Antibiotic duration and timing of the switch from intravenous to oral route for bacterial infections in children: systematic review and guidelines

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Few studies are available to inform duration of intravenous antibiotics for children and when it is safe and appropriate to switch to oral antibiotics. We have systematically reviewed antibiotic duration and timing of intravenous to oral switch for 36 paediatric infectious diseases and developed evidence-graded recommendations on the basis of the review, guidelines, and expert consensus. We searched databases and obtained information from references identified and relevant guidelines. All eligible studies were assessed for quality. 4090 articles were identified and 170 studies were included. Evidence relating antibiotic duration to outcomes in children for some infections was supported by meta-analyses or randomised controlled trials; in other infections data were from retrospective series only. Criteria for intravenous to oral switch commonly included defervescence and clinical improvement with or without improvement in laboratory markers. Evidence suggests that intravenous to oral switch can occur earlier than previously recommended for some infections. We have synthesised recommendations for antibiotic duration and intravenous to oral switch to support clinical decision making and prospective research.

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Introduction

Antibiotics are commonly prescribed for children in hospital, but few data are available to inform optimal duration of therapy. In view of the global crisis of antimicrobial resistance, the need for evidence-based recommendations for the optimal duration of intravenous and oral antibiotics, and when to switch from the intravenous to the oral route, is crucial (appendix reference [AR] 1). Shorter antibiotic courses can potentially affect antimicrobial resistance, and have already been advocated for a few infections (AR 2 and 3). So far, there has been no systematic review of the evidence guiding the minimum duration of intravenous antibiotics before switching to oral treatment for infections in children.

We aimed to determine, in children younger than 18 years with bacterial infections, the minimum intravenous and total antibiotic duration required to achieve outcomes similar to or better than those with traditional longer durations administered for specific infections. We then aimed to make evidence-based recommendations for optimal intravenous and total antibiotic duration and criteria for intravenous to oral switch.

Methods

The Australian and New Zealand Paediatric Infectious Diseases Australasian Stewardship of Antimicrobials in Paediatrics (ANZPID-ASAP) group of the Australasian Society for Infectious Diseases collaborated on this study. Using 2009 PRISMA guidelines (appendix), the group systematically reviewed the literature on intravenous and total duration of antibiotics and the timing of switching from the intravenous to oral route for 36 infections in children younger than 18 years. Evidence-based recommendations synthesised from the review findings, relevant guidelines, and consensus opinion of the group were produced (appendix). There were four review coordinators (BJM, DA, DI, PAB) and 18 review contributors.

Search strategy and selection criteria

The group searched MEDLINE from 1946 to Nov 21, 2014, and the Cochrane Central Register of Controlled Trials (up to Nov 21, 2014) using a standard overall strategy for all infections, and then separately with specific terms for each infection (appendix). Further information was obtained from secondary references identified from articles, and relevant guidelines. All study types published in peer-reviewed journals and published conference abstracts, except single case reports, were included. Studies were limited to those in human beings and reported in English, but no restrictions on year of publication were applied. Studies included were those of children younger than 18 years diagnosed with a bacterial infection for whom data about intravenous, oral, or total antibiotic duration and outcomes were reported. When data were scarce in children and the infection was likely to be similar in children and adults, relevant adult studies identified from other information sources were also reviewed. Interventions assessed were comparison between different intravenous antibiotic durations, comparison between different oral antibiotic durations, comparison between the use of intravenous and oral antibiotics, intravenous or oral antibiotic durations, and criteria for intravenous to oral switch. Outcome measures sought were clinical improvement or recovery and persistence of infection, complications, and recurrence of infection. No restriction was set on follow-up duration because of the differing natural histories of included infections. This study is registered with PROSPERO, number CRD42014015460.

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See Online for appendix

Quality assessment and data extraction

The titles and abstracts of all studies resulting from the database search of each bacterial infection were screened and the full texts of all potentially relevant articles were reviewed by two independent investigators (one contributor and one coordinator), with disagreements resolved by discussion or a third coordinator. Risk of bias was assessed (appendix) at study level according to adapted grading of evidence and recommendations by the Australian National Health and Medical Research Council (NHMRC; AR 4). Risk of bias affected data synthesis by attributing weight according to the assessed bias in the study. No specific assessment was made for reporting bias, though it has been identified in our review where deemed possible. Negative studies were included. Data extracted and synthesised were ages of participants, underlying comorbidities (eg, immunocompromised), type of bacterial infection, duration of intravenous antibiotics, duration of oral antibiotics, persistent or recurrent infection, and complications of infection. The only simplification made was that if a systematic review included multiple similar studies with similar outcomes not all of them were independently cited. Data synthesis and recommendations incorporated the level of evidence and weighted the risk of bias accordingly.

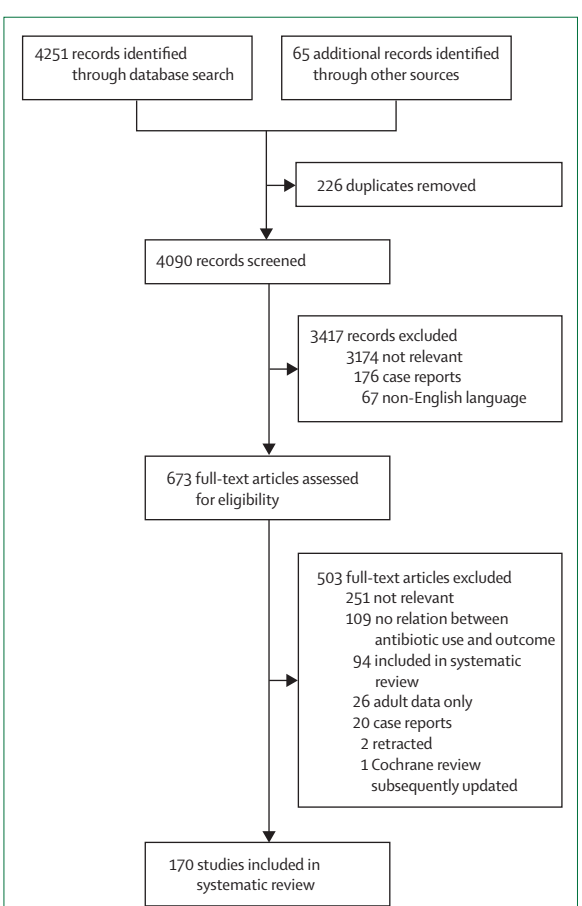

Figure: **Study profile**

Guidelines

Evidence-graded recommendations were made for intravenous and total antibiotic duration and timing of intravenous to oral switch for bacterial infections in children. These guidelines were made on the basis of a synthesis of the literature from the systematic review, relevant current guidelines (AR 5–28), and expert consensus opinion from the ANZPID-ASAP group. In making recommendations, the group applied grading of evidence strength and consistency according to the adapted NHMRC criteria (appendix; AR 4).

Role of the funding source

No funding was provided for this study.

Findings

Our search identified 4090 abstracts. 671 potentially relevant articles were assessed for eligibility, of which 170 studies met the inclusion criteria (figure). Most studies were not of high quality, with only 61 (36%) being randomised controlled trials or systematic reviews (appendix). Specific infections were reviewed individually, and for most of them there were no systematic reviews or trials of antibiotic duration or intravenous to oral switch.

Bacteraemia and endocarditis

Antibiotic duration for meningococcal bacteraemia can depend on coexistent meningococcal meningitis. In two trials of all-cause bacterial meningitis, children with meningococcal meningitis with or without meningococcaemia who were improving were randomised to short (4–5 days) versus long (7–10 days) duration of intravenous antibiotics; no deaths or relapses were recorded in either group.[1,2] In observational studies, 4 days of intravenous antibiotics for meningococcaemia is not associated with excess mortality or relapse.[3,4]

In two systematic reviews including several different study types and a large retrospective study of occult pneumococcal bacteraemia, no differences in serious complications between intravenous and oral antibiotics were recorded.[5–11] However, children who remained febrile at follow-up (median 33 h) were more likely to have developed focal infections or persistent bacteraemia if they were treated with oral antibiotics.[11] Results from another series showed that intravenous antibiotics given for fewer than 2 days and oral antibiotics for 10 days did not result in any complications.[12] For bacteraemia with associated pneumonia, initial intravenous antibiotics led to a lower admission rate than did oral-only antibiotics and improved condition at follow-up.[13]

In a small trial of neonates with *Staphylococcus aureus* bacteraemia, Chowdhary and colleagues[14] showed higher treatment failures with 7 days of intravenous antibiotics than with 14 days. Three retrospective series documented wide variations in median duration of intravenous antibiotics (5–162 days).[15–17] In a study of neonates with meticillin-resistant *S aureus* (MRSA) bacteraemia, the

mean duration of vancomycin treatment for those without any complications was 9·7 days (SD 5·1), although recurrences were greater with fewer than 14 days of antibiotics than with 14 days or longer.[18] Children with MRSA bacteraemia without endocarditis had a median antibiotic duration of 22 days (IQR 12–29), with bacteraemia persisting for a median of 6 days (IQR 2–7), despite effective antibiotics.[19]

Results from a retrospective study of uncomplicated Gram-negative bacteraemia (including *Pseudomonas aeruginosa*) in children showed no difference in mortality or recurrence between short (median 10 days, IQR 10–10) and longer course (14, 14–17) of intravenous antibiotics.[20] In Hakki and colleagues' retrospective study[21] of mostly adults with *P aeruginosa* bacteraemia after stem-cell transplantation, risk of recurrence was increased but not significantly so (p=0·06) when fewer than 14 days of antibiotics was compared with 14 days or more. The only data on antibiotic duration in multiresistant Gram-negative bacteraemia are from a study in critically ill adults: after onset of bacteraemia length of stay in hospital was the same for patients with sensitive (median 27 days, IQR 9–63·5) as with resistant Enterobacteriaceae bacteraemia (35 days, IQR 10–77), suggesting lack of need for long-term antibiotics with Gram-negative resistance (AR 29). Two studies of bacteraemia caused by non-typhoid salmonellae showed no difference in complications or recurrence between less than 7 days of antibiotics and 7 days or more.[22,23]

Outcomes in retrospective studies[24–26] of central venous catheter (CVC) infection with *S aureus* or Gram-negative organisms in children and adults vary: salvage can be successful if bacteraemia clears rapidly (AR 30 and 31). In two studies of CVC-associated *S aureus* bacteraemia in children, median intravenous antibiotic duration was 10 days[24] and 14 days,[26] with duration, CVC removal, and recurrence being unrelated. In adults, longer durations decrease complications.[16,27,28] After line removal for CVC infections with coagulase-negative staphylococci and *Bacillus* species, short intravenous courses (3–5 days and 5–7 days, respectively) are non-inferior than longer courses.[29–31] Results from small series in immunocompetent and immunocompromised children showed that CVC-associated bacteraemia resolved with 7–21 days of intravenous antibiotics, but no studies have compared antibiotic durations with line removal or retention.[32–36] A few studies of anti-infective locks have yielded mixed results, and larger studies are awaited.

No trials in childhood infective endocarditis exist, so practice is usually extrapolated from adult data. Results from retrospective studies in children show that antibiotic durations are unrelated to complications or recurrence (all-cause 4–6 weeks,[37,38] *S aureus* 2–6 weeks of intravenous with long-term oral use,[39] *Streptococcus pneumoniae* 4–8 weeks of intravenous use).[40] Guidelines for treatment of viridans streptococci rely on adult data, which show that shorter durations (2–4 weeks) are effective for susceptible isolates (AR 32–35). Oral antibiotics alone were used in six patients for a median of 6 weeks with no recurrences in one small study published in 1977.[41]

CNS infections

In a systematic review of bacterial meningitis in children no difference in outcomes between 4–7 days and 7–14 days of antibiotics was recorded,[2,42–46] and results from observational studies show low failure rates with 4–7 days.[47,48] However, potential selection bias could reduce the applicability of the results. A large trial in resource-poor countries found similar outcomes with 5 or 10 days of ceftriaxone,[1] although the study lacked power to assess individual organisms. Failures have occurred after treatment for up to 14 days for *Listeria monocytogenes* meningitis,[49] and 21 days of treatment is recommended for Gram-negative meningitis (AR 36). Intraventricular antibiotics increase mortality so are not recommended (AR 37 and 38).

In a large retrospective study of childhood brain abscess, there was no difference in morbidity or mortality between patients who received less than 6 weeks, 6 weeks, or more than 6 weeks of antibiotics, and no difference in outcome by amount of intravenous versus oral antibiotics in patients who received 6 weeks of antibiotics in total.[50] In an observational study, children with positive cultures and clinical improvement received 2 weeks of intravenous antibiotics followed by 4 weeks of oral antibiotics with no increase in recurrence.[51] Studies mostly in adults have assessed intravenous durations of 1–2 weeks, with intravenous to oral switch based on clinical improvement and normalisation of C-reactive protein and found no recurrences (AR 39 and 40).[52]

Results of studies of ventriculoperitoneal shunt infection in children show that, irrespective of antibiotic duration, the highest chance of cure is with shunt removal.[53,54] For simple shunt infection the mean effective intravenous antibiotic duration was 9·7 days (SD 1·7) and with intraventricular antibiotics 6 days (SD 1·7) to 8 days (range 3–17).[55,56] For complicated shunt infection (eg, multicompartment hydrocephalus), 3 weeks of intravenous and 2 weeks of intraventricular antibiotics were effective.[57] In three studies, shunt reinfection was not associated with duration of antibiotics.[58–60] In one study with shunt retention, if there was no blockage or infection with *S aureus*, intravenous or intraventricular antibiotics for 14 days resulted in no recurrence by 6 months.[61]

Respiratory infections

In pharyngitis and otitis media, either antibiotics are not needed or oral antibiotics are prescribed, so they are not included in this Review.

In a small trial in children and adults with drained peritonsillar abscess, a comparison of intravenous and oral antibiotics showed no difference in complications or recovery time.[62] In two studies of drainage and initial intravenous antibiotics the median length of stay was

2–3 days as a proxy for intravenous antibiotic duration, although no information about postdischarge antibiotics was given.[63,64] In adults, drainage followed by single-dose intravenous and 7 days of oral antibiotics is effective[65] (AR 41), although resolution can occur with drainage alone or antibiotics alone.[63,66]

In four retrospective series of children with drained retropharyngeal abscess the average intravenous duration was 3–6 days and oral duration 7–10 days, with no clinically significant complications.[67–70] 51 (75%) children in one study were managed with antibiotics alone.[68] Clinical symptoms such as return of neck mobility and toleration of oral fluids and diet were indications for intravenous to oral switch.[69,70] Oral durations varied from 7–9 days on the basis of symptom improvement to 3–6 weeks on the basis of CT resolution with no major complications with either duration, suggesting that 7–9 days is sufficient.[69,70]

Three retrospective and one prospective series with low complication, low recurrence rates, or both found average durations of treatment with intravenous antibiotics of 4·5–7 days for uncomplicated mastoiditis and 7·8–11 days for mastoiditis with mastoidectomy,[71–74] followed by an average of 7–9 days of oral antibiotics.[71,73] C-reactive protein and erythrocyte sedimentation rate (ESR) did not predict length of stay or oral antibiotic duration in one study in which patients without intracranial complications received 7–10 days of oral antibiotics after discharge and at least 15 days if there were intracranial complications.[75] No difference in rate of readmission to hospital between intravenous and oral outpatient treatment after mastoidectomy was found.[76]

Of four trials of acute sinusitis comparing 10–14 days of antibiotics with placebo, two favoured treatment and two found no difference in outcomes.[77–80] Results from two systematic reviews suggested that children with severe illness (fever >39°C, 3 days of purulent nasal discharge, headache, facial pain) can benefit from antibiotics[81] and that those with non-severe illness are likely to improve after 7 days with or without antibiotics.[82] Authors of a Cochrane review[83] and a systematic review[84] calculated that eight children needed to be treated with antibiotics to achieve one additional cure, and results from the systematic review showed that the efficacy of antibiotics was not established. A trial compared 3 with 5 days of azithromycin, and showed similar clinical resolution.[85] No difference in outcomes was found in a systematic review in adults comparing short (3–7 days) with longer durations of antibiotics (AR 42).

Only retrospective, hospital-based case series of acute cervical lymphadenitis have been published and most start intravenous antibiotics, but they probably represent a minority of cases.[86–88] Durations vary widely for intravenous use from 2 to 22 days and 7 to 10 days for oral use; longer durations were often associated with surgical drainage.[86–90] Recurrence rates in all studies were low.

A Cochrane review of children aged 2–59 months with non-severe pneumonia found no difference in outcomes for 3 versus 5 days of antibiotics.[91] Four additional trials in children aged up to 12–16 years found no difference between 3–5 days of antibiotics and longer durations.[85,92–94] In comparisons of intravenous with oral antibiotics for moderately severe pneumonia, three trials and a Cochrane review showed similar resolution of fever and oxygen requirement.[95–98] However, severe pneumonia (oxygen saturation <85%, shock requiring intravenous fluid bolus) or complicated disease (immunocompromised, chronic lung or heart disease, pleural effusion at diagnosis) were excluded. In their systematic review in children younger than 5 years in resource-poor settings, Lassi and colleagues[99] concluded that 3 days of oral antibiotics was sufficient for non-severe pneumonia.

A systematic review of all aspects of ventilator-associated pneumonia in children yielded no paediatric data for antibiotic duration, so on the basis of adult data the recommendation was to stop antibiotics after 3 days if cultures were negative or after 8 days with clinical or biomarker improvement (AR 43). All other studies are in adults: results from systematic reviews, trials, and a prospective study comparing short course (7–8 days) with longer course (10–15 days) antibiotics showed no difference in mortality (AR 44–49). In one study a higher recurrence rate of ventilator-associated pneumonia was recorded with 8 days of antibiotics than with 15 days if sputum culture yielded non-fermentative Gram-negative bacilli (eg, *Pseudomonas* spp, *Acinetobacter* spp), but this recurrence did not lead to higher mortality (AR 44). Declining inflammatory markers including C-reactive protein (AR 50) and procalcitonin (AR 51) are associated with better outcomes, but have not been used to guide intravenous to oral switch. A Cochrane review of short-course versus long-course antibiotics for hospital-acquired pneumonia in critically ill adults found no increase in mortality when procalcitonin was used to guide antibiotic cessation (AR 52).

No studies of antibiotic duration for pleural empyema in children exist. A systematic review of operative versus non-operative management found mean antibiotic durations of 12·8 days (SD 3·8) and 21·3 days (SD 7·9), respectively, although whether the route was intravenous or oral was not specified.[100] In another systematic review, length of stay in hospital (as a proxy for intravenous antibiotic duration) was similar with an average of 6 days for both groups.[101] In studies comparing different antibiotics but with the same duration, 14 days or more of intravenous antibiotics were used with relapse being uncommon.[102,103] In a retrospective series of *S pneumoniae* empyema, there was no difference in intravenous antibiotic duration and outcomes between penicillin-sensitive and penicillin-resistant strains, suggesting that longer durations for resistant bacteria are unnecessary.[104]

Few studies of lung abscess in children have been done. A comparison of antibiotics alone (with or without percutaneous drainage) with surgical drainage found a mean of 18 days of intravenous antibiotics in the medical

(antibiotic only) group compared with 26 days in the surgical group with similar mean oral durations (13–17 days), which were unrelated to clinical or radiological improvement or mortality.[105] Three other retrospective series found a mean total antibiotic duration ranging from 24 to 40 days.[106–108] Two trials in adults stipulated a minimum of 6 days of intravenous antibiotics, but did not relate duration to clinical improvement (AR 53 and 54).

Musculoskeletal infections

In two systematic reviews, short course intravenous antibiotics (<7 days[109] and 3–4 days[110]) for uncomplicated acute osteomyelitis had similar cure rates to longer courses, with one of them[110] suggesting that a total of 3 weeks was sufficient.[109–112] In a large trial, after a median of 4 days of intravenous treatment, no difference in cure between 16 and 26 days of oral antibiotics was seen.[113] Some studies base intravenous to oral switch on clinical response and others include C-reactive protein.[113] Data are lacking for complicated acute osteomyelitis, but experts suggest longer-term intravenous duration. Although not powered to find a difference, an analysis of bacteraemic bone and joint infection in children showed no difference in mean intravenous antibiotic duration (4 days) or outcomes between patients with and without bacteraemia.[114]

The inadequate evidence available for subacute and chronic osteomyelitis in children was highlighted in a systematic review of 14 small observational studies; the conclusion was that long courses of antibiotics are no more effective than shorter courses, and that 2 days of intravenous plus 6 weeks of oral antibiotics will suffice.[115] A Cochrane review in adults found no difference between intravenous and oral antibiotics (AR 55). In a retrospective study, adolescents whose prosthetic spinal rod was removed because of chronic infection received 2–3 days of intravenous and 10 days of oral antibiotics with no recurrence.[116] There are no studies of antibiotic duration when prosthetic material remains.

Although the conclusion from a systematic review of acute septic arthritis in children was that the ideal antibiotic duration was not defined,[117] results from subsequent small trials and observational data showed that administration of 7 days or more of intravenous antibiotics followed by 3–4 weeks of oral antibiotics is effective and safe.[112,118–123] In a definitive large trial, children with culture-positive septic arthritis were randomised after 2–4 days of intravenous antibiotics to complete a total of either 10 or 30 days of oral antibiotics, and there were no differences in treatment success.[124] As with osteomyelitis, concurrent bacteraemia can be treatable with shorter duration intravenous antibiotics.[114]

For pyomyositis in children, in two retrospective series the mean duration of intravenous antibiotics was 11–13 days and of oral antibiotics 20–30 days,[125,126] whereas two other series described 4–7 days of intravenous antibiotics with a mean total of 2–6 weeks, all with low complication rates.[127,128] Intravenous to oral switch was based on clinical improvement and reduced inflammatory markers.[126–128] When surgery is required, intravenous antibiotics are usually continued until postoperatively.[126]

Skin and soft tissue infections

The conclusion from a Cochrane review of adults and adolescents with cellulitis was that extended intravenous antibiotics were unnecessary.[129] In prospective studies of children with moderate or severe uncomplicated cellulitis (rapidly spreading erythema, tenderness, lymphangitis, systemic symptoms) initially treated with intravenous antibiotics, most have recorded successful switch to oral antibiotics after 2–3 days of intravenous antibiotics.[130,131] In retrospective studies, a median of 2 days of intravenous followed by 7 days of oral antibiotics did not result in complications.[132,133]

A prospective study including children with preseptal cellulitis found a median intravenous duration of 2 days (IQR 2–3) and oral 7 days (5–7) with no complications or recurrence.[131] Intravenous to oral switch was based on reduced swelling and erythema. Retrospective series have reported success without complications with 2–3 days of intravenous and 7–8 days of oral antibiotics.[132,134–137]

In two retrospective series of children with orbital cellulitis, a mean of 9·3 days (SD 3·6) of intravenous antibiotics (total 21·0 days, SD 3·0 days)[138] and median of 4 days (range 2–8) of intravenous antibiotics[139] were given with no long-term complications. One small study compared orally bioavailable antibiotics with historical intravenous cases, and although antibiotic durations were not reported no difference in mean length of stay or complications was noted.[140]

A study of MRSA skin abscesses of less than 5 cm diameter found no benefit from antibiotics for drained abscesses.[141] A larger trial in children of skin abscesses of all sizes and causal organisms compared 10 days of oral co-trimoxazole with placebo after incision and drainage.[142] There was no difference in failure rate, and a difference in new lesion formation at 10 days had disappeared by 3 months; treatment failure did not correlate with abscess size.

Results from a trial of systemic antibiotics versus placebo in superficial surgical site infection with local wound treatment showed that antibiotics increased bacterial clearance without clinical benefit.[143] The conclusion from a systematic review of adults with deep surgical site infection after spinal instrumentation was that spinal rod removal could shorten intravenous and oral antibiotic duration.[144] In children, small case series suggest that for removed prostheses 1–2 weeks of intravenous and 6 weeks of oral antibiotics are sufficient,[145,146] whereas for retained prostheses 4–6 weeks of intravenous and several months of oral antibiotics might be necessary.[147,148] In one study, normalisation of C-reactive protein and ESR was used to guide intravenous to oral switch.[147] Postsurgical mediastinitis is a specific deep surgical site infection for

which common durations of 4–6 weeks of intravenous antibiotics are extrapolated from scanty adult data (AR 56). In a retrospective study in children and neonates with postsurgical mediastinitis, the median duration of intravenous antibiotics was 11 days (range 7–28), with no recurrences or deaths.[149] Whether oral antibiotics were used after intravenous administration is unclear.

Abdominopelvic infections

According to a Cochrane review of all ages after appendicectomy, prophylactic intravenous antibiotics were superior to placebo for prevention of wound infection and intra-abdominal abscess.[150] For paediatric studies the difference was no longer statistically significant but favoured single-dose preoperative antibiotics.[151] Studies of antibiotics versus surgery in children with appendicitis are too small to apply a recommendation (AR 57).

Results of a systematic review of complicated appendicitis in children showed that limiting total antibiotic duration to 3 days was not associated with higher complication rates.[152] In three trials and a retrospective review no difference in clinical improvement or complications were seen when shorter intravenous and total antibiotic durations were compared with longer durations, the shortest regimen being a mean of 3·4 days [SD 1·7] intravenous and no oral antibiotics.[153–156] No definitive criteria are available for stopping or switching intravenous antibiotics, but children[157] and adults (AR 58) with intra-abdominal sepsis have low complication rates if intravenous antibiotics are stopped when patients are afebrile and tolerating diet.

No outcome studies of antibiotic duration in acute cholangitis in children exist. In a study that included several children, failure to respond early to intravenous antibiotics was associated with mortality (AR 59). The only study that included children exclusively assessed clinical outcomes in acute cholangitis after the Kasai procedure (biliary bypass surgery for biliary atresia) according to institutional protocol: all antibiotics were administered intravenously for at least 2 weeks. After 1 week, 30 (75%) of the children had improved and no child needed more than 3 weeks of antibiotic treatment.[158]

There are no studies in children of either prophylaxis of infection in acute necrotising pancreatitis or treatment of established infection of pancreatic necrosis. A Cochrane review (AR 60), a systematic review (AR 61), and a trial (AR 62), all in adults only, found that antibiotics did not reduce mortality or pancreatic infection. Conversely one systematic review of antibiotics started within 72 h of symptoms showed reduced mortality compared with placebo (AR 63). However, since pancreatitis in adults is different from that in children, paediatric practice relies on expert experience and the use of prophylactic antibiotics is rare. Although antibiotic use is less controversial in established pancreatic

	Minimum intravenous antibiotic duration (level of evidence*)	Criteria for switch to oral antibiotic	Minimum total antibiotic duration (level of evidence*)	Comments
Bacteraemia and endocarditis				
Meningococcal bacteraemia	4–5 days (C-III)	No oral switch	4–5 days (C-III)	Duration applicable for uncomplicated bacteraemia
Pneumococcal bacteraemia	Occult afebrile at 24 h: 0 days (B-I); occult febrile at 24 h: 1 day (C-IV); non-occult/septic: 7–10 days (D-IV)	Oral only; afebrile, rapid improvement; no oral switch	7–10 days; 7–10 days; 7–10 days	Occult: usually febrile, but not septic and no major focus. If ongoing fever repeat blood culture, consider other focal investigations (eg, lumbar puncture, chest imaging [C-IV]); Non-occult: if associated pneumonia, initial intravenous until improvement then total 7–10 days (C-IV)
Staphylococcus aureus bacteraemia	7–14 days (D-IV)	No oral switch	MSSA: 7–14 days (D-IV), MRSA: 14 days (D-IV), longer if persistent positive cultures or complications (D-expert opinion)	If associated with endocarditis, refer to endocarditis guideline, if associated with osteomyelitis or septic arthritis, intravenous duration can be shortened to 4–7 days if condition is improving quickly and is uncomplicated, with remainder oral (C-III)
Gram-negative bacteraemia	10 days (C-III)	No oral switch	10 days (C-III) specific bacteria: pseudomonas in HSCT: 14 days (D-IV) non-typhoidal salmonellae: 7 days (D-IV)	If multiresistant, duration is from first negative culture; if associated with UTI, intravenous duration may be shortened to 5–7 days if uncomplicated and improving quickly (D-IV), with remainder oral (D-expert opinion)
CVC-associated bacteraemia	7 days (B-III) CoNS in neonates, line removed, cultures cleared: 3–7 days (C-IV)	No oral switch	Additional duration dependent on the bacteria cultured (refer to relevant guideline)	CVC removal if blood cultures positive after 72 h of appropriate antibiotics (B-III); no bacteria absolutely necessitate CVC removal, but *Pseudomonas aeruginosa* and *Staphylococcus aureus* have been harder to clear in some studies
Bacterial endocarditis	4–6 weeks depending on organism and antibiotic choice (C-III), except sensitive viridans streptococci	No oral switch	Viridans streptococci (D-IV) MIC ≤0·12 mg/L: 2 weeks or 4 weeks MIC >0·12–2 mg/L: 4–6 weeks MIC >4 mg/L: 4–6 weeks *S aureus* (D-IV) MSSA uncomplicated: 4 weeks MSSA complicated or MRSA: 6 weeks	For MIC ≤0·12 mg/L, 2 weeks if benzylpenicillin (or ceftriaxone) + gentamicin, 4 weeks if benzylpenicillin (or ceftriaxone) alone

(Table continues on next page)

	Minimum intravenous antibiotic duration (level of evidence*)	Criteria for switch to oral antibiotic	Minimum total antibiotic duration (level of evidence*)	Comments
(Continued from previous page)				
Central nervous system infections				
Bacterial meningitis	7–21 days depending on organism (D-IV)	No oral switch (D-IV)	*Neisseria meningitidis*: 5–7 days (B-II) *Haemophilus influenzae*: 7–10 days (C-II) *Streptococcus pneumoniae*: 10–14 days (C-II) Group B streptococci: 14–21 days (D-IV) Gram-negative bacilli: 21 days (D-IV) *Listeria monocytogenes*: 21 days (D-IV)	Nil
Brain abscess and subdural empyema	2–4 weeks (B-III)	Clinical improvement (afebrile, normal conscious level), CRP normal (C-III)	6 weeks (C-III)	Pus drainage where possible (B-III), ideally before antibiotics. Antibiotic duration is likely to be longer when drainage cannot occur (D-expert opinion); decision to switch to oral includes antibiotic CNS penetration and adherence
Ventriculoperitoneal shunt infection	Uncomplicated: 10 days (C-III); complicated: 21 days (C-III)	No oral switch; no oral switch	Uncomplicated: 10 days intravenous (with or without intraventricular antibiotics); Complicated: 21 days intravenous (with or without intraventricular antibiotics); might need longer, aiming for 7 days post CSF clearance (D-expert opinion)	Shunt removal (B-III), with alternative CSF drainage; if conservative treatment in CoNS infection, shunt should be removed if CSF not sterilised (D-expert opinion); Complicated: multi-compartmental hydrocephalus, ventriculitis, multiple organisms, severe peritonitis, or remaining prosthetic material. Intraventricular antibiotics (particularly aminoglycosides) should be avoided in neonates (A-I)
Respiratory infections				
Peritonsillar abscess (quinsy)	1–2 days following successful drainage (C-IV)	As soon as tolerated	10 days (A-I)	Nil
Retropharyngeal abscess	3–5 days for conservative or surgical management (D-IV)	Afebrile, neck mobility, tolerating oral diet (D-IV)	10–14 days (D-expert opinion)	Even if abscess is drained, intravenous antibiotics needed for surrounding tissue involvement
Mastoiditis	5 days (D-IV)	Clinical improvement	12–15 days based on clinical progress (D-expert opinion)	Longer courses might be required for intracranial complications; refer to brain abscess guideline
Acute bacterial sinusitis	0 days (C-I) Systemically unwell or high risk of suppuration: 1–2 days (D-expert opinion)	Clinical improvement	Moderate or severe: 7 days after improvement in symptoms (C-I); usually 10–14 days (D-expert opinion)	Nil
Acute cervical lymphadenitis	0 days (D-expert opinion) Systemically unwell or rapid progression: 2–3 days (D-IV)	Clinical improvement including reduction in fever, pain, and size	5–7 days (D-expert opinion)	May be longer if slow progression or abscess formation (D-IV)
Community-acquired pneumonia	0 days (A-I) Severe or complicated: initial intravenous treatment (D-expert opinion)	Clinical improvement	Mild: 3 days (A-I) Moderate or severe uncomplicated: ≤7 days of antibiotics (B-I)	Oral antibiotics can be used in most children including children requiring hospital admission (A-I); if associated with bacteraemia refer to the relevant guideline Severe or complicated: O_2 sats <85%, shock receiving intravenous bolus, immunocompromised, chronic lung or heart disease
Ventilator-associated pneumonia	Initial treatment (D-expert opinion)	No bacteraemia, clinical improvement, toleration of oral drugs	Good clinical response: 7 days (B-II) Non-fermentative Gram-negative bacilli in sputum: 10 days (D-expert opinion) (eg, *Pseudomonas* spp, *Acinetobacter* spp)	Although there is no minimum intravenous duration most patients will start intravenous antibiotics because they are ventilated; if associated with bacteraemia refer to the relevant guideline
Pleural empyema	Initial treatment (D-expert opinion)	Afebrile for 1–2 days, chest drain removed	7 days (D-expert opinion)	Patients can remain febrile for several days on adequate treatment; antibiotic duration might need to be much longer (up to 6 weeks) dependent on disease severity
Lung abscess	Initial treatment (D-expert opinion)	Afebrile, clinical improvement	4–6 weeks (D-expert opinion)	Abscess >6 cm: continue until resolved or cavity small and stable size (D-expert opinion)
Musculoskeletal infections				
Acute osteomyelitis	Uncomplicated: 3–4 days (A-I)	Afebrile, clinical improvement, CRP or ESR decreasing (A-II)	3–4 weeks (A-II) Complicated (delayed presentation, associated wound or abscess): longer duration intravenous administration is likely to be required (D-expert opinion)	If associated with bacteraemia, initial intravenous but may be shortened to 4–7 days if improving quickly and uncomplicated, with remainder oral for total duration as for non-bacteraemic infection (C-III)
Subacute or chronic osteomyelitis	Clinically well and no prosthetic material: 0 days (D-expert opinion); prosthetic material: initial treatment (D-expert opinion)	As soon as tolerated; clinical improvement (D-expert opinion)	No evidence to support a minimum total duration; no evidence to support a minimum total duration	If prosthetic material is present, biofilm active antibiotics for a long duration are likely to be necessary (D-expert opinion); cure might not be possible without removal of prosthetic material

(Table continues on next page)

	Minimum intravenous antibiotic duration (level of evidence*)	Criteria for switch to oral antibiotic	Minimum total antibiotic duration (level of evidence*)	Comments
(Continued from previous page)				
Septic arthritis	2–4 days (A-II)	Afebrile, clinical improvement, CRP or ESR decreasing (A-II)	2–3 weeks (A-II) Complicated (delayed presentation, associated wound or abscess): longer duration intravenous route is likely to be required (D-expert opinion)	If associated with bacteraemia, initial intravenous route but may be shortened to 4–7 days if improving quickly and uncomplicated, with remainder oral route for total duration as for non-bacteraemic infection (C-III)
Pyomyositis	2–5 days (C-IV)	Clinical improvement	2–3 weeks (C-IV)	Pus should be drained (C-IV)
Skin and soft tissue infections				
Cellulitis	Mild: 0 days; moderate or severe: 1–3 days (C-IV)	Clinical improvement: reduction in fever and erythema	5–7 days (C-IV)	If associated with deep infection or osteomyelitis, refer to relevant guideline; moderate or severe: rapidly spreading erythema, tenderness, lymphangitis, systemic features
Preseptal (periorbital) cellulitis	2–3 days (C-IV)	Clinical improvement: reduction in fever and erythema	7–10 days (C-IV)	Nil
Orbital cellulitis	3–4 days (C-IV)	Clinical resolution of fever, erythema, and pain	7–10 days (C-IV)	Intraorbital abscesses should be drained, with non-operative management in selected patients (C-IV); if symptoms persist intravenous antibiotics should continue while investigating for complications (D-expert opinion)
Skin abscesses and boils	If effectively drained: 0 days (B-II)	As soon as tolerated	0 days (B-II)	If associated with cellulitis, refer to relevant guideline. Treatment recommendations unaffected by abscess size
Superficial surgical site infection	0 days (B-II)	As soon as tolerated	If started, 5–7 days (D-expert opinion)	Local wound management and delay starting antibiotics, especially if symptoms occur within 48 h of surgery (B-II)
Deep surgical site infection	No prosthetic material: initial treatment (B-III); prosthetic material: 4–6 weeks (D-expert opinion)	No oral switch if short duration; clinical improvement	No minimum recommendation, duration dependent on clinical improvement; if prosthetic material present, very long-term antibiotics might be necessary (D-expert opinion)	Wound should be surgically debrided (B-III). Mediastinitis might be treatable with shorter than 4–6 weeks' antibiotics, but there is insufficient evidence for this recommendation; prosthetic material should be removed if possible
Abdominopelvic infections				
Appendicitis: uncomplicated	Single preoperative dose (A-I)	No oral switch	Single preoperative dose only (A-I)	Surgical prophylaxis; non-operative antibiotic management has been used but studies are too small to recommend this approach
Appendicitis: complicated, intra-abdominal infection	Initial treatment (B-III)	Clinical improvement, normal bowel function (B-III)	3–7 days (B-III); stop when signs of infection have resolved (B-III)	Complicated: perforation, peritonitis, pus in peritoneum. Antibiotics do not need to be changed on the basis of culture results if improving (B-III)
Acute cholangitis	Initial treatment (C-III)	No recommendation	No minimum duration, depends on clinical improvement (D-expert opinion)	If there is accompanying bacteraemia refer to the relevant guideline
Pancreatitis	Prevention of infection: 0 days (C-I); treatment of infection: initial treatment (D-IV)	Not applicable; no recommendation	0 days (C-I); no minimum duration, dependent on clinical improvement (D-expert opinion)	The only evidence for antibiotic use for pancreatitis in children is for treatment of established infection. If complications of bacteraemia or pneumonia occur refer to the relevant guideline; ..
Necrotising enterocolitis	7-10 days (C-IV)	No oral switch	7–10 days (D-expert opinion) with further duration if lack of clinical improvement	Antibiotics can be discontinued after 2–3 days if necrotising enterocolitis is thought unlikely (D-expert opinion)
Genitourinary infections				
Lower UTI	0 days Age <3 months: initial treatment	Clinical improvement	3–4 days (A-I)	If associated with bacteraemia, refer to bacteraemia guideline
Pyelonephritis	0 days (A-I) Age <3 months or not tolerating orals: initial treatment	Clinical improvement, or as soon as tolerating orals	10 days (A-I) In a child who rapidly improves 7 days may be sufficient (D-expert opinion)	If associated with bacteraemia, refer to bacteraemia guideline
Epididymitis	0 days	Clinical improvement	Negative urinalysis: no antibiotic (C-III) Positive urinalysis: oral antibiotic (B-III) for 2 weeks (D-expert opinion)	Nil

MSSA=meticillin-sensitive *S aureus*. MRSA=meticillin-resistant *S aureus*. UTI=urinary tract infection. HSCT=haemopoietic stem-cell transplantation. CVC=central venous catheter. MIC=minimum inhibitory concentration. CoNS=coagulase-negative staphylococci. CRP=C-reactive protein. CSF=cerebrospinal fluid. *Grading of evidence is shown in appendix.

Table: **Recommendations for minimum intravenous and total duration of antibiotics and timing of intravenous to oral switch**

infection, no studies in adults or children have addressed duration of antibiotics in this condition.

A Cochrane review of antibiotics for necrotising enterocolitis identified only two studies that assessed antibiotic choice but not duration (AR 64). However, one study specified 10–14 days of intravenous antibiotics in each arm,[159] and a retrospective study compared two different intravenous regimens administered for 7–10 days,[160] both of which had low complication rates. Oral antibiotics are not recommended.

Genitourinary infection

In a Cochrane review of childhood lower urinary tract infection no difference in persistent bacteriuria or recurrence was noted between 2–4 days and 7–14 days of oral antibiotics.[161] Results from a subsequent Cochrane review showed that single-dose antibiotic was associated with more persistent bacteriuria than was 10 days of antibiotics, although no difference in symptom duration or recurrence occurred.[162] A large retrospective study of infants younger than 6 months found no difference in treatment failure between intravenous antibiotics for 3 days or less and 4 days or more.[163]

A Cochrane review and trial of acute pyelonephritis in children treated with 10–14 days of antibiotics, found no difference in duration of fever or renal damage between all intravenous antibiotics, 3 days of intravenous followed by oral antibiotics, or all oral administration.[164,165] Similarly, a Cochrane review in all ages with pyelonephritis found no difference between different routes of administration.[166] Some data on antibiotic duration for urinary tract infection with Gram-negative bacteraemia suggest that shorter intravenous durations than recommended for bacteraemia alone (ie, 10 days) could be sufficient (eg, a mean of 6 days with varying subsequent oral durations; AR 65).[167,168] In a trial comparing 3 days of intravenous antibiotics with no intravenous administration, followed by 14 days of oral antibiotics for febrile urinary tract infection, there was no difference in recurrence rate between groups, even with bacteraemia.[168] However, only 13 of 306 patients had bacteraemia, so numbers are too small to recommend a minimum duration this short. In the largest retrospective multicentre study of infants with bacteraemic urinary tract infection, no relapses occurred with a mean intravenous antibiotic duration of 7·8 days (SD 4·0), with the lowest mean duration at any institution of 5·5 days (SD 3·0), suggesting that shorter courses could be appropriate in healthy infants who have recovered.[169]

There are no studies of antibiotic duration in epididymitis, but the question of whether antibiotics are needed at all has been addressed. In prepubescent boys, antibiotics are usually recommended for epididymitis associated with abnormal urine (AR 11). Two retrospective studies of urinalysis in epididymitis found low rates of abnormal urine (1–7%), although in one of them 128 boys (91%) received antibiotics (AR 66 and 67). In a prospective study, 36 (84%) of 43 boys without pyuria received no antibiotics, while the five (10%) with pyuria received antibiotics, although duration was not stated.[170] At a mean follow-up of 3 months, there were no complications in the group that did not receive antibiotics.

Discussion

We have reviewed the evidence for minimum intravenous and total antibiotic duration in children younger than 18 years with bacterial infections, comparing shorter courses with traditionally longer durations. In many infections, especially when clinical improvement is rapid, emerging data suggest that traditional long durations of intravenous antibiotics might be unnecessary and that intravenous to oral switch can occur earlier. In most of the other infections evidence for routine longer courses is sparse. The frequent use of traditionally longer courses indicates the paucity of evidence and lack of consensus guidelines and, in the face of this gap, natural clinical instincts to take a conservative approach with patient care. However, longer durations of antibiotics are associated with increased antimicrobial resistance, so the cost must be weighed against the potential benefits, especially if these benefits are unproven.

We have therefore derived evidence-based recommendations for minimum intravenous and total antibiotic duration for all bacterial infections reviewed, and graded the recommendation according to the quality of the evidence (table). We have also taken into account information from available guidelines (AR 5–28). Although the evidence is generalisable for most patients, recommendations should be used as a framework to tailor treatment individually in the context of each patient's condition, including underlying immunodeficiency, infection severity, and rate of

***Panel:* General principles guiding intravenous to oral switch of antibiotics**

Clinical condition

- Clinically stable without signs of severe sepsis (fever alone need not prevent switch)

Ability to absorb oral antibiotics

- Able to tolerate oral medication (not vomiting or nil by mouth)
- No impairment to absorption (eg, mucositis)
- Older than 28 days (<28 days not an absolute contraindication, but absorption variable)

Availability of an appropriate oral antibiotic

- Antibiotic treats the identified or expected organism
- Antibiotic available in appropriate or palatable paediatric formulation
- Antibiotic has sufficient penetration of affected tissues

Practical issues

- Adherence to oral antibiotics
- The family agrees with the plan

recovery. For example, immunocompromised patients might need longer total durations for some infections because of diminished immune defences to combat infection.

In addition to recommendations for specific infection, review of the contributing articles has highlighted general principles that should be considered when deciding whether the switch from intravenous to oral antibiotics is suitable, including clinical condition, ability to absorb oral antibiotics, and availability of an appropriate oral choice for children (panel).

In an era of increasing antimicrobial resistance, strategies to reduce antibiotic overuse are crucial. Optimising the duration of intravenous and oral antibiotics aims to provide the shortest safe duration of antibiotics to treat infection. By reviewing the available evidence systematically, we have synthesised recommendations in the context of available guidelines for antibiotic duration and criteria for intravenous to oral switch. These recommendations can be used to support clinical decision making and, where data are scarce, as a basis for prospective research on optimal antibiotic durations.

Contributors

BJM coordinated contributors to review one or more infections, completed one or more topics as described for all other authors, collated the search and review data in PRISMA format from all contributors, independently verified the searches and reviews, substantially edited the reviews and recommendations, and compiled and approved the final report. DA conceived the project, compiled the list of topics, coordinated the search strategy, coordinated contributors to review one or more infections, and completed one or more topics as described for all other authors, and approved the final report. DI conceived the project, substantially edited the reviews and recommendations, and approved the final report. PAB completed one or more topics as described for all other authors, collated the search and review data in PRISMA format from all contributors, independently verified the searches and reviews, substantially edited the reviews and recommendations, and compiled and approved the final report. All other authors completed one or more topic literature reviews as follows: performed the search, screened and selected relevant studies, synthesised the data, and drafted the literature review and recommendations. They also reviewed the final report to ensure consensus and approved the final report.

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Declaration of interests

We declare no competing interests.

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References

1 Molyneux E, Nizami SQ, Saha S, et al. 5 versus 10 days of treatment with ceftriaxone for bacterial meningitis in children: a double-blind randomised equivalence study. *Lancet* 2011; **377:** 1837–45.

2 Roine I, Ledermann W, Foncea LM, Banfi A, Cohen J, Peltola H. Randomized trial of four vs seven days of ceftriaxone treatment for bacterial meningitis in children with rapid initial recovery. *Pediatr Infect Dis J* 2000; **19:** 219–22.

3 Viladrich PF. Four days of penicillin therapy for meningococcal meningitis. *Arch Intern Med* 1986; **146:** 2380–82.

4 Tuncer AM, Gür I, Ertem U, et al. Once daily ceftriaxone for meningococcemia and meningococcal meningitis. *Pediatr Infect Dis J* 1988; **7:** 711–13.

5 Rothrock SG, Green SM, Harper MB, Clark MC, McIlmail DP, Bachur R. Parenteral vs oral antibiotics in the prevention of serious bacterial infections in children with *Streptococcus pneumoniae* occult bacteremia: a meta-analysis. *Acad Emerg Med* 1998; **5:** 599–606.

6 Fleisher GR, Rosenberg N, Vinci R, et al. Intramuscular versus oral antibiotic therapy for the prevention of meningitis and other bacterial sequelae in young, febrile children at risk for occult bacteremia. *J Pediatr* 1994; **124:** 504–12.

7 Harper MB, Bachur R, Fleisher GR. Effect of antibiotic therapy on the outcome of outpatients with unsuspected bacteremia. *Pediatr Infect Dis J* 1995; **14:** 760–67.

8 Bass JW, Steele RW, Wittler RR, et al. Antimicrobial treatment of occult bacteremia: a multicenter cooperative study. *Pediatr Infect Dis J* 1993; **12:** 466–73.

9 McCarthy PL, Grundy GW, Spiesel SZ, Dolan TF. Bacteremia in children: an outpatient clinical review. *Pediatrics* 1976; **57:** 861–68.

10 Rothrock SG, Harper MB, Green SM, et al. Do oral antibiotics prevent meningitis and serious bacterial infections in children with *Streptococcus pneumoniae* occult bacteremia? A meta-analysis. *Pediatrics* 1997; **99:** 438–44.

11 Bachur R, Harper MB. Reevaluation of outpatients with *Streptococcus pneumoniae* bacteremia. *Pediatrics* 2000; **105:** 502–09.

12 Bradley JS, Ching DK, Hart CL. Invasive bacterial disease in childhood: efficacy of oral antibiotic therapy following short course parenteral therapy in non-central nervous system infections. *Pediatr Infect Dis J* 1987; **6:** 821–25.

13 Chumpa A, Bachur RG, Harper MB. Bacteremia-associated pneumococcal pneumonia and the benefit of initial parenteral antimicrobial therapy. *Pediatr Infect Dis J* 1999; **18:** 1081–85.

14 Chowdhary G, Dutta S, Narang A. Randomized controlled trial of 7-day vs. 14-day antibiotics for neonatal sepsis. *J Trop Pediatr* 2006; **52:** 427–32.

15 Denniston S, Riordan F. *Staphylococcus aureus* bacteraemia in children and neonates: A 10 year retrospective review. *J Infect* 2006; **53:** 387–93.

16 Walker TM, Bowler ICJW, Bejon P. Risk factors for recurrence after *Staphylococcus aureus* bacteraemia. A retrospective matched case-control study. *J Infect* 2009; **58:** 411–16.

17 Tan TQ, Mason EO, Ou CN, Kaplan SL. Use of intravenous rifampin in neonates with persistent staphylococcal bacteremia. *Antimicrob Agents Chemother* 1993; **37:** 2401–06.

18 Chuang YY, Huang YC, Lee CY, Lin TY, Lien R, Chou YH. Methicillin-resistant *Staphylococcus aureus* bacteraemia in neonatal intensive care units: an analysis of 90 episodes. *Acta Paediatr* 2004; **93:** 786–90.

19 Creel AM, Durham SH, Benner KW, Alten JA, Winkler MK. Severe invasive community-associated methicillin-resistant *Staphylococcus aureus* infections in previously healthy children. *Pediatr Crit Care Med* 2009; **10:** 323–27.

20 Park SH, Milstone AM, Diener-West M, Nussenblatt V, Cosgrove SE, Tamma PD. Short versus prolonged courses of antibiotic therapy for children with uncomplicated Gram-negative bacteraemia. *J Antimicrob Chemother* 2014; **69:** 779–85.

21 Hakki M, Limaye AP, Kim HW, Kirby KA, Corey L, Boeckh M. Invasive *Pseudomonas aeruginosa* infections: high rate of recurrence and mortality after hematopoietic cell transplantation. *Bone Marrow Transplant* 2007; **39:** 687–93.

22 Yen M-H, Huang Y-C, Chiu C-H, Lin T-Y. Duration of antimicrobial therapy for non-typhoid Salmonella bacteremia in healthy children. *J Microbiol Immunol Infect* 2002; **35:** 94–98.

23 Tsai M-H, Huang Y-C, Chiu C-H, et al. Nontyphoidal Salmonella bacteremia in previously healthy children: analysis of 199 episodes. *Pediatr Infect Dis J* 2007; **26:** 909–13.

24 Carrillo-Marquez MA, Hulten KG, Mason EO, Kaplan SL. Clinical and molecular epidemiology of *Staphylococcus aureus* catheter-related bacteremia in children. *Pediatr Infect Dis J* 2010; **29:** 410–14.

25 Nazemi KJ, Buescher ES, Kelly REJ, Karlowicz MG. Central venous catheter removal versus in situ treatment in neonates with enterobacteriaceae bacteremia. *Pediatrics* 2003; **111:** e269–74.

26 Srinivasan A, Seifried S, Zhu L, et al. *Staphylococcus aureus* bacteremia in pediatric patients with cancer. *Pediatr Infect Dis J* 2010; **29:** 172–74.

27 Jernigan JA, Farr BM. Short-course therapy of catheter-related *Staphylococcus aureus* bacteremia: a meta-analysis. *Ann Intern Med* 1993; **119:** 304–11.

28 Raad II, Sabbagh MF. Optimal duration of therapy for catheter-related *Staphylococcus aureus* bacteremia: a study of 55 cases and review. *Clin Infect Dis* 1992; **14:** 75–82.

29 Hemels MAC, van den Hoogen A, Verboon-Maciolek MA, Fleer A, Krediet TG. Shortening the antibiotic course for the treatment of neonatal coagulase-negative staphylococcal sepsis: fine with three days. *Neonatology* 2012; **101:** 101–05.

30 Linder N, Lubin D, Hernandez A, Amit L, Ashkenazi S. Duration of vancomycin treatment for coagulase-negative Staphylococcus sepsis in very low birth weight infants. *Br J Clin Pharmacol* 2013; **76:** 58–64.

31 Kassar R, Hachem R, Jiang Y, Chaftari A-M, Raad I. Management of Bacillus bacteremia: the need for catheter removal. *Medicine* 2009; **88:** 279–83.

32 Hartman GE, Shochat SJ. Management of septic complications associated with Silastic catheters in childhood malignancy. *Pediatr Infect Dis J* 1987; **6:** 1042–47.

33 Flynn PM, Shenep JL, Stokes DC, Barrett FF. In situ management of confirmed central venous catheter-related bacteremia. *Pediatr Infect Dis J* 1987; **6:** 729–34.

34 King DR, Komer M, Hoffman J, et al. Broviac catheter sepsis: the natural history of an iatrogenic infection. *J Pediatr Surg* 1985; **20:** 728–33.

35 Olson TA, Fischer GW, Lupo MC, et al. Antimicrobial therapy of Broviac catheter infections in pediatric hematology oncology patients. *J Pediatr Surg* 1987; **22:** 839–42.

36 Rao JS, O'Meara A, Harvey T, Breatnach F. A new approach to the management of Broviac catheter infection. *J Hosp Infect* 1992; **22:** 109–16.

37 Johnson JA, Boyce TG, Cetta F, Steckelberg JM, Johnson JN. Infective endocarditis in the pediatric patient: a 60-year single-institution review. *Mayo Clin Proc* 2012; **87:** 629–35.

38 Niwa K, Nakazawa M, Tateno S, Yoshinaga M, Terai M. Infective endocarditis in congenital heart disease: Japanese national collaboration study. *Heart* 2005; **91:** 795–800.

39 Røder BL, Wandall DA, Frimodt-Møller N, Espersen F, Skinhøj P, Rosdahl VT. Clinical features of *Staphylococcus aureus* endocarditis: a 10-year experience in Denmark. *Arch Intern Med* 1999; **159:** 462–69.

40 Lindberg J, Prag J, Schonheyder HC. Pneumococcal endocarditis is not just a disease of the past: an analysis of 16 cases diagnosed in Denmark 1986–1997. *Scand J Infect Dis* 1998; **30:** 469–72.

41 Phillips B, Watson GH. Oral treatment of subacute bacterial endocarditis in children. *Arch Dis Child* 1977; **52:** 235–37.

42 Lin TY, Chrane DF, Nelson JD, McCracken GHJ. Seven days of ceftriaxone therapy is as effective as ten days' treatment for bacterial meningitis. *JAMA* 1985; **253:** 3559–63.

43 Kavaliotis J, Manios SG, Kansouzidou A, Danielidis V. Treatment of childhood bacterial meningitis with ceftriaxone once daily: open, prospective, randomized, comparative study of short-course versus standard-length therapy. *Chemotherapy* 1989; **35:** 296–303.

44 Martin E, Hohl P, Guggi T, Kayser FH, Fernex M. Short course single daily ceftriaxone monotherapy for acute bacterial meningitis in children: results of a Swiss multicenter study. Part I: clinical results. *Infection* 1990; **18:** 70–77.

45 Singhi P, Kaushal M, Singhi S, Ray P. Seven days vs 10 days ceftriaxone therapy in bacterial meningitis. *J Trop Ped* 2002; **48:** 273–79.

46 Karageorgopoulos DE, Valkimadi PE, Kapaskelis A, Rafailidis PI, Falagas ME. Short versus long duration of antibiotic therapy for bacterial meningitis: a meta-analysis of randomised controlled trials in children. *Arch Dis Child* 2009; **94:** 607–14.

47 Craig JC, Abbott GD, Mogridge NB. Ceftriaxone for paediatric bacterial meningitis: a report of 62 children and a review of the literature. *N Z Med J* 1992; **105:** 441–44.

48 Scholz H, Hofmann T, Noack R, Edwards DJ, Stoeckel K. Prospective comparison of ceftriaxone and cefotaxime for the short-term treatment of bacterial meningitis in children. *Chemotherapy* 1998; **44:** 142–47.

49 Mylonakis E, Hohmann EL, Calderwood SB. Central nervous system infection with *Listeria monocytogenes*. 33 years' experience at a general hospital and review of 776 episodes from the literature. *Medicine* 1998; **77:** 313–36.

50 Felsenstein S, Williams B, Shingadia D, et al. Clinical and microbiologic features guiding treatment recommendations for brain abscesses in children. *Pediatr Infect Dis J* 2013; **32:** 129–35.

51 Madhugiri VS, Sastri BVS, Srikantha U, et al. Focal intradural brain infections in children: an analysis of management and outcome. *Pediatr Neurosurg* 2011; **47:** 113–24.

52 Carpenter J, Stapleton S, Holliman R. Retrospective analysis of 49 cases of brain abscess and review of the literature. *Eur J Clin Microbiol Infect Dis* 2007; **26:** 1–11.

53 James HE, Walsh JW, Wilson HD, Connor JD, Bean JR, Tibbs PA. Prospective randomized study of therapy in cerebrospinal fluid shunt infection. *Neurosurgery* 1980; **7:** 459–63.

54 James HE, Walsh JW, Wilson HD, Connor JD. The management of cerebrospinal fluid shunt infections: a clinical experience. *Acta Neurochir (Wien)* 1981; **59:** 157–66.

55 James HE, Bradley JS. Aggressive management of shunt infection: combined intravenous and intraventricular antibiotic therapy for twelve or less days. *Pediatr Neurosurg* 2008; **44:** 104–11.

56 Arnell K, Enblad P, Wester T, Sjölin J. Treatment of cerebrospinal fluid shunt infections in children using systemic and intraventricular antibiotic therapy in combination with externalization of the ventricular catheter: efficacy in 34 consecutively treated infections. *J Neurosurg* 2007; **107:** 213–19.

57 James HE, Bradley JS. Management of complicated shunt infections: a clinical report. *J Neurosurg Pediatr* 2008; **1:** 223–28.

58 Kestle JRW, Garton HJL, Whitehead WE, et al. Management of shunt infections: a multicenter pilot study. *J Neurosurg Pediatr* 2006; **105:** 177–81.

59 Simon TD, Mayer-Hamblett N, Whitlock KB, et al. Few patient, treatment, and diagnostic or microbiological factors, except complications and intermittent negative cerebrospinal fluid (CSF) cultures during first CSF shunt infection, are associated with reinfection. *J Ped Infect Dis* 2014; **3:** 15–22.

60 Simon TD, Hall M, Dean JM, Kestle JRW, Riva-Cambrin J. Reinfection following initial cerebrospinal fluid shunt infection. *J Neurosurg Pediatr* 2010; **6:** 277–85.

61 Brown EM, Edwards RJ, Pople IK. Conservative management of patients with cerebrospinal fluid shunt infections. *Neurosurgery* 2006; **58:** 657–65.

62 Sexton DG, Babin RW. Peritonsillar abscess: a comparison of a conservative and a more aggressive management protocol. *Int J Pediatr Otorhinolaryngol* 1987; **14:** 129–32.

63 Kara N, Spinou C. Appropriate antibiotics for peritonsillar abscess: a 9 month cohort. *Otorhinolaryngol Head Neck Surg* 2010; **40:** 20–24.

64 Segal N, El-Saied S, Puterman M. Peritonsillar abscess in children in the southern district of Israel. *Int J Pediatr Otorhinolaryngol* 2009; **73:** 1148–50.

65 Maharaj D, Rajah V, Hemsley S. Management of peritonsillar abscess. *J Laryngol Otol* 1991; **105:** 743–45.

66 Lamkin RH, Portt J. An outpatient medical treatment protocol for peritonsillar abscess. *Ear Nose Throat J* 2006; **85:** 658–60.

67 Kirse DJ, Roberson DW. Surgical management of retropharyngeal space infections in children. *Laryngoscope* 2001; **111:** 1413–22.

68 Al-Sabah B, Bin Salleen H, Hagr A, Choi-Rosen J, Manoukian JJ, Tewfik TL. Retropharyngeal abscess in children: 10-year study. *J Otolaryngol* 2004; **33:** 352–55.

69 McClay JE, Murray AD, Booth T. Intravenous antibiotic therapy for deep neck abscesses defined by computed tomography. *Arch Otolaryngol Head Neck Surg* 2003; **129:** 1207–12.

70 Page C, Biet A, Zaatar R, Strunski V. Parapharyngeal abscess: diagnosis and treatment. *Eur Arch Otorhinolaryngol* 2008; **265:** 681–66.

71 Quesnel S, Nguyen M, Pierrot S, Contencin P, Manach Y, Couloigner V. Acute mastoiditis in children: a retrospective study of 188 patients. *Int J Pediatr Otorhinolaryngol* 2010; **74:** 1388–92.

72 Pang LHY, Barakate MS, Havas TE. Mastoiditis in a paediatric population: a review of 11 years experience in management. *Int J Pediatr Otorhinolaryngol* 2009; **73:** 1520–24.

73 Kaplan SL, Mason EO, Wald ER, et al. Pneumococcal mastoiditis in children. *Pediatrics* 2000; **106:** 695–99.

74 Niv A, Nash M, Peiser J, et al. Outpatient management of acute mastoiditis with periosteitis in children. *Int J Pediatr Otorhinolaryngol* 1998; **46:** 9–13.

75 Psarommatis IM, Voudouris C, Douros K, Giannakopoulos P, Bairamis T, Carabinos C. Algorithmic management of pediatric acute mastoiditis. *Int J Pediatr Otorhinolaryngol* 2012; **76:** 791–96.

76 Moore JA, Wei JL, Smith HJ, Mayo MS. Treatment of pediatric suppurative mastoiditis: is peripherally inserted central catheter (PICC) antibiotic therapy necessary? *Otolaryngol Head Neck Surg* 2006; **135:** 106–10.

77 Wald ER, Chiponis D, Ledesma-Medina J. Comparative effectiveness of amoxicillin and amoxicillin-clavulanate potassium in acute paranasal sinus infections in children: a double-blind, placebo-controlled trial. *Pediatrics* 1986; **77:** 795–800.

78 Wald ER, Nash D, Eickhoff J. Effectiveness of amoxicillin/clavulanate potassium in the treatment of acute bacterial sinusitis in children. *Pediatrics* 2009; **124:** 9–15.

79 Kristo A, Uhari M, Luotonen J, Ilkko E, Koivunen P, Alho O-P. Cefuroxime axetil versus placebo for children with acute respiratory infection and imaging evidence of sinusitis: a randomized, controlled trial. *Acta Paediatr* 2005; **94:** 1208–13.

80 Garbutt JM, Goldstein M, Gellman E, Shannon W, Littenberg B. A randomized, placebo-controlled trial of antimicrobial treatment for children with clinically diagnosed acute sinusitis. *Pediatrics* 2001; **107:** 619–25.

81 Smith MJ. Evidence for the diagnosis and treatment of acute uncomplicated sinusitis in children: a systematic review. *Pediatrics* 2013; **132:** e284–96.

82 Rosenfeld RM, Singer M, Jones S. Systematic review of antimicrobial therapy in patients with acute rhinosinusitis. *Otolaryngol Head Neck Surg* 2007; **137** (suppl)**:** S32–45.

83 Morris P, Leach A. Antibiotics for persistent nasal discharge (rhinosinusitis) in children. *Cochrane Database Syst Rev* 2002; **4:** CD001094.

84 Cronin MJ, Khan S, Saeed S. The role of antibiotics in the treatment of acute rhinosinusitis in children: a systematic review. *Arch Dis Child* 2013; **98:** 299–303.

85 Ficnar B, Huzjak N, Oreskovic K, Matrapazovski M, Klinar I. Azithromycin: 3-day versus 5-day course in the treatment of respiratory tract infections in children. Croatian Azithromycin Study Group. *J Chemother* 1997; **9:** 38–43.

86 Georget E, Gauthier A, Brugel L, et al. Acute cervical lymphadenitis and infections of the retropharyngeal and parapharyngeal spaces in children. *BMC Ear Nose Throat Disord* 2014; **14:** 8.

87 Baek MY, Park KH, We JH, Park SE. Needle aspiration as therapeutic management for suppurative cervical lymphadenitis in children. *Korean J Pediatr* 2010; **53:** 801–04.

88 Luu TM, Chevalier I, Gauthier M, Carceller AM, Bensoussan A, Tapiero B. Acute adenitis in children: clinical course and factors predictive of surgical drainage. *J Paediatr Child Health* 2005; **41:** 273–77.

89 Tanir G, Tonbul A, Tuygun N, Aydemir C, Ertan U. Soft tissue infections in children: a retrospective analysis of 242 hospitalized patients. *Jpn J Infect Dis* 2006; **59:** 258–60.

90 Neff L, Newland JG, Sykes KJ, Selvarangan R, Wei JL. Microbiology and antimicrobial treatment of pediatric cervical lymphadenitis requiring surgical intervention. *Int J Pediatr Otorhinolaryngol* 2013; **77:** 817–20.

91 Haider BA, Saeed MA, Bhutta ZA. Short-course versus long-course antibiotic therapy for non-severe community-acquired pneumonia in children aged 2 months to 59 months. *Cochrane Database Syst Rev* 2008; **2:** CD005976.

92 Peltola H, Vuori-Holopainen E, Kallio MJ, SE-TU Study Group. Successful shortening from seven to four days of parenteral beta-lactam treatment for common childhood infections: a prospective and randomized study. *Int J Infect Dis* 2001; **5:** 3–8.

93 Ferwerda A, Moll HA, Hop WC, et al. Efficacy, safety and tolerability of 3 day azithromycin versus 10 day co-amoxiclav in the treatment of children with acute lower respiratory tract infections. *J Antimicrob Chemother* 2001; **47:** 441–46.

94 Harris JA, Kolokathis A, Campbell M, Cassell GH, Hammerschlag MR. Safety and efficacy of azithromycin in the treatment of community-acquired pneumonia in children. *Pediatr Infect Dis J* 1998; **17:** 865–71.

95 Atkinson M, Lakhanpaul M, Smyth A, et al. Comparison of oral amoxicillin and intravenous benzyl penicillin for community acquired pneumonia in children (PIVOT trial): a multicentre pragmatic randomised controlled equivalence trial. *Thorax* 2007; **62:** 1102–06.

96 Addo-Yobo E, Chisaka N, Hassan M, et al. Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study. *Lancet* 2004; **364:** 1141–48.

97 Hazir T, Fox LM, Nisar YB, et al. Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. *Lancet* 2008; **371:** 49–56.

98 Lodha R, Kabra SK, Pandey RM. Antibiotics for community-acquired pneumonia in children. *Cochrane Database Syst Rev* 2013; **6:** CD004874.

99 Lassi ZS, Das JK, Haider SW, Salam RA, Qazi SA, Bhutta ZA. Systematic review on antibiotic therapy for pneumonia in children between 2 and 59 months of age. *Arch Dis Child* 2014; **99:** 687–93.

100 Avansino JR, Goldman B, Sawin RS, Flum DR. Primary operative versus nonoperative therapy for pediatric empyema: a meta-analysis. *Pediatrics* 2005; **115:** 1652–59.

101 Mahant S, Cohen E, Weinstein M, Wadhwa A. Video-assisted thoracoscopic surgery vs chest drain with fibrinolytics for the treatment of pleural empyema in children: a systematic review of randomized controlled trials. *Arch Pediatr Adolesc Med* 2010; **164:** 201–03.

102 Palacios GC, Gonzalez SN, Perez FL, Cuevas SF, Solorzano SF. Cefuroxime vs a dicloxacillin/chloramphenicol combination for the treatment of parapneumonic pleural effusion and empyema in children. *Pulm Pharmacol Ther* 2002; **15:** 17–23.

103 Belet N, Uysal S, Bernay E, Gurses N. Postpneumonic empyema in childhood. *Indian J Pediatr* 2001; **68:** 11–14.

104 Paganini H, Guiñazú JR, Hernández C, Lopardo H, Gonzalez F, Berberian G. Comparative analysis of outcome and clinical features in children with pleural empyema caused by penicillin-nonsusceptible and penicillin-susceptible *Streptococcus pneumoniae*. *Int J Infect Dis* 2001; **5:** 86–88.

105 Tan TQ, Seilheimer DK, Kaplan SL. Pediatric lung abscess: clinical management and outcome. *Pediatr Infect Dis J* 1995; **14:** 51–55.

106 Chan P-C, Huang L-M, Wu P-S, et al. Clinical management and outcome of childhood lung abscess: a 16-year experience. *J Microbiol Immunol Infect* 2005; **38:** 183–88.

107 Nagasawa KK, Johnson SM. Thoracoscopic treatment of pediatric lung abscesses. *J Pediatr Surg* 2010; **45:** 574–78.

108 Tseng YL, Wu MH, Lin MY, Lai WW, Liu CC. Surgery for lung abscess in immunocompetent and immunocompromised children. *J Pediatr Surg* 2001; **36:** 470–73.

109 Le Saux N, Howard A, Barrowman NJ, Gaboury I, Sampson M, Moher D. Shorter courses of parenteral antibiotic therapy do not appear to influence response rates for children with acute hematogenous osteomyelitis: a systematic review. *BMC Infect Dis* 2002; **2:** 16.

110 Howard-Jones AR, Isaacs D. Systematic review of duration and choice of systemic antibiotic therapy for acute haematogenous bacterial osteomyelitis in children. *J Paediatr Child Health* 2013; **49:** 760–68.

111 Kolyvas E, Ahronheim G, Marks MI, Gledhill R, Owen H, Rosenthall L. Oral antibiotic therapy of skeletal infections in children. *Pedaitrics* 1980; **65:** 867–71.

112 Jaberi FM, Shahcheraghi GH, Ahadzadeh M. Short-term intravenous antibiotic treatment of acute hematogenous bone and joint infection in children: a prospective randomized trial. *J Pediatr Orthop* 2002; **22:** 317–20.

113 Peltola H, Pääkkönen M, Kallio P, Kallio MJT. Short- versus long-term antimicrobial treatment for acute hematogenous osteomyelitis of childhood. *Pediatr Infect Dis J* 2010; **29:** 1123–28.

114 Pääkkönen M, Kallio PE, Kallio MJT, Peltola H. No need for prolonged intravenous antibiotics in bacteremic bone and joint infections of childhood. 33rd Annual Meeting of the European Bone and Joint Infection Society; Utrecht; Sept 11–13, 2014. F108.

115 Howard-Jones AR, Isaacs D. Systematic review of systemic antibiotic treatment for children with chronic and sub-acute pyogenic osteomyelitis. *J Paediatr Child Health* 2010; **46:** 736–41.

116 Clark CE, Shufflebarger HL. Late-developing infection in instrumented idiopathic scoliosis. *Spine* 1999; **24:** 1909–12.

117 Kang S-N, Sanghera T, Mangwani J, Paterson JMH, Ramachandran M. The management of septic arthritis in children: systematic review of the English language literature. *J Bone Joint Surg Br* 2009; **91:** 1127–33.

118 Ballock RT, Newton PO, Evans SJ, Estabrook M, Farnsworth CL, Bradley JS. A comparison of early versus late conversion from intravenous to oral therapy in the treatment of septic arthritis. *J Pediatr Orthop* 2009; **29:** 636–42.

119 Peltola H, Pääkkönen M, Kallio P, Kallio MJT, OM-SA Study Group. Clindamycin vs first-generation cephalosporins for acute osteoarticular infections of childhood—a prospective quasi-randomized controlled trial. *Clin Microbiol Infect* 2012; **18:** 582–89.

120 Pääkkönen M, Kallio MJT, Kallio PE, Peltola H. Shortened hospital stay for childhood bone and joint infections: analysis of 265 prospectively collected culture-positive cases in 1983–2005. *Scand J Infect Dis* 2012; **44:** 683–88.

121 Nelson JD, Bucholz RW, Kusmiesz H, Shelton S. Benefits and risks of sequential parenteral—oral cephalosporin therapy for suppurative bone and joint infections. *J Pediatr Orthop* 1982; **2:** 255–62.

122 Jagodzinski NA, Kanwar R, Graham K, Bache CE. Prospective evaluation of a shortened regimen of treatment for acute osteomyelitis and septic arthritis in children. *J Pediatr Orthop* 2009; **29:** 518–25.

123 Kocher MS, Mandiga R, Murphy JM, et al. A clinical practice guideline for treatment of septic arthritis in children: efficacy in improving process of care and effect on outcome of septic arthritis of the hip. *J Bone Joint Surg Am* 2003; **85-A:** 994–99.

124 Peltola H, Pääkkönen M, Kallio P, Kallio MJT, Osteomyelitis-Septic Arthritis (OM-SA) Study Group. Prospective, randomized trial of 10 days versus 30 days of antimicrobial treatment, including a short-term course of parenteral therapy, for childhood septic arthritis. *Clinic Infect Dis* 2009; **48:** 1201–10.

125 Pannaraj PS, Hulten KG, Gonzalez BE, Mason EO, Kaplan SL. Infective pyomyositis and myositis in children in the era of community-acquired, methicillin-resistant *Staphylococcus aureus* infection. *Clin Infect Dis* 2006; **43:** 953–60.

126 Moriarty P, Leung C, Walsh M, Nourse C. Increasing pyomyositis presentations among children in Queensland, Australia. *Pediatr Infect Dis J* 2015; **34:** 1–4.

127 Unnikrishnan PN, Perry D, George H, Bassi R, Bruce C. Tropical primary pyomyositis in children of the UK: an emerging medical challenge. *Int Orthop* 2010; **34:** 109–13.

128 Miller NJK, Duncan RDD, Huntley JS. The conservative management of primary pyomyositis abscess in children: case series and review of the literature. *Scott Med J* 2011; **56:** 181–81.

129 Kilburn SA, Featherstone P, Higgins B, Brindle R. Interventions for cellulitis and erysipelas. *Cochrane Database Syst Rev* 2010; **6:** CD004299.

130 Gouin S, Chevalier I, Gauthier M, Lamarre V. Prospective evaluation of the management of moderate to severe cellulitis with parenteral antibiotics at a paediatric day treatment centre. *J Paediatr Child Health* 2008; **44:** 214–18.

131 Ibrahim LF, Hopper SM, Babl FE, Bryant PA. Who can have parenteral antibiotics at home?: a prospective observational study in children with moderate/severe cellulitis. *Pediatr Infect Dis J* 2016; **35:** 269–74.

132 Hopper SM, Ibrahim LF, Babl FE, Bryant PA. A comparison of treatment at home or in hospital for moderate/severe cellulitis in children. *Arch Dis Child* 2014; **99** (suppl 2)**:** A246–47.

133 Kam AJ, Leal J, Freedman SB. Pediatric cellulitis: success of emergency department short-course intravenous antibiotics. *Pediatr Emerg Care* 2010; **26:** 171–76.

134 Moubayed SP, Vu T-TV, Quach C, Daniel SJ. Periorbital cellulitis in the pediatric population: clinical features and management of 117 cases. *J Otolaryngol Head Neck Surg* 2011; **40:** 266–70.

135 Upile NS, Munir N, Leong SC, Swift AC. Who should manage acute periorbital cellulitis in children? *Int J Pediatr Otorhinolaryngol* 2012; **76:** 1073–77.

136 Goldman RD, Dolansky G, Rogovik AL. Predictors for admission of children with periorbital cellulitis presenting to the pediatric emergency department. *Pediatr Emerg Care* 2008; **24:** 279–83.

137 Brugha RE, Abrahamson E. Ambulatory intravenous antibiotic therapy for children with preseptal cellulitis. *Pediatr Emerg Care* 2012; **28:** 226–28.

138 Nageswaran S, Woods CR, Benjamin DK Jr, Givner LB, Shetty AK. Orbital cellulitis in children. *Pediatr Infect Dis J* 2006; **25:** 695–99.

139 Emmett Hurley P, Harris GJ. Subperiosteal abscess of the orbit: duration of intravenous antibiotic therapy in nonsurgical cases. *Ophthal Plast Reconstr Surg* 2012; **28:** 22–26.

140 Cannon PS, Mc Keag D, Radford R, Ataullah S, Leatherbarrow B. Our experience using primary oral antibiotics in the management of orbital cellulitis in a tertiary referral centre. *Eye (Lond)* 2009; **23:** 612–15.

141 Lee MC, Rios AM, Aten MF, et al. Management and outcome of children with skin and soft tissue abscesses caused by community-acquired methicillin-resistant *Staphylococcus aureus*. *Pediatr Infect Dis J* 2004; **23:** 123–27.

142 Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. *Ann Emerg Med* 2010; **55:** 401–07.

143 Huizinga WK, Kritzinger NA, Bhamjee A. The value of adjuvant systemic antibiotic therapy in localised wound infections among hospital patients: a comparative study. *J Infect* 1986; **13:** 11–16.

144 Lall RR, Wong AP, Lall RR, Lawton CD, Smith ZA, Dahdaleh NS. Evidence-based management of deep wound infection after spinal instrumentation. *J Clin Neurosci* 2015; **22:** 238–42.

145 Soultanis K, Mantelos G, Pagiatakis A, Soucacos PN. Late infection in patients with scoliosis treated with spinal instrumentation. *Clin Orthop Relat Res* 2003; **411:** 116–23.

146 Hester SM, Fisher JF, Lee MR, Macomson S, Vender JR. Evaluation of salvage techniques for infected baclofen pumps in pediatric patients with cerebral palsy. *J Neurosurg Pediatr* 2012; **10:** 548–54.

147 Smith JT, Smith MS. Can infection associated with rib distraction techniques be managed without implant removal? *Spine* 2011; **36:** 2176–79.

148 Calkins CM, Shew SB, Sharp RJ, et al. Management of postoperative infections after the minimally invasive pectus excavatum repair. *J Pediatr Surg* 2005; **40:** 1004–08.

149 Anslot C, Hulin S, Durandy Y. Postoperative mediastinitis in children: improvement of simple primary closed drainage. *Ann Thorac Surg* 2007; **84:** 423–28.

150 Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendicectomy. *Cochrane Database Syst Rev* 2005; **3:** CD001439.

151 Lee SL, Islam S, Cassidy LD, Abdullah F, Arca MJ, Committee FT2APSAOACT. Antibiotics and appendicitis in the pediatric population: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee Systematic Review. *J Pediatr Surg* 2010; **45:** 2181–85.

152 Snelling CMH, Poenaru D, Drover JW. Minimum postoperative antibiotic duration in advanced appendicitis in children: a review. *Pediatr Surg Int* 2004; **20:** 838–45.

153 Rice H, Brown RL, Gollin G, et al. Results of a pilot trial comparing prolonged intravenous antibiotics with sequential intravenous/oral antibiotics for children with perforated appendicitis. *Arch Surg* 2001; **136:** 1391–95.

154 Fraser JD, Aguayo P, Leys CM, et al. A complete course of intravenous antibiotics vs a combination of intravenous and oral antibiotics for perforated appendicitis in children: a prospective, randomized trial. *J Pediatr Surg* 2010; **45:** 1198–202.

155 Lelli L, Drongowski R, Raviz S, Wilke L, Heidelberger K, Hirsch R. Historical changes in the postoperative treatment of appendicitis in children: impact of medical outcome. *J Pediatr Surg* 2000; **35:** 239–45.

156 Taylor E. The efficacy of postoperative oral antibiotics in appendicitis: a randomized prospective double-blinded study. *Am Surg* 2004; **70:** 858–62.

157 Hoelzer DJ, Zabel DD, Zern JT. Determining duration of antibiotic use in children with complicated appendicitis. *Pediatr Infect Dis J* 1999; **18:** 979–82.

158 Wong KKY, Fan AH, Lan LCL, Lin SCL, Tam PKH. Effective antibiotic regime for postoperative acute cholangitis in biliary atresia—an evolving scene. *J Pediatr Surg* 2004; **39:** 1800–02.

159 Faix RG, Polley TZ, Grasela TH. A randomized, controlled trial of parenteral clindamycin in neonatal necrotizing enterocolitis. *J Pediatr* 1988; **112:** 271–77.

160 Scheifele DW, Ginter GL, Olsen E, Fussell S, Pendray M. Comparison of two antibiotic regimens for neonatal necrotizing enterocolitis. *J Antimicrob Chemother* 1987; **20:** 421–29.

161 Michael M, Hodson EM, Craig JC, Martin S, Moyer VA. Short versus standard duration oral antibiotic therapy for acute urinary tract infection in children. *Cochrane Database Syst Rev* 2003; **1:** CD003966.

162 Fitzgerald A, Mori R, Lakhanpaul M, Tullus K. Antibiotics for treating lower urinary tract infection in children. *Cochrane Database Syst Rev* 2012; **8:** CD006857.

163 Brady PW, Conway PH, Goudie A. Length of intravenous antibiotic therapy and treatment failure in infants with urinary tract infections. *Pediatrics* 2010; **126:** 196–203.

164 Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev* 2014; **7:** CD003772.

165 Bocquet N, Sergent Alaoui A, Jais J-P, et al. Randomized trial of oral versus sequential IV/oral antibiotic for acute pyelonephritis in children. *Pediatrics* 2012; **129:** e269–75.

166 Pohl A. Modes of administration of antibiotics for symptomatic severe urinary tract infections. *Cochrane Database Syst Rev* 2007; **4:** CD003237.

167 Honkinen O, Jahnukainen T, Mertsola J, Eskola J, Ruuskanen O. Bacteremic urinary tract infection in children. *Pediatr Infect Dis J* 2000; **19**: 630.

168 Hoberman A, Wald ER, Hickey RW, et al. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. *Pediatrics* 1999; **104:** 79–86.

169 Schroeder AR, Shen MW, Biondi EA, et al. Bacteraemic urinary tract infection: management and outcomes in young infants. *Arch Dis Child* 2015; **101:** 125–30.

170 Lau P, Anderson PA, Giacomantonio JM, Schwarz RD. Acute epididymitis in boys: are antibiotics indicated? *Br J Urol* 1997; **79:** 797–800.