INTRAVENOUS TO ORAL ANTIMICROBIAL SWITCH

PRACTICE GUIDELINE©

DOCUMENT SUMMARY/KEY POINTS

- Intravenous antibiotics are important for treatment of serious infections, but are sometimes continued for longer than necessary, and associated with risks of catheter-related infection, increased hospital length of stay, and selection pressure for antimicrobial resistance. Switching to oral formulations should occur when safe to do so.
- Oral therapy limits use of vascular access devices and the associated complications in addition to benefits such as lower cost, more efficient drug administration and opportunity for earlier discharge
- Table 1 summarises the available evidence and guidelines for the duration of antibiotic use in key paediatric conditions after systematic review.

READ ACKNOWLEDGEMENT

- Read Acknowledge Only – Medical, Pharmacy and Nursing Staff

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Background

In many infections, especially when clinical improvement is rapid, there is data to suggest that traditional long durations of intravenous antibiotics might be unnecessary and that switching to oral formulation can occur earlier. Oral therapy avoids the need for a vascular access device, and is usually associated with less serious adverse effects than parenteral therapy. Oral therapy also has the advantage of lower cost, greater efficiency of drug administration and opportunity for earlier discharge.[1,2]

Table 1 summarises evidence-based recommendations for minimum intravenous and total antibiotic duration for common bacterial infections in children. Evidence and recommendations have been graded according to the quality of the evidence and information from available guidelines.

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 recovery. For example, immunocompromised patients might need longer total durations for some infections because of diminished immune defences to combat infection.[3]

General principles guiding IV to oral antibiotic switch[3]

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 (e.g. mucositis)
Older than 28 days (<28 days not an absolute contraindication, but absorption variable)

Availability of an appropriate oral antibiotic that will:

Treat the identified or expected organism(s)
Is available in appropriate/palatable paediatric formulation *(contact Pharmacy to discuss available options if a proprietary product is not available)*
Sufficiently penetrates affected tissues

Practical issues

Adherence to oral antibiotics
The family agrees with the plan

Information for parents and carers

Parent and carer information leaflets designed to facilitate discussion and promote shared decision making are available in various languages and may be downloaded directly from the Clinical Excellence Commission:
http://www.cec.health.nsw.gov.au/patient-safety-programs/medication-safety/antimicrobial-stewardship/quah/iv-to-oral-antibiotic-switch

Examples of antimicrobials with good oral absorption[1,4]

Antimicrobial	Oral Bioavailability
Azithromycin	34-52%
Clindamycin	90%
Ciprofloxacin	60-80%
Fluconazole	>90%
Linezolid	100%
Metronidazole	~80%
Moxifloxacin	~90%
Rifampicin	Similar plasma levels achieved with oral
Trimethoprim-sulfamethoxazole	Similar plasma levels achieved with oral

Guidelines for Antibiotic Duration and IV-Oral Switch in Children[3]

Infection	Minimum IV antibiotic duration	Criteria for switch to oral antibiotic	Minimum total antibiotic duration	Notes
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*: fever at 24h? Afebrile: 0 days [B-I] Febrile: 1 day [C-IV] Non-occult (septic): 7-10 days [D-IV]	 Oral only Afebrile, improved No oral switch	 7-10 days [C-IV] 7-10 days [C-IV] 7-10 days [C-IV]	*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] If associated pneumonia, initial IV 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 endocarditis, refer to endocarditis guideline If associated osteomyelitis/septic arthritis, IV duration may be shortened to 4-7 days if improving quickly and 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 *Salmonella*: 7 days [D-IV]	If multi-resistant, duration is from first negative culture If associated UTI, IV duration may be shortened to 5-7 days if uncomplicated and improving quickly [D-IV], with remainder oral [D-expert opinion] *HSCT – haematopoietic stem cell transplant
Central venous catheter (CVC)-associated bacteraemia	7 days [B-III] CoNS* in neonates, line removed, cultures cleared: 3-7 days [C-IV]	No oral switch No oral switch	Additional duration dependent on the bacteria cultured (refer to relevant guideline)	CVC removal if blood cultures positive after 72 hours of appropriate antibiotics [B-III]. No bacteria absolutely necessitate CVC removal, but *Pseudomonas aeruginosa* and *S. aureus* have been harder to clear in some studies. *CoNS – coagulase negative staphylococci
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 ≤0.12mg/L: 2 weeks[1]or 4 weeks[2] MIC >0.12mg/L: 4-6 weeks *S. aureus* [D-IV] MSSA uncomplicated: 4 weeks MSSA complicated or MRSA: 6 weeks	[1]If benzylpenicillin (or ceftriaxone) + gentamicin [2]If benzylpenicillin (or ceftriaxone) alone

Infection	Minimum IV antibiotic duration	Criteria for switch to oral antibiotic	Minimum total antibiotic duration	Notes
Central nervous system infections				
Bacterial meningitis	7-21 days depending on organism [D-IV]	No oral switch [D-IV]	*N. meningitidis*: 5-7 days [B-II] *H. influenzae*: 7-10 days [C-II] *S. pneumoniae*: 10-14 days [C-II] Group B streptococci: 14-21 days [D-IV] Gram-negative bacilli: 21 days [D-IV] *L. monocytogenes*: 21 days [D-IV]	Nil
Brain abscess and subdural empyema	2-4 weeks [B-III]	Clinical improvement (afebrile, alert), CRP normal [C-III]	6 weeks [C-III]	Pus drainage if possible [B-III], ideally before antibiotics. Duration likely to be longer if no drainage [D-expert opinion] Decision to switch to oral includes antibiotic CNS penetration and adherence.
Ventriculo-peritoneal shunt infection	Uncomplicated: 10 days [C-III] Complicated: 21 days [C-III]	No oral switch No oral switch	Uncomplicated: 10 days IV (with or without intraventricular antibiotics) Complicated: 21 days IV (with or without intraventricular antibiotics). May 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 sterilized [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				
Streptococcal pharyngitis/ tonsillitis*	0 days [A-I]	As soon as tolerated	10 days [A-I]	Duration based on using penicillin *Pharyngitis and *otitis media excluded from Lancet ID article due to space limitations and usually not IV
Peritonsillar abscess (quinsy)	1-2 days following successful drainage [C-IV]	As soon as tolerated	10 days [A-I]	Nil
Otitis media*	0 days [A-I]	As soon as tolerated	5 days if treated [A-I] More severely unwell children: up to 10 days [D-expert opinion] Tympanic membrane perforation if indigenous: ≤14 days [D-expert opinion]	Withhold antibiotics for 48 hours in most children [A-I] Consider antibiotics if symptoms persist for 48 hours (earlier in children age <6 months [D-expert opinion]) Unwell or systemic symptoms – treat immediately with antibiotics [D-expert opinion] *Otitis media excluded from Lancet ID as above

Infection	Minimum IV antibiotic duration	Criteria for switch to oral antibiotic	Minimum total antibiotic duration	Notes
Respiratory infections cont.				
Retro-pharyngeal 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, IV antibiotics for surrounding tissue involvement
Mastoiditis	5 days [D-IV]	Clinical improvement	12-15 days based on clinical progress [D-expert opinion]	Longer courses may be required for intracranial complications; refer to brain abscess guideline
Acute bacterial sinusitis	0 days [C-I] Systemically unwell/high risk of suppuration: 1-2 days [D-expert opinion]	Clinical improvement	Moderate-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/ 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 IV treatment [D-expert opinion]	Clinical Improvement Clinical improvement	Mild: 3 days [A-I] Moderate/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 bacteraemia refer to the relevant guideline *Severe/complicated: O2 sats<85%, shock receiving IV bolus, immunocompromise, chronic lung/heart disease
Ventilator-associated pneumonia	Initial treatment [D-expert opinion]	No bacteraemia, clinical improvement, tolerating orals	Good clinical response: 7 days [B-II] Non-fermentative Gram-negative bacilli in sputum: 10 days [D-expert opinion] (eg *Pseudomonas*, *Acinetobacter*)	Although there is no minimum IV duration the majority of patients will start IV due to being ventilated If associated bacteraemia refer to the relevant guideline
Pleural empyema	Initial treatment [D-expert opinion]	Afebrile for 1-2 days, chest drain removed	7 days	Patients can remain febrile for several days on adequate treatment. Antibiotic duration may need to be much longer (up to 6 weeks) depending on disease severity
Lung abscess	Initial treatment [D-expert opinion]	Afebrile, clinical improvement	4-6 weeks [D-expert opinion]	Abscess >6cm: continue until resolved or cavity small and stable size [D-expert opinion]

Infection	Minimum IV antibiotic duration	Criteria for switch to oral antibiotic	Minimum total antibiotic duration	Notes
Musculoskeletal infections				
Acute osteomyelitis	Uncomplicated: 3-4 days [A-I]	Afebrile, clinical improvement, CRP/ESR decreasing [A-II]	3-4 weeks [A-II] Complicated (delayed presentation, associated wound or abscess): longer duration IV is likely to be required [D-expert opinion]	If associated bacteraemia, initial IV 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]	There is no evidence to support a minimum total duration There is 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 may not be possible without prosthetic material removal
Septic arthritis	2-4 days [A-II]	Afebrile, clinical improvement, CRP/ESR decreasing [A-II]	2-3 weeks [A-II] Complicated (delayed presentation, associated wound or abscess): longer duration IV is likely to be required [D-expert opinion]	If associated bacteraemia, initial IV 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]
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/severe*: 1-3 days [C-IV]	Clinical improvement – fever and erythema reduction	5-7 days [C-IV]	If associated deep infection or osteomyelitis, refer to the relevant guideline *Moderate/severe: rapidly spreading erythema, tender, lymphangitis, systemic features
Preseptal (periorbital) cellulitis	2-3 days [C-IV]	Clinical improvement 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]	Intra-orbital abscesses should be drained, with non-operative management in selected patients [C-IV]. If symptoms persist IV antibiotics should continue while investigating for complications [D-expert opinion]

Infection	Minimum IV antibiotic duration	Criteria for switch to oral antibiotic	Minimum total antibiotic duration	Notes
Skin and soft tissue infections				
Skin abscesses and boils	If effectively drained: 0 days [B-II]	As soon as tolerated	0 days [B-II]	If associated cellulitis, refer to the 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 hours post 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 prolonged antibiotics may be necessary [D-expert opinion]	The wound should be surgically debrided [B-III] Mediastinitis may be treatable with shorter than 4-6 weeks but there is insufficient evidence to recommend this Prosthetic material should be removed if possible.
Abdominopelvic infections				
Appendicitis – uncomplicated	Single pre-operative dose [A-I]	No oral switch	Single pre-operative dose only [A-I]	Surgical prophylaxis only 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 based on 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 [C-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 in 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 NEC is considered unlikely [D-expert opinion]

Infection	Minimum IV antibiotic duration	Criteria for switch to oral antibiotic	Minimum total antibiotic duration	Notes
Genitourinary infections				
Lower urinary tract infection (UTI)	0 days Age <3m: initial treatment	Clinical improvement	3-4 days [A-I]	If associated bacteraemia, refer to bacteraemia guideline
Pyelonephritis	0 days [A-I] Age <3m 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 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

Note: 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 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 A)

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Appendix A: Grading of evidence and recommendations

Grading of Recommendations

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Grading of Evidence

Evidence level	Study Intervention Type	Study quality & risk of bias	
		High quality	Low Quality
I	A systematic review of level II studies	A	B
II	A randomised controlled trial	B	C
III	All other types of study with some type of control or comparison: pseudo-randomised, comparative with concurrent controls, cohort, case-control, interrupted time series	C	D
IV	Case series with either post-test or pre-test/post-test outcomes	D	D
Expert Opinion	Case reports, historical practice, guidelines and expert opinion	D	D