



**ANTIBIOTIC DURATION AND TIMING OF  
THE SWITCH FROM INTRAVENOUS TO  
ORAL ROUTE FOR BACTERIAL  
INFECTIONS IN CHILDREN**  
SYSTEMATIC REVIEW AND GUIDELINES

PEDIATRIC DEPARTMENT 1

27/02/2020



# THE LANCET Infectious Diseases

Volume 18, Issue 6, June 2018

www.thelancet.com/infection



## Articles

Detection of Zika virus in amniotic fluid of fetuses with microcephaly

See page 653

## Articles

When did hepatitis C virus genotype 1a spread in North America?

See page 698

## Review

What sequelae of Ebola virus disease will survivors face?

See page e82

The Lancet Infectious Diseases has an **Impact Factor of 27.516**® and ranks first among infectious diseases journals (2018 Journal Citation Reports®, Clarivate Analytics 2019).



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

*Brendan J McMullan, David Andresen, Christopher C Blyth, Minyon L Avent, Asha C Bowen, Philip N Britton, Julia E Clark, Celia M Cooper, Nigel Curtis, Emma Goeman, Briony Hazelton, Gabrielle M Haeusler, Ameneh Khatami, James P Newcombe, Joshua Osowicki, Pamela Palasanthiran, Mike Starr, Tony Lai, Clare Nourse, Joshua R Francis, David Isaacs, Penelope A Bryant, on behalf of the ANZPID-ASAP group*

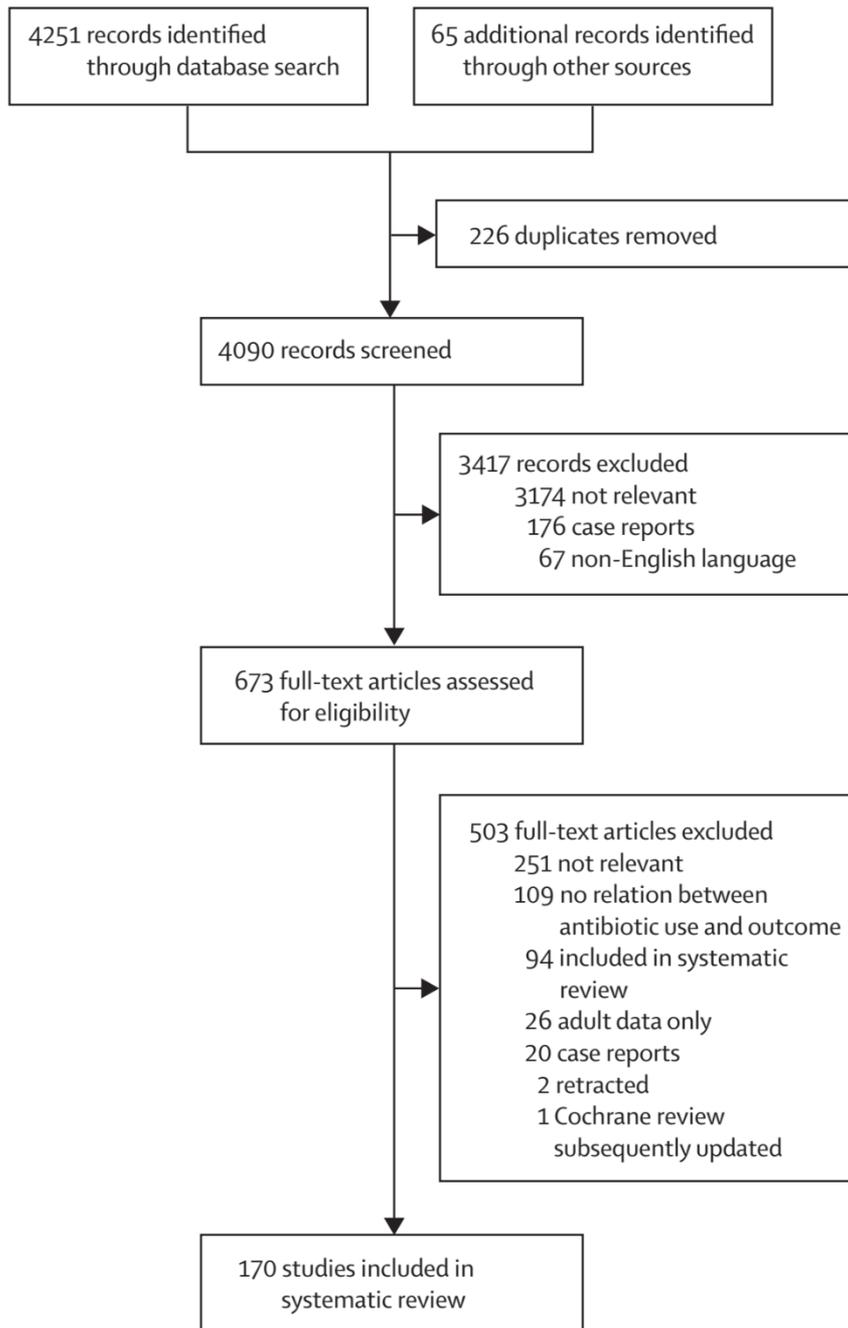
Few studies are available to inform duration of intravenous antibiotics for children and when to switch to oral antibiotics. We have systematically reviewed antibiotic duration and timing of switch for 36 paediatric infectious diseases and developed evidence-graded recommendations, review, guidelines, and expert consensus. We searched databases and obtained information on studies and relevant guidelines. All eligible studies were assessed for quality. 4090 articles were included. Evidence relating antibiotic duration to outcomes in children for some infections came from meta-analyses or randomised controlled trials; in other infections data were from retrospective studies. Outcomes of intravenous to oral switch commonly included defervescence and clinical improvement with no difference in laboratory markers. Evidence suggests that intravenous to oral switch can occur safely and is recommended for some infections. We have synthesised recommendations for antibiotic duration and oral switch to support clinical decision making and prospective research.



# WHY WE CHOOSE THIS TOPIC?

- 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. Shorter antibiotic courses can potentially affect antimicrobial resistance, and have already been advocated for a few infections.
- 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.





# FINDINGS

Our search identified 4090 abstracts. 673 potentially relevant articles were assessed for eligibility, of which 170 studies met the inclusion criteria. After that, only 61 (36%) being RCT or systematic reviews.



# BACTERAEEMIA & ENDOCARDITIS

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b><i>Meningo.</i> bacteraemia</b>	4–5 days (C-III)	No oral switch	4–5 days (C-III)	7-14 days or afebrile 4-5 days
<b><i>Pneumo.</i> bacteraemia</b>	Occult afebrile at 24 h: 0 day (B-I); Occult febrile at 24 h: 1 day (C-IV);  Septic: 7–10 days (D-IV)	Oral only  Afebrile, rapid improvement  No oral switch	7–10 days  7–10 days  7–10 days	7-10 days
<b><i>Staph.aureus</i> bacteraemia</b>	7–14 days (D-IV)	No oral switch	<i>MSSA</i> : 7–14 days (D-IV), <i>MRSA</i> : 14 days (D-IV), longer if persistent positive cultures or complications (D-expert opinion)	7-14 days

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b>Gram negative bacteraemia</b>	10 days (C-III)	No oral switch	10 days (C-III) specific bacteria: <i>Pseudo.</i> : 14 days (D-IV) Non-typhoidal salmon.: 7 days (D-IV)	14 days
<b>CVC-associated bacteraemia</b>	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)	The same
<b>Bacterial endocarditis</b>	4–6 weeks depending on organism and antibiotic choice (C-III)	No oral switch	Viridans strep. (D-IV) MIC ≤0.12 mg/L: 2w or 4w MIC >0.12–2 mg/L: 4–6w MIC >4 mg/L: 4–6w <i>S aureus</i> (D-IV) MSSA uncomplicated: 4w MSSA complicated or MRSA: 6w	Min 2w (4-8w)

# CNS INFECTIONS

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b>Bacterial meningitis</b>	7–21 days depending on organism (D-IV)	No oral switch (D-IV)	<i>Neis.meningitidis</i> : 5–7 days (B-II) <i>H.influenzae</i> : 7–10 days (C-II) <i>Strep.pneumoniae</i> : 10–14 days (C-II) Gr.B strep.: 14–21 days (D-IV) Gram-negative bacilli: 21 days (D-IV) <i>Lis.monocytogenes</i> : 21 days (D-IV)	5-7 days  7-10 days  10-14 days  21 days  14-21 days
<b>Brain abscess and subdural empyema</b>	2–4 weeks (B-III)	Clinical improve. (afebrile, normal conscious level), CRP normal (C-III)	6 weeks (C-III)	4 – 8w

# RESPIRATORY INFECTIONS

	<b>Min intravenous antibiotic duration</b>	<b>Criteria for switch to oral antibiotic</b>	<b>Min total antibiotic duration</b>	<b>CH2 Guidelines</b>
<b>Peritonsillar abscess (quinsy)</b>	1–2 days following successful drainage (C-IV)	As soon as tolerated	10 days (A-I)	Almost oral antibiotic 10 days
<b>Retropharyngeal abscess</b>	3–5 days for conservative or surgical management (D-IV)	Afebrile, neck mobility, tolerating oral diet (D-IV)	10–14 days (D-expert opinion)	The same
<b>Acute bacterial sinusitis</b>	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)	Almost oral antibiotic 10 days

	<b>Min intravenous antibiotic duration</b>	<b>Criteria for switch to oral antibiotic</b>	<b>Min total antibiotic duration</b>	<b>CH2 Guidelines</b>
<b>Acute cervical lymphadenitis</b>	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)	N/A
<b>Community-acquired pneumonia</b>	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)	Uncomplicated: 7-10 days or afebrile after 7 days  Complicated: 4w or afebrile after 2w
<b>Pleural empyema</b>	Initial treatment (D-expert opinion)	Afebrile for 1–2 days, chest drain removed	7 days (D-expert opinion)	3-4 weeks

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b>Ventilator-associated pneumonia</b>	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, <i>Pseudo. spp</i> , <i>Acineto. spp</i> )	N/A
<b>Lung abscess</b>	Initial treatment (D-expert opinion)	Afebrile, clinical improvement	4–6 weeks (D-expert opinion)	The same



# MUSCULOSKELETAL INFECTIONS

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b>Acute osteomyelitis</b>	Uncomplicated: 3–4 days (A-I)	Afebrile, clinical improvement, CRP decreasing (A-II)	3–4 weeks (A-II) Complicated (associated wound or abscess): longer duration intravenous administration is likely to be required (D-expert opinion)	Clinical improvement (after 7 days): switch to oral.  Antibiotic duration: 3 months (?)
<b>Subacute or chronic osteomyelitis</b>	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	N/A

	<b>Min intravenous antibiotic duration</b>	<b>Criteria for switch to oral antibiotic</b>	<b>Min total antibiotic duration</b>	<b>CH2 Guidelines</b>
<b>Septic arthritis</b>	2–4 days (A-II)	Afebrile, clinical improvement, CRP decreasing (A-II)	2–3 weeks (A-II) Complicated (wound or abscess): longer duration intravenous route is likely to be required (D-expert opinion)	The same



# SKIN AND SOFT TISSUE INFECTIONS

	<b>Min intravenous antibiotic duration</b>	<b>Criteria for switch to oral antibiotic</b>	<b>Min total antibiotic duration</b>	<b>CH2 Guidelines</b>
<b>Cellulitis</b>	Mild: 0 days  Moderate or severe: 1–3 days (C-IV)	Clinical improvement: reduction in fever and erythema	5–7 days (C-IV)	7-10 days
<b>Preseptal (periorbital) cellulitis</b>	2–3 days (C-IV)	Clinical improvement: reduction in fever and erythema	7–10 days (C-IV)	N/A
<b>Orbital cellulitis</b>	3–4 days (C-IV)	Clinical resolution of fever, erythema, and pain.	7–10 days (C-IV)	N/A

	<b>Min intravenous antibiotic duration</b>	<b>Criteria for switch to oral antibiotic</b>	<b>Min total antibiotic duration</b>	<b>CH2 Guidelines</b>
<b>Skin abscesses and boils</b>	If effectively drained: 0 days (B-II)	N/A	0 days (B-II)	Oral antibiotic: 7 days
<b>Superficial surgical site infection</b>	0 days (B-II)	As soon as tolerated	If started, 5–7 days (D-expert opinion)	The same
<b>Deep surgical site infection</b>	No prosthetic material: initial treatment (B-III)  Prosthetic material: 4–6w (D-expert opinion)	No oral switch if short duration  Clinical improvement	No minimum recommendation, duration dependent on clinical improvement; if prosthetic material present, very longterm antibiotics might be necessary (D-expert opinion)	The same

# ABDOMINOPELVIC INFECTIONS

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b>Appendicitis: uncomplicated</b>	Single preoperative dose (A-I)	No oral switch	Single preoperative dose only (A-I)	The same
<b>Appendicitis: complicated, intra-abdominal infection</b>	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)	The same
<b>Acute cholangitis</b>	Initial treatment (C-III)	No recommendation	No minimum duration, depends on clinical improvement (D-expert opinion)	The same

	<b>Min intravenous antibiotic duration</b>	<b>Criteria for switch to oral antibiotic</b>	<b>Min total antibiotic duration</b>	<b>CH2 Guidelines</b>
<b>Pancreatitis</b>	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 same
<b>Necrotising enterocolitis</b>	7-10 days (C-IV)	No oral switch	7–10 days (D-expert opinion) with further duration if lack of clinical improvement	The same



# GENITOURINARY INFECTIONS

	Min intravenous antibiotic duration	Criteria for switch to oral antibiotic	Min total antibiotic duration	CH2 Guidelines
<b>Lower UTI</b>	0 days  Age <3 months: initial treatment	Clinical improvement	3–4 days (A-I)	The same
<b>Pyelonephritis</b>	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)	14 days  Clinical improvement after 4 days and urine culture (-): switch oral
<b>Epididymitis</b>	0 days	N/A	Negative urinalysis: no antibiotic (C-III)  Positive urinalysis: oral antibiotic (B-III) for 2 weeks (D-expert opinion)	N/A

# GENERAL PRINCIPLES GUIDING INTRAVENOUS TO ORAL SWITCH OF ANTIBIOTICS

## Clinical condition

- Clinically stable without signs of severe sepsis

## 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)



# GENERAL PRINCIPLES GUIDING INTRAVENOUS TO ORAL SWITCH OF ANTIBIOTICS

## 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



HAPPY  
**DOCTOR'S**  
DAY

