

Date

June 1, 2012

Title

Anti-Infective Treatment for Pediatric Community-acquired Pneumonia (CAP) – Inpatient and Outpatient

Purpose of GREAT

The purpose of this document is to highlight recent evidence-based recommendations for anti-infective selection in infants and children with community acquired pneumonia from the Infectious Diseases Society of America (IDSA) and the British Thoracic Society (BTS) guidelines (*BTS 2011, [CCHMC 5a]*); (*IDSA 2011, [CCHMC 5a]*). Adoption of this evidence will guide practice change at the point of care.

CCHMC Clinical Question

In children 3 months to 18 years of age, does the selection of antibiotic differ by age or care location for the management of CAP?

Target Population

Inclusion:

- otherwise healthy children from 3 months to 18 years of age who present with simple CAP

Exclusions:

- children requiring intensive care on admission
- pneumonia began within 48 hours after a hospital admission
- likely aspiration of a foreign body or stomach contents
- medical condition that uniquely alters pathophysiology and/or care options related to pneumonia, including:
 - congenital, acquired, or drug induced immunocompromise
 - chronic lung disease such as cystic fibrosis

Recommendations (See [CCHMC](#); [BTS](#); and [IDSA](#) Tables of Recommendation Strengths)

Outpatients:

1. It is recommended that amoxicillin be used as first-line therapy for previously healthy, appropriately immunized children 3 months to 18 years of age with mild to moderate CAP suspected to be of bacterial origin. Amoxicillin provides appropriate coverage for *Streptococcus pneumoniae* (*S. pneumoniae*), the most prominent invasive bacterial pathogen (*BTS 2011, [CCHMC 5a]* [*BTS B*]; (*IDSA 2011, [CCHMC 5a]* [*IDSA strong/moderate*]). See Table 1: Outpatient Anti-infective Treatment Recommended by Age and Indication for Treatment.

Note 1: Anti-infective therapy is not routinely required for children < 2years of age (*BTS 2011, [CCHMC 5a]*) or preschool-aged children with mild symptoms of lower respiratory tract infection, because viral pathogens are responsible for the great majority of clinical disease but review is prudent if symptoms persist (*BTS 2011, [CCHMC 5a]*); (*IDSA 2011, [CCHMC 5a]*).

Note 2: Atypical bacterial pathogens (e.g., *M. pneumoniae*), and less common lower respiratory tract bacterial pathogens, may also need to be considered in management decisions (*BTS 2011, [CCHMC 5a]*); (*IDSA 2011, [CCHMC 5a]*).

Table 1: Outpatient Anti-infective Treatment Recommended by Age and Indication for Treatment

Indication for Treatment	Infant/Preschool-Aged Children	School-Aged Children and Adolescents
First-line for presumed viral CAP	No antibacterial agent; consider treatment for influenza as appropriate	No antibacterial agent; consider treatment for influenza as appropriate
First-line for presumed bacterial CAP	Amoxicillin	Amoxicillin
First-line for non-immunized	3 rd generation cephalosporin or amoxicillin-clavulanate	3 rd generation cephalosporin or Amoxicillin-clavulanate
Suspicion of atypical bacterial cause	If high suspicion of atypical bacterial cause consider infectious disease consult	Azithromycin, clarithromycin, doxycycline (for children >7 years old with suspected atypical cause), (levofloxacin or moxifloxacin if < 8years old and allergic to macrolides
Alternative if allergy to first-line	6 months to 5 years – 3 rd generation cephalosporin, clindamycin	3 rd generation cephalosporin, clindamycin,
Alternative if allergy to alternative	Levofloxacin	Levofloxacin

(Adapted from British Thoracic Society (BTS) and Infectious Diseases Society of America (IDSA) guidelines (BTS 2011, [CCHMC 5a]); (IDSA 2011, [CCHMC 5a])

Inpatients:

- It is recommended that ampicillin or penicillin G be administered to the fully immunized infant or school-aged child admitted to a hospital with CAP when local epidemiologic data document lack of substantial high-level penicillin resistance for invasive *S. pneumoniae* (IDSA 2011, [CCHMC 5a] [IDSA strong/moderate]). See Table 2 Inpatient Anti-infective Treatment Recommended by Age and Indication for Treatment.

Table 2: Inpatient Anti-infective Treatment Recommended by Age and Indication for Treatment

Indication for Treatment	Infant / Preschool-Aged Children	School-Aged Children and Adolescents
First-line	Amoxicillin/ampicillin (intravenous)	Amoxicillin/ampicillin (intravenous)
First-line for non-immunized and those with life threatening infections	3 rd generation cephalosporin	3 rd generation cephalosporin
Atypical bacterial infection	Azithromycin <i>In addition</i> to beta-lactam therapy if atypical bacteria are significant considerations. <i>Instead of</i> beta-lactam if findings are characteristic of atypical infection	Azithromycin <i>In addition</i> to beta-lactam therapy if atypical bacteria are significant considerations. <i>Instead of</i> beta-lactam if findings are characteristic of atypical infection
<i>Staphylococcus aureus</i> (S. aureus)	Vancomycin or clindamycin <i>In addition</i> to beta-lactam therapy if clinical, laboratory, or imaging characteristics are consistent with infection caused by <i>S. aureus</i>	Vancomycin or clindamycin <i>In addition</i> to beta-lactam therapy if clinical, laboratory, or imaging characteristics are consistent with infection caused by <i>S. aureus</i>
Alternative if allergy to first -line	3 rd generation cephalosporin, clindamycin	3 rd generation cephalosporin, clindamycin
Alternative if allergy to alternative	Levofloxacin	Levofloxacin

(Adapted from BTS and IDSA guidelines (BTS 2011, [CCHMC 5a]); (IDSA 2011, [CCHMC 5a]).

Implementation

Relevant CCHMC Evidence-Based Implementation Tools:

Community-Acquired Pneumonia, Health Topic for Parents <http://www.cincinnatichildrens.org/health/p/pneumonia/>

Applicability

It is challenging to share, implement, and monitor new evidence across a community setting with many individual practices and no common electronic patient health record.

Outcome or Process Measures

At Cincinnati Children's Hospital Medical Center the goal is that 90% of eligible children that present to the Emergency Department or are admitted with simple CAP will be prescribed the recommended antibiotic.

Supporting Information

Background/Purpose of Development

The purpose of this GREAT is to share and implement the most current evidence regarding appropriate antibiotic choice for children presenting with CAP.

Many pathogens are responsible for CAP in children, most prominently viruses and bacteria. Viral etiologies of CAP have been documented in up to 80% of children younger than 2 years of age (*IDSA 2011, [CCHMC 5a]*).

Before the widespread use of pneumococcal vaccines, reports of epidemiologic investigations on the etiology of CAP cited *S. pneumoniae* as the most commonly documented bacterial pathogen, occurring in 4% to 44% of all children investigated. Pathogens responsible for "atypical pneumonia" have been identified in 3% to 23% of children studied, with *M. pneumoniae* most often identified in older children and *C. pneumoniae* in infants (*IDSA 2011, [CCHMC 5a]*).

Resistance to anti-infectives among bacterial pathogens is increasing and is of concern; an important factor in this increase is the overuse of these agents. The management of pneumococcal infections has been challenged by the development of resistance. In children with pneumonia, the nature of the infecting organism is almost never known at the initiation of treatment and the choice of antibiotic is therefore determined by the reported prevalence of different pathogens in children by age group, knowledge of resistance patterns of expected pathogens circulating within the community, and the immunization status of the child (*BTS 2011, [CCHMC 5a]*).

Limiting exposure to any anti-infective, whenever possible, is preferred. Limiting the spectrum of activity of anti-infectives to that specifically required to treat the identified pathogen is preferred. Using the proper dosage of anti-infective to be able to achieve a minimal effective concentration at the site of infection is important to decrease the development of resistance (*IDSA 2011, [CCHMC 5a]*).

Issues to consider when reviewing the evidence:

1. Recommendations came from two quality national guidelines, British Thoracic Society (BTS), and Infectious Diseases Society of America (IDSA) (*BTS 2011, [CCHMC 5a]*); (*IDSA 2011, [CCHMC 5a]*).
2. Appraisal of Guidelines for Research and Evaluation II (AGREE II) was performed on each of these guidelines by three independent reviewers (*AGREE 2009, [CCHMC 5a]*). Appraisal summaries are included below.
3. For detail of the complete care management of children with CAP these guidelines may be accessed via the links below.

AGREE II Appraisal Results

IDSA GUIDELINE

1.SCOPE AND PURPOSE	93%
2.STAKEHOLDER INVOLVEMENT	63%
3.RIGOR OF DEVELOPMENT	67%
4.CLARITY AND PRESENTATION	93%
5.APPLICABILITY	47%
6.EDITORIAL INDEPENDENCE	78%

BTS GUIDELINE

1.SCOPE AND PURPOSE	93%
2.STAKEHOLDER INVOLVEMENT	56%
3.RIGOR OF DEVELOPMENT	74%
4.CLARITY AND PRESENTATION	89%
5.APPLICABILITY	42%
6.EDITORIAL INDEPENDENCE	83%

AGREE II Purpose Overview

The Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument was developed to address the issue of variability in guideline quality. To that end, the AGREE instrument is a tool that assesses the methodological rigour and transparency in which a guideline is developed.

IDSA: <http://cid.oxfordjournals.org/content/early/2011/08/30/cid.cir531.full.pdf+html>

BTS: <http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Pneumonia/Guidelines/CAP%20children%20October%202011.pdf>

Search Strategy

Search from 2006 to current, performed in November, 2011:

1. National Guideline Clearinghouse: (www.ngc.gov)

The initial electronic search for guidelines resulted in two nationally available guidelines for the treatment of adult patients presenting with CAP, which were eliminated as not related to the population of interest. One pediatric guideline was found that was due for revision so was not included in these recommendations.

2. Ovid/Medline Search:

1. community-acquired Infections/ or exp pneumonia/ or community-acquired pneumonia.mp.	70873
2. limit 1 to (english language and humans and yr="2006 -Current")	11343
3. limit 2 to "all child (0 to 18 years)"	3156
4. limit 3 to guideline	2

Two pediatric guidelines for the management of CAP were published in the fall of 2011.

Reference List (Evidence Level in []; See Table of Evidence Levels following references)

1. **AGREE_NextStepsConsortium:** The AGREE II Instrument [Electronic version]. Retrieved November 10, 2010, from <http://www.agreetrust.org>, 2009 / CCHMC, [5a]E.
2. **BTS, B. T. S. S. o. C. C., Harris, Michael, Clark, Julia, Coote, Nicky, Fletcher, Penny, Harnden, Anthony, McKean, Michael, Thomson, Anne,:** British Thoracic Society guidelines for the management of community acquired pneumonia in children: update 2011. *Thorax*, 66 Suppl 2: ii1-23, 2011 / CCHMC, [5a]____ E.
3. **IDSA, I. D. S. o. A. B., JS; Byington, CL; Shah, SS; Alverson, B; Carter, ER; Harrison, C; Kaplan, SL; Mace, SE; McCracken Jr, GH; Moore, MR; St Peter, SD; Stockwell, JA; and Swanson, JT,:** The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 53(7), 2011 / CCHMC, [5a]E.

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Conflicts of Interest were declared for each team member:

- No financial conflicts of interest were found.
 No external funding was received for development of this recommendation.

Table of Language and Definitions for Recommendation Strength (see note above):

Language for Strength	Definition
It is strongly recommended that... It is strongly recommended that... not...	When the dimensions for judging the strength of the evidence are applied, there is high support that benefits clearly outweigh risks and burdens. <i>(or visa-versa for negative recommendations)</i>
It is recommended that... It is recommended that... not...	When the dimensions for judging the strength of the evidence are applied, there is moderate support that benefits are closely balanced with risks and burdens.
There is insufficient evidence and a lack of consensus to make a recommendation...	
<i>Given the dimensions below and that more answers to the left of the scales indicate support for a stronger recommendation, the recommendation statement above reflects the strength of the recommendation as judged by the development group. (Note that for negative recommendations, the left/right logic may be reversed for one or more dimensions.)</i>	
1. Grade of the Body of Evidence	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low
<i>Comments: Based on the body of evidence for these recommendations within two quality national guidelines</i>	
2. Safety / Harm (Side Effects and Risks)	<input type="checkbox"/> Minimal <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Serious
<i>Comments: Misuse of anti-infective may lead to extension of illness or antibiotic resistance</i>	
3. Health benefit to patient	<input type="checkbox"/> Significant <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Minimal
<i>Comments:</i>	
4. Burden on patient to adhere to recommendation	<input type="checkbox"/> Low <input checked="" type="checkbox"/> Unable to determine <input type="checkbox"/> High
<i>Comments:</i>	
5. Cost-effectiveness to healthcare system	<input checked="" type="checkbox"/> Cost-effective <input type="checkbox"/> Inconclusive <input type="checkbox"/> Not cost-effective
<i>Comments: Potential for decrease in misuse of anti-infectives</i>	
6. Directness of the evidence for this target population	<input checked="" type="checkbox"/> Directly relates <input type="checkbox"/> Some concern of directness <input type="checkbox"/> Indirectly relates
<i>Comments:</i>	
7. Impact on morbidity/mortality or quality of life	<input type="checkbox"/> High <input checked="" type="checkbox"/> Medium <input type="checkbox"/> Low
<i>Comments: Appropriate timeframe for illness resolution has more potential if appropriate anti-infective agent is selected</i>	

Note: Full tables of evidence grading system available in separate document:

- [Table of Evidence Levels of Individual Studies by Domain, Study Design, & Quality](#) (abbreviated table below)
- [Grading a Body of Evidence to Answer a Clinical Question](#)
- [Judging the Strength of a Recommendation](#) (dimensions table above, other abbreviated tables below)

CCHMC Table of Evidence Levels (see note above)

Quality level	Definition
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5a or 5b	General review, expert opinion, case report, consensus report, or guideline
5	Local Consensus

†a = good quality study; b = lesser quality study

BTS Table: Brief Description of Generic Levels of Evidence and Guideline Statement Grades

Evidence level	Definition	Guideline statement grade
Ia	A good recent systematic review of studies designed to answer the question of interest	A+
Ib	One or more rigorous studies designed to answer the question, but not formally combined	A-
II	One or more prospective clinical studies which illuminate, but do not rigorously answer, the question	B+
III	One or more retrospective clinical studies which illuminate, but do not rigorously answer, the question	B-
IVa	Formal combination of expert views	C
IVb	Other information	D

(BTS 2011, [CCHMC 5a])

IDSA Table: Strength of Recommendation and Quality of Evidence

Strength of recommendation and quality of evidence	Clarity of balance between desirable and undesirable effects	Methodologic quality of supporting evidence (examples)	Implications
Strong recommendation			
High-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Consistent evidence from well-performed RCTs ^a or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances; further research is unlikely to change our confidence in the estimate of effect.
Moderate-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances; further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for ≥1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence	Recommendation may change when higher quality evidence becomes available; further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low-quality evidence (rarely applicable)	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for ≥1 critical outcome from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher quality evidence becomes available; any estimate of effect for ≥1 critical outcome is very uncertain.
Weak recommendation			
High-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patients or societal values; further research is unlikely to change our confidence in the estimate of effect.
Moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Alternative approaches are likely to be better for some patients under some circumstances; further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low-quality evidence	Uncertainty in the estimates of desirable effects, harms, and burden; desirable effects, harms, and burden may be closely balanced	Evidence for ≥1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low-quality evidence	Major uncertainty in estimates of desirable effects, harms, and burden; desirable effects may or may not be balanced with undesirable effects may be closely balanced	Evidence for ≥1 critical outcome from unsystematic clinical observations or 2very indirect evidence	Other alternatives may be equally reasonable; any estimate of effect, for at ≥1 critical outcome, is very uncertain.

^a RCTs, randomized controlled trials.

(IDSA 2011, [CCHMC 5a])

Copies of this Evidence Recommendation Excerpts document and related tools (if applicable, e.g., screening tools, algorithms, etc.) are available by request at ebdminfo@cchmc.org and may be distributed by any organization for the global purpose of improving child health outcomes.

Please cite as: Cincinnati Children's Hospital Medical Center: Evidence Recommendation Excerpts Community-acquired pneumonia, anti-infective selection from BTS and IDSA guidelines, GREAT 001, pages 1-6, June 1,-2012.

This Evidence Recommendation Excerpts document has been reviewed against quality criteria by 2 independent reviewers from the CCHMC Evidence Collaboration.

For more information about CCHMC Evidence Recommendation Excerpts contact the Evidence Collaboration at EBDMinfo@cchmc.org.

Note

This Evidence Recommendation Excerpts document addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of published guideline current at the time of the guideline search. This Evidence Excerpt does not preclude using care modalities proven efficacious in studies published subsequent to the dissemination of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.