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Antimicrobial Therapy in Community-Acquired Pneumonia in Children

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Abstract

Purpose of Review Empirical antibiotic therapy remains the cornerstone of treatment in community-acquired pneumonia (CAP). However, the best option for empirical antibiotics for treatment on an ambulatory basis, as well as in those requiring hospitalization, is still unclear. This review tries to answer the question regarding the most appropriate antibiotics in different settings in children with CAP as well as duration of therapy.

Recent Findings Recent studies have provided insights regarding use of oral antibiotics in children with mild to moderate CAP, and severe CAP with lower chest retractions but no hypoxia. In view of rapidly emerging resistance among various causative pathogens, several new drugs have been currently approved, or are under trial for CAP in children.

Summary Current knowledge suggests that the choice of antibiotics for ambulatory treatment of CAP is oral amoxicillin with a duration of 3–5 days. Children with CAP with lower chest retractions but no hypoxia can be treated with oral amoxicillin. Severe pneumonia can be treated with intravenous antibiotics consisting of penicillin/ampicillin with or without an aminoglycoside. Several new drugs have been developed and approved for use in CAP caused by multidrug-resistant organisms, but these should be used judiciously to avoid emergence of further resistance. Future research is needed regarding the safety and efficacy of newer drugs in children.

Keywords Acute lower respiratory tract infection · Children · Community-acquired pneumonia · Pneumococcal

Introduction

Pneumonia is the most important cause of under-five mortality worldwide with a much higher burden in developing countries. The global estimated annual incidence of community-acquired pneumonia (CAP) is 120–256 million cases with 1.4 million dying every year [1–3]. Of this, the contribution from children under 5 years is 1 million every year accounting for 16% of all deaths with 90–95% of deaths occurring in developing countries [4, 5]. India is among the leading countries with the highest number of deaths in children under 5 years of age. In 2015, of the 5.9 million deaths globally in the under 5 age group, 1.2 million deaths occurred in India alone [6]. Despite the advances in diagnostic tests and improvement in immunization coverage and treatment of CAP in children, the mortality remains high, particularly in developing countries. The antibiotic therapy remains the cornerstone of treatment in CAP along with other supportive care. However, despite various formulations of national and international guidelines for antibiotic therapy in CAP, the optimal choice and duration of antibiotics in CAP is still in debate. We performed this narrative review to describe the current literature available regarding the antibiotic therapy in CAP in children and tried to formulate an opinion regarding the optimum choice and duration of antibiotics for the same.

Methods

The objective of this review was to identify the literature regarding antibiotic therapy for community-acquired pneumonia in children. We reviewed various guidelines on CAP and searched PubMed/ Medline and Google Scholar for relevant articles from 1988 to March 2018 by using the following keywords: "antibiotics," "antimicrobials," "antibiotic therapy," "drugs," "drug options," "community-acquired pneumonia," "CAP," "children," "pediatric" as well as combinations

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of these. We also searched the articles from the last 5 years for identifying advances and newer options in antibiotic therapy for CAP in children. As this was not a systematic review, we identified relevant articles for inclusion in this review.

Results and Discussion

Challenges to the Treatment of CAP in Children

The biggest challenge to determining the best treatment for CAP in children is that there has been no validated definition of pneumonia in children. The World Health Organization (WHO) definition of pneumonia has a good sensitivity but poor specificity for the diagnosis of pneumonia and is predominantly for the use in countries with high infant mortality due to pneumonia [7–9]. It is largely defined as the presence of signs and symptoms of respiratory distress along with evidence of involvement of lung parenchyma, either clinically or radiologically [10]. The etiology of pneumonia in children are viruses, bacteria, and atypical pathogens, like *Mycoplasma pneumoniae*. The frequency for each etiology varies with age (Table 1) [11]. It is very difficult to differentiate viral or bacterial pneumonia clinically, particularly in cases of severe pneumonia. Difficulty in collecting satisfactory pulmonary samples for microbiological diagnosis, and a lack of rapid diagnostic tests that help to differentiate between viral and bacteriological etiology, makes the identification of a causative agent difficult. Hence, the treatment of CAP is largely empirical. There are several debates of antimicrobial therapy in CAP in children-outpatient versus hospital treatment; oral vs intravenous routine severe pneumonia; short course versus long duration; choice of initial empirical antibiotics; and need for combination therapy. Currently, the inadvertent use of antimicrobials in CAP has resulted in antibiotic resistance, and hence provides a great challenge for the treatment of severe pneumonia requiring hospitalization and hospital-acquired pneumonia. There is little progress in terms of newer antibiotics available for the treatment of CAP in children. The following sections will describe the current evidence available addressing these debates and challenges.

Antibiotic Therapy in CAP

Based upon the severity of pneumonia, children can be grouped into three categories—outpatients, those requiring hospital admission, and those requiring intensive care [12]. Criteria for hospitalization are given in Table 2 [12]. WHO classifies the severity of CAP into only two categories based upon the need for ambulatory treatment or hospital admission [7].

Outpatient Treatment

Choice of Antibiotics The antibiotic therapy is an important measure of outcome in CAP besides host factors and virulence of organism. As the etiological diagnosis of CAP is difficult, the treatment is largely empirical. The appropriate choice of initial empirical antibiotics has great impact on outcome. Children with mild to moderate CAP or non-severe pneumonia per WHO definition can be treated on outpatient basis. As viruses are the major pathogens for CAP in preschool children, antibiotics are not required most of the times [7, 12]. Oral co-trimoxazole (trimethoprim plus sulfamethoxazole) and amoxicillin are the most extensively studied antibiotics

Table 1 Etiology of community-acquired pneumonia in children by age group

	Common	Less common	Rare
1–3 months	Streptococcus pneumoniae Chlamydia pneumoniae Respiratory viruses Enterovirus	Group A Streptococcus Group B Streptococcus Haemophilus influenzae	Varicella zoster virus
4 months–< 5 years	Streptococcus pneumoniae Respiratory viruses	Mycoplasma pneumoniae Group A Streptococcus Haemophilus influenzae Staphylococcus aureus	Moraxella
≥ 5 years	Streptococcus pneumoniae Mycoplasma pneumoniae Respiratory viruses	Staphylococcus aureus Chlamydia pneumoniae	Group A Streptococcus
Immunocompromised (all ages)	As with age group plus Fungi, Burkholderia, Pseudomonas		

Table 2 Criteria for hospitalization in children with CAP

Criteria for hospitalization
Children and infants who have moderate to severe CAPas defined by: • Tachypnea, respiratory rate, breaths/min: ○ Age 0–2 months: > 60 ○ Age 2–12 months: > 50 ○ Age 1–5 years: > 40 ○ Age > 5 years: > 20 • Dyspnea • Retractions (suprasternal, intercostals, or subcostal) • Grunting • Nasal flaring • Apnea • Altered mental status • Pulse oximetry measurement, <90% on room air
Infants less than 3–6 months of age with suspected bacterial CAP
Children and infants with suspected or documented CAP caused by a pathogen with increased virulence, such as community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA)
Children and infants for whom there is concern about careful observation at home or who are unable to comply with therapy or unable to be followed up

for outpatient treatment for CAP in children. In the past, several studies have demonstrated that co-trimoxazole is less efficacious and has high treatment failure rates compared to oral amoxicillin [13–15]. Currently, oral amoxicillin is the treatment of choice for non-severe pneumonia and is also endorsed by WHO [7]. Recently, the review by Cochrane collaboration has reported the similar failure rates (odds ratio (OR) 1.18, 95% confidence interval (CI) 0.91 to 1.51) and cure rates (OR 1.03, 95 CI 0.56 to 1.89) with the use of both these antibiotics indicating that amoxicillin can be considered as alternative to co-trimoxazole [16]. The Infectious Disease Society of America (IDSA) also recommends amoxicillin as the first-line drug in adolescents and school-aged children who are previously healthy and immunized for age [12]. Other antibiotics studied are amoxicillin-clavulanic acid, procaine penicillin, and cephalosporins (cefpodoxime). While procaine penicillin has not been shown to be better than co-trimoxazole or amoxicillin [17–19], Jibril et al. reported better cure rates with amoxicillin-clavulanic acid compared to amoxicillin alone (OR 10.44, 95% CI 2.85 to 38.21) [20]. A multicentric study comparing cefpodoxime and amoxicillin-clavulanic acid for non-severe pneumonia showed similar cure rates at 10 days of treatment in both groups (OR 0.69, 95% CI 0.18 to 2.60) [21]. Hence, amoxicillin-clavulanic acid and cefpodoxime may be considered second-line oral drugs for ambulatory treatment of pneumonia.

The Cochrane collaboration in 2015 reviewed the role of macrolides in CAP due to mycoplasma in children and observed that response rates were similar between groups treated with or without a macrolide in most studies. However, in one study, the resolution of clinical illness was 100% in the azithromycin group, while it was 77% in the non-azithromycin group in CAP due to Mycoplasma, Chlamydia, or both [22]. The IDSA guidelines also recommend macrolide antibiotics in children strongly suspected to have CAP due to an atypical pathogen in outpatient settings [12].

Dose of Antibiotics Various studies have been conducted to determine the ideal dose of an antibiotic for non-severe pneumonia. A double dose of co-trimoxazole in comparison with the standard dose showed no significant difference in clinical cure rates in a study by Rasmussen et al. [23]. The dose of amoxicillin most commonly prescribed routinely and in various studies is 40–50 mg/kg/day in three divided doses [19, 24, 25]. A systematic review from India revealed that pneumococcal resistance to penicillin is in the range of 3–20% with the majority having intermediate resistance to penicillin. This indicates that the continuation of the usual doses of amoxicillin in areas with intermediate resistance to penicillin still have high levels of resistance detected [26•]. However, in western countries due to the high prevalence of penicillin non-susceptible *S. pneumoniae*, higher doses up to 90 mg/kg/day are recommended [27, 28].

In view of the wide variation of penicillin-resistant pneumococcal diseases across the world, a higher dose (90 mg/kg/day) of amoxicillin may be considered for suspected pneumococcal CAP while countries with a low or intermediate prevalence of penicillin resistance of pneumococcal CAP may continue to use 40–50 mg/kg/day.

Duration of Antibiotic Therapy The duration of treatment has also been reduced from previous 5–7 days to 3–5 days. The 3-day treatment with oral amoxicillin has been shown to be equally effective as 5-day therapy in developing countries in which pneumonia was defined using the WHO definition [15, 24]. While a recent study by Greenberg et al. showed that a 5-day course was non-inferior compared to a 10-day course of oral amoxicillin, a 3-day course was associated with high failure rates in a developed country particularly in radiologically confirmed pneumonia [27]. These observations suggest that radiologically confirmed pneumonia should be treated with 5 days of antibiotics.

A prospective double-blind study on children below 5 years of age with non-severe pneumonia in Pakistan compared a 3-day normal dose amoxicillin regimen with a placebo and reported no difference in failure rate at 72 h (7.2 vs 8.3%, p = 0.60) [28]. Similarly, a prospective double-blind study carried out in India on children under 5 years of age with non-severe pneumonia compared a 3-day regimen of low to normal dose oral amoxicillin versus placebo, and observed no significant difference in clinical failure (defined as severe or very severe pneumonia, oxygen saturation < 90% before or on day 4, fever, or persistence of non-severe pneumonia on day 4). It also observed a clinical failure rate of 19.9% in the amoxicillin

group and 24% in the placebo group ($p = 0.34$, number needed to treat in order to avoid one clinical failure= 24) [29]. These studies highlight the role of viruses as causative agents in non-severe pneumonia. From these observations, it may be inferred that the majority of non-severe pneumonia diagnosed in children may be due to a viral infection, and that a 3-day course of antibiotics may be sufficient for WHO-defined non-severe pneumonia.

Inpatient Treatment

Choice of Empirical Antibiotics In developing countries, where immunization against pneumococcus is rarely performed, injectable penicillin/ampicillin plus gentamicin is the first choice of antibiotics in hospitalized children with severe CAP [30]. Chloramphenicol has been shown to be inferior to this combination therapy in various studies [30, 31]. Williams et al. compared narrow-spectrum antibiotic therapy (penicillin/ampicillin) with broad-spectrum antibiotic therapy (cefotaxime/ceftriaxone) in hospitalized children with uncomplicated CAP during the first 2 days and found narrow-spectrum antibiotics to be as effective as broad-spectrum antibiotics in terms of length of stay (LOS), duration of intravenous therapy, readmission rates, or overall costs [32]. However, in areas with presence of high levels of penicillin resistance, or for infants and children with life-threatening infection, including those with empyema, empiric therapy with a broad-spectrum antibiotic like a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) should be prescribed [12]. WHO has recommended co-amoxiclav or ceftriaxone as second-line treatment in cases of less satisfactory improvement after 48 h of ampicillin/gentamicin therapy [7]. Also, Breuer et al. found a shorter hospital stay, duration of fever, and duration of IV treatment with broad-spectrum antibiotics in children who received oral therapy for CAP prior to hospitalization [33]. While IDSA recommends empiric macrolide therapy (oral or parenteral), in addition to an optional β-lactam antibiotic in hospitalized children with CAP, a multicenter prospective study by Williams et al. in 1418 children hospitalized with radiologically confirmed pneumonia, comparing β-lactam monotherapy and β-lactam plus macrolide combination therapy showed no difference in length of hospital stay, ICU admission, re-hospitalizations, and self-reported recovery at follow-up [34•]. This implies a major role of viruses and typical bacteria as an etiology for CAP rather than atypical micro-organisms.

If a possibility of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) CAP is considered on basis of fast deterioration, associated skin or soft tissue abscesses, complication after measles, or pneumatoceles or pneumothorax on chest radiograph, clindamycin is recommended [35].

Oral Antibiotics for Severe Pneumonia Children with pneumonia and lower chest indrawing, classified as severe pneumonia, forms a large group. These children were treated with oral amoxicillin or intravenous ampicillin or aqueous penicillin G with similar outcome in terms of cure rates, failure rates, need for hospitalization, and relapse rates [19, 27]. However, the results were better than co-trimoxazole. A recent systematic review demonstrated similar failure rates in children receiving oral antibiotics and those receiving parenteral antibiotics [13% (288/2208) versus 13.8% (302/2183), (OR 0.93; 95% CI 0.78, 1.11)] [36••]. Therefore, it is recommended that children with pneumonia with chest indrawing but no hypoxia may be treated on an ambulatory basis with oral amoxicillin. It is specifically favorable in developing countries where it may be cost effective and resource friendly.

Duration of Antibiotic Therapy The optimal duration of antibiotic therapy for CAP requiring hospitalization is still under debate. Based upon the two randomized controlled trials, the empirical treatment of CAP during hospitalization for duration of 5 and 7 days had similar efficacy. Another randomized controlled trial in 312 children with intervention group of discontinuation of antibiotics at day 5 and control group of discontinuation at the discretion of physician showed the similar clinical success at days 10 and 30 since admission with significant reduction to antibiotic exposure in intervention group. Hence, the current recommendations are to treat for 5 days in the absence of documented cause according to various international guidelines. WHO recommends 5 days of antibiotic treatment in severe and very severe pneumonia [7]. In western settings, longer duration (up to 10 days) has been recommended [12].

Antibiotic Resistance and Therapeutic Options

In the last few decades, inadvertent and irrational use of antibiotics has increased the problem of antimicrobial resistance globally. This is also true for CAP in children where there is growing evidence of pneumonia caused by multidrug-resistant (MDR) bacteria.

S. pneumoniae is virtually penicillin-susceptible. However, there is increasing evidence of growing numbers of penicillin-resistant strains of pneumococcus. Penicillin-resistant *S. pneumoniae* (PRSP) constituted 14.8% of the *S. pneumoniae* isolates in global surveillance by TEST trial from 2004 to 2011 with a major contribution from the Asian/Pacific region (30%) followed by Africa (28%) and in the Middle East (25%) [37]. Based upon MIC levels, susceptibility of *S. pneumoniae* to β-lactams is quantified as ≤ 0.5 mg/L and resistance as > 2 mg/L as defined by the European Committee on Antibiotic Susceptibility Testing (EUCAST)

[38]. Modification of the pneumococcal cell wall penicillin-binding proteins is the major mechanism causing their decreased but not absent affinity to penicillin and other β-lactams. Therefore, higher dosages of β-lactam antibiotics leading to higher concentrations and good tissue distribution, as in the lung, may overcome resistance. In countries where penicillin non-susceptible pneumococcus exceeds 25%, high-dose penicillin or high-dose amoxicillin should be considered as empirical treatment of pneumococcal CAP [39, 40]. Third-generation cephalosporins like ceftriaxone are a better alternative for penicillin non-susceptible *S. pneumoniae* CAP based upon their pharmacokinetic/pharmacodynamic parameters [41]. Pneumococcal resistance to macrolides has been reported in various studies, and as the mutations causing resistance affect macrolide binding to ribosomes, it cannot be overcome by increasing the dose of macrolides [42]. Hence, empirical monotherapy with macrolides should be avoided in CAP in children. Various options to treat penicillin non-susceptible pneumococcal CAP are high-dose ampicillin, piperacillin, ceftriaxone, cefotaxime, respiratory fluoroquinolones (levofloxacin and moxifloxacin), ertapenem, meropenem, imipenem, and clindamycin [43, 44].

MRSA is an important cause of CAP in children because of increased severity of infection and higher mortality rate. Though MRSA is mostly seen in association with healthcare-associated infections, CA-MRSA CAP is unique as it is associated with higher morbidity and mortality despite its occurrence in immunocompetent children. The pathogenicity is attributed to the production of exotoxins [45]. Hence, the antibiotics acting via inhibition of ribosomal synthesis can help block toxin production by MRSA independent of their bactericidal/bacteriostatic properties. Linezolid has been shown as superior to vancomycin in a randomized trial of 200 adult patients in terms of efficacy (clinical response in terms of cure rate of 57.6 vs 46.6% respectively at the end of the study), and adverse effects but had no difference in terms of 60 days mortality [46]. So, linezolid may be considered as the first choice in CA-MRSA CAP due to lesser side effects than vancomycin (renal toxicity in particular), higher clinical effectiveness, and availability of an oral preparation. A combination of vancomycin and clindamycin may have equivalent activity to linezolid for CA-MRSA CAP [47]. Other drugs for MRSA are teicoplanin, daptomycin, clindamycin, and trimethoprim/sulfamethoxazole. However, there are several concerns regarding their use in CA-MRSA CAP. Daptomycin is inappropriate for the treatment of pneumonia as it does not achieve good concentration in the lung due to inactivation by surfactant [48]. Clindamycin and trimethoprim/sulfamethoxazole, though useful for treatment of CA-MRSA skin infections, has substantial concern due to rapid development of resistance as monotherapy in CAP. Therefore, these antibiotics should not be considered as usual treatment options for CA-MRSA CAP.

Macrolide resistance in *M. pneumoniae* in children has been increasing rapidly. In most cases, infections are mild to moderate, and signs and symptoms tend to resolve spontaneously without specific therapy. A few cases have increased severity of infection, which may also be attributed to macrolide resistance. However, the recent Japanese Guidelines for the Management of Respiratory Infectious Diseases recommend treatment with macrolides alone despite the presence of macrolide resistance up to 80% [49]. Other alternative drugs are tetracyclines and fluoroquinolones, which may be considered in severe cases of CAP due to *M. pneumoniae* with macrolide resistance. But concerns are regarding their safety in the pediatric population [50–52].

Newer Antibiotics for Community-Acquired Pneumonia

Due to increasing drug resistance, there is urgent need of newer drugs with activity against resistant organisms. There is great hindrance to the development of novel agents due to difficulties in discovering new classes of agents. In spite of these hurdles, there are advances in the last few years regarding novel agents for CAP, and various drugs are in phase 1 and phase 2 trials.

A newly developed fifth-generation cephalosporin, ceftaroline fosamil, has been approved for use in adults with CAP due to drug-resistant organisms based upon FOCUS trials. It is a bactericidal drug effective against a broad spectrum of microbial agents including resistant gram-positive pathogens involved in CAP, such as MRSA and MDR *S. pneumoniae*. Its increased affinity to MRSA penicillin-binding protein 2A results in greater ant-MRSA activity. It is well tolerated, with similar adverse events to other cephalosporins [53].

Tigecycline is the first broad-spectrum, iv, glycylcycline antibiotic for the treatment of CAP approved by FDA in 2010. It is a synthetic analogue of the tetracyclines, designed to overcome resistance mechanisms of ribosomal protection, and active efflux [54]. Two non-inferiority, randomized, double-blind, multinational, phase III studies compared the safety and efficacy of tigecycline in comparison with levofloxacin in the treatment of CAP and showed better cure rates with tigecycline. However, it was associated with more adverse effects of nausea and vomiting [55, 56]. Also, a few meta-analyses have shown increased mortality risk associated with tigecycline [57, 58]. A recent pooled analysis of these two studies showed similar efficacy of tigecycline with levofloxacin except for patients with risk factors like diabetes where tigecycline performed better than levofloxacin [59].

Telavancin is a new glycopeptide approved for hospital-acquired pneumonia. The mechanism of action is by inhibition of bacterial cell wall synthesis as well as disruption of cell

membrane barrier function by binding to specific target lipid II in the bacterial cell membrane. It demonstrates bactericidal activity against gram-positive pathogens including MRSA, and its long half-life allows it to be administered once daily [60, 61].Two non-inferiority randomized controlled trials comparing telavancin and vancomycin in adults for skin and soft tissue infections and nosocomial pneumonia showed equal efficacy in cure rates and eradication rates. However, its safety and effectiveness have not been established in children.

The ketolides represent a subclass of macrolide antibiotics designed to be effective against macrolide-resistant respiratory pathogens. Their mechanism of action is very similar to erythromycin A, i.e., inhibition of protein synthesis by interaction with the peptidyl transferase site of the bacterial 50S ribosomal subunit. The high affinity binding to ribosomes of ketolides make them more effective than macrolides. Cethromycin has in vitro activity against penicillin and macrolide-resistant organisms. In two non-inferiority trials, cethromycin has been shown to be non-inferior to clarithromycin with similar efficacy and safety [54]. Another ketolide, solithromycin, was compared with moxifloxacin in 860 adults with CAP, and was found to be non-inferior to oral moxifloxacin [55]. However, its clinical efficacy and safety is still to be determined in children.

Besides, various other drugs for CAP are under development. Omadacycline, an aminomethylcycline (tetracycline analogue), is active against MDR *S. pneumoniae* and MRSA, as well as some gram-negative pathogens. It is more effective than tetracyclines as it is able to overcome two most common mechanisms of resistance, i.e., the tetracycline efflux and ribosome protection. Currently, the drug is in phase 3 trials [56]. It is also available in oral formulation to be administered once a day. The most common adverse effects in clinical trials are nausea, transient rise in heart rate, and reversible elevation of liver enzymes.

Another antimicrobial drug that is effective against common etiological agents for CAP along with MRSA is lefamulin. This molecule belongs to a new class of antibiotics known as the pleuromutilins. Its mechanism of action involves inhibition of protein synthesis by binding to A and P sites of 50S bacterial ribosome and interfering with peptidyl transferase center, thus preventing the first peptide bond formation and further peptide chain elongation. This is also considered to be effective against vancomycin-resistant MRSA and is under evaluation [57]. The drug underwent phase 2 clinical trials for skin and soft tissue infections and phase 3 trials for CAP and showed promising results in both conditions in adults when compared to vancomycin. These trials also showed that the drug is well tolerated with minimal side effects. The FDA approval is still awaited for this drug. There are however no trials in pediatric population.

Novel quinolones such as nemonoxacin [58] and zabofloxacin [62•] have been studied in adults for safety and efficacy in adults with CAP. These are non-fluorinated quinolones that selectively inhibit the bacterial DNA topoisomerase activity. These were found to be non-inferior to levofloxacin in terms of efficacy and safety in phase 2 trials in CAP in Taiwan. These are still to be approved by US FDA here.

A new antimicrobial agent tedizolid, an oxazolidinone, has been found to be effective against linezolid-resistant MRSA. Tedizolid phosphate is a prodrug that is converted by plasma phosphatases to microbiologically active tedizolid in vivo. Tedizolid inhibits bacterial translation and protein synthesis. Additionally, it does not interact with serotonergic agents and appears to have no serotonin syndrome [63]. It has been approved by FDA in 2014. Additionally, multiple new therapies for antibiotic-resistant gram-negative bacilli, including extended spectrum β-lactam-resistant Enterobacteriacae and *Acinetobacterbaumanii*, are under active investigation [64].

A few new classes of antimicrobials for CAP are currently under phase 1 and 2 trials and may be approved in the near future [62•].

Conclusion

Empirical antibiotic therapy is one of the most important parts of treatment of CAP in children and adults. Most of the cases can be treated on outpatient basis for which oral amoxicillin is the drug of choice with 3 days duration equally effective to 5 days therapy. Few children require hospitalization and the initial choice of empirical antibiotic therapy is intravenous ampicillin/gentamicin combination. Third-generation cephalosporins are a reasonable choice in non-responding cases. Clindamycin can be added in case of a high suspicion of MRSA CAP. A macrolide alone, or in combination with third-generation cephalosporin, may be considered only if there is high suspicion of pneumonia by atypical pathogens. There is increasing recognition of antibiotic resistance among various pathogens in CAP. Many new drugs have been developed against drug-resistant pathogens and a few drugs are under development. Rational use of antibiotics with choosing narrow-spectrum drugs and the shortest possible duration may help in reducing the drug resistance.

Compliance with Ethical Standards

Conflict of Interest Samriti Gupta, Rakesh Lodha, and S.K. Kabra declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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