

ority margin of 10% (Yoon *et al.*, 2013). According to the Agency for Healthcare Research and Quality (2013), second-generation cephalosporins are considered an alternative treatment for mild exacerbations of COPD, with no risk factors for poor outcome.

Cefuroxime has been used in the treatment of acute otitis media and acute sinusitis (Ip *et al.*, 2005; Brook, 2007). In one study, oral cefuroxime 250 mg every 12 hours was more effective than oral penicillin in eradicating group A beta-hemolytic streptococcal (GABHS) tonsillitis–pharyngitis (Adam *et al.*, 2000). More recently, a meta-analysis involving 35 trials comparing cephalosporin with penicillin treatment of GABHS tonsillopharyngitis in children was carried out by Casey and Pichichero (2004); cefuroxime was statistically superior in clinical improvement and bacterial eradication of GABHS. As a group, the second-generation cephalosporins showed similarly higher bacterial cure rates. However, because of variable rates of resistance among *S. pneumoniae* and because of the introduction of the conjugated pneumococcal vaccines, both the prevalence of *H. influenzae* and proportion of beta-lactamase-producing *H. influenzae* extrapolated from middle ear fluid cultures of children with acute otitis medium have markedly increased (Casey *et al.*, 2010). IDSA guidelines no longer recommend second- and third-generation oral cephalosporins for empiric monotherapy of acute bacterial rhinosinusitis, and amoxicillin–clavulanate is considered the first-line therapy in both children and adults (Chow *et al.*, 2012).

## 7b. Uncomplicated urinary tract infection

Acute uncomplicated urinary tract infections (UTIs) in adults include episodes of acute cystitis and acute pyelonephritis in otherwise healthy individuals (without structural and functional abnormalities within the urinary tract, kidney diseases, or co-morbidity that could lead to more serious outcomes). The main Gram-negative bacteria involved are *E. coli*, *K. pneumoniae*, and *P. mirabilis*; *S. saprophyticus* is the most common Gram-positive isolate. The wide use of second-generation cephalosporins to treat UTIs has led to an increasing resistance, even though susceptibility rates vary among the countries. Data collected from the Antimicrobial Resistance Epidemiological Survey on Cystitis (ARESC) study have shown reduced cefuroxime susceptibility in almost 20% of all *E. coli*, 6.5% of *K. pneumoniae*, and 4.8% of *P. mirabilis* isolates, with susceptibility rates  $\leq 80.9\%$  in Italy and Spain (Schito *et al.*, 2009). This is in line with a 7-year surveillance study in Spain reporting resistance rates  $> 30\%$  in *E. coli* isolates (Sorlozano *et al.*, 2014). Data from a multicenter study in China have found in *E. coli* resistance rates to fluoroquinolones and to second- and third-generation cephalosporin ranging from 49.4% to 57.5% (Qiao *et al.*, 2013). Moreover UTI pathogens can carry ESBL genes that further decrease cefuroxime activity. Efficacy of fosfomycin and nitrofurantoin against *E. coli* ESBL and non-ESBL producers and *K. pneumoniae* has been demonstrated in previous studies, so they are currently among the first-line agents recommended

for empirical treatment of uncomplicated UTIs. Cefuroxime use should be limited to those situations with a demonstrated or highly probable susceptibility.

Oral cefuroxime has been regarded as less effective than trimethoprim sulfamethoxazole and fluoroquinolones for most organisms causing UTI. However, the drug does concentrate in the urine and is active against all but ESBL- or AmpC-producing *E. coli*. Cefuroxime can be used as an alternative agent, especially during pregnancy. In complicated UTI or pyelonephritis, it can be used as a switch to oral therapy after initial clinical improvement, based on organism susceptibility (Nicolle, 2002).

## 7c. Skin and skin structure infection

Generally, unlike cephalexin, which has good activity against *S. aureus*, cefuroxime has little role in the treatment of skin and soft-tissue infection (Stevens *et al.*, 2005). Oral penicillin for 10 days has been recommended as treatment of choice for perianal streptococcal dermatitis in children. In a small prospective unblinded study, treatment with cefuroxime achieved a more rapid clinical improvement compared with oral penicillin (Meury *et al.*, 2008). It is considered an alternative regimen for the treatment of infected animal bite wounds, although the addition of anaerobic coverage is required (Stevens *et al.*, 2014; Goldstein *et al.*, 1988).

## 7d. Intraabdominal infection

Cefuroxime, in combination with metronidazole, has been shown to have an equal success rate of mild to moderate community-acquired intraabdominal infection compared with piperacillin–tazobactam monotherapy (Ohlin *et al.*, 1999) or imipenem monotherapy (Angeras *et al.*, 1996). According to the Surgical Infection Society (SIS) and the IDSA guidelines, cefuroxime plus metronidazole is among the recommended regimens to treat mild to moderate community-acquired intraabdominal infection in adult patients (Solomkin *et al.*, 2010). However it should not be used to treat suspected infection with ESBL-producing organisms because of its poor efficacy against these strains.

## 7e. Meningitis

Even though cefuroxime may penetrate the CSF in patients with meningeal inflammation, it is not recommended for the treatment of meningitis. Its efficacy is inferior to ceftriaxone, and treatment with cefuroxime in children has been associated with increased hearing impairment (Schaad *et al.*, 1990). Reduced rates of susceptibility for cefuroxime were found among *Neisseria meningitidis* strains isolated from 18 African countries in the “meningitis belt” between 2000 and 2006 that were tested for susceptibility to beta-lactams antibiotics (Hedberg *et al.*, 2009).

One study has shown cefuroxime has efficacy as a single agent for prophylaxis in patients undergoing transsphenoidal surgery (Little *et al.*, 2011).