Both penicillin and amoxycillin should be tested in antimicrobial surveillance for *Streptococcus pneumoniae*

The recently published [1] surveillance recommendations of the ESCMID Study Group for Antimicrobial Resistance Surveillance (ESGARS) state that ‘Antibiotics to be included in surveillance studies should be selected in such a way as to ensure the highest sensitivity in detecting the possible presence of a particular antibiotic resistance mechanism’. This is appropriate if the goal of the surveillance is purely epidemiological, i.e., designed to monitor the presence of resistance mechanisms, but is inappropriate if the goal of the surveillance is to provide clinically relevant information to clinicians, particularly for the selection of antimicrobial agents for use in empirical therapy. The authors also state that the information obtained from the ‘sentinel’ antibiotics can be used to ‘infer’ the activity of other agents, and that this information should be provided to clinicians, ‘who do not necessarily need to be aware of all the details regarding the method of inference and its application’. While this method may be adequate for some antimicrobial agents, it may not be appropriate to use penicillin resistance to predict the clinically relevant activity of amoxycillin.

*Streptococcus pneumoniae* is one of the most common bacterial pathogens recovered from patients with community-acquired pneumonia, acute bacterial sinusitis, acute exacerbations of chronic bronchitis, acute otitis media, bacteremia and meningitis. The 1998–2000 Alexander Project demonstrated penicillin resistance rates of 41% and 26% in France and Spain, respectively [2]. Penicillin-resistant isolates of *S. pneumoniae* (PRSP) are often resistant to other antimicrobial agents prescribed commonly, such as macrolides, trimethoprim–sulphamethoxazole and the oral cephalosporins, further limiting the treatment options available to physicians. In western Europe, 62% of PRSP isolates were also resistant to macrolides, and 92% were resistant to trimethoprim–sulphamethoxazole. However, only 8% of PRSP isolates from western Europe were resistant to amoxycillin. In addition, amoxycillin was the only non-quinolone agent tested that had in-vitro activity for ≥90% of the *S. pneumoniae* isolates tested in all of the countries analysed [2].

It is also inappropriate to use penicillin MICs to predict the MICs of amoxycillin, since these are not identical and may differ by one or more dilutions. This is especially significant for isolates with MICs near the penicillin resistance breakpoint of ≥2 mg/L, as such isolates often have MICs that are one dilution higher or lower for amoxycillin, depending on the precise penicillin-binding protein mutation present.

The key difference between oral amoxycillin and oral penicillin is the pharmacokinetic profile. Oral amoxycillin achieves markedly higher serum concentrations than does penicillin. This is because amoxycillin is stable in the presence of gastric acid and is absorbed readily after oral administration. Penicillin is less stable in gastric acid and only c. 30% is absorbed into the blood after oral administration. In addition, the protein binding of amoxycillin is only c. 17% compared to 80% for penicillin V, so there is significantly more amoxycillin to act on infecting pathogens [3–5]. The key pharmacokinetic/pharmacodynamic parameter correlating with efficacy of the β-lactams is the period of time for which serum levels remain above the MIC for the infecting pathogen ($T > MIC$). For β-lactams in general, a $T > MIC$ that is ≥40% of the dosing interval is predictive of efficacy; however, efficacy was demonstrated with amoxycillin when the $T > MIC$ was c. 35–40% of the dosing interval in an animal model of respiratory tract infection [6]. Many amoxycillin formulations prescribed commonly (including 875 mg twice-daily, 875 mg three-times-daily and 500 mg three-times-daily) provide a $T > MIC$ that is ≥40% of the dosing interval for isolates with an MIC of 2 mg/L. This corresponds with the NCCLS susceptibility breakpoint for *S. pneumoniae*, which was based on the pharmacokinetic/pharmacodynamic profile of amoxycillin, proven efficacy in animal models against *S. pneumoniae* isolates with MICs of 2 mg/L, and studies demonstrating clinical efficacy in patients infected with *S. pneumoniae* strains with MICs ≤2 mg/L [7].

At the NCCLS susceptibility breakpoint of ≤2 mg/L, penicillin-intermediate isolates, as well as most penicillin-resistant isolates, are considered susceptible to amoxycillin. This becomes significant in countries where high-dose formulations of amoxycillin, or amoxycillin-containing agents such as Augmentin SR (2000/125 mg...
twice-daily) or Augmentin ES-600, are approved. These high-dose formulations provide an amoxicillin $T > \text{MIC}$ of 46–49% of the dosing interval for isolates with amoxicillin MICs of 4 mg/L, thereby providing coverage for an even larger percentage of PRSP isolates.

The efficacy of amoxicillin against PRSP has also been demonstrated in the clinic. In a large phase III clinical programme that included studies of community-acquired pneumonia, acute bacterial sinusitis and acute exacerbations of chronic bronchitis, 50 (96.1%) of 52 patients with PRSP infection, including 13 of 15 isolates with amoxicillin MICs of 4–8 mg/L, were treated successfully with amoxicillin–clavulanate 2000/125 mg twice-daily [8]. In paediatric phase III otitis media studies, Augmentin ES-600 (90/6.4 mg/kg/day) eradicated 31 (91%) of 34 PRSP isolates by the primary endpoint visit (on-therapy) [9].

In conclusion, in an era of increased resistance to many of the antimicrobial agents used commonly today, treatment options are limited. Penicillin-intermediate and/or -resistant isolates of \textit{S. pneumoniae} that are reported falsely as resistant to amoxicillin, or amoxicillin-containing formulations, would reduce the availability of treatment options and could lead to the use of less appropriate agents, such as the fluoroquinolones, which may need to be reserved for treatment failures. This is a particular concern with paediatric patients, for whom fluoroquinolones are not approved for common respiratory tract infections. Therefore, if surveillance studies on \textit{S. pneumoniae} are to be used by clinicians to help determine therapeutic options, both penicillin and amoxicillin should be tested.

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Performance of the Focus ELISA test for detection of herpes simplex virus type-2-specific antibodies in Chinese STD patients

Herpes simplex virus type-2 (HSV-2) infection is one of the most common sexually transmitted infections, with a significantly increased incidence worldwide. Effective intervention has been complicated, in part, by the absence of methods to differentiate HSV-1 from HSV-2-infected individuals accurately and easily. During the past 15 years, many tests for detecting antibodies to HSV-1 or HSV-2 have been developed. The recent article by Ashley-Morrow et al. [1] described the performance of the HerpeSelect HSV-2 ELISA (Focus Technologies, Cypress, CA, USA) in ten different geographical locations. This test has been introduced into sexually transmitted disease (STD) services in China, and has also been used in epidemiological and interventional projects.