



Resistance to Streptococcus pneumoniae in Brazil

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Streptococcus pneumoniae (pneumococcus) is the main etiological agent of pneumonias and invasive diseases in children and adults. It is estimated that in developing countries, pneumococcus is responsible for more than one million deaths per year of children younger than five years of age, most due to pneumonia. Pneumococcal diseases affect needier populations more severely, even worsening the social situation of these populations. Although pneumonias cause a large number of deaths, other mucosal diseases caused by pneumococcus are more common. The use of antibiotics to treat otitis and sinusitis caused by pneumococcus has been associated with the appearance and spread of antibiotic-resistant strains.

Acute otitis media (AOM) is an important disease because it affects the younger pediatric population and also because it is the bacterial disease most often diagnosed in pediatrics. In the United States, AOM is responsible for 24 million visits to physicians per year and for the consumption of 240 million dollars in antibiotics. Approximately three fourths of children three years old or less are observed to have at least one AOM episode. This figure seems to be growing, as there has been an increase in the number of medical appointments because of AOM, from 10 million visits in 1975 to 24.5 million in 1990.

In general, acute otitis media (AOM) is triggered by a viral infection of the upper respiratory tract that causes edema in the ear canal. This leads to accumulation of fluid and mucus, which become secondarily infected by bacteria that colonize the nasopharynx, particularly *S. pneumoniae*. Pneumococcal infections start in the nasopharynx. Infants, children and adolescents can be nasal carriers of *S. pneumoniae*. Studies carried out with longitudinal follow-up of children from birth have demonstrated that most children are colonized by pneumococcus at least once during childhood. A study performed in Fortaleza (Northeast Brazil) with 900 children found 55% of these children and infants showed colonization. In S. Paulo, other studies detected 35% to 45% of normal children to be colonized.

Once it is known that the infection is always preceded by colonization, a higher frequency of pneumococcal infection can be observed in younger children, who are colonized most often. Most studies in Brazil have focused on patients who had invasive infections, but an increase in pneumococcal bacterial resistance has drawn attention in the last few years. The first data on bacterial resistance were

from a study performed between 1989 and 1993 that found that in 10% of strains not susceptible to penicillin, almost all had intermediate resistance. Carried out in several Latin American countries, the SIREVA study evaluated the bacterial resistance of pneumococci to penicillin in cases between 1997 and 1999. The study was published in 2001. It showed 19% of strains had intermediate resistance and 1.8% of strains in Brazil had full resistance. More recent data (2006) indicate 19.6% intermediate resistance and 13.8% full resistance.

Sih and colleagues, evaluating 300 children with diagnostic puncture between 1990 and 1995, performed the only Brazilian study on the middle ear. This study detected pneumococci in 16%, with an intermediate resistance to penicillin in 56% of those. Strains colonizing the nasopharynx were detected in children with AIDS, and 22% of those had intermediate resistance to penicillin. The penicillin-resistance of strains isolated from HIV-positive children was not higher than that in the general population. Penicillin-resistance in invasive infections was 17%, compatible with what was found in the nasopharynx.

Another study with 80 children in 2000 isolated pneumococcus from the nasopharynx in 52% of the children, with 40% of those strains having intermediate resistance. In 2005, we evaluated colonization by pneumococci in infants younger than six months of age. We found that approximately 25% were colonized at six months of age (**Table 1**). Among the strains found in these patients, 25% were non-susceptible to penicillin. This demonstrates early colonization, possibly by non-susceptible strains.

Table 1. Pneumococcal colonization in infants below six months of age

Infants N = 139	Total
Colonization /3 ms	17.3% (24/139)
Colonization/ 6 ms	16.5% (22/133)
Colonization/ 3 or 6 ms	26.6% (37/139)
Colonization by pneumococci non-susceptible to penicillin	35 (25%)
Use of antibiotics up to 6 months	35 (25%)

Between 2000 and 2001, 55 patients with invasive pneumococcal infections were evaluated. During this period, we detected non-susceptibility to penicillin in 34% and full resistance in 8.6% of the strains.

The definition of resistance to penicillin by *S. pneumoniae* is given in the evaluation of the Minimum Inhibitory Concentration (MIC). Strains with MIC < 0.1 µg/ml are considered to be susceptible; MIC between 0.1 and 1.0 have intermediate resistance, and MIC above 1.0 µg/ml have full resistance. These criteria were recently altered. The criteria were maintained for meningitis and were altered for strains from other origins. When a strain has MIC < 4.0 µg/ml, it is considered to be susceptible; those with a MIC = 4.0 µg/ml are considered to be intermediate, and with a MIC > 4.0 µg/ml there is full resistance. This evaluative criterion makes the rate of resistance very low, as it selects for strains that are resistant

from a clinical point of view. The objective of this alteration was to achieve better correlation between data acquired *in vivo* and those acquired *in vitro*.

Conclusion

Resistance of *S. pneumoniae* to penicillin is increasing in São Paulo. Evaluation of nasopharyngeal colonization is a good method, as it is a simple and easy way to obtain bacteria and can reflect progression of bacterial resistance in the community. We lack Brazilian data related to infections of the middle ear.

Recommended readings

1. Di Fabio JL, Castañeda E, Agudelo CI et al. Evolution of *Streptococcus pneumoniae* serotypes and penicillin susceptibility in Latin America, Sireva-Vigia Group, 1993-1999. *Pediatr Infect Dis J* 2001;20:959-67.
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3. Brandileone MC, Vieira VS, Casagrande ST et al. Prevalence of serotypes and antimicrobial resistance of *Streptococcus pneumoniae* strains isolated from Brazilian children with invasive infections. Pneumococcal Study Group in Brazil for the SIREVA Project. *Regional System for Vaccines in Latin America. Microb Drug Resist* 1997;3:141-6.
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5. Lopes C, Berezin and – Pneumococcal colonization and vaccine in pregnancy- 6th international simposium on Pneumococci and Pneumococcal diseases 8-12 June 2008 Reykjavik, Iceland
6. Dagan R, Jacobs MR, Greenberg D. Pneumococcal Infections' In: RD Feigin, JD Cherry, GJ eds. *Textbook of Pediatric Infectious Diseases* 5th ed: Saunders Co Philadelphia, PA, 2004: 1204-1258.