



**ACADEMIC EXAMS**  
AT THE FACULTY OF MEDICINE OF THE UNIVERSITY OF LISBON  
INSTITUTE OF ADVANCED TRAINING

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**Masters:**

Clinical Microbiology (4th Edition)

**Name of Student:**

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**Subject of Thesis:**

Five years of Prevenar – impact of conjugated vaccine 7 – in the colonisation by *Streptococcus Pneumoniae* in children at nursery schools in the greater Lisbon area.

**Date of Defence:**

21/05/2009

**Mark:**

Very Good

**Jury:**

**President:** Professor J. Melo Cristino (FMUL)

**Orientator:** Professor Hermínia de Lencastre (ITQUNL)

**Jury Members:** Professor Mário Ramirez (FMUL)



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**ABSTRACT**

Pneumococcal disease, caused by *Streptococcus pneumoniae*, leads to a wide range of important human pathologies, from common upper respiratory tract infections to severe invasive manifestations such as pneumonia, meningitis and septicemia. Thus it is a major public health problem all over the world.

The increase in pneumococcal resistance to antimicrobial drugs, and the spread of resistant strains all over the world, underline the importance of control through vaccination. A 7-valent pneumococcal conjugate vaccine 7-valent (PCV7) has been available in Portugal since 2001. This vaccine protects against seven serotypes and has been shown to induce antibody production and immunological memory in very young children (less than 2 years of age).

One of the advantages of this vaccine is that it reduces nasopharyngeal carriage by the serotypes included in it. Since colonization is the starting point for invasive disease and transmission, colonization studies are important to understand the impact of PCV7.

It has been observed that, following vaccination with PCV7, a reduction in nasopharyngeal carriage of serotypes included in the vaccine and an increase in carriage of non vaccine serotypes (NVT) occurs.

This is the first study in Portugal aiming to understand the impact of PCV7 on genetic diversity of pneumococcal population colonizing vaccinated and unvaccinated children attending day-care centers five years after its introduction. We compared circulating clones in 2006 with those detected in 2001 and determined if majority clones had evolved in the same way, if introduction of new clones had occurred as well as capsular switching events. For that we characterized by serotyping 463 isolates from 2001 (before vaccination) and 387 isolates from 2006.

A significant increase of genetic and serotype diversity was observed among NVT strains. Also a significant raise of some serotypes after vaccine introduction was detected and the impact of PCV7 within a serotype was not equal since we detected different behaviour between different clones. Emergence, expansion and *de novo* acquisition led to a significant raise in resistance of NVT strains. When comparing vaccinated with unvaccinated children we concluded that in terms of serotype and genetic diversity there were no significant differences. According to these results significant changes on NVT strains are occurring and clones that are not PCV7 targets are emerging, showing that surveillance studies are required.

**Key Words:** *Streptococcus pneumoniae*, colonization, pneumococcal conjugate vaccine, serotype, clone.