



# Predicting Patient Response to Pneumococcal 23-vaccine (PPV23) Using Age, Baseline Immunoglobulins, and Pneumococcal Serotypes

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## INTRODUCTION

Humoral immunodeficiency is the most common form of primary immunodeficiency (PID). Although genetic testing is becoming more readily accessible, measurement of antibody response to vaccinations continues to remain crucial in the evaluation and diagnosis of primary immunodeficiency disorders. The 23-valent pneumococcal polysaccharide vaccine (PPV23) remains the vaccine of choice to evaluate T-cell-independent immune responses during the initial laboratory workup of PID patients.

In the diagnostic evaluation for humoral immunodeficiency, the level of anti-pneumococcal antibodies in the patient's serum before and after vaccination are measured to determine whether an appropriate antibody response has occurred to the vaccination. Most researchers agree that a pneumococcal-serotype-specific 2-fold to 4-fold increase or a serotype-specific concentration of 1-1.5 ug/ml at one-month post-vaccination produces long-term protection. If the patient responds to less than 50-70% of the serotypes examined, the patient can be identified as having a deficient production of antibodies in a T-cell-independent manner.

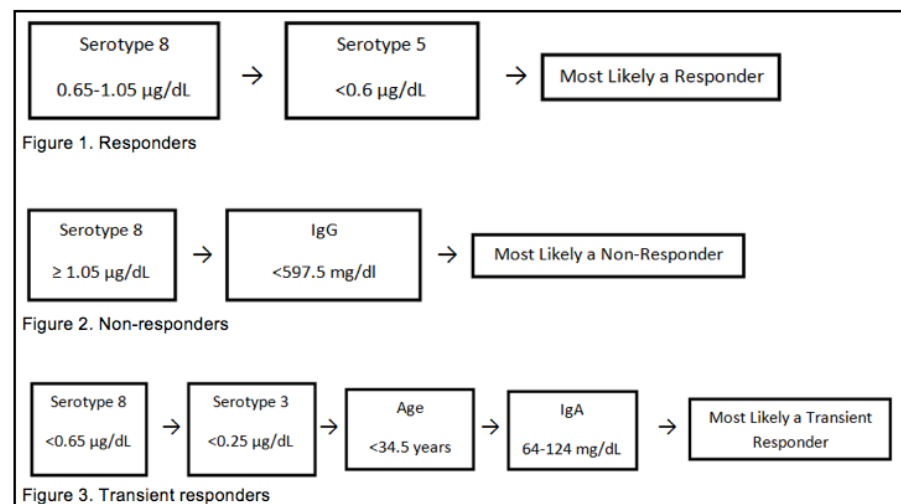
Although there are guidelines on how to interpret the overall vaccine response, there is a paucity of evidence on the significance of individual pre-vaccination serotype concentrations as a possible predictor of immunodeficiency or future risk of immunodeficiency. We performed a statistical investigation of pre-vaccination immunoglobulin (Ig) levels of the individual pneumococcal polysaccharide serotype in PPV23 to determine if there is any statistical correlation between individual pneumococcal polysaccharide serotypes and possible response patterns

## METHODS

A retrospective chart analysis over a six-year period of all of the patients with immune disorders that were seen between 2001 and 2007 was performed. All sex, age, and race groups were included. Four hundred ninety-two patients were screened. Patients were excluded if they had a specifically defined PID, did not follow-up for repeat PPV23 titers in the defined 4-8 weeks and when applicable, 6-8 months time frame. A total of 300 patients met the inclusion criteria and were included in the study.

A statistical evaluation of pre- and post-vaccination pneumococcal titer levels, serum Ig levels, and age of individuals with recurrent infections was performed to predict their response post-vaccination. All patients who responded at the 4-8 week check-up were seen between 6-8 months for an additional set of titers. An ordinal method was used to determine statistical significance for the pre- and post-vaccination pneumococcal titer levels, serum Ig levels, and age.

Patients were separated into three distinct categories based on their post PPV23 pneumococcal titers: responders, non-responders, and transient responders. Subjects were placed in the responder group if they showed an adequate increase in titers values to protective levels throughout the 6-8-month period and/or showed clinical improvement. A transient responder was defined by an initial protective response at the 4-8-week visit, but with subsequent follow up testing demonstrating a decrease in titer values by one-half from their first post-vaccination levels and/or showed initial clinical improvement in disease but showed a clinical decline after six months. Non-responders were defined as subjects who did not respond to the vaccination and had little to no clinical improvement post vaccination.



## RESULTS

Individually, none of the variables could predict response between groups. In turn, a sequence was made in order to accurately predict the responder status using age, IgG levels, IgA levels, and pre-titers levels. If a pre-vaccine titer to serotype 8 was between 0.65 and 1.05 µg/mL and serotype 5 was less than 0.6 µg/mL the patient will most likely respond to the vaccine (Responder) (Figure 1). If a pre-vaccine titer to serotype 8 was greater than 1.05 µg/mL and the serum IgG was less than 597.5 mg/dL the patient would most likely not respond to the vaccine (Non-Responder) (Figure 2). If the serotype 8 was less than 0.65 µg/mL, serotype 3 was less than 0.25 µg/mL, the age was less than 34.5 years, and the IgA was between 64 and 124 mg/dL, the patient would most likely be a transient responder (Transient) (Figure 3).

## CONCLUSIONS

- The diagnosis of humoral immunodeficiency is based upon clinical history as well as quantitative serologic investigation.
- Research of pneumococcal pre-vaccination titers in determining post-vaccination responder status has been sparse.
- Our data demonstrates that specific pneumococcal serotype titers, immunoglobulin levels, and age may be able to predict vaccination responder status of patients undergoing immunological evaluation for humoral immunodeficiency.
- The ability to help identify the responder status, especially transient status, prior to vaccination would aid in guiding appropriate patient management and follow-up.