Test Definition: PNTOR

Streptococcus pneumoniae IgG Antibodies, Total, with Reflex, Serum

Overview

Useful For

Assessing the IgG antibody response to active immunization with nonconjugated 23-valent pneumococcal vaccines

Assessing the IgG antibody response to active immunization with conjugated 13-valent, 15-valent and 20-valent pneumococcal vaccines

Determining the ability of an individual to produce an antibody response to polysaccharide antigens, as part of an evaluation for humoral or combined immunodeficiencies

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
PN23M	S. pneumoniae IgG Ab,23 serotypes,S	Yes	No

Testing Algorithm

If the result is 41.0 mcg/mL or greater and less than 181.0 mcg/mL, then *Streptococcus pneumoniae* IgG antibodies for 23 serotypes will be performed at an additional charge.

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

This test is the preferred test for patients being evaluated for possible immunodeficiency or for assessment of pneumococcal vaccination response (initial evaluation).

The preferred test for patients previously tested for *Streptococcus pneumoniae* antibodies (as part of follow up testing or part of pre/post vaccine assessment) is PNTO / *Streptococcus pneumoniae* IgG Antibodies, Total, Serum.

The preferred test for patients previously tested for *S pneumoniae* serotypes (as part of follow up testing or part of

pre/post vaccine assessment) is PN23M / *Streptococcus pneumoniae* IgG Antibodies, 23 Serotypes, Serum.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL Serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Specimen Minimum Volume

Serum: 0.3 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Streptococcus pneumoniae is a gram-positive bacterium that causes a variety of infectious diseases in children and adults, including invasive disease (bacteriemia and meningitis) and infections of the respiratory tract (pneumonia and otitis media).(1) More than 90 serotypes of *S. pneumoniae* have been identified, based on varying polysaccharides found in the bacterial cell wall. The serotypes responsible for disease vary with age and geographic location. Bacterial polysaccharides induce a T-cell independent type II humoral immune response. In adults and older children, bacterial polysaccharides are effective in generating an immune response that results in production of IgG antibodies and generation of long-lived plasma cells and memory B cells.(2) *S. pneumoniae* purified polysaccharide vaccines (PPSV) that contain a total of 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F) are available; these are referred to as PPSV23.(3) These 23 serotypes were included because, as a group, they account for approximately 90% of invasive pneumococcal infections. Antibody responses develop in 75% to 85% of nonimmunocompromised adults and older children approximately 4 to 6 weeks following immunization with purified

polysaccharide vaccines. A meta-analysis estimated an efficacy of 74% for prevention of invasive pneumococcal disease in adults vaccinated with pneumococcal polysaccharide vaccine (PPSV23).(4) In contrast, immune responses to polysaccharide antigens in children younger than 2 years are generally weak.

Active immunization of children younger than 2 years requires vaccines prepared of polysaccharides conjugated to an immunogenic carrier protein (Corynebacterium diphtheria strain C7), which results in a T-cell dependent antibody response.(3) In children younger than 6 years, prior to the availability of routine *S. pneumoniae* vaccination, 7 serotypes (4, 6B, 9V, 18C, 19F, and 23F) accounted for 80% of invasive disease and up to 100% of all isolates that were found to be highly resistant to treatment with penicillin. The first pneumococcal conjugated vaccine (PCV) available for children younger than 2 years contained these 7 serotypes (PCV7). The vaccine was highly effective, with invasive disease in children younger than 5 years reduced from 99 to 21 cases per 100,000 population from 1998 to 2008.(5) In addition, it was demonstrated that after PCV7 became part of the routine vaccination schedule, only 2% of invasive disease was associated with any of the serotypes present in the vaccine. Instead, approximately 61% of the invasive disease was caused by an additional 6 serotypes (1, 3, 5, 6A, 7F, and 19A). This led to development of a 13-valent conjugated vaccine, known as pneumococcal conjugate vaccine (PCV13). More recently, additional pneumococcal conjugate vaccines have been approved, specifically 15-valent (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F) and 20-valent (1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F) vaccines, known as PCV15 and PCV20, respectively.

Conjugated pneumococcal vaccination is included in the routine childhood schedule, with 4 doses of PCV13 or PCV15 administered at 2, 4, 6, and 12 to 15 months.(6) For adults younger than 65 years, a single dose of PCV20 or a single dose of PCV15 followed 1 year later with a single dose of PPSV23 is recommended.(7) This same pneumococcal vaccination strategy is recommended for adults 19 to 64 years with immunocompromising conditions, cochlear implants, cerebrospinal fluid leaks, or other chronic health conditions.

Patients with intrinsic defects in humoral immunity, such as common variable immunodeficiency, may have impaired antibody responses to pneumococcal vaccination.(8,9) Selective antibody deficiency is a recognized clinical entity in patients older than 2 years and is characterized by recurrent bacterial respiratory infections, absent or subnormal antibody response to a majority of polysaccharide antigens, and normal or increased immunoglobulin concentrations, including IgG subclasses, in the context of intact humoral response to protein antigens. In several other primary immunodeficiencies, including Wiskott-Aldrich syndrome, autoimmune lymphoproliferate syndrome, and DiGeorge syndrome, IgG subclass deficiencies may also result in impaired antibody responses to polysaccharide antigens.

Reference Values

> or =9.7 mcg/mL

Interpretation

Low antipneumococcal antibody concentrations (<9.7 mcg/mL) indicate a poor response to the pneumococcal vaccine, while high concentrations (>270.0 mcg/mL) indicate a robust vaccine response. Results falling in the modest (9.7-40.9 mcg/mL), intermediate (41.0-180.9 mcg/mL), and moderate (181.0-270.0 mcg/mL) categories may warrant serotype-specific antibody testing, to be determined at the discretion of the physician.

When comparing pre- and post-vaccination samples, an increase in antibody concentrations is generally considered to be indicative of a normal vaccine response. However, the specific fold increase is influenced substantially by the

antibody concentration observed in the pre-vaccination sample.

Cautions

The humoral immune response to *Streptococcal pneumoniae* vaccination is affected by multiple factors, including age, immune status, vaccination history, prior infections, and carrier status.

Protective concentrations of IgG antibodies, or those required to prevent infection from *Streptococcus pneumoniae,* have not been defined.

Quantitation of the IgG antibody response to pneumococcal serotypes does not provide any information on their functional capacity (opsonization efficiency).

Supportive Data

The utility of measuring the total IgG response to Streptococcus pneumoniae vaccination was assessed in a study published by Parker et al.(10) In a cohort of healthy individuals (n=77), a median 9-fold increase in IgG reactivity was observed 4 to 6 weeks after vaccination, with median IgG concentrations of 41 mcg/mL and 375 mcg/mL in pre- and post-vaccination samples, respectively. Based upon data in the healthy control group, a concentration of 77 mcg/mL was established as the threshold for defining a normal vaccination response. Using this cut-off, in a cohort of individuals with humoral primary immunodeficiencies, 62.7% (64/102) had results below this cut-off following vaccination, compared to 3.9% (3/77) in the healthy control group.(10) While measurement of antibodies against Streptococcus pneumoniae is not diagnostic for any specific disease, it can be used to understand the nature and magnitude of immunoglobulin deficiencies in patients with suspected humoral immune disorders.

Clinical Reference

1. Weisberg SS. Pneumococcus. Dis Mon. 2007;53(10):495-502. doi:10.1016/j.disamonth.2007.09.013
2. Grabenstein JD, Manoff SB. Pneumococcal polysaccharide 23-valent vaccine: long-term persistence of circulating antibody and immunogenicity and safety after revaccination in adults. Vaccine. 2012;30(30):4435-4444
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4. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev. 2013;2013(1):CD000422
5. Paradiso PR. Advances in pneumococcal disease prevention: 13-valent pneumococcal conjugate vaccine for infants and children. Clin Infect Dis. 2011;52(10):1241-1247
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7. Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine among U.S. children: Updated recommendations of the Advisory Committee on Immunization Practices - United States, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(37):1174-1181
8. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015;136(5):1186-205.e2078
9. Orange JS, Ballow M, Stiehm ER, et al. Use and interpretation of diagnostic vaccination in primary immunodeficiency: a working group report of the Basic and Clinical Immunology Interest Section of the American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol. 2012;130(3 Suppl):S1-S24
10. Parker AR, Park MA, Harding S, Abraham RS. The total IgM, IgA and IgG antibody responses to pneumococcal

polysaccharide vaccination (Pneumovax 23) in a healthy adult population and patients diagnosed with primary immunodeficiencies. Vaccine. 2019;37(10):1350-1355

Performance

Method Description

Testing for IgG antibodies to *Streptococcus pneumoniae* serotypes is performed using a laboratory-developed immunoassay.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Tuesday

Report Available

2 to 8 days

Specimen Retention Time

12 weeks

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

86317
86317 x 23 (if appropriate)

LOINC® Information

MAYO CLINIC LABORATORIES

Test Definition: PNTOR

Streptococcus pneumoniae IgG Antibodies, Total, with Reflex, Serum

Test ID	Test Order Name	Order LOINC® Value
PNTOR	S. pneumoniae IgG Ab, with reflex,S	43236-9

Result ID	Test Result Name	Result LOINC® Value
PNTOR	S. pneumoniae IgG Ab, with reflex,S	43236-9