Test Definition: PN23

S. pneumoniae IgG Ab,23 serotypes,S

Overview

Useful For

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

Assessing the IgG antibody response to active immunization with conjugated, 13-valent 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

Method Name

MicrospherePhotometry

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume:0.5 mL

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

Streptococcus pneumoniae is a gram-positive bacteria that causes a variety of infectious diseases in children and adults, including invasive disease (bacteremia and meningitis) and infections of the respiratory tract (pneumonia and otitis media).(1,2) In 2009, it is estimated that *S pneumoniae* was responsible for approximately 43,500 infections and 5,000 deaths in the United States. More than 90 serotypes of *S pneumoniae* have been identified, based on varying polysaccharides that are 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. Vaccines containing bacterial polysaccharides can be effective in generating an immune response that results in production of IgG antibodies and generation of long-lived plasma and memory B cells, which can protect an individual against bacterial disease. Active immunization of adults and children older than 2 years is performed with nonconjugated polysaccharide vaccines (Pneumovax and Pnu-Immune 23) that contain a total of 23 serotypes, namely 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F.(3) These 23 serotypes were included because, as a group, they account for approximately 90% of invasive pneumococcal infections. Antibody responses develop in approximately 75% to 85% of nonimmunocompromised adults and older children approximately 4 to 6 weeks following immunization. Immunization with a 23-valent vaccine is recommended for all adults 65 years of age and older, and for adults 18 to 64 years of age with certain chronic diseases (heart disease, lung disease, type I diabetes, liver disease), those who are immunocompromised (congenital or acquired immunodeficiencies, malignancy, solid-organ transplant), and those with functional or anatomic asplenia.(3)Â

In contrast to adults and older pediatrics, immune responses to polysaccharide antigens in children younger than 2 years of age are generally weak. Active immunization of children younger than 2 years requires multiple injections of vaccine prepared from purified polysaccharides conjugated to an immunogenic carrier (*Corynebacterium diphtheria* strain C7 protein), which results in a T-cell dependent antibody response. In children younger than age 6, 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 conjugated vaccine available for children younger than age 2 (Prevnar) contained these 7 serotypes.(4,5) The vaccine was highly effective, with invasive disease in children younger than age 5 reduced from 99 to 21 cases per 100,000 population from 1998 to 2008. In addition, it was demonstrated that after Prevnar became part of the routine vaccination schedule, only 2% of invasive disease was associated with any of the serotypes present in the 7-valent conjugate vaccine. Instead, approximately 61% of the invasive disease was caused by an additional 6 serotypes, including 1, 3, 5, 6A, 7F, and 19A. This led to development of a 13-valent *S pneumoniae* polysaccharide conjugate vaccine, which is marketed as Prevnar13. Prevnar13 is approved for administration to all children ages 6 weeks to 71 months, and has replaced the previous 7-valent Prevnar vaccine.(6)

Patients with intrinsic defects in humoral immunity, such as common variable immunodeficiency, may have impaired antibody responses to pneumococcal vaccination. Further, impaired polysaccharide responsiveness, also known as 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 the polysaccharide antigens, and normal or increased immunoglobulin levels, including IgG subclasses, in the context of an intact humoral response to protein antigens. In several other primary immunodeficiencies, including Wiskott-Aldrich syndrome, autoimmune lymphoproliferative syndrome, and DiGeorge syndrome, IgG-subclass deficiencies may also result in impaired antibody responses to polysaccharide antigens.

Reference Values

Results are reported in mcg/mL.

Serotype	Normal Value
1 (1)	> or =2.3
2 (2)	> or =1.0
3 (3)	> or =1.8
4 (4)	> or =0.6
5 (5)	> or =10.7
8 (8)	> or =2.9
9N (9)	> or =9.2
12F (12)	> or =0.6
14 (14)	> or =7.0
17F (17)	> or =7.8
19F (19)	> or =15.0
20 (20)	> or =1.3
22F (22)	> or =7.2
23F (23)	> or =8.0
6B (26)	> or =4.7
10A (34)	> or =2.9
11A (43)	> or =2.4
7F (51)	> or =3.2
15B (54)	> or =3.3
18C (56)	> or =3.3
19A (57)	> or =17.1
9V (68)	> or =2.6
33F (70)	> or =1.7

Interpretation

As a general guideline, nonimmunocompromised adults develop IgG antibodies approximately 4 to 6 weeks following nonconjugated vaccination. A study conducted at the Mayo Clinic assessed IgG antibody concentrations prior to and following vaccination in a cohort of 100 healthy adults who met stringent exclusion criteria, including lack of previous pneumococcal vaccination or pneumonia associated with *Streptococcus pneumoniae* infection. Based on this data, reference ranges were established that most effectively discriminated between prevaccination and postvaccination antibody concentrations. Antibody concentrations greater than or equal to the reference value for at least 50% of serotypes in either a pre- or postvaccination specimen or a 2-fold or greater increase in antibody concentrations for at least 50% of serotypes when comparing the pre- to the postvaccination results would be consistent with a normal response to *S pneumoniae* vaccination.

Serotype-specific antibodies may persist for up to 10 years following immunization or infection.

Cautions

The humoral immune response to *Streptococcus pneumoniae* is age dependent and the database of IgG antibody concentrations to different serotypes is incomplete.

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

Quantitation of the IgG antibody response to pneumococcal serotypes does not provide any information on the functional capacity of the serotype-specific antibodies generated (opsonization efficiency).

Clinical Reference

1. Weisberg SS: Pneumococcus. Dis Mon 2007 October;53(10):495-502

2. Braido F, Bellotti M, De Maria A, et al: The role of pneumococcal vaccine. Pulm Pharm Ther 2008 August;21(4):608-615

3. Nuorti JP, Whitney CG: Updated recommendations for prevention of invasive pneumococcal disease among adults using the 23-valent pneumococcal polysaccharide vaccine (PPSV23). Morb Mortal Wkly Rep 2010 September;59(34)1102-1106

4. Moffitt KL, Malley R: Next generation pneumococcal vaccines. Curr Opin Immunol 2011 June;23(3):407-413

5. Paradiso PR: Advances in pneumococcal disease prevention: 13-valent pneumococcal conjugate vaccine for infants and children. Clin Infect Dis 2011 May;52(10):1241-1247

6. Nuorti JP, Whitney CG: Prevention of pneumococcal disease among infants and children-Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine. MMWR Recomm Rep 2010 Dec;59(RR-11):1-18

7. Jacob GL, Homburger HA: Simultaneous Quantitative Measurement of IgG Antibodies to Streptococcus Pneumoniae Serotypes by Microsphere Photometry. J Allergy Clin Immunol 2004;113(2) Suppl (Abstract 1049,Â S288)

8. Plikaytis BD, Holder PF, Pais LB, et al: Determination of parallelism and nonparallelism in bioassay dilution curves. J Clin Microbiology 1994 October;32:2441-2447

9. Plikaytis BD, Goldblatt D, Frasch CE, et al: An analytical model applied to a multicenter pneumococcal enzyme-linked immunosorbent assay study. J Clin Microbiol 2000 June;38(6):2043-2050

10. Park MA, Snyder MR, Smith C, et al: New guidelines for interpretation of IgG pneumococcal antibody data: results from a cohort study of healthy adults. Clin Immunol 2010 May;135(2):38

Performance

Method Description

IgG antibodies to *Streptococcus pneumoniae* serotypes are measured by microsphere photometry. Purified pneumococcal polysaccharides coupled covalently to polystyrene microspheres bind IgG antibodies in patients' sera during the first incubation. After incubation, the microspheres are washed and incubated with phycoerythrin-conjugated antihuman IgG antibody. The concentration of IgG antibodies to each polysaccharide is determined by comparison to dose-response curves calculated from serial dilutions of a serum pool from immunized adults with known concentrations of antibodies to each polysaccharide (secondary standard). The secondary standard is traceable to a standard reference preparation (FDA 89-SF) that contains known concentrations of IgG antibodies to 23 different *S pneumoniae* serotypes. Dose-response curves prepared from serial dilutions of the secondary standard parallel the dose-response curves of the primary reference preparation for all polysaccharides.(Jacob GL, Homburger HA: Simultaneous Quantitative Measurement of IgG Antibodies to *Streptococcus Pneumoniae* Serotypes

by Microsphere Photometry. Poster Presentation; AAAAI 60th Annual Meeting, March 19-23, 2004. San Francisco, CA. J Allergy Clin Immunol Vol 113, No 2, [Abstract 1049, pS288] 2004; Plikaytis BD, Holder PF, Pais LB, et al: Determination of parallelism and nonparallelism in bioassay dilution curves. J Clin Microbiol 1994;2441-2447; Plikaytis BD, Goldblatt D, Frasch CE, et al: An analytical model applied to a multicenter pneumococcal enzyme-linked immunosorbent assay study. J Clin Microbiol 2000;38:2043-2050)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

4 to 6 days

Specimen Retention Time

8 weeks

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

86317 x 22

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
PN23	S. pneumoniae IgG Ab,23 serotypes,S	42366-5

Result ID	Test Result Name	Result LOINC Value
23979	Serotype 1 (1)	85954-6
23949	Serotype 2(2)	86039-5
23950	Serotype 3 (3)	86080-9
23951	Serotype 4 (4)	86107-0
23952	Serotype 5 (5)	86130-2

Result ID	Test Result Name	Result LOINC Value
23953	Serotype 8 (8)	86147-6
23954	Serotype 9N (9)	86169-0
23955	Serotype 12F (12)	85977-7
23956	Serotype 14 (14)	85991-8
23957	Serotype 17F (17)	86009-8
23958	Serotype 19F (19)	86024-7
23959	Serotype 20 (20)	86045-2
23960	Serotype 22F (22)	86052-8
23961	Serotype 23F (23)	86064-3
23962	Serotype 6B (26)	27118-9
23963	Serotype 10A (34)	86098-1
23964	Serotype 11A (43)	86122-9
23965	Serotype 7F (51)	25296-5
23966	Serotype 15B (54)	40973-0
23967	Serotype 18C (56)	27395-3
23968	Serotype 19A (57)	40974-8
23969	Serotype 9V (68)	30153-1
23970	Serotype 33F (70)	40969-8