Specific Antibody Deficiency (SAD) / Specific Polysaccharide Antibody Deficiency (SPAD)

Most people have normal blood levels of the 3 main Immunoglobulin / antibody types that protect them from disease-causing bacteria and viruses (IgM, IgA and IgG *IgG has 4 different sub-types, IgA has 2). Unfortunately, some people who produce normal immunoglobulin levels (normal quantities) lack the ability to produce protective IgG antibodies against **certain types of bacteria** that frequently cause upper and lower respiratory tract infections. This "hole" in the immune system is called Specific Antibody Deficiency (SAD) or sometimes termed "Specific Polysaccharide Antibody Deficiency" (SPAD).

Definition of Specific Antibody Deficiency

Each individual IgG antibody molecule type is uniquely designed to protect against a specific type of disease-causing organism and these "specific antibodies," are formed either in response to natural exposures (Infections), or through exposure to vaccines. Specific antibodies can be measured in the laboratory, and these levels (called titers) are used to help diagnose active or past diseases or to assess problems with protective immunity.

Bacteria such as: Streptococcus pneumoniae, Neisseria meningitidis, Klebsiella pneumoniae and Hemophilus influenza-B surround themselves with a capsule of Polysaccharides (sugars) that hides their cell surface proteins from the immune system. A normal immune system is capable of making protective antibodies against most foreign proteins and can also make effectively antibodies against sugar capsules. Unfortunately, a small number of people do not make protective immunity after infections with encapsulated bacteria and so they can get these infections again and again. Since Streptococcus pneumoniae bacteria are the most common causes of ear and sinus infections, persons with recurrent ear and sinus infections should be testing to evaluate their immunity against these bacteria. When natural immunity is found to be low, a vaccine called Pneumovax (PPSV-23) is used to boost these antibody levels (PPSV-23 contains 23 types of Strep. pneumo.). Children and adults who have normal, or near normal levels, of IgG, IgM and IgA but fail to develop protective immune responses after vaccination with PPSV-23, are diagnosed with Specific Antibody Deficiency (SAD / SPAD). *Most experts agree that a protective level of antibody to Streptococcus pneumoniae bacteria is >1.3 mcg/ml.

Specific IgG antibodies are very important in fighting infections; however, contributions from other components of the immune system are often needed to effectively eradicate bacteria and viruses. White blood cells (Neutrophils, monocytes and lymphocytes), serum Complement proteins and IgM and IgA antibodies are often involved in effective immune responses. The co-existence of an IgA, or an IgG subclass deficiency with PPSV-23 unresponsiveness can make the risk for recurrent infections even higher.

Clinical Presentation of Specific Antibody Deficiency

Recurrent ear infections, sinusitis, bronchitis and occasionally pneumonia or meningitis are the most frequently observed illnesses in patients with SAD. While some patients will show an increased

frequency of infection beginning in the first few years of life, the onset of recurrent infections may occur much later as an adult. Often a child with SAD will first come to the physician's attention because of recurrent ear infections. Children receive 4 pneumococcal vaccinations (Prevnar-13) before the age of 2 however, some children fail to respond adequately to this vaccine and remain unprotected. In general, the infections suffered by persons with SAD are not as dangerous as those suffered by those who have very low levels of IgG, IgM and/or IgA; *like Common Variable Immune Deficiency (CVID). CVID is an example of an Immunodeficiency where there are defects in both Immunoglobulin protection and white blood cell (Lymphocyte) functions.

Diagnosis of Specific Antibody Deficiency

When Specific Antibody Deficiency is suspected in children or adults, the recommended initial evaluation includes measurement antibody titers to Streptococcus pneumoniae and quantitative Immunoglobulin level testing (IgG, IgM, IgA). Although there have been over 100 serotypes (strains) of S. pneumonia isolated, 23 of these strains are currently responsible for about 90% of all pneumococcal infections. If initial testing shows low natural antibody protection to the most common types of *Streptococcus pneumoniae*, repeat testing is done one month after vaccination with PPSV23 (Pneumovax) *Although there is another pneumococcal vaccine, called Prevnar-20 / PCV-20, this vaccine is not used for an initial immune system assessment.

A study performed in our clinic found that patients between 1-8 year of age who had been immunized with the only ½ of the adult dose (0.25cc instead of 0.5cc) responded well to the lower dose and experienced fewer vaccine-related side-effects. It is has been found that Immunologically normal individuals respond well to the majority of the serotypes found in the unconjugated 23-serotype vaccines (PPSV-23) after age 1 and ***typically*** retain protective antibody levels for about 5 years or more *Occasionally, some persons with SAD will loose their protective vaccine generated antibodies faster than 5 years. There are some persons with SAD who will lose antibody protection faster than others and may need more frequent re-vaccinations. The criteria for the diagnosis of SAD have been somewhat controversial however, most Immunologists now agree that one month after receiving the PPSV-23 vaccine, both children and adults with normal total IgG levels (with or without IgG subclass deficiency) are likely to have SAD /SPAD if they responded inadequately (levels <1.3 ug/ml) to less than 70% of the 23 different vaccine serotypes (< 17 / 23).

As of 2016, it is recommended that children under 15 months of age receive a 4 shot series of Prevnar (PCV13), this conjugated pneumococcal vaccine (Sugar capsules bound to Diptheria proteins) may be more likely to stimulate an immune response to pneumococci than PPSV-23 however, the immune response to PCV13 (or PCV-20) vaccines cannot be used to diagnose SAD. In our experience, when persons with SAD are vaccinated with conjugated vaccines (PCV-13 or 20), there is rarely any notable improvement in antibody protection above that seen initially with PPSV-23.

Inheritance of Specific Antibody Deficiency

No clear-cut pattern of inheritance has been observed with SAD however, anecdotally, SAD seems to run in many families (Genetic factors are likely).

The Natural History of Specific Antibody Deficiency.

The natural history of patients with SAD is not completely understood. SAD seems to be diagnosed more often in adults, possibly because many physicians mistakenly assume that children who receive PCV13 will always mount a good vaccine response and therefore, they rarely test for vaccine responses this age group. Unfortunately, this assumption is often found to be incorrect, especially when children stand-out from their peers in terms of recurrent ear and sinus infections. Immune testing for pneumococcal antibodies should be considered for any child who has received the PCV-13 series but still appears to have more frequent respiratory infections. Some children diagnosed with SAD may "outgrow" this condition however, adults with similar symptoms and a poor response to PPSV-23 vaccination are less likely to improve over time. Both IgG subclass deficiencies and SAD may evolve into a more severe immune condition called ***Common Variable Immunodeficiency*** (CVID). Because it is not possible to determine which SAD patients will progress, periodic re-evaluation of immunoglobulin levels and specific antibody titers is necessary in persons diagnosed with SAD who show clinical worsening with a pattern of frequent respiratory infections.

Treatment of Specific Antibody Deficiency

Patients with SAD frequently suffer from recurrent or chronic infections of the ears, and para-nasal sinuses. Treatment of these infections usually requires antibiotics however, anecdotally, we have found that prophylactic daily nasal rinsing with **hypertonic** saline and **xylitol** (Using a NeilMed bottle) may reduce the risk for recurrent infections *Hypertonic saline seems to inhibit Pneumococcal bacterial growth and Xylitol can decrease bacterial adherence to mucous membranes of the nose. The "wait and see" approach for recurrent sinusitis without prophylactic sinus rinsing is rarely a fruitful strategy. One goal of aggressive (early) treatment of infections is to prevent permanent damage to the ears and lungs that might result in hearing loss or chronic lung disease from scarring. Another goal is to maintain patients as symptom-free as possible so that they may pursue the activities of daily living at home, school or work. Sometimes antibiotics may be used for prevention (prophylaxis) of infections however, this is strategy not a part of our routine practice. Laboratory cultures of purulent discharge blown from the nose (Not nasal swabs) may be useful for directing effective antibiotic selection and, in our practice, frequently isolated unusual pathogens (MDRSP, MRSA, Gram neg. bacteria etc.) has significantly impacted our prescribing habits.

The effectiveness of Immunoglobulin replacement therapy for person with SAD, with or without IgG subclass deficiency, is not as clear-cut as it is for those with more severe Immunodeficiency like CVID. ***For the great majority of patients with SAD, infections can be controlled with culture-directed antibiotics and High-salt / Xylitol sinus rinsing and IgG replacement therapy is not necessary.*** However, for occasional patients, whose frequent infections cannot be controlled, other risk factors for recurrent sinusitis, such as sinus structural problems or severe environmental allergy, should be investigated.

Since many young children appear to outgrow SAD as their immune systems mature, it is important to periodically re-evaluate for specific antibody levels and consider periodic re-immunization with the pneumococcal vaccines. If the diagnosis of SAD is made in a teenager or adult, resolution of this Immunodeficiency is less likely to occur.

Expectations for Patients with Specific Antibody Deficiency

The outlook for patients with SAD is generally good if there are minimal other risk factors. If the use of hypertonic saline / xylitol sinus rinses fails to effectively mitigate against recurrent infections, sinus surgery to correct anatomic anomalies and allergy shots for severe allergic rhinitis should be considered.

*Anecdotally, at Alamo Asthma & Allergy Associates we have found that many persons with SAD / SPAD respond well to COVID vaccinations (Making high titers of IgG to spike protein) however, about 7% of persons under age 60 in the general population are non-responders to COVID vaccine and so eventually; finding non-responders among the SAD population would also be expected.

Portions of this information were adapted from the *IDF Patient & Family Handbook for Primary Immunodeficiency Diseases FIFTH EDITION*. Copyright 2013 by Immune Deficiency Foundation, USA. These pages contain general medical information and anecdotal clinical experiences which cannot be applied safely to any individual case. Medical knowledge and practice can change rapidly. Therefore, this information should not be used as a substitute for professional medical advice.
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