AS WE DISCUSSED in previous columns, an antibody deficiency disorder can be diagnosed in two ways: 1) deficient serum IgG levels, usually accompanied by deficient IgA and/or IgM levels, in a patient who also fails to make appropriate specific antibodies (such as in X-linked agammaglobulinemia) or 2) normal IgG, IgA and IgM serum levels in a patient who fails to make specific antibodies.

Whether a patient makes specific antibodies can be determined by performing pre- and post-immunization antibody titer analyses to pneumococcal vaccine. For instance, a poor response to pneumococcal vaccination, whether a patient has low IgG (and/or IgA and IgM) levels or normal serum IgG, IgA and IgM levels, can be a determinant of a specific antibody deficiency (SAD). However, many medical and insurance personnel may be confused by a SAD diagnosis for patients with normal serum IgG, IgA and IgM levels, even though these patients respond poorly to pneumococcal vaccination. It's a common misconception that if the IgG serum levels are normal, then the humoral immune system must be normal. That is wrong! The humoral immune system (antibodies and complement proteins) may be within normal parameters only when appropriate specific antibody levels are made and maintained after pneumococcal vaccination.

Currently, 23 different strains of pneumococcal bacteria are used to make up the pneumococcal vaccine. Since each strain will result in the production of a “unique” antibody, the term “serotype” is used to denote each strain and the antibody directed against it. Therefore, 23 pneumococcal serotypes can be identified in the vaccine, and they are composed of 23 unique antibodies and the “strength” of each antibody response, which is called the “titer.” Thus, 23 serotype titers can be determined from the pneumococcal vaccine.

To perform a pneumococcal assay, first a blood sample is taken from a patient (pre-immunization serum), and then the pneumococcal vaccine is given. In approximately four weeks, another blood sample is obtained for the post-immunization serum. Both sera are then assayed to obtain specific titer values.

The number of serotype titers analyzed has changed over the years. Initially, as few as four serotypes were analyzed. This grew to seven, 10, 12, 14, 15 and, now, to the full 23 serotypes. Many studies comparing the assay regarding the potential for diagnosing an antibody deficiency have looked at the responses of 10 to 15 serotypes. Based on these studies, a consensus has developed concerning the interpretation of the results. In general, a titer value exceeding 1.3 mcg/mL is defined as protection against the specific pneumococcal serotype tested, whereas values less than 1.3 mcg/mL are defined as not protective. Previously, the titer value was considered a meaningful immune response if there was a fourfold increase between the pre- and post-immunization titers (example: if pre = 4 mcg/mL, then post >16 mcg/mL would be considered normal). Now, if the pre-immunization titer is greater than 1.3 mcg/mL, then a twofold increase may be accepted as normal (example: if pre = 4 mcg/mL, then post >8 mcg/mL is considered normal). For nonprotective pre-immunization titers, the post-immunization titer values should increase into the protective range, with a threefold increase expected. For very low pre-immunization titers, a fourfold increase into the protective post-immunization range is expected.

The next issue considered is the “number” of appropriately protective post-immunization serotype titers. For children between 2 and 6 years of age, “normal” is defined by having more than 50 percent of the post-immunization titers well into the protective range, with titer increases of twofold to fourfold, depending on how low the pre-immunization titers were. For adults, it is 75 percent.

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Editor’s Note: This Immunology 101 column, introduced in the April-May 2010 issue of IG Living, is intended to be a basic course in immunology.