

# SELECTIVE IgA DEFICIENCY



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**DEFINITION:** Selective IgA Deficiency is the severe deficiency or total absence of the IgA class of immunoglobulins in the blood serum and secretions. There are five types (classes) of immunoglobulins or antibodies in the blood: IgG, IgA, IgM, IgD, and IgE. The immunoglobulin class present in the largest amount in blood is IgG, followed by IgM and IgA. IgD and IgE are present in very small amounts in the blood.

Of these immunoglobulin classes, it is primarily IgM and IgG that protect the bloodstream, body tissues, and internal organs from infection. It is also important that the body is protected at surfaces that come in close contact with the environment. These sites are the mucosal surfaces: the mouth and nose, the throat, the airways within the lung, the gastrointestinal tract, the eyes, and the genitalia. The IgA antibodies (which are transported in secretions to mucosal surfaces) play a major role in protecting mucosal surfaces from infection. IgG, IgM and IgE antibodies are also found in secretions at mucosal surfaces, but not in the same amount as the IgA antibody. This is why IgA is known as the secretory antibody. If our mucosal surfaces were spread out they would cover any area equal to one and one half tennis courts, so the importance of IgA in protecting our mucosal surfaces cannot be overstated.

IgA has some special chemical characteristics. It is present in secretions as two antibody molecules attached by a component called the J chain ("J" for "joining") (*see chapter on Immune System*). In order for these antibodies to be secreted, they must also be attached to another molecule called the secretory piece. The IgA unit that protects the mucosal surfaces is actually composed of

two IgA molecules joined by the J chain and attached to the secretory piece.

Individuals with Selective IgA Deficiency do not produce IgA. They do, however, produce all the other immunoglobulin classes. In addition, the function of their T-lymphocytes, phagocytic cells and complement system are normal or near normal. Hence, this condition is known as "Selective" IgA Deficiency.

The cause or causes of Selective IgA Deficiency are unknown. It is likely that there are a variety of causes for Selective IgA Deficiency and that the cause may differ from patient to patient. Individuals with Selective IgA Deficiency have B-lymphocytes that appear to be normal, but do not mature into IgA producing plasma cells.

**CLINICAL FEATURES:** Selective IgA Deficiency is the most common primary immunodeficiency disease. Studies have indicated that as many as one in every five hundred people have Selective IgA Deficiency. Many of these individuals have relatively mild illnesses and are generally not sick enough to be seen by a doctor. Therefore, they are never discovered to have IgA deficiency. In fact, the majority of individuals with Selective IgA Deficiency are relatively healthy and free of symptoms. In contrast, there are also individuals with Selective IgA Deficiency who have significant illnesses. Currently, it is not understood why some individuals with IgA deficiency have almost no illness while others are very sick. Studies have suggested that some patients with IgA deficiency may be missing a fraction of their IgG (the IgG2 subclass) and that may be one explanation of why some patients with IgA deficiency are more susceptible to infection than others.

A common problem in IgA deficiency is susceptibility to infections. Recurrent ear infections, sinusitis, bronchitis and pneumonia are the most common infections seen in patients with Selective IgA Deficiency. This is easy to understand because IgA protects mucosal surfaces from infections. These infections may become chronic. Furthermore, the infection may not completely clear with treatment, and patients may have to remain on antibiotics for longer than usual.

A second major problem in IgA deficiency is the occurrence of autoimmune diseases. In autoimmune diseases an individual produces antibodies or T-lymphocytes which react with his/her own tissues with resulting damage to these tissues. Some of the more frequent autoimmune diseases associated with IgA deficiency are: Rheumatoid Arthritis, Systemic Lupus Erythematosus and Immune Thrombocytopenic Purpura (ITP). These autoimmune diseases may cause sore and swollen joints of the hands or knees, a rash on the face, anemia (a low red blood cell count) or thrombocytopenia (a low platelet count). Other kinds of autoimmune disease may affect the endocrine system and/or the gastrointestinal system.

Allergies may also be more common among individuals with Selective IgA Deficiency than among the general population. The types of allergies vary. Asthma is one of the common allergic diseases that occurs with Selective IgA Deficiency. It has been suggested that asthma may be more severe, and less responsive to therapy, in individuals with IgA deficiency than it is in normal individuals. Another type of allergy associated with IgA deficiency is food allergy, in which patients have reactions to certain foods. Symptoms associated with food allergies are diarrhea or abdominal cramping. It is not certain whether there is an increased incidence of allergic rhini-

tis (hay fever) or eczema in Selective IgA Deficiency.

Another unusual, but important, form of allergy may also occur in IgA deficiency. In people whose blood contains no IgA, IgA from other individuals may be recognized by the immune system as a foreign protein. Because antibodies are normally made against foreign proteins, some people with Selective IgA Deficiency make an IgG or IgE antibody against IgA. In this situation, if an IgA deficient person who has antibodies against IgA receives a blood product that contains IgA, an allergic reaction may result. Although allergic reactions to IgA are very uncommon, it is important that every patient with Selective IgA Deficiency is aware of the potential risk of transfusion reactions if they receive blood or blood products.

**DIAGNOSIS:** The diagnosis of Selective IgA Deficiency is usually suspected because of either chronic or recurrent infections, allergies, autoimmune diseases, or chronic diarrhea. The diagnosis is established when tests of the patient's blood serum demonstrate a marked reduction or near absence of IgA with normal levels of the other major classes of immunoglobulins (IgG and IgM). Most patients make antibodies normally. An occasional patient may also have IgG2 subclass deficiency and associated antibody deficiency (*see chapter on IgG Subclass Deficiency*). The numbers and functions of T-lymphocytes are normal.

Several other tests that may be important include a complete blood count, measurement of lung function, and a urinalysis. Other tests that may be obtained in specific patients include measurement of thyroid function, measurement of kidney function, measurements of absorption of nutrients by the GI tract, and the test for antibodies directed against the body's own tissues (autoantibodies).

**TREATMENT:** The currently available preparations of gamma globulin do not contain significant amounts of IgA. Even if such products could be prepared, there is no way to cause IgA administered by injection to find its way to the mucous membranes that lack this immunoglobulin. Therefore, it is not currently possible to replace IgA in IgA deficient patients. However, an occasional patient who has IgA deficiency also has IgG2 subclass deficiency with a deficiency of antibody production. In these individuals, the use of replacement gamma globulin may be helpful in diminishing the frequency of infections (*see also chapter on Specific Medical Therapy*).

Treatment of the problems associated with Selective IgA Deficiency should be directed toward the particular problem. For example, patients with chronic or recurrent infections need appropriate antibiotics. Ideally, antibiotic therapy should be directed at the specific organism causing the infection. It is not always possible to identify these organisms, however, and the use of broad-spectrum antibiotics may be necessary. Certain patients who have chronic sinusitis or chronic bronchitis may need to stay on long term antibiotic therapy. It is important that the doctor and the patient communicate closely so that appropriate decisions can be reached for therapy.

There are a variety of therapies for the treatment of autoimmune diseases. Anti-inflammatory drugs, such as aspirin or ibuprofen, are used in diseases that cause joint inflammation. Steroids may be helpful in a variety of autoimmune diseases. If autoimmune disease results in an abnormality of the endocrine system, replacement therapy with hormones may be necessary.

Treatment of the allergies associated with IgA deficiency is similar to treatment of allergies in general. It is not known whether immunotherapy (allergy shots) is helpful in the allergies associated with Selective IgA Deficiency.

As a matter of precaution, it may also be desirable to test the blood of a patient with Selective IgA Deficiency for antibodies against IgA in order to prepare for the possibility that the patient may need a blood transfusion.

The most important aspect of therapy in IgA deficiency is close communication between the patient (and/or the patient's family) and the physician so that problems can be recognized and treated as soon as they arise.

**EXPECTATIONS:** Although Selective IgA Deficiency is one of the milder forms of immunodeficiency, it may result in severe disease in some people. Therefore, it is difficult to predict the long-term outcome in a given patient with Selective IgA Deficiency. In general, the prognosis in Selective IgA Deficiency depends on the prognosis of the associated diseases. It is important for physicians to continually assess and reevaluate patients with Selective IgA Deficiency for the existence of associated diseases and the development of more extensive immunodeficiency. For example, rarely, IgA deficiency will progress to become Common Variable Immunodeficiency with its deficiencies of IgG and IgM. The physician should be notified of anything unusual, especially fever, productive cough, skin rash or sore joints. The key to a good prognosis is adequate communication with the physician and the development of effective therapeutic strategies as soon as disease processes are recognized.

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