

Immunodeficiency: Antibody

Caroline Ward, University of Bristol, UK



There are several mechanisms by which a person may fail to produce adequate levels of antibodies (Ab), resulting in a clinical antibody deficiency and an inability to eliminate microbial pathogens effectively from the body. Without early recognition and adequate replacement of Ab, structural damage to organs may occur due to recurrent infections. Fortunately, these conditions are rare – however this means that it can be difficult to diagnose them quickly.

Causes

Ab deficiencies may be primary, or secondary to other conditions.

Causes of secondary Ab deficiency include common conditions like **haematological malignancies** and **immunosuppressive drug therapy**, e.g. after **organ transplantation** or for **autoimmune conditions** like **rheumatoid arthritis**. In these cases, there are decreased B-cell numbers, so Ab are not made in adequate quantities. Rarer causes include protein loss, for example due to malnutrition or protein-losing enteropathy. Since Ab are proteins, this can also lead to Ab deficiency.

Primary Ab deficiencies are rare conditions. The commonest is **IgA deficiency**, which often remains undetected as it does not always produce clinical symptoms. Next most common are the **common variable immunodeficiency disorders (CVIDs)** and these represent a group of probable genetic conditions with the unifying phenotype of Ab deficiency, although there are other associated conditions including lymphoma, granuloma and a variety of autoimmune diseases. Ab failure can occur at any age and the hallmark recurrent infections may develop after the onset of other complications. Other primary Ab deficiencies include **Bruton's X-linked agammaglobulinaemia** and **hyper-IgM syndrome**.

Features of Ab deficiency

Infections are suspicious if they are:

SEVERE
PERSISTENT
UNUSUAL
RECURRENT

Patients with recurrent (several in a year) severe infections, especially with encapsulated bacteria, that do not clear after a normal course of antibiotics and that may be due to unusual organisms (e.g. ureaplasma) should be suspected of having an Ab deficiency and referred to a clinical immunologist. The diagnosis is confirmed by measuring serum immunoglobulin levels and by administration of test immunisations with pneumococcus and influenza vaccine, with the level of specific Ab produced being assayed three weeks later.

Treatment

It is not currently possible to cure primary Ab deficiency, so lifelong therapy is required. This involves the **intra-venous or sub-cutaneous infusion of Ab preparations** at 2–3 week intervals. The Ab used are purified from pooled blood donations and are very expensive. In addition, since patients may still have infections despite treatment, it is important to be vigilant for signs of structural damage, e.g. with regular **CT scans** of the chest looking for **bronchiectasis**. Despite treatment, patients still require longer courses of antibiotics to treat breakthrough infections. Patients are likely to develop associated conditions, including autoimmune and malignant diseases, so it is important to detect and treat these.

If an Ab deficiency is secondary to another condition, the patient may recover when the underlying problem is treated or it may persist despite treatment of the cause or removal of the drug responsible. These people may also need therapy with exogenous Ab.