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IgA deficiency and autoimmunity.

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Abstract

IgA is the most abundant immunoglobulin in the human body, and performs a very specialized role which involves mucosal immunity, development of tolerance and protection against infection. IgA is the key immunoglobulin in the respiratory and gastrointestinal tracts, which provide the most intimate interface between the environment and self. Normal levels of IgA are based on early studies consisting of only small numbers of patients. The international consensus definition of IgA deficiency is a level of 0.07g/l after the age of four years in the absence of IgG and IgM deficiencies. The epidemiology of IgA deficiency reveals interesting variances between geographical regions - the incidence in Caucasians being much higher than that in Asians. IgA deficiency has also been found to co-exist with autoimmune diseases, allergies and malignancies. The association with autoimmunity is particularly interesting because it suggests a common genetic linkage that could potentially also explain the diversity in geoepidemiology. Both MHC and non-MHC associations have been described and the 8.1 haplotype has been significantly associated with autoimmunity in IgA deficiency patients over controls. Non-MHC genetic associations include IFIH1 and CLEC16A. The mutations leading to IgA deficiency have not been defined, but in some cases of IgA deficiency it has been suggested that the pathogenesis involves a failure in switched memory B cells that can lead to this cohort experiencing an increased incidence of recurrent bacterial infections or autoimmune diseases. Attempts to investigate the role of cytokines that can induce IgA synthesis in cells of patients with IgA deficiency, such as IL21 or the combination of CD40L/anti-CD40, IL-4 and IL10, are underway.