

ADRENAL ANTIBODIES

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This article describes adrenal antibodies and explains how tests for these antibodies can be used to diagnose and sometimes predict autoimmune adrenal insufficiency.

Testing for Adrenal Antibodies

Tests for adrenal antibodies are used to diagnose autoimmune adrenal insufficiency. The term adrenal antibodies refers to several different autoantibodies that are directed against the adrenal cortex, the outer layer of tissue surrounding each of the adrenal glands. Adrenal antibodies are also known as adrenocortical antibodies or, more accurately, adrenocortical autoantibodies (ACA). ACA destroy adrenal tissue, interfering with hormone production, by damaging various adrenal proteins, particularly the 21-hydroxy enzymes. For this reason, 21-hydroxy or 21-OH antibodies are considered more sensitive indicators of autoimmune adrenal insufficiency. Other adrenal antibodies that may occur but are rarely tested for include antibodies to 17-alpha-hydroxylase and antibodies to the P450 side-chain cleavage enzyme (P450_{scc} antibodies). Today, most doctors order tests for both ACA and 21-OH antibodies to evaluate patients for adrenal insufficiency.

Adrenal Insufficiency

Approximately 75-80 percent of all cases of primary adrenal insufficiency or Addison's disease have an autoimmune origin. That is, about 75-80 percent of patients with Addison's disease have adrenal antibodies. 100 percent of patients with autoimmune polyglandular syndromes have adrenal antibodies. Besides autoimmunity, other causes of Addison's disease include infection, metastatic cancers, conditions of adrenal leukodystrophy, hemorrhage in patients on high doses of anticoagulant medications, congenital disorders, and patients with antiphospholipid syndrome. The highest levels of ACA are usually seen early in the disease course and high titers correlate with disease severity.

It's still uncertain if the production of adrenal antibodies by the immune system is the result of an autoantigen-driven immune mechanism or the consequence of adrenal tissue destruction. Recent theories of autoimmune disease suggest that autoantibodies primarily target tissue enzymes, such as 21-OH, and that this is the primary mode of tissue destruction. This suggests that autoantibodies are more likely the cause than the consequence.

Incidence of Adrenal Antibodies

Some people with a family history of autoimmune adrenal disease and also autoimmune thyroid disease, autoimmune hypoparathyroidism, primary ovarian failure, atrophic gastritis, vitiligo or insulin-dependent diabetes mellitus may also have adrenal antibodies without having any signs of adrenal insufficiency. In a study of 3,020 patients with the

autoimmune disorders listed above, 26 patients or 0.9 percent of people with non-adrenal autoimmune disorders were found to have ACA. 19 of these patients were studied over the course of 4-5 years to see if they eventually developed adrenal insufficiency. The other patients either started corticosteroid therapy and had to drop out of the study or were no longer available. Of the 19 patients, 3 had 21-OH antibodies before developing ACA antibodies indicating that tests for 21-OH antibodies may be more sensitive indicators of adrenal autoimmunity in some cases.

All of the patients were evaluated for adrenal insufficiency using tests for ACTH (adrenocorticotropin hormone), cortisol, aldosterone, ACTH stimulation tests, and plasma rennin activity, which is an indicator of fluid balance. Using these testing parameters to grade patients, 5 stages of adrenal insufficiency (with 5 being most severe) can be determined, with the grades showing both aldosterone and cortisol deficiencies. Although the patients in this study initially had no symptoms of adrenal disease, 15 of 19 had test abnormalities at the start of the study that gave them adrenal insufficiency scores between 1 and 4. It should be noted that most studies show that symptoms of adrenal insufficiency often do not occur until 90 percent of the adrenal gland tissue has been destroyed.

All patients (9 of 19 or 42 percent) of these subjects (representing less than 0.05 percent of autoimmune disease patients) who were found to be in stage 2 or 3 of adrenal insufficiency at the onset of the study progressed to stage 3 or 4 by the end of the study. An additional 32 percent of patients, who initially had stage 1 results progressed to stages between 2-4. In 26% of patients (all females), antibodies declined and patients showed no signs of adrenal insufficiency at the end of the study. The patients who showed signs of increased adrenal insufficiency at the end of the study showed significant increases in their levels of ACA and 21-OH antibodies by the end of the study.

A similar study involving 2571 patients also showed an ACA prevalence rate of 0.9 percent in patients with other non-adrenal autoimmune disorders. This study also showed that the HLA marker B8 and to a lesser extent DR3 are associated with the development of ACA. Patients with autoimmune thyroid disease, gluten sensitivity and type 1 antibodies also have a high association with these markers.

These studies show that the presence of adrenal antibodies in adults doesn't necessarily predict progressive adrenal disease, and that higher antibody levels correlate with disease severity. Positive results for 21-OH antibodies are also more sensitive indicators of aggressive disease. However, other studies have shown that the presence of 21-OH antibodies in children is more predictive for future development of Addison's disease. The initial concentration of the antibodies also clearly correlated with disease progression. For this reason children with diabetes are now being routinely tested for these antibodies.

Additional follow-up with these and other studies show that although patients with other autoimmune diseases may develop adrenal antibodies, the highest risk of developing autoimmune adrenal insufficiency occurs in relatives of patients with autoimmune adrenal insufficiency (both Addison's disease and the polyglandular autoimmune

syndromes I and II), and patients with other autoimmune hypoparathyroidism, chronic yeast infection (*Candida albicans* infection or candidiasis) and premature ovarian failure.

References:

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