

Epithelial Skin Antibody

DIAGNOSTIC TESTS FOR IMMUNOBULLOUS DISEASES OF SKIN AND MUCOUS MEMBRANES

Introduction

- Autoimmune blistering diseases affect skin and mucous membranes and are caused by the deposition of specific antibodies on cutaneous structures.
- In pemphigus (all types), antibodies bind to cell surfaces (formerly referred to as intercellular substance) of epidermal and stratified squamous epithelial cells in and around affected areas. Because of this, blistering occurs within the epidermis of hairy and glabrous skin or within epithelium of mucous membranes. Cell surface antibodies circulate in the blood in up to 80 percent of patients with pemphigus. Therefore, detection of circulating cell surface antibodies can be used as a sensitive and specific diagnostic test for pemphigus. In addition, levels of these antibodies correlate with disease activity and can be used to monitor response to therapy. In most types of pemphigus, IgG antibodies bind to cell surface proteins. In a rare form of pemphigus, IgA antibodies bind to cutaneous cell surfaces and are detectable when they circulate in blood.
- In pemphigoid (all types), blistering occurs in a subepidermal or subepithelial location, and IgG antibodies bind to basement membrane zone components. These antibodies circulate in the blood in up to 80 percent of patients and bind to the epidermal side of skin split at the basement membrane zone. Dermal binding may also be present in pemphigoid, demonstrating a combined pattern with both epidermal and dermal localization. In epidermolysis bullosa acquisita, blistering also occurs in a subepidermal location, and IgG antibodies also bind to basement membrane zone components. However, in epidermolysis bullosa acquisita, IgG basement membrane zone antibodies bind exclusively to the dermal side of split skin. Therefore, detection of circulating IgG basement membrane zone antibodies, along with their basement membrane zone localization, can be used as sensitive and specific diagnostic tests for pemphigoid and epidermolysis bullosa acquisita. Moreover, these tests permit distinguishing the two diseases, whereas tissue studies will show similar findings in both diseases.
- Herpes gestationis, also referred to as pemphigoid gestationis, is a variant form of pemphigoid occurring in pregnancy and the puerperium in which complement-activating, basement membrane-binding antibodies are present in the circulation. With modification in indirect immunofluorescence testing to add a fresh source of complement, these antibodies can be detected for diagnosis (test number 0092105).
- Linear IgA bullous dermatosis and bullous disease of childhood are subepidermal blistering diseases in which IgA antibodies bind to basement membrane zone components. These antibodies circulate in blood in up to 80 percent of patients. Testing for IgA basement membrane zone antibodies is a sensitive and specific test for these diseases and permits distinguishing them from other subepidermal blistering diseases.

Clinical Significance

- The clinical courses of various cutaneous blistering diseases differ, as do their responses to treatment. Although immunobullous diseases have certain clinical and histological features that characterize them, often their presentation is atypical and/or shows overlap with other diseases. Therefore, it is important that diagnostic tests are able to distinguish them. Diagnosis of immune-mediated diseases of skin and other epithelial organs is aided by specific immunodermatologic testing.
- Testing for cell surface antibodies is important in establishing the diagnosis of pemphigus (all types). Desmoglein antibody testing (performed as a separate test, 0090649), in conjunction with both IgG and IgA cell surface antibody testing, can help distinguish types of pemphigus. Moreover, because antibody titers correlate with disease severity, the results can be used to monitor disease activity and response to treatment.
- Testing for basement membrane zone antibodies is important in establishing the diagnosis of pemphigoid (all types) and epidermolysis bullosa acquisita. Localization of antibody binding distinguishes the types of subepidermal immunobullous diseases, knowledge of which is useful in planning therapy. Testing for antibodies to specific bullous pemphigoid antigens (performed as a separate test, 0092566), in conjunction with both IgG and IgA basement membrane zone antibody testing, may be useful in monitoring disease activity and response to treatment.

Indications for Ordering

- Testing for epidermal antibodies is appropriate for patients suspected of having or known to have immunobullous disease, including all types of pemphigus, all types of pemphigoid, herpes gestationis, epidermolysis bullosa acquisita, linear IgA bullous dermatosis, and childhood immunobullous disease.
- Cell surface and basement membrane zone antibody testing by indirect immunofluorescence is well established for the diagnosis of these diseases alone or in conjunction with direct immunofluorescence of tissue (test number 0092572). This testing is helpful in distinguishing subtypes of subepidermal immunobullous disease; there is no other testing to do so. An important consideration is the clinical variability with which immune-mediated skin diseases present. Pemphigoid may have an urticarial phase for months or longer before blistering develops, and several disorders may resemble common dermatoses, potentially causing delay in diagnosis and treatment if not tested appropriately.
- Because normal individuals may have low titer circulating cell surface or basement membrane zone antibodies, interpretation of results should be done along with clinical correlation.

Interpretation

- Cell surface and basement membrane zone serum antibody titers < 1:10 are negative. Titers of 1:10 are borderline/indeterminate, and continued monitoring of patient for disease activity is recommended. Low titer cell surface antibodies may rarely be found in patients with burns, drug reactions, fungal infections, or other inflammatory diseases. Low titer cell surface and basement membrane zone antibodies may be found rarely in normal individuals.
- Positive results are any of the following:
 - IgG cell surface (intercellular substance) antibody titer > 1:10
 - IgA cell surface (intercellular substance) antibody titer > 1:10
 - IgG basement membrane zone antibody titer > 1:10 (see pattern)
 - IgA basement membrane zone antibody titer > 1:10 (see pattern)
- BMZ Pattern:
 - Epidermal or combined, epidermal and dermal: IgG basement membrane zone antibody binding pattern is diagnostic of pemphigoid (all types).
 - Dermal IgG basement membrane zone antibody binding pattern is diagnostic of epidermolysis bullosa acquisita.
 - Epidermal, combined, or, rarely, dermal: IgA basement membrane zone binding pattern is diagnostic of linear IgA bullous dermatosis.

Related Tests

- IgG Desmoglein 1 & Desmoglein 3 (0090649)
- Bullous Pemphigoid (180 kDa & 230 kDa) Antigens, IgG (0092566)
- Cutaneous Direct Immunofluorescence, Biopsy (0092572)

References

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4. Harman KE. New laboratory techniques for the assessment of acquired immunobullous disorders. *Clin Exp Dermatol* 2002;27:40–6.
5. Anhalt GJ, Diaz LA. Research advances in pemphigus. *JAMA* 2001;285:652–4.

Test Information

0090299

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For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.