



<u>Procedure</u>	<u>Result</u>	<u>Units</u>	<u>Ref Interval</u>	<u>Accession</u>	<u>Collected</u>	<u>Received</u>	<u>Reported/</u> <u>Verified</u>
Pemphigus Antibody Panel, IgG	See Note	f@		19-128-402215	07-May-19 17:09:00	10-May-19 07:45:00	14-May-19 13:54:29
EER Pemphigus Antibody Panel, IgG	See Note	f@		19-128-402215	07-May-19 17:09:00	10-May-19 07:45:00	14-May-19 13:54:29
Basement Membrane Zone Ab Panel	See Note	f@		19-128-402215	07-May-19 17:09:00	10-May-19 09:16:00	14-May-19 13:54:03
EER Basement Membrane Zone Ab Panel	See Note	@		19-128-402215	07-May-19 17:09:00	10-May-19 09:16:00	15-May-19 09:58:03

* Abnormal, # = Corrected, C = Critical, f = Footnote, H = High, L = Low, t = Interpretive Text, @ = Reference Lab

07-May-19 17:09:00 Pemphigus Antibody Panel, IgG:
IMMUNODERMATOLOGY LABORATORY

Specimen(s):
1. Serum specimen

Clinical/Diagnostic Information:
No clinical information provided.

DIAGNOSTIC INTERPRETATION

Negative/normal IgG Pemphigus Antibody Panel for IgG cell surface antibodies with positive IgG basement membrane zone antibodies (pemphigoid or epidermolysis bullosa acquisita) by indirect immunofluorescence and concurrent testing consistent with pemphigoid

(See Results, Comments, and separate concurrent Basement Membrane Zone Antibody Panel testing report with positive findings and additional comments)

RESULTS

Indirect Immunofluorescence

Cell Surface IgG Antibodies

IgG: Negative, monkey esophagus substrate
Negative, intact human skin substrate

Positive IgG basement membrane zone antibodies, monkey
esophagus and intact human skin substrates

Reference Range:

Positive - Titer greater than 1:10
Borderline - Titer 1:10
Negative - Titer less than 1:10

(H = high/positive)

Enzyme Linked Immunosorbent Assay (ELISA)

Desmoglein (DSG) 1 and 3 IgG Antibodies

IgG desmoglein 1 antibodies: 0 units

Reference Range:

Positive (H) = Greater than 20 units
Borderline/Indeterminate = 14-20 units
Negative = Less than 14 units

IgG desmoglein 3 antibodies: 0 units

Reference Range:

Positive (H) = Greater than 20 units
Borderline/Indeterminate = 9-20 units
Negative = Less than 9 units

(H = high/increased; units = units/mL serum)

COMMENTS

Specific

The negative IgG cell surface antibodies by indirect immunofluorescence testing and normal IgG desmoglein 1 and IgG desmoglein 3 antibody levels by ELISAs are against, but do not rule out, the diagnosis of pemphigus vulgaris

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or pemphigus foliaceus and other IgG pemphigus variants. These findings do not rule out other immunobullous diseases.

Notably, IgG basement membrane zone antibody staining is present on both intact skin and monkey esophagus substrates. IgG basement membrane zone antibodies characteristically are found in pemphigoid and epidermolysis bullosa acquisita. Concurrent Basement Membrane Zone Antibody Panel testing demonstrates positive findings consistent with pemphigoid (separate report with additional comments). Clinical correlation is needed.

General

Greater than 80 percent of patients with pemphigus have positive epithelial cell surface antibodies in their sera identified by indirect immunofluorescence. Serum antibody titers correlate with disease activity. Cell surface antibodies are implicated in the pathophysiology of pemphigus and are not typically detected in normal individuals, in patients with other diseases or in patients with pemphigus whose disease activity is minimal and/or under therapeutic control. IgG cell surface antibodies characteristically are positive by indirect immunofluorescence in IgG pemphigus variants, including pemphigus foliaceus and pemphigus vulgaris, and IgA cell surface antibodies characteristically are positive in IgA pemphigus and also may be observed in some pemphigus variants along with positive IgG cell surface antibodies.

If indicated to further evaluate for IgA cell surface antibodies, add-on testing may be requested on this specimen for IgA Pemphigus Antibody (ARUP test number 0092106) by contacting ARUP Client Services at 1-800-242-2787 option 2.

Antibodies in serum from individuals with pemphigus bind to desmogleins, which are calcium-dependent adhesion molecules in cell surface desmosomes; such antibodies are detected by enzyme linked immunosorbent assay (ELISA) testing. Specific reactivity to the type of desmoglein may be helpful in determining pemphigus subtypes; IgG desmoglein 1 autoantibodies predominate in patients with pemphigus foliaceus, and IgG desmoglein 3 autoantibodies, with or without accompanying desmoglein 1 autoantibodies, predominate in patients with pemphigus vulgaris. Overlapping expression with autoantibodies to both desmogleins 1 and 3 typically is associated clinically with both mucosal and skin lesions. ELISA testing for IgG desmoglein 1 and IgG desmoglein 3 antibodies is highly sensitive, with greater than 90 percent of pemphigus patients showing increased levels of one or both antibodies. Desmoglein antibodies are not increased in normal individuals. IgG desmoglein levels by ELISA testing also correlate with disease activity.

TESTING METHODS

Indirect Immunofluorescence

Cell Surface IgG Antibodies

The patient's serum is progressively diluted in calcium-containing buffer beginning at 1:10 in three two-fold screening dilutions, layered on sections of intact normal human skin and monkey esophagus substrates, and stained with fluorescein-conjugated anti-IgG using Analyte Specific Reagents (ASRs). When positive, the serum is further diluted in two-fold reductions to the limiting dilution of antibody detection or to a maximum dilution of 1:40,960. These tests were developed and their performance characteristics determined by the Immunodermatology Laboratory at the University of Utah. They have not been cleared or approved by the U.S. Food and Drug Administration. ASRs are used in many laboratory tests necessary for standard medical care and generally do not require FDA approval. These tests should not be regarded as investigational or for research only. [Immunofluorescence studies, one antibody on two substrates]

Enzyme Linked Immunosorbent Assay (ELISA)

Desmoglein 1 and desmoglein 3 IgG serum antibody levels determined by U.S. Food and Drug Administration-approved ELISAs (Mesacup, MBL BION). [Two ELISAs]

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Immunodermatologist
Electronically signed 5/13/2019 11:36:10PM

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(800)522-2787 - www.aruplab.com
Julio C. Delgado, M.D. M.S., Director of Laboratories

Example Report

Patient Age/Gender: 72 years Female
Printed: 26-Jun-19 07:42:48

07-May-19 17:09:00 EER Pemphigus Antibody Panel, IgG:
Access ARUP Enhanced Report using either link below:

-Direct access:

-Enter Username, Password: <https://erpt.aruplab.com>
Username:
Password:

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07-May-19 17:09:00 Basement Membrane Zone Ab Panel:
IMMUNODERMATOLOGY LABORATORY

Specimen(s):
1. Serum specimen

Clinical/Diagnostic Information:
No clinical information provided.

DIAGNOSTIC INTERPRETATION

Consistent with pemphigoid

(See Results, Comments, and separate concurrent IgG Pemphigus Antibody Panel testing report with negative/normal findings for IgG cell surface antibodies and additional comments)

RESULTS

Indirect Immunofluorescence

Basement Membrane Zone (BMZ) IgG and IgA Antibodies

IgG: Positive, titer greater than 1:40,960 (H), monkey
esophagus substrate
Positive, epidermal pattern, titer 1:20,480 (H), human
split skin substrate

IgA: Negative, monkey esophagus substrate
Negative, human split skin substrate

Reference Range:

Positive (H) - Titer greater than 1:10
Borderline - Titer 1:10
Negative - Titer less than 1:10

Pattern on Human BMZ Split Skin:

IgG epidermal or epidermal-dermal combined BMZ
antibody pattern = pemphigoid

IgG dermal BMZ antibody pattern = epidermolysis
bullosa acquisita

IgA epidermal, epidermal-dermal combined, or,
dermal BMZ antibody pattern = linear IgA bullous
dermatosis

(H = high/positive)

Enzyme Linked Immunosorbent Assay (ELISA)

Bullous Pemphigoid (BP) 180 and 230 IgG Antibodies

IgG BP 180 antibodies: 115* units (H)

Reference Range:

Positive (H) = Greater than or equal to 9 units
Negative = Less than 9 units

IgG BP 230 antibodies: 108* units (H)

Reference Range:

Positive (H) = Greater than or equal to 9 units
Negative = Less than 9 units

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Collagen VII IgG Antibodies

IgG Collagen VII antibodies: 3 units

Reference Range:

Positive (H) = Greater than or equal to 9 units
Slightly increased, positive (H) = 7-8 units
Normal/negative = 0-6 units

(H = high/increased; units = units/mL serum)

COMMENTS

Specific

The positive IgG basement membrane zone antibodies on monkey esophagus substrate with epidermal localization on split skin substrate by indirect immunofluorescence and increased IgG BP 180 and IgG BP 230 antibody levels and a normal IgG type VII collagen antibody level by ELISAs, support the diagnosis of pemphigoid without evidence for the diagnosis of epidermolysis bullosa acquisita or linear IgA bullous dermatosis. Concurrent IgG Pemphigus Antibody Panel testing demonstrates negative/normal findings for IgG cell surface antibodies with corroborating findings of positive IgG basement membrane zone antibodies by indirect immunofluorescence on both monkey esophagus and intact skin substrates (separate report with additional comments).

IgG BP 180 antibody levels correlate with disease activity in some patients with pemphigoid. Clinical correlation is needed with consideration for monitoring antibody profiles and levels to aid in assessing disease expression and activity, including response to therapy.

General

Approximately 80 percent of patients with bullous pemphigoid, epidermolysis bullosa acquisita, and linear IgA bullous dermatosis have positive serum antibodies to basement membrane zone components. Approximately 20 percent of patients with mucous membrane/cicatrical pemphigoid have positive serum antibodies to basement membrane zone components. The pattern of staining on split skin specifies disease.

Major molecular structures in the basement membrane zone to which IgG pemphigoid antibodies bind have been identified and termed "BP 180" for a 180 kDa bullous pemphigoid antigen and "BP 230" for a 230 kDa bullous pemphigoid antigen. BP 180 is a transmembrane component of the basement membrane zone with collagen-like domains. BP 230 is located in the hemidesmosomal plaque of basal cells in the epidermis. Serum levels of IgG BP 180 and IgG BP 230 antibodies are in the negative range in normal individuals. Patients with pemphigoid may show reactivity to multiple basement membrane zone components in addition to or other than the BP 180 and BP 230 epitopes expressed in these ELISAs.

Collagen VII is a component of anchoring fibrils within epithelial basement membrane zone (skin and mucous membranes), and patients with epidermolysis bullosa acquisita characteristically develop IgG antibodies to collagen VII. Patients with inflammatory bowel disease, including Crohn's disease and ulcerative colitis, with and without mucocutaneous manifestations of epidermolysis bullosa acquisita and patients with bullous lupus erythematosus also may develop antibodies to collagen VII. The major epitopes for epidermolysis bullosa acquisita antibody reactivity reside in the non-collagenous amino-terminal domain, NC1, with minor epitopes in the non-collagenous carboxy-terminal domain, NC2, of the three identical alpha chains that comprise collagen VII. This ELISA contains combined purified recombinant antigens from both NC1 and NC2 for detection of IgG antibodies in serum. The reference range for this assay indicates a threshold level at 6 units/mL, and levels above this threshold may correlate with disease activity. The IgG type VII collagen antibody level by ELISA is a sensitive diagnostic marker together with dermal pattern IgG basement membrane zone antibody reactivity on split skin substrate by indirect immunofluorescence in patients with epidermolysis bullosa acquisita and in a subset of patients with bullous lupus erythematosus, although patients with these disorders may demonstrate antibodies to basement membrane zone antigens in addition to or other than the collagen VII epitopes expressed in this ELISA.

TESTING METHODS

Indirect Immunofluorescence

Basement Membrane Zone (BMZ) IgG and IgA Antibodies

The patient's serum is progressively diluted beginning at 1:5 in three two-fold screening dilutions, layered on sections of monkey esophagus substrate and human basement membrane zone split skin substrate, and stained with fluorescein-conjugated anti-IgA and anti-IgG using Analyte Specific Reagents (ASRs). When positive, the serum is

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further diluted in two-fold reductions to the limiting dilution of antibody detection or to a maximum dilution of 1:40,960. These tests were developed and their performance characteristics determined by the Immunodermatology Laboratory at the University of Utah. They have not been cleared or approved by the U.S. Food and Drug Administration. ASRs are used in many laboratory tests necessary for standard medical care and generally do not require FDA approval. These tests should not be regarded as investigational or for research only. [Immunofluorescence studies, two antibodies on two substrates with two limiting dilution end-point titers]

Enzyme Linked Immunosorbent Assay (ELISA)

IgG BP 180 and IgG BP 230 serum antibody levels determined by U.S. Food and Drug Administration-approved ELISAs (Mesacup, MBL BION).
[Two ELISAs]

Collagen VII IgG serum antibody level determined by ELISA (Mesacup, MBL International). This test was developed and its performance characteristics determined by the Immunodermatology Laboratory at the University of Utah. It has not been cleared or approved by the U.S. Food and Drug Administration. [One ELISA]

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07-May-19 17:09:00 EER Basement Membrane Zone Ab Panel, EER Pemphigus Antibody Panel, IgG, Pemphigus Antibody Panel, IgG, Basement Membrane Zone Ab Panel:

Performed at: ARUP - University Hospital Laboratory 50 N. Medical Drive Salt Lake City UT 84132