Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1954
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Basement Membrane Zone Antibody Panel

ARUP test code 3001410

Basement Membrane Zone Ab Panel

See Note

CLINICAL INFORMATION
Urticarial and erythematous patches, occasional blisters, and milia.

Specimen Details
S22-IP0000515 - Serum; Collected: 6/22/2022; Received: 6/22/2022

DIAGNOSTIC INTERPRETATION

Negative/normal IgG and IgA basement membrane zone (pemphigoid, epidermolysis bullosa acquisita, linear IgA disease) antibodies

(See Results and Comments)

RESULTS
Indirect Immunofluorescence (IIF)

Basement Membrane Zone (BMZ) IgG and IgA Antibodies

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

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

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

Localization Pattern on Human BMZ Split Skin:
Epidermal (roof) or combined epidermal-dermal (roof and floor) IgG and/or IgG4 BMZ antibodies = pemphigoid (including pemphigoid gestationis, bullous pemphigoid, mucous membrane pemphigoid)

Dermal (floor) IgG and/or IgG4 BMZ antibodies = epidermolysis bullosa acquisita or bullous lupus erythematosus or anti-laminin-332 pemphigoid or anti-p200 (laminin gamma-1) pemphigoid or another rare pemphigoid subtype

Epidermal (roof), combined epidermal-dermal (roof and floor), or, dermal (floor) IgA BMZ antibodies = linear IgA disease (including linear IgA bullous dermatosis and chronic bullous disease of childhood)

(H) = high/positive

H=High, L=Low, *=Abnormal, C=Critical

Enzyme-Linked Immunosorbent Assay (ELISA)

Bullous Pemphigoid (BP)180 and BP230 IgG Antibodies

IgG BP180 antibody level: 3 U/mL

Reference Range:
Normal (negative) = Less than 9 U/mL
Increased (H) (positive) = 9 U/mL and greater

IgG BP230 antibody level: 1 U/mL

Reference Range:
Normal (negative) = Less than 9 U/mL
Increased (H) (positive) = 9 U/mL and greater

Type VII Collagen IgG Antibodies

IgG type VII collagen antibody level: 0 U/mL

Reference Range:
Normal (negative) = Less than 7 U/mL
Slightly increased (H) (positive) = 7-8 U/mL
Increased (H) (positive) = 9 U/mL and greater

COMMENTS

Specific

The negative IgG and IgA basement membrane zone antibodies by indirect immunofluorescence testing and normal IgG BP180, IgG BP230, and IgG type VII collagen antibody levels by ELISAs are against, but do not rule out, the diagnoses of bullous pemphigoid, epidermolysis bullosa acquisita, and linear IgA disease. The results do not rule out the diagnosis of mucous membrane/cicatricial pemphigoid because patients with this pemphigoid subtype may not have detectable circulating basement membrane zone antibodies, although, when present, they can be helpful diagnostically.

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations. Clinical correlation is needed, including with direct immunofluorescence findings on a biopsy specimen and treatment status, with consideration for monitoring serum antibody profiles by indirect immunofluorescence and antibody levels by ELISAs to aid in assessing disease expression and activity, particularly with persistent, progressive, or changing disease.

General

Approximately 80 percent of patients with bullous pemphigoid, epidermolysis bullosa acquisita, and linear IgA bullous dermatosis have positive antibodies to basement membrane zone components in their sera detected by indirect immunofluorescence. Approximately 50 percent of patients with mucous membrane/cicatricial pemphigoid demonstrate antibodies to basement membrane zone components detected by indirect immunofluorescence. The immunoglobulin class of basement membrane zone antibodies and pattern of antibody localization on split skin substrate distinguish the diseases. Positive serum IgA epithelial basement membrane zone antibodies are highly specific diagnostic markers for linear IgA disease. IgA basement membrane zone antibodies by indirect immunofluorescence may be found in variant presentations of mucous membrane pemphigoid and epidermolysis bullosa acquisita. Moreover, IgA basement membrane zone antibodies may be co-expressed with IgG basement membrane zone antibodies in some patients with pemphigoid including mucous membrane/cicatricial pemphigoid and, characteristically,

in linear IgA/IgG bullous dermatosis.

Major molecular structures in the basement membrane zone to which IgG pemphigoid antibodies bind have been identified and termed "BP180" for a 180 kDa bullous pemphigoid antigen (also known as bullous pemphigoid antigen 2, BPAG2, or type XVII collagen, COL17) and "BP230" for a 230 kDa bullous pemphigoid antigen (also known as bullous pemphigoid antigen 1, BPAG1). BP180 is a transmembrane component of the basement membrane zone with collagen-like domains; the non-collagenous 16A (NC16A) antigenic domain of BP180 has been identified as a main antigenic target. BP230 is in the hemidesmosomal plaque of basal cells in the epidermis. Serum levels of IgG BP180 and IgG BP230 antibodies are determined by ELISA, and serum levels of IgG BP180 antibodies may correlate with disease activity in pemphigoid, diminishing with treatment response. Up to 7 percent of individuals who do not have pemphigoid, including patients with other immunobullous diseases, have increased levels of IgG BP180 and/or BP230 antibodies by ELISAs. Patients with pemphigoid may show reactivity to multiple basement membrane zone components in addition to or other than the BP180 and BP230 epitopes expressed in the tested ELISAs.

Type VII collagen 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 type VII collagen. An increased serum IgG type VII collagen antibody level by ELISA provides support for the diagnosis of epidermolysis bullosa acquisita and a subset of bullous lupus erythematosus together with dermal localization (floor) of IgG basement membrane zone antibodies on split skin substrate by indirect immunofluorescence. Patients with inflammatory bowel disease, including Crohn disease and ulcerative colitis, with and without mucocutaneous manifestations of epidermolysis bullosa acquisita, may demonstrate increased levels of antibodies to type VII collagen. The major epitopes for 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 type VII collagen. The tested ELISA contains combined purified recombinant antigens from both NC1 and NC2 for detection of IgG antibodies. Serum antibody levels above the reference range threshold of 6 U/mL may correlate with disease activity. Patients with epidermolysis bullosa acquisita or bullous lupus erythematosus may develop antibodies to basement membrane zone antigens in addition to or other than the type VII collagen epitopes displayed in this ELISA, and patients with other epithelial antibody-associated disorders may develop overlapping basement membrane zone antibody expression with an increased level of IgG type VII collagen antibodies.

TESTING METHODS
Indirect Immunofluorescence (IIF)

IgG and IgA Epithelial Basement Membrane Zone (BMZ) Antibodies

Patient serum is progressively diluted beginning at 1:5 in three two-fold screening dilutions, layered on sections of human skin split at the basement membrane zone and monkey esophagus substrates, and reacted with fluorescein isothiocyanate (FITC)-conjugated antibodies to IgG and IgA. 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. The limiting-dilution, end-point titer is reported for each substrate, and the pattern of staining on split skin substrate also is reported. This indirect immunofluorescence testing 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 FDA (US Food and Drug Administration). FDA clearance or approval currently is

not required for this testing performed in a CLIA-certified laboratory (Clinical Laboratory Improvement Amendments) and intended for clinical use. [Indirect immunofluorescence, two antibodies on two substrates (IIF X 4)]

Enzyme-Linked Immunosorbent Assay (ELISA)

IgG BP180 and IgG BP230 serum antibody levels determined by U.S. Food and Drug Administration (FDA)-approved ELISAs (Mesacup, MBL BION). [Two ELISAs]

IgG type VII collagen serum antibody level determined by ELISA (Mesacup, MBL International). The performance characteristics of this ELISA testing were determined by the Immunodermatology Laboratory at the University of Utah. The testing has not been cleared or approved by the FDA (US Food and Drug Administration). FDA clearance or approval currently is not required for this testing performed in a CLIA-certified laboratory (Clinical Laboratory Improvement Amendments) and intended for clinical use. [One ELISA]

Electronically signed by [redacted]
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CLIA Number: 46D0681916

EER Basement Membrane Zone Ab Panel

See Note

Authorized individuals can access the ARUP Enhanced Report using the following link:

[redacted]

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Basement Membrane Zone Ab Panel	22-173-113932	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER Basement Membrane Zone Ab Panel	22-173-113932	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical