ARUP LABORATORIES
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Jonathan R. Genzen, MD, PhD, Chief Medical Officer

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

Physician: Doctor, Example

Patient: Patient, Example

DOB	12/31/1940
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Pemphigoid Antibody Panel

ARUP test code 0092001

EER Pemphigoid Antibody Panel

See Note

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

[redacted]

Pemphigoid Antibody Panel

See Note

CLINICAL INFORMATION
Eczematous lesions and generalized pruritus.

Specimen Details
[redacted] - ; Collected: 1/8/2024; Received: 1/9/2024

DIAGNOSTIC INTERPRETATION

Negative/normal Pemphigoid Antibody Panel

(See Results and Comments including further testing considerations)

RESULTS
Indirect Immunofluorescence (IIF)

Basement Membrane Zone (BMZ) IgG, IgG4, and IgA Antibodies

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

IgG4: 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, some types of mucous membrane pemphigoid)

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

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)

IgA and IgG basement membrane zone antibodies may be co-expressed in basement membrane zone antibody-associated diseases

(H) = high/positive

Enzyme-Linked Immunosorbent Assay (ELISA)

Bullous Pemphigoid (BP)180 and BP230 IgG Antibodies

IgG BP180 antibody level: 4 U/mL
Reference Range:
Normal (negative) = Less than 9 U/mL
Increased (H) (positive) = 9 U/mL and greater

IgG BP230 antibody level: 3 U/mL

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

(H) = high/positive
U = antibody level in ELISA units

COMMENTS

Specific

The negative IgG, including IgG4, and IgA basement membrane zone antibodies by indirect immunofluorescence testing and the normal IgG BP180 and IgG BP230 antibody levels by ELISAs are against, but do not rule out, the diagnoses of bullous pemphigoid, epidermolysis bullosa acquisita, and linear IgA disease/linear IgA bullous dermatosis. 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.

Also, in patients with epidermolysis bullosa acquisita and in a subset of patients with bullous lupus erythematosus, the IgG type VII collagen antibody level by ELISA may be a more sensitive diagnostic marker than basement membrane zone antibody reactivity by indirect immunofluorescence. If clinically indicated to further evaluate the immunopathological profile, additional testing with respect to basement membrane zone antibodies or other epithelial cell surface/intercellular substance (pemphigus) antibodies may be performed on this specimen by contacting ARUP Client Services at 1-800-242-2787, option 2, with add-on test request(s) for:
- Collagen Type VII Antibodies, IgG by ELISA (ARUP test number 2010905), and/or
- Pemphigus Antibody Panel, IgG (ARUP test number 0090650),
- Pemphigus Antibodies, IgA by IIF (ARUP test number 0092106).

Detection, levels, and patterns of diagnostic antibodies may

fluctuate with disease manifestations. Clinical correlation is needed, including direct immunofluorescence findings on a biopsy specimen and treatment status. Monitoring serum antibody profiles by indirect immunofluorescence and antibody levels by ELISAs may aid in assessing disease expression and activity, particularly with persistent, progressive, or changing disease and in response to therapy.

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. IgG4 subclass reactivity by indirect immunofluorescence may be more sensitive than IgG in some patients with pemphigoid and epidermolysis bullosa acquisita. The immunoglobulin class of basement membrane zone antibodies and pattern of antibody localization on split skin substrate (also known as salt split skin) 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 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 located in the hemidesmosomal plaque of basal cells in the epidermis. Serum levels of IgG BP180 and IgG BP230 antibodies are determined by ELISA, which may be more sensitive than indirect immunofluorescence. 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 in the tested ELISAs. Type VII collagen is a component of anchoring fibrils within epithelial basement membrane zone (skin and mucous membranes) and is an antigenic target of IgG autoantibodies in patients with epidermolysis bullosa acquisita and in a subset of patients with bullous lupus erythematosus and, potentially, as overlapping basement membrane zone antibody expression in patients with other epithelial antibody-associated disease. Tests that detect antibodies with specificity for other basement membrane zone antigens, including laminin-332, p200 (laminin gamma-1), and alpha6beta4 integrin, may be more sensitive than indirect immunofluorescence but are not currently available, except laminin-332 IgG antibodies in select laboratories. Mucous membrane involvement is predominant in anti-laminin-332 pemphigoid. Recognition of the association of this pemphigoid variant with underlying or developing malignancy (typically solid tumor) in up to one third of cases is critical so

appropriate clinical evaluation is conducted. Patients with anti-p200 (laminin gamma-1) pemphigoid tend to be younger than those with bullous pemphigoid and have lesions that clinically resemble both bullous pemphigoid and the inflammatory epidermolysis bullosa acquisita variant that may include mucosal involvement. For those patients with antibodies to alpha6beta4 integrin, alpha6 epitopes primarily are targeted in oral pemphigoid, and beta4 epitopes primarily are targeted in ocular pemphigoid.

TESTING METHODS
Indirect Immunofluorescence (IIF)

IgG, IgG4, 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. FITC-conjugated anti-IgG4 is tested to increase test sensitivity (maximum serum dilution of 1:20). 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, three antibodies on two substrates (IIF X 6)]

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]

Electronically signed by [redacted] on 01/09/24 at 1:02 PM.
Performed At: IMMUNODERMATOLOGY LABORATORY
417 S. WAKARA WAY, SUITE 2151
SALT LAKE CITY, UT 84108
Medical Director: KRISTIN M. LEIFERMAN, MD
CLIA Number: 46D0681916

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
EER Pemphigoid Antibody Panel	24-008-124096	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Pemphigoid Antibody Panel	24-008-124096	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