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

Physician: Doctor, Example

Patient: Patient, Example

DOB	6/24/1928
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Immunobullous Disease Panel, Epithelial

ARUP test code 3001409

EER Immunobullous Disease Panel

See Note

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

Immunobullous Disease Panel

See Note

IMMUNODERMATOLOGY REPORT

Specimen(s):
1. Serum specimen

Clinical/Diagnostic Information:
No clinical information provided.

DIAGNOSTIC INTERPRETATION

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

Negative/normal IgG, including IgG4, and IgA cell surface (pemphigus) antibodies

(See Results and Comments)

RESULTS
Indirect Immunofluorescence

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:
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

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

IgG dermal BMZ antibody pattern = epidermolysis bullosa acquisita

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

Cell Surface IgG and IgA Antibodies

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

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

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)

Bullous Pemphigoid (BP) 180 and 230 IgG Antibodies

IgG BP 180 antibodies: 1 unit

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

IgG BP 230 antibodies: 2 units

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

Collagen VII IgG Antibodies

IgG Collagen VII antibodies: 2 units

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

Desmoglein (DSG) 1 and 3 IgG Antibodies

IgG desmoglein 1 antibodies: 3 units

Reference Range:
Positive (H) = Greater than 20 units
Borderline/indeterminate = 14-20 units
Negative = Less than 14 units

IgG desmoglein 3 antibodies: 5 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 and IgA basement membrane zone antibodies by indirect immunofluorescence testing and normal IgG BP 180, IgG

BP 230, 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 bullous dermatosis. The results do not rule out the diagnosis of mucous membrane/cicatricial pemphigoid because a large proportion of patients with this pemphigoid subtype do not have detectable circulating basement membrane zone antibodies.

The negative IgG and IgA cell surface antibodies by indirect immunofluorescence testing are against, but do not rule out, the diagnoses of pemphigus vulgaris, pemphigus foliaceus, other types of IgG pemphigus, and IgA pemphigus. The normal IgG desmoglein 1 and IgG desmoglein 3 antibody levels by ELISAs also are against, but do not rule out, the diagnosis of active pemphigus foliaceus or pemphigus vulgaris.

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations. Clinical correlation is needed, including correlation with direct immunofluorescence findings on a biopsy specimen and/or treatment status, with consideration for monitoring serum antibody profiles and levels 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. Approximately 20 percent of patients with mucous membrane pemphigoid, including cicatricial pemphigoid, demonstrate antibodies to basement membrane zone components. The pattern of staining on split skin substrate 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 and is a principal antigenic target in mucous membrane pemphigoid. 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, and serum levels of IgG BP 180 antibodies may correlate with disease activity in pemphigoid, diminishing with treatment response. 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.

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 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

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

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 type VII collagen epitopes expressed in this ELISA..

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.

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

IgG and IgA Epithelial Basement Membrane Zone and Cell Surface Antibodies

The patients serum is progressively diluted beginning at 1:5 in four two-fold screening dilutions, layered on sections of human skin split at the basement membrane zone, intact human skin, and monkey esophagus substrates, and stained with fluorescein-conjugated anti-IgG and anti-IgA 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, two antibodies on three substrates]

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]

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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]

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

[redacted], MD
Immunodermatologist
Electronically signed 5/11/2019 11:08:41PM
Performed at: ARUP - University Hospital Laboratory 50 N. Medical Drive Salt Lake City UT 84132

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
EER Immunobullous Disease Panel	19-127-120308	5/7/2019 2:52:00 PM	5/9/2019 8:23:37 AM	5/13/2019 2:10:00 PM
Immunobullous Disease Panel	19-127-120308	5/7/2019 2:52:00 PM	5/9/2019 8:23:37 AM	5/13/2019 1:28:00 PM

END OF CHART