ARUP Laboratories
500 Chipeta Way – Salt Lake City, UT 84108
(800)522-2787 - www.aruplab.com
Julio C. Delgado, M.D. M.S., Director of Laboratories

*****Example Report*****

Patient Age/Gender: Unknown Unknown
Printed: 20-May-19 09:15:43

Procedure	Result	Units	Ref Interval	Accession	Collected	Received	Reported/ Verified
EER Immunobullous Disease Panel	EERUnavailable @			19-137-101276	17-May-19 06:49:00	17-May-19 06:58:00	20-May-19 09:00:36
Immunobullous Disease Panel	See Note f@			19-137-101276	17-May-19 06:49:00	17-May-19 06:58:00	20-May-19 09:00:36

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

17-May-19 06:49:00 Immunobullous Disease Panel:

IMMUNODERMATOLOGY REPORT

Specimen(s):
1. Serum specimen

Clinical/Diagnostic Information:
No clinical information provided.

DIAGNOSTIC INTERPRETATION

Consistent with pemphigoid (See Results and Comments)

RESULTS
Indirect Immunofluorescence

Basement Membrane Zone (BMZ) IgG and IgA Antibodies

IgG: Negative, monkey esophagus substrate
Positive, epidermal pattern, titer 1:160 (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

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: 27 units (H)

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

IgG BP 230 antibodies: 1 unit

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

Collagen VII IgG Antibodies

IgG Collagen VII antibodies: 1 unit

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: 9 units

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

IgG desmoglein 3 antibodies: 1 unit

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

These results, demonstrating positive IgG basement membrane zone antibodies with epidermal localization on split skin substrate by indirect immunofluorescence and an increased IgG BP 180 antibody level by ELISA, support the diagnosis of pemphigoid. IgG BP 180 antibody levels correlate with disease activity in some patients with pemphigoid. Monitoring antibody profiles by indirect immunofluorescence and antibody levels by ELISAs may be useful in assessing disease expression and activity, including response to therapy.

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.

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/cicatricial pemphigoid have positive antibodies to basement membrane zone components in their sera. 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, and serum levels of IgG BP 180 correlate with disease activity in some patients with pemphigoid. Patients with pemphigoid may show reactivity

to 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.

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 patient’s 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 with one limiting dilution end-point titer]

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]

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

Kristin Leiferman, MD
17-May-19 06:49:00 EER Immunobullous Disease Panel,Immunobullous Disease Panel:
Performed at: ARUP - University Hospital Laboratory 50 N. Medical Drive Salt Lake City UT 84132