Pemphigoid Antibody Panel

ARUP LABORATORIES

Patient: [redacted]
DOB: [redacted] Age: [redacted] Sex: [redacted]
Patient Identifiers: [redacted]

Visit Number (FIN): [redacted]

Client: [redacted]

Physician: [redacted]

ARUP Test Code: 0092001

Collection Date: 06/23/2022
Received in lab: 06/23/2022
Completion Date: 06/23/2022

Immunodermatology Serum Test Report Navigation Guide

The Immunodermatology TESTING REPORT from the University of Utah follows "See Note" and is arranged as outlined below on the following pages:

CLINICAL INFORMATION
This content is provided by the ordering clinician and includes the reason for testing.

Specimen Details
This includes specimen identification with collected and received dates.

DIAGNOSTIC INTERPRETATION
This is a synopsis of key findings from the testing and their diagnostic relevance.

RESULTS
This section reports the discrete finding and value of each test component, along with the reference range.

COMMENTS
Specific

These comments provide an explanation of the test results as they relate to clinical considerations, and include reference to any concurrent and/or previous testing.

General

These comments summarize fundamental information about the test(s) and the component(s) assessed to aid in interpretation of their clinical applicability.

TESTING METHODS
The section lists the procedures performed, the test source(s), and the applicable laboratory developed test disclaimer(s).

TEST RESULTS SUMMARY CHART
A chart tabulating results of tests ordered for the patient by the same client is included if previous and/or concurrent testing has been performed.

ELISA RESULTS GRAPH
A graph of ELISA results also is included if previous and/or concurrent testing has been performed; the graph may be found on a subsequent page.

For testing algorithm and additional information, refer to:
arupconsult.com/content/immunobullous-skin-diseases-screening

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Laboratory Director

Chart continues on following page(s)

HEALTH
UNIVERSITY OF UTAH

Department of Dermatology
Immunodermatology Laboratory

Immunodermatology.uofumedicine.org

[redacted] *MD - Co-Director*
[redacted] *MD - Co-Director*
[redacted] *MD*
[redacted] *MD*

417 S. Wakara Way, Suite 2151
Salt Lake City, UT 84108

Phone: 1-801-581-7139 or 1-866-266-5699
Fax: 1-801-585-5695

IMMUNODERMATOLOGY LABORATORY REPORT

[redacted]

Submitter

ARUP Sendouts

Pemphigoid Antibody Panel (Final result)

TESTING REPORT follows "See Note"
See Note

CLINICAL INFORMATION
Tense blisters on urticarial base with pruritus. Presumptive diagnosis is bullous pemphigoid.

Specimen Details
S22-IP0000535 - Serum; Collected: 6/23/2022; Received: 6/23/2022

DIAGNOSTIC INTERPRETATION

Pemphigoid Antibody Panel monitoring, consistent with pemphigoid

(See Results, Comments, and Previous and Current Test Results Summary Chart with Graph of ELISA results in the Enhanced Electronic Report/EELR and/or available upon request)

RESULTS
Indirect Immunofluorescence (IIF)

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

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

IgG4: Detected, titer 1:10 (Borderline), monkey esophagus substrate

Copy For:
IP1212

Printed: 6/23/2022 5:42 PM
Page: 1 of 7

[redacted]
PCP: Unspecified

Positive, epidermal localization (roof), titer 1:20 (H), 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)

Enzyme-Linked Immunosorbent Assay (ELISA)

Bullous Pemphigoid (BP)180 and BP230 IgG Antibodies

IgG BP180 antibody level: 49 U/mL (H)

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

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Laboratory Director

Chart continues on following page(s)

[redacted]

PCP: Unspecified

The findings, demonstrating positive IgG4 basement membrane zone antibody reactivity with epidermal localization on split skin substrate by indirect immunofluorescence and an increased IgG BP180 antibody level by ELISA, provide support for the diagnosis of pemphigoid. Previous testing showed similar findings, supporting the diagnosis of pemphigoid including pemphigoid variants, and also a normal IgG type VII collagen antibody level by ELISA on one determination. See chart for summary of previous and current basement membrane zone antibody test results at end of report (below); a graph of the ELISA results is available in the Enhanced Electronic Report/EELR and/or available upon request by contacting ARUP Client Services at 1-800-242-2787, option 2, and ask to speak with the Immunodermatology Laboratory at the University of Utah regarding patient results.

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations, and IgG BP180 antibody levels correlate with disease activity in some patients with pemphigoid. Clinical correlation is needed, including treatment status, with consideration for continued monitoring of serum antibody profiles by indirect immunofluorescence and antibody levels by ELISAs to aid in assessing disease expression and activity, including response to therapy.

General

Approximately 80 percent of patients with bullous pemphigoid and epidermolysis bullosa acquisita have positive IgG and/or IgG4 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 (also known as salt split skin) distinguish the diseases. IgG4 subclass reactivity by indirect immunofluorescence may be more sensitive than IgG in some patients with pemphigoid and epidermolysis bullosa acquisita.

Positive serum IgA epithelial basement membrane zone antibodies are highly specific diagnostic markers for linear IgA disease and are present in up to 80 percent of patients with linear IgA bullous dermatosis. Titers of positive IgA basement membrane zone antibodies may be useful markers in following disease expression and activity. IgA basement membrane zone antibodies may be found in variant presentations of mucous membrane pemphigoid and epidermolysis bullosa acquisita. 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. When co-expressed, the presence of two antibody classes with reactivity toward basement membrane zone may have implications for disease severity and treatment considerations.

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

[redacted]
PCP: Unspecified

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 and is a principal 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, 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 displayed 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.

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 Assays (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]

[redacted]

PCP: Unspecified

TEST RESULTS SUMMARY CHART
Basement Membrane Zone (BMZ) Antibodies

Serum Number	Date of Specimen	IgG and IgG4 BMZ Titers	IgA BMZ Titers	BP 180	BP 230	Col VII
20-0234	03/26/20	IgG ME Neg IgG SS Neg IgG4 ME 1:5 IgG4 SS Epi, 1:20	ME Neg SS Neg	52	4	NA
20-2225	11/15/20	IgG ME Neg IgG SS Neg IgG4 ME 1:10 IgG4 SS Epi, 1:20	ME Neg SS Neg	57	4	NA
21-0025	01/06/21	IgG ME Neg IgG SS Epi, 1:10 IgG4 ME 1:20 IgG4 SS Epi, >1:20	ME Neg SS Neg	67	6	NA
21-0654	05/20/21	IgG ME Neg IgG SS Epi, 1:20 IgG4 ME 1:10 IgG4 SS Epi, 1:20	ME Neg SS Neg	59	5	NA
21-0722	07/24/21	IgG ME Neg IgG SS Epi, 1:10 IgG4 ME 1:10 IgG4 SS Epi, 1:20	ME Neg SS Neg	53	4	2
22-0513	06/22/22	IgG ME Neg IgG SS Neg IgG4 ME 1:10 IgG4 SS Epi, 1:20	ME Neg SS Neg	49	3	NA

ELISA Reference Ranges:

IgG BP180 and IgG BP230 Antibody Levels
Normal (negative) = Less than 9 U/mL
Increased (H) (positive) = 9 U/mL and greater

IgG Type VII Collagen Antibody Level
Normal (negative) = Less than 7 U/mL

[redacted]

PCP: Unspecified

```
Slightly increased (H) (positive) = 7-8 U/mL
        Increased (H) (positive) = 9 U/mL and greater

Chart Key:

IgG BMZ   = IgG basement membrane zone (BMZ) antibodies by
            indirect immunofluorescence
IgG4 BMZ  = IgG4 basement membrane zone (BMZ) antibodies
            by indirect immunofluorescence
IgA BMZ   = IgA basement membrane zone (BMZ) antibodies by
            indirect immunofluorescence

ME = Antibody absence (negative) or antibody presence
     (positive endpoint titer) on monkey esophagus (ME)
     substrate
SS = Antibody absence (negative) or antibody presence
     (positive pattern and endpoint titer) on split skin
     (SS) substrate

Epi  = epidermal localization (roof) on split skin
       substrate (IgG - pemphigoid including bullous
       pemphigoid, some mucous membrane pemphigoid, and
       other pemphigoid variants; IgA - linear IgA disease
       including linear IgA bullous dermatosis and chronic
       bullous disease of childhood)
Derm = dermal localization (floor) on split skin substrate
       (IgG - epidermolysis bullosa acquisita, bullous
       lupus erythematosus, anti-laminin-332 pemphigoid,
       anti-p200 (laminin gamma-1) pemphigoid, other
       rare pemphigoid subtypes; IgA - linear IgA disease
       including linear IgA epidermolysis bullosa
       acquisita)
Comb = combined epidermal-dermal localization (roof and
       floor) on split skin substrate (IgG -
       pemphigoid and pemphigoid variants; IgA - linear
       IgA disease)

BP180 = IgG BP180 antibody level (U/mL) by ELISA
BP230 = IgG BP230 antibody level (U/mL) by ELISA
Col VII = IgG Collagen VII antibody level (U/mL)
          by ELISA

Neg = Negative
NA  = Not Assayed
```

Electronically signed by [redacted], MD, on 06/23/22 at 5:42 PM.

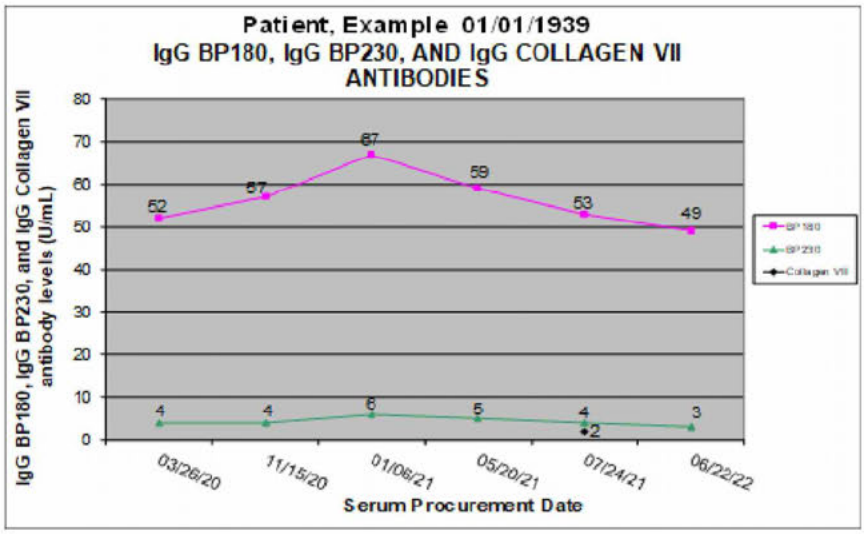
ELISA RESULTS GRAPH (may be found on next page)

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Laboratory Director

Chart continues on following page(s)

[redacted]

PCP: Unspecified



Resulting Laboratory

IMMUNODERMATOLOGY LABORATORY 801-581-7139
University of Utah
417 S. Wakara Way, Suite 2151
Salt Lake City, UT 84108
Director: [redacted], MD

Copy For:
IP1212

Printed: 6/23/2022 5:42 PM
Page: 7 of 7