

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

Physician: Doctor, Example

**Patient: Patient, Example**

**DOB:** Unknown  
**Gender:** Unknown  
**Patient Identifiers:** 01234567890ABCD, 012345  
**Visit Number (FIN):** 01234567890ABCD  
**Collection Date:** 00/00/0000 00:00

**Paraneoplastic Pemphigus (Paraneoplastic Autoimmune Multiorgan Syndrome) Expanded Antibody Panel by IIF With ELISA**

ARUP test code 3016534

EER Paraneoplastic Pemphigus Expanded Ab

See Note

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

[Redacted Link]

Paraneoplastic Pemphigus Expanded Ab

See Note

**CLINICAL INFORMATION**

Mucosal involvement with extensive erosions and targetoid, urticarial, and scaly skin lesions. Presumptive diagnosis is pemphigus, including paraneoplastic pemphigus, versus drug reaction, Stevens-Johnson syndrome.

**Specimen Details**

[Redacted] - ; Collected: 11/20/2024; Received: 11/22/2024

**DIAGNOSTIC INTERPRETATION**

Consistent with paraneoplastic pemphigus/paraneoplastic autoimmune multiorgan syndrome:

- Positive IgG epithelial antibody reactivity with rodent bladder substrates, including rat bladder, by indirect immunofluorescence; and
- Increased IgG envoplakin antibody level by ELISA

(See Results and Comments)

**RESULTS**

Indirect Immunofluorescence (IIF)

**Paraneoplastic Pemphigus IgG Antibodies**

IgG: Positive, cell surface, titer 1:40 (H),  
rat bladder substrate  
Positive, basement membrane zone, titer 1:10 (H),  
rat bladder substrate  
  
Positive, cell surface, titer 1:40 (H),  
mouse bladder substrate  
Positive, basement membrane zone, titer 1:10 (H),  
mouse bladder substrate

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

Negative, intercalated discs, mouse heart substrate

Negative, portal tracts, mouse liver substrate

Reference Range:

Negative - Titer less than 1:5

Borderline - Titer 1:5

Positive (H) - Titer greater than 1:5

Positive, cell surface/intercellular substance,  
monkey esophagus substrate

Positive, basement membrane zone,  
monkey esophagus substrate

Reference Range:

Negative - Titer less than 1:10

Borderline - Titer 1:10

Positive (H) - Titer greater than 1:10

(H) = high/positive

Enzyme-Linked Immunosorbent Assay (ELISA)

Envoplakin IgG Antibodies

IgG envoplakin antibody level: 1.07 ratio U/mL (H)

Reference Range:

Normal (negative) = Less than 1.00 ratio U/mL

Increased (H) (positive) = 1.00 ratio U/mL and greater

(H) = high/positive

U = antibody level in ELISA units

COMMENTS

Specific

IgG antibodies reacting with rodent substrates, including cell surface/intercellular substance and basement membrane zone antibodies with rat and mouse bladder substrates and cell surface/intercellular substance and basement membrane zone antibodies with monkey esophagus substrate, as detected in this indirect immunofluorescence testing, along with an increased level of IgG envoplakin antibodies by ELISA, support the diagnosis of paraneoplastic pemphigus (PNP), also known as Paraneoplastic Autoimmune Multiorgan Syndrome (PAMS). Antibody reactivity with intercalated discs in rodent heart and/or portal tracts in rodent liver by indirect immunofluorescence is supportive when antibody reactivity with rodent bladder, either or both rat and mouse, substrate is present.

Various serum epithelial antibodies may be found in PNP/PAMS and other paraneoplastic presentations by various tests with differing sensitivities. Among the several possible epithelial targets, IgG envoplakin antibodies develop in many patients with PNP/PAMS and rarely in patients with other immunobullous diseases. Moreover, when increased, IgG envoplakin antibody levels correlate with extent of mucocutaneous paraneoplastic pemphigus disease expression.

Clinical correlation is needed. If indicated to further evaluate the immunopathological profile, additional testing may be performed on this serum specimen by contacting ARUP Client Services at 1-800-242-2787, option 2, with add-on test request(s):

For comprehensive testing that includes the epithelial antibody tests below, order

- Immunobullous Disease Antibody Panel (ARUP test number 3001409);

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Alternatively, to assess for specific disease-associated epithelial antibodies or individual antibody targets, order

- Pemphigus Antibody Panel, IgG (ARUP test number 0090650),
- Pemphigus Antibodies, IgA by IIF (ARUP test number 0092106), and/or
- Basement Membrane Zone Antibody Panel (ARUP test number 3001410);

Or

- Desmoglein 1 and Desmoglein 3 (Pemphigus) Antibodies, IgG by ELISA (ARUP test number 0090649),
- Bullous Pemphigoid (BP180 and BP230) Antibodies, IgG by ELISA (ARUP test number 0092566), and
- Collagen Type VII Antibody, IgG by ELISA (ARUP test number 2010905).

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations. Monitoring of serum antibody profiles by indirect immunofluorescence testing 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.

If it would be helpful to discuss the patient case with this report, including request for additional testing on this serum specimen, contact 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.

#### General

Paraneoplastic pemphigus (PNP), also known as paraneoplastic autoimmune multiorgan syndrome (PAMS), may affect all ages and develops as a severe mucocutaneous blistering and erosive disease in association with malignancies, most often hematologic (lymphoma, leukemia) and sarcoma. It also may develop in association with benign neoplasia, especially Castleman disease, which is the most frequent association in children and adolescents. Antibodies targeting the various types of epithelia can lead to involvement of various organs and tissues, for example, eyes, lungs, gastrointestinal tract, kidney, and thyroid and is the basis of the name, paraneoplastic autoimmune multiorgan syndrome.

Positive indirect immunofluorescence testing results indicate the presence of serum antibodies to multiple epithelia (simple, columnar, transitional) with several possible epithelial targets, predominantly to plakins (envoplakin, periplakin, desmoplakin I, desmoplakin II, epiplakin, plectin, BP230), also cadherins (desmoglein 1, desmoglein 3; desmocollin 1, desmocollin 2, desmocollin 3), alpha-2-macroglobulin-like-1 (A2ML1), laminin 332, and/or BP180 and support a diagnosis of paraneoplastic pemphigus (paraneoplastic autoimmune multiorgan syndrome). Increased IgG envoplakin antibodies develop in many patients with PNP/PAMS and rarely in patients with other immunobullous diseases. The tested ELISA identifies IgG antibodies to the N-terminal recombinant fragment of envoplakin. Specificity of the test has been reported to be high at 96-99 percent and sensitivity of the test more variably reported at 55-86 percent. Envoplakin and periplakin are principal antigenic targets in the disease, and, based on the high sensitivity, an increased IgG envoplakin antibody level is a diagnostic marker for paraneoplastic pemphigus (paraneoplastic autoimmune multiorgan syndrome). IgG envoplakin antibody levels correlate with extent of mucocutaneous paraneoplastic pemphigus disease expression. After successful tumor therapy, envoplakin antibody levels decrease significantly.

For positive antibody panel testing results without known malignancy, perform aggressive evaluation for

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neoplasia/malignancy and, if not found, monitor for developing malignancy. For negative results, correlate with histopathological examination of formalin-fixed tissue in addition to direct immunofluorescence findings on a perilesional mucocutaneous biopsy specimen and epithelial antibodies in serum characteristic of other immunobullous diseases; negative paraneoplastic pemphigus antibody findings by indirect immunofluorescence and ELISA testing do not rule out paraneoplastic/malignancy-associated disease. Other known paraneoplastic epithelial autoantibody associations include nonclassical, intercellular IgG/IgA dermatosis and anti-laminin 332 pemphigoid.

TESTING METHODS

Indirect Immunofluorescence (IIF)

IgG Paraneoplastic Pemphigus Antibodies

The patient serum is progressively diluted in calcium-containing buffer beginning at 1:5 in three two-fold screening dilutions, layered on rodent substrates, including rat bladder, mouse bladder, mouse heart, and mouse liver, and also on monkey esophagus substrate, and reacted with fluorescein isothiocyanate (FITC)-conjugated antibody to IgG. When positive on rodent substrate(s), 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 rodent substrate. 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, one antibody on five substrates (IIF X 5) with two limiting dilution, end-point titers (antibody titer X 2)]

Enzyme-Linked Immunosorbent Assay (ELISA)

IgG envoplakin serum antibody level determined by ELISA (Euroimmun US, Inc.). The performance characteristics of this test have been validated by the University of Utah Immunodermatology Laboratory and meet specifications required by the Clinical Laboratory Improvement Amendment of 1988 (CLIA). The test has CE Mark certification as an in vitro diagnostic in the European Union. The testing has not been cleared or approved by the US Food and Drug Administration (FDA). The testing was performed in a CLIA-certified laboratory and is intended for clinical purposes. [One ELISA]

Electronically signed by [REDACTED] on 11/22/24 at 7:19 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

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VERIFIED/REPORTED DATES				
Procedure	Accession	Collected	Received	Verified/Reported
EER Paraneoplastic Pemphigus Expanded Ab	24-325-116938	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Paraneoplastic Pemphigus Expanded Ab	24-325-116938	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**

*Unless otherwise indicated, testing performed at:*

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

Patient: Patient, Example  
ARUP Accession: 24-325-116938  
Patient Identifiers: 01234567890ABCD, 012345  
Visit Number (FIN): 01234567890ABCD  
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