MAYO CLINIC LABORATORIES

# Test Definition: BPAB

Bullous Pemphigoid, BP180 and BP230, IgG Antibodies, Serum

## Overview

### Useful For

Initial screening test in the diagnosis of bullous pemphigoid and its variants

Complementing the standard serum test of indirect immunofluorescence utilizing primate esophagus substrate and primate salt-split skin substrate (CIFS / Cutaneous Immunofluorescence Antibodies [IgG], Serum)

### Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum Red

### Specimen Required

**Collection Container/Tube:**

**Preferred:** Red top

**Acceptable:** Serum gel

**Submission container/tube:** Plastic vial

**Specimen Volume:** 1 mL

**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.

### Specimen Minimum Volume

0.5 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | OK |
| Gross lipemia | OK |
| Gross icterus | OK |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Serum Red | Refrigerated (preferred) | 14 days | |
| | Frozen | 30 days | |
| | Ambient | 14 days | |

## Clinical & Interpretive

### Clinical Information

Bullous pemphigoid (BP) is a chronic pruritic blistering disorder found mainly in aged persons, characterized by the development of tense blisters over an erythematous or urticarial base. IgG anti-basement membrane zone antibodies are found in the serum of patients, and linear IgG and C3 sediment is found on the basement membrane zone of the lesion. Several well characterized variants exist including localized, mucous membrane predominant and pemphigoid gestationis, also referred to as herpes gestationis.

Target antigens of the autoantibodies in BP patient serum are BP230 and BP180, also called BPAG1 and BPAG2. Molecular weight of these antigens is 230 kDa and 180 kDa, respectively. BP180 is thought to be the direct target of the autoantibody because of its location along the basement membranes, and the autoantibody against BP230 is thought to be secondarily produced.

### Reference Values

BULLOUS PEMPHIGOID 180:
<20 RU/mL (negative)
> or =20 RU/mL (positive)

BULLOUS PEMPHIGOID 230:
<20 RU/mL (negative)
> or =20 RU/mL (positive)

### Interpretation

Antibodies to bullous pemphigoid (BP) BP180 and BP230 have been shown to be present in most patients with pemphigoid. Adequate sensitivities and specificity for disease are documented and Mayo Clinic's experience demonstrates a very good correlation between BP180 and BP230 results and the presence of pemphigoid (see Supportive Data). However, in those patients strongly suspected to have pemphigoid, either by clinical findings or by routine biopsy and/or direct immunofluorescence, and in whom the BP180/BP230 assay is negative, follow-up testing by CIFS / Cutaneous Immunofluorescence Antibodies [IgG], Serum is recommended.

Antibody titer may correlate with disease activity in some patients. Patients with severe disease may be expected to have high titers of antibodies to BP. Titers may decrease with clinical improvement.

### Cautions

As with other diagnostic test procedures, the results obtained with bullous pemphigoid (BP) BP180 and BP230 enzyme-linked immunosorbent assay kit serve only as an aid to diagnosis and should not be interpreted as diagnostic in themselves.

Performance of the assay in pediatric patients has not been established.

Performance of the assay on other matrices besides serum has not been established.

## Supportive Data

Thirty-two classic bullous pemphigoid (BP), 15 mucous membrane pemphigoid, and 7 other pemphigoid variants, diagnosed by direct immunofluorescence, routine histology, and clinical presentation were tested. Controls included 47 patients with other autoimmune blistering disorders and 42 age-matched controls without skin disease. Forty of 54 (74%) patients with BP and variants tested positive for BP180 and/or BP230 autoantibodies. Of these patients, 28 of 32 (88%) with classical BP, 8 of 15 (53%) with mucous membrane predominant (MMP), and 4 of 7 (57%) of other pemphigoid variants, tested positive.

The calculated sensitivities in classical BP were 54% for BP180 alone and 56% for BP230 alone. The sensitivity increased to 88% with both tests combined, which is comparable to that of indirect immunofluorescence (IIF) (88%). In MMP the calculated sensitivities were 47% for BP180 alone, 13% for BP230 alone, and 53% for both combined. This was slightly less than the sensitivity of IIF (67%). Only 5 of 47 (11%) and 2 of 47 (4%) control patients with other autoimmune blistering disorders were positive for BP180 and BP230 autoantibodies respectively. Interestingly, the 2 patients positive for BP230 autoantibody had paraneoplastic pemphigus. One of 42 (2%) and 0 normal controls tested positive for BP180 and BP230 respectively.

The calculated specificities for BP180, BP230, and IIF were 93%, 98%, and 92% respectively.

## Clinical Reference

1. Liu Z, Diaz LA, Troy JL, et al: A passive transfer model of the organ-specific autoimmune disease, bullous pemphigoid, using antibodies generated against the hemidesmosomal antigen, BP180. J Clin Invest. 1993 Nov;92(5):2480-2488
2. Matsumura K, Amagai M, Nishikawa T, Hashimoto T: The majority of bullous pemphigoid and herpes gestationes serum samples react with the NC16a domain of the e180-kD bullous pemphigoid antigen. Arch Dermatol Res. 1996 Aug;288(9):507-509
3. Stanley JR, Hawley-Nelson P, Yuspa SH, Shevach EM, Katz SI: Characterization of bullous pemphigoid antigen: a unique basement membrane protein of stratified aqueous epithelia. Cell. 1981 Jun;24(3):897-903
4. Hamada T, Nagata Y, Tomita M, Salmhofer W, Hashimoto T: Bullous pemphigoid sera react specially with various domains of BP230, most frequently with C-terminal domain, by immunblot analyses using bacterial recombinant proteins covering the entire molecule. Exp Dermatol. 2001 Aug;10(4):256-263
5. Rico MJ, Korman NJ, Stanley JR, Tanaka T, Hall RP: IgG antibodies from patients with bullous pemphigoid bind to localized epitopes on synthetic peptides encoded by bullous pemphigoid antigen cDNA. J Immunol. 1990 Dec 1;145(11):3728-3733
6. Wieland CN, Comfere NI, Gibson LE, Weaver AL, Krause PK, Murray JA: Anti-bullous pemphigoid 180 and 230 antibodies in a sample of unaffected subjects. Arch Dermatol. 2010 Jan;146(1):21-25
7. Montagnon CM, Tolkachjov SN, Murrell DF, Camilleri MJ, Lehman JS: Subepithelial autoimmune blistering dermatoses: Clinical features and diagnosis. J Am Acad Dermatol. 2021 Jul;85(1):1-14
8. Montagnon CM, Lehman JS, Murrell DF, Camilleri MJ, Tolkachjov SN: Subepithelial autoimmune bullous dermatoses: disease activity assessment and therapy. J Am Acad Dermatol. 2021 Jul;85(1):18-27

## Performance

### Method Description

This enzyme-linked immunosorbent assay (ELISA) method detects and measures serum levels of antibodies of certain pemphigoid diseases. Calibrators and patient sera are added to microwells coated with bullous pemphigoid (BP) BP180 and BP230 antigens, allowing antibodies to react with the immobilized antigens. After washing to remove any unbound serum proteins, horseradish peroxidase-conjugated IgG is added and incubated. Following another wash step, the peroxidase substrate is added and allowed to incubate for an additional period. Stop solution is then added to each well to cancel the enzyme reaction and to stabilize the color development. The assay can be quantified by measuring the reaction photometrically and plotting the results. The amount of antigen specific bound antibody is proportional to the color intensity.(Package inserts: Anti-BP180-NC16A-4X ELISA [IgG], Form EA_1502-2G_A_US_D04.doc. EuroImmun; Version: 7/6/11; Anti-BP230-CF ELISA [IgG], Form EA_1502-1G_A_UK_C03.doc. EuroImmun; Version: 5/9/11)

### PDF Report

No

### Day(s) Performed

Varies

### Report Available

1 to 5 days

### Specimen Retention Time

30 days

### Performing Laboratory Location

Rochester

## Fees & Codes

### Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

### Test Classification

This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

83516 x 2

# Test Definition: BPAB

Bullous Pemphigoid, BP180 and BP230, IgG Antibodies, Serum

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| BPAB | BP 180 and 230, Serum | 92671-7 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 606816 | BP 180, S | 53842-1 |
| 606817 | BP 230, S | 53843-9 |