

## ■ INTRODUCTION

Bullous pemphigoid (BP) is a chronic, autoimmune, subepidermal, blistering disease of the skin. It rarely involves mucous membranes. BP is characterized by the presence of (1) immunoglobulin IgG and complement deposits in the skin of patients and (2) of the presence in the serum of immunoglobulin G (IgG) autoantibodies specific for the basement membrane zone antigens such as to BP230 ( BPAg1) and BP180 (BPAg2).

## ■ CLINICAL FEATURES

BP is uncommon, and its frequency is unknown. No racial predilection is apparent. BP primarily affects elderly individuals in the fifth through seventh decades of life, with an average age at onset of 65 years. A few cases of BP of childhood onset have been reported in the literature. The cause of BP is not known. Clinically BP may present with several distinct clinical presentations such as generalized bullous, vesicular, vegetative, generalized erythroderma, urticarial, and nodular. It can affect any part of the skin surface, with a predilection on the flexural areas of the skin. Oral and ocular mucosa involvement rarely occurs and, when seen, is of minor clinical significance.

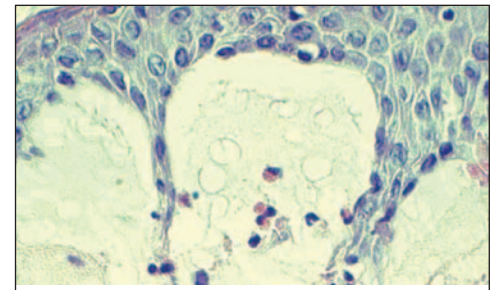
## ■ DIAGNOSIS

BP diagnosis is by biopsy and serum analysis of the presence of autoantibodies to the basement membrane zone (BMZ). Biopsy studies include H&E and direct immunofluorescence (IF). Direct IF studies show the presence of immunoglobulins and complement in the BMZ with a linear pattern. Serum studies detect the presence of autoantibodies to BMZ antigens by indirect IF using primate esophagus and/or split skin. For H&E biopsy should be taken from the edge of a blister and for direct IF studies biopsy should be from normal-appearing perilesional skin.

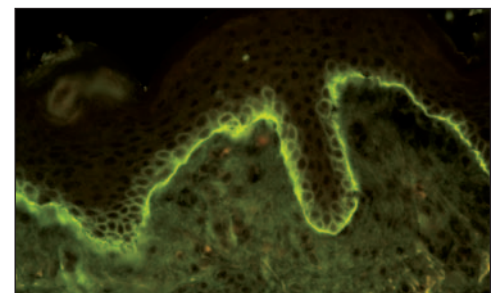
The H&E examination demonstrates subepidermal blister. The inflammatory infiltrate is typically polymorphous, with an eosinophil predominance. Direct IF studies demonstrate in vivo deposits of IgG (70-90% of patients) and complement C3 deposition (90-100% of patients) in a linear band at the BMZ. This pattern of immunoreactants is also observed in other sub-epidermal bullous diseases such as mucous membrane pemphigoid (MMP) and epidermolysis bullosa acquisita (EBA). In summary, a combination of clinical, histological, and IF studies are the most reliable in diagnosis of BP.



CLINICAL: Bulla on the skin



H & E showing subepidermal blister containing eosinophils



Direct IF showing linear deposits of C3 in the BMZ

DIAGNOSTIC CRITERIA	SENSITIVITY	SPECIFICITY
Clinical	63%	95%
Histological	27%	98%
Direct IF	90%	95%
Indirect IF	59%	99%
Clinical, Direct & Indirect IF	98%	98%

# BULLOUS PEMPHIGOID

BP can be differentiated from EBA by localizing the site of immunodeposits on the peri-lesional biopsy split at the lamina lucida junction by incubating the patient's skin biopsy in high salt. These antigen localization studies can be performed on specimens that have been submitted for routine IF studies. Similar studies of antigen localization can also be performed on serum. Based on the site of localization of immune deposits differentiation between BP and EBA can reliably be made as summarized to the right.

## TREATMENT

Topical steroids are effective however their use in extensive disease may be limited by side effects and practical factors. The effectiveness of the addition of plasma exchange or azathioprine to corticosteroids has not been fully established. Combination treatment with tetracycline and nicotinamide may be useful.

METHODS OF DIFFERENTIATION	BP	EBA
Serum tests for BMZ antibodies on salt split skin	Roof Roof & Floor	Floor
Direct IF on normal salt split skin (may be performed on same specimen submitted for DIF)	Roof Roof & Floor	Floor
"Antigen Mapping" for Type IV collagen and Laminin on lesional biopsy	Floor	Roof

## SUGGESTED READING

Liu Z, Diaz LA. Bullous pemphigoid: end of the century overview. *J Dermatol.* 2001;28:647-50.

Fleming TE, Korman NJ: Cicatricial pemphigoid. *J Am Acad Dermatol.* 2000;43:571-91;

Walsh SR, Hogg D, Mydlarski PR. Bullous pemphigoid: from bench to bedside. *Drugs.*2005; 65:905-26.

Khumalo N, Kirtschig G, Middleton P, Hollis S, Wojnarowska F, Murrell D. Interventions for bullous pemphigoid. *Cochrane Database Syst Rev.* 2005;(3):CD002292.

## SPECIMEN SUBMISSION

Specimen collection kits are available free of charge. Please call (800) 537-8378 for an immediate shipment. Use appropriate tube(s) as follows:

Immunofluorescence:  
Lesional biopsy: Red tube  
Normal biopsy: Purple tube  
H&E biopsy: Green tube  
Serology: Orange tube

Specimens can be shipped by courier services, U.S. Postal Service and overnight carriers free of charge. Results are reported in two business days of specimen receipt via mail, fax and through IMMCO Online, a HIPAA-compliant web tool at [www.immco.com](http://www.immco.com).



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