

EPIDERMOLYSIS BULLOSA AQUISITA



■ INTRODUCTION

Epidermolysis Bullosa Acquisita (EBA) is a chronic autoimmune sub-epidermal blistering disease of the skin and mucous membranes. EBA is characterized by blisters, scars, and milia primarily in trauma-prone areas such as the extensor surfaces of elbows, knees, ankles, and buttocks.

■ CLINICAL FEATURES

Two distinct phenotypes of EBA have been described: non-inflammatory (classical) EBA and inflammatory EBA. Both types may present as indicated above, however, inflammatory EBA can also mimic other sub-epidermal bullous disorders such as bullous pemphigoid, mucous membrane pemphigoid, and linear IgA dermatosis. Most EBA occurring in adults is classical EBA, while EBA in childhood is rare and usually of the inflammatory type. One feature that distinguishes presentation of adult EBA from the childhood form is mucosal involvement. In adult EBA mucosal involvement occurs in approximately 50% of cases as compared with childhood EBA in which mucosal involvement occurs in the majority of cases. In 1970 the first diagnostic criteria for EBA was established. It included:

- spontaneous or trauma induced blisters resembling hereditary dystrophic EB adult onset
- negative family history for EB
- exclusion of other bullous disorders

Since being established, the criteria have been modified and now include the presence of a sub-epidermal bullous disorder with immunoglobulin deposits at the basement membrane zone in perilesional skin appearing as a linear pattern with sublamina densa deposits through immunoelectron microscopy or through direct and indirect immunofluorescence studies of the presence of immune deposits on the dermal side of the split.

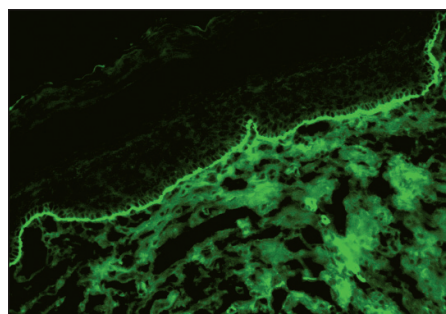
■ DIAGNOSIS

To establish the diagnosis of EBA, the following tests should be performed:

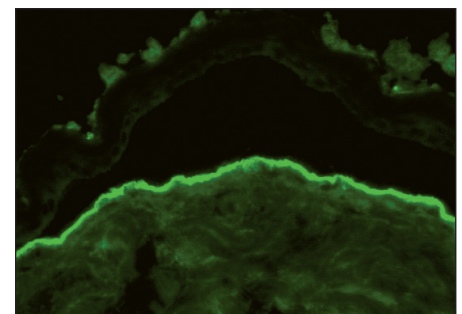
- H & E biopsy taken from the edge of a new blister
- Direct immunofluorescence on normal-appearing perilesional skin
- Indirect immunofluorescence using the patient's serum on a salt-split normal skin substrate

H & E studies of EBA cases exhibit papillary edema and vacuolar alterations with subsequent formation of a sub-epidermal blister. Classical EBA demonstrate little

inflammatory infiltrate as compared with the inflammatory type of EBA. Because of the variable clinical and histological manifestations it is difficult to diagnose EBA by this method alone. Immunological investigations are a very important component for proper diagnosis. Direct immunofluorescence studies on the perilesional skin or mucosa demonstrate the presence of IgG accompanied by complement C3 along the basement membrane zone with a linear pattern. Other immunoreactants such as IgM and IgA may also be in evidence. Indirect immunofluorescence tests of sera on a combination of monkey and guinea pig esophagus substrates and high salt split skin sections are used to detect EBA antibodies. These antibodies can be distinguished from pemphigoid antibodies by their localization in skin where a split is induced at the *lamina lucida* by 1 M NaCl. In contrast, bullous pemphigoid (BP) antibodies react primarily or exclusively in the roof of split skin preparations while the EBA type antibodies bind exclusively to the floor.



Direct IF: Linear deposits of IgG at BMZ



Indirect IF: EBA antibodies on salt split skin

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■ TREATMENT

Classical EBA may be refractory to many treatments such as to corticosteroids, methotrexate and cyclophosphamide. The inflammatory type of EBA responds more favorably to treatment with dapsone and prednisone. Other agents such as cyclosporine in high dose, IV immunoglobulins, and plasmapheresis may also be of help. Supportive therapy is of utmost importance in EBA.

■ SUGGESTED READING

Hallel-Halevy D, Nadelman C, Chen M, Woodley DT. Epidermolysis bullosa acquisita: update and review. *Clin Dermatol.* 2001;19:712-8.

Mayuzumi M, Akiyama M, Nishie W. et al. Childhood epidermolysis bullosa acquisita with autoantibodies against the noncollagenous 1 and 2 domains of type VII collagen: case report and review of the literature. *Br J Dermatol.* 2006;155:1048-52.

Trigo-Guzman FX, Conti A, Aoki V, et al. Epidermolysis bullosa acquisita in childhood. *J Dermatol.* 2003 Mar;30:226-9.

Rinaggio J, Neiders ME, Aguirre A, Kumar V. Using immunofluorescence in the diagnosis of chronic ulcerative lesions of the oral mucosa. *Compend Contin Educ Dent.* 1999;20:943-4.

METHODS OF DIFFERENTIATION	BP	EBA
Serum tests for the presence of BMZ antibodies on normal split skin	Roof Roof & Floor	Floor
Immunofluorescence tests on normal salt split skin biopsy (may be performed on same specimen submitted for routine IF studies)	Roof Roof & Floor	Floor

OPTIMAL BIOPSY SITE FOR IMMUNOLOGICAL INVESTIGATIONS:

Tissue	Site
Skin or Mucosa	Take one biopsy from a perilesional area, adjacent to active or new blister
	Take one biopsy from an adjacent or normal area at least 3 mm from a lesion

SPECIMEN SUBMISSION

Specimen collection kits are available free of charge. Please call [\(800\) 537-8378](tel:8005378378) 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.



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