# Autoimmune Bullous Disease

Mariana A. Phillips, M.D.

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<tr>
<th>Disease</th>
<th>Immunology/Autoantigen</th>
<th>Primary Lesion</th>
<th>Distribution</th>
<th>Distinctive Pathology</th>
<th>Associated Disease</th>
<th>Associated Drugs</th>
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<tbody>
<tr>
<td>Bullous Pemphigoid</td>
<td>BPAg1 (230 kDa)</td>
<td>Tense blister on normal or erythematous base</td>
<td>Lower abd, inner anterior thigh, flexor forearms, may be anywhere 10-35% with oral mucosal involvement</td>
<td>Subepidermal blister with superficial dermal infiltrate with eos 50% with Eosinophilia</td>
<td>No increase in cancer, age appropriate screening</td>
<td>Furosemide, Captopril, Enalapril, Nalidix Acid, PCN, Penicillamine, Sulfasalazine</td>
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<td>BPAg2-NC16A (180 kDa)</td>
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<td></td>
<td>IF: Linear C3 &amp; IgG at BMZ</td>
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<td>IgG4 &gt; IgG1</td>
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<td>Tense vesicle bulla on erythematous or urticarial base, rupture easily</td>
<td>Mucous membranes</td>
<td>Oral &amp; conjunctiva most common; Esophageal, rectal, genital, nasopharyngeal</td>
<td>Blister in lamina lucida with mixed infiltrate — may see Plasma cells, EOS, PMNs</td>
<td>Penicillamine, Clonidine</td>
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<td>Cicatricial Pemphigoid</td>
<td>BPAg2-NC16A &amp; a more distal site Lammin 5-a3 LAD1, a6b4 Type VII collagen IF: Linear IgG and C3 at BMZ</td>
<td>Tense vesicle bulla on erythematous or urticarial base, rupture easily</td>
<td>Mucous membranes</td>
<td>Oral &amp; conjunctiva most common; Esophageal, rectal, genital, nasopharyngeal</td>
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<td>Epidermolysis Bullosa</td>
<td>IgG to NC1 of Type VII collagen (Anchoring fibrils) a-chain-290kDa 145 kDa-NC1 domain IF: Linear IgG at BMZ</td>
<td>Blister on non-inflamed skin Scarring and milia cyst formation</td>
<td>Classic – acral with alopecia &amp; nail dystrophy BP-like widespread with accentuation in skin folds Brunsting-Perry – head &amp; neck involved</td>
<td>Mucosal form</td>
<td>Subepidermal blister in the sublamina densa PMN predominant</td>
<td>Inflammatory bowel disease Diabetes Thyroiditis Myeloma Bullous SLE Lymphoma</td>
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<td>Aquisa</td>
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<td>Herpes Gestationis</td>
<td>IgG1 &amp; C3 BPAg2 NC16A domain C3 is the main factor! IF: Linear C3 at BMZ</td>
<td>Erythematous papules Papulo-vascular Urticaria Tense Bulla Extremely pruritic</td>
<td>Per-umbilical, abdomen, may involve palms, soles, chest, back Mucosa spared</td>
<td>Necrosis of basal cells with vaculization Bullous teardrop shaped blister Edema of dermal papilla</td>
<td>Grave’s disease Hydatidiform mole, choriocarcinoma Usually in 4th to 7th month of pregnancy or in post partum period No increase in maternal mortality May recur at delivery, oral contraceptive use, menstruation, and subsequent pregnancy</td>
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<td>Chronic Bullous Disease</td>
<td>Linear IgA1 + C3, IgG</td>
<td>Pruritic tense blister on inflammatory base</td>
<td>Perineum, perioral region, “collarette of blister” Lower trunk and thighs +oral lesion</td>
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<td>HLA B6</td>
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<td>of Childhood</td>
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**References**

### Disease Immunology/ Autoantigen Primary Lesion Distribution Distinctive Pathology Associated Disease Associated Drugs

**Linear IgA Dermatosis**
- Linear IgA1; antigen unknown LAD-1 (97kDa, 120 kDa); Type VII collagen.
- IF: Linear IgA at BMZ + IgG/C3
- Annular/ grouped papules, vesicles, bulla, urticaria
- Pruritic, symmetrical, extensors — elbows, knees, buttocks.
- 70% with oral lesions
- Subepidermal bulla, neutrophils along BMZ; perivascular lymphocytic infiltrate
- Lymphoid malignancies
- Thyroid disease
- Vancomycin
- Lithium
- Diclofenac

**Dermatitis Herpetiformis**
- IgA1 + C3 granular deposits at BMZ.
- IF is + in normal appearing skin (IgA & C3 deposits not affected by treatment with dapsone, does decrease with gluten free diet)
- Papulovesicle + hemorrhagic Urticarial plaques
- Symmetrically on extensor surface; elbows, knees, buttocks, sacral shoulders
- Blister in lamina lucida
- Neutrophilic microabscesses in dermal papilla + EOS
- Accumulation of PMN in BMZ
- Late – necrosis of keratinocytes
- Gluten sensitive enteropathy
- Increased GI lymphoma
- DM, SLE, vitiligo, Non-Hodgkin’s, Sjogren’s
- HLA-B8
- HLA-DR3
- DQ-α2

**Pemphigus Foliaceus**
- IgG to 160 kDa Desmogliens 1 and 2; IgG4- complement independent
- IF: intercellular IgG throughout epidermis
- Pemphigus Erythematosus: +ANA, +lupus band test, IgG and complement intracellular and at BMZ
- Scaly crusted erosions on erythematous base
- Seborrheic distribution — face, scalp, trunk
- Rarely Mucosa inv. Fogo selvagem-endemic to Brazil
- Blister just below stratum corneum in granular layer with acantholysis
- Exocytosis of EOS
- Perivascular infiltrate with EOS
- Myasthenia gravis
- Thymoma
- Penicillamine
- Captopril
- Piroxicam

**Pemphigus Vulgaris**
- IgG to Desmogliens 3 in mucosal predominant
- IgG to both Desmogliens 1 and 3 in mucosal and cutaneous disease
- IgG4- complement independent
- Painful, not pruritic flicced Blisters on normal skin
- Occur anywhere In majority of pts, mucous membrane involvement will be the presenting symptom
- Suprabasilar blister with acantholysis and acantholytic cells in the blister cavity
- Pemphigus vegetans – intraepidermal eosinophilic abscesses
- Dyskeratosis, suprabasilar acantholysis with basal cell vacuolar change and exocytosis
- Non-Hodgkin’s Lymphoma
- Leukemia (CLL)
- Thymoma (6%)
- Waldenstrom’s macroglobulinemia
- Castleman’s disease (HHV-8)

**Paraneoplastic Pemphigus**
- IgG and C3 Dsg 1, DSG 3, Plectin, BPAg1, Envoiplakin, Penplakin
- 250, 230, 210, 190, 170 kDa proteins involved
- IgG and C3 IF: IgG and C3 intercellular and linear along BMZ
- blisters on erythematous skin
- Severe oral and conjunctival involvement
- Intraepidermal eosinophilic abscesses
- Penicillamine
- Captopril
- Drugs are not implicated as often as in pemphigus foliaceus

If you would like to contribute to this popular, widely-read feature, please contact the editor, Dean Monti at dmonti@aad.org.