



Shannon Hart, DO, is a PGY-2 at the KCU-GME Consortium/ADCS Orlando Dermatology Residency Program.



Nathaniel A. Marroquin, DO, is a PGY-2 at the KCU-GME Consortium/ADCS Orlando Dermatology Residency Program.



Ryan Ottwell, DO, FAAD, is a dermatologist at the Oklahoma State University Center for Health Science, Department of Surgery – Dermatology.

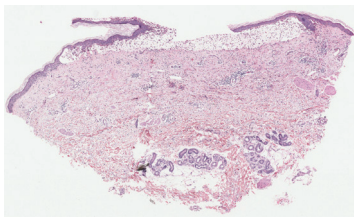
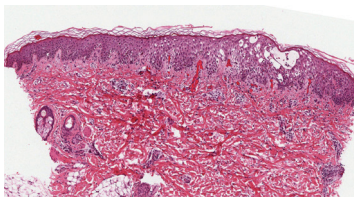
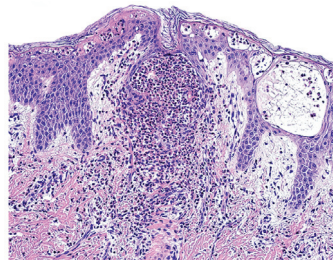
Eosinophilic spongiosis differential diagnosis = HAAPPIE

By Shannon Hart, DO, Nathaniel A. Marroquin, DO, and Ryan Ottwell, DO, FAAD

Diagnosis	Histopathologic features	Other important fodder	Histology image*
H: Herpes gestationis (pemphigoid gestationis)	- Subepidermal blister with eosinophils ± neutrophils - Eosinophilic spongiosis - Papillary dermal edema	- Direct immunofluorescence (DIF) shows linear deposition of C3 along the basement membrane zone (BMZ), n-serrated pattern - Pattern is identical to bullous pemphigoid - Salt-split testing shows staining to the roof of the blister (epidermal side)	
A: Arthropod bite	- Wedge-shaped (V-shaped) superficial & deep perivascular infiltrate with eosinophils, lymphocytes, and histiocytes - Overlying spongiosis ± epidermal necrosis	- Pronounced spongiosis may lead to blister/bullae formation → bullous arthropod reaction - Flame figures may occur secondary to eosinophilic degeneration - Consider evaluating for underlying hematologic malignancy or latent Epstein-Barr virus infection in patients who present with atypical or exaggerated reactions to arthropod bites	
A: Allergic contact dermatitis (ACD)	- Characterized by spongiosis (spongiotic dermatitis) with acute, subacute, and chronic forms - Acute ACD characterized by a normal basket-weave orthokeratosis, spongiosis with eosinophilic exocytosis and a dermal inflammatory infiltrate comprised eosinophils, lymphocytes, and histiocytes - Pronounced epidermal edema may lead to vesicle formation - In subacute and chronic ACD, spongiosis becomes less prominent, and the epidermis shows acanthosis with overlying hyperkeratosis or parakeratosis	- Type IV delayed hypersensitivity reaction - Langerhans cell microabscesses in the epidermis are associated with ACD but are not specific for the diagnosis - No keratinocyte necrosis (vs. ICD which shows keratinocyte necrosis)	
P: Pemphigus (vulgaris)	- Intraepidermal blister - Suprabasilar acantholysis with preservation of basal keratinocytes, "tombstoning" - No keratinocyte necrosis - Blister cavity contains acantholytic keratinocytes and eosinophils	- DIF shows intercellular deposition of IgG and C3 - creating a "chicken-wire" pattern - Acantholysis may involve hair follicles (vs. Hailey-Hailey disease which spares hair follicles)	

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Diagnosis	Histopathologic features	Other important fodder	Histology image*
P: (bullous) Pemphigoid	- Subepidermal blister with eosinophils ± neutrophils† - Eosinophilic spongiosis - Papillary dermal edema	- Perilesional DIF demonstrates linear deposition of IgG and C3 at the dermoepidermal junction, exhibiting an n-serrated pattern - Indirect immunofluorescence on salt-split skin reveals immunoreactant localization to the blister roof	
I: Incontinentia pigmenti	Vesicular stage: - Eosinophil-rich spongiosis producing intraepidermal vesicles with marked eosinophilic exocytosis - Scattered keratinocyte apoptosis may be seen Verrucous stage: - Marked hyperkeratosis and papillomatosis with minimal spongiosis and few eosinophils - Conspicuous dyskeratosis forming whorled and clustered aggregates within the epidermis and stratum corneum Hyperpigmented stage: - Evidence of pigment incontinence with multiple melanophages in the dermis Hypopigmented stages: - Thinning of the epidermis is present, along with reduced melanin within the basal layer - Pilosebaceous structures and eccrine sweat glands are entirely absent - Apoptotic keratinocytes may also be observed within the epidermal layer	- X-linked dominant disorder due to mutations in IKBKG (NEMO) gene - Vesicular stage observed at birth and up to 1 month of age - Verrucous stage observed up to 2 years of age - Hyperpigmented stage observed up to adolescence - Hypopigmented stage may be observed throughout adulthood - Note that necrotic keratinocytes are a classic finding	 Vesicular stage
E: Erythema toxicum neonatorum‡	- Subcorneal, intraepidermal, or intrafollicular pustules composed of eosinophils, with occasional neutrophils - Superficial dermal edema and eosinophilic infiltration	Smear of pustule contents stained with Wright stain demonstrates numerous eosinophils	

* All histology slides were obtained from PathPresenter.com with their permission. The authors thank PathPresenter and the pathologists who contribute to their website.

† Autoantibodies activate complement (→ neutrophil recruitment) and trigger a Th2 response with IL-5 (→ eosinophil recruitment); both cells release proteases that damage the dermal-epidermal junction and cause subepidermal blistering.

‡ Erythema toxicum neonatorum histology image permission was obtained from Dr. Ranata Joffe, originally published in Dermatopathology: Practical & Conceptual (January to March 2006, Volume 12, Issue 1).

References:

- Elston, D. M., Ferringer, T. C., Ko, C., High, W. A., & DiCaudo, D. J. (2025). *Dermatopathology* (4th ed.). Elsevier.
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