

# Pemphigus foliaceus

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## Pathologist's perspective

Clinically pemphigus foliaceus is primarily a pustular, crusting and erosive disease. Cytologically and histologically it is characterised by the presence of granulocytes with acantholytic cells.

Acantholysis is defined as a loss of cohesion between epidermal cells and can occur due to:

1. Breakdown of existing desmosomes due to autoantibodies to components (desmogleins, desmocollins) that reduce function and/or signalling, e.g. Pemphigus foliaceus, pemphigus vulgaris.
2. External proteases that breakdown the protein constituents, e.g. *Trichophyton* spp, *Staphylococcus* spp.
3. Hereditary defects in the synthesis of intercellular bridges (desmosomes), e.g. Darriers disease.

Acantholytic cells are usually individualised and more rounded due to loss of desmosome structure/function. However, they are still intact, metabolically active and capable of DNA synthesis. They can have intensely blue (cytology) or eosinophilic (histology) cytoplasm but are not keratinised. Nuclei are usually central and can appear relatively normal with visible nucleoli. Eventually acantholytic cells will degenerate and die. Acantholysis of groups of adjacent keratinocytes leads to vesicle or pustule formation.

In dogs, pemphigus foliaceus occurs due to IgG autoantibodies to desmocollin-1 resulting in superficial acantholysis. In comparison, pemphigus vulgaris in dogs occurs due to autoantibodies to desmoglein-3 resulting in suprabasal acantholysis.

Pemphigus erythematosus is a similar intraepidermal acantholytic disease to pemphigus foliaceus but also has a cytotoxic/interface pattern similar to lupus erythematosus diseases. Despite this, clinically it is a milder disease restricted to the face and probably reflects a variant of pemphigus foliaceus as currently it does not seem prognostically different.

In cats, pemphigus foliaceus is also due to autoantibodies but the target within the desmosomal complex has not been identified yet.

Pemphigus foliaceus is the most common acantholytic disease in veterinary species but there are other.

## Acantholytic diseases in companion animals

1. Pemphigus foliaceus/erythematosus.
2. Pustular drug eruptions.
3. Superficial pustular dermatophytosis.
  - a. Usually *Trichophyton* spp.
  - b. Dogs and horses.
4. Bullous impetigo.
  - a. Staphylococcal
5. Paraneoplastic pemphigus.
6. Pemphigus vulgaris.
7. Squamous cell carcinoma.
8. Epitheliotrophic lymphoma.
9. Hailey-Hailey/Darriers disease.

## Diagnosis of pemphigus foliaceus

Diagnosis can be made cytologically or histologically with consideration of the clinical lesions, distribution and ruling out other differential diagnoses outlined above. However, histology is the only diagnostic technique that can identify vascular lesions which Zhou *et al.* (2021) demonstrated were significantly associated with presence of concurrent systemic disease, longer times to remission and higher incidence of adverse effects to treatment.

Cytology and histology of intact pustules in pemphigus foliaceus usually indicate acantholytic cells with well-preserved granulocytes (neutrophils or eosinophils) and no bacterial involvement. Histologically pustules are usually subcorneal to intraepidermal with acantholytic cells and granulocytes. There are also usually serocellular crusts from ruptured pustules with acantholytic cells, degenerate granulocytes which may also have bacteria present which can be confused with superficial pyoderma. However, pustules from pemphigus foliaceus will usually have higher numbers of acantholytic cells than superficial pyodermas or dermatophytosis.

Ideally intact pustules should be sampled for cytology or histology to minimise confusion with a superficial pyoderma. A recent study (Spriggs 2024) confirmed significantly higher numbers of acantholytic cells from intact pustules than beneath crusts in pemphigus foliaceus. Cytology from impression smears of intact pustules indicated an average of  $\geq 5$  acantholytic cells/500x field had a sensitivity of 84–100% and specificity of 95–97% for the diagnosis of pemphigus foliaceus. However, the same study also confirmed significantly increased numbers of acantholytic cells beneath crusts in pemphigus foliaceus as compared to superficial pyoderma which means that crusts can still be diagnostically useful.

This is important as intact pustules can be difficult to find clinically, especially in cats or chronic canine cases due to self-trauma and episodic waves of active lesions. Crusts are also useful for dermatophyte or bacterial culture if a resistant infection is a differential diagnosis therefore should be submitted fresh in suspect cases.

Crust preservation is also important for histology which is one of the main reasons why surgical preparation and clipping is contraindicated for dermatopathology biopsies. Biopsies should always include any adherent crusts even if they are dislodged during the biopsy process. Multiple incisional or 8mm punch biopsies are usually adequate especially if they include intact pustules.

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