

# Pemphigus in the dog and cat. Part 2: Diagnosis and management

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## DIAGNOSIS

The clinical features of the pemphigus group of conditions, together with cytological and histological examination, form the basis for diagnosis. However these dermatoses are uncommon to rare. The primary role of the clinician is to rule out more common differential diagnoses. The major differential diagnoses of each condition are listed in Tables 1–3.

**TABLE 1: Differential diagnosis of pemphigus foliaceus**

Bacterial folliculitis  
Impetigo  
Dermatophytosis  
Keratinisation defects  
Pemphigus erythematosus  
Demodicosis

**TABLE 2: Differential diagnosis of pemphigus erythematosus**

Bacterial folliculitis  
Zinc responsive dermatitis  
Dermatophytosis  
Keratinisation defects  
Dermatomyositis  
Discoid lupus erythematosus

**TABLE 3: Differential diagnosis of pemphigus vulgaris**

Bullous pemphigoid  
Epidermolysis bullosa  
Systemic lupus erythematosus  
Erythema multiforme  
Ulcerative dermatitis (Rough Collie and Sheltie)  
Epitheliotropic lymphoma

## DIAGNOSTIC APPROACH

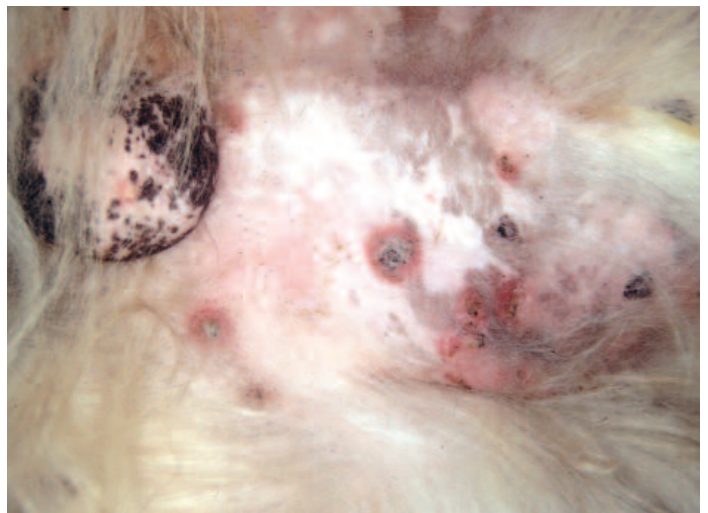
The approach to the diagnosis of the pemphigus group of conditions relies on the following:

1. History
2. Clinical examination
3. Diagnostic tests
  - a. Skin scrapings and hair plucks (rules out demodicosis and dermatophytosis)
  - b. Exfoliative cytology (demonstrates acantholysis and rules out bacterial pyoderma)
  - c. Skin biopsy (definitive diagnosis).

The primary diagnostic feature of all the pemphigus group of conditions is acantholysis. This feature can be seen in other dermatoses including dermatophytosis and bacterial pyoderma, and so care is required in the interpretation of this finding.

## Cytological examination

Ideally, material should be taken from an intact pustule (Fig. 1). These lesions are very transient however, especially in pemphigus foliaceus and erythematosus. If only a few intact pustules are available, these should be reserved for histological examination. If pustules are available, these should be carefully opened and the extruded material carefully spread onto a slide.



**Fig. 1:** Intact pustules should be sampled if available.



Fig. 2: Crusting lesions in a cat with pemphigus foliaceus.



Fig. 3: Examination of a purulent exudate from the nail fold of a cat may be useful.

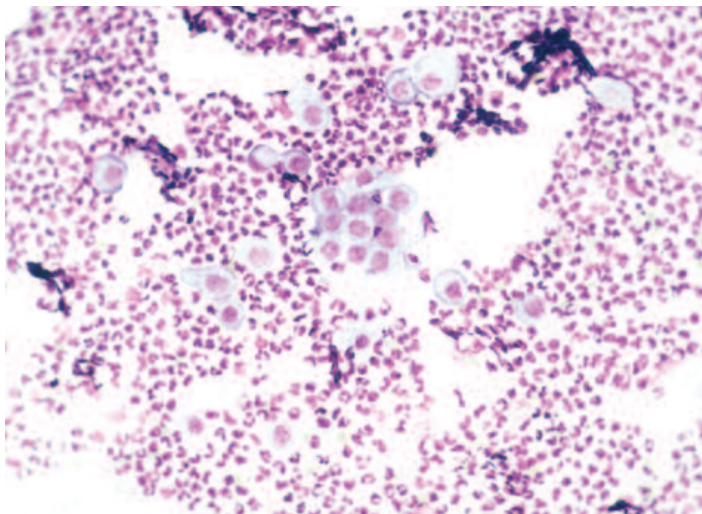


Fig. 4: Cytology sample from a dog with pemphigus: note acantholytic cells and non-degenerative neutrophils.

#### TABLE 4: Cytological features of pemphigus conditions

Non-degenerative neutrophils  
 Acantholytic cells (rounded and sometimes surrounded by neutrophils)  
 Lack of significant bacterial infection

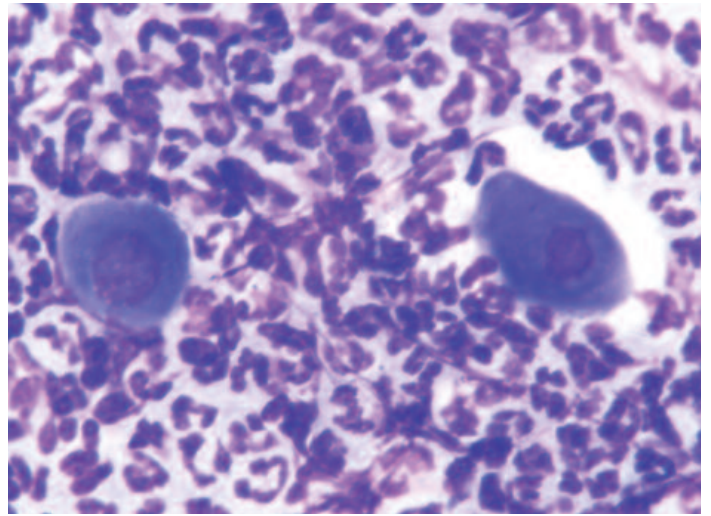


Fig. 5: Close up demonstrating the rounded appearance of the acantholytic cells.

Material often needs to be taken from areas of crusting (Fig. 2). Crusts are gently removed, and a slide is touched gently onto moist eroded areas. Examination of material from the nail beds of affected cats may also be useful (Fig. 3).

In all cases, samples should be taken from several sites; acantholysis can appear to be present in one sample and completely absent in another. Cytological features to be looked for are listed in Table 4 (Figs. 4 and 5).

If significant bacteria are present, especially intracellular in location, or if degenerate neutrophils are present, then antibacterial therapy should be given prior to resampling and before skin biopsy samples are taken.

#### Skin biopsy

Diagnosis of the pemphigus conditions is by the demonstration of acantholysis in histological sections. This is made more difficult by the poor preservation of intact, often superficial pustules, and the ability of other conditions to produce very similar features. Ideally, early pustular lesions should be sampled and multiple (4-5) biopsies should be taken if possible. Even the rotational forces of a punch biopsy can disrupt lesions, and so if possible elliptical biopsies should be taken; however the need for general anaesthesia needs to be weighed up against the choice of technique.

If pemphigus vulgaris is suspected, biopsies of lips and skin are more reliable than samples taken from

**TABLE 5: Histological signs of pemphigus foliaceus**

Large subcorneal pustules  
Non-degenerate neutrophils  
Acantholytic cells  
The pustules may extend into follicular epithelium  
Care to rule out dermatophytosis (PAS stain if suspected)  
If apoptosis is present consider drug reaction

**TABLE 6: Histological signs of pemphigus erythematosus**

Large subcorneal pustules  
Non-degenerate neutrophils  
Acantholytic cells  
Interface dermatitis  
Basal cell damage

**TABLE 7: Histological signs of pemphigus vulgaris**

Supra-basilar cleft  
Rows of basal cells seen (tombstones)  
Hair follicles may be involved

**TABLE 8: Histological signs of paraneoplastic pemphigus**

Supra-basilar cleft  
Rows of basal cells seen (tombstones)  
Hair follicles may be involved  
Intra-epidermal pustules (throughout epidermis)  
Significant apoptosis

the oral cavity. The margins of recent ulcers may also be diagnostic. The histological features of the pemphigus conditions are listed in Tables 5-8.

Immunocytochemistry and immunofluorescence may be used to aid diagnosis but these techniques are complex and difficult to interpret.

#### PROGNOSIS

The prognosis of pemphigus foliaceus and erythematosus is guarded to good, with most cases responding to treatment, although some may require long-term management. The prognosis of pemphigus vulgaris is guarded to poor, with very few documented cases surviving for more than two years.

Drug-related pemphigus carries a good prognosis provided the offending drug can be identified and withdrawn.

The prognosis of paraneoplastic pemphigus depends upon the prognosis and management of the underlying neoplasia.

#### MANAGEMENT

There are numerous discussions of the management of autoimmune disease available, and the basic features of management will be discussed here.

The most common treatment for the pemphigus group of conditions is the use of oral glucocorticoids, sometimes in combination with azathioprine or cyclophosphamide in the dog or with chlorambucil in the cat. If a drug-related pemphigus is suspected, all possible offending drugs should be withdrawn, and the animal should be fed foodstuffs free from preservatives.

Glucocorticoids are initially used at a dose of 1 mg/kg q 12h or 24h, and are continued until lesions have reduced or resolved. If lesions settle then pustules appear to return, further cytology should be taken to rule out new lesions being caused by bacterial pyoderma due to immunosuppression. If vomiting occurs with the glucocorticoids then enteric-coated prednisolone may be better tolerated.

Once the patient is in remission, the dosage is slowly tapered to alternate day therapy and then gradually withdrawn.

If lesions do not resolve, or if recurrence occurs at a high dose of glucocorticoids, azathioprine may be added at 2 mg/kg q 24h. Although azathioprine is usually well tolerated in the dog, routine haematology should be performed every two weeks to assess for blood dyscrasias. Other side effects including GI effects and liver toxicity have been reported.

An alternative to azathioprine in the dog is cyclophosphamide at 5-10 mg/kg q 24h. Again side effects may occur, with haemorrhagic cystitis, GI signs and bone marrow depression all possible.

In the cat, the drug of choice to accompany glucocorticoids is chlorambucil at 0.1-0.2 mg/kg q 24h or on alternate days.

It must be remembered that these products, other than the glucocorticoids, are all unlicensed drugs, and owners should not handle immunosuppressive drugs without wearing gloves.

Other treatments used for the pemphigus group include gold salts (chrysotherapy) and a combination of tetracycline and nicotinamide. The former may be difficult to obtain and is expensive; the latter is only appropriate in very mild cases but well worth trying (particularly when trying to wean off steroids).

#### CONCLUSIONS

Again it must be emphasised that the pemphigus group of conditions are uncommon to rare. Once a diagnosis is made robust therapy is required, and may be needed long-term.

*These multiple choice questions are based on the above text. Answers appear on page 59.*

- 1. Which of the following are differential diagnoses for pemphigus foliaceus:**
  - a. dermatophytosis
  - b. dermatomyositis
  - c. Vogt-Koyanagi-Harada syndrome
  - d. bullous pemphigoid
  
- 2. What is the essential pathological change common to all the pemphigus conditions:**
  - a. lichenoid infiltrate
  - b. spongiosis
  - c. acantholysis
  - d. acanthosis
  
- 3. Which diagnostic tests are most useful to diagnose pemphigus conditions:**
  - a. exfoliative cytology
  - b. skin biopsy
  - c. immunofluorescence
  - d. clinical biochemistry
  
- 4. Which of the following drugs are useful in management of pemphigus foliaceus in the cat:**
  - a. prednisolone
  - b. dexamethasone
  - c. azathioprine
  - d. chlorambucil

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