

AKITA CLUB OF AMERICA GENETICS AND HEALTH COMMITTEE

PEMPHIGUS

What is Pemphigus?

Structure of the Skin

Normal skin or epidermis is made of up several layers of different cells. In addition to skin cells, these layers also contain:

- melanocytes which produce pigment
- Langerhans' cells which are part of the immune system
- Merkel cells which are part of the nervous system

Underneath the visible skin are layers of living skin cells that divide and move upward, changing in character, composition, and shape as they do so. So the oldest cells are on the outside and began their life on the inside at the bottom.

This bottom layer of "baby" cells is called the stratum basale or basal layer. The cells are keratinocytes, because production of the structural protein keratin begins here. This single layer of keratinocytes sits atop the cells of the dermis or deeper tissue layer.

As these cells divide, they move upward into the next skin layer, the stratum spinosum or prickle cell layer, one or two layers thick in most places. Their name comes from little spines or prickles.

Cells in the next layer are characterized by tiny granules, which give it the name stratum granulosum or granular layer. It's usually only one or two layers deep, but is thicker around the hair follicles. These cells have more keratin, but are still alive; they still divide to form new cells.

At the top is the stratum corneum or horny layer, what is visible to us as skin. Much deeper than the other layers, its overlapping plate-like cells--think of a house that has been reroofed several times, each one being laid over the other--are actually dead and fully keratinized. They flake off easily, but they form a tough layer of protection for the living cells underneath.

Even tougher is the stratum lucidum. This specialized skin makes up the skin of the foot pads and nose leather of the dog and it is also dead. In these areas, the other skin layers may also be thicker.

Symptoms of Pemphigus Complex

Pemphigus is a disease that results when the body's immune defenses attack its own skin. Something interferes with the recognition process and treats the skin as if it were a foreign substance. Actually, Pemphigus is a complex of diseases differentiated by the skin layer which is attacked. It is found across many species, including humans, cats, dogs, and horses.

The most severe form is Pemphigus Vulgaris. The attachment of the basal and prickle cell layers is

attacked. Fluid filled blisters called vesicles form and eventually break open, resulting in painful ulcerated sores. These are most common in areas where normal skin meets specialized skin, like the skin of the lips, nose, eyes, pads, nails, as well as the mucosal skin of the mouth.

Pemphigus Erythematosus is similar but involves the outer skin layer or stratum corneum. It looks like a mild case of Pemphigus Foliaceus and may be more prevalent in collies. The ulcerated sores are usually restricted to the facial area and are very similar to those found in discoid lupus. Indeed, some researchers feel they are related in some fashion.

Bullous Pemphigoid involves the whole epidermal layer and is most common in humans. Fortunately, the incidence of all Pemphigus in humans is lower than in dogs. Nonetheless, many research projects look for relationship between Pemphigus in humans and other animals.

The rarest form found in dogs is Pemphigus Vegetans. Wart-like sores appear, usually, over the entire body.

The most common form is Pemphigus Foliaceus, affecting Dobermans, Bearded Collies, Newfoundlands, and several spitz breeds, among others. Generally speaking, Akitas seem to be affected more drastically than other breeds. The attack here is against the granular cells' attachment to each other. As these cells separate, crusty sores and lesions develop, mostly around the eyes, nose, ears, feet, and groin.

Affected dogs may have pronounced dandruff, and hair loss. The skin may be hyperpigmented, and the pads may slough off. They display lethargy, stiffness, decreased appetite, and depression. If secondary infections are present, they may also have a fever.



Above: Before and after treatment photos. Unfortunately, this dog died of treatment complications.

Notice the "black skin" that results from hyperpigmentation. This can be a complication of hypothyroidism as well. This dog was diagnosed with both Pemphigus and thyroid problems.

Photos courtesy of Nancy Lamm.



Causes

Because Pemphigus is an autoimmune disease, an underlying genetic component is suspected. Possibly, these individuals are predisposed to developing some form of Pemphigus in the presence of the right triggers. A number of these are recognized in humans, and some may apply to dogs as well. Certainly, further research into possible causative agents is warranted.

In humans, the complex is associated with exposure to pesticides, especially organophosphates and organochlorines, and with treatment by various drugs. Commonly reported in humans is the use of d-penicillamine to treat rheumatoid arthritis. In dogs, adverse reactions to trimethoprim-sulfonamide (Tribrissen) is the most often reported. Also reported are reactions to Ampicillin, Cimetidine, Diethylcarbamazine, Procainamide, Sulphonamides, Thiabendazole, and Triamcinolone. However, since many of these are commonly prescribed, the incidence is probably quite low. ([ProVet website](#) look under *Drug related skin reactions*)

Human patients with lymphomas have also developed pemphigus. Researchers into canine lymphoma are unaware of any such association in dogs. (Personal communication, Dr. J. Modiano). The presence of gram negative bacteria in patients that later manifested Pemphigus raises questions about infective agents as either causing or exacerbating Pemphigus. Also under investigation are viruses of the herpetoviridae family, such as herpes simplex and Cytomegalovirus (CMV).

Certain types of food may trigger Pemphigus in humans. Groups include phenols, tannins, and thiols, and avoiding them may lead to remission of symptoms. Whether this applies to dogs is undetermined.

Photosensitivity is a problem for affected individuals across species, especially those with Pemphigus Erythematosus. Exposure to ultraviolet radiation or even x-rays can make affected cases worse and are reported to have induced Pemphigus in dogs. ([Pemphigus Article](#), Brenner, Sara, *et al.*, *Pemphigus: An acronym for a disease with multiple causes*. **The International Pemphigus Foundation Website**)

Diagnosis

Unfortunately, sores typical of Pemphigus can also be due to a lot of different causes, including allergies, drug reactions, systemic lupus erythematosus, discoid lupus, and skin cancers. Superficial pyodermas (hot spots) can also be confused with Pemphigus lesions.

Diagnosis **MUST** be made by a qualified professional's examination of a skin biopsy. This may be done with a local anesthesia and should be taken from an affected area.

Prognosis and Treatment

Before the advent of immunosuppressive drugs, Pemphigus in humans often proved fatal because of secondary infections and/or damage to the mucosal linings of the mouth and esophagus. The same is probably true for dogs. ([Oral Manifestations of Autoimmune Blistering Diseases](#). Chan, Lawrence, *et. al.*, *Oral manifestations of autoimmune blistering disease*, **EMedicine Website**)

Pemphigus Erythematosus

The prognosis for those with Pemphigus Erythematosus is better than with other members of the Pemphigus complex. Exposure to sunlight and other radiation should be minimized. Helpful in early treatment are topical sunscreens and topical glucocorticoids as well as supplementation with Vitamin E and Omega complex fatty acids. If symptoms progress further, tetracycline and niacinamide may produce a remission of symptoms. (White, Sd. *et. al.*, Use of tetracycline and niacinamide for treatment of autoimmune skin disease in 31 dogs, *J Am Vet Med Assoc.* 1992 May 15;200(10):1497-500)

If the disease progresses, oral glucocorticoids as well as immunosuppressive drugs such as Azathioprine or Chlorambucil might be necessary. However, these drugs are not without significant risk.

Recently, J. Griffies, *et. al.*, reported some promising results in treating both Discoid Lupus and Pemphigus Erythematosus with topical application of 0.1% tacrolimus, an immunomodulator produced by a fungus. Remission with just tacrolimus alone occurred in some dogs, while others were able to decrease or discontinue steroids. (Griffies, Joel D., *et. al.*, Topical 0.1% Tacrolimus for the treatment of discoid lupus erythematosus and Pemphigus Erythematosus in dogs. *J. Am. An. Hosp. Assoc.* 2004, Jan-Feb; 40(1):29-41)

Pemphigus Foliaceus

The mortality rate for dogs affected with Pemphigus Foliaceus dogs is still high for a variety of reasons. (Gomez, S., D.O. Morris, M. Rosenbaum, and M Goldschmidt, *Outcome and complications associated with treatment of pemphigus foliaceus in dogs: 43 cases (1994-2000)*, *J Am Vet Med Assoc.* 2004 Apr 15;224(8):1312-6).

Immunosuppression is essential, so affected dogs always receive corticosteroids, usually for the remainder of their lives. Because corticosteroids can have serious side-effects, these dogs must be closely monitored. They may drink more water than normal and can develop urinary incontinence. Cortisone stimulates the appetite, so they eat more, and metabolic changes may result, making them more susceptible to weight gain. Long-term steroid use can bring on diabetes.

Most dogs are treated with a combination of steroids and stronger immune suppressants. The most common is Azathioprine, but its effectiveness isn't obvious for some time after it is started. This drug can cause problems with bone-marrow production, so follow-up blood testing is necessary.

Open sores present a convenient hosting ground for bacteria, so secondary infections are frequently a problem. Cephalexin is most commonly used, and baths with special antimicrobial soaps may also help. One of the most significant findings in the Gomez study was a significantly decreased mortality rate in dogs treated concurrently with antimicrobials.

In the 43 affected dogs they followed, Gomez, *et. al.*, found no difference in survival time between dogs treated solely with steroids vs. those treated with a combination of steroids and azathioprine. However, they did report a high incidence of dogs that either died from or were euthanized because of complications of corticosteroid treatment. In theory at least, using azathioprine to keep steroid doses low should increase the survival chances of dogs that might otherwise have succumbed early to problems related to high-dose

steroids.

Gomez, et. al., reported a fatality rate of 60.5% in the dogs they followed, due not so much to the disease itself as to difficulties in treatment. Successful treatment requires a lot of cooperation and coordination between veterinarians and owners. For a variety of reasons ranging from expense to poor response to treatment (probably side effects of medications), many owners euthanized their dogs. Almost all the deaths in this study (88.4%) occurred before ten months of treatment.

Pemphigus Foliaceus seems to affect more males than females (Gomez reported the ratio at 30:13), gender wasn't significant to survival rates. Of the 17 dogs that were alive when the study terminated, four were no longer symptomatic and were no longer on any kind of treatment. In these dogs, Pemphigus might have been induced by drugs. This would be consistent with other reports in dogs and humans.

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