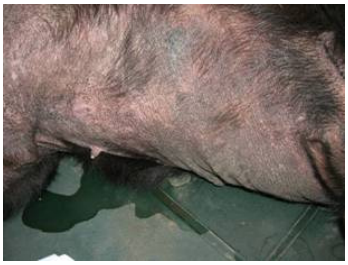
Atopic Dermatitis In Dogs and the Epidermal Barrier Defect.

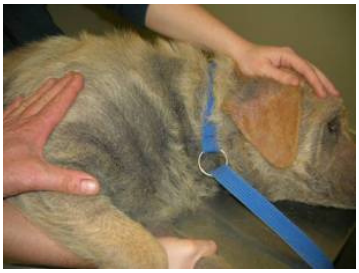
Hydration of the skin and treatment of the dysfunction of the epidermal barrier has long been a cornerstone of the management of atopic dermatitis in humans. In veterinary dermatology, we have lagged behind our human colleagues in this area while perhaps leading them in the area of immunotherapy for atopic dermatitis.

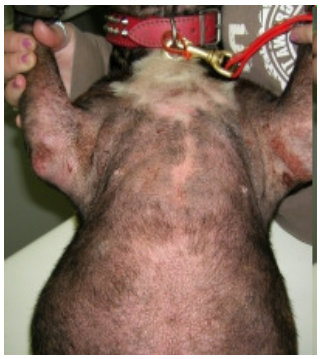
There is little doubt that atopic dogs have a skin barrier defect. This not only causes dry skin through increased trans epidermal water loss (which in itself is a cause of irritation and itch). Furthermore, defects in the skin barrier function result in increased access of allergens to the immune cells of the skin and also increased adhesion and surface proliferation of micro-organisms.

Hydration and Restoring the Epidermal Barrier



Major cornerstone of managing human atopic dermatitis.





The cells of the epidermis, called keratinocytes, can be likened to bricks floating in a sea of lipids. Intracellular lipids are produced within lamellar bodies in the lower layers of the epidermis and then released into the intracellular space by a process of exocytosis. There is a hydrolipid film on the surface of the epidermis which is produced by intracellular lipids, secretions of the apocrine sweat glands and lipid rich ceruminal glands.

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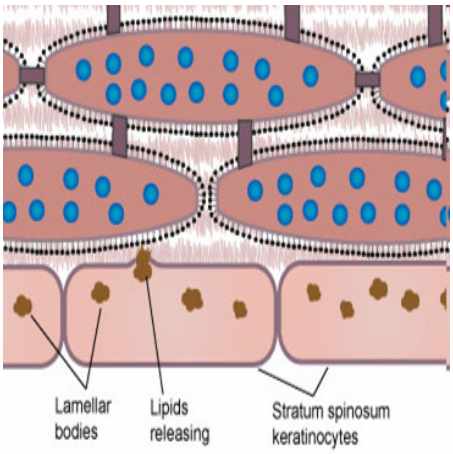
Bricks and Mortar Model of the Epidermis

- Surface hydrolipid film
- Keratinocytes in a “sea” of lipids
- Tight junctions between keratinocytes



- Adhesion and proliferation of microorganisms
- Ingress of allergens
- Drying via increased transepidermal water loss

There is no doubt that in dogs with atopic dermatitis there is a barrier defect. The evidence is overwhelming. The question that remains to be answered is whether they barrier defect seen atopic dogs is a primary lesion responsible for the development of the disease or is a major complication of the disease and results in its perpetuation.

In humans, approximately 30% of atopic individuals have no detectable IgE either by blood test or by intradermal allergen test. These humans are referred to as having “ intrinsic atopic dermatitis” . In the case of humans, there is a strong body of opinion that believes the barrier defects identified in humans are indeed the primary cause in these “intrinsic atopics”.

In dogs, a subset of atopic individuals also are negative to both intradermal and blood IgE tests. These dogs are referred to as having “atopic-like dermatitis”. At this stage it is a bit of a chicken and egg argument over the barrier defect comes first in these dogs or develops later as a result of the disease due to non-IgE based immune reactions.

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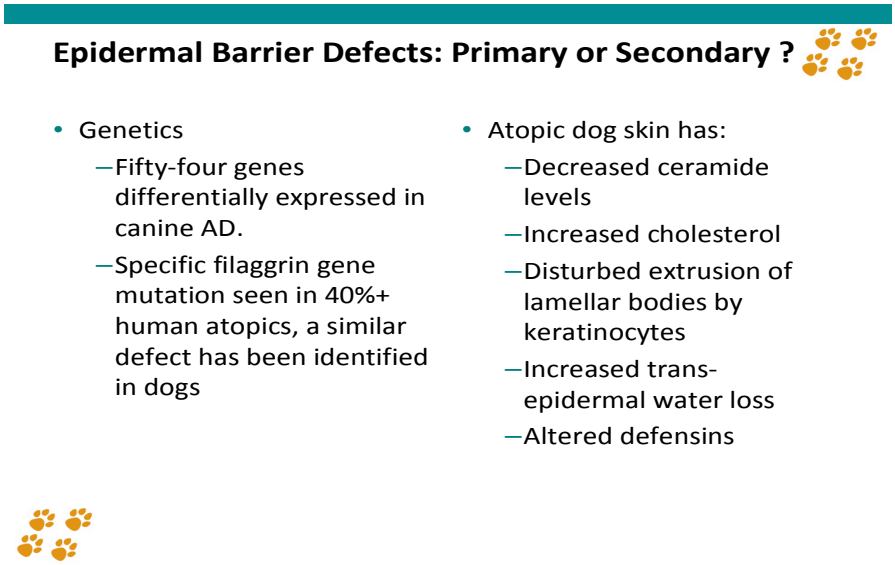
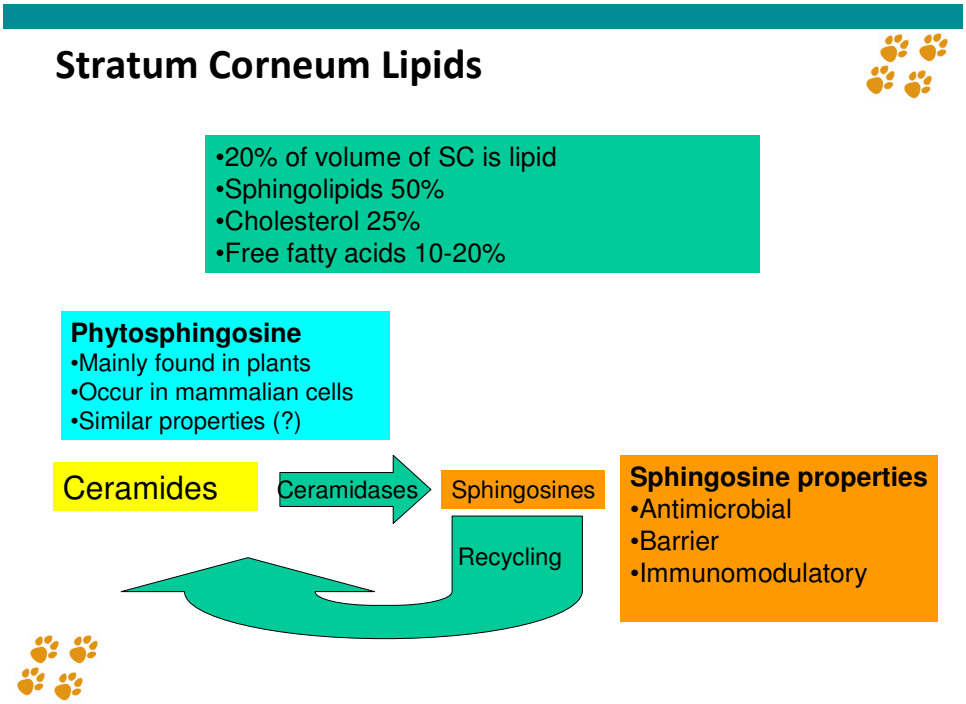




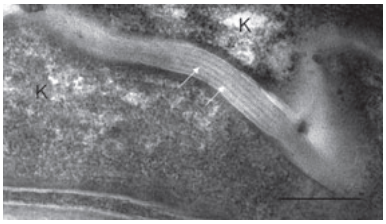
Approximately, 50% of the intercellular lipids in the epidermis are sphingolipids. Ceramides from the lamellar bodies are converted by ceramidases to sphingosines. Sphingosines have antimicrobial, moisturiser and immunomodulatory properties. Atopic dogs not only have decreased levels of sphingolipids in the epidermis but also altered ratios of the different ceramides found in normal skin.

We are seeing some new compounds containing phytosphingosine on the market. Phytosphingosine is mainly found in plants and may have similar properties to animal sphingosine.

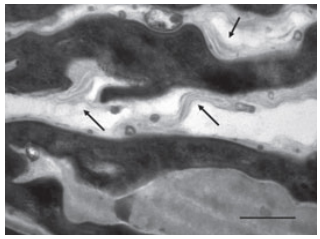
Marsella and co-workers (2010) have demonstrated visible abnormalities in the lipid lamellae of non-lesional skin in atopic dogs. Furthermore, they have demonstrated

that these defects are exacerbated when these atopic dogs are exposed to allergens to which they have been sensitised.

Lipid Lamellae Stratum Corneum



Normal dog non lesional stratum corneum.



Atopic dog non lesional stratum corneum.

Abnormal structure exacerbated by allergen challenge.

Marsalla 2010

The slide below describes the two classical classes of moisturisers. Hydroscopic agents that draw water into the skin osmotically and emollients that provide a a greasy seal on the surface. Standard sorbolene is a mixture of both types of agents.

Moisturizers

- Hygroscopic ((humectant) agents
  - Attract water into stratum corneum.
  - Urea, glycerin, lactic acid and propylene glycol.
- Emollients (Paraffin/mineral oil)
  - Decrease epidermal water loss
  - Form a barrier between skin and potential allergens.

Moisturizers
- PAW Nutriderm 1:2 spray
- Propylene glycol 25-33% spray
- Sorbolene (glycerin and paraffin oil + additives)
- Alpha Keri bath oil 1:50 spray

Bathing and wetting the skin
Benefit or harm (?)
Emollients may be MORE effective without bathing

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In Australia, we have at present only one registered Veterinary sphingolipid-containing moisturising agent. Paws Nutriderm Conditioner contains a ceramide complex and other moisturising agents that both dogs and clients find very acceptable. The ability to diluted the product 1:2 with water and use it as a daily spray makes it both an economical and highly effective moisturising agent.

Sphingolipid Moisturizers

Some studies in humans to indicate superiority

Optimal lipid balance yet to be determined in humans & dog.

Veterinary placebo controlled studies lacking

Good clinical results

Add 200ml tube to 400ml water.

What is the best moisturising agent for dogs? An easy answer may be "the one that clients will use" and very greasy mixtures such as 30% propylene glycol or one in 50 Alfa-kerri oil may suit some clients but many find these mixtures producing an unacceptable greasy feel to the coat.

Sphingolipid-containing barrier repair agents have gained a significant place in the management of human atopic dermatitis. In humans and dogs, there is still a lack of large scale controlled studies to determine the best moisturiser composition. The author's experience using Paws Nutriderm conditioner spray has been very positive and the author has found a high level of client acceptance of this product.

The author is currently trialling a regime of using 0.025% budesonide (the active corticosteroid in many nasal sprays) in a moisturising base of 30% propylene glycol and 10% glycerine on a twice a week basis. On days in between budesonide treatment, the Paws Nutriderm Conditioner spray is used.

Clinicians always need to be aware of the possibility of contact sensitivity developing to ANY topical agent, including corticosteroids!

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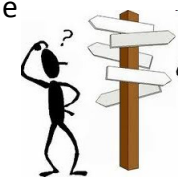
In conclusion, addressing the barrier dysfunction known to be present in atopic dogs is not only logical that has minimal potential for harm and low cost and presents us with the ability to minimise the amount of corticosteroid that we need to control these dogs.

Barrier Repair Therapy - Conclusions

- **Topical and oral lipid complexes alter diseased skin structure and composition resulting in improved barrier function**
  - Decreased doses of corticosteroids and cyclosporine
  - Increased immunotherapy efficiency
  - Decreased number of infections
  - Cost effective
  - Low toxicity
  - Not a monotherapy “cure”



Further reading:

Transmission electron microscopy studies in an experimental model of canine atopic dermatitis .Marsella R et al (2010)
www.ncbi.nlm.nih.gov/pubmed/20042040

Unravelling the skin barrier: a new paradigm for atopic dermatitis and house dust mites. Marsella R and Samuelson D (2009)
http://www.ncbi.nlm.nih.gov/pubmed/20178491

A new moisturizer containing physiologic lipid granules alleviates atopic dermatitis. Na J et al (2010)
http://www.ncbi.nlm.nih.gov/pubmed/19626524

Therapeutic Implications of a Barrier-Based Pathogenesis of Atopic Dermatitis. Elias PM and Wakefield JS (2010)
http://www.ncbi.nlm.nih.gov/pubmed/21174234

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