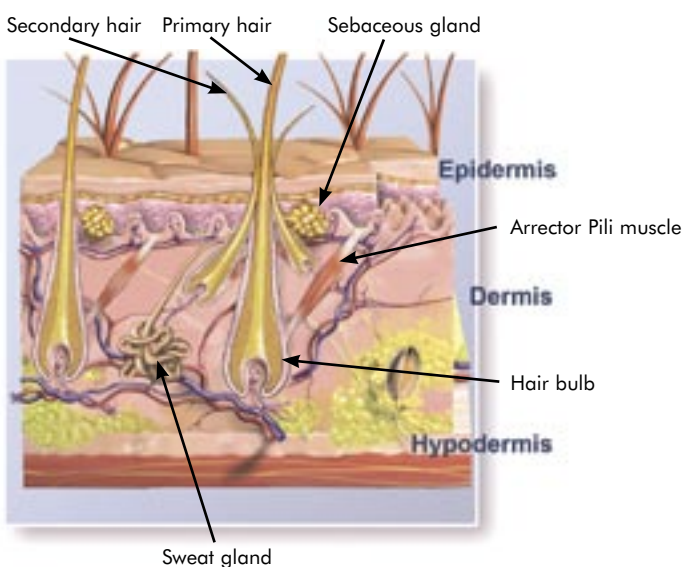# Canine Skin – it's what's inside that counts – The importance of nutrition –

Good nutrition is essential for skin health. Normal keratinisation requires an adequate supply of several skin essential nutrients: protein, fatty acids, zinc, copper, Vitamin A, and B vitamins (Chesney 1993). Deficiencies in numerous essential amino acids, fatty acids, vitamins or minerals can cause deviations in skin structure or function: epidermal atrophy occurs with protein, calorie and vitamin deficiencies. Hyperkeratosis or acanthosis can occur with magnesium, zinc, pantothenic acid, pyridoxine, biotin, Vitamin A or essential fatty acid deficiencies, while parakeratosis is symptomatic of zinc deficiency. Pigment changes may be seen with deficiencies of copper, cysteine or panthothenic acid. Alopecia or changes in the sebaceous glands may occur with zinc, biotin or riboflavin deficiencies. In addition to these direct effects, suboptimal nutrition may increase susceptibility to parasites, such as mange mites, fleas and lice, as well as enhance susceptibility to skin infections (Marks 1991; Chesney 1995; Berardesca 1990).

Providing minimum nutrient requirements by definition should eliminate all dermatological signs associated with dietary deficiencies. However, certain animals may have genetic or metabolic differences that may respond to intakes greater than those considered adequate to avoid recognised dietary deficiencies.

Cross Section of Canine Skin

Secondary hair   Primary hair   Sebaceous gland
Epidermis
Arrector Pili muscle
Dermis
Hair bulb
Hypodermis
Sweat gland

The Role of Protein in Skin and Coat Health

Skin contains a significant amount of protein and serves as a major source of protein reserves when intake is inadequate. (Muller 1989) The hair shaft is composed primarily of alpha-keratin protein. Specific skin effects from gross protein deficiency include hyperkeratosis, epidermal hyperpigmentation, flaky skin, loss of hair pigmentation, and increased hair fragility. (Mosier 1978; Latham 1991) This may be seen as crusty lesions with patchy alopecia and dry, brittle hair coats. Microscopic changes include puffing and flaking of the keratin layer and foamy-looking collagen layers. (Mosier 1978) Hair root changes occur in protein malnutrition, with an increased number of follicles in telogen phase and a decreased number in anagen phase (McLaren 1987). Subclinical protein deficiency may be less noticeable. Suboptimal protein intake can decrease hair production and decrease fibre diameter, length and breaking strength (Galbraith 1998; Sahlu 1992; Shimoshima 1988). However, increasing dietary protein or sulphur amino acid intake increased the rate of division of cells in the follicle bulb matrix, which increased keratin gene expression, protein deposition and follicle growth rate (Galbraith 1998; Matheson 1999). Therefore, optimal protein may be beneficial for enhanced hair coat quality.

Suboptimal protein intake can decrease hair diameter, length and breaking strength.

The amino acids proline, glycine, lysine and arginine are essential building blocks of collagen, the principal component of the dermis. Arginine is required for wound healing and also facilitates the availability of immune cells to the wound site for healing. Glycine and proline are the major amino acids in elastin, a key protein in the skin. Lysine has an important function in the constitution of the cross-links between the molecules to build the fibrils and fibres of collagen.

The Role of Omega-6 and Omega-3 Fatty Acids in Skin and Coat Health

Within the skin, the Omega-6 and Omega-3 fatty acids serve three main functions: a structural component of cells membranes, maintenance of the epidermal water barrier and precursors for the production of pro- and anti-inflammatory eicosanoids.

Fatty acids serve as a structural component of the phospholipids of cellular membranes, where they maintain fluidity and normal permeability. If tissue permeability is disrupted, it can lead to nutrient and water loss, altered receptor function and enzyme activity, and altered cytokine production. (White, 1995) As a precursor for the production of anti-inflammatory eicosanoids, Omega-3 fatty acids can play a major role in inflammatory disease.

Generalised flaky desquamation, coarse lustreless hair coats or alopecia, pruritus and skin lesions are among the most recognised signs of essential fatty acid deficiency. Fatty acids, which make up the bulk of cellular membranes, maintain the membrane fluidity and flexibility that is critical for normal cell function. This is true for all cells, but the effects of deficiency are most visible in the skin. Dry scaly skin, hyperkeratinisation, greasy seborrhoea, and alopecia may result from deficient Omega-6 fatty acid intake. Arachidonic acid is critical for regulating epidermal proliferation, while linoleic acid controls transepidermal migration of molecules, including water, through the skin. (Campbell 1993) Linoleic acid is also a major lipid in sebum and an integral part of the intercellular lipid layer of the skin, which contributes to the skin's function as a protective organ. (Scott 2001)

Immune-Modulatory Effects of Fatty Acids

Polyunsaturated fatty acids in both the Omega-6 and Omega-3 families can have immuno-modulatory effects. The primary Omega-6 fatty acid in cell membranes is arachidonic acid (AA), which serves as the precursor for the production of prostaglandin E_2 (PGE_2), leukotriene B_4 (LTB_4) and 12-hydrodroxyeicosatetraenoic acid (12-HETE), all potent inflammatory mediators (White 1995). If the diet is enriched with long chain Omega-3 fatty acids, part of the AA in cell membranes can be replaced by eicospentaenoic acid (EPA) and docosahexaenoic acid (DHA). (Schoenherr 1997; White 1992; Drevon 1992; Waldron 2000). EPA then may be used instead of AA for the production of eicosanoids, resulting in a different and less inflammatory set of compounds (e.g., PGE_3, LTB_5 and 15-HETE instead of PGE_2, LTB_4 and 12-HETE) Schoenherr 1997; Drevon 1992, Waldron 2000).Thus, the substitution of Omega-3 for part of the Omega-6 fatty acids results in a reduction in inflammation that would be beneficial in inflammatory conditions. Evidence to support this theory has been generated in multiple studies using various *in vitro* and *in vivo* models of inflammation (Grimble 1998; Miles 1998).

Canine specific studies are consistent with other studies. When normal dogs were fed 1.8 to 3.4% of dietary fatty acids as Omega-3 fatty acids (ALA, EPA and DHA) for 6 to 12 weeks, there was a significant reduction in LTB_4 production with a concurrent increase in LTB_5 production. This change was detectable in skin, circulating neutrophils and plasma. (Vaughn 1993) In another study, dogs were fed diets containing either linseed oil (also called flaxseed oil), a source of C18 Omega-3 fatty acids, or menhaden oil, a source of the longer chain Omega-3 fatty acids EPA and DHA. (Waldron 2000) Both sources resulted in incorporation of Omega-3 fatty acids into neutrophil membranes, with a resulting reduction in LTB_4 and increased LTB_5 ion production. However, the effects were significantly greater in the EPA and DHA fed dogs compared to the ALA fed dogs. (Waldron 2000) Clinical evidence to date suggests that up to 50% of patients with inflammatory and pruritic conditions may respond positively to Omega-3 fatty acid intake, especially EPA and DHA (Schoenherr 1997).

The Role of Vitamins in Skin and Coat Health

Riboflavin deficiency can cause a dry flaky dermatitis with reddening of the skin and hair loss. Biotin deficiency can cause the hair to become thin or lose pigment and the skin to become dry and flaky or greasy. (Mosier, 1978) Pantothenic acid deficiency can lead to loss of hair pigment and hair loss.

Vitamin A deficiency can appear like an essential fatty acid deficiency and lead to dry, scaly skin. (Mosier, 1978) Excessive vitamin A also causes skin lesions that appear similar to those of vitamin A deficiency, including dry skin, alopecia and pruritus. On the other hand, vitamin A or related compounds have been used topically to treat various skin problems in humans. Retinoic acid (a form of vitamin A) has been shown to be involved in regulation of epidermal keratinocytes by regulating gene transcription (Volberg,1992). Dietary supplementation with vitamin A has been used to treat seborrhoea in American Cocker Spaniels while topical treatments have been used for a number of skin conditions in various breeds. (Sousa 1998) The vitamin A supplement, given at 10 to 25 times the requirement of 100 IU/kg body weight/day, appeared most useful in patients with marked follicular plugging and hyperkeratosis. (Codner 1993) Active vitamin D (1,25-dihydroxycholecalciferol) has been investigated in human medicine as a treatment for psoriasis and ichthyosis, both hyperproliferative conditions (Holick 1995). Cells of the outer root sheath and epidermal cells have vitamin D receptors. *In vitro* data shows that active vitamin D inhibits the proliferation of keratinocytes and dermal fibroblasts.

Vitamin E functions as a natural antioxidant and together with selenium helps to maintain the stability of cell and lysosomal membranes. Vitamin E, a scavenger of free radicals, protects cutaneous cells from the oxidative damage caused by the free radicals, which are produced by damaged skin and environmental insults. *In vitro* data from a model for canine atopy has shown that vitamin E can decrease the production and release of inflammatory mediators, thus providing a potential benefit in inflammatory dermatoses (Gueck 2002).

The Role of Minerals in Skin and Coat Health

Zinc is critical for normal skin development, and deficiency leads to parakeratosis and dermatitis. Zinc-responsive dermatitis generally is reported in puppies or zinc-sensitive breeds (primarily Siberian Huskies and Alaskan Malamutes), although it can occur in other breeds. Some older dogs with poor hair coats and scaly skin also may improve with zinc supplementation (Mosier, 1985). Zinc bioavailability can be influenced by the zinc source, as well as by dietary phytate, supplemental calcium and other variables. Affected dogs have scaling, crusting skin lesions, hyperkeratosis and secondary skin infections that respond to dietary change or zinc supplementation.

Maintaining Skin Hydration

The stratum corneum plays a pivotal role in preventing excessive water loss from the body (Chesney,1993; Hattingh,1973). The extracellular space of the stratum corneum contains glycolipids and glycosaminoglycans as well as several immunologically important substances. The glycolipids appear to be critical in supporting the water barrier function of the stratum corneum. Water diffuses out from the body and is lost at the skin surface. This water loss is referred to as transepidermal water loss (TEWL) and is driven by the steep concentration gradient between the hydrated internal body tissues with a moisture content of approximately 75% and the drier external atmosphere (Chesney,1993; Marks, 1991). Normal skin contains 10 to 40% water, with about 35% water in the stratum corneum considered optimal. (Marks 1991) Moisture content in canine skin depends on anatomic location, with ear pinna, chest and groin skin having the highest moisture levels (Chesney, 1995). Low skin hydration is associated with increased TEWL and reduced skin surface lipid content. Such changes are characteristic of defective epidermal barrier function and typical of atopic dermatitis and various scaly dermatoses (Berardesca 1990, Linde 1992, Thune 1988). Atopic

dogs also show abnormal water-absorptive (hygroscopic) and water-holding capacity (Chesney 1995).

Low skin hydration can result in potential skin surface disturbances eg changes in microflora content, sebum production or ability to adapt to the environment

Optimal hydration of the stratum corneum is the single most important factor influencing microfloral growth at the skin surface (Muller 1989). Moisture moving outward through the skin hydrates the cells prior to being evaporated into the atmosphere. Dry skin is characterised by a lack of moisture in the keratinised stratum corneum. Disturbances in keratinisation or other disorders in the stratum corneum may increase its permeability, allowing either increased water loss or over-hydration. An over-moist stratum corneum is a less efficient barrier while an abnormally dry stratum corneum becomes brittle and inflexible, resulting in painful fissures as well as breaks in the physical barrier of protection. (Marks 1991) Some environmental factors that have been shown to affect skin hydration and TEWL include diet, bathing, soaps, shampoos and moisturisers (Thune 1988; Campbell 1996; Campbell 1995; Stender 1990). Dietary alterations of protein, amino acids and lipids may influence hydration and moisture kinetics. A deficiency of protein or essential amino acids can lead to dry skin, among other changes. Adequate dietary

The Connection Between Atopy and Food Allergy in Dogs

Canine atopy is reported to affect between 3 and 15% of the canine population. Up to 80% of these dogs also are flea allergic and up to 30% are food allergic (Chalmers 1994). Atopic dermatitis is defined as a genetically predisposed inflammatory and pruritic allergic skin condition induced by IgE antibodies to environmental allergens, such as pollens, moulds and house dust (Chalmers 1994). Exposure to environmental allergens occurs via contact with skin, respiratory mucosa or gastrointestinal mucosa, although the respiratory route is most common. Likewise, food allergic dermatitis is thought to be an IgE-mediated condition, with allergen exposure occurring via the gastrointestinal mucosa. Food allergy in humans is considered to be an IgE-mediated hypersensitivity in most cases, and thus shares the same pathogenic mechanism as atopic dermatitis (Ermel 1997; Hillier 2001).

Typical features common to both atopic dermatitis and food allergic dermatitis in dogs include: young age at onset; pruritus of the ears, axilla, inguinal area and distal limbs; frequent occurrence of otitis and recurrent secondary bacterial or yeast infections (Hillier 2001). In dogs with a non-seasonal presentation of these clinical signs, it may be difficult to impossible to distinguish between the two conditions on a clinical basis alone (Hillier 2001). In addition, the presence of food allergy may contribute to the development or exacerbation of atopy, especially if the gastrointestinal mucosa is compromised as a result (Hillier 2001; Chandra 1997; Chesney 2002).

In humans and dogs, atopy and food allergy frequently occur together. Food allergy was confirmed in approximately 25% of human patients with atopic eczema (Chandra 1993). Nearly one third (32.7%) of 58 atopic dogs entered into an elimination diet trial were confirmed to be food allergic (Chesney 2002). A significant reduction in pruritus was observed in atopic dogs (confirmed atopic based on positive serum IgE response to inhalant allergens or mites) fed a hypoallergenic diet over an 8-week period (Puigdemont 2003, unpublished data). On the other hand, of 52 dogs with food allergy confirmed by challenge, 12 were considered atopic (Chesney 2002) and 6 more were confirmed atopic by intradermal skin testing (Carlotti 1990). Among the 6 skin-test positive atopic dogs, half were successfully controlled simply by managing the concurrent food allergy.

Factors Influencing Development of Allergic Conditions

The likelihood of an individual patient developing food sensitivity depends in part on permeability of the gut, the presence of allergy to other foods or inhalants, as well as other factors (Chandra 1997). Heredity is a major predisposing factor in allergic conditions in humans. The likelihood of an infant developing atopy or food allergy is 37% if one parent was atopic and 62% if both parents were affected (Chandra 1997). This may also be true in dogs, based on breed and familial predisposition, but the mode of inheritance is unknown (Chalmers 1994).

Current evidence suggests that dogs with cutaneous food allergy may be predisposed to developing atopic dermatitis (Hillier 2001). This may be due to an underlying immune (Th1/Th2) imbalance, or it may be a result of compromised gastrointestinal mucosa. Since the gastrointestinal mucosa is a primary barrier to prevent absorption of potential allergenic proteins, a breach in this barrier increases the likelihood of allergens entering the body and contacting the gut associated lymphoid tissue (GALT), thus increasing the risk of sensitisation or allergic response (Chandra 1997).

Gastrointestinal permeability and transmucosal antigen transfer are increased in humans with atopy and food allergy, and the absorbed dietary antigens can contribute to clinical signs of atopy (Chesney 2002; Majamaa 1997). This appears to be associated with clinical or subclinical intestinal inflammation. In dogs, food allergy often manifests with primary gastrointestinal signs. In addition, some food allergic dogs with skin lesions also demonstrate mild gastrointestinal disturbances. Thus, it is likely that some degree of gastrointestinal compromise exists in dogs, as well as humans, with atopy or food allergic dermatitis.
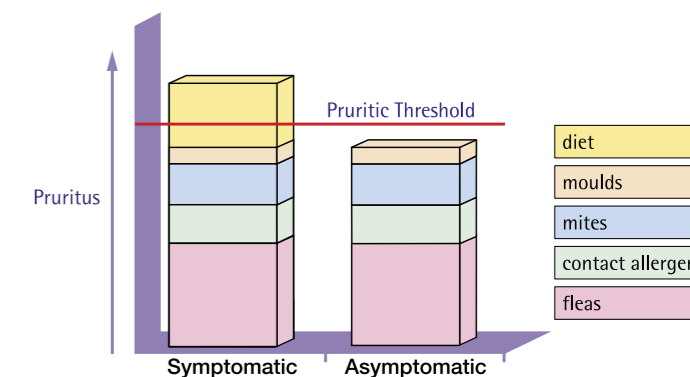
A pruritic dog with concurrent atopy and food allergy may drop below the pruritic threshold by the effective control of only one allergen.

Once sensitised, the body's response to an allergen is the same but individuals' pruritic responses appear to differ. This may be due to variations in the pruritic threshold, which can differ between dogs and with the same animal at different times (Chalmers 1994). It also may relate to the concept of "summation," which suggests that multiple allergies or non-allergenic pruritic stimuli are additive in effect. Thus, a pruritic dog with concurrent atopy and food allergy, for example, may drop below the pruritic threshold by effective control of only one of these conditions. Non-allergenic factors, such as stress, dry skin, hot weather etc can also contribute to pruritus via non-immunologic means and must be considered in the diagnosis and management of pruritic pets (Chalmers, 1994).

A pruritic dog with concurrent atopy and food allergy may drop below the pruritic threshold by effective control of only one of these conditions.

Clinical Implications

Atopy and food allergy are relatively common conditions in humans and pets, and may occur concurrently. The immunopathogenesis of atopy has strong similarities among humans, dogs and cats, and both allergic conditions appear to share a common pathophysiology.

Food allergy is diagnosed by response to veterinary supervised elimination and challenge feeding trials. The diagnosis of atopy in dogs and cats is usually considered a process of elimination, confirmed by intradermal or serum testing for suspect allergens. In various studies, a large percentage of atopic dogs responded to a hypoallergenic diet with a clinically significant (up to 100%) reduction in pruritus. This effect may have been due to a reduction in the overall antigen exposure, dropping the animals below their pruritic threshold. This phenomenon may make the identification more difficult, but can make management easier.

Thus, the use of a hypoallergenic diet or a diet with limited and uncommon proteins may prove useful not only in the identification and management of food allergy, but also in the management of atopy. In some atopic patients, feeding an appropriate hypoallergenic diet may be adequate to significantly reduce the clinical signs associated with pruritus.

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