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Nutritional dermatoses and the contribution of dietetics in dermatology

ABBREVIATIONS USED IN THIS CHAPTER

DGLA: dihomo-gamma-linolenic acid
DHA: docosahexaenoic acid
EPA: eicosapentaenoic acid
IgE: immunoglobulin E
ME: metabolizable energy
PUFA: polyunsaturated fatty acid
TEWL: transepidermal water loss

Nutritional dermatoses and the contribution of dietetics in dermatology

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Ralf Mueller graduated in Munich, Germany in 1985, and worked in several large and small animal practices before completing a residency in veterinary dermatology at the University of California, Davis in 1992. In 1992 he moved to Melbourne, Australia where together with his partner and wife Dr. Sonya Bettenay he was director in a veterinary dermatology specialist practice and consultant at the University of Sydney. In 1999, he became Assistant Professor in Veterinary Dermatology at the College of Veterinary Medicine and Biomedical Sciences, Colorado State University and finished his habilitation thesis at Zurich University, Switzerland. In 2004, he accepted a position as chief of the veterinary dermatology service at the University of Munich, Germany. He has published over 80 studies, articles, book chapters and books.

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The skin is a major organ with many different functions. Obviously, it is important for social interactions, giving each individual its characteristic appearance. It also serves as a barrier to maintain a stable internal environment. The skin plays a major role in the immune response to external factors, but also has a distinctive role in metabolism, sensory perception and temperature regulation amongst others. An imbalanced intake of nutrients such as amino acids, fatty acids, vitamins or trace elements disrupts the barrier function and the immune protection provided by the skin. The cat may become more sensitive to infection and may develop allergic reactions more easily. Skin and coat are a mirror of a cat's health and the quality of its food. Nutrition has a special place in feline dermatology, not only as an essential factor in the prevention of skin diseases, but also as a therapy for allergies and metabolic dermatopathies.

1 - Risk factors

► Breed specificities

In contrast to dogs where several skin conditions can be directly related to nutrition, there is little evidence of a link between a breed, nutrient and a specific disease in the feline literature. However, the Siamese seems to have an increased tendency to food allergy (see section on "Dietary hypersensitivities").

► Color of the coat

The color of a cat is a complex feature and influenced by genetics, environment (temperature, UV intensity and humidity all alter the coat's color by degrading the pigmentation) and nutrition (many nutrients play a role in pigment production).

The selection of colors in pure breed cats has become a specialist's hobby. Pigmentation is linked to the distribution of melanin in the hair shaft. Eumelanin (black to brown) and pheomelanin (red to yellow) combine to form the various shades of a cat's coat. The likelihood to produce eumelanin or pheomelanin is genetically determined but the enzyme which catalyzes the conversion from tyrosine can be a limiting factor. Pigment synthesis in the melanocytes depends on the supply of specific amino acids:
- phenylalanine and tyrosine are melanin precursors **(Figure 1)**
- cysteine is needed for the production of pheomelanin. It contains a high proportion of sulphur.

A dietary deficiency in tyrosine (or its precursor, phenylalanine) has been shown to induce a reddish change in the black hair of cats **(Figure 2)**. Similarly the deep orange colored cats turned pale orange when experimentally fed a diet lacking tyrosine *(Yu et al, 2001)*.

According to the *National Research Council (NRC)* 2006, the adequate intake for an adult cat corresponds to 0.38 g of phenylalanine and tyrosine per kg of metabolic weight i.e. a level of 3.83 g per 1000 kcal of metabolizable energy (ME). In a 4000 kcal ME/kg diet, it represents a minimum level of 15.3 g/kg of dry matter. To maximize black hair color, an equal quantity or greater of tyrosine to that of phenylalanine is required *(NRC, 2006)*.

FIGURE 1 - SYNTHESIS OF MELANIN FROM PHENYLALANINE

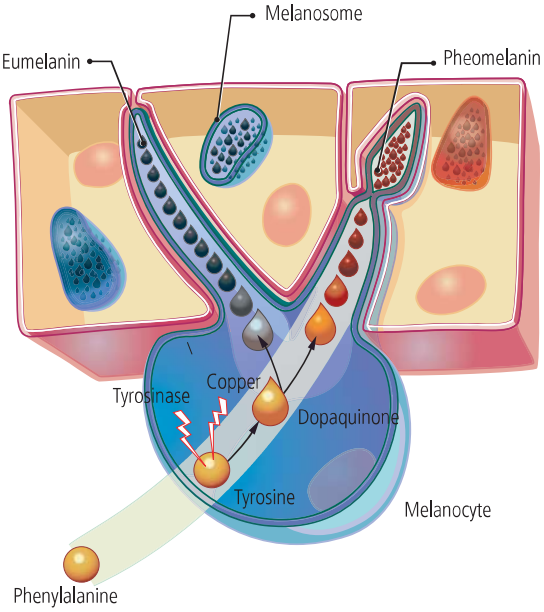

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Figure 2 - Influence of dietary tyrosine intake on color intensity in black cats. *Diets that cause the color of hair to change from black to reddish-brown are associated with a reduction in melanin in hair, a decreased total melanin concentration and low concentrations of tyrosine in plasma.*

► Environmental factors

White cats are prone to squamous cell carcinoma, especially on the ear pinna and nose. Neoplastic changes are often preceded by solar dermatitis (sun burn). Solar radiation is the most ubiquitous mutagen but except indoor confinement, very little can be done to prevent exposure to sun light and the related free radicals. Research has shown the benefits of antioxidants in preventing UV light induced skin tumors and supplementation of antioxidants in the food may thus be useful *(Liebler & Burr, 2000)*.

► Age and physiological states

In health and disease, age and physiological stage can greatly influence the quality of skin and coat. Growth, gestation, lactation, and old age will modify the nutritional requirements and are likely to interfere with the supply of nutrients to the cutaneous structures.

► Obesity

The physical constraints related to excessive weight reduce the ability of the cat to groom. This can lead to skin and/or coat conditions such as matted hair or anal sac impaction. Any other painful factor limiting the range of movement such as arthritis or idiopathic cystitis will have similar consequences.

► Concurrent diseases

The skin is a large organ requiring numerous macro and micro nutrients. Any condition interfering with the absorption of those nutrients will have consequences on the skin and coat **(Table 1)**.

► Nutritional balance

There is no published evidence of "generic food skin diseases" in the cat but, usually, when the diet is unbalanced, cutaneous signs often precede weight loss **(Table 2)**.

2 - Nutritional dermatosis

Nutritional dermatoses may affect cats in many different ways which are listed in **Table 2**.

► Specific nutritional imbalances

> Protein deficiency

Hair consists of 95% protein, and is rich in sulphur amino acids such as methionine and cystine. The growth of hair and renewal of the skin will absorb 30% of dietary protein *(Scott et al, 2001)*. Any situation where protein requirements are not fulfilled will lead to poor coat and skin with generalized scaling, loss of pigment, poor hair growth, easy shedding, thin, dull and brittle hair.

Protein deficiency can either be due to a lack of supply i.e. poor quality diet, unbalanced home prepared food, low protein diet or to protein loss related to a systemic illness such as protein losing gastro-enteropathy, nephropathy, hepatopathy, or chronic bleeding. The reason for the nutritional imbalance needs to be identified and corrected.

TABLE 1 - VARIOUS CONDITIONS INTERFERING WITH THE ABSORPTION OF NUTRIENTS

Nutrients	Diseases or diets
Proteins	Any systemic disease inducing protein loss or impairing protein absorption (i.e: gastroenteropathy, hepatopathy, nephropathy, chronic bleeding)
Fats	Digestive disorders, neoplastic or inflammatory diseases leading to malabsorption or maldigestion Renal or liver diseases
Vitamins and minerals	Polyuria-polydipsia, large consumption of white raw eggs, unbalanced vegetarian diets

TABLE 2 - CUTANEOUS SIGNS OF AN UNBALANCED DIET

- Widespread scaling
- Crusting (non allergic miliary dermatitis)
- Patchy alopecia
- Lack of pigment
- Poor hair growth
- Thin, brittle, dull hair
- Seborrhea oleosa
- Recurring pyoderma
- Impaired wound healing
- Chronic or recurrent otitis

> Essential fatty acid deficiencies

Essential fatty acids are not synthesized by the organism, thus their supplementation in the diet is "essential". They are primarily the precursors of two families of polyunsaturated fatty acids (PUFA), omega-6 fatty acids and omega-3 fatty acids.

PUFA fulfill five main functions:
- incorporation in the structure of the cell membrane, which gives it its flexibility and permeability
- production of eicosanoids (leukotrienes, prostaglandins, etc.)
- maintenance of the skin barrier permeability (especially omega-6 fatty acids)
- cholesterol metabolism and transport
- immunomodulation through an influence on antigen presenting cells and T lymphocytes

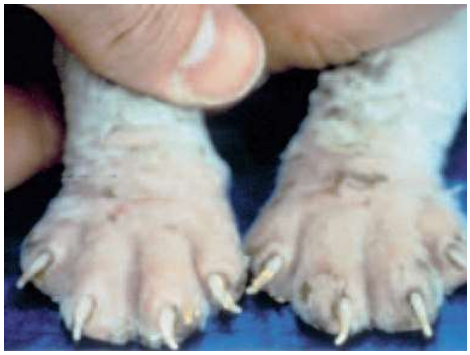
PUFA deficiencies are observed in animals suffering from malassimilation or animals fed with poor-quality diets or diets that have been overheated for a lengthy period. The cutaneous signs are xerosis, dull hair and a keratoseborrheic disorder. The response to PUFA supplementation is rapid.

- ***Linoleic acid***, a precursor of omega-6 fatty acids, is abundant in most vegetable oils. It represents more than 70% of the fatty acids in evening primrose oil and more than 50% in sunflower oil, corn and soy oils.

DERMATOLOGICAL CONSEQUENCES OF SOME SPECIFIC DEFICIENCIES IN AMINO-ACIDS IN DOMESTIC SHORT HAIR CATS

Dermatological consequences of isoleucine deficiency in a short hair cat. Note the crusty material around the eyes, nose pad and mouth. The hair coat is rough. In this kitten, bilateral conjunctivitis and bacterial infection with staphylococci suggest impaired resistance to common dermal bacteria.

Isoleucine deficiency resulted in desquamation of the outer layer of the epidermis on the pads of the paws with cracking.



Dermatological consequences of a deficiency of sulphur containing amino-acids in a domestic short hair cat. Note the hyperkeratosis and swelling of the paws.

Deficiency of sulphur containing amino-acids. Swelling, reddening and hyperkeratosis of the nail bed.

Cats are deficient in Δ-6 desaturase which is the enzyme needed for the first step of the transformation of linoleic acid into arachidonic acid. Thus linoleic acid and arachidonic acid are both essential nutrients for the cat **(Figure 3)**.

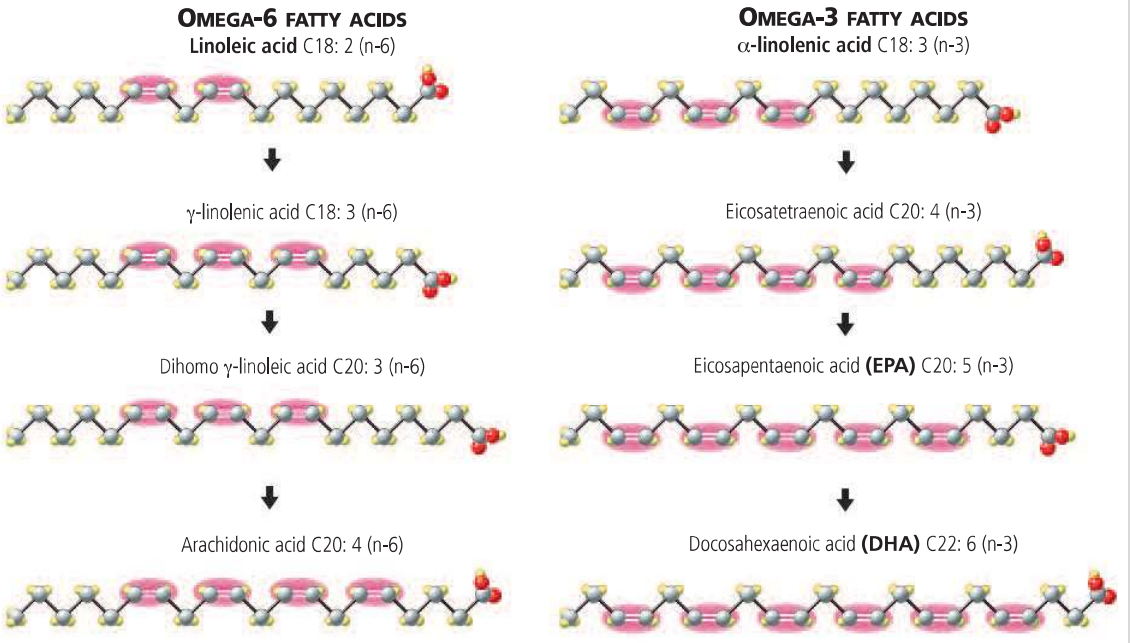
- ***Alpha linolenic acid***, a member of the omega-3 fatty acids, is found in green vegetables, fruits, grasses and plankton, and in concentrated form in the oil of plants like soy, flax, or linseed. The oils of fish from cold waters contain very high levels of two long-chain fatty acids derived from alpha linolenic acid: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) **(Figure 3)**. These two fatty acids participate in the fluidity of the cell membranes.

In addition to their anti-inflammatory, anti-neoplastic, immuno-stimulant, and cardio-protective properties, omega-3 fatty acids are also often used as anti-pruritic agents. Even in situations of an open wound or post-surgery, the benefit of supplementation still outclasses the mild reduction of perfusion which could potentially impede the healing process *(Scardino et al, 1999)*.

> Zinc deficiency

Zinc is a key element in many cellular mechanisms. Considering the fast turn over of epidermal cells, zinc is particularly necessary for a healthy skin and coat. Zinc is also needed for the biosynthesis of fatty acids, for the metabolism of vitamin A and for the inflammatory and immune response. Absolute dietary deficiency has not been reported in the cat but absorption of zinc can be inhibited by excessive levels of calcium, iron or copper due to competition for the absorption channels. Phytate present in cereals chelates zinc and will reduce its dietary availability. Other conditions preventing the absorption of zinc such as enteritis can also lead to depletion of the metal but usually the symptoms of the protein deficiency will be clinically apparent before signs of zinc deficiency occur.

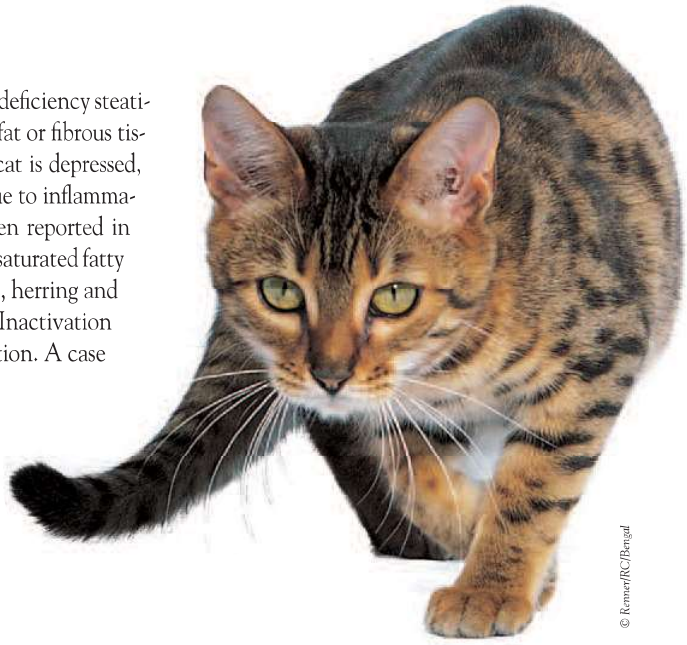
FIGURE 3 - HEPATIC SYNTHESIS OF LONG-CHAIN OMEGA-6 AND OMEGA-3 FATTY ACIDS FROM THEIR RESPECTIVE PRECURSORS



> Vitamin E deficiency

Pansteatitis (synonyms: feline vitamin E deficiency, vitamin E deficiency steatitis or yellow fat disease) is characterized by diffuse nodules of fat or fibrous tissue, especially in the groin or on the ventral abdomen. The cat is depressed, febrile, and reluctant to move or jump. Palpation is painful due to inflammation of the subcutaneous fat. Nutritional pansteatitis has been reported in young and obese cats fed a diet containing large amounts of unsaturated fatty acids and/or insufficient vitamin E. Canned red tuna, sardines, herring and cod but also diets based on pig brain have been incriminated. Inactivation of vitamin E can occur during food processing or by fat oxidation. A case of pansteatitis associated with a pancreatic tumor has been described *(Fabbrini et al, 2005)*.

Histologically, the subcutaneous fat will exhibit ceroid deposits which are pathognomonic of the condition. In lesions without ceroid, specific staining will have to be performed to differentiate pansteatitis from pancreatic or traumatic panniculitis *(Gross et al, 2005)*.



Cats have high requirements in terms of water-soluble B vitamins and they are unable to convert β-carotene into retinol (active form of vitamin A). These characteristics show that cats are adapted to a carnivorous diet: under natural conditions, they do not lack these vitamins since they are present in large quantities in animal tissues.

> Vitamin A deficiency

Cats are unable to convert β-carotene from plants to vitamin A and thus need to receive preformed vitamin A. Among several functions, vitamin A is required for ocular function but also for skin turn over. With vitamin A deficiency, the cat will exhibit a poor coat, alopecia and generalized scaling. The supply of a balanced, meat containing diet is usually sufficient to cure the condition. Vitamin A supplements are not recommended in the cat when fed a complete food because of the risk of hypervitaminosis A.

> Hypervitaminosis A

This condition was rather common in the past when cats were fed raw liver. It is still seen occasionally when the owner gives large amounts of cod liver oil supplement. The signs are mainly osteo-articular due to the cat's inability to move. As a consequence, the cat will be unable to groom properly, resulting in an unkempt, matted coat.

> Vitamin B deficiency

B complex vitamins are treated as a group. They are water soluble vitamins that cannot be stored. Biotin, riboflavin, niacin, inositol, pantothenic acid and pyridoxine are important for the quality of the skin barrier and deficiencies will lead to dry flaky seborrhoea accompanied by alopecia, anorexia, weight loss and pruritus.

Biotin deficiency sometimes occurs with consumption of numerous uncooked eggs. The avidin in the egg white binds to biotin and blocks its absorption. This will lead to a papulocrustous dermatitis.

A deficiency in riboflavin will lead to head and neck alopecia in cats. Niacin deficiency has also been described in cats fed a low protein high corn diet. Niacin and pyridoxine deficiencies can be produced experimentally. However, appropriately formulated commercial pet food contains high quantities of these vitamins.

Supplementation of B vitamins might be necessary with anorexia or polyuria. Vitamin B complex can be found in brewer's yeast and in balanced commercial food. Certain B vitamins work in synergy with histidine to improve the barrier function of the epidermis and decrease the TEWL (transepidermal water loss) *(Watson et al, 2006)*.

TABLE 3 - VARIOUS CLINICAL EXPRESSIONS OF ADVERSE FOOD REACTIONS IN CATS

Cutaneous problems	Miliary dermatitis Self-induced alopecia Head & neck pruritus Eosinophilic granuloma
Gastrointestinal problems	Vomiting Diarrhea Flatulence Weight loss

> Dietary hypersensitivities

The term dietary hypersensitivity or food allergy is used by many veterinarians and owners as a broad term to describe any immunological and non-immunological reactions to ingredients of the diet that result in a clinical adverse reaction in an otherwise healthy cat. This adverse reaction may occur in the form of gastrointestinal problems and/or cutaneous abnormalities typically associated with self trauma due to pruritus **(Table 3)**.

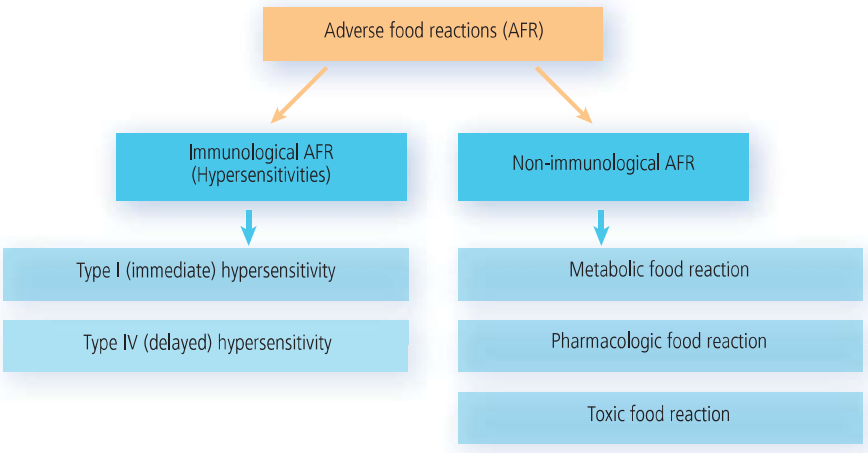
In the cat, adverse food reactions are considered to be relatively more common than in the dog *(Scott et al, 2001)*. In one search of feline records in a number of veterinary colleges, feline adverse food reaction occurred in 10% of the patients presented with allergic skin disease *(Chalmers & Medleau, 1989)*. It was the second most common disorder after flea bite hypersensitivity. However, another more recent report suggested atopic dermatitis to be much more common than adverse food reaction (73 versus 23% of 90 cats) *(Prost, 1998)*. This may reflect the different location, different setting of private dermatology referral practice versus veterinary teaching hospitals, the increased awareness of other hypersensitivities besides flea hypersensitivity in the cat, and/or owners increasingly willing to pursue involved diagnostic procedures for their pets. The prevalence of food hypersensitivity in humans is reported to be approximately 10% in infants *(Bock, 1987)* and 2% in adults *(Young et al, 1994)*. No such data is available for cats to the authors' knowledge.

> Etiology

In humans, non-immunological food reactions like toxic food reactions (e.g. toxins secreted by *Salmonella spp.*), pharmacologic reactions (e.g. caffeine) and metabolic reactions (e.g. lactase deficiency) comprise the majority of food-related problems *(Sampson, 2003)*. The term hypersensitivity is used more stringently only for immunologically mediated reactions to food ingredients. Type I hypersensitivities are most common, although type IV mediated food hypersensitivities and mixed forms have been described **(Figure 4)**.

In cats, type I hypersensitivity has been presumed as edema is the predominant clinical sign in some cats *(Walton, 1967)*. However, in most clinical cases, the pathophysiological mechanism is not determined and adverse food reaction is diagnosed exclusively by the association between diet and clinical signs.

FIGURE 4 - PATHOGENESIS OF ADVERSE FOOD REACTION



> Break in immune tolerance

In healthy humans, intact food antigens penetrate the gastrointestinal tract and enter the circulation without any clinical signs because most individuals develop tolerance to ingested antigens. This tolerance may be based on the induction of regulatory T cells *(Smith et al, 2000; Zivny et al, 2001)* or T cell anergy (where T cells are stimulated by antigen presenting cells via MHC class II molecules but without appropriate costimulatory signals) *(Chehade & Mayer, 2005)*. Maintenance of this immune tolerance depends on a variety of factors listed in **Table 4**.

In humans with a genetic predisposition for atopy, class switching of B cells leads to the production of antigen-specific IgE. A breakdown in oral tolerance and development of hypersensitivity may occur when food allergens penetrate the mucosal barrier and reach IgE antibodies bound to mast cells. Degranulation of these mast cells leads to mediator release, inflammatory cell influx and subsequent clinical signs. In the cat, little is known about the mechanisms underlying oral tolerance and hypersensitivity.

TABLE 4 - FACTORS INFLUENCING THE MAINTENANCE OF IMMUNE TOLERANCE
(Chehade & Mayer, 2005)

Antigen dose
- High dose: T cell anergy
- Low dose: activation of regulatory T cells

Antigen form
- Soluble antigens are tolerated better than particulate antigens

Host genetics
Commensal flora
Host age
Gastrointestinal barrier function

> Dietary allergens

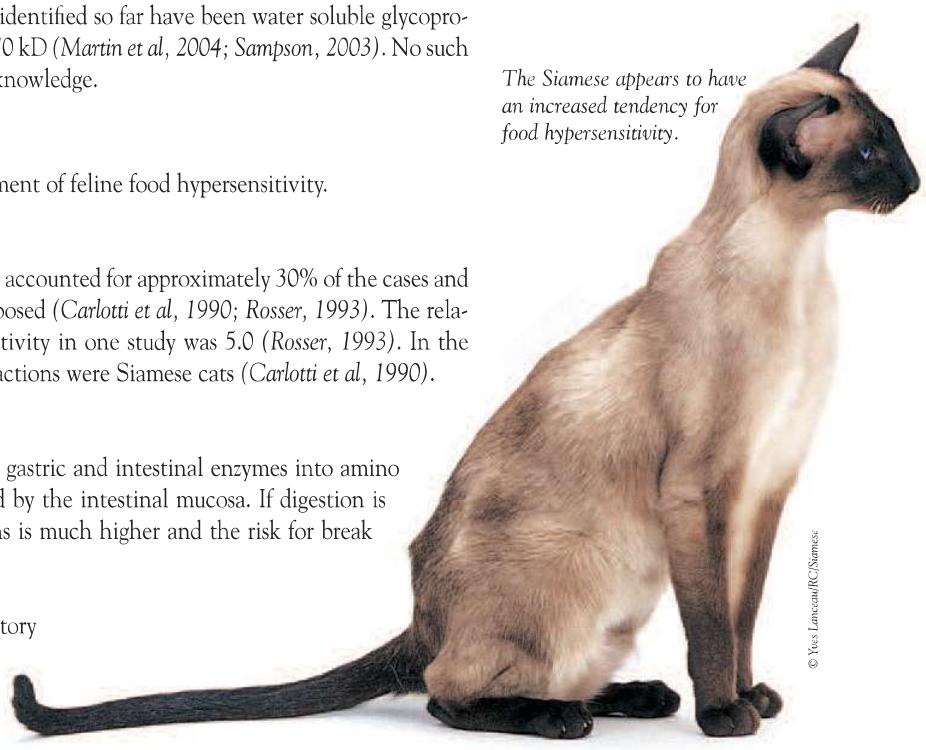
In three studies the most common allergens involved based on provocative challenge were fish, beef and dairy products *(Guaguere, 1993; Walton, 1967; White & Sequoia, 1989)*. One third of the cats could not tolerate any commercially prepared diet without recurrence of clinical signs. A list of reported offending allergens is given in **Table 5**.

TABLE 5 - ALLERGENS INVOLVED IN FELINE ADVERSE FOOD REACTIONS

Beef	Eggs
Chicken	Fish
Clam juice	Horse
Cod liver oil	Lamb/Mutton
Commercial foods	Pork
Dairy products	Rabbit

In one study, almost 30% of 55 cats with chronic gastrointestinal problems showed food hypersensitivity *(Guilford et al, 2001)*. Half of these cats reacted to more than one protein. The clinical feature identified to be most sensitive for the diagnosis of adverse food reaction was the concurrent occurrence of gastrointestinal and cutaneous signs.

In humans and dogs, the major food allergens identified so far have been water soluble glycoproteins with molecular weights ranging from 10-70 kD *(Martin et al, 2004; Sampson, 2003)*. No such data is available for the feline to the authors' knowledge.


© Yves Lanceau/RC/Siamese

The Siamese appears to have an increased tendency for food hypersensitivity.

Predisposing factors

Many factors may be involved in the development of feline food hypersensitivity.

Genetic predisposition
In two studies, Siamese or Siamese cross breeds accounted for approximately 30% of the cases and a genetic predisposition for those cats was proposed *(Carlotti et al, 1990; Rosser, 1993)*. The relative risk factor of Siamese for food hypersensitivity in one study was 5.0 *(Rosser, 1993)*. In the other report, 3 of 10 cats with adverse food reactions were Siamese cats *(Carlotti et al, 1990)*.

Maldigestion
Dietary proteins are typically broken down by gastric and intestinal enzymes into amino acids and small peptides which are assimilated by the intestinal mucosa. If digestion is defective, the molecular weight of the proteins is much higher and the risk for break down of tolerance increased.

This explains why chronic intestinal inflammatory disease may be conducive to the development of dietary hypersensitivity. However, if


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Figure 5 - Consequences of pruritus in a domestic short hair cat. *Face, head, pinnae and neck can all be affected in various combinations.*

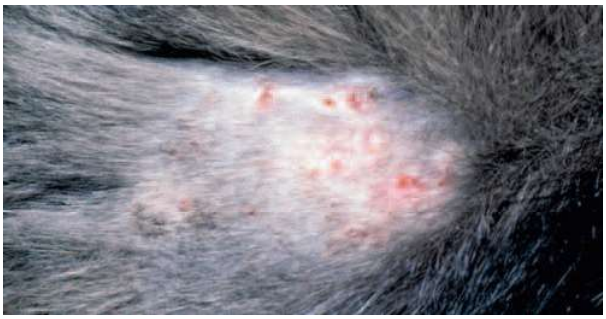
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Figure 6 - Characteristic lesion of miliary dermatitis in a domestic short hair cat. *Small papules and crusts on the trunk characteristic of military dermatitis.*


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Figure 7 - Consequences of an allergic pruritus in a domestic short hair cat. *Noninflammatory alopecia on the flanks and lateral thighs.*

the gastrointestinal inflammation seen in cats with chronic bowel problems was originally due to other causes and led to food hypersensitivity or if this hypersensitivity is solely responsible for the inflammatory changes is not known at this point.

Other hypersensitivities

Concurrent hypersensitivities such as flea bite hypersensitivity or atopic dermatitis are known in dogs with dietary intolerance and may also be a complicating factor in cats. In one of the first reports studying feline food hypersensitivity, 3 of 14 cats had concurrent hypersensitivities *(White & Sequoia, 1989)*. In a recent article, 6 of 16 cats with allergies were diagnosed with a combination of adverse food reaction and atopic dermatitis *(Waisglass et al, 2006)*. Another report described 90 allergic cats, 16 cats had an exclusive adverse food reaction, 4 cats had concurrent atopic dermatitis and adverse food reaction and one cat was additionally allergic to fleas *(Prost, 1998)*. Thus almost a quarter of cats with an adverse food reaction had concurrent hypersensitivities.

Clinical features

In the cat, clinical signs of adverse food reactions vary from pruritus with associated self trauma, eosinophilic granuloma, respiratory signs to gastrointestinal problems.

Head and neck pruritus

Head and neck pruritus was reported in cats with dietary hypersensitivity *(Guaguere, 1993; Medleau et al, 1986; Stogdale et al, 1982)*. Alopecia, crusting, erosions and ulcerations are seen in the affected area as a consequence of self trauma **(Figure 5)**. Pruritus is often severe and may be non-responsive to medical therapy. Secondary infections with bacteria or yeast are not uncommon. Pruritus and thus lesions can spread to other body sites and become generalized with time.

Miliary dermatitis

Small papules and crusts either localized (frequently on the head and neck) **(Figure 6)** or generalized are also seen with dietary hypersensitivities *(Mueller, 2000, Scott et al, 2001)*. In one study, 21% of the cats with adverse food reaction showed this reaction pattern *(White & Sequoia 1989)*. In another study, almost half of the cats with adverse food reactions had military dermatitis *(Carlotti et al, 1990)*.

Non-inflammatory alopecia

Self-induced, bilaterally symmetrical alopecia with no macroscopic lesions is also a common reaction pattern associated with feline adverse food reaction *(Mueller, 2000; Scott et al, 2001)*. Most commonly affected sites are the ventrum, inguinal area, thighs and flanks **(Figure 7)** Owners may or may not observe excessive grooming as a cause of the alopecia, as some cats do not exhibit that behavior in the presence of humans ("closet groomers"). In one report, 10% of all cats with adverse food reaction showed exclusively alopecia. In another report of 21 cats with presumptive psychogenic alopecia, adverse food reaction was diagnosed in more than half of the cats *(Waisglass et al, 2006)*.

Eosinophilic granuloma

Eosinophilic plaques are the most frequently reported lesion of the eosinophilic granuloma complex in cats with adverse food reactions, but other lesions such as linear granuloma have been reported *(Carlotti et al, 1990; White & Sequoia, 1989)*. Eosinophilic plaques are well circumscribed, erythematous, severely pruritic and often ulcerated plaques typically on the abdomen or medial thighs **(Figure 8)**. Linear granulomas are non pruritic, raised, firm, yellowish plaques, most commonly on the caudal thighs **(Figure 9)**.

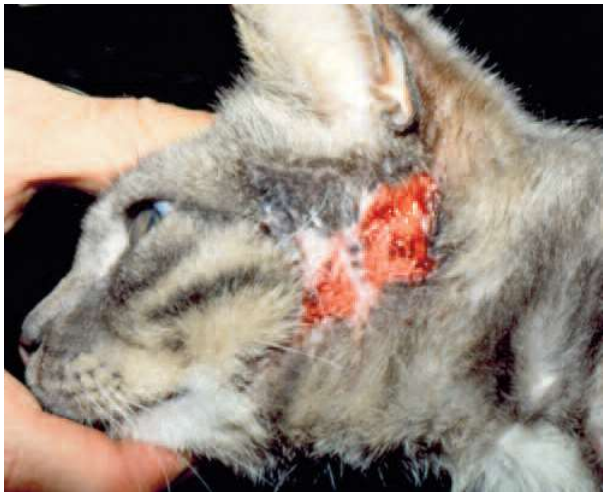


Figure 8 - Facial eosinophilic plaque in a domestic short hair cat.

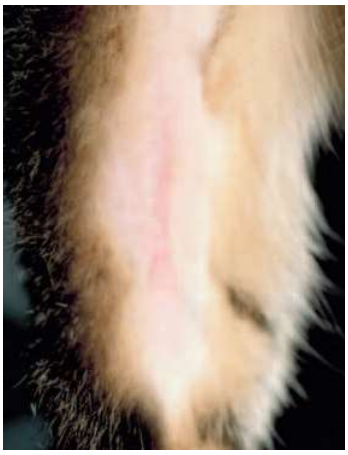


Figure 9 - Linear granuloma on the caudal thigh of a domestic short hair cat.

Gastrointestinal problems

Vomiting, diarrhea and/or flatulence may be clinical signs of feline adverse food reaction *(Guilford et al, 2001; Stogdale et al, 1982)*. Vomition may occur within minutes after eating or hours after the meal and often occurs infrequently. In many cats, diarrhea is due to large bowel dysfunction and thus excessive straining to defecate, mucus and/or blood in the feces may be seen. In one study of 55 cats with chronic gastrointestinal problems, almost one third were diagnosed as food sensitive based on resolution of clinical signs with an elimination diet and recurrence of those signs, when challenged with the previous diet. Most of these cats had a history of vomiting (56%) and a quarter of the cats exhibited chronic diarrhea. The remaining 3 cats had both clinical signs *(Guilford et al, 2001)*.

Diagnosis

Cutaneous signs of feline adverse food reactions usually present themselves as reaction patterns with a number of possible underlying causes, thus a thorough diagnostic work-up is essential in these patients. The list of differential diagnoses depends on the presenting cutaneous reaction pattern and is shown in **Table 6**. Diagnostic tests or trial therapies to rule out differential diagnoses depend on the presenting signs and may include evaluation of cutaneous cytology, superficial and deep skin scrapings, fungal cultures, ectoparasite treatment trials and skin biopsies.

TABLE 6 - IMPORTANT DIFFERENTIAL DIAGNOSES OF CUTANEOUS REACTION PATTERNS ASSOCIATED WITH FELINE ADVERSE FOOD REACTIONS

Reaction pattern	Differential diagnoses
Miliary dermatitis	• Allergies (flea bite hypersensitivity, atopic dermatitis, adverse food reaction, mosquito-bite hypersensitivity) • Ectoparasites (scabies, cheyletiellosis, ear mites) • Infections (dermatophytosis, bacterial infection) • Immune-mediated diseases (pemphigus foliaceus) • Neoplasia (mast cell tumor)
Self-induced alopecia	• Allergies (flea bite hypersensitivity, atopic dermatitis, adverse food reaction) • Psychogenic alopecia • Drug reaction
Head & neck pruritus	• Allergies (atopic dermatitis, adverse food reaction) • Ectoparasites (scabies, ear mites) • Otitis externa • Neoplasia (epitheliotrophic T cell lymphoma)
Eosinophilic granuloma	• Allergies (flea bite hypersensitivity, atopic dermatitis, adverse food reaction) • Idiopathic eosinophilic granuloma

TABLE 7 - EXAMPLES OF PROTEIN SOURCES FOR ELIMINATION DIETS IN CATS

• Duck	• Pheasant
• Goat	• Rabbit
• Horse	• Venison
• Ostrich	

Intradermal testing/serum testing for food allergen-specific IgE

It is tempting to measure dietary allergen-specific IgE to identify the offending dietary allergen(s) and to use the results to choose a new diet. Although sometimes recommended by individuals and laboratories offering these tests, at this time there is no evidence available to the authors to justify such tests. In the dog, published data show that these tests are unreliable *(Jackson & Hammerberg, 2002; Jeffers et al, 1991; Kunkle & Horner, 1992; Mueller & Tsohalis, 1998; Wilhelm & Favrot, 2005)*. In the cat, only one report evaluated serum antigen-specific IgE in cats with adverse food reactions *(Guilford et al, 2001)*. Only half of the cats with confirmed adverse food reaction had a positive test result. The majority of cats either tolerated the food antigen that they had tested positive for or they had never been exposed to it and thus hypersensitivity seemed unlikely. Only 25% of the cats showed results that were consistent with the results of their elimination diet and re-exposures.

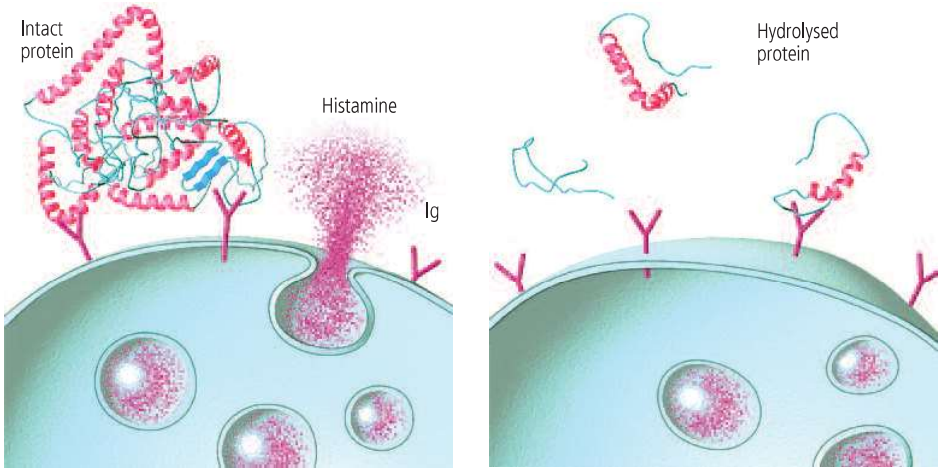
Home-prepared elimination diets

The only reliable means to diagnose adverse food reaction in the cat is currently a commercial or a home-prepared elimination diet with a protein source the cat has not been exposed to *(Mueller, 2000; Scott et al, 2001)*. Examples of possible protein sources are given in **Table 7**. Such a diet is typically not nutritionally balanced, but may be fed in adult animals for short periods of time (for the trial period, up to 12 weeks) without clinically apparent adverse effects. The protein source should be boiled, grilled or prepared in a microwave. The method of preparation depends on the individual circumstances, owner and cat. Some cats will accept a mixture of a protein and a carbohydrate source, in these cases a combination of both may be fed. However, most cats will prefer a diet based on protein sources only. Although taurine levels in meat are sufficient for cats *(Wills, 1991)*, particularly young animals on a home-prepared elimination diet may benefit from vitamin and mineral supplementation without flavors or additives *(Scott et al, 2001; Wills, 1991)*.

Commercial elimination diets

As alternative protein sources are sometimes difficult to obtain and require preparation, some owners may only be willing to use a commercial diet. Although numerous hypoallergenic diets are on the market, it is important to remember that the frequency of an adverse reaction to a protein is first and foremost related to the frequency this particular protein is fed to our feline companions. Lamb, fish and chicken, in the past considered first choices for elimination diets, are sometimes reported to be implicated in adverse food reactions of individual cats. These ingredients can still be effective in individual patients but only food with proteins that exclusively come from selected sources that the patient was not exposed to previously are acceptable.

FIGURE 10 – LOWER ALLERGENICITY OF HYDROLYSED PROTEINS VERSUS INTACT PROTEINS



Degranulation of mast cells (which leads to the release of histamine, responsible for inflammation), results from the binding of two amino acid sequences or epitopes on two immunoglobulins located on the mast cell surface. The lower the molecular weight of the protein, the lower the likelihood of containing these two amino-acid sequences.

Alternatively, hydrolysed diets may be fed. These foods are formulated on the basis of protein hydrolysates. The purpose of the hydrolysation is to fractionate the proteins into small peptides of low molecular weight **(Figure 10)**.

These peptides are less antigenic and more digestible and thus offer less stimulation to the gastrointestinal immune system. Thus, hydrolysed diets are theoretically the most suitable commercial elimination diets. In the dog, studies have documented clinical improvement of allergic patients on hydrolysed diets *(Biourge et al, 2004; Loeffler et al, 2004; Loeffler et al, 2006)*. No such studies have been conducted in cats to the authors' knowledge.

If there are several cats in the household, either the hypersensitive cat must be prevented from access to the other cats' food, or all the cats must be given the same elimination diet. © Yves Lanceau/RC/ European Shorthair

Concomitant treatments

Antipruritic and/or antimicrobial treatment may be indicated during the elimination diet. The cat may also have concurrent disease that requires continuous administration of drugs. In these cases, the prescription of flavored medication must be avoided, as small amounts of offending allergens may lead to clinical signs and prevent remission with the diet. If medication is usually administered with food, any potential protein source previously fed must be avoided.

Special circumstances

Multi-pet households

If more than one animal lives in the same household, then the other animals must be fed separately. This is only possible, if the animals are housed completely separately or if the other animals feed rapidly and thus will empty their food bowl in a very short time when placed into a room without the patient with suspected adverse food reaction. Otherwise it is prudent to feed all the animals in the household the same elimination diet to avoid accidents, where the patient consumes additional food from other pets that will most likely prevent clinical improvement.

Outdoor cats

Many cats either live predominantly outdoors or at least have free and unlimited access to the outside. They may wander into other back yards or houses and help themselves to pet food available there. Thus, ideally these patients need to be kept indoors for the duration of the diet, which can be difficult for the cat and owner.

Cats that typically hunt mice or birds will continue that habit during the dietary trial. Ideally these patients should be kept indoors for the duration of the elimination and challenge dietary trials.

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Fussy eaters

Some cats may not like the new food offered to them during the diet trial. Cats can be determined and few owners will tolerate refusal of any given diet for more than a couple of days. With a home-prepared diet, warming up the food, salting it very slightly or preparing it differently may entice the cat to accept it. With commercial diets, a gradual change from the original food to the diet over three or four days may increase the chance of acceptance. If neither of these measures is helpful, a new elimination diet may need to be formulated.

Monitoring the diet

Compliance with the diet can be difficult not only considering the patient, but also the owner. A thorough client education supported by written instructions will increase the chances of success. Every family member and visiting friends must be informed of the need for strict adherence to the agreed diet trial.

A telephone call a few days after instituting the diet will be helpful in identifying possible problems. At that time, any

Table 8 - Example of pruritus scores

Note	Description
0	Absence of pruritus
1	Discrete pruritus, not spontaneously described by the owner, less than one hour per day
2	Moderate pruritus, spontaneously described by the owner, one to three hours per day
3	Significant pruritus, three to six hours per day
4	Very significant pruritus, permanent, observed in consultation, sleeping problems

questions the owners may have are answered. Regular appointments after three to four and six to eight weeks are needed to monitor compliance, motivate and emotionally support the owner. Depending on the food and the cat, weight gain or weight loss may ensue. The owner must be instructed to monitor the cat's weight and if there is weight gain, diet intake should be decreased. If the patient loses weight, more food should be offered.

Length of the diet and interpretation of results

A diet trial should be conducted for six to eight weeks. If remission is achieved faster, then of course the diet can be discontinued earlier. After the diet trial, the previous food is fed again and should lead to a recurrence of clinical signs within hours to at the most, two weeks. At this point reinstitution of the elimination diet with subsequent resolution of clinical signs confirms the diagnosis of adverse food reaction. If however after two weeks no deterioration has occurred, then improvement was due to other factors such as treating secondary infections, change of seasons or concurrent ectoparasite treatment trial.

If there is spectacular improvement and complete remission occurs, judgement of success is simple. However, if there is partial improvement, interpretation is more difficult. Scoring systems for pruritus **(Table 8)** and/or lesions or digital photographs may be helpful in these patients. A provocative test is as important in these patients as in the cats with complete remission on the diet to ascertain the diagnosis.

Sequential rechallenge with the introduction of one protein source every one or two weeks allows correct identification of the offending allergen(s). Although many owners are reluctant to perform such a sequential rechallenge due to the associated emotional and organizational efforts, knowledge of the type of allergens involved frequently permits a wider choice of diets likely to be tolerated long term. Alternatively, the elimination diet may be continued long term. With a home-prepared diet, a nutritionist should be consulted to balance the diet and avoid nutritional deficiencies.

3 - Metabolic diseases

► Metabolic epidermal necrosis/necrolytic migratory erythema

Necrolytic migratory erythema is a skin disease in humans, that most commonly occurs secondary to a glucagon-secreting pancreatic tumor *(Tierney & Badger, 2004)*. However, liver disease, internal malignancies other than pancreatic tumors and even glucocorticoid administration have been reported as causes of this disease *(Mullans & Cohen, 1998; Tierney & Badger, 2004)*.

In the dog and cat, the terms diabetic dermatopathy, hepatocutaneous syndrome, metabolic epidermal necrosis or superficial necrolytic dermatitis have all been used, but a standard nomenclature has not been accepted *(Scott et al, 2001)*. In the dog, the most common causes are liver disease, hyperadrenocorticism, diabetes mellitus, pancreatic tumors and phenobarbital administration *(Gross et al, 1993; March et al, 2004; Torres et al, 1997; Yoshida et al, 1996)*. Two of the four cats reported in the literature had hepatopathies and the remaining two had pancreatic tumors *(Beardi, 2003; Godfrey & Rest, 2000; Kimmel et al, 2003; Patel et al, 1996)*. The exact pathogenesis of metabolic epidermal necrosis has not been elucidated, but a deficiency of amino acids, fatty acids and/or zinc is discussed in the dog *(Outerbridge et al, 2002; Tierney & Badger, 2004)*.

Clinical signs in the cat include stomatitis, gingivitis, alopecia, scaling and mild crusting. The skin lesions are bilaterally symmetrical and affect the axillae, ventrum, and inguinal area as well as the tail. Foot pads and mucocutaneous junctions were affected in one cat. Skin biopsies show diagnostic features of severe parakeratosis with underlying severe edema of the upper epidermis, and irregular epidermal hyperplasia with mild to moderate inflammation of the underlying dermis and

appendages. Ultrasonography of the liver may reveal a diffusely coarse echotexture with a reticular pattern or a pancreatic mass.

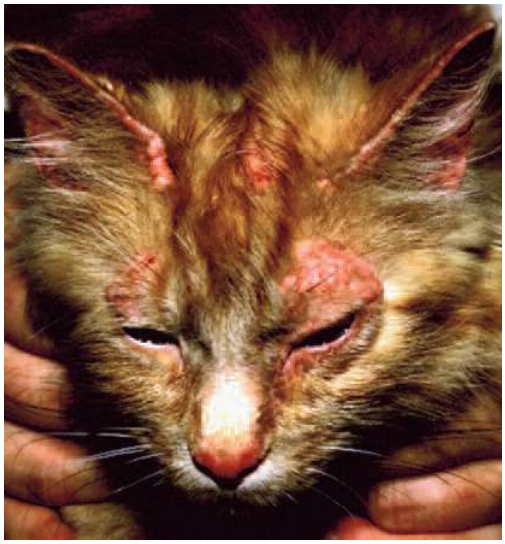
Treatment of human necrolytic migratory erythema involves removal of the pancreatic tumor, skin lesions subsequently resolve without further therapy *(Chastain, 2001; Zhang et al, 2004)*. In dogs, removal of a pancreatic tumor has also resulted in complete clinical remission *(Torres et al, 1997)*. However, in most patients, advanced liver disease is the cause. In these patients, high quality proteins such as eggs in association with zinc and fatty acid supplementation may be helpful. In severe cases, intravenous amino acid infusion may lead to temporary remission *(Gross et al, 1993, Outerbridge et al, 2002)*. However, if the underlying disease cannot be treated successfully, the prognosis is poor. To date, successful treatment of this disease in the cat has not been reported.

TABLE 9 - CAUSES OF FELINE XANTHOMAS

- Diabetes mellitus
- Chronic administration of megestrol acetate
- Congenital lipoprotein lipase deficiency
- High dietary fat intake
- Idiopathic

► Xanthoma

Feline xanthomas are benign granulomatous lesions with several possible causes **(Table 9)**. Hereditary hyperlipoproteinemia is one possible etiology *(Grieshaber, 1991; Johnstone et al, 1990; Jones et al, 1986)*. It may be due to congenital deficiency of lipoprotein lipase, an enzyme responsible for hydrolysis of the lipids in the chylomicrons and the release of free fatty acids in the peripheral tissues *(Bauer & Verlander, 1984)*. Xanthomas have also been reported in cats with diabetes mellitus *(Jones et al, 1986; Kwochka & Short, 1984)*. A case series of 5 cats described frequent high fat treats such as cream, butter and ice cream as possible causes, all of these cats responded to a low fat diet *(Vitale et al, 1998)*. Leakage with extra- and intracellular deposition of lipoproteins from the capillaries into the tissue is suspected to occur in humans and may also occur in cats. Idiopathic feline xanthoma may also exist *(Denerolle, 1992)*.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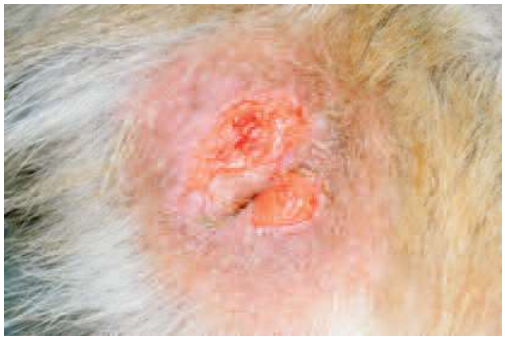
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Figure 11 - A DSH cat with facial alopecia, erythema, and papules due to xanthoma. *Clinical signs of xanthomas in cats include white to yellowish papules, plaques and nodules that may or may not be ulcerated.*

Lesions most commonly develop on the head, particularly the preauricular area and pinnae **(Figure 11)**. Bony prominences may also be affected.

The diagnosis is confirmed histologically. A nodular to diffuse granulomatous inflammation with foamy macrophages and multinucleated giant cells is characteristic. Diabetes mellitus or excess dietary fat intake should be ruled out as underlying causes.

Treatment consists of addressing the underlying disease and feeding a low fat diet (< 25 % of calories of the diet provided by fat). If diabetes mellitus is treated successfully, the diet may be changed back to normal. In patients with idiopathic or congenital xanthomas, it may be prudent to continue the low-fat diet for the remainder of the pets life.

Lesions due to a specific underlying cause resolve spontaneously once the underlying cause is addressed successfully. A low-fat diet is recommended and will be particularly useful in cats with the idiopathic form of xanthoma.

4 - Nutritional therapy in dermatology

► Dull coat, xerosis

The coat's sheen is connected to the composition of sebum secreted by sebaceous gland secretions and stored in the hair follicles. The lipids in the composition of sebum are species and in the dog breed specific *(Dunstan et al, 2000)*, but the production and the quality of the sebum is also influenced by food *(Macdonald et al, 1983)*. Dryness of the skin (xerosis) is caused by decreased water

content. The increased water loss through evaporation may be due to low humidity conditions of the environment or an increased transepidermal water loss. In cats, linoleic acid deficiency has been shown to be a possible cause for the latter *(Macdonald et al, 1983)*.

► Color change of black coats to reddish brown

In some black cats, the coat color changes to a reddish brown. This color change is associated with low tyrosine plasma concentrations, has been induced in cats given a tyrosine-deficient diet, and is reversed by diets containing a high concentration of tyrosine or phenylalanine. Current dietary recommendations for dietary tyrosine and phenylalanine for kittens are below those required to support maximal melanin synthesis in black adult cats. The requirement appears to be greater than a combination of 4.5 g tyrosine plus 12 g phenylalanine/kg diet but less than 24 g phenylalanine alone/kg diet *(Yu et al, 2001)*.

► Skin wound healing

To maximize wound healing and to be able to formulate appropriate nutritional supplements in the pre- and post-surgery period in humans, nutritionists have studied the stimulation of re-epithelialization and of the immune system to decrease the chance of secondary wound infections. A number of oral preparations are available in human medicine, but similar products for cats are not available to the authors' knowledge.

Protein and zinc deficiencies are associated with delayed wound healing and care should be taken to optimize protein and zinc intake in wounded animals *(Robben et al, 1999)*.

Iron and vitamin C are involved in hydroxylation of proline, a major amino acid in the structure of collagen. Iron deficiency affects the quality of the scar tissue.

Omega-3 fatty acids have a positive effect on wound healing in dogs *(Scardino et al, 1999)*. A vitamin E supplement helps protect PUFA's from oxidation. Similarly, the positive role of curcumin, aloe vera and bromelaine has been shown in the canine wound healing process *(Fray et al, 2004)*. To the authors's knowledge, no such data exists for cats.

► Feline allergic skin disease

Feline atopic dermatitis is a multifactorial disease. However, in contrast to human or canine atopic dermatitis, the cat presents with a number of clinical reaction patterns *(Bettenay, 2000; Rees, 2001)* **(Table 4)**. Additional common causes for these reaction patterns are flea bite hypersensitivity and adverse food reactions (see above). Nutrition may be used in several ways in these feline patients.

> Reduction in inflammation with polyunsaturated fatty acids

Long chain polyunsaturated fatty acids have been shown to alleviate the symptoms of miliary dermatitis *(Harvey, 1993; Harvey, 1991; Lechowski et al, 1998)*. The fatty acid profile in plasma of affected cats was different than that of normal cats and omega-3 supplementation increased plasma concentrations of EPA and DHA and decreased dihomo-gamma-linolenic acid (DGLA), corresponding to clinical improvement. A combination of fish oil (omega-3) and evening primrose oil (omega-6) had a higher response rate than fish oil alone *(Harvey, 1993)*. Some cats with eosinophilic granuloma, another reaction pattern frequently associated with feline allergies, also respond to fatty acid supplementation *(Scott et al, 2001)*.

A diet that does not contain adequate levels of tyrosine and/or phenylalanine to permit the complete synthesis of melanin induces a coat color change in black cats. The color becomes reddish brown.

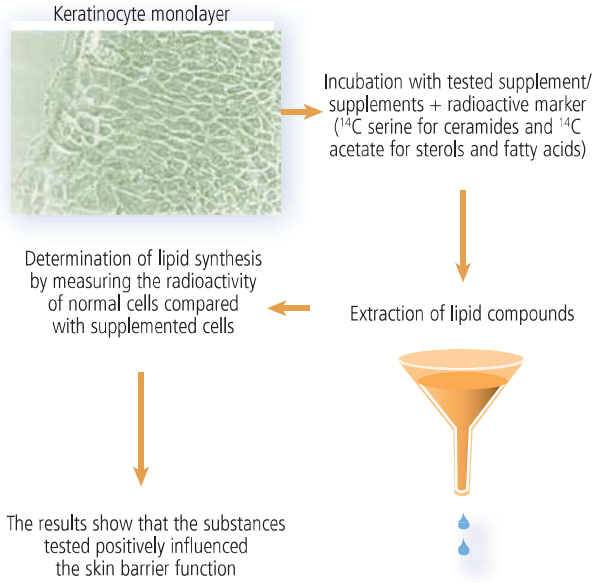
> Prevention or control of dietary hypersensitivities

Up to 40% of cats with atopic dermatitis have concurrent adverse food reactions *(Waisglass et al, 2006)*. Such possible dietary hypersensitivities may be addressed by either using food sources avoiding the offending protein allergens or by using a hydrolysed diet where the antigens are of such small size that an allergic reaction may be prevented in many patients.

> Re-establishment of the skin barrier

Defects in intercellular ceramides in canine atopic epidermis have been described and presumably allow increased transepidermal water loss, increased penetration by antigens and increased adherence of staphylococci similar to what is seen in human patients with atopic dermatitis. In vitro studies (keratinocytes cultures) conducted by the Waltham Centre for Pet Nutrition have shown that some nutrients (in particular nicotinamide, pantothenic acid, histidine, inositol and choline) improve the structure and the function of the skin. Others (pyridoxine and proline) stimulate the synthesis of ceramides *(Watson et al, 2006)* **(Figure 12)**.

FIGURE 12 – MEASURING THE SYNTHESIS OF SKIN LIPIDS
(From Watson, 2003)



In vivo studies have confirmed this approach. After nine weeks of supplementation with a supplement composed of nicotinamide, pantothenic acid, histidine, inositol and choline, the cutaneous water loss was significantly reduced in atopic dogs. The reduction in water loss and so xerosis can have a positive effect of reducing allergen penetration, and also limit bacterial and fungal colonization, which may cause the development of atopic dermatitis. Unfortunately, no such reports exist for the cat to the authors' knowledge.

► Miscellaneous skin diseases

> *Urticaria pigmentosa*

Essential fatty acids were reported to be helpful in the control of exacerbations of feline urticaria pigmentosa, a maculopapular eruption of the ventral trunk with a perivascular to diffuse mastocytic and eosinophilic infiltrate in the dermis *(Noli et al, 2004)*.

> Dermatosparaxis/cutaneous asthenia

Dermatosparaxis is an inherited connective tissue disease characterized by excessive fragility and hyperextensibility of the skin. Because vitamin C is necessary in collagen synthesis, it may be useful in the treatment of feline patients with this disease. Although in contrast to dogs, two cats with dermatosparaxis treated with vitamin C did not improve *(Scott et al, 2001)*, one of the authors has seen improvement in two cats with this syndrome treated with vitamin C.

> Feline acne

Feline acne is a disorder characterized by comedones and crusts on the chin and lips **(Figure 13)** and the idiopathic form is considered a disorder of follicular keratinization *(Scott et al, 2001)*. It responds to a number of topical antimicrobial agents, but cats with recurrent feline acne have been reported to also benefit from fatty acid supplementation *(Rosenkrantz, 1991)*.

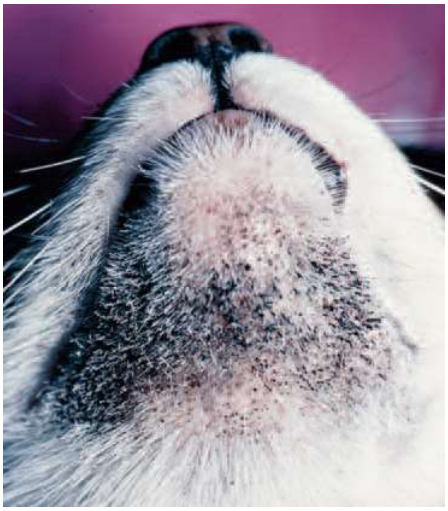

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Figure 13 - Domestic short hair cat with acne. *Comedones and small crusts on the ventral chin.*

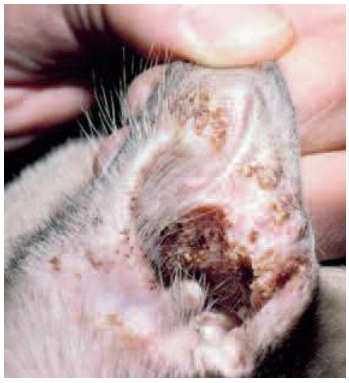

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Figure 14 - A cat with pemphigus foliaceus. Crusts on the medial pinnae.

TABLE 10 - EXAMPLES OF NUTRITIONAL RECOMMENDATIONS FOR LIMITING THE RISK OF FOOD ALLERGIES IN CHILDREN
(Sampson, 2004)

- Breastfeeding for three to six months
- Use of hydrolysates if breastfeeding is not possible
- Avoidance of peanuts and seafood during pregnancy and breastfeeding
- Avoidance of high-risk foods (peanuts, hazelnuts, seafood) before three years of age

> Various immune-mediated diseases

Pemphigus foliaceus is a pustular and crusting skin disease **(Figure 14)** characterized by acantholysis of keratinocytes. Typically, immunosuppressive therapy with glucocorticoids or chlorambucil is recommended to treat feline pemphigus foliaceus. However, vitamin E and fatty acid supplementation have been reported to be useful in individual patients *(Scott et al, 2001)*. Similarly, vitamin E and essential fatty acids have been recommended as adjunctive treatment of feline discoid lupus erythematosus *(Scott et al, 2001)*.

► Prophylactic nutrition

In feline dermatology, nutritional interventions have been almost exclusively devoted to therapeutic functions. In human dermatology, nutrition is also used preventively. The problem with preventive nutritional intervention is the identification of the patient at risk. Although most cats kept as pets are domestic short hair cats and most diseases lack clear breed predispositions in the feline, some rare dermatoses show breed predisposition such as adverse food reactions in Siamese and thus may be suited to such interventions. Prospective controlled clinical studies are needed to evaluate the benefit of such an approach.

> Highly digestible foods

In human medicine, hydrolysates are mainly used in the prevention of adverse food reactions for high-risk children or their mothers to reduce the risk that clinical manifestations of atopy will develop **(Table 10)**. If such an approach is useful in feline medicine remains to be elucidated.

> Probiotics

In humans there is a significant difference between the intestinal flora of normal and that of atopic babies *(Bjorksten et al, 2001)*. Similarly, it has been shown, that supplementation of pregnant and breastfeeding mothers with *Lactobacillus rhamnosus* significantly decreases the clinical manifestations in their children *(Kalliomaki et al, 2003)*. In addition, supplementation with lactobacilli has improved the clinical signs of atopic children *(Rosenfeldt et al, 2003)*.

In the cat, the addition of probiotics in food or capsules presents technical problems. In a recent study, none of the probiotic supplements tested contained all the claimed bacteria *(Weese & Arroyo, 2003)*. However, it is possible to include probiotics in dry food and an effect on the feline immune response was observed after supplementation *(Marshall-Jones et al, 2006)*. If these probiotics could be used for the prevention or treatment of atopic disease awaits further study.

Conclusion

Food plays a fundamental role in cutaneous homeostasis and in the treatment of many inflammatory dermatoses. The study of diet is therefore an integral part of the dermatological history. The correction of dietary imbalances (with respect to fatty acids and tyrosine in particular) is a necessary factor in good dermatological therapy.

The treatment of many dermatoses involves the use of nutrients that reinforce the skin barrier function, or modulate the immune system, either as anti-inflammatory or as immunostimulatory agents. In the future, it is likely that more emphasis will be placed on the possible use of food for prophylactic purposes. Furthermore, the exact type and dose of optimal fatty acid supplementations and probiotics will need to be determined to greatly benefit our feline patients.

Frequently asked questions about the contribution of dietetics in dermatology

Q	A
Which nutritional deficiencies are most commonly implicated in feline dermatology?	Essential fatty acid and tyrosine deficiency are possible deficiencies leading to skin disease in cats.
Do cats get zinc deficiency?	In contrast to dogs, zinc deficiency has not been reported in cats.
Are adverse food reactions common?	In cats, adverse food reactions are more frequently seen than in the dog. An adverse food reaction should be considered particularly when head and neck pruritus are observed or there are concurrent gastrointestinal signs associated with the skin disease.
Which foods are the most likely to cause allergic reactions?	Fish, beef and dairy products are the most commonly reported food allergens in the cat. However, this may simply be due to the widespread use of these ingredients in cat food.
Is white meat less allergic than red meat?	This belief is incorrect. The color of the meat does not have any influence on its potential allergenic or hypoallergenic character. The risk increases with the quantity of meat ingested. Red meats such as venison are widely and successfully used as a basis for elimination diets, simply because these foods are not typically found in cat foods.
How do you diagnose atopic dermatitis in a cat?	Atopic dermatitis in the cat may present as a variety of cutaneous reaction patterns. These cutaneous reaction patterns in turn may be caused by many different diseases. Thus, the differential diagnoses for each patient with potential atopic dermatitis need to be ruled out prior to the diagnosis of atopic dermatitis. For example, all cats with potential atopy need to undergo strict flea control and an elimination diet to rule out flea bite hypersensitivity and adverse food reaction.
Can atopic dermatitis be controlled simply with PUFA supplementation?	Yes, but if the response is unsatisfactory after 6-12 weeks of treatment, other therapeutics should be used.
Can diet be the cause of non-inflammatory "endocrine" alopecia in the cat?	Years ago, non-inflammatory alopecia was considered a hormonal disease. However, true endocrine alopecia in cats is very rare. Subsequently, this disease was diagnosed as psychogenic alopecia. Some patients indeed develop psychogenic alopecia and responded to behavioral therapy. However, many of these cats are actually allergic cats; the overgrooming and alopecia is a response to pruritus. An elimination diet to rule out adverse food reaction is an essential diagnostic tool in every cat with non-inflammatory alopecia.

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Focus on:

Borage oil

Borage *(Borago officinalis)* is a plant originally from Syria. It is now grown in North Africa and various countries of Europe, including France, Britain, Germany and the Netherlands. The first traces of its use are from the first century AD. Traditionally, the young leaves were consumed in salads or soups and the flowers gave a refreshing flavor to wine.

Borage seeds

Borage blooms over two months, which means that not all the seeds become mature at the same time. It is important to only harvest the mature seeds, which look like grains of pepper, as they have twice the oil content of green seeds (30% vs. 15%).

Harvesting may be done naturally – recovering the seeds as they fall by rolling out a tarp between the rows – or mechanically, using small carts to catch the seeds, which are loosened by vibration.

Borage oil

The seeds dry out naturally somewhere cool in the shade. To avoid mold, they must be used shortly after harvesting. The oil is obtained by grinding and pressing the seeds. The procedure is performed in a cold environment. Above 50 °C (122°F), the fatty acids risk being denatured.

Unparalleled gamma-linolenic acid (GLA) content

The oil is obtained by pressing the borage seeds. Their unsaturated fatty acid content is 80% and they have a large content of a particular fatty acid of the omega-6 family, known as gamma-linolenic acid (GLA). GLA is normally synthesized from linoleic acid.

Most vegetable oils have a very high linoleic acid content, but the only oils that contain a beneficial quantity of GLA are borage oil, the oil of blackcurrant seeds and evening primrose oil.

Linoleic acid undergoes successive transformations to produce all the fatty acids of the omega-6 family. Each step is triggered by a particular enzyme. The metabolism of unsaturated fatty acids in cats remains a controversial subject. Some authors feel that Δ6 desaturase is ineffective in cats *(Sinclair et al., 1979)*. More recent studies *(Pawlosky et al., 1994)* show that the conversion of linoleic acid to GLA is possible, with increased efficacy when the animal is deficient. This process however remains limited in the cat. In this study, the authors reported that only 0.06% of the ingested linoleic acid was converted to GLA.

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Nutritional benefit of GLA

Borage oil is widely used in nutrition and cosmetology. It is used in products designed to rejuvenate the skin. It is especially indicated for the dry skin of cats that tend towards seborrhea. Cats respond very well to the addition of GLA to the diet.

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The supplementation of GLA promotes the increased production of type 1 prostaglandins over the production of type 2 prostaglandins, which are much more pro-inflammatory. Borage oil is accordingly potentially beneficial in all situations demanding an anti-inflammatory effect.

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Comparison of the GLA content of different vegetable oils

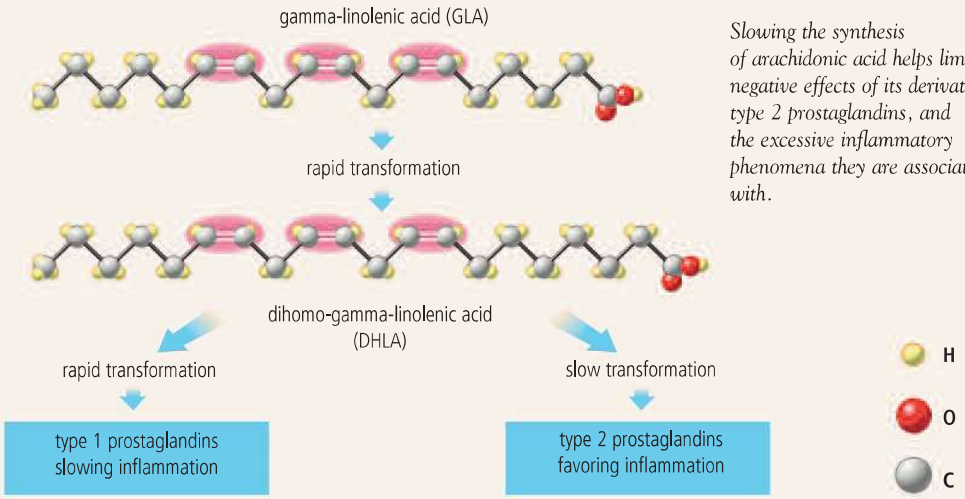
Vegetable sources	Linoleic acid%	Gamma-linolenic acid (GLA)%
Borage	35 to 40	20 to 25
Blackcurrant seeds	45 to 50	15 to 20
Evening primrose	70 to 80	8 to 12
Soy	50 to 55	-
Olive	8 to 10	-

Borage oil has the highest GLA concentration.

The beneficial effects of GLA have been studied most in dermatology. Major alterations to the condition of the skin (dull hair, scaling and skin ulcers that do not heal easily) are observed in cats fed for 18 months with a food containing sunflower seed oil, which is rich in linoleic acid, as the sole source of fat *(Frankel & Rivers, 1978)*. Substituting half the sunflower seed oil with evening primrose oil, which is rich in GLA, helps obtain a fast improvement in the condition of the skin in these animals. Reversion to the original diet results in deterioration of the condition of the skin again. This study therefore confirms the benefit of high GLA oil supplementation to alter linoleic acid desaturation.

Other studies show the benefit of GLA intake in feline dermatology. In cats with papulo-squamous dermatitis, the dietary incorporation of evening primrose oil, helped to obtain better therapeutic results than sunflower oil, *(Harvey, 1993a)*. With feline miliary dermatitis, the efficacy of GLA administration was improved when it was combined with fish oil *(Harvey, 1993b)*.

ORIGIN OF THE BALANCE BETWEEN TYPE 1 AND 2 PROSTAGLANDINS



Slowing the synthesis of arachidonic acid helps limit the negative effects of its derivatives, type 2 prostaglandins, and the excessive inflammatory phenomena they are associated with.

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Protein composition of cat hair

The daily protein requirement to regenerate skin cells and stimulate hair growth is estimated at almost 30% of the daily protein intake (Scott et al, 2001).

There is little data on the amino acid composition of hair. It is determined through hydrolysis with hydrochloric acid for 24 hours. This method may however lead to the degradation of some amino acids or underestimate the content when hydrolysis is incomplete. Studies *(Robel & Crane, 1972; Darragh et al, 1996)* have reported alternative techniques to minimize these inaccuracies. *Hendriks et al* (1998) reported that the color or sex of the animal has no impact on the amino acid composition of the hair.

TABLE 1 - AMINO ACID COMPOSITION OF THE HAIRS OF CATS AND SOME OTHER MAMMALS
(From Hendriks et al, 1998)

Amino acid	Content (mol/100 mol of residue)				
	Cat	Dog	Horse	Sheep	Human
Cysteine	15.9	16.7	14.4	13.1	17.8
Methionine	0.9	0.9	0.2	0.5	0.6
Aspartate	5.6	5.3	6.0	5.9	4.9
Threonine	6.4	6.2	6.5	6.5	6.8
Serine	10.6	10.5	9.6	10.8	11.7
Glutamate	11.4	11.1	11.3	11.1	11.4
Glycine	9.5	7.8	6.4	8.6	6.4
Alanine	5.1	5.1	5.5	5.2	4.6
Valine	4.9	4.9	5.9	5.7	5.8
Isoleucine	2.5	2.5	3.6	3.0	2.6
Leucine	6.7	6.1	7.5	7.2	5.8
Tyrosine	3.0	2.7	1.9	3.8	2.0
Phenylalanine	2.3	1.7	2.5	2.5	1.6
Histidine	1.2	0.9	1.1	0.8	0.9
Lysine	2.9	3.9	2.9	2.7	2.7
Arginine	6.1	6.3	7.9	6.2	5.8
Proline	4.9	7.3	7.8	6.6	8.4

The total nitrogen content of cat hair is said to be 15.1% *(Hendriks et al, 1998)*. This author also reported that amino acids represent 86% of the hair mass in this species. The remainder is divided between non-nitrogen compounds: minerals, sterols and complex lipids.

The amino acid composition of cat hair is similar to that of dogs, sheep, horses and humans, although the proline content in cats is lower than in the other species. The most abundant amino acids in cat hair protein are cysteine, serine, glutamic acid and glycine **(Table 1)**. Sulphur containing amino acids can account for up to 37% of the total amino acids *(Swift & Smith, 2000)*. They build cysteine bridges, which are essential to hair construction. Cysteine is also involved in the enzymatic production of pheomelanin *(Granholm, 1996)*.

Animal color or sex has no impact on the amino acid composition of the hair.

Key points

for covering protein requirement with respect to hair growth

The quantity of amino acids required for hair growth in a given period of the year can be estimated by multiplying the amino acid concentration in each cat hair by the hair growth rate during that period of the year *(Hendriks et al, 1998)*. The daily protein requirement to regenerate skin cells and stimulate hair growth is estimated at almost 30% of daily protein intake *(Scott et al, 2001)*.

The effects of general protein deficiency:

- Initially, a drop in the diameter of the hair and reduction in the size of the hair bulb
- Subsequently, the hair becomes dull and fragile, growing more slowly and falling out faster.

Isolated deficiency of sulfur amino acids (cysteine, methionine) may lead to the same clinical signs.

Studies show the impact of a deficiency of tyrosine and phenylalanine, a melanin precursor. After a few weeks red hairs begin to appear, especially in black cats. Supplementation reverses this phenomenon. The hairs of reddish cats (which have pheomelanin pigments) also take on a lighter color in response to deficiency *(Morris et al, 2002; Anderson et al, 2002; Yu et al, 2001)*. *Morris et al* (2002) show that around three times as much phenylalanine and tyrosine is needed to obtain optimal coloration of a black coat than is needed for the normal growth of a kitten. These authors recommend a minimum intake of 18 g/kg of dry dietary matter.

Around three times as much phenylalanine and tyrosine is needed to obtain optimal coloration of a black coat than is needed for the normal growth of a kitten.

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