Fatty Acid Supplementation:

Does It Work for Dogs with Ear and Skin Disease?

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BASIC FATTY ACID METABOLISM

All mammals synthesize fatty acids *de novo* up to palmitic acid (16:0), which may be elongated to stearic acid (18:0) and converted into oleic acid (18:1). Plants, unlike mammals, can insert additional double bonds into oleic acid and produce the polyunsaturated fatty acids (PUFA), linoleic acid (LA, 18:2n-6) and alpha-linolenic acid (ALA, 18:3n-3). Both LA and ALA are considered essential fatty acids (EFA) because animals cannot synthesize them from other series of fatty acids; thus, they must be supplied by the diet.

Dietary PUFA serve as substrates that may be metabolized to form important, biologically active compounds. To produce those metabolites, a number of cells contain a group of enzymes that desaturate (introducing a double bond between carbon atoms), elongate (increasing length of fatty acid chain) and oxygenate fatty acids.

All PUFA are categorized based on the position of the first double bond in the structure from the terminal end. The two most important PUFA series are the omega-6 series (the first double bond is located at the sixth carbon atom) and the omega-3 series (the first double bond is located at the third carbon atom). In the omega-6 series, linoleic acid can be desaturated to yield gamma-linolenic acid (GLA, 18:3n-6), which is elongated to dihomo-gamma-linolenic acid (DGLA, 20:3n-6) and ultimately desaturated again to produce arachidonic acid (AA, 20:4n-6) in the animal.

Many marine plants, especially algae, elongate chains and add double bonds to ALA to yield omega-3 PUFA with 20 and 22 carbon atoms and five or six double bonds. Formation of these long-chain omega-3 PUFA by marine algae and their transfer through the food chain to fish account for the abundance of eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3) in certain marine fish oils.

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AA and EPA act as precursors for the synthesis of eicosanoids, a significant group of immunoregulatory molecules that function as local hormones and mediators of inflammation. The amounts and types of eicosanoids synthesized are determined by the availability of the PUFA precursor and by the activities of the enzyme system to synthesize them. In most conditions the principal precursor for these compounds is AA, although EPA competes with AA for the same enzyme systems. The eicosanoids produced from AA appear to be more inflammatory than those formed from EPA. Ingestion of oils containing omega-3 PUFA results in a decrease in membrane AA levels since omega-3 PUFA replace AA in the substrate pool and also produces an accompanying decrease in the capacity to synthesize eicosanoids from AA. In contrast, eicosanoids derived from EPA promote less inflammatory activity and may alter vascular function. Inflammatory eicosanoids produced from AA may be depressed when animals consume foods with high levels of omega-3 fatty acids.

WHAT'S NEW IN FATTY ACIDS?

Resolvins and Protectins

Beneficial actions of polyunsaturated fatty acids were noted many years ago but the underlying mechanisms for these effects are poorly understood. It is clear that arachidonic acid is transformed into many potent bioactive compounds such as prostaglandins, leukotrienes and lipoxins. The departure of fatty acids from simply playing structural roles in cell membranes and/or as energy stores came largely from the recognition of the rapid transformation of arachidonic acid to these potent eicosanoids by both cyclooxygenase and lipoxygenase mechanisms. As discussed earlier, many of the classic prostaglandins and leukotriene mediators are pro-inflammatory and play a decisive role in inflammation and/or in systems where prostaglandins are key physiologic regulators.

In sharp contrast, it has become clear in recent years that counter-regulatory substances such as lipoxins are generated during the resolution of acute inflammation, and that these serve as agonists for endogenous anti-inflammatory mechanisms. This constitutes the first evidence that the resolution of inflammation, which was once thought to be a passive process, is actually an active process that involves up-regulating specific pro-resolution circuits. Thus, resolution of inflammation is an active endogenous process aimed at protecting the host from exacerbated inflammation.

The molecular mechanisms underlying the beneficial actions of polyunsaturated fatty acids remain an area of active research. Investigators have recently identified a variety of novel oxygenated products generated by enzymatic processes from the precursor omega-3 fatty acids EPA and DHA. These new compounds possess potent actions in the resolution of inflammation and may also have neuroprotective properties. The term *resolvin* (resolution phase interaction products) has been proposed for some of these compounds since they display both potent anti-inflammatory and immunoregulatory properties, reducing neutrophil traffic and the magnitude of the inflammatory response. The term *protectin* has been proposed for another class of these compounds with protective actions in neural and retinal tissues.

Resolvins are derived from both EPA (E series) and DHA (D series). Both the D and E classes of resolvins appear as biosynthetic products involving cell-to-cell interaction with vascular endothelial cells and are potent regulators of leukocyte infiltration. Specifically, resolvin E1 (RvE1) has been shown to dramatically reduce dermal inflammation, peritonitis, colitis, periodontitis, dendritic cell migration and interleukin (IL)-12 production. Resolvins of the D series block tumor necrosis factor-alpha activity and act as potent regulators to limit leukocyte infiltration into inflamed brain, skin and peritoneum.

Among the essential fatty acids, DHA is concentrated in the central nervous system, neurons and retina where it is thought to regulate membrane fluidity and ion fluxes. The term *docosanoids* has been proposed to describe products generated from DHA. DHA-derived docosatrienes have neuroprotective action in retinal cells and can improve the sequelae associated with stroke and dementia. The terms protectin or neuroprotectin describe these compounds, which are rapidly generated from DHA and released locally into tissues. The effects of protectins on neural pain receptors and pathways are unknown. There is emerging evidence that resolvins and docosanoid compounds may also have immunoregulatory actions by influencing antigen-presenting cells and T-cell traffic.

Fatty acid supplementation has been used for many years to help manage patients with a variety of inflammatory diseases and associated pain. The underlying mechanisms for the beneficial effects of fatty acid supplementation have been poorly understood. Resolvins and protectins, which are generated from EPA and DHA, are 'switched-on' in the resolution phase of an inflammatory response, thus acting as 'braking-signals' in inflammation and reducing leukocyte-mediated injury in several different tissues. The discovery of resolvins and protectins offers molecular mechanisms that could underlie some of the beneficial actions of dietary fatty acid supplementation observed in many clinical settings.

Use of Fatty Acid Supplementation for Patients with Seborrhea

Fats and fatty acids have been recommended for many years as supplements to improve the sheen and luster of hair. In the past, animal and vegetable sources of fat were recommended to improve coat quality. Investigators showed that dogs with seborrhea have abnormally low cutaneous levels of linoleic acid and increased cutaneous levels of oleic acid.[1] These low cutaneous levels are found despite normal food and serum fatty acid concentrations. Following supplementation for 30 days with a vegetable oil high in linoleic acid (sunflower oil), the cutaneous fatty acid concentrations return to near normal and clinical signs of seborrhea improved.[1] This suggests that clinical signs of seborrhea in dogs may be partly attributable to a localized deficiency of linoleic acid, increased levels of arachidonic acid in the skin or both. However, other investigators found no significant differences in the serum and skin fatty acid profiles of normal and a small number of seborrheic dogs.[2]

Seborrhea sicca is also associated with increased transepidermal water loss, which can be reversed with cutaneous administration of vegetable oils rich in linoleic acid.[3] Transepidermal water loss can also be decreased by supplementing the food with alpha-linolenic acid.[3] Further studies are needed to determine the effects of supplementation of food with other fatty acids and to determine the optimal dose of fatty acid supplements for patients with seborrhea.

Recommendation for use of fatty acids to help manage seborrhea: For patients with seborrhea, increase the total amount of dietary fatty acids including use of supplements or foods with higher levels of omega-6 fatty acids from vegetable oils and/or higher levels of omega-3 fatty acids from flaxseed. This is best accomplished with a variety of fatty acid supplements or foods designed for pets with “sensitive skin.”

Use of Fatty Acid Supplementation for Patients with Inflammatory Skin Diseases (Including Canine Ear Disease)

The use of fatty acids as antipruritic agents in dogs and cats has been the subject of numerous studies and considerable debate. The inflammation associated with allergic skin disease may be partially caused by abnormal essential fatty acid metabolism and inappropriate eicosanoid synthesis. A unique feature of skin is that it lacks Δ-6- and Δ-5-desaturase enzyme activity, and thus is incapable of making AA from LA or EPA from ALA. Skin can elongate GLA to DGLA and EPA to DHA. Normal dogs metabolize dietary sources of ALA to EPA and DHA elsewhere in the body. These fatty acids are then incorporated into the skin. DGLA, EPA and DHA in cutaneous cellular membranes may decrease inflammation through competition with AA for metabolic enzymes or because of the anti-inflammatory nature of the eicosanoids produced. The rationale for specifically administering products high in GLA is that GLA can be incorporated into the skin, where it is rapidly elongated to DGLA. Because skin lacks desaturase enzymes, DGLA is not further metabolized to arachidonic acid. As a result, DGLA competes with AA for metabolic enzymes. Thus, there is a decrease in AA-derived eicosanoids and an increase in the anti-inflammatory eicosanoids.

ALA is an omega-3 PUFA that is metabolized to EPA and DHA, and incorporated into the skin of normal dogs. Findings suggest that atopic dermatitis in human beings is associated with a deficiency of Δ-6-desaturase activity, which prevents the rapid conversion of ALA to EPA and DHA in atopic individuals. Comparable studies using atopic dogs and cats have not been published. However, one study suggested that subsets of atopic dogs exist with different fatty acid metabolic capabilities.[4]

The use of fatty acids for treating atopic dermatitis and chronic pruritus has been extensively studied in dogs. Unfortunately, most of these studies have been uncontrolled, nonblinded clinical trials using low doses of fatty acids for short periods. Well-controlled clinical studies using placebos and high doses of fatty acids for six weeks or more showed decreased pruritus in 0 to more than 50% of the patients.[5] Dogs that did not have decreased pruritus still showed improvement in other clinical signs, including less erythroderma and skin edema. The benefit of fatty acid supplementation is maximized in dogs if other contributing diseases such as adverse reactions to food, flea hypersensitivity, bacterial pyoderma and *Malassezia* dermatitis are controlled. Overall, it is probably safe to inform clients that 50 to 65% of dogs with allergic dermatitis and otitis externa will improve with modification in fatty acid intake, if secondary bacterial and yeast infections are controlled. Synergistic effects have been documented between fatty acid supplementation and use of other antipruritic agents such as antihistamines and glucocorticoids.

Recommendation for use of fatty acids for inflammatory skin disease in dogs: Deliver 50 to 250 mg total omega-3 fatty acids/kg body weight/day, or 0.8 to 3.0% total omega-3 fatty acids in the food (dry matter basis) with omega-6 to omega-3 ratio of 2:1 to 5:1. This is best accomplished using a therapeutic food specifically formulated with high levels of omega-3 fatty acids.

HOW TO USE FATTY ACID SUPPLEMENTATION

It is clear that dietary fatty acid levels well above those needed to avoid fatty acid deficiency benefit some patients with seborrhea, arthritis, allergic skin disease, chronic kidney disease, heart disease and cancer.[6] Dietary omega-3 fatty acid concentrations can be increased by using a supplement (usually cold water marine oils) or changing to food(s) that contains flaxseed, fish meal and/or fish oil as major ingredients. Dietary GLA concentrations can be increased by using a supplement with evening primrose, borage or black currant oil. Most commercial pet foods already exceed the omega-6 essential fatty acid requirement for linoleic acid by using vegetable oil and/or vegetable ingredients in their formula. Many commercial pet foods also contain levels of omega-3 fatty acids higher than those found in popular fatty acid supplements **(Tables 1 and 2)**.

What is less clear are answers to the following questions:

1. Which fatty acid or combination of fatty acids is most effective?
2. What ratio of omega-6 to omega-3 fatty acids is optimal?
3. What absolute amount of omega-6 and omega-3 fatty acids is appropriate in normal animals and what amount is effective in animals with clinical disease?
4. What levels of other nutrients (vitamins, trace minerals) are needed to allow fatty acid therapy to be effective?
5. What level of total dietary fat is needed to optimize fatty acid metabolism and clinical efficacy?

Although definitive answers to these questions are lacking in many situations, laboratory and clinical studies in a number of species have established a daily dosage for total omega-3 fatty acids that seems to be a reasonable starting point for patients with inflammatory and other diseases. An initial dose of 50 to 250 mg of total omega-3 fatty acids (ALA, EPA and/or DHA) per kg body weight per day seemed to be effective in a large number of studies.[5]

This total dose can be supplied through a combination of appropriate foods and supplements. It is important to note that many therapeutic foods contain much higher levels of fatty acids than those found in typical fatty acid supplements. Use of fatty acids for management of a wide variety of conditions will be easier and more cost effective if an appropriate food is used versus adding a fatty acid supplement to the regular diet.

The risks and side effects of high levels of dietary fatty acids are few. Soft feces, overt diarrhea, flatulence, vomiting and halitosis ("fishy breath") are most commonly noted at typical levels of fatty acid supplementation. More serious potential side effects include hemorrhage due to reduced platelet function, decreased plasma vitamin E concentrations and increased susceptibility to oxidative injury. Hemorrhagic problems have not been recognized in dogs consuming levels of omega-3 fatty acids found in pet foods and typical supplements.

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Table 1.

The total essential fatty acid intake for a 10-kg dog eating 600 kcal per day of selected commercial foods.

Foods*	Total omega-6 FA (mg)	Total omega-3 FA (mg)	EPA + DHA (mg)
Hill's® Prescription Diet® a/d® Canine/Feline Critical Care, moist	7,716	3,078	1,981
Hill's® Prescription Diet® b/d® Canine Aging & Alertness, dry	5,478	1,584	89
Hill's® Prescription Diet® d/d® Canine Skin Support Potato & Duck Formula, dry	5,184	1,170	522
Hill's® Prescription Diet® d/d® Canine Skin Support Duck Formula, moist	4,932	1,248	593
Hill's® Prescription Diet® d/d® Canine Skin Support Potato & Salmon Formula, dry	4,302	2,154	1,516
Hill's® Prescription Diet® d/d® Canine Skin Support Salmon Formula, moist	5,148	4,350	2,673
Hill's® Prescription Diet® d/d® Canine Skin Support Potato & Venison Formula, dry	5,238	1,140	499
Hill's® Prescription Diet® d/d® Canine Skin Support Venison Formula, moist	4,950	1,098	440
Hill's® Prescription Diet® i/d® Low Fat GI Restore Canine, dry	3,426	1,500	9
Hill's® Prescription Diet® d/d® Canine Skin Support Rice & Egg Formula, dry	5,028	1,134	637
Hill's® Prescription Diet® j/d® Canine Mobility, moist	4,104	6,066	2,284
Hill's® Prescription Diet® j/d® Canine Mobility, dry	4,284	5,712	1,234
Hill's® Prescription Diet® n/d® Canine, moist	2,724	10,764	8,426
Hill's® Prescription Diet® z/d® ULTRA Allergen Free Canine, moist	6,174	762	114
Hill's® Prescription Diet® z/d® ULTRA Allergen Free Canine, dry	6,528	792	75
Hill's® Science Diet® Adult Advanced Fitness Original Dog, dry	6,924	900	20
Hill's® Science Diet® Adult Lamb Meal & Rice Recipe Dog, dry	4,968	1,008	16
Hill's® Science Diet® Mature Adult Active Longevity™ Original , dry	5,754	870	8
Hill's® Science Diet® Adult Light Dog, dry	5,778	984	6
Hill's® Science Diet® Adult Sensitive Skin Canine, dry	7,266	2,184	58
Hill's® Science Diet® Adult Healthy Mobility™ Canine, dry	5,466	2,106	876
Hill's® Science Diet® Puppy Healthy Development Original, dry	5,706	1,668	682
Hill's® Science Diet® Puppy Large Breed, dry	3,972	2,016	630
Hill's® Ideal Balance™ Grain Free Natural Salmon & Potato Recipe, Adult, Dry	4,776	1,476	826
Hill's® Science Diet® Senior 11+, Small & Toy Breed Age Defying, dry	5,256	1,938	779
Hill's® Science Diet® Puppy, Small & Toy Breed, dry	6,114	1,824	734

Foods (continued)*	Total omega-6 FA (mg)	Total omega-3 FA (mg)	EPA + DHA (mg)
Hill's® Science Diet® Healthy Advantage™ Adult Canine, dry	5,706	744	50
Hill's® Science Diet® Healthy Advantage™ Puppy, dry	6,762	2,448	738
Iams® ProActive Health Chunks®, dry	5,124	360	33
Eukanuba® Puppy Growth Formula	5,736	858	453
Eukanuba® Adult Weight Control Small Breed, dry	4,386	528	N/A
Eukanuba® Healthy Joints, Canine, dry	4,884	684	N/A
Eukanuba® Senior Maintenance Dog Food, dry	4,500	600	267
Iams Veterinary Formulas® Skin & Coat Plus Response™ FP, dry	N/A	N/A	N/A
Iams Veterinary Formulas® Skin & Coat Plus Response™ FP, moist	N/A	N/A	N/A
Purina Veterinary Diets® DRM Dermatologic Management® Canine Formula, dry	1,668	1,668	N/A
Purina Veterinary Diets® JM Joint Mobility® Canine Formula, dry	2,670	1,512	N/A
Royal Canin Veterinary Diet® Hypoallergenic Selected Protein Adult PD Formula, Canine, dry	2,802	798	N/A
Royal Canin Veterinary Diet® Hypoallergenic Selected Protein Adult PV Formula, Canine, dry	1,728	714	324
Royal Canin Veterinary Diet® Hypoallergenic Selected Protein Adult PW Large Breed Formula, Canine, dry	2,046	918	480
Royal Canin Veterinary Diet® Hypoallergenic Selected Protein Adult PR Formula, Canine, moist	6,528	1,044	N/A
Royal Canin Veterinary Diet® Hypoallergenic Selected Protein Moderate Calorie Adult PW, Canine, moist	5,664	1,404	N/A
Royal Canin Veterinary Diet® Skin Support SS™, Canine, dry	1,380	N/A	3,000
Royal Canin Veterinary Diet® Hypoallergenic Hydrolyzed Protein Adult HP, Canine, dry	7,050	1,128	444
Royal Canin Veterinary Diet Canine Hypoallergenic Hydrolyzed Protein Moderate Calorie, dry	5,442	1,170	559
Royal Canin Veterinary Diet Canine Hypoallergenic Hydrolyzed Protein Small Breed, dry	6,498	1,194	540
Royal Canin Veterinary Diet® Mobility Support JS 23, dry	4,062	1,314	870
Royal Canin Veterinary Diet® Mobility Support JS 24 Large Breed, dry	3,954	1,848	1,297
Natural Choice Senior 7+ Chicken, Whole Brown Rice & Oatmeal Formula, dry	5,658	600	207
Natural Choice Venison & Whole Brown Rice Formula, dry	5,700	426	17
Natura® California Natural Herring & Sweet Potato Formula Adult Canine, dry	1,224	N/A	2,436
Old Mother Hubbard® Wellness Core Grain Free Original Formula Adult Dog Food, dry	4,194	648	98

Table 2.

The total essential fatty acid (FA) intake for a 10-kg dog receiving one of the selected supplements.

Supplements*	Amount	Total omega-6 FA (mg)	Total omega-3 FA (mg)	EPA + DHA (mg)
Dechra EicosaCaps™ Omega 3&6 / GlenHaven EFA2N	1 capsule	291	N/A	26.3
Dechra EicosaDerm Omega 3 / GlenHaven EFA1N	2 ml	N/A	N/A	600
Free Form Snip Tips Small Dogs & Cats	1 capsule	N/A	N/A	434
Nordic Naturals® Omega-3 Pet™ Medium to Large Breed Dog	2.5 ml	N/A	713	552
Nordic Naturals® Omega-3 Pet™ Soft Gels	1 soft gel	N/A	310	240
Nordic Naturals® Pet Cod Liver Oil Medium to Large Breed Dogs	2.5 ml	32	575	437
NutraMax® Welactin® Canine Liquid	6 ml	N/A	1,450	1,250
NutraMax® Welactin® Canine Softgels	1 softgel	N/A	300	255
Solgeval Derma-3® Small Breeds	1 softgel	N/A	N/A	183
Solgeval Derma-3® Liquid	1 pump	N/A	N/A	300
Solgeval Derma-3® Free Form Liquid	1 pump	N/A	N/A	264
Solgeval Actis® Omega-Dog	2 ml	152	N/A	450
Vedco NutriVed™ O.F.A. Granules	1 scoop	539	127	87
Vedco NutriVed™ O.F.A. Liquid	4 ml	1,764	312	64
Vétoquinol AllerG-3™ Small Breeds	1 softgel	N/A	N/A	183
Vétoquinol AllerG-3™ Liquid	1 pump	N/A	N/A	300
Virbac Omegaderm® Cats & Small Dogs	1 packet	1,486	N/A	299
Virbac Omegaderm® Medium & Large Dogs	1 packet	2,973	N/A	598
Virbac Allerderm EFA-Caps®	1 capsule	48	N/A	130
Virbac Allerderm EFA-Caps® HP	1 capsule	88	N/A	200

N/A = not available

*Manufacturer's published values or analytical values available in May 2013.