# FLEA CONTROL A WHOLE NEW WORLD

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Fleas are a common and important external parasite of dogs and cats. The most common flea species infesting dogs and cats in North America and in many areas of the world is *Ctenocephalides felis felis*, the cat flea.[1,2] Cat fleas are voracious blood feeders consuming up to 15 times their body weight in blood daily and female fleas use that blood to produce up to twice their bodyweight in eggs daily.[1-3] So it does not take long before a flea infestation can get completely out of hand. These fleas can cause allergic skin disease (FAD), produce anemia through their blood feeding activities, transmit tapeworms and bacterial pathogens.[1,2] It is therefore important for the health and well-being of our pets that we control these harmful parasites.

It must be understood that it often takes several weeks to eliminate a flea infestation. That is because all flea infestations of dogs and cats originated from a flea-infested environment and it takes time to eradicate the immature stages living in the carpet or outdoors. Once these fleas jump on a dog or cat they will feed, mate and female fleas will begin laying eggs within 24 hours.[1-3] Then within a few days each female flea will be producing 40 – 50 eggs per day, with hundreds and potentially thousands of eggs being deposited into the home or yard.[3] The in-home and potentially outdoor premises rapidly becomes infested with egg, larvae, pupae and emerging adult fleas, often referred to as the flea biomass.

Historically veterinarians and pet owner treated the premises directly through the application of insecticides and insect growth regulators into the carpet and yard.[4] This was done in an attempt to kill emerging fleas and prevent development of eggs & larvae. Premises treatments were considered necessary to break the flea lifecycle. The primary reason that premises treatments were necessary was that prior to the mid-1990s topical products (dips, sprays, collars, powders etc..) had no substantial duration of residual activity.[5] Premises treatments were difficult to conduct, time consuming, expensive, environmentally unfriendly and often ineffective.

However, with modern topical and systemic residual flea products, control of infestations in the premises is now achieved by preventing flea reproduction.[6,7] Reproduction is halted either through the use of highly effective residual adulticides that kill most newly acquired fleas before they begin reproduction (killing fleas within 24 hours after jumping on treated pet) or through the use of insect growth regulators (or insecticides) with ovicidal activity to kill any eggs that might be produced.[6,7] Simply if you cannot reproduce as a species you go extinct in the local premises.

When focusing on residual adulticides it is the residual speed of kill of a product that is of utmost importance.[8] Residual speed of kill relates to how rapidly a product kills newly acquired fleas at some time point (days or weeks) after administration. If a product can kill newly acquired fleas fast enough it can prevent flea reproduction and markedly reduce the amount of salivary proteins injected by the fleas, thus minimizing or eliminate FAD symptoms.[5,8]

Although modern residual flea adulticides provide prolonged adulticidal activity, it has been determined that efficacy and speed of kill of most products will decrease over time following

administration.[5,9-12] As the residual efficacy decreases and fleas are not killed within 24 hours, female fleas can live long enough to produce eggs.[5,9,10] Therefore, it is important to use a product that is effective enough to suppress reproduction between scheduled reapplications. Residual efficacy can also be affected by under-dosing by clients, bathing or swimming that can reduce insecticide levels of topical formulations, poor G.I. absorption with oral products and natural variability in susceptibility or outright resistance.[13]

Proper administration of effective residual flea products to all dogs and cats means no more fleas reproducing and no more eggs dropping into the environment. Therefore, within 2 to 7 days, eggs that were previously deposited have developed into larvae, within 1 to 2 weeks the larvae have now developed into pupae, and 1 to 4 weeks later those pupae are now adult fleas. As these fleas emerge and jump on treated pets they are hopefully being killed by the flea product. Therefore within 3 to 8 weeks or occasionally as long as 3 months, all the adult fleas and immature life stage biomass should be gone.[6,7]

How bad a flea infestation becomes and how rapidly a flea infestation is eliminated is not only affected by the product used, but also by environmental conditions. Relative humidity in the microenvironment is primary determining factor in flea populations. This is because flea larvae are weak link in the life-cycle chain and are very susceptible to heat and desiccation.[1,2] In addition, the rate of flea development and therefore how rapidly the biomass is exhausted can be very temperature dependent.[1,2]

If a flea infestation continues beyond the expected 3 to 8 weeks (or longer), a commonly encountered problem is an untreated flea host in the home or maybe the product itself is not stopping reproduction. An interesting assessment of product performance entails the evaluation of gender structure of newly emerged fleas in these homes.[14] While most insect species exhibit protrandry (males tend to emerge before females), *C. felis* belong to a much smaller group that exhibits protogny (females tend to develop before males).[15] The first fleas to emerge from a cohort of eggs are females, followed by both males and females and then lastly almost exclusively males. It has been demonstrated that if flea reproduction is inhibited by insecticidal treatments administered to a pet, then a gender shift in premises flea population takes place overtime from a female dominated population towards a more male dominated population.[14] In a recent field investigation, 60% of the unfed fleas collected in premises light traps on day 0 were female, whereas by 28-30 days following treatment with oral afoxolaner, 78% of the unfed fleas collected in the traps were male. This was a clear and rapid gender shift, indicative of cessation of flea reproduction.

Another issue that must be expected in a small number of homes is that the flea infestation may get worse before it gets better.[7] These cases are referred to as “Red-line homes”. By definition a red-line home is a house were premises trap flea counts increase > 20% over day 0 trap counts within 1 to 4 weeks post-treatment.[14] These surges in emerging fleas occurs because of a large preexisting biomass in the indoor premises. Such surges in emerging fleas and resulting increase in flea numbers on household pets can give the perception of product failure. Often extensive and frequent mechanical intervention (vacuuming, washing pet bedding and area and throw rugs, etc..) and even application of insecticides into the premises may be necessary in these cases.

Fluralaner, afoxolaner, lotilaner and sarolaner are recently introduced oral flea and tick adulticides in the isoxazoline class of drugs. These drugs work as GABA-Chloride antagonists causing over excitation of the insect and arachnid nervous system and rapid ectoparasite death.[16-

[18] These compounds have demonstrated rapid and persistent efficacy against fleas and multiple species of ticks].

Following the administration of a fluralaner chew, efficacy has been maintained against fleas in both field and laboratory studies for 12 weeks against fleas. A single dose of a fluralaner chew killed newly acquired female fleas rapidly enough that no eggs were laid after repeated infestations for 120 days.[19] In field studies evaluating dogs not managed with associated medications, afoxolaner, fluralaner and sarolaner not only managed flea infestations, but also managed clinical signs associated with FAD and pruritus.[20,21]

Following administration of fluralaner or afoxolaner, flea populations on pets were reduced by 99.0% and 99.3%, respectively within 7 days.[20] Flea populations on the fluralaner treated dogs were 0 (100% efficacy) on days 54-60 and 82-86 after the administration of a single dose on day 0. Administration of 3 monthly doses of afoxolaner reduced flea populations by 100% on days 82-86. Flea numbers in indoor-premises were markedly reduced in both treatment groups by days 82-86, with 100% and 98.9% reductions in flea trap counts in the fluralaner and afoxolaner treatment groups, respectively. Marked improvement was observed in FAD lesion scoring, Atopic Dermatitis lesions scoring (CADESI-4) and pruritus scores with both formulations.

Spinosad first became available as an oral treatment for the control of flea infestations on dogs in late 2007. A multi-clinic, investigator-blinded study was undertaken in client-owned dogs to investigate and compare the flea control provided by 3 consecutive monthly treatments of oral spinosad (SPN) or fipronil/(s)—methoprene topical (FSM) spot-on.[22] The first household dog meeting enrollment criteria and with at least 10 fleas (whole-body flea count) served as the index dog in a household against which primary objectives were set. Allocation was based on pruritus scores at the enrollment visit and on single or multiple pet household. Index pets were randomized to treatment with either SPN or FSM, dispensed on day 0 for at-home administration by owners. All other household dogs and cats, maximum 4 pets per household, were dispensed the same treatment as the index dog (spinetoram was dispensed for cats in SPN households). Subsequent treatments were dispensed when index dogs were returned for whole-body flea counts and pruritus-scoring at visits on days 30 and 60, with final assessments on day 90 (± 5 days on each occasion). Primary endpoints were the number of flea-free index dogs in each group one month after the final treatment, the reduction in owner-reported pruritus, and the reduction from baseline in mean flea counts. One hundred twenty-eight index dogs were enrolled (65 in the SPN arm; 63 in the FSM arm) at 10 clinics in Florida (6), North Carolina (2), Louisiana (1), and Texas (1). On day 0, geometric mean flea counts were 57.7 (range: 10-1,469) and 44.8 (10-717) for the SPN and FSM groups, respectively. On Day 90, 55 of 58 (95%) and 21 of 55 (38%) index dogs completing the study were flea-free in SPN and FSM groups, respectively; mean SPN pruritus scores declined to 0.92 (6.67 on day 0), and to 3.83 (6.33 on day 0) for FSM; geometric mean flea counts (% control) were 0.08 (99.9%) and 5.19 (88.4%), for SPN and FSM groups, respectively.

Flea allergy dermatitis or flea bite hypersensitivity is the most common dermatologic disease of domestic dogs. Cats are also afflicted with FAD, which is one of the major causes of feline miliary dermatitis. Historically, it has been said that one flea is all that is necessary to maintain the clinical signs of FAD and therefore total flea eradication is necessary. Newer adulticides such as fipronil, imidacloprid, metaflumizone, nitenpyram, selamectin, and spinosad have had a positive clinical effect on dogs and cats with FAD. However, data on flea biology and the effect of these products on flea feeding bring into question the once perceived dogma of the 'one flea bite'.[5] Adult cat fleas begin feeding almost immediately once they find a host, with many fleas feeding within minutes. In one study, 25–60% of fleas were blood fed within 5 min and in another study the

volume of blood consumed by fleas was quantifiable within 5 min Feeding is so rapid that partially digested blood can be defaecated in as little as 2–6 min after fleas acquire a host. After rapid transit through the flea, the excreted blood dries within minutes into reddish black faecal pellets or long tubular coils (flea dirt). While initiation of feeding is rapid, daily blood consumption is voracious. Female cat fleas can consume up to ten times their body weight in blood the very first day. They are on the host and peak consumption occurs within a few days at 15 times their body weight (13.6 lL) daily. With such rapid and voracious blood feeding, is it reasonable to assume that residual insecticides can truly prevent flea biting and feeding?

A study was conducted at Kansas State University, Manhattan KS, USA to evaluate the residual activity of fipronil and imidacloprid on egg production and blood feeding. There were two objectives to these studies 1) to evaluate if these compounds will kill newly acquired fleas prior to them feeding and 2) to determine how long these compounds will prevent viable egg production after application. In the first experiment six cats were treated with either a fipronil spray (0.29% w/w) formulation, an imidacloprid spot-on (9.1% w/w) formulation at labeled rates or were left as untreated controls. Surprisingly when 100 *Ctenocephalides felis* were placed on cats 6 days after treatment with imidacloprid or fipronil, the percent of fleas that fed and consumed blood was 89 and 92%, respectively.[5] While the adulticidal efficacy of the products was 100%, neither product killed fleas before the vast majority could bite, feed and consume at least some quantity of blood.

In another study conducted in Europe it was determined that the topical application of imidacloprid or fipronil to cats did not prevent fleas from biting and feeding. Unconfined fleas placed on cats treated with imidacloprid and fipronil had reductions in the percent of fleas blood feeding of 49.6 and 39.5%, respectively, on day seven; while reductions in percent of fleas feeding on day 28 was 0 and 3.4%, respectively. While topical applications of dichlorvos/fenitrothion or permethrin did reduce the percent of fleas feeding by greater than 80%, these compounds also did not completely prevent flea bites or feeding. The data on percent of fleas feeding on imidacloprid and fipronil treated cats in the European study differ from the data in the Kansas State University Study. This likely occurred due to the known reduced susceptibility of the KSU flea strain to imidacloprid and fipronil.

Another study conducted at KSU using dogs evaluated the ability of a 65% permethrin spot-on, a 13.8% fenthion spot-on and an 8% Chlorpyriphos collar to reduce blood feeding by fleas.[5] At two weeks post-treatment evaluation of the blood fed status of fleas revealed that an average of 66.7% of fleas from permethrin treated dogs had fed. Fleas from chlorpyrifos collared dogs and fenthion treated dogs averaged 53.0 and 37% blood fed status, respectively. In this study the percent of fleas feeding on organophosphate and pyrethroid treated dogs was considerably higher than in the study conducted in Europe. It was later determined that the flea strain used in the KSU study was tolerant/resistant to certain organophosphates and pyrethroids.

Additional research has now been conducted to quantify the amount of blood consumed by fleas on insecticide treated cats.[23] In this study fleas were confined for 24 hours in confinement feeding chambers attached to treated cats once a week for four 4 weeks. Confinement feeding chambers were used so that fleas and their feces could be collected for quantification and analysis. Cats were treated on day 0 with fipronil, imidacloprid, selamectin at label rates or were left untreated. In addition, another group of cats was administered nitenpyram one hour prior to each weekly infestations. After each 24-hour infestation fleas and feces were removed, microcell removed and the quantity of blood consumed and excreted was determined spectrophotometrically using the Drabkin's Reagent Method. Fleas placed on imidacloprid and fipronil-treated cats seven days post-treatment had reductions in blood consumption of 90.78 and 69.77%, respectively.

Whereas, at 14 days post-treatment fleas on fipronil-treated cats had no statistically significant reduction in blood consumption as compared to fleas on untreated controls while fleas on imidacloprid-treated cats consumed 55.73% less blood as fleas on controls. Then by three weeks post-treatment fleas on imidacloprid-treated cats had no statistically significant reduction in blood consumption as compared to fleas on untreated controls. Of particular interest was that fleas placed on cats treated orally with nitenpyram never consumed more than 1.63% (98.37% reduction) as much blood as fleas placed on control cats. Topically applied, but transdermally absorbed selamectin also had a pronounced effect upon blood consumption of fleas. Even on day 28 post-treatment there was an 88.9% reduction in blood consumption as compared to fleas on untreated controls.

As stated previously compounds such as fipronil, imidacloprid, metaflumizone, and selamectin and spinosad have had a major impact on reducing the occurrence of FAD. However, the data from the qualitative and quantitative studies demonstrates that these compounds do not stop flea bites nor completely stop flea feeding. Therefore, it appears their role in managing FAD is likely related to a decrease in prolonged flea feeding and thereby the amount of salivary protein delivered to the pet and in the long term reducing flea numbers. It is this author's opinion that FAD is related to the degree of hypersensitivity of an individual animal, the numbers of fleas feeding and amount of antigen injected. This certainly brings into question the old dogma of a single flea bite eliciting an FAD reaction, at least in the majority of clinically afflicted animals. If a single flea bite was responsible, it appears no flea product would provide much relief, at least not until the flea population was eradicated. Also of importance to note is that regardless rather as to whether an insecticide works topically or systemically may be irrelevant in the management of fleas or FAD, since in the one study the systemically active compounds had a pronounced effect on blood feeding.[5]

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