

# Control of flea populations in a simulated home environment model using lufenuron, imidacloprid or fipronil

D. E. JACOBS, M. J. HUTCHINSON and W. G. RYAN\*

Department of Pathology and Infectious Diseases, The Royal Veterinary College (University of London) and \*Merial Animal Health, Iselin, NJ, U.S.A.

**Abstract.** Control strategies were evaluated over a 6-month period in a home simulation model comprising a series of similar carpeted pens, housing matched groups of six cats, in which the life-cycle of the flea *Ctenocephalides felis felis* Bouché (Siphonaptera: Pulicidae) had been established. Additional adult fleas were placed on the cats at intervals to mimic acquisition of extraneous fleas from outside the home. Treatment strategies included a single subcutaneous deposition of injectable lufenuron supported by initial treatments with a short-acting insecticidal spray, or monthly topical applications of imidacloprid or fipronil. An untreated control group indicated that conditions were suitable for flea replication and development. Controls had to be combed on 18 occasions to remove excessive flea burdens and two developed allergic reactions. Lufenuron cats were combed once and required two insecticidal treatments in the first month to achieve control. Even so, small flea burdens were constantly present thereafter. Imidacloprid and fipronil treatments appeared to give virtually complete control throughout. Single fleas were found on imidacloprid cats on two occasions, whereas none were recovered from fipronil cats at any time after the first treatment. Tracer cats were used to monitor re-infestation rates at the end of the trial period. Small numbers of host-seeking fleas were demonstrated in all treatment pens, indicating that total eradication had not been accomplished. It is concluded that the home environment simulation model incorporating tracer animals could provide a powerful tool for studying flea population dynamics under controlled conditions but improved techniques are needed for quantifying other off-host life-cycle stages.

**Key words.** *Ctenocephalides*, cat flea, control, dichlorvos/fenitrothion, fipronil, imidacloprid, lufenuron.

## Introduction

Flea infestations continue to be an almost ubiquitous problem in dogs and cats. Fortunately, considerable advances have been made in flea control methodology in recent years (Rust & Dryden, 1997). In particular, topically applied insecticides are now available which have prolonged activity on the animal. For example, spot-on formulations of fipronil and imidacloprid each provide at least 4 weeks' protection from reinfestation

(Cunningham *et al.*, 1997; Jacobs *et al.*, 1997a). Carefully timed treatments with these products can therefore prevent continued contamination of the domestic environment by ensuring that most, if not all, newly acquired fleas are killed before oviposition starts (Carlotti & Jacobs, 2000). In experimental models, monthly treatments of cats with fipronil or imidacloprid gave apparently complete control of flea populations even when small numbers of adults were placed on the animals to mimic infestations acquired outside the home (Jacobs *et al.*, 1997b; Hutchinson *et al.*, 1998). An alternative approach to environmental control is to use an insect growth regulator (IGR) to ensure that any flea eggs deposited by pets within the home are infertile. Lufenuron is a systemic IGR that

Correspondence: Professor Dennis Jacobs, Department of Pathology and Infectious Diseases, The Royal Veterinary College, North Mymms, Hatfield, Herts AL9 7TA, U.K. E-mail: djacobs@rvc.ac.uk

will induce infertility in fleas feeding on cats for up to 6 months following administration by subcutaneous injection (Franc & Cadiergues, 1997). As lufenuron is not adulticidal, concurrent insecticidal treatments may be necessary to eliminate resident fleas in the early stages of a control programme. Both methods of depleting the reservoir of off-host life-cycle stages offer an attractive alternative to the application of relatively large quantities of biologically active chemicals directly into the domestic environment.

Flea population dynamics within a household are influenced by a number of uncontrollable variables and, consequently, experimental models have been developed for evaluating intervention strategies with both dogs (Blagburn *et al.*, 1995) and cats (Fisher *et al.*, 1996). In these, matched groups of animals are kept in separate but identical carpeted pens in a common airspace. The flea life-cycle is established within each pen, with the carpets providing conditions suitable for the development of the off-host stages. The effectiveness of each control programme is assessed by comparing the mean adult flea burdens of groups of matched animals in treatment and control pens. Although this comparison provides a good assessment of the overall level of protection, it gives little indication of the challenge to which animals are exposed at any point in time, as newly acquired fleas are likely to succumb to insecticidal residues before they can be counted.

The present study had two objectives. The first was to compare three intervention strategies for controlling fleas on cats and the second was to evaluate the potential use of 'tracer' cats for monitoring environmental challenge in home simulation studies. 'Tracers' are parasite-free animals that are used in addition to the principal test animals for the purpose of measuring the rate of acquisition of parasites during a defined time period. They are commonly used in field experiments evaluating parasite control strategies in farm animals (see, for example, Jacobs *et al.*, 1995) but have not previously been employed for the current purpose.

## Materials and Methods

An overview of the experimental design is provided in Table 1. Day 0 is defined as the first treatment date. Twenty-four adult Domestic Short Haired (DSH) cats (four males and 20 females) were assigned to blocks of four on the basis of sex and flea susceptibility. The latter was determined by placing 40 unfed adult fleas on each cat on day -45 and counting the numbers that had established the following day, when surviving fleas were removed and destroyed. Cats within each block were allocated randomly to four groups. Each group was housed in a separate carpeted pen in the same room of a controlled environment animal house complying with local animal welfare standards. The pens were separated by solid walls and strict precautions were taken to prevent transfer of fleas or chemical traces between groups. Ambient conditions were mostly around 21–22°C and 40–60% relative humidity.

Group 1 was kept as an untreated control. Cats in Group 2 each received lufenuron (Program Injectable Suspension for Cats, Novartis) by subcutaneous injection on day 0. Each cat in

this group was, in addition, sprayed with a dichlorvos/fenitrothion preparation (Nuvan Top, Novartis) on the same day. Groups 3 and 4 were given imidacloprid (Advantage for Cats, Bayer) or fipronil (Frontline Spot On Cats, Merial), respectively, as spot-on topical applications administered six times at monthly intervals (on the 23rd day of each month). All treatments contained 10% active ingredient and were applied according to label directions using the appropriate pre-packaged applicator for the weight of each animal (i.e. lufenuron and imidacloprid: cats <4 kg 0.4 mL, >4 kg 0.8 mL; fipronil: 0.5 mL per cat irrespective of weight).

To establish the flea life-cycle within the pens, each cat was initially infested with 40 cat fleas (*Ctenocephalides felis felis* Bouché, RVC03 strain) on day -40. To simulate the roaming cat bringing extraneously acquired fleas into a household, additional burdens of 10 fleas were applied twice monthly (12 and 5 days before each treatment date) to the imidacloprid and fipronil groups from day 18 and to the lufenuron group from day 25. Fleas were counted by a standardized combing procedure (Jacobs *et al.*, 1997b) on days -26, -19, -14, -1 and monthly from day 29. On each occasion, all the fleas up to a maximum of 30 were replaced on the cat of origin. In order to maintain flea burdens within acceptable limits, additional ('welfare') combings were conducted if a group displayed exaggerated grooming activity. This part of the study was completed on day 180 when the principal test cats were removed from their pens.

A further 12 flea-free untreated DSH cats were allocated as 'tracers' to the four pens on the basis of their flea susceptibility measured, as before, on days 174/175. They were placed in the pens on day 180 and flea counts were performed on days 181 and 182.

The number of live fleas recovered from each animal on each day was transformed to the natural logarithm of (count + 1) for calculation of geometric means. Direct comparisons between groups were not possible because combing on welfare grounds had reduced flea numbers in some groups.

## Results

Mean flea burdens on the cats in each group had increased from 4.0–6.6 on day -14 to 11.7–37.6 by day -1. The untreated control cats required welfare combings on 18 occasions (on days 2, 13, 16, 18, 19, 22, 49, 51, 54, 57, 124, 128, 132, 135, 139, 142, 146 and 159). Despite the frequent removal of fleas from this group, the mean flea burden remained between 7.9 and 45.7 at each scheduled examination (Table 2) with a maximum of 87.7 recorded on day 18. Two control cats developed signs of flea allergic dermatitis and were replaced by substitutes on days 19 and 22, respectively.

Cats in the lufenuron group were seen to be scratching during the first 3 weeks following treatment and a welfare combing was required on day 18 when a mean count of 78.2 was recorded. Consequently, a second, unscheduled, application of dichlorvos/fenitrothion was made on day 19. Thereafter, means of 5.0–6.9 fleas were recovered at each subsequent scheduled examination (Table 2). With the

**Table 1.** Overview of experimental design.

Number of animals	Trial cats:	Four groups of six
	Tracer cats:	Four groups of three
Allocation procedure	Day -45:	All trial cats infested with 40 fleas
	Day -44:	Fleas on cats counted and destroyed; flea counts used to allocate trial cats to groups; groups assigned to carpeted pens
Establishment of flea life-cycle in pens	Day -40:	All trial cats infested with 40 fleas; flea eggs allowed to accumulate in carpets
Treatments	Control:	No treatment given
	Lufenuron:	Single injection on day 0 plus dichlorvos/fenitrothion spray day 0 and when needed
	Imidacloprid:	Spot-on treatment day 0 and monthly thereafter
	Fipronil:	Spot-on treatment day 0 and monthly thereafter
Simulation of extraneous re-infestation		10 fleas applied monthly to each trial cat in treated groups 12 and 5 days prior to each scheduled treatment date (starting day 18 for fipronil and imidacloprid groups; day 25 for lufenuron group)
Scheduled flea counts		Trial cats were combed on days -14, -1, 29, 60, 90, 121, 152, 180 All fleas up to a maximum of 30 were replaced on cat of origin
Welfare flea combings		Groups were combed when excessive grooming or other clinical signs became evident; all fleas to maximum of 30 replaced
Tracer cats	Day 174:	Each tracer cat infested with 40 fleas
	Day 175:	Fleas counted and destroyed; flea counts used for allocation to groups
	Day 180:	Trial cats removed from pens; flea-free tracer cats put into pens
	Days 181/182:	Flea counts performed on tracer cats

**Table 2.** Geometric mean flea counts and range (in brackets) for untreated controls and groups of cats treated on Day 0 with injectable lufenuron and with topical dichlorvos/fenitrothion on days 0 and 19, or with imidacloprid or fipronil on day 0 and at monthly intervals.

Day of trial	Control	Lufenuron and dichlorvos/fenitrothion	Imidacloprid	Fipronil
-14	4.0 (0-24)	4.6 (1-11)	4.5 (1-33)	6.6 (0-21)
-1	35.1 (14-67)	37.6 (26-55)	11.7 (5-36)	30.2 (13-43)
29	45.7 (37-68) <sup>a</sup>	5.4 (3-14) <sup>c</sup>	0.1 (0-1)	0
60	17.7 (7-38) <sup>b</sup>	5.0 (0-26)	0	0
90	7.9 (3-16)	5.9 (1-19)	0	0
121	36.6 (20-60)	6.1 (1-20)	0	0
152	28.2 (12-45) <sup>c</sup>	6.9 (2-21)	0.1 (0-1)	0
180	9.8 (6-20) <sup>d</sup>	5.7 (1-17)	0	0

Superscripts denote number of welfare combings prior to that observation point: a=6; b=4; c=7; d=1; e=1.

exception of one cat on one occasion (day 60), all cats in this group had fleas at every scheduled examination, with individual counts throughout the post-treatment period ranging from 1 to 26. A count of 137 was recorded on day 18.

No fleas were found on any fipronil-treated cat after day 0 (Table 2). In the imidacloprid group, a single flea was recovered from one cat on two occasions (days 29 and 152).

No adverse reactions to any treatment were observed during the study.

Flea counts on tracer cats were similar for the three pens housing medicated cats, while tracers in the control pen

appeared to acquire greater numbers (Table 3). The group size was too small for statistical confirmation.

## Discussion

The *C. felis* life-cycle was established in each pen by infesting the cats with adult fleas and allowing the eggs they produced to accumulate and develop on the carpets. Initially, flea burdens were adequately controlled by the grooming behaviour of the cats (Hinkle *et al.*, 1998; Eckstein & Hart, 2000). By day -1,

**Table 3.** Individual flea counts (with geometric means in brackets) of tracer cats placed in pens that had been occupied by untreated controls or groups of cats treated on day 0 with injectable lufenuron and with topical dichlorvos/fenitrothion on days 0 and 19, or with imidacloprid or fipronil on day 0 and at monthly intervals.

Day of trial	Control	Lufenuron and dichlorvos/fenitrothion	Imidacloprid	Fipronil
181	4, 7, 10 (6.6)	0, 2, 5 (1.6)	0, 4, 7 (2.4)	1, 3, 6 (2.8)
182	3, 4, 5 (3.9)	0, 3, 3 (1.5)	0, 2, 2 (1.1)	0, 1, 2 (0.8)
181 + 182	(10.5)	(3.8)	(3.1)	(3.8)

however, host-seeking adults were emerging from pupae in the carpet in sufficient numbers to cause flea burdens on the cats to increase rapidly. The first treatments were therefore given at a stage in flea population development that, in the absence of overt flea allergy dermatitis, might be recognized as an impending problem by a pet owner. Repeated welfare combings were needed in the control group to keep infestations within limits acceptable on welfare grounds and two cats showing early signs of flea bite hypersensitivity were withdrawn from the trial. These results indicate that experimental conditions were suitable for the flea population to build up to massive levels if left unchecked.

In the lufenuron group, two insecticidal treatments (on days 0 and 19) were required to protect cats from the overt effects of continued re-infestation derived from flea eggs dropped prior to day 0. The dichlorvos/fenitrothion combination used in this study has good initial activity against an established flea burden but gives only partial protection from reinfestation thereafter. Fisher *et al.* (1993), for example, recorded 99% efficacy one day after treatment, falling to 46% at 8 days. After the second treatment, flea numbers stabilized at a tolerable level. It is not known what proportion of the flea burden during this period was derived from eggs that had hatched on the carpet or from the additional 'extraneous' adult fleas placed on the cats. Even though experimental conditions were favourable for flea development, monthly fipronil or imidacloprid treatments gave virtually complete control as measured by monthly combing of the cats. No welfare combings were required and no cats developed hypersensitivity reactions.

When fipronil- or imidacloprid-treated cats become re-infested, flea mortality commences within a few hours (Postal *et al.*, 1996; Everett *et al.*, 2000). The great majority of newly arrived fleas will therefore have succumbed before they can be detected by combing. This is especially true in home simulation models as observations are generally restricted to weekly, fortnightly or monthly intervals because flea counting is a labour-intensive activity (taking 10–15 min per cat in our protocols). Such data give useful information on the overall clinical protection afforded by a control strategy but provide only a crude indication of the influence of treatment on the numbers of off-host life-cycle stages. This study has shown that tracer cats can be used to provide additional information on re-infestation rates. Thus, at day 180, when zero counts were recorded from all the fipronil- and imidacloprid-treated

animals, the net re-infestation rate (i.e. the true number of newly arrived fleas less the number lost through grooming) was 0.5–0.6 fleas per cat per day for the three treatment groups and 1.8 per day for the controls. The control figure would presumably have been higher if the tracers had been used earlier in the study when higher flea burdens were accumulating on these cats. The use of tracer cats during a trial is, however, limited by the risk of fighting when new cats are introduced to an established social group and by the fact that maximum pen occupancy is determined by animal welfare regulations.

The origin of the small numbers of host-seeking fleas detected by tracers in the treatment pens between days 180 and 182 is unknown. They probably reflect delayed emergence from pupae already present in the carpet before day 0 (i.e. the pupal window, as described by Silverman & Rust, 1985). However, the possibility that occasional fleas on treated animals can succeed in producing small numbers of fertile eggs before succumbing to the effects of the insecticide or IGR cannot be excluded. Whatever the explanation, their demonstration emphasizes the difficulty in attaining complete eradication of a flea population and the need for a long-term approach to flea control.

Other methods for quantifying off-host life-cycle stages were attempted during the course of this study but gave inconsistent results. For example, samples were cut from the carpet at intervals and incubated. Adult fleas were recovered from most samples taken from the control pen throughout the trial, but only from those collected up to day 30 in the treated pens. The numbers of adults recovered, however, did not correlate with other observations, presumably because flea larvae are unlikely to be evenly or randomly distributed across the carpets. The 'white sock technique', in which the numbers of adult fleas jumping onto white fabric dragged across the floor are counted, proved to be too insensitive to be useful at the levels of infestation encountered in this study.

In conclusion, monthly treatments with fipronil or imidacloprid gave virtually complete protection against flea infestation under conditions that were highly favourable for flea development, even though small numbers of extraneous fleas were being added to the system at regular intervals. Under similar circumstances, injectable lufenuron supported by initial insecticidal treatments and a welfare combing gave adequate but incomplete longer term control, with small flea burdens

constantly present. The use of tracer cats demonstrated that total eradication of the flea population had not been achieved in any group 180 days after the start of the intervention strategies. The home environment simulation model incorporating tracer animals could provide a powerful tool for studying flea population dynamics under controlled conditions but improved techniques need to be devised for quantifying other off-host life-cycle stages.

## References

- Blagburn, B.L., Hendrix, C.M., Vaughan, J.L., Lindsay, D.S. & Barnett, S.H. (1995) Efficacy of lufenuron against developmental stages of fleas (*Ctenocephalides felis felis*) in dogs housed in simulated home environments. *American Journal of Veterinary Research*, **56**, 464–467.
- Carlotti, D.N. & Jacobs, D.E. (2000) Therapy, control and prevention of flea allergy dermatitis in dogs and cats. *Veterinary Dermatology*, **11**, 83–98.
- Cunningham, J., Everett, R., Hunter, J.S., McCall, J.W., McTier, T.L., Tanner, P. *et al.* (1997) Residual efficacy of Frontline Top Spot for the control of fleas and ticks in the dog. *Proceedings of the North American Veterinary Conference, Orlando, 11–15 January 1997*.
- Eckstein, R.A. & Hart, B.L. (2000) Grooming and control of fleas in cats. *Applied Animal Behaviour Science*, **68**, 141–150.
- Everett, R., Cunningham, J., Arther, R., Bledsoe, D.L. & Mencke, N. (2000) Comparative evaluation of speed of flea kill of Advantage (imidacloprid) and Revolution (selamectin) on dogs. *Compendium on Continuing Education for the Veterinary Surgeon*, **22** (4A) (Suppl.), 9–11.
- Fisher, M.A., Hutchinson, M.J., Jacobs, D.E. & Dick, I.G.C. (1993) Efficacy of fenthion against the flea, *Ctenocephalides felis*, on the cat. *Journal of Small Animal Practice*, **34**, 434–435.
- Fisher, M.A., Jacobs, D.E., Hutchinson, M.J. & Dick, I.G.C. (1996) Evaluation of flea control programmes for cats using fenthion and lufenuron. *Veterinary Record*, **136**, 386–389.
- Franc, M. & Cadiegues, M.C. (1997) Use of injectable lufenuron for treatment of infestations of *Ctenocephalides felis* in cats. *American Journal of Veterinary Research*, **58**, 140–142.
- Hinkle, N.C., Koehler, P.G. & Patterson, R.S. (1998) Host grooming efficiency for regulation of cat flea (Siphonaptera: Pulicidae) populations. *Journal of Medical Entomology*, **35**, 266–269.
- Hutchinson, M.J., Jacobs, D.E., Fox, M.T., Jeannin, Ph. & Postal, J.-M. (1998) Evaluation of flea control strategies using fipronil on cats in a controlled simulated home environment. *Veterinary Record*, **142**, 356–357.
- Jacobs, D.E., Fisher, M.A., Hutchinson, M.J., Bartram, D.J. & Veys, P. (1995) An evaluation of abamectin given at turnout and six weeks after turnout for the control of nematode infections in calves. *Veterinary Record*, **136**, 386–389.
- Jacobs, D.E., Hutchinson, M.J., Fox, M.T. & Krieger, K.J. (1997b) Comparison of flea control strategies using imidacloprid or lufenuron on cats in a controlled simulated home environment. *American Journal of Veterinary Research*, **58**, 1260–1262.
- Jacobs, D.E., Hutchinson, M.J. & Krieger, K.J. (1997a) Duration of activity of imidacloprid, a novel adulticide for flea control, against *Ctenocephalides felis* on cats. *Veterinary Record*, **140**, 259–60.
- Postal, J.M., Le Nain, S., Fillon, F. & Longo, F. (1996) Efficacy of a 10% fipronil spot-on formulation against cat flea infestations (*Ctenocephalides felis*) in cats. *Proceedings of the British Dermatology Group Satellite Meeting, British Small Animal Veterinary Association Congress, Birmingham, U.K., April, 1996*, 69.
- Rust, M.K. & Dryden, M.W. (1997) The biology, ecology, and management of the cat flea. *Annual Review of Entomology*, **42**, 451–473.
- Silverman, J. & Rust, M.K. (1985) Extended longevity of the pre-emerged adult cat flea (Siphonaptera: Pulicidae) and factors stimulating emergence from the pupal cocoon. *Annals of the Entomological Society of America*, **78**, 763–768.

Accepted 21 September 2000