Efficacy of Indoor Residual Spraying Using Lambda-Cyhalothrin for Controlling Nontarget Vector Fleas (Siphonaptera) on Commensal Rats in a Plague Endemic Region of Northwestern Uganda

JEFF N. BORCHERT,[1,2] REBECCA J. EISEN,[1] LINDA A. ATIKU,[3] MARK J. DELOREY,[1] JOSEPH T. MPANGA,[3] NACKSON BABI,[3] RUSSELL E. ENSCORE,[1] AND KENNETH L. GAGE[1]

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ABSTRACT Over the past two decades, the majority of human plague cases have been reported from areas in Africa, including Uganda. In an effort to develop affordable plague control methods within an integrated vector control framework, we evaluated the efficacy of indoor residual spraying (IRS) techniques commonly used for mosquito control for controlling fleas on hut-dwelling commensal rodents in a plague-endemic region of Uganda. We evaluated both the standard IRS spraying (walls and ceiling) and a modified IRS technique that included insecticide application on not only on walls and ceiling but also a portion of the floor of each treated hut. Our study demonstrated that both the standard and modified IRS applications were effective at significantly reducing the flea burden and flea infestation of commensal rodents for up to 100 d after application, suggesting that IRS could potentially provide simultaneous control of mosquito and fleaborne diseases.

KEY WORDS indoor residual spray, *Rattus rattus*, plague, flea, lambda-cyhalothrin

Plague is a severe, rodent-associated bacterial disease that is transmitted primarily by fleas. The causative agent *Yersinia pestis* (Lehmann and Neumann) van Loghem is reported to infect numerous vertebrate species and is transmitted by at least 80 different flea species (Pollitzer 1954, Gage and Kosoy 2005). Although plague presents in several clinical manifestations, bubonic plague is the most common and is typically associated with rodents and their fleas (Gage 1998). Commensal rats (*Rattus* spp.) and their fleas are important sources of human infection in many regions of the world, especially in areas that have heavy rat infestations in human dwellings. Rodent incursions often occur in plague-endemic regions of Africa and are believed responsible for the majority of plague cases and plague-related deaths documented in recent decades (Gage 1998, WHO 2010). In Uganda, plague is endemic in the northwestern districts of Arua and Nebbi (Winters et al. 2009). From 1999 to 2008, these districts reported to the Ugandan Ministry of Health an average of ≈206 (range, 11–462) suspect human cases per year (Centers for Disease Control and Prevention [CDC], unpublished data).

Previous research in the Arua and Nebbi districts indicated that the black rat, *Rattus rattus* L., was the most frequently captured rodent in both peridomestic areas and inside huts and that the majority of fleas acquired from *R. rattus* were *Xenopsylla cheopis* Rothschild or *Xenopsylla brasiliensis* Baker (Orach 2003, Eisen et al. 2008, Amatre et al. 2009). These rat fleas are believed to play an important role in plague epizootics and epidemics (Hopkins 1949, Pollitzer 1954, Kilonzo et al. 1992) because they are efficient vectors of *Y. pestis* in laboratory studies (Pollitzer 1954, Gage and Kosoy 2005, Eisen et al. 2007), readily feed on humans when encountered (Verjbitski 1908, Kwochka 1987), and were implicated as vectors in past epidemiological studies (Gage 1998). Therefore, commensal rats and their fleas provide key targets for plague control interventions.

As malaria control campaigns were initiated after the Second World War and became widespread in many developing nations, some studies suggested the onset of indoor insecticide spraying for mosquito control contributed to the control of other vectorborne diseases, including plague and leishmaniasis (Patel et al. 1960, Akiev 1982, Elias et al. 1989). Although these anecdotes appear in past literature, the effectiveness of mosquito control spray campaigns against the vectors of *Y. pestis* was never evaluated. In Africa, malaria control campaigns using indoor residual spraying (IRS) began in the early 1940s and were concentrated mostly in the urban areas of political and economic importance (Kouznetsov 1977). Because of the subsequent failures to control malaria in Africa, tropical regions of the continent were mostly overlooked in the large-scale World Health Organization (WHO) global malaria eradication plans implemented between 1957 and 1969, with the exception of a few

[1] Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, 3150 Rampart Rd., Fort Collins, CO 80522.
[2] Corresponding author, e-mail: gqx1@cdc.gov.
[3] Uganda Virus Research Institute, P.O. Box 49, Plot 51–59 Nakiwongo, Entebbe, Uganda.

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selected regions including pilot programs in Uganda (1959–1963) (De Zulueta et al. 1961, 1964; Kouznetsov 1977, Hay et al. 2004; Enayati and Hemmingway 2010). These small-scale IRS programs were performed sporadically during the following decades, but their impacts on plague in Uganda were never evaluated (UMCP 2005). Currently, IRS is part of the Uganda Malaria Control Strategic Plan that is supported in part by the President's Malaria Initiative (PMI) (UMCP 2005, Verhaeghen et al. 2010) and covers only a portion of the country (six districts in north central Uganda), but not including the plague-endemic region of northwestern Uganda. Since 2007, these districts have consistently had >90% of their households sprayed with IRS by the PMI program (USAID 2010). Uganda historically used DDT, malathion, and lambda-cyhalothrin for mosquito control, with the latter also being used to control tsetse fly, *Glossina fuscipes fuscipes* Newstead, the primary regional vector of trypanosomiasis (Najera et al. 1967, Okoth et al. 1991, Bukirwa et al. 2009). In addition to its ability to kill the mosquito vectors of human malaria, lambda-cyalothrin is efficacious against fleas (Syngenta 2007).

Because no long-term and cost-effective method for plague control in rural African villages has been identified, our goal was to determine whether IRS methods using lambda-cyhalothrin typically used for mosquito control in Uganda would simultaneously control the fleas of rodents. The objectives of the current study were to evaluate the effect of the standard IRS technique used in Uganda and a modified IRS approach on flea loads of *R. rattus* captured inside homes.

Materials and Methods

Study Areas. Field studies were conducted in the Arua and Nebbi districts of northwestern Uganda. These areas are characterized by intense agriculture, dense human population, and highly fragmented land use (MAYAN 2005). The two districts are bisected by the northern tip of the Albertine Rift escarpment (Plumtree et al. 2007) with the easternmost low lying areas characterized by sandy soil and low rainfall and the western, higher areas characterized by lush vegetation, fertile soil and ample water sources. More detailed descriptions of the ecological characteristics of the area were reported previously (Amatre et al. 2009, Winters et al. 2009, Borchert et al. 2010). Village homes included in this study were typical of the predominant hut style in this region and consisted of square or round structures constructed of mud and waddle with a grass, thatched roof. Floors were dirt and often smeared with a combination of mud and bovine feces, creating a hardened surface after drying (Southall 1956, Middleton 2002).

Five villages were assigned to each of the three treatments (standard IRS treatment, modified IRS treatment, and control) in the Arua and Nebbi districts (Fig. 1) (Note: Since this research was conducted, the political boundary of the Nebbi District was split into two districts, Nebbi and Zombo. All villages listed as residing in the Nebbi District in this article, now reside in the newly formed Zombo District.) Villages were matched in triplicate (one treatment, modified treatment, and control) as closely as possible with respect to location, elevation, geographical extent of the village, human population size, agricultural practices, and housing construction type. In each village, 100 huts were randomly selected for study.

Capturing and Processing Rodents. Periodic rodent trapping was conducted to evaluate the efficacy of the insecticidal spraying against rodent fleas. Collections were performed 2 d before spraying and on days 20, 40, 60, 80, and 100 post-IRS. The day of spraying was defined as day 0. In all standard treatment, modified treatment and control villages, two Tomahawk traps (48.3 by 17.1 by 17.1 cm, Tomahawk Trap Co., Tomahawk, WI) were set inside each study hut, for 200 traps per village in total. Both traps were placed on the ground against the inside of hut walls. Traps were collected the next morning. Upon capture, rats were sedated by inhalation of halothane, identified to species based on morphological appearance and measurements (e.g., length of body, tail, right hind foot, and ear) (Delany 1975), and thoroughly combed with a small pocket comb to recover fleas (Gage 1999). All fleas collected from each rat were combined and stored in microcentrifuge tubes containing 70% alcohol and later identified to species following published taxonomic keys (Hopkins 1947, Haselbarth 1966, Smit 1973). A passive integrative transponder chip (AVID, AVID Identification Systems, Norcross, CA) was placed on the dorsal surface of each rodent subcutaneously between the shoulder blades. Rodents were then released at the point of capture. On the final day of trapping (day 100), captured rodents were processed as described above and then euthanized via an overdose of halothane.

Voucher flea specimens were submitted to the Centers for Disease Control and Prevention, Division of Vector-Borne Diseases and voucher small mammal specimens were submitted to Makerere University (Kampala, Uganda) for verification of species identification. All animal-handling procedures were performed according to protocols approved by the Centers for Disease Control and Prevention, Division of Vector-Borne Diseases (ACUC 09-022, Fort Collins, CO).

Application of Insecticide. Two days after the first rodent collection, two methods of IRS application were performed. For the standard application, insecticide was applied to the walls and ceiling of each hut. For the modified application, insecticide was applied to the walls, ceiling and a 1-m perimeter area around the inside floor, against the wall of the huts. Control villages received no treatment. IRS was performed using lambda-cyhalothrin (ICON CS, Syngenta Corp., Basel, Switzerland) and applied at 25 mg/m^2, as recommended for control of mosquitoes (WHO 2009a). Both methods used a 10-liter hand-pump sprayer (Chapin Manufacturing, Batavia, NY). Application methods were based on the standard IRS application

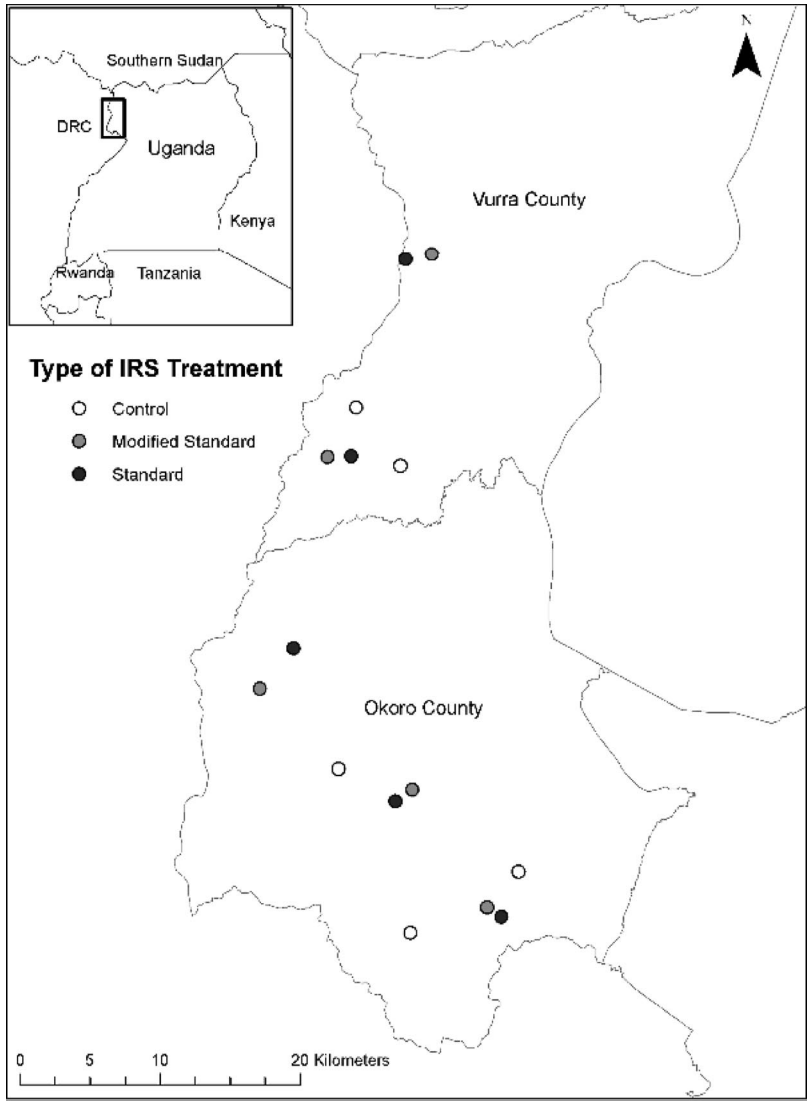


Fig. 1. Locations of study villages in the Arua and Nebbi districts.

methods as recommended by WHO (2002). Residents were instructed not to plaster their huts during the duration of the study.

Statistical Analysis. Because of the high number of rats without fleas, a hurdle model with a truncated Poisson distribution was fit to the data. The same set of predictors was used in both the zero and count portions of the hurdle model. Treatment was included as a main effect; day posttreatment was considered a continuous variable, and linear and quadratic functions of day were included. Treatment-specific trends over time were allowed by including interaction terms between treatment and day posttreatment. Finally, random effects for village and for hut within village were added. To test whether treatment differences existed over time, we used Scheffé method for multiple comparisons with overall type I error of $P = 0.05$. All analyses were run using SAS 9.2 statistical software (SAS Institute, Cary, NC).

Results

In total, 489 huts (97.8%) were treated in the standard IRS villages and 490 huts (98.0%) in the modified IRS villages. The most common reasons for noncompliance were residents not present at time of spraying or refusal. Although we made an effort to discourage residents from plastering their huts during the study, many huts were plastered during the Christmas holiday, which fell between the day 20 and day 40 trapping sessions. In these areas, residents will occasionally apply a new layer of plaster mixed from cow dung and mud to repair cracks and holes in their huts. Residents plastered 94 (19.2%) huts in standard treat-

Table 1. Number and species of fleas collected from rats inside traditional huts in northwestern Uganda

Village (treatment group)[a] (no. captures)	No. fleas on *R. rattus* collected in villages					
	X. cheopis[b]	*X. brasiliensis*[b]	*D. lypusus*[b]	*Ct. bacopus*/ *Ct. c. cabirus*[b]	Other[c]	Unknown
Offa A/B (S) (244)	149	1	1	0	0	3
Pomosi (S) (309)	35	0	1	1	0	0
Akwerali (S) (270)	0	12	3	0	0	0
Aliza/Ngira (S) (220)	1	37	2	0	2	0
Anyiku/Godrombo (S) (285)	2	33	1	1	2	3
Olli/Yapi (MS) (287)	59	2	0	1	2	0
Paganza (MS) (425)	19	0	2	1	0	0
Olli-Nebbi (MS) (466)	6	33	0	1	2	0
Mawa/Angenja (MS) (183)	0	13	0	0	4	1
Ocungulir/Akoth (MS) (397)	1	40	1	1	0	0
Tabanzu (C) (295)	144	10	2	1	4	3
Kaza (C) (207)	69	0	5	1	1	6
Oyaragada (C) (241)	17	137	14	5	8	2
Jupakonja (C) (281)	1	218	3	2	3	9
Gbalia (C) (276)	0	159	10	1	12	0
Total (4,386)	503	695	45	16	40	27

[a] S, standard treatment; MS, modified standard treatment; and C, control.
[b] *Xenopsylla cheopis, Xenopsylla brasiliensis, Dinopsylla lypusus, Ctenopthalmus bacopus/Ctenophthalmus calceatus cabirus.*
[c] Other flea species: *Xenopsylla* spp., *Afristivalus torvus* Rothschild (syn. *Stivalus torvus* in Hopkins 1947), *Ctenocephalides felis* Bouché, *Echidnophaga gallinacea* Westwood.

ment villages, 31 (6.3%) in the modified standard huts, and 202 (40.4%) in control huts. To determine whether plastering at Christmas compromised our study by affecting flea populations on rats, we compared the proportion of rats having at least one flea from huts that had been plastered versus those that had not been plastered. Plastering did not significantly change the overall proportion of rats with fleas ($F = 0.39$; df = 1, 3,162; $P = 0.47$) regardless of time point ($F = 0.45$; df = 5, 3,162; $P = 0.19$) or treatment ($F = 0.56$; df = 2, 3,162; $P = 0.43$).

In total, we recorded 4,386 (1,300 from control villages, 1,328 from standard IRS villages, and 1,758 from modified IRS villages) captures during 18,000 trap-nights. *R. rattus* comprised 100% of captured rodents (Table 1).

In total, 1,326 fleas, representing at least nine species, were collected. Table 1 lists the number of fleas captured throughout the study for both pretreatment and posttreatment trapping periods combined. Two flea species, *X. cheopis* and *X. brasiliensis*, represented 90.3% ($n = 1198$) of fleas collected (Table 1). *Dinopsyllus lypusus* Jordan & Rothschild was the next most commonly encountered species, representing 3.4% ($n = 45$) of fleas collected. *Ctenophthalmus bacopus* Jordan and *Ctenophthalmus calceatus cabirus* Jordan & Rothschild (syn. *Ct. cabirus* in Hopkins 1947) represented 1.2% ($n = 16$) of fleas collected.

The percentage of *R. rattus* infested (having at least one flea) differed significantly from the control for both the standard and modified IRS treatment sites at all time points after insecticide application ($F = 91.0$; df = 15, 3,171; $P < 0.001$) (Table 2; Fig. 2). There was no statistical difference in the proportion of infested rodents during the pretreatment session ($F = 0.27$; df = 2, 3,171; $P = 0.76$). Proportions of rats with fleas in the two treatment groups did not differ from each other at each time point after insecticide application.

Table 2. Percentage of rats infested with fleas collected from village groups in Arua and Nebbi districts

Village (grouping)	Treatment/ Control	Percentage (%) rats infested with fleas (no. rats examined)					
		Pre-treatment	20d	40d	60d	80d	100d
Offa A/B (a)	Standard	73.7 (38)	9.09 (33)	12.12 (33)	4.08 (49)	12.82 (39)	9.62 (52)
Olli/Yapi (a)	Modified standard	57.1 (42)	2.04 (49)	2.17 (46)	4.55 (44)	2.50 (40)	4.55 (66)
Tabanzu (a)	Control	42.5 (40)	20.45 (44)	24.53 (53)	34.04 (47)	22.45 (49)	11.29 (62)
Pomosi (b)	Standard	32.6 (46)	0.00 (56)	0.00 (43)	2.13 (47)	1.59 (63)	1.85 (54)
Paganza (b)	Modified standard	22.1 (68)	1.32 (76)	0.00 (59)	0.00 (61)	0.00 (74)	0.00 (87)
Kaza (b)	Control	31.9 (47)	28.57 (42)	12.90 (31)	14.29 (28)	4.17 (24)	22.86 (35)
Akwerali (c)	Standard	17.4 (46)	0.00 (52)	0.00 (41)	2.38 (42)	2.17 (46)	0.00 (43)
Olli (Nebbi) (c)	Modified standard	34.5 (58)	0.00 (66)	0.00 (79)	1.14 (87)	1.22 (82)	2.13 (94)
Oyaragada (c)	Control	25.0 (44)	52.17 (46)	26.83 (41)	38.24 (35)	40.63 (32)	20.93 (43)
Aliza/Ngira (d)	Standard	34.0 (47)	0.00 (44)	0.00 (31)	0.00 (33)	3.70 (27)	5.26 (38)
Mawa/Angenja (d)	Modified standard	42.1 (19)	0.00 (29)	0.00 (35)	0.00 (45)	0.00 (27)	7.14 (28)
Jupakonja (d)	Control	40.4 (47)	26.19 (42)	37.21 (43)	41.67 (48)	40.74 (54)	46.81 (47)
Anyiku/Godrombo (e)	Standard	33.3 (48)	4.08 (49)	3.77 (53)	4.65 (43)	2.33 (43)	10.20 (49)
Ocungulir/Akoth (e)	Modified standard	30.3 (66)	0.00 (69)	1.41 (71)	0.00 (65)	0.00 (62)	6.25 (64)
Gbalia (e)	Control	30.9 (55)	28.81 (59)	30.61 (49)	30.61 (29)	30.56 (36)	39.58 (48)

Table 3. Mean number of fleas collected from rats in village groups in Arua and Nebbi districts, Uganda

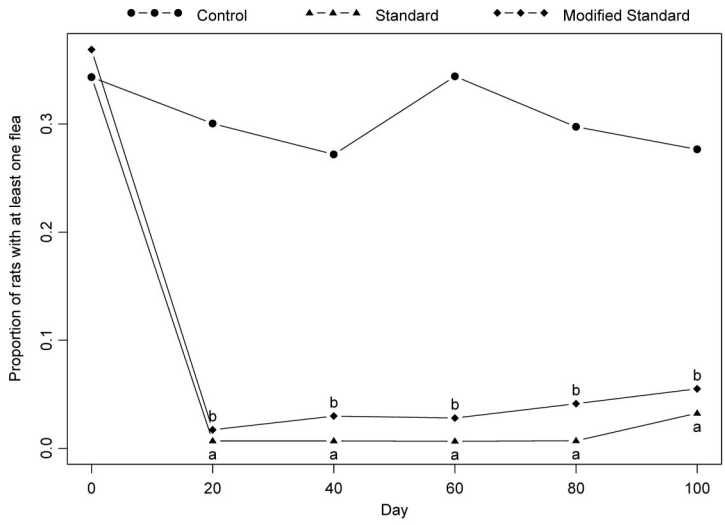
Village (grouping)	Treatment/ control	Mean no. fleas recovered					
		Pretreatment	20 d	40 d	60 d	80 d	100 d
Offa A/B (a)	Standard	2.97	0.24	0.15	0.08	0.23	0.13
Olli/Yapi (a)	Modified Standard	1.29	0.02	0.04	0.07	0.03	0.05
Tabanzu (a)	Control	0.93	0.39	0.58	0.64	0.78	0.16
Pomosi (b)	Standard	0.67	0.00	0.00	0.02	0.02	0.02
Paganza (b)	Modified Standard	0.31	0.01	0.00	0.00	0.00	0.00
Kaza (b)	Control	0.66	0.52	0.26	0.21	0.04	0.43
Akwerali (c)	Standard	0.28	0.00	0.00	0.02	0.02	0.00
Olli (Nebbi) (c)	Modified Standard	0.69	0.00	0.00	0.02	0.01	0.02
Oyaragada (c)	Control	0.34	1.35	0.63	0.85	1.09	0.33
Aliza/Ngira (d)	Standard	0.81	0.00	0.00	0.00	0.04	0.05
Mawa/Angenja (d)	Modified Standard	0.84	0.00	0.00	0.00	0.00	0.07
Jupakonja (d)	Control	0.79	0.52	0.74	1.46	0.91	0.87
Anyiku/Godrombo (e)	Standard	0.63	0.04	0.04	0.05	0.02	0.10
Ocungulir/Akoth (e)	Modified Standard	0.53	0.00	0.03	0.00	0.00	0.09
Gbalia (e)	Control	0.87	0.58	0.59	0.52	0.50	0.77

Among those rats found infested with fleas, the mean number of fleas per rat was not statistically different within the treatment and control groups ($F = 0.98$, df = 212, $P = 0.40$).

Consistent with the percentage of *R. rattus* infested with at least one flea on treatment sites, comparisons of the mean number of fleas per rat did not differ between the control and both treatment groups at the pretreatment but were significantly lower on both treatment groups compared with the control group ($F = 5.3$; df = 15, 3,171; $P < 0.001$) after treatment took place (Table 3; Fig. 3). The mean number of fleas on rats in the two treatment groups did not differ from each other at each time point after insecticide application.

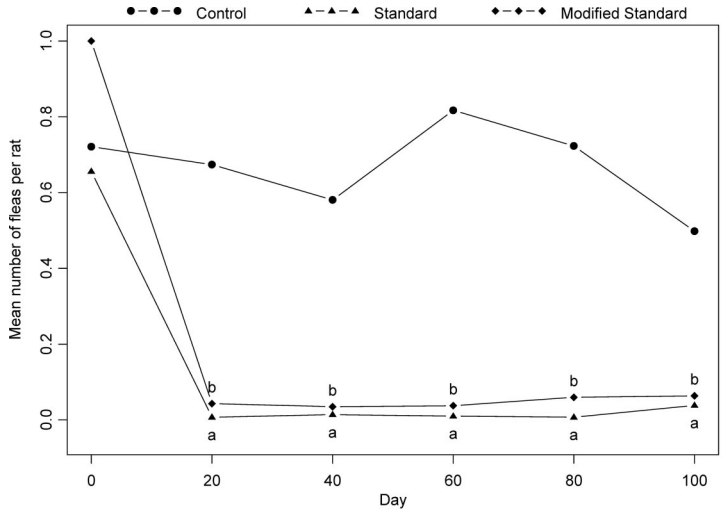
Discussion

In this study, both the standard and modified IRS applications of lambda-cyhalothrin reduced flea loads on *R. rattus* for at least 100 d. The modified application did not improve results in comparison to the standard application, implying that either technique has potential to control fleas on *R. rattus* in northwestern Uganda. We observed dripping and mist from the sprayer falling to the floor when applying IRS to the ceiling of huts on both standard and modified treatment groups. Although insecticide was not directly applied, standard treatment hut floors received some insecticide application. In the West Nile region where our study was conducted, most human plague cases occur between August and early January (Winters et al. 2009). Because we demonstrated a reduction in fleas on rodents for at least 3 mo in our evaluation, IRS application using lambda-cyhalothrin could provide additional protection for residents during the peak months of the plague transmission season and perhaps even longer based on other reports indicating that this formula (ICON CS) was effective against mosquitoes for as long as 10 mo on mud surfaces (Syngenta 2007).



[a]Pooled standard treatment vs. control comparison (Scheffe's method). Significantly lower than controls ($P < 0.001$).
[b]Pooled modified treatment vs. control comparison (Scheffe's method). Significantly lower than controls ($P < 0.001$).

Fig. 2. Proportion of rodents infested with fleas collected in Arua and Nebbi districts (combined villages).



[a]Pooled standard treatment vs. control comparison (Scheffe's method). Significantly lower than controls ($P < 0.001$).
[b]Pooled modified treatment vs. control comparison (Scheffe's method). Significantly lower than controls ($P < 0.001$).

Fig. 3. Mean number of fleas collected from rats in Arua and Nebbi districts (combined villages).

Suppressing adult flea populations for even limited durations could disrupt ongoing transmission of plague and might depress flea numbers past a critical point where it is no longer possible to maintain an epizootic during the remainder of the plague season. The exact rodent flea infestation threshold required to maintain *Y. pestis* transmission in enzootic or epizootic states is unknown. However, early research reported that a flea index of ≥1.0 was high enough to support rodent-to-rodent transmission of plague (Politzer 1954). Later average estimates ranged from 9.4 to 15.8 *X. cheopis* per rat for epizootic transmission (Lorange et al. 2005, Eisen et al. 2007). In our study, conducted during an interepizootic period, pretreatment thresholds were at or below one flea per rat and were reduced to <0.1 flea per rat after treatment. These findings suggest that the use of IRS could effectively prevent transmission of plague bacteria by maintaining flea loads below perceived critical thresholds for transmission.

In our study locations, we observed that the drive to plaster huts, especially during the Christmas holidays (to beautify the residence), was widespread and part of the local culture but had no apparent effect on flea populations on rats. In contrast, others reported that plastering of huts after insecticide application decreased the effectiveness of IRS and considered an impediment to IRS campaigns for mosquito control (Sharp et al. 1990, Mnzava et al. 1998, Govere et al. 2000). Likewise, plastering activities (without the addition of chemicals to the plaster) were thought to control the free-living fleas inside huts (Kilonzo et al. 1997), but the effectiveness of this was questioned in a later study (Laudisoit et al. 2007).

We observed rats moving throughout huts on the ground, in the grass roofs of the huts, along the tops of walls, and in between huts of the same homestead (CDC, unpublished data) during our study. Rodent contact with the walls and surfaces of the huts probably exposed them to the insecticide used in our treatments. Whether insecticide was then translocated to nesting areas is unknown, but this has been hypothesized in other studies to control off-host nest dwelling fleas (Gage et al. 1997). If translocation does indeed occur, it could result in control of not only adult fleas but also subadult or newly emerged fleas in the nest, thus increasing the impact and duration of flea control. Similarly to previous studies (Eisen et al. 2008, Borchert et al. 2010), *X. cheopis* and *X. brasiliensis* were the predominant fleas found on commensal rats in this area.

Repeated exposure of insects to insecticides can lead to the development of resistance in arthropod vectors of disease (Roberts and Andre 1994). Reports exist of insecticide resistance to DDT occurring in fleas after the use of the insecticide to control mosquitoes (Patel et al. 1960, Busvine and Pal 1969) and insecticide resistance in fleas was reported in Africa (WHO 1992). Use of pyrethroid insecticides has already caused the development of insecticide resistance in Ugandan mosquitoes (Morgan et al. 2010) and the possibility of insecticide resistance occurring in fleas after exposure to lambda-cyhalothrin is certainly possible. Our group is currently running baseline susceptibility studies of local fleas to lambda-cyhalothrin (ICON CS) as well as investigations to determine the presence of resistance genes in fleas. There are currently 12 different chemicals in four chemical classes available for IRS application (WHO 2009a) and rotating among these available chemicals could discourage resistance from occurring (Roberts and Andre 1994). The choice of insecticide for use in control operations needs to be considered because if insecticide resistance develops (either in mosquitoes or fleas), control programs could become ineffective and the further usefulness of a particular insecticide will

be limited. Therefore, the judicious use and possible withholding of effective insecticides for use in response situations might be critical to ensure that adequate tools are available for controlling plague epidemics.

The cost of insecticides varies among the chemicals and efforts must be made to select a cost-effective and affordable insecticide to maintain the sustainability of control programs. For example, ICON CS cost the equivalent of ≈US$9.00/sachet in our study and approximately three huts were spayed using each diluted sachet. Therefore, the insecticide cost was ≈US$3.00/hut, not including additional overhead, labor and transport costs resulting in a fairly significant investment in an area with limited disease control resources. Because plague control programs in developing nations often suffer from underfunding (WHO 2008), the potential to combine plague control with already existing and funded mosquito control programs may help prevent and control the disease. To illustrate this point, malaria control programs received 1.7 billion dollars of international funding in 2009 worldwide (WHO 2009b) and many of the 45 countries in Africa that are endemic for malaria also recorded plague cases from 1987 to 2009 (including Uganda) (WHO 2008, 2010). This region would greatly benefit from the added benefit of plague control from IRS application programs for malaria control where the endemicity of the diseases overlap.

In summary, our study demonstrated that the use of indoor residual spraying for control of mosquitoes in Uganda also reduced on-host flea vectors of plague for at least 100 d. Future studies are needed to assess the effect of IRS on the human incidence of both plague and malaria in the same localities and studies pinpointing the best timing for insecticide application to be effective against both diseases.

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