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ROLE OF URBAN MICE IN TRANSMISSION OF *TOXOPLASMA GONDII*

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Abstract *Toxoplasma gondii* is a protozoan parasite capable of infecting most warm blooded animals. The parasite can cause spontaneous abortions and foetal abnormalities and induce serious illness in immuno-compromised patients. Humans are intermediate hosts and can become infected via cat faeces. Previous research confirmed high levels of infection (59%) in urban mice (*Mus domesticus*) caught in domestic properties in a residential area of Manchester, United Kingdom and concluded that they play an important role in maintaining *Toxoplasma* infection. This new study aimed to investigate whether this high level of infection was generally found in other urban locations. Traps were laid in a number of UK locations and the 119 mice collected were screened for *Toxoplasma*. A prevalence of 51% infection was confirmed and this was not significantly different from the levels found in the earlier study confirming that high prevalence of infection is a common feature of urban mice. These findings suggest that urban mice may play an important role in the persistence and transmission of *Toxoplasma* infection in urban areas. This is significant since, in the UK, little consideration is given to the role of urban mice in the propagation of human pathogens. Their classification as a nuisance rather than a public health pest continues to thwart the implementation of effective control strategies to ameliorate the health threats posed by the presence of mice in urban settings.
Key Words *Mus domesticus* disease transmission, *Toxoplasma gondii*

INTRODUCTION

The urban house mouse (*Mus domesticus*) is highly successful in exploiting the human environment and its continued survival and proliferation owes much to its capacity to adapt to life in close association with people and to its nocturnal habits, enabling foraging activities to go largely unnoticed (Rowe, 1973; Shenker, 1973). Within the United Kingdom, house mice tend to live almost entirely inside buildings, increasing the opportunities for direct and indirect contact with people, posing a potential threat to public health through the zoonotic diseases they may carry.

Toxoplasma gondii is an intracellular protozoan parasite capable of infecting almost all warm-blooded animals including humans. Its impact lies in its ability to cause spontaneous abortions and foetal abnormalities, and to induce serious illness in immuno-compromised subjects. Cats are the only known definitive host for *T. gondii*, and acquire the infection in one of two main ways: via consumption of infected intermediate host prey (such as mice) or via ingestion of oocysts within their food or water (Dubey and Beattie, 1988). Infected cats may produce more than 100 million oocysts in its faeces, which can remain viable in the environment for over a year (Jackson et al., 1988; Frenkel, 2000). Cats cease shedding oocysts in their faeces approximately 14 days after the initial infection. The prevalence of *T. gondii* infection in cat populations will depend upon the availability of and contact with infected prey species such as small mammals, where infection levels depend upon access to and ingestion of infected oocysts and/or infected tissue or transmission of the infection via a congenital route (Dubey and Beattie, 1988).

Humans are intermediate hosts and can become infected by three main routes, horizontally through the ingestion of food and/or water contaminated with oocysts excreted by infected cats, by consumption of tissue cysts in undercooked meat, and vertically via transplacental tachyzoites from mother to foetus. As the infective oocysts excreted by the cat are considered a major source of infection, the advice typically given to vulnerable groups such as pregnant women focuses on the avoidance of contact with cats and cat faeces.

Human toxoplasmosis ranges from an asymptomatic episode to chronic and even life threatening illness. Those with a robust immune system usually experience a mild and self-limiting illness, although tissue cysts of the parasite may remain present for many years. Women who acquire the infection during pregnancy have a 45% chance of transplacentally transferring the parasite to the foetus. In 1992 the incidence of prenatal infection with *T. gondii* in human neonates was estimated as 0.3-1.6 per 1000 births in the UK (Zadik et al., 1995). Effects on the foetus ranged from sub clinical infection to intrauterine death in 10% of cases (Remington and Desmonts, 1990; Chatterton, 1992).

Experimental infection of both the house mouse (*Mus domesticus*) and the field mouse (*Apodemus sylvaticus*) with infective oocysts demonstrated a high frequency of vertical transmission (i.e. repeated transplacental transmission from one generation to the next) (Thiermann, 1957; Beverley, 1959; Remington, et al., 1961; De Roever-Bonnet, 1969; Owen and Trees, 1998; Marshall et al., 2004). Consequently, *T. gondii* infection levels could theoretically persist within a mouse population in the absence of felid-derived oocysts. This would suggest that within the urban context, mice could be important intermediate hosts in facilitating the persistence of the parasite.

Murphy et al. (2008) trapped urban mice in the Cheetham Hill area of Manchester, UK from domestic dwellings and screened them for the presence of *Toxoplasma gondii* infection. Infection rates varied depending on the test used. PCR-based detection found high levels of infection (59% infected), but low levels using serological detection (1% infected). The authors suggested that the discrepancy in results could indicate the importance of vertical transmission of the parasite within this host. Previous studies had indicated that serological detection methods might not be accurate for detection of the parasite when it was vertically transmitted (Suzuki and Kobayashi, 1990; Owen and Trees, 1998), due to the occurrence of tolerance amongst newborn mice. Sixteen of the mice caught during the trapping phase were pregnant, and the foetuses of these females were screened for *T. gondii* infection. Marshall et al. (2004) found that 75% of these foetuses tested positive for *T. gondii* infection, confirming that vertical transmission was occurring at a high rate amongst this mouse population.

Whilst mice do not pose a direct risk of infection to the human population, they could be an important reservoir for the parasite, enabling it to survive until such times as a cat is introduced and the cycle is completed. High risk groups such as pregnant women could then be infected by handling cat faeces. Effective control of the infection would therefore require a rigorous mouse control strategy to eradicate this reservoir. To test the reliability of the results reported by Murphy et al. (2008) in the Cheetham Hill area of Manchester, mice from other locations in the UK were trapped and tested for *Toxoplasma* infection.

MATERIALS AND METHODS

Six Local Authority pest management service units, five in the Greater Manchester area and one in the South West of England, and one commercial organisation in Manchester, agreed to place snap traps in locations where they were undertaking control programmes to eradicate mouse infestations. Captured mice were collected by a member of the research team and screened for the presence of *Toxoplasma* infection. Brain samples were dissected out using aseptic techniques and the presence of T. gondii was detected using the nested polymerase chain reaction (PCR) amplification of the Surface Antigen Gene 1 (SAG1) (Savva et al., 1990). Samples that showed no amplification products were checked for the ability to amplify using primers to mouse tubulin (Terry et al., 2001) and were rechecked for SAG1 amplification using higher and lower DNA concentrations to ensure true negativity. PCR products were analysed using the techniques described by Terry et al. (2001).

RESULTS AND DISCUSSION

During the fieldwork phase, 119 mice were captured. The number of mice captured within each of the six locations ranged from 2 to 82 (Table 1). Mice were caught in 50 separate domestic properties and 1 commercial site and the numbers captured per property ranged from 1 to 18, with a mean of 2.3 per property.

Table 1. Prevalence of *Toxoplasma* infection in the mice caught in seven locations.

Location	Total no. mice caught (No. properties)	No. testing positive for *Toxoplasma* infection	% testing positive for *Toxoplasma* infection
GMLA 1*	82(34)	43	52
GMLA 2	2(1)	2	100
GMLA 3	9(4)	3	33
GMLA 4	9(7)	1	11
GMLA 5	7(6)	5	71
SWLA	6(missing)	6	100
GMComm	4(1)	1	25
Total	**119**	**61**	**51**

* GMLA – Greater Manchester Local Authority; SWLA – Southwest England LA; GMComm – commercial site in Greater Manchester

The percentages testing positive for *Toxoplasma* infection at each site ranged from 11 – 100% with an overall infection rate of 51%. The overall infection rates from this study did not differ significantly from the infection rates reported in Murphy et al. (2008) work ($\chi^2 = 1.6$; $p = 0.21$) and confirms the reliability of these earlier findings.

As the definitive host, cats play an important role in the propagation of *Toxoplasma* infection. However, earlier work found that the infection status of mice did not have a direct relationship with the presence of a cat within the property where the mouse had been captured, with 92% of mice testing positive being caught in properties where the resident confirmed that no cat was present (Table 2). In this study the data relating to cats was less complete. However, for properties where information about cats was provided, 44 of the 45 mice (98%) which tested positive for *Toxoplasma* were trapped in properties where the owner confirmed that no cat was present (Table 2).

Table 2. Distribution of mice positive for *Toxoplasma* and the presence of cats in urban properties.

Toxoplasma status	Cheetham Hill study (Murphy et al. 2008)		Current study	
	Cats present	Cats absent	Cats present	Cats absent
No. mice testing positive/total no. positive mice	10/117	107/117	1/45	44/45
% infected	9%	91%	2%	98%

Urban mice appear to play an important role in the maintenance of *Toxoplasma gondii* in the urban environment, in the absence of a definitive host. If contact with the definitive host was the only mechanism by which urban mice could become infected with *Toxoplasma*, then infection rates would be predicted to be higher in adult mice because they would have had more opportunities for environmental exposure to the oocysts shed by the definitive host. Mice were split into three age categories (juvenile/adolescent/adult) depending on weight (<10 g/10-15 g/>15 g) and the rates of infection within each of the three age groups examined (see Table 3). In both studies the rates of infection were similar in all three age categories, and indeed when tested showed no significant differences between the three age groups ($\chi^2 = 0.76$; $p = 0.68$) suggesting that exposure to oocysts may not be the only route of infection and that vertical transmission between an infected mother and foetus must also play a role in propagating the infection (Marshall et al., 2004).

Table 3. Prevalence of *Toxoplasma* infection in juvenile/adolescent/adult mice

Age category	Juveniles	Adolescents	Adults	Total
CHEETHAM HILL STUDY (Murphy et al., 2008)				
No infected/total	73/119	26/47	18/34	117/200
% infected	61%	55%	53%	59%
CURRENT STUDY				
No infected/total	14/25	22/41	25/53	61/119
% infected	56%	54%	47%	51%

CONCLUSIONS

The previous work reported by Murphy et al. (2008) was undertaken within a small geographical area (6 hectares) and whilst the high levels of *Toxoplasma* infection (59%) were remarkable, it was important that an attempt was made to replicate this result in mice caught in other urban locations. An infection rate of 51% found in the mice captured from geographically dispersed urban locations confirms the reliability of the infection rates reported in earlier work.

Transmission of *Toxoplasma* infection vertically within mouse populations is an important finding and raises issues relating to the control of mice in urban settings. In the UK the urban mouse is viewed as a nuisance pest and local approaches to control have developed over time, leading to significant variations in the services offered to those living in infested domestic properties. In order to break the cycle of *Toxoplasma* infection and thus reduce its public health impact, it is important that cats do not consume infected mice. Work by Murphy et al. (2005) confirmed that in Cheetham Hill mice were able to migrate between properties and reactive treatment regimes (treating only those properties where residents had requested it), whilst cropping a proportion of the mouse population present, would not eradicate it and *Toxoplasma* infection would be maintained (via, in the main, vertical transmission routes) in that environment. Treating all adjoining properties and checking the effectiveness of the treatments adopted, whilst costly initially, would ensure eradication from each block and break the *Toxoplasma* cycle. This proactive approach, treating all properties within a block where a mouse infestation had been confirmed was adopted in Cheetham Hill and led to the complete eradication of chronic mouse infestations within that area. Whilst the early costs of adopting this approach may be substantial, these must be balanced against the long term health benefits to those living infested properties.

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