Review TRENDS in Parasitology Vol.20 No.2 February 2004

Wilderness in the city: the urbanization of *Echinococcus multilocularis*

Peter Deplazes[1], Daniel Hegglin[1], Sandra Gloor[2] and Thomas Romig[3]

[1]Institute of Parasitology, University of Zürich, Winterthurerstr. 266a, CH-8057 Zürich, Switzerland
[2]SWILD – Work Group Urban Ecology and Wildlife Research, Wuhrstr. 12, CH-8003 Zürich, Switzerland
[3]Section Infectiology, University of Ulm, Robert-Koch-Str. 8, D-89081 Ulm, Germany

A distinct increase in fox populations, particularly in urban areas, has been observed in Europe. This is of particular concern in endemic regions of the small fox tapeworm *Echinococcus multilocularis*, the aetiological agent of human alveolar echinococcosis. Novel tools have facilitated the investigation of the ecology of urban foxes and have demonstrated the urban wildlife cycle of *E. multilocularis*. Such studies are essential for estimating the risk of transmission to humans and to determine the basics for the development of control strategies.

Echinococcus multilocularis is typically perpetuated in a wildlife (sylvatic) cycle that includes foxes (genera *Vulpes* and *Alopex*) as definitive hosts and different species of rodent (mainly Arvicolidae) as intermediate hosts [1]. In some endemic areas, other species of wild carnivores, such as coyote, wolf and raccoon dog, are involved as definitive hosts. In addition, a synanthropic cycle exists in some rural communities with domestic dogs as definitive hosts, which acquire the infection from wild rodents [2–4].

In the core European area of human alveolar echinococcosis (AE), a consistently high prevalence of 35–65% of *E. multilocularis* in red foxes has been recorded [1,5,6], and foxes are probably responsible for most of the environmental contamination with *E. multilocularis* eggs. Furthermore, recent studies have shown that *E. multilocularis* has a wider geographical range than was previously anticipated and there are reports on increasing *E. multilocularis* prevalences in some regions [7,8]. Within the past 10–20 years, the population dynamics of the definitive host of *E. multilocularis* have changed drastically in many parts of Europe [9]. Rabies, an important factor for the mortality of red foxes, has disappeared because of the successful vaccination campaigns [9,10] and, as a result, foxes have extended their distribution increasingly to urban areas over the past few decades [11].

However, retrospectively, no direct correlation between fox population densities and the incidence of human AE could be demonstrated. In Switzerland, the countrywide average incidence of human AE (0.10–0.18 new cases per 100 000 individuals per year) has not varied between 1956 and 1992, suggesting a stable epidemiological situation despite the high variations in fox densities during this time [1]. However, there is overwhelming evidence that any shift towards synanthropic transmission of *E. multilocularis* leads to heavy infection pressure to the human population. This was the case in areas where domestic dogs became involved in the parasite's life cycle (e.g. in parts of Alaska and in some regions of China), resulting in very high prevalences of human AE of up to 4.0% [3,4].

Today, foxes are present in many central and western European cities and towns, and urban fox densities often exceed rural ones. Foxes have become well adapted to urban life. They use specific habitats such as allotment gardens and residential areas during the night and rest sites during the day (S. Gloor, PhD Thesis, University of Zürich, 2002). The increasingly close contact between people and foxes in urban areas calls for a monitoring of the situation. Although there are no indications yet that the number of AE cases in urban areas is on the rise, it remains to be seen if the increasing presence of the parasite will lead to a temporally delayed increase in the future. In this review, we focus on the urban *E. multilocularis* transmission in respect of the changing fox ecology and possible risks of human infection.

The urban fox phenomenon

Red foxes living in urban areas have been known in Britain since the 1930s [12]. In the 1970s and 1980s, urban fox densities of up to five family groups per km^2 were recorded. Because these observations were unique, urban foxes were initially thought to be an isolated British phenomenon [13,14].

In the 1970s and 1980s, continental fox populations suffered heavily from a rabies epizootic, a zoonosis not present in the UK. Subsequently, fox populations decreased drastically. However, fox populations recovered from 1985 onwards (e.g. [9,15]) because of successful oral vaccination campaigns against rabies, which started in Switzerland in 1978 [16] and were widely extended to other regions of western and central Europe in the following years [9].

Coinciding with the population recovery in rural areas, more and more foxes have been recorded from large conurbations. A survey of town officials and persons responsible for wildlife management revealed that foxes are present in 28 of the 30 largest Swiss cities [11]. Urban foxes have also been recorded from other parts of the distribution area of the red fox, including: Oslo, Norway [17]; Arhus, Denmark [18]; Stuttgart, Germany [7]; Toronto, Canada [19]; and Sapporo, Japan [20].

Corresponding author: Peter Deplazes (deplazesp@access.unizh.ch).

 1471-4922/$ - see front matter doi:10.1016/j.pt.2003.11.011

In Zürich, Switzerland, urban foxes have been known since the 1960s, but remained apparently rare until the mid-1980s. Between 1985 and 1997, the annual numbers of foxes shot or found dead in Zürich increased 20-fold [11].

To study the spatial and habitat use of the urban fox population of Zürich, 22 adult foxes (13 females and nine males) from urban and peri-urban areas were observed by radiotracking (S. Gloor, op. cit.), revealing that their home ranges were relatively small (Figure 1a) and were comparable with those observed in British cities with high fox densities (e.g. [21,22]). According to preliminary home range analyses, the home ranges of female foxes were 28.8 ± 22.7 ha, and the home ranges of resident male foxes were 30.8 ± 11.0 ha estimated by the area of a 100% minimum convex polygon (MCP). The tracked foxes were classified into urban or rural according to the amount of urban area within their home ranges. There was an obvious separation between rural and urban foxes: the border between the city and the surrounding grassland and forest was hardly ever crossed (S. Gloor, op. cit.) (Figure 1a). The spatial separation of rural and urban foxes was also demonstrated by food analyses of their stomachs and by toxicological investigations [23,24]. Moreover, microsatellite analyses revealed a reduced gene flow between urban and rural populations [25]. Genetic differences were lower between different rural fox populations compared with adjacent rural and urban fox populations.

Overlapping home ranges of foxes of the same sex and observations of more than two adult foxes at breeding dens indicate the establishment of family groups [26] (S. Gloor, op. cit.). In the Zürich area covered by the radiotracked resident foxes (6.7 km^2), 23 dens with cubs were known in 1999. The fox density in the area would be 6.9 adult foxes per km^2, assuming two adult foxes per breeding den, or 10.3 adult foxes per km^2, with three adult foxes per den. Recent studies in a suburban area south of Munich, Germany, arrived at estimates of 10 adults per km^2, based on radiotracking of seven urban foxes (A. König and T. Romig, unpublished).

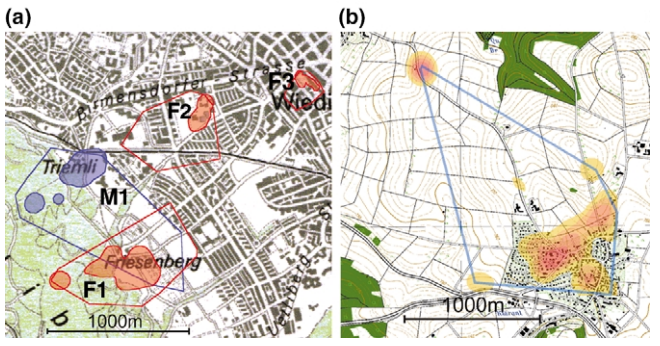

Figure 1. Examples of seasonal home range areas of **(a)** urban and peri-urban, and **(b)** rural foxes. (a) Home ranges of three female foxes (red; F1, F2 and F3) and one male fox (blue; M1) in the urban and peri-urban area of Zürich. The home range areas of F1 (100% MCP: 42.5 ha; 222 locations) and M1 (100% MCP: 68.2 ha; 173 locations) were mainly located outside of the urban border. F2 (100% MCP: 27.1 ha; 190 locations) and F3 (100% MCP: 4.8 ha; 186 locations) were urban foxes that never left the built-up area. (b) Home range of one female fox in a rural town (Böhringen) of the Swabian Jura (Germany). The home range (95% MCP: 169 ha) is larger than those of urban foxes, and activity is divided between nightly activity in town and day-time rest sites >1 km outside. The yellow/red areas indicate density of location (N = 206), with the red areas representing the highest density. Figure 1b is courtesy of D. Thoma, Stuttgart, Germany. Abbreviations: F, female; M, male; MCP, minimum convex polygon.

Different studies have pointed out the crucial significance of anthropogenic food resources for the urbanization of foxes [27,28]. In Zürich, >50% of an average stomach contents of foxes were found to be anthropogenic and it has been estimated that the overall food supply of households, allotment gardens and public areas would be sufficient to feed a much higher number of foxes than are currently present [24].

Foxes have adapted to synanthropic life in larger cities, but it appears that they increasingly use anthropogenic food sources within villages and small towns (with populations of 1000–3000 people) in rural settings. An ongoing study in a rural area of the Swabian Jura in southwest Germany has shown that, unlike typical urban foxes, very few of these animals are 'resident' (i.e. present day and night) within small towns and villages. The reason could be owing to a rather limited tolerance by the inhabitants towards foxes in their vicinity, such that any animal behaving conspicuously, or attempting to establish a den or resting place within the settlement, could be shot. A radiotracking study of foxes caught in or near such villages has revealed interesting adaptations to this situation. Whereas some animals are foraging at night both in the settlement area and in the adjacent open country, others prefer the settlement area for their activity and spend the day in dens, which can be several kilometres away from town (D. Thoma and T. Romig, unpublished). This hybrid behaviour is reflected in the size of the home ranges, which are larger than those of true 'urban' foxes, but are smaller than those from non-synanthropic foxes in rural areas (Figure 1b). These small-town foxes are potentially important as sources of human infection with *E. multilocularis* because the foxes can acquire the parasite by feeding on rodents on the surrounding grassland and defecating within built-up areas.

Echinococcus multilocularis in urban settings

In the past five years, the occurrence of *E. multilocularis* in urban foxes has been reported from several European cities (e.g. Copenhagen [29], Geneva [30], Stuttgart [7] and Zürich [31]). To date, the urban transmission of *E. multilocularis* has been most comprehensively documented in Zürich. Over a period of 26 months (1996–1998), foxes were examined for intestinal infections with *E. multilocularis* and other helminths (Table 1). Seasonal differences in the prevalence of *E. multilocularis* were found only in urban subadult (4–12 months old) male foxes, which were significantly less-frequently infected in summer than in winter. The prevalence of *E. multilocularis* in 252 foxes sampled during winter differed significantly between 47% in the urban and 67% in the adjacent recreational area. A similar prevalence gradient is observed in Geneva and Stuttgart (Table 1). However, the presence of *E. multilocularis* is not limited to large cities. A preliminary survey of 67 foxes collected in the built-up area of the rural town Oberammergau (Bavaria, Germany) indicated a prevalence of 39% (T. Romig and A. König, unpublished).

The distribution of the *E. multilocularis* biomass, as expressed by worm numbers per fox, is highly aggregated (overdispersed) in several studies on rural and urban foxes [31,32]. In one study, as few as 10 foxes (8%) were infected

Table 1. Small intestinal helminths found in urban foxes[a]

	Zürich (1996–1998) (*n* = 388)		Geneva (1998–2001) (*n* = 160)		Stuttgart (1995–2003) (*n* = 492)	
	P (%)	CI	P (%)	CI	P (%)	CI
Echinococcus multilocularis	44.3	39.3–49.4	43.1	35.3–51.2	16.8	13.8–20.6
Taenia spp.	16.5	13.0–20.7	38.1	30.6–46.1	13.4	10.6–16.8
Mesocestoides spp.	4.4	2.7–7.1	4.4	1.8–8.8	18.5	15.2–22.2
Dipylidium caninum	0.5	0.1–2.1	2.5	0.7–6.3	–	–
Toxocara canis	47.4	42.4–52.5	71.9	64.2–78.7	41.3	37.1–45.9
Hookworms	66.8	61.8–71.4	78.8	71.6–84.8	13.4	10.6–26.8
Ref.	[31]		[30]		–[b]	

[a]Abbreviations: CI, upper and lower 95% confidence interval; *n*, number of foxes investigated; P, prevalence.
[b]T. Romig, unpublished.

with more than 10 000 specimens and harboured 72% of the total biomass of *E. multilocularis* in this fox population [31]. Therefore, a few highly infected foxes are responsible for most of the environmental egg contamination. For *E. multilocularis*, different mechanisms could contribute to this phenomenon. On the basis of the few available experimental data, the time of egg excretion of *E. multilocularis* (patency) by definitive hosts lasts only a few months. Most of the worm burden is apparently eliminated within 2–3 months [33], but residual worm burdens can persist for several additional months. To date, most of the experimental studies were performed with heavily infected hosts and, therefore, a crowding effect that limits survival cannot be excluded. Furthermore, intestinal immunity against *E. multilocularis* is not well understood. Indeed, an age-dependent distribution of the parasite biomass in definitive host populations has been described for *Echinococcus granulosus* in dogs [34] and *E. multilocularis* in foxes [5,31]. In both subadult and adult foxes, an overdispersed pattern of *E. multilocularis* distribution was observed, but a total of 82.7% of the worm burden was detected in 68 subadult foxes of a total sample of 133 animals [35]. Therefore, the age distribution within a fox population should have a significant impact on the population's capacity for *E. multilocularis* and consequently on infection pressure.

Environmental contamination with *E. multilocularis* eggs can be estimated by novel immunological and molecular methods (Box 1). Analyses of 647 fox faecal specimens collected within Zürich revealed coproantigen-positive samples of 10–60% in different areas. The spatial distribution of coproantigen-positive samples (Figure 2a) was in accordance with the different prevalences found in necropsied foxes [31] and provided evidence for a high contamination with *E. multilocularis* in recreational areas in the outskirts. Furthermore, *E. multilocularis*-infected rodents were found in these highly contaminated areas (Figure 2b). The highest prevalence of *E. multilocularis* was found in *Arvicola terrestris* (9.1%), followed by *Clethrionomys glareolus* (2.4%), but no infections were detected in 154 *Apodemus* sp. [36]. However, *Microtus* spp, another important group of intermediate hosts, were not investigated in sufficient numbers in this study. In nine out of ten trapping sites along the city border, *E. multilocularis*-infected rodents were caught (Figure 2b), demonstrating an urban cycle of the parasite. Within the city area of Stuttgart, 12% of 33 muskrats (*Ondatra zibethicus*) were infected, indicating that this species could act as an important link in the urban transmission of *E. multilocularis* when suitable habitats (lakes) are present (T. Romig, unpublished). In Sapporo, there is a high level of contamination with *E. multilocularis* around fox dens located in the urban fringe [20]. However, the authors pointed out that the life cycle of *E. multilocularis* might not easily be maintained in the urban area, whereas the outskirts offer a good habitat for *Clethrionomys rufocanus,* the most important intermediate host in this area.

Echinococcus multilocularis infection in domestic carnivores

The presence of an urban wildlife cycle of *E. multilocularis* is now documented in several European cities. Hence, there is an increasing risk of infection with *E. multilocularis* for domestic dogs and cats by preying on metacestode-infected rodents. Both dogs and cats can reach extremely high population densities in urban areas. According to the Zürich dog tax statistics, there are 0.7 dogs per ha and the cat population is estimated to be around three times higher. In Brooklyn, New York, densities of free roaming domestic cats of up to 4.9 individuals per ha have been recorded [37], exceeding more than tenfold the highest recorded population densities of urban foxes [26,38]. However, the zoonotic significance of *E. multilocularis* infections in cats is probably limited because of the retarded development and a markedly reduced egg production of worms infecting this host species [39].

In certain epidemiological situations in Alaska and China, high prevalences of *E. multilocularis* have been found in domestic dogs (1–12%), which apparently are the main sources for infections in humans within villages [3,4]. In other endemic areas, such as Europe, USA and Japan, the epidemiological significance of domestic carnivores is uncertain, and extended risk analyses with sufficient numbers of human cases are needed for statistical analyses. Nevertheless, there is some evidence supporting the risk of transmission from dogs to people [40].

In central Europe, necropsy studies undertaken on dogs and cats have revealed local *E. multilocularis* prevalences of 0.4–5.6% [6,41]. Such studies have the disadvantage that the necropsied animals are usually a selected population and that only a small number of animals can be examined. Only in the past ten years has the development of coproantigen tests enabled the survey of larger numbers of living animals from the normal

Box 1. Methods for diagnosis of intestinal *Echinococcus multilocularis* infection

The gold standard for diagnosing intestinal infection in definitive hosts is the sedimentation and counting technique (SCT) at necropsy (Table I). For mass screening of foxes, the intestinal scraping technique (IST), a less laborious technique, is used. The disadvantages of these methods are: (i) the high logistical requirements; and (ii) the need for special safety precautions. Serological screening using crude parasite antigens or an affinity-purified antigen (Em2 antigen) has been considered unsuitable for reliable diagnosis of intestinal *E. multilocularis* infection [53]. Two novel approaches for diagnosis of intestinal *E. multilocularis* infection, the detection of *E. multilocularis*-specific coproantigens in enzyme-linked immunosorbent assay (ELISA) and of copro-DNA by polymerase chain reaction (PCR), have been successfully implemented. These methods have proved their value for the diagnosis in both live and dead animals. Coproantigen detection is the method of choice for mass screening because it is sensitive, fast and cheap. In diagnostic PCR, two different genes have been targeted, the U1 small nuclear RNA gene [54] and the mitochondrial 12S ribosomal RNA (rRNA) gene [55]. However, the use of PCR for routine diagnostic or large-scale purposes is hampered by the laborious DNA extraction from faecal material. PCR is the only method for identifying *E. multilocularis* from morphologically indistinguishable taeniid eggs isolated from faecal or environmental samples.

For studies on faecal samples collected in the field, the sampling strategy was evaluated carefully [20,32,36]. In rural areas, coproantigen detection in field samples did reflect the different prevalences in fox populations, as assessed from foxes at necropsy. In urban areas that were highly contaminated with fox faeces, coproantigen results represent the level of contamination with *E. multilocularis* rather than a prevalence of the parasite, because the possibility of multiple samples being collected from the same animal cannot be excluded.

Table 1. Diagnostic methods for the detection of *Echinococcus multilocularis* in definitive hosts or in field faecal samples[a]

Test system	Stage detected	Test characteristics	Advantages	Disadvantages	No. of investigations per person per day	Refs
SCT	Intestinal stages	SE and SP ≈ 100%; reference method	Morphological identification of intestinal helminths and their stages, precise quantification	Application at necropsy only, laborious for mass screening	10 animals (necropsy included)	[31,53]
IST	Intestinal stages	SE = 78% (compared with SCT); SP ≈ 100%; screening test	Morphological identification of all intestinal helminths and their stages, semi-quantification	Application at necropsy only, laborious	20 animals (necropsy included)	[31,53]
CELISA	Antigens of intestinal stages	SE ≈ 80% (compared with SCT), SP = 95–99% [42]; SE ≈ 87% (compared with SCT), SP ≈ 70% [29]; routine test for mass screening[b]	Allows *in vivo* and post-mortem diagnosis, testing of field faecal samples, rapid and easy performance, prepatent infection detectable	*Echinococcus* genus-specific, worm burden cannot be quantified	200 samples	[42,56][b]
Egg isolation and identification by PCR	*E. multilocularis* eggs	SE 94% (compared with SCT)[c], SP = 100% [57]; confirmation test for cELISA-positive samples	Allows *in vivo* and post-mortem diagnosis and testing of field faecal samples, allows concentration of eggs, little PCR inhibition	Laborious procedure, detects only patent infections, worm burden cannot be quantified	15 samples	[57]
PCR (total DNA)	DNA of eggs and intestinal stages	SE = 89% (compared with IST)[d], SP = 100% [55]; SE = 82% (compared with SCT)[c], SP = 96% [58]	Allows *in vivo* and post-mortem diagnosis, and testing of field faecal samples	Limited amount of material, laborious DNA extraction, inhibition of PCR, worm burden cannot be quantified	15 samples	[55,58]

[a]Abbreviations: cELISA, coproantigen enzyme-linked immunosorbent assay; IST, intestinal scraping technique; PCR, polymerase chain reaction; SCT, sedimentation and counting technique; SE, sensitivity; SP, specificity.
[b]A commercial test is available (Chekit® Echinotest; http://www.bommeli.com).
[c]Target gene: U1 small nuclear RNA gene [54].
[d]Target gene: mitochondrial 12S ribosomal RNA gene [55].

population (Box 1). Hence, low prevalences of *E. multilocularis* of 0.3% and 0.4%, respectively, were found in the densely populated part of eastern Switzerland in 660 randomly selected, living domestic dogs and in 263 cats by detection of specific coproantigen and confirmation of positive results by PCR [42]. In a rural area of western Switzerland, higher prevalences of 7% in 86 dogs and of 3% in 33 cats were recorded [43].

To estimate the relative significance of foxes, dogs and cats as carriers of *E. multilocularis,* the prevalences and

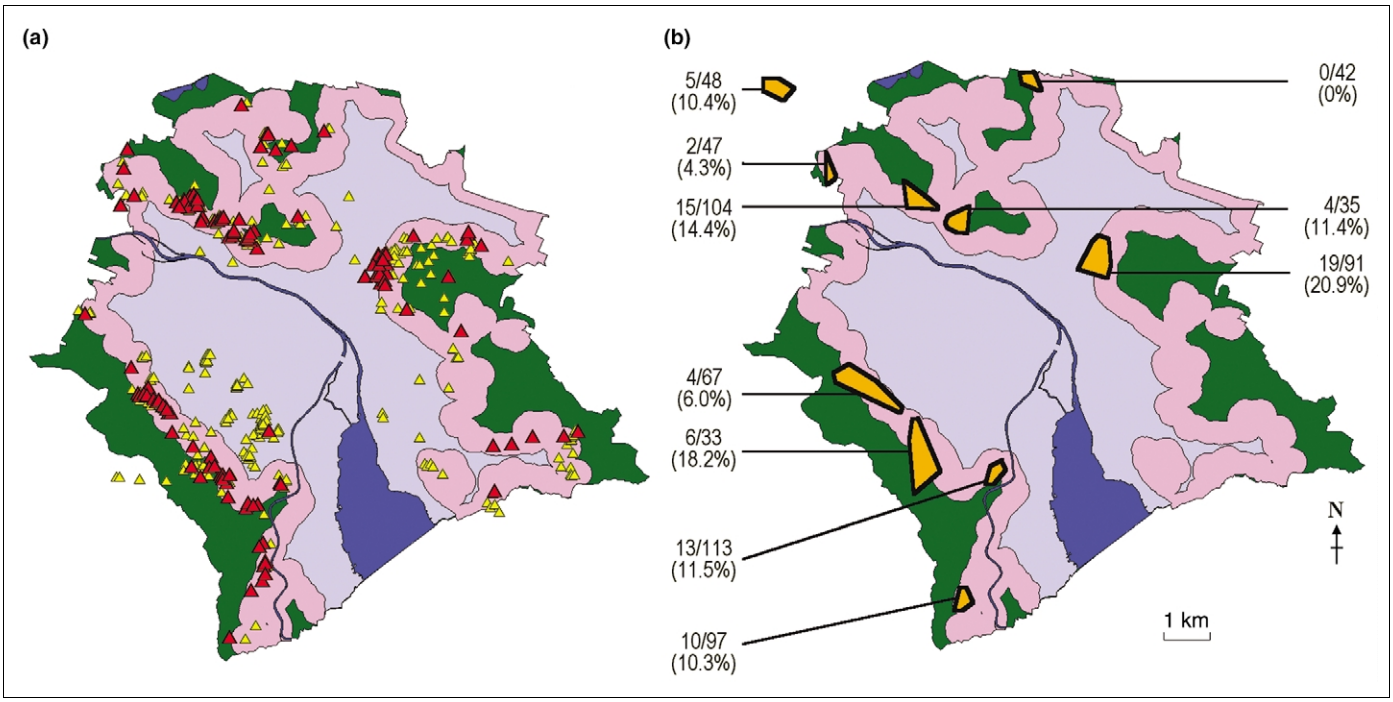

Figure 2. *Echinococcus multilocularis* in Zürich. **(a)** Distribution of coproantigen-positive (red triangles) and -negative (yellow triangles) fox faeces. **(b)** Number of *Arvicola terrestris* positive for *E. multilocularis* from total animals investigated. Key: blue, rivers and lakes; green, urban periphery with forests and agricultural area; lilac, central urban area; orange polygons, trapping areas for *A. terrestris*; pink, urban border area. Figure is modified from Ref. [36].

population sizes of these definitive hosts have to be considered. On the basis of the prevalences in a highly endemic area in eastern Switzerland, ~1500 foxes, 145 dogs and 550 cats were estimated to be infected with *E. multilocularis* in this region [1]. However, not considered in this calculation were the lower susceptibility of cats, the differences in biotic potential between definitive hosts and the impact of transmission routes to humans. Dogs infected with *Taenia* species are known to be contaminated with *Taenia* eggs adhered to the coat all over the whole body and, in selected cases, it was possible to detect *E. multilocularis* proglottids or eggs (confirmed by PCR) in the peri-anal region of infected dogs (Figure 3; P. Deplazes, unpublished). Furthermore, because dogs often roll in fox faeces, the dogs' coats could represent another indirect source of infection.

The patency and survival of *E. multilocularis* in the definitive host is restricted to several months [33]. Therefore, it is pertinent to consider incidence rates covering the life span of dogs or cats to quantify the possible risk of transmission to humans. On the basis of the scarce information of survival and reproduction of *E. multilocularis* in the definitive host, it can be calculated (based on a uniform infection pressure) that dogs or cats, even in populations with very low prevalences, are exposed to a relatively high risk (~10%) of being infected with *E. multilocularis* at least once during their life (Figure 4). However, in rural dogs, which have higher prevalence rates, the probability of being infected once within the first three years of life is ~50%.

Irrespective of the relative risk significance of dogs and cats for humans, it should be stressed that animals with access to rodents in endemic areas should be regarded as potential sources of human infection and be regularly treated with anthelmintics [44].

Options on control of AE in urban areas

The high prevalence of *E. multilocularis* in growing urban fox populations, the environmental contamination with eggs and the emerging public awareness concerning urban zoonoses could justify implementation of control strategies in the future. Apart from ongoing, carefully planned information campaigns about this zoonosis and its potential risks [45], research on possible control strategies is of major interest.

A reduction in the abundance of intermediate rodent hosts is very difficult and controversial from the ecological point of view. The impact of fox culling is questionable and depends on different parameters (e.g. [46]). A general reduction in fox numbers can hardly be achieved with

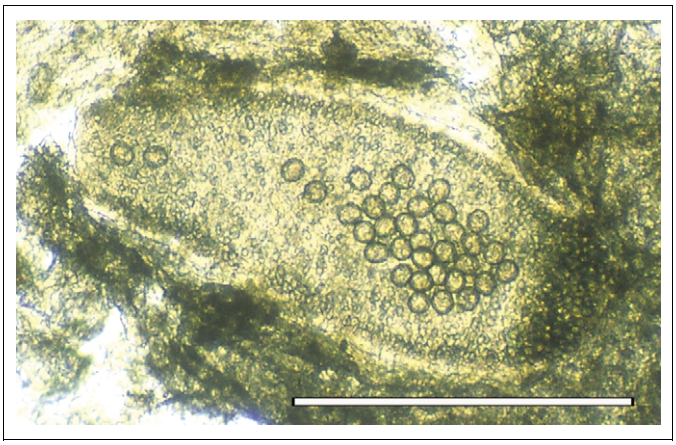

Figure 3. A proglottid of *Echinococcus multilocularis* from the peri-anal region of a coproantigen-positive dog excreting taeniid eggs confirmed by polymerase chain reaction as being *E. multilocularis* eggs. Scale bar = 0.5 mm.

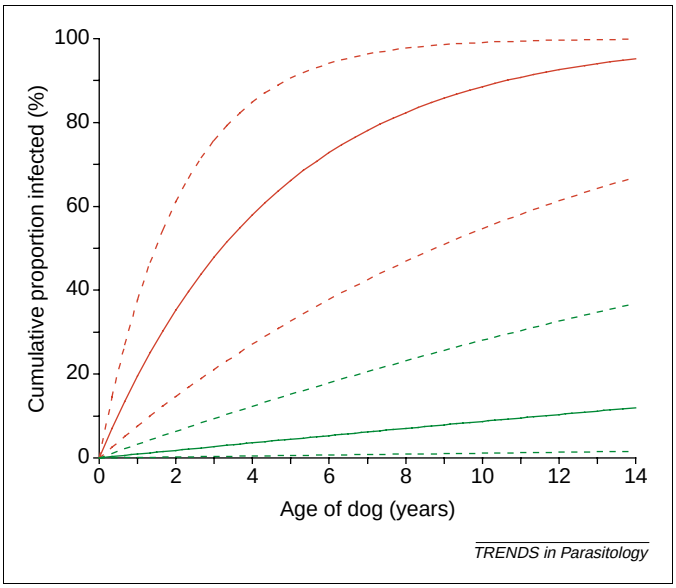

Figure 4. Age-dependant proportion of dogs being infected at least once with *Echinococcus multilocularis* in their lifetime. Cumulative predicted proportion of dogs infected for a representative Swiss dog population (solid green line, prevalence 0.3%; broken green line, 95% confidence interval: 0.04–1.09%) [42] and for a rural farm dog population (solid red line, prevalence 6.9%; broken red line, 95% confidence interval: 2.60–14.57%) [43]. Duration of egg excretion was assumed to be no longer than 120 days.

conventional methods. Furthermore, subadult foxes have a stronger spatial dynamic because of their dispersing behaviour (e.g. [47]). Consequently, hunting mainly affects the population structure by causing a proportional increase of juvenile foxes [13]. These are known to harbour up to 85% of the total biomass of *E. multilocularis* found in a fox population [31]. Therefore, culling could have a counterproductive effect on zoonosis prevention and could even facilitate disease transmission [48].

Several attempts have been made to control *E. multilocularis* by anthelmintic treatment of wild foxes. The first study, in southern Germany, demonstrated the general feasibility of such an approach [49] and, in consecutive field trials, experience was gathered on large-scale application under different levels of endemicity. In one trial (3500 km^2 area within a high endemicity region of southwest Germany), baits containing praziquantel were distributed in densities of 20 per km^2 using small aircraft, according to the protocol of concurrent rabies immunization campaigns. After 1.5 years of repeated baiting at six-week intervals, prevalences calculated from shot foxes were reduced from an initial prevalence of 64% (95% confidence intervals: 59–69%) to 18% (95% confidence intervals: 13–24%) [5]. During a further 1.5 years of baiting at three-month intervals, the prevalence remained low, whereas within two years of gradual discontinuation of baiting, the prevalence reversed to almost pre-control levels (T. Romig, unpublished). The results of this study are in agreement with a similar large-scale trial in northeastern Germany [50]. There, the study area of 5000 km^2 contained two circumscribed endemic foci and a low-endemic periphery. Bait distribution was similar to the study above, with one year at six-week intervals, followed by a further year at three-month intervals. Prevalences were strongly reduced from 15.6–26.8% in the year before control to 1.9–6.2% in the last year of control in the endemic area, and from 4.1–7.1% to 0.0–1.0% in the low-endemic area, respectively [50].

In all studies addressing anthelmintic intervention against sylvatic *E. multilocularis* transmission, prevalences in foxes decreased considerably, but eradication was not achieved. For improvement of control efficacy, potential factors responsible for persistence of the transmission need to be elucidated. One potentially important parameter is the sub-population of foxes having home ranges in or near human settlements. Such foxes are less likely to have access to baits dispersed by aircraft. However, they are still exposed to *E. multilocularis* infection by rodent populations in or near towns. Fox densities in cities and towns are frequently higher than those in the open landscape [22,38]. Because of obviously closer contact with the humans, the inclusion of such synanthropic fox populations in control strategies is a matter of priority. *Echinococcus multilocularis* control in urban foxes could either be a part of large-scale intervention measures or a strategy on its own by concentrating on areas of more-intense contact between foxes and humans.

Fox baiting in urban areas has so far not been critically evaluated. A camera trap study in Zürich based on 'movement photos' revealed that domestic cats and foxes were most frequently photographed at baiting places, but neither the cats nor the few observed stone martens and badgers fed on the baits, as documented by 'removal photos' (D. Hegglin, PhD Thesis, University of Zürich, 2003). Most of the removed baits were taken by foxes (48%), but also hedgehogs (19%), dogs (9%), snails (10%) and mice (4%) consumed the baits [51].

The cycle of *E. multilocularis* in urban settings seems to be determined by the small home ranges of foxes and the distribution of suitable intermediate hosts. Therefore, local interference in the cycle that reduces the infection pressure in defined areas that are intensively used by humans (e.g. public parks, swimming pool areas, private gardens) should be feasible. Field experimental studies in Zürich on the control of *E. multilocularis* infection in such areas by manually distributing praziquantel-containing baits (50 baits km^{-2} per month) have shown that a reduction of infection pressure on defined small urban patches with a high *E. multilocularis* egg contamination is feasible and also results in a significant lower prevalence in the intermediate hosts [52]. Within six bait areas of 1 km^2, the portion of *E. multilocularis* coproantigen-positive faeces dropped from 24.6% to 5.5%, and the prevalence in *A. terrestris* from 8.4% to 1.0% after 16 months of treatment. In the six control areas (also 1 km^2 each), the portion of coproantigen-positive faeces and the prevalence in *A. terrestris* remained unchanged [52].

So far, no resistance of tapeworms to any anthelmintics has been observed, even in *E. granulosus* control programs with continuous treatment of dogs over many years. However, long-term consequences of praziquantel treatment in wild carnivore populations should be carefully monitored.

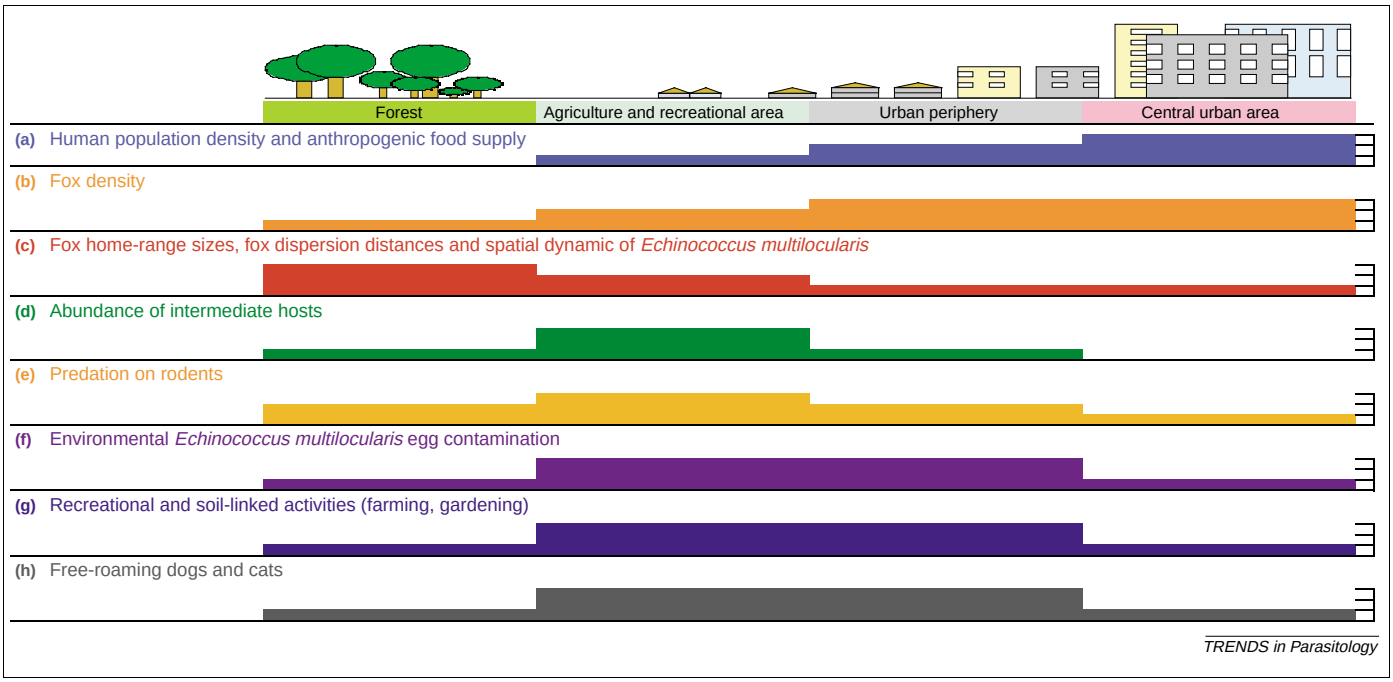

Figure 5. Factors affecting the urban cycle of *Echinococcus multilocularis* and the infection pressure with *Echinococcus multilocularis* eggs. The relative impact of the different factors according to the degree of urbanization is indicated by the magnitude of the bars. **(a)** Increasing human population density from rural area (forest) towards the city centre is linked with an increase of anthropogenic food supply [24]. **(b)** This surplus of food resource allows high fox densities in urban areas [59]. **(c)** High fox densities correlate with small home ranges and small dispersion distances [22]. This restricted spatial behaviour of urban foxes also limits the spatial dynamic of *E. multilocularis* because the final host species are much more mobile than the intermediate host species. **(d)** Along the urban border areas, there are large meadows for agricultural and recreational use, which offer a suitable habitat for *Arvicola terrestris* and *Microtus arvalis*, two of the intermediate hosts of major importance in western Europe [60]. **(e)** Rodents are less accessible for predation by foxes in forest than in open landscapes. As the supply of voles decreases towards the city centre, predation of voles by foxes is also less frequent [24] (D. Hegglin, unpublished). **(f)** In the borderland between rural and urban habitat, high fox population densities intersect with suitable habitats for voles and, as a consequence, environmental *E. multilocularis* egg contamination is the highest [36]. **(g)** At the same time, this area is intensively used by a broad section of the public for recreational and soil-linked activities, and **(h)** densities of domestic cats and dogs, which can acquire the parasite by preying on infected voles, are high.

Conclusions

On the basis of the high prevalence of *E. multilocularis* in the growing fox populations, the total biomass has probably increased significantly in the past 20 years in central Europe. As illustrated in Figure 5, various factors determine the degree of *E. multilocularis* egg contamination, which reaches a maximum in villages and urban peripheries where rural and urban habitats intersect. Because the public intensively uses these areas, they could play an important role for transmission of human AE and should be considered as public health importance. Furthermore, the establishment of the *E. multilocularis* cycle in urban and peri-urban areas has enhanced the potential risk of infection for domestic definitive hosts. Recent data from the European Register of Alveolar Echinococcosis (http://www.uni-ulm.de/uni/fak/medizin/biodok/abteilung/echiweb.htm) document the significance of this dangerous infection [40]. Continuous monitoring of this potentially emerging zoonosis throughout Europe has therefore been recommended [40]. Control strategies aimed at the domestic dog and cat population [44], as well as baiting strategies for rural or urban foxes, are feasible and can significantly reduce the environmental contamination with *E. multilocularis* eggs, even if only applied locally. However, introduction of such long-lasting control programs is not only an epidemiological issue, but also a political issue.

Acknowledgements

We acknowledge the support of our research activities by the Swiss National Science Foundation (grant no. 31–47031.96), the Swiss Federal Office of Veterinary Medicine, Berne, the Swiss Federal Office for Education and Science (EU FAIR Projekt CT97–3515/BBW Nr. 97.0586), and the European Commission (Project Echinorisk, Contract QLK2-CT-2001–01995). We are grateful to Andreas König, Dorothea Thoma and Claude Fischer for the provision of unpublished observations.

References

1 Eckert, J. and Deplazes, P. (1999) Alveolar echinococcosis in humans: the current situation in Central Europe and the need for countermeasures. *Parasitol. Today* 15, 315–319
2 Petavy, A.F. *et al.* (1991) Life cycles of *Echinococcus multilocularis* in relation to human infection. *J. Parasitol.* 77, 133–137
3 Schantz, P.M. *et al.* (1995) Epidemiology and control of hydatid disease. In *Echinococcus and Hydatid Disease* (Thompson, R.C.A. and Lymbery, A.J., eds) pp. 233–331, CAB International
4 Craig, P.S. *et al.* (2000) An epidemiological and ecological study on human alveolar echinococcosis transmission in Gansu, China. *Acta Trop.* 77, 167–177
5 Romig, T. *et al.* (1999) Bekämpfung von *Echinococcus multilocularis* in einem Hochendemiegebiet Süddeutschlands. In *Tagung der Fachgruppe 'Parasitologie und Parasitäre Krankheiten'* (Society, G.V.M., ed.), pp. 172–183, Verlag der Deutschen Veterinärmedizinischen Gesellschafte e. V.
6 Eckert, J. *et al.* (2001) Geographic distribution and prevalence. In *WHO/OIE Manual on Echinococcosis in Humans and Animals* (Eckert, J. *et al.*, eds), pp. 100–142, Office International des Epizooties
7 Romig, T. *et al.* (1999) *Echinococcus multilocularis* in animal hosts: new data from western Europe. *Helminthologia* 36, 185–191
8 Sréter, T. *et al.* (2003) *Echinococcus multilocularis*: an emerging pathogen in Hungary and Central Eastern Europe? *Emerg. Infect. Dis.* 9, 384–386
9 Chautan, M. *et al.* (2000) Role of rabies in recent demographic changes in red fox (*Vulpes vulpes*) populations in Europe. *Mammalia* 64, 391–410
10 Breitenmoser, U. *et al.* (2000) The final phase of the rabies epizootic in Switzerland. *Schweiz. Arch. Tierheilkd.* 142, 447–454

11 Gloor, S. *et al.* (2001) The rise of urban fox populations in Switzerland. *Mamm. Biol.* 66, 155–164
12 Harris, S. and Rayner, J.M.V. (1986) A discriminant analysis of the current distribution of urban foxes (*Vulpes vulpes*) in Britain. *J. Anim. Ecol.* 55, 605–611
13 Harris, S. (1977) Distribution, habitat utilization and age structure of a suburban fox (*Vulpes vulpes*) population. *Mamm. Rev.* 7, 25–39
14 Macdonald, D.W. and Newdick, M.T. (1982) The distribution and ecology of foxes, *Vulpes vulpes* (L.), in urban areas. In *Urban Ecology: Proceedings of the Second European Ecological Symposium* (Bornkamm, R. *et al.*, eds), pp. 123–135, Blackwell Scientific Publications
15 Vos, A.C. (1994) Reproductive-performance of the red fox, *Vulpes vulpes*, in Garmisch-Partenkirchen, Germany, 1987–1992. *Mamm. Biol.* 59, 326–331
16 Wandeler, A.I. *et al.* (1988) Oral immunization of wildlife against rabies: concept and first field experiments. *Rev. Infect. Dis.* 10, S649–S653
17 Christensen, H. (1985) Urban fox population in Oslo. *Revue d'Ecologie* 40, 185–186
18 Moller Nielsen, S. (1990) The food of rural and suburban woodland foxes *Vulpes vulpes* in Denmark. *Nat. Jutl.* 23, 25–32
19 Adkins, C.A. and Stott, P. (1998) Home ranges, movements and habitat associations of red foxes *Vulpes vulpes* in suburban Toronto, Ontario, Canada. *Can. J. Zool.* 244, 335–346
20 Tsukada, H. *et al.* (2000) Preliminary study of the role of red foxes in *Echinococcus multilocularis* transmission in the urban area of Sapporo, Japan. *Parasitology* 120, 423–428
21 Doncaster, C.P. and Macdonald, D.W. (1991) Drifting territoriality in the red fox *Vulpes vulpes*. *J. Anim. Ecol.* 60, 423–440
22 Trewhella, W.J. *et al.* (1988) Dispersal distance, home-range size and population density in the red fox (*Vulpes vulpes*): a quantitative analysis. *J. Appl. Ecol.* 25, 423–434
23 Dip, R. *et al.* (2001) Comparison of heavy metal concentrations in tissues of red foxes from adjacent urban, suburban, and rural areas. *Arch. Environ. Contam. Toxicol.* 40, 551–556
24 Contesse, P. *et al.* The diet of urban foxes (*Vulpes vulpes*) and the availability of anthropogenic food in the city of Zürich, Switzerland. *Mamm. Biol.* (in press)
25 Wandeler, P. *et al.* (2003) The city-fox phenomenon: genetic consequences of a recent colonization of urban habitat. *Mol. Ecol.* 12, 647–656
26 Baker, P.J. *et al.* (2000) Flexible spatial organization of urban foxes, *Vulpes vulpes*, before and during an outbreak of sarcoptic mange. *Anim. Behav.* 59, 127–146
27 Harris, S. (1981) The food of suburban foxes (*Vulpes vulpes*), with special reference to London. *Mamm. Rev.* 11, 151–168
28 Doncaster, C.P. *et al.* (1990) Feeding ecology of red foxes (*Vulpes vulpes*) in the city of Oxford, England. *J. Mammal.* 71, 188–194
29 Kapel, C.M.O. and Saeed, I. (2000) *Echinococcus multilocularis* – en ny zoonotisk parasit I Denmark. *Dansk Veterinaer. Tidsskrift* 83, 14–16
30 Fischer, C. *et al.* (2003) Relation in the presence of various parasites in the red fox (*Vulpes vulpes*) in Geneva. *Swiss Med. Wkly.* 133, S61
31 Hofer, S. *et al.* (2000) High prevalence of *Echinococcus multilocularis* in urban red foxes (*Vulpes vulpes*) and voles (*Arvicola terrestris*) in the city of Zürich, Switzerland. *Parasitology* 120, 135–142
32 Raoul, F. *et al.* (2001) Assessment of the epidemiological status of *Echinococcus multilocularis* in foxes in France using ELISA coprotests on fox faeces collected in the field. *Int. J. Parasitol.* 31, 1579–1588
33 Nonaka, N. *et al.* (1996) Time course of coproantigen excretion in *Echinococcus multilocularis* infections in foxes and an alternative definitive host, golden hamsters. *Int. J. Parasitol.* 26, 1271–1278
34 Torgerson, P.R. *et al.* (2003) Modelling the transmission dynamics of *Echinococcus granulosus* in dogs in rural Kazakhstan. *Parasitology* 126, 417–424
35 Deplazes, P. *et al.* (2002) Urban transmission of *Echinococcus multilocularis*. In *Cestode Zoonoses: Echinococcosis and Cysticercosis* (Craig, P. and Pawlowski, Z., eds), pp. 287–297, IOS Press
36 Stieger, C. *et al.* (2002) Spatial and temporal aspects of urban transmission of *Echinococcus multilocularis*. *Parasitology* 124, 631–640
37 Calhoon, R. and Haspel, C. (1989) Urban cat populations compared by season, subhabitat and supplemental feeding. *J. Anim. Ecol.* 58, 321–328
38 Harris, S. and Rayner, J.M.V. (1986) Urban fox (*Vulpes vulpes*) population estimates and habitat requirements in several British cities. *J. Anim. Ecol.* 55, 575–591
39 Thompson, R.C.A. (1995) Biology and systematics of *Echinococcus multilocularis*. In *Echinococcus and Hydatid Disease* (Thompson, R.C.A. and Lymbery, A.J., eds), pp. 1–50, CAB International
40 Kern, P. *et al.* (2003) European echinococcosis registry: human alveolar echinococcosis, Europe, 1982–2000. *Emerg. Infect. Dis.* 9, 343–349
41 Petavy, A.F. *et al.* (2000) *Echinococcus multilocularis* in domestic cats in France. A potential risk factor for alveolar hydatid disease contamination in humans. *Vet. Parasitol.* 87, 151–156
42 Deplazes, P. *et al.* (1999) *Echinococcus multilocularis* coproantigen detection by enzyme-linked immunosorbent assay in fox, dog, and cat populations. *J. Parasitol.* 85, 115–121
43 Gottstein, B. *et al.* (2001) Is high prevalence of *Echinococcus multilocularis* in wild and domestic animals associated with disease incidence in humans? *Emerg. Infect. Dis.* 7, 408–412
44 Deplazes, P. and Eckert, J. (2001) Veterinary aspects of alveolar echinococcosis – a zoonosis of public health significance. *Vet. Parasitol.* 98, 65–87
45 Bontadina, F. *et al.* (2001) INFOX – Kommunikation für ein konfliktarmes Zusammenleben von Menschen und Stadtfüchsen. *For. Snow Landsc. Res.* 76, 267–284
46 Heydon, M.J. and Reynolds, J.C. (2000) Fox (*Vulpes vulpes*) management in three contrasting regions of Britain, in relation to agricultural and sporting interests. *J. Zool.* 251, 237–252
47 Harris, S. and Trewhella, W.J. (1988) An analysis of some of the factors affecting dispersal in an urban fox (*Vulpes vulpes*) population. *J. Appl. Ecol.* 25, 409–422
48 Tuyttens, F.A.M. *et al.* (2000) Spatial perturbation caused by a badger (*Meles meles*) culling operation: implications for the function of territoriality and the control of bovine tuberculosis (*Mycobacterium bovis*). *J. Anim. Ecol.* 69, 815–828
49 Schelling, U. *et al.* (1997) Chemotherapy with praziquantel has the potential to reduce the prevalence of *Echinococcus multilocularis* in wild foxes (*Vulpes vulpes*). *Ann. Trop. Med. Parasitol.* 91, 179–186
50 Tackmann, K. *et al.* (2001) A field study to control *Echinococcus multilocularis*-infections of the red fox (*Vulpes vulpes*) in an endemic focus. *Epidemiol. Infect.* 127, 577–587
51 Hegglin, D. *et al.* Baiting red foxes in an urban area: a camera trap study. *J. Wildl. Manage.* (in press)
52 Hegglin, D. *et al.* (2003) Anthelmintic baiting of foxes against urban contamination with *Echinococcus multilocularis*. *Emerg. Infect. Dis.* 9, 1266–1272
53 Eckert, J. *et al.* (2001) Echinococcus in animals: clinical aspects, diagnosis and treatment. In *WHO/OIE Manual on Echinococcosis in Humans and Animals* (Eckert, J. *et al.*, eds), pp. 72–99, Office International des Epizooties
54 Bretagne, S. *et al.* (1993) Detection of *Echinococcus multilocularis* DNA in fox faeces using DNA amplification. *Parasitology* 106, 193–199
55 Dinkel, A. *et al.* (1998) Detection of *Echinococcus multilocularis* in the definitive host: coprodiagnosis by PCR as an alternative to necropsy. *J. Clin. Microbiol.* 36, 1871–1876
56 Sakai, H. *et al.* (1998) Coproantigen detection in a survey of *Echinococcus multilocularis* infection among red foxes, *Vulpes vulpes schrencki*, in Hokkaido, Japan. *J. Vet. Med. Sci.* 60, 639–641
57 Mathis, A. *et al.* (1996) An improved test system for PCR-based specific detection of *Echinococcus multilocularis* eggs. *J. Helminthol.* 70, 219–222
58 Monnier, P. *et al.* (1996) Improvement of a polymerase chain reaction assay for the detection of *Echinococcus multilocularis* DNA in faecal samples of foxes. *Vet. Parasitol.* 67, 185–195
59 Saunders, G. *et al.* (1993) Urban foxes (*Vulpes vulpes*): food acquisition, time and energy budgeting of a generalized predator. In *Mammals as Predators* (Vol. 65) (Dunstone, N. and Gorman, M.L., eds), pp. 215–234, Oxford University Press
60 Giraudoux, P. *et al.* (2002) Transmission ecology of *Echinococcus multilocularis* in wildlife: what can be learned from comparative studies and multiscale approaches? In *Cestode Zoonoses: Echinococcosis and Cysticercosis* (Craig, P. and Pawlowski, Z., eds), pp. 251–266, IOS Press