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Efficacy of anthelmintic baiting of foxes against *Echinococcus multilocularis* in northern Japan

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ABSTRACT

Field application of anthelmintic baits against *Echinococcus multilocularis* in red foxes (*Vulpes vulpes*) was conducted on Nemuro Peninsula at the eastern edge of Hokkaido, Japan. The total study area was 412 km^2, of which 135 km^2 were used for bait distribution. Commercial baits containing 50 mg praziquantel were distributed by car along roads outside towns and villages in a density of 15/km^2. Additional baits were distributed around fox breeding dens. Baiting was done from November 1999 to January 2006 at an average frequency of 4.3 distribution rounds per years (in total 27 rounds). Prevalence in foxes collected in the baiting and non-baiting areas were determined by necropsy. Base prevalence (before baiting) was 49.4% (CI95%: 43.7–55.0) in the baiting area and 70.5% (CI95%: 60.2–79.2) in the non-baiting area. During the first and second half of the baiting period, the prevalence in the baited area changed to 26.2% (CI95%: 14.4–42.3) and later to 15.8% (CI95%: 7.9–28.4), but remained at a high level in the neighboring non-baited area with 60.4% (CI95%: 45.3–73.9) and 65.0% (CI95%: 40.9–83.7). Our data show, that significant prevalence reduction (but not elimination) of *E. multilocularis* in foxes can be achieved by this method under epidemiological conditions, which are fundamentally different from those in Europe where most previous studies have been done.

1. Introduction

The fox tapeworm *Echinococcus multilocularis* is the causative agent of alveolar echinococcosis (AE), one of the most severe parasitic zoonoses in the temperate and cold regions of the northern hemisphere. Globally, AE is estimated to cause the annual loss of 650,000 disability-adjusted life years (Torgerson and Craig, 2011). Fox populations and the prevalence of *E. multilocularis* have been increasing in many regions, and foxes have adapted to man-made environments, in Japan as well as in Europe (Tsukada et al., 2000; Gloor et al., 2001; Deplazes et al., 2004; Romig et al., 2006). Recent reports show that the parasite has the potential to invade previously non-endemic countries or regions, and national regulations to prevent introduction e.g. via infected companion animals or via translocation of wildlife seem to be of little effect (Davidson et al., 2012). In this situation, effective methods to counteract transmission of this wildlife-transmitted zoonosis are highly desirable.

There are few options for such countermeasures. Vaccinations for humans or animals will not be available in the foreseeable future. Risk-based anthelmintic treatment of domestic dogs and improved knowledge about transmission routes are assumed to decrease the infection pressure to humans, but will have little impact on the

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persistence of the parasite's lifecycle (Kern et al., 2004; Hegglin et al., 2008; Deplazes et al., 2011). Concerning host animal control, large-scale destruction of rodents is unfeasible, and an effective control of foxes by intense hunting or trapping is not practical and accepted in most affected regions (Hegglin and Deplazes, 2013).

Several field trials to assess the efficacy of anthelmintic baiting against *E. multilocularis* in foxes have been carried out in Europe (Hegglin and Deplazes, 2013). Longitudinal studies in areas of up to 5000 km^2, where praziquantel baits were repeatedly distributed by aircraft, demonstrated a marked decrease of cestode prevalence in foxes, although elimination in the treated areas was not achieved (Tackmann et al., 2001; Romig et al., 2007). Likewise, local application of baits in small and fragmented urban settings gave promising and sustainable results (Hegglin and Deplazes, 2008). After 3 years of a baiting trial in southern Germany, where both large-scale and local applications were combined, the prevalence of *E. multilocularis* in foxes was effectively reduced to sporadic occurrence (König et al., 2008).

Hokkaido, the northernmost island of Japan, is the only area of the country where AE is endemic. Up to the present, more than 600 human cases have been recorded since 1937. The life cycle of *E. multilocularis* in Europe is closely linked to the presence of agriculturally managed open grassland without cover of higher vegetation, which is the habitat of the main intermediate hosts (common vole *Microtus arvalis* and fossorial water vole *Arvicola scherman*) (Giraudoux et al., 2002; Romig et al., 2006). In contrast, the main intermediate hosts species in Hokkaido are red-backed voles of the genus *Myodes* (mainly *M. rufocanus*), which inhabit woodlands and open habitats with dense coverage of plants such as bamboo grass (*Sasa* spp.) (Ohbayashi, 1996; Takahashi and Uraguchi, 1996; Kaneko et al., 1998). Therefore, baiting methods evaluated in Europe cannot be uncritically applied in Japan. Small scale trials to evaluate the efficacy of fox chemotherapy were carried out in Hokkaido. Praziquantel tablets in baits made from fish products were placed near fox dens every month for 13 months in a 90 km^2 area in eastern Hokkaido (Tsukada et al., 2002). It was shown that coproantigen ELISA positive rate of fox feces decreased from 60% to 30%. A similar bait, containing praziquantel powder, was used in a 110 km^2 area on Hokkaido, where prevalence in foxes decreased from 58% to 11% within 4 years (Inoue et al., 2007).

Here, we report a study in eastern Hokkaido using a method to distribute praziquantel in commercial baits (Droncit® bait) in a standardized and time-efficient schedule by car along roads. A preliminary description of this study, with incomplete data, had been published in Japanese language (Takahashi et al., 2002).

2. Materials and methods

The study was conducted within the administrative boundary of Nemuro (412 km^2), which is located at the eastern edge of Hokkaido with a human population of 29,000 (December 2012 census). The area is composed of pastures, other grasslands, woodlands and residential areas. The study area was divided into a baiting area (135 km^2) and control area (277 km^2) (Fig. 1). The baiting area consists of a peninsula and is inhabited by >90% of the total population of Nemuro. Fox baits containing 50 mg praziquantel (Droncit® bait, Bayer AG, Leverkusen, Germany) were distributed by car along roads at a density of 15 baits/km^2. Additional baits were distributed around fox breeding dens once in each breeding season (a total of 103 dens were treated with 20–30 baits each during the study period). From November 1999 to January 2006, 27 rounds of bait distribution were done (4.3 rounds annually on average). For practical reasons, the number of rounds was 1–2 in the cold season and 2–4 from spring to autumn. Sub-samples of baits (n = 93–139) were checked for their disappearance rate at day 3 after distribution during 10 baiting rounds from 1999 to 2002. To evaluate the efficacy of baiting, foxes were examined by necropsy for the presence of *E. multilocularis* worms. Foxes were shot by local hunters in winter, some samples were additionally obtained between spring and autumn. The collection of samples was as evenly spread over the study areas as practically possible. In total, 411 and 163 foxes were collected from the baiting and control areas, respectively, during a pre-baiting period (April 1994 to March 1999) and the baiting period (November 1999 to March 2006). Further, the prevalence was monitored for 2 years after the last bait distribution in the baiting area (76 foxes), while for logistical reasons foxes could not be obtained in relevant numbers from the control area. Fox carcasses were kept frozen at −20 °C until examination. Necropsy was done in a safety laboratory equipped for handling of biohazardous material. The small intestine was transferred to a tray with water and slit open longitudinally. The mucosa was detached from the intestine using a metal scraper. Thereafter, the removed mucosa and intestine contents were macroscopically examined under water cover for adult worms. Parasites were confirmed using a microscope. Graphical displays and prevalence 95% confidence

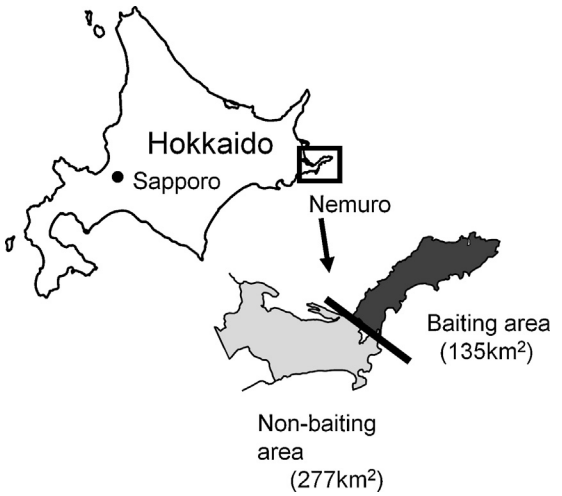

Fig. 1. Study area (total 412 km^2) in Nemuro city, Hokkaido, Japan.