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Mathematical modeling of *Echinococcus multilocularis* transmission

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## **Abstract**

A mathematical model for the transmission cycle of *Echinococcus multilocularis* would be useful for estimating its prevalence, and the model simulation can be instrumental in designing various control strategies. This review focuses on the epidemiological factors in the *E. multilocularis* transmission cycle and the recent advances of mathematical models for *E. multilocularis* transmission.

*Keywords:* *Echinococcus multilocularis*; Fox; Mathematical model; Vole.

## 1. Introduction

*Echinococcus multilocularis* is distributed in central Europe, North America, and northern and central Eurasia [1]. In Japan, human alveolar Echinococcus (HAE) caused by *E. multilocularis* has spread throughout the mainland of Hokkaido [2], making it desirable to design effective control strategies against HAE. It is difficult to elucidate the source of infections due to the long incubation period [3]. A mathematical model for the transmission cycle of *E. multilocularis* would be useful for estimating its prevalence, and the model simulation can be instrumental in designing various control strategies. A few models about *E. multilocularis* transmission have been proposed since 1995 [4-6]. This review focuses on the epidemiological factors in the *E. multilocularis* transmission cycle and the recent advances of mathematical models for *E. multilocularis* transmission.

*E. multilocularis* carries out its transmission cycle in two hosts; the definitive hosts are canines, while the intermediate hosts are mainly rodents and ungulates [1, 7-9]. Individuals are infected by the accidental ingestion of parasite eggs. The intermediate hosts are infected by ingesting parasite eggs voided in the feces of infected definitive hosts, while the definitive hosts are infected by preying on the intermediate hosts that have hydatid cysts. A mathematical model which quantitatively describes the

transmission of *E. multilocularis* needs to include the following components [5, 10]

1. dynamics of definitive host population
2. dynamics of intermediate host population
3. predator-prey relationship between the definitive hosts (canines) and the intermediate hosts (rodents)
4. longevity of parasite eggs in the environment.

## **2. Dynamics of definitive hosts**

Foxes mainly maintain the transmission cycle of *E. multilocularis*. The major definitive host is the red fox (*Vulpes vulpes*) for most endemic regions, or the arctic fox (*Alopex lagopus*) for the tundra zone of Eurasia and North America [1, 7, 9, 11]. The dynamics of the fox population show marked seasonal variations because foxes are wild animals. Therefore, a quantitative transmission model needs to include a host population dynamic component [5]. In Hokkaido, Japan, the breeding season of red foxes is generally early spring (the last third of March - the first third of April) and newborns after weaning, which might be exposed to *E. multilocularis* infection, emerge from their dens one month after birth [12]. Generally, for any wild animal the death rate of juveniles is significantly higher than that of adults. The death rate of juvenile (under 1

year old) red foxes in Hokkaido was estimated to be 2.5 times higher than that of adults [5]. The seasonal population model of red fox density in Hokkaido is shown in Fig. 1. The arctic fox population is also influenced by emigration and immigration due to long-distance traveling [11].

### **3. Dynamics of intermediate hosts**

Rodents mainly maintain the transmission cycle of *E. multilocularis* as the intermediate hosts, and the species that are involved in the cycle vary in different endemic regions [1, 9]. In Hokkaido, the major intermediate host is the gray-sided vole (*Clethrionomys rufocanus*) [7]. The gray-sided vole breeds in three seasons of the year (all seasons except winter) [13, 14]. The survival rate of voles depends on the season and age, with that for the first month of life being lower than that of >1 month [13, 14], while the survival rate in winter is higher than that in summer [15]. Besides the season variation, the dynamics of the vole population vary on a large scale annually, and have certain geographical characteristics [16]. There is no necessity to consider emigration or immigration in the dynamics of the vole population because of the small size of home ranges [13].

#### **4. Transmission processes of *Echinococcus multilocularis***

The definitive host is infected with *E. multilocularis* by preying on rodents which harbor multilocular *Echinococcus* with infectious protoscoleces. Therefore, the prevalence of *E. multilocularis* is affected by the average number (NVF) of voles ingested by a fox each day, which depends on the density of the vole population and on the depth of the snow factors [17, 18], which were introduced into the transmission model [5].

The intermediate host is infected by ingesting *E. multilocularis* eggs voided in the feces of infected definitive hosts. The duration of the egg's infectious ability is mainly affected by temperature and humidity. The tenacity of eggs is sensitive to elevated temperature, to very low temperature and to desiccation [19]. The experimental formula for the longevity ( $d$  days) of eggs at temperature ( $t$  °C) was established as  $d = \exp[-0.135(t-43.7)]$  [20].

#### **5. Mathematical models of *Echinococcus multilocularis* transmission**

A deterministic model for the transmission of a parasite essentially describes its transmission cycle as a set of differential equations. Roberts and Aubert [4] constructed a simple deterministic *E. multilocularis* transmission model to evaluate the effect of

control by addition of praziquantel in France. Ishikawa et al. [5] proposed a model that took into account the influence of the dynamics of both the definitive and the intermediate host populations and the seasonal effects on the longevity of *E. multilocularis* eggs and NVF to describe the mechanism of seasonal transmission in Hokkaido quantitatively. Hansen et al. [6] tried to develop a stochastic transmission model from the Roberts and Aubert model to devise a hypothesis that would fit well with the prevalence data during the pre- and post-control periods in the northern Germany. In these models [4-6], each host population is broadly divided into three epidemiology classes. Moreover, in the quantitative model shown in Fig.2 [5], the infected egg-producing class in foxes is subdivided into two subclasses according to whether egg production is abundant or not.

The basic reproductive rate ( $R_0$ ) is the theoretically maximum number of secondary infections.  $R_0$  was estimated from the Roberts and Aubert model [4] or the model of Ishikawa et al. excluding seasonal factors [5] as follows:

$$R_0 = \frac{\lambda_f \lambda_v \overline{N_f}}{\delta_v (1 + \delta_v \tau_v) (1 + \delta_f \tau_f) (1 + \delta_f \eta_t)} \eta_t$$

$$R_0 = \frac{s_f \overline{NVF} \lambda_v \overline{N_f}}{\delta_v (1 + \delta_v \tau_v) (1 + \delta_f \tau_f) (1 + \delta_f \eta_h)} \left( \rho \eta_h + \frac{\eta_l}{1 + \delta_f \eta_l} \right)$$



The symbols  $\lambda_a, \delta_a, \tau_a, s_f, \overline{NVF}, \overline{N_f}, \eta_t, \eta_h, \eta_l$ , and  $\rho$  represent the infectious contact rate ( $a=s, v$ ), the death rate ( $a=s, v$ ), the period of no egg production ( $a=f$ ) or for acquiring infectious protoscoleces ( $a=v$ ) expressed as days after infection, the conditional probability of maturity of worms ( $f$ ), the average NVF, the average of density ( $f$ ), the durations of total, high and low egg production, and the multiplicative factor caused by high egg production, with the suffixes  $f$  and  $v$  standing for fox and vole, respectively.

The seasonal variations of the prevalence and the density of infected foxes were simulated for the two endemic regions in Hokkaido, Japan: Nemuro and Abashiri, where the average prevalence rates (1995-2000) were 53% and 48%, respectively. There is a great difference between the two regions in terms of snowfall. Comparison of two regions using the model simulation shows that the winter density of the infected foxes is maintained at a certain level in Nemuro, while it falls to a low level in Abashiri, which leads to the difference of the winter prevalence between Nemuro and Abashiri (Fig. 3) [5].

## 6. Risk of HAE

The risk to the human population of being infected with HAE has a close relation to the amount of *E. multilocularis* eggs that maintain infectious ability in the environment. A comparative study on the risk of HAE between Sapporo, the capital of Hokkaido, and Nemuro was carried out by simulating the seasonal fluctuation in *E. multilocularis* egg dispersion in the environment based on the model [5].

## **7. Prospects**

Recent advances in mathematical modeling of *E. multilocularis* transmission were summarized here. There has been steady progress in mathematical modeling of *E. multilocularis* transmission into consideration taking seasonal factors. Further follow-up studies based on field data will be needed to precisely estimate the effects of control strategies against *E. multilocularis* using model simulations.

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## Legends

### Fig. 1

The seasonal population dynamics models for foxes and voles in Hokkaido. The solid line and the dotted line shows the variations in fox and vole density /km<sup>2</sup>, respectively [5]

### Fig. 2

The basic scheme for the model of the *Echinococcus multilocularis* transmission cycle between foxes (the major definitive host) and voles (the major intermediate host).

### Fig. 3

Seasonal variations in the density/km<sup>2</sup> of foxes infected with *E. multilocularis* (solid line) and the prevalence of *E. multilocularis* in the fox population (broken line). The black and gray lines show the Nemuro and Abashiri situations, respectively [5].