Biology

Microbiology & Immunology fields

Okayama University   *Year* 2003

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A Model for the Transmission of *Echinococcus multilocularis* in Hokkaido, Japan

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Abbreviations:

HAE, human alveolar echinococcosis; NVF, the average number of voles ingested by a fox a day;

Abstract

A mathematical model for *Echinococcus multilocularis* transmission would be useful to estimate its prevalence and manage control strategies. We propose a mathematical model which quantitatively describes the transmission of *E. multilocularis* in Hokkaido, Japan. The model takes into account the influence of the dynamics of both the definitive and the intermediate host populations, which show large scale seasonal variations as they are wild animals. The simulations based on the model clarify the mechanism for the seasonal transmission of *E. multilocularis* quantitatively, notwithstanding a lack of seasonal prevalence data. At present, human alveolar echinococcosis is prevalent throughout the mainland of Hokkaido. The risk of being infected with alveolar echinococcosis in the human population has been investigated by analyzing the seasonal fluctuation of parasite egg dispersal in the environment, which should be necessary for planning more suitable preventive measures against *E. multilocularis*.

Keywords: **Computer simulation, *Echinococcus multilocularis*, Hokkaido, Japan, Transmission model**

Introduction

We propose a mathematical model to describe the transmission of _Echinococcus multilocularis_ quantitatively. A mathematical model can help in studying estimates of prevalence and the effects of control measures under various assumptions. A simple mathematical model was constructed by Roberts et al. (1995) to evaluate the effect of control by the addition of praziquantel to bait in France.

On the main island of Hokkaido, Japan, the first case of human alveolar echinococcosis (HAE) was reported in 1965 at Nemuro, in eastern Hokkaido (Yamamoto et al., 1966). Nowadays, HAE has spread throughout the mainland of Hokkaido (Annual Reports of the Council for alveolar Echinococcus in Hokkaido 1984-1994, Department of Health and Welfare, the Hokkaido Government; Doi, 1995). _E. multilocularis_ maintains the transmission cycle in two hosts; the definitive host is canines, while the intermediate hosts are mainly rodents and ungulates. In Hokkaido, the major definitive host is the red fox (_Vulpes vulpes_), and the major intermediate host, the gray-sided vole (_Clethrionomys rufocanus_) (Ohbayashi, 1996). The intermediate hosts are infected by ingesting parasite eggs in voided feces of infected definitive hosts, while the definitive hosts are infected by preying on voles that have hydatid cysts. Humans are infected by the accidental ingestion of parasite eggs.

The transmission of _E. multilocularis_ is subject to the influence of the dynamics for both the definitive and the intermediate host populations, which vary greatly between seasons because they are wild animals (Saitoh et al. 1998). Seasonal forcing was accounted for in the model to more precisely analyze the prevalence of _E. multilocularis_ in the host population. The ecological and epidemiological parameters used in the model were determined on the basis of field surveys in Hokkaido, Japan.

We carried out simulations of the model to study the seasonal transition in the prevalence of _E. multilocularis_ in the population of foxes in Nemuro and Abashiri provinces, eastern Hokkaido. We also investigated the risk of being infected with HAE in the human population through simulations of the model, assuming that the risk would depend on the abundance of parasite eggs in the environment. Consideration for the mechanism of seasonal transmission can be helpful in designing strategies for the control of _E. multilocularis_.

Materials and Methods

Study Area

Hokkaido is the northernmost island of Japan. The vole is the most common small mammal in Hokkaido. The Forest Agency of the Japanese Government has been carrying out a monitoring census of vole populations in forests all over Hokkaido since 1954. A statistical report on hunting (Department of Health and Welfare, the Hokkaido Government, 2000) showed that the population of red foxes was on the increase until around 1980, and thereafter was fairly constant. Epidemiological surveys on _E. multilocularis_ have been carried out by the Department of Health and Welfare of the Hokkaido Government in Annual Reports of the Council for alveolar echinococcus in Hokkaido. We focused on two infected provinces, Nemuro and Abashiri, located in eastern Hokkaido, to allow us to adjust the model with the aid of ecological, epidemiological and meteorological parameters. Table 1 shows the prevalence of _E. multilocularis_ in the fox population in the above provinces.

[Table 1]

Life cycle of _E. multilocularis_

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The life cycle of *E. multilocularis* consists of a free-living eggs phase in the environment and parasite stages in each of the two hosts. The vole has protoscoleces of *E. multilocularis* one or two months after orally ingesting eggs. The experimental infections in voles (*C. rufocanus*) showed that all voles had susceptibility to *E. multilocularis* eggs, that the infectious protoscoleces in hydatid cysts increased with time, and that the protoscoleces were first detected in some voles at 41 days after ingestion, and in all voles by 44 days (Yagi and Ito, 1998). Thus, we adopted 45 days as the period (τ_v) for the acquisition of infectiousness against the definitive host in voles.

The definitive host is infected with *E. multilocularis* by preying on voles which harbor multilocular echinococcus with infectious protoscoleces. In the experimental infection of foxes, parasite eggs were initially detected in the feces at 29-33 days after infection (Nonaka et al., 1996), and at 29-32 days (Yagi and Ito, 1998), but not detected thereafter until 66-84 days after infection (Nonaka et al., 1996). Abundant eggs were excreted from the experimentally infected foxes during the initial week of egg output, and thereafter the number of eggs fell off rapidly (Yagi and Ito, 1998). Thus, our model uses 30 days as the period (τ_f) for the maturity of *E. multilocularis* in foxes, 7 days as the duration (τ_h) of high parasite egg production and 60 days as that (τ_l) of low parasite egg production, respectively.

Longevity of *E. multilocularis* eggs

The longevity of *E. multilocularis* eggs is influenced by environmental factors. Especially, the duration of the egg's infectious ability is swayed by temperature and humidity (Yagi and Itoh, 1999). The experimental formula for the longevity (*d* days) in temperature ($t\ ^{o}C$) was obtained as $d = \exp\ (-0.135\ (t - 43.4))$ from experimental

infections in mice (Ishige et al., 1993). However, this formula is inapplicable to low temperatures (Yagi and Ito, 1999). As the seasonal climate effect on the longevity of eggs governs the transmission dynamics of _E. Multilocularis_ from foxes to the intermediate hosts, we assume in the model that the seasonal transmission rate from foxes to voles is in proportion to the relative seasonal longevity (e_r) of eggs as compared with the longevity of eggs at 13.8 ^oC (temperature in autumn in Nemuro province), which is calculated by the experimental formula with the proviso that the upper bound of longevity is fixed at 100 days, in due consideration of a low temperature period and of the limitations of the formula. The relative longevity of eggs in Nemuro and Abashiri provinces is shown in Table 2. The relative longevity will be used in the model for the risk of the human population being infected with HAE.

[Table 2]

Dynamics of Host populations

As the populations of the host animals show large scale seasonal variations, it is important in terms of the dynamics of the transmission of _E. multilocularis_ to consider such seasonal fluctuations.

The breeding season of red foxes (_V. vulpes_) in Hokkaido is generally from the last third of March to the first third of April. Newborns emerge from their dens after weaning, which has been assessed at about one month (Uraguchi and Takahashi, 1998). We assumed that newborns would be exposed to _E. multilocularis_ infection after weaning. The average litter size was estimated as 4.05 in Nemuro (Uraguchi and Takahashi, 1998), and 4.0 in Koshimizu (Abe, 1971), both in the eastern part of Hokkaido. The birth rate (b_f) in the population of foxes can be expressed by the product of litter size, sex ratio and percentage of breeding females; we adopted $b_f = 1.8$ where

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the values of litter size, sex ratio and percentage of breeding females were taken as 4.0, 0.5 and 90%, respectively. Generally, for any wild animal the death rate of juveniles is significantly higher than that of adults. We estimated the death rates of juveniles (under one year old) (δ_j) and adults (δ_a) as 0.82 and 0.33, respectively, on the assumption that the annual growth rate of the fox population would remain stable, based on the census data of the age structure (Uraguchi and Takahashi 1991; Uraguchi and Takahashi 1998). These figures are in accordance with the data obtained in Kushiro and Nemuro; $\delta_j =$ 0.86 and 0.84 in 1971-72 and 1977-79, and $\delta_a = 0.33$ and 0.39, respectively (Yoneda, 1981). The density (N_f) of the fox population per 1 km^2 has been used as a measure in the model. It was estimated that $N_f = 0.7$~1.0 before the breeding season at Nemuro in 1986-96 (Uraguchi and Takahashi 1998).

The gray-sided vole (*C. rufocanus*) breeds in three seasons of the year (except winter). Only females passing the winter become pregnant in spring, and the spring-born females then mature during the summer to comprise a major part of the breeding population in the autumn. Thus, the pregnancy rate is higher in spring and autumn than in summer (Kaneko et al., 1998). The maturation period is about 30-60 days, and the gestation period is 18-19 days (Abe, 1968). A typical litter size is 4-7, with an average of 5.3 (Fujimaki, 1981; Yoccoz et al., 1998), and the order of decreasing litter size was reported as spring, autumn and summer (Fujimaki, 1975). The percentage of breeding females is higher in spring and autumn than in summer (Ota, 1984). The birth rate (b_v) in the vole population that can be written as a product of litter size, sex ratio which is assumed to be 0.5, and percentage of breeding females has two peaks a year, one in spring and one in autumn. The survival rate of voles depends on the season and age, with the survival rate for the first month of life being lower than that of

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more than one month (Ohta, 1984), while the survival rate in winter is higher than that in summer (Dewa, 1975). Although the dynamics of vole populations in Hokkaido vary on a large scale annually and have certain geographical characteristics such as a periodical fluctuation with a 3.5-4.5 year cycle in the northern and eastern areas of Hokkaido, we assumed the condition that the annual growth rat

e of the vole population would remain stable and assigned age- and season- dependent death and birth rates which would result from age- and season- dependent litter sizes, as well as the percentage of breeding females, as shown in Table 4b, c. As a measure of the abundance of the vole population, the model uses the density (N_v) of the vole population per 1 km^2. It was estimated that $N_v = 0.30$ % 10^3 in spring (before the breeding season), giving 2.84 % 10^3 in autumn in Nemuro (1984-1993), and $N_v = 0.63$ % 10^3 in spring, or 1.74 % 10^3 in autumn in Abashiri (1983-1992) (Census data on vole populations from the Forest Agency of the Japanese Government).

Transmission model of _E. multilocularis_

We propose a deterministic model for the transmission of _E. multilocularis_. The model works well provided that there are no immigrations or emigrations of foxes in a target area, while there is no need to take in any immigrations or emigrations of voles owing to their narrow and exclusive home range (Saitoh, 1991; Ishibashi et al., 1998). The fox population is divided into four epidemiological classes: negative, infected but not parasite egg producing, high parasite egg producing, and low parasite egg producing, which are symbolized by x_1, x_2, x_3, x_4, respectively. The vole population is divided into three classes: negative, infected but not yet infectious, and infectious (holding protoscoleces in hydatid cysts), which are designated y_1, y_2, y_3, respectively. Each epidemiological class of fox populations is classified into two age groups: juveniles (_j_)

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and adults (a), while each epidemiological class of the vole population is classified into 5 age groups: newborn (0), one month (1), two months (2), three months (3), more than four months (4). The symbols of age groups ($a, j, 0 \sim 4$) are used as suffixes of the above variables for epidemiological classes.

[Table 3]

   E. multilocularis can be transmitted to a fox when it ingests an infected vole holding protoscoleces in hydatid cysts. Therefore, the prevalence of *E. multilocularis* in the fox population is affected by their food habits, that is, the average number (NVF) of voles ingested by a fox each day. NVF depends on the density of the vole population and on the meteorological condition of the depth of snow (Abe, 1975; Yoneda, 1981). Thus, we introduce a food habit function $f(N_v, d_s)$ for vole density (N_v) and the depth of snow (d_s) as NVF. We assume that $f(N_v, d_s) = 0$ for $d_s > 50$ (cm), because a fox cannot prey on voles that live under deep snow. A fox feeds on voles by preference, but it does have other available food (Yoneda, 1981). Thus, it has been assumed in the model that the NVF increases swiftly at a low fox density, while the increasing degree of NVF is reduced at a high density, and that NVF becomes saturated with the maximum number (m_N) of voles ingested by a fox each day at a fairly high density, which was estimated as 8 (Abe, 1975). Applying the logistic distribution (W) to the relationship between NVF and N_v, the food habit function is written as:

$$f(N_v, d_s) = g(d_s)\, m_N\, W(N_v,),$$

$$W(N_v) = 1/(1 + \exp(-k(N_v - N_v))$$

where $g(d_s)$ stands for the function which obstructs foxes from preying on voles whose value decreases from 1 ($d_s < 10$) to 0 ($d_s > 50$). The shape parameters k and N_v are chosen as 0.003 and $1.2 \% 10^3$ from experimental data. The transfer rates among

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epidemiological classes in the fox population are composed of several epidemiological parameters. The symbol λ signifies the infection rate from the negative stage (x_1) to the infected, but no egg production, stage (x_2) and R, the recovery rate from the high production of eggs-stage (x_4) to the negative stage (x_1) in due consideration of super infection, while P_j, P_a, and Q_j, Q_a signify the transfer rates for the age groups of juveniles (j) and adults (a) from the infected but no egg production stage (x_2) to the high production of eggs-stage (x_3), and from the high production stage (x_3) to the low production stage (x_4), respectively. These transfer rates are expressed by the following formulae:

$$\lambda(t) = s_0\, f(N_v(t), d_s(t))\, y_3(t) / N_v(t)$$

$$P_p(t) = (1 - \delta_{f,\,p})^{\tau_f}\, \lambda(t - \tau_f), \qquad (p = j, a)$$

$$Q_p(t) = (1 - \delta_{f,\,p})^{\tau_f + \tau_h}\, \lambda(t - (\tau_f + \tau_h)), \quad (p = j, a)$$

$$R(t) = \lambda(t) / (\exp(\tau_l\, \lambda(t)) - 1)$$

In the above formula, s_0 denotes the conditional probability that protoscoleces in a vole can mature in a fox; s_0 is assessed as 0.9 because of the high probability of infection with inoculated protoscoleces.

Voles can be infected with _E. multilocularis_ by oral injection of free-living eggs that are excreted by the infected foxes. We introduce the transfer factors μ_0, μ and ρ. μ_0 is the basic infectious contact rate from the low egg producing class of foxes at the standard temperature, while μ is the infectious contact rate from the low egg producing class that is obtained by multiplying μ_0 by e_r (the relative seasonal longevity of eggs). ρ is the multiplicative factor for the basic infectious contact rate from the high egg producing class. Due to a lack of direct survey data, we will investigate the values of μ_0 and ρ on the basis of prevalence data for the populations of foxes and voles in the next

section. In the model, we assume that a vole at the infected but not yet infectious stage moves to the infectious stage after τ_v days, and that no voles recover from _E. multilocularis_.

The basic scheme of the model is shown in Fig. 1a (case for the population of foxes) and 1b (case for the population of voles), and the parameters used in the model are tabulated with the assumed and adjusted values in Table 4a.

[Fig. 1a, b]

[Table 4a, b, c]

Results

Dynamics models of Host populations

In order to act in concert with the transmission model for _E. multilocularis_, we prepared a seasonal population dynamics model of foxes for stable annual growth rate (the density per 1 km^2 in spring being 1.0) on the basis of the ecological parameters in Table 4a. We also prepared a seasonal population dynamics model of voles for the stable annual growth rate (the density per 1 km^2 in spring being 0.3 % 10^3) on the basis of the ecological parameters in Table 4a-c.

[Fig. 2]

Fitting parameters

The basic reproductive rate (R_0) is the maximal number of secondary infections that is theoretically possible when one infected fox is introduced into a susceptible population: any secondary cases derive from the intermediate populations that are infected through eggs produced by one infected fox. The basic reproductive rate of the model, which can be calculated on the simplified assumption that any seasonal factors

or any super infection are ignored, is expressed by the combination of several

parameters in the model as:

$$R_0 = \left(\mu_0\,\Box_h + \frac{\mu_0\,\rho}{1 + \frac{\delta}{f}\rho}\right)\frac{1}{1 + \frac{\delta}{f}}\cdots\frac{1}{1 + \frac{\delta}{v}}\cdots\frac{1}{1 + \frac{\delta}{h}}\cdots\frac{s_0\,\bar{f}N_f}{\delta}$$

The symbols, f, δ_f and δ_v, represent the average of NVF, the average of the daily death

rates for the total population of foxes and that for the total population of voles,

estimated as 6.6, 3.26 × 10^{-3} and 1.19 × 10^{-2}, respectively, while the other symbols in

the formula are referred to in Table 4a. In the previous sections, we assigned the

estimated or adjusted values to all the above parameters, except for two transfer factors,

the infectious contact rate from the low egg producing class (μ_0) and the multiplier of

the basic infectious contact rate from the high egg producing class (ρ). Applying these

values in the formula, R_0 can be written as a function of μ_0, ρ and N_f:

$$R_0 \approx 1.45 \times 10^{4}\,(1 + 1.39 \times 10^{-1}\,\rho)\,\mu_0\,N_f$$

It is difficult to decide the two parameters, μ_0 and ρ, in accordance with the field data

because of the presence of free-living eggs in the environment, although it is more

important to decide a pertinent value of μ_0 than of ρ. Since the ratio of parasite egg

discharge in the high production period compared to that in the low production period

was found to be more than five times greater in the experimental infection of foxes

(Yagi and Ito, 1998), ρ is limited to within the scope of (1, 10) and a value of 5 is

adopted in the following simulations. When the permissible range of R_0 is arranged

from 1 to 20, the value of μ_0 is allowed to vary within the range (4.0 × 10^{-5} - 8.1 × 10^{-4}),

(2.7 × 10^{-5} - 5.4 × 10^{-4}) or (1.9 × 10^{-5} - 3.8 × 10^{-4}) at $\rho = 1$, 5 or 10, respectively, on

choosing 1.5/ km^2 as N_f the average density of foxes. We examined the highest, lowest

and average yearly prevalence rates of _E. multilocularis_ in the fox population for the

range (μ_0) from 0.1 % 10^{-4} to 5.0 % 10^{-4} in steps of 1.0 % 10^{-5} with the model

simulations under the Nemuro situation. The curves for the prevalence rates are shown

in Fig. 3.

[Fig. 3]

When the permissible ranges of the highest and average prevalence rates (%) have their

limits set to (55, 90) and (40, 75) making allowance for Table 1, the value of μ_0 is

allowed the bounds (1.0 % 10^{-4}- 3.4 % 10^{-4}). We carry out simulations within these

bounds in the next section.

Simulations for the prevalence of _E. multilocularis_

The transmission model for _E. multilocularis_ was programed by Fortran 90 to

work on any computer under the Microsoft Windows TM platform.

Firstly, to investigate the effect of seasonal transitions on the prevalence of _E. multilocularis_ in both host populations, foxes and voles, under the situations in Nemuro

and Abashiri, Eastern Hokkaido, we planned the simulations where μ_0 was chosen as

1.5 % 10^{-4} the value that realized the average prevalence rates during 1995-2000 in

Nemuro (53%) and Abashiri (48%) (Table 1). There is a great difference between the

two provinces in terms of snowfall. The Japan Meteorological Agency (1986-97)

reported that the average depth of snow in the winter three months (January-March) was

36.1 _cm_, 66.2 _cm_, and that the number of days beyond 50 _cm_ deep was 0 days and 72

days in Nemuro and Abashiri, respectively. The simulations indicate that the density of

infected foxes goes down to its lowest during the second third of March (Nemuro), and

the first third of April (Abashiri) before the breeding season, thereafter reaching its peak

during the second third of June due to an increase in infected juveniles. Although the

prevalence rate in fox populations is highest during the first third of October due to a

decrease in the total population,   the timing of the lowest prevalence rate is synchronized with that of the lowest infectious density. This result also shows that there are some differences in the winter prevalence of the fox populations between the Nemuro and Abashiri areas, that is, the winter density of infected foxes maintains a certain level in Numero, while it falls to a low level in Abashiri.

[Fig. 4]

Secondly, we investigated the risk to the human population of being infected with HAE using model simulations. In this article, such a risk is expressed as the proportion of parasite eggs in the environment relative to the maximum abundance in Nemuro area, which is referred to as the hazard index. The simulations were also carried out for the situation in the environs of Sapporo, the capital of Hokkaido, where the fox population density was assumed to be half as much as that in Nemuro. The simulation for Nemuro indicates that the hazard index is highest during the first third of June when infected juveniles begin to discharge parasite eggs, and that it goes down for a while during a high temperature period and then rises again to reach a second peak in October. A comparative study indicates that the hazard index fluctuates widely and has a sharp peak in the Nemuro conditions (high density of fox population), while it varies little mildly and remains at a low level throughout the whole year in the environs of Sapporo (low density).

[Fig. 5]

Discussion

It is important to consider the connection between the model and reality. It is unavoidable for the transmission model for *E. multilocularis* to have a somewhat complicated structure, and consequently to involve many ecological, as well as

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epidemiological, parameters because *E. multilocularis* has a complicated life cycle

ranging between two kinds of hosts. Through experimental and field data, we obtained

estimated values for all parameters with two exceptions (μ_0, ρ) and the number of

exceptional parameters is low considering the complicity of the model. We set bounds

for the above two parameters on the basis of field data for the prevalence rate of *E.*

multilocularis, so that the model fits regional situations where *E. multilocularis*

prevails.

A distinctive feature of the model is the division of the production stage of foxes

into two classes according to egg output; this is adequate for investigating the risk of

infection in the human population with HAE. In the model, we have considered neither

the acquisition of immunity nor intensity of infection which is related to the

protoscolece burden in the voles that are preyed on by the fox. Further precise research

on transmission models based on the intensity of infection, or models incorporating

immunity is desirable, tracking the progress of experimental infections in foxes.

The process of transmission of *E. multilocularis* from foxes to voles is

controlled by the state of free living eggs in the environment whose longevity depends

on environmental factors. We considered the effect of air temperature on the longevity

of eggs, but not the effect of humidity, which also influenced longevity (Yagi and Itoh,

1999). This leaves some room for consideration that there would be some lag time

between the discharge of eggs from foxes and the oral ingestion of eggs by voles, and

that the free living eggs would accumulate in the environment. However, to avoid a

more complicated structure in this model, we assumed that the discharge of eggs had an

immediate contribution to the transmission of *E. multilocularis* in voles.

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On the other hand, the process transmitting *E. multilocularis* from voles to foxes seems more clear, as it is governed by the predation of voles. We think that the introduction of a food habit function for foxes, which depends on the vole density and depth of snow, is adequate to describe the above transmission stage.

For the allowable bounds ($1.0 \% \ 10^{-4}$- $3.4 \% \ 10^{-4}$) of the basic infectious contact rate (μ_0), the bounds of the highest, the average and the lowest yearly prevalence rates (%) in the population of voles were estimated as (2.8, 12.2), (1.1, 4.7) and (0.4, 1.6), respectively, while the Annual Report of the Council for alveolar echinococcus in Hokkaido, 2001-2002 (Department of Health and Welfare, the Hokkaido Government) reported that the prevalence rate in the vole population of Nemuro , Northern Hokkaido varied widely from 0.0% to 17.3%, and that its average for twenty years (1981-2000) was 4.6%. The above bounds of μ_0 seem adequate to use in simulations from the view point of prevalence in voles; it takes into account the difficulty in finding the exact prevalence rate of vole populations in the field, as well as the fact that there are some hot spots of infected voles with *E. multilocularis*.

The effect of super infection introduced into the model has a great influence on the prevalence of *E. multilocularis* in fox populations. A comparative study shows that the highest and average yearly prevalence rates in the fox population with super infection are about 1.4-1.6 and 1.4-1.8 fold higher than those without super infection for $\mu_0 > 1.4 \% \ 10^{-4}$, and that the highest prevalence rate without super infection asymptomatically tends towards the equilibrium prevalence rate, which is calculated on the simplified assumption (referred to in Fitting parameter- subsection) and is given as the formula on the basic reproductive rate (R_0): $0.65 (1-1/R_0)$, as μ_0 tends to be larger.

The field data on the prevalence in Nemuro (Table 1) support the effect of super infection in the model.

Although little is known about the seasonal transition in the prevalence of _E. multilocularis_ due to a lack of seasonal prevalence data in the populations of foxes and voles, the simulation clarifies the mechanism of seasonal transmission for _E. multilocularis_ quantitatively, and this can be helpful in designing strategies for its control. Bearing in mind that the peak density of infected foxes does not necessarily coincide with that of the prevalence rate (Fig. 4), it is essential to pay more attention to the transition, rather than the density, when attempting to control the source of infection. A difference in the prevalence rate between Nemuro and Abashiri was also indicated by the field data (Table 1; Saitoh and Takahashi, 1998); the simulation showed that this was caused by a difference in snowfall between the two provinces.

The hazard index depends not only on the air temperature, but also other environmental factors, including humidity. Although we have only taken the air temperature into account with the hazard index, it is reasonable to assume that there is some danger an individual would be infected with HAE during the high hazard index period as shown in Fig. 5. Eckert et al. (2002) proposed preventive measures and safety precautions to prevent human echinococcosis. These included education, careful handling of wild berries and vegetables and etc., but they did not mention the seasonal fluctuations of egg dispersal in the environment which were shown in the present report. Consideration for seasonal fluctuations in parasite egg dispersal in the environment is necessary when planning more suitable preventive measures against _E. multilocularis_, although there may be different types of seasonal fluctuations of egg dispersal according to the countries or provinces, as shown between Nemuro and Sapporo in the

present article. Therefore, further careful research is necessary before planning

measures according to each country and province because there may be various types of

seasonal fluctuations of temperature, snow fall and ecological factors such as the

population of vole predators.

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Table 1. Prevalence of *Echinococcus multilocularis* in the fox populations [a]

year	Nemuro			Abashiri		
	number examined	number positive	prevalence rate (%)	number examined	number positive	prevalence rate (%)
1995	82	62	75.6	28	12	42.9
1996	97	38	39.2	20	5	25.0
1997	89	28	31.5	22	10	45.5
1998	60	46	76.7	35	23	65.7
1999	23	7	30.4	22	10	45.5
2000	39	27	69.2	19	10	52.6
total	390	208	53.3	146	70	47.9

[a] Derived from the Department of Health and Welfare, the Hokkaido Government in Annual Report of the Council for alveolar echinococcus in Hokkaido, 2001-2002

Table 2. The relative longevity of *Echinococcus multilocularis* eggs

season	Nemuro		Abashiri	
	mean air [a] temperature	relative [b] longevity	mean air [a] temperature	relative [b] longevity
spring	8.74	1.86	11.24	1.43
summer	16.16	0.74	18.53	0.53
autumn	13.89	1	13.71	1.02
winter	-0.02	1.86	-1.14	1.86

[a] Derived from the Japan Meteorological Agency,   1994-1999

[b] The standard temperature was set as 13.89 in autumn in Nemuro

Table 3. The variables used in   the Echinococcus transmission model

Host	Symbol [a]	Description (density per 1 km^2)
fox	$x_{1,p}$	negative
	$x_{2,p}$	infected, no parasite egg producing
	$x_{3,p}$	infected, high parasite egg producing
	$x_{4,p}$	infected, low parasite egg producing
	N_f	total density
vole	$y_{1,q}$	negative
	$y_{2,q}$	infected but not yet infectious
	$y_{3,q}$	infectious (holding protoscoleces in hydatid cysts)
	N_v	total density

[a] $p = j, a$ representing the age group of juveniles and adults; $q = 0\text{-}4$ representing the age groups of newborns, one month olds, two month olds, three month olds and more than four month olds, respectively

Table 4a. The model parameters together with their assumed and adjusted values

Description	Symbol	Estimated value
fox birth rate per year	b_f	1.8
vole birth rate per month ($q = 2,3,4$)	$b_{v,q}$	see Table 4b
fox death rate per year (juveniles)	$d_{f,j}$	0.82
fox death rate per year (adults)	$d_{f,a}$	0.33
vole death rate per month ($q = 0,1,2,3,4$)	$d_{v,q}$	see Table 4c
period of no parasite egg production in foxes (days after infection)	t_f	30
duration of high parasite egg production (days)	t_h	7
duration of low parasite egg production (days)	t_l	60
period for acquiring infectious protoscoleces in voles (days after ingestion)	t_v	45
the conditional probability of maturity in foxes	s_0	0.9
the basic infectious contact rate [a]	m_0	$(1.0 \sim 3.4) \times 10^{-4}$
multiplicative factor caused by high egg production	r	1~10

[a] see text;

Table 4b. The assigned values for age- and season- dependent birth rates of voles

Age group (q)	litter Size			percentage of breeding females			birth rate ($b_{v,q}$)		
	Sp [a]	Su [b]	Au [c]	Sp [a]	Su [b]	Au [c]	Sp [a]	Su [b]	Au [c]
2	0	4.5	5.2	0	50	50	0	1.13	1.3
3	0	4.5	5.2	0	60	85	0	1.35	2.21
4	6.2	4.8	5.3	100	70	100	3.1	1.68	2.65

[a] Sp, spring; [b] Su, summer; [c] Au, autumn;

Table 4c. The assigned values for age- and season- dependent death rates of voles

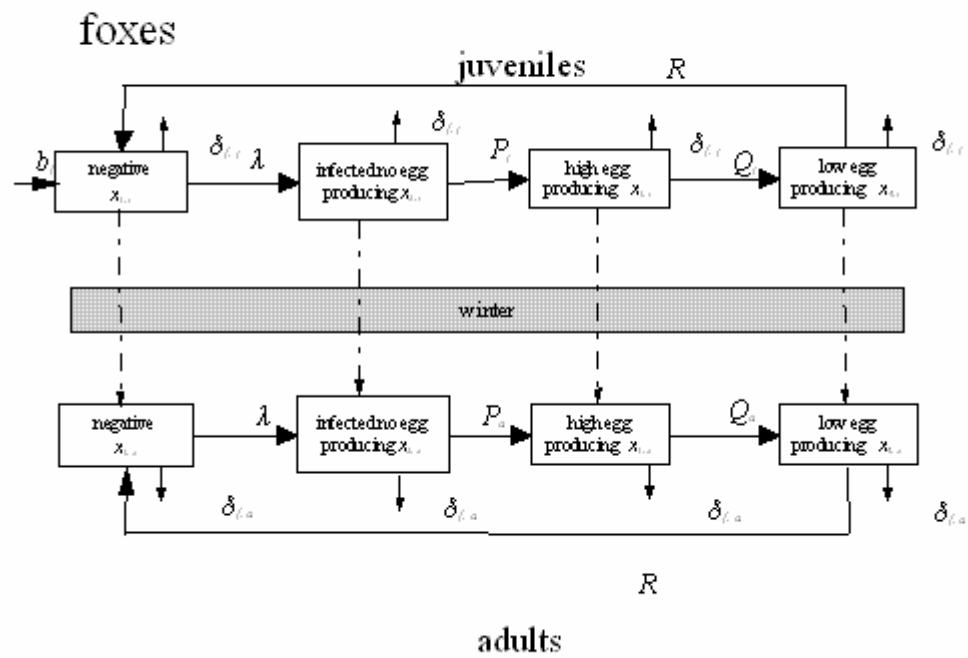| Age group (q)	death rate ($d_{v,q}$)			
	spring	summer	autumn	winter
0	0.5	0.5	0.5	0.25
1	0.25	0.25	0.25	0.25
2	0.2	0.2	0.2	0.25
3	0.2	0.2	0.2	0.25
4	0.25	0.25	0.25	0.25

Legends

Fig. 1a, b. The basic schemes of the transmission model for _E. multilocularis_ in the fox populations (a) showing the transfers among 4 epidemiological classes, and the vole populations (b) showing the transfers among 3 epidemiological classes, the division into 5 age groups being omitted.

Fig. 2. The seasonal population dynamics models of foxes and voles. The solid line and the dotted line show the variations of fox or vole density per 1 km^2 on the basis of our population dynamics models, respectively.

Fig. 3. The prevalence rate in the fox population corresponding to the basic infectious contact rate (m_0) in the model. The solid line, the broken line and the dotted line show the highest, the average and the lowest yearly prevalence rates, respectively.

Fig. 4. Seasonal variations in the density per 1 km^2 of infected foxes for _E. multilocularis_ (solid lines) and seasonal variations in the prevalence rate of _E. multilocularis_ in the fox population (broken lines). The black and gray lines show the Nemuro and Abashiri situations, respectively.

Fig. 5. Seasonal variations in the hazard index. The solid line shows the Nemuro situation, and the dotted line, the environs of Sapporo.

foxes

juveniles R

b | negative $x_{i,t}$ $\delta_{i,t}$ λ infected no egg producing $x_{i,t}$ $\delta_{i,t}$ P_i high egg producing $x_{i,t}$ $\delta_{i,t}$ Q_i low egg producing $x_{i,t}$ $\delta_{i,t}$

winter

negative $x_{i,a}$ λ infected no egg producing $x_{i,a}$ P_a high egg producing $x_{i,a}$ Q_a low egg producing $x_{i,a}$

$\delta_{i,a}$ $\delta_{i,a}$ $\delta_{i,a}$ $\delta_{i,a}$

R

adults

voles

b_r → [negative y_1] → [infected but not infectious y_2] → [infectious y_3]

δ_r δ_r δ_r