<table>
<thead>
<tr>
<th>項目</th>
<th>内容</th>
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<tr>
<td>項目</td>
<td>掲載された学術的研究論文を紹介し、テキストをカスタマイズし、ナレーションを提供する方法について説明します。</td>
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<td>項目</td>
<td>熱帯医学の研究を取り上げ、その成果を示します。</td>
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<td>項目</td>
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<td>資料の利用上の注意や制限について説明します。</td>
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Transmission Dynamics of *Dirofilaria immitis* in a Southwestern Part of Japan

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**Abstract:** The transmission dynamics of *Dirofilaria immitis* were studied by using reported data in Nagasaki City and Omura City, Japan. The catalytic model was applied to the age distribution of positive rate for microfilariae of *D. immitis* in dogs. Using the force of infection obtained by applying the catalytic model, the critical vector density for the disappearance of *D. immitis* was estimated. Transmission frequencies of *D. immitis* in the two places were calculated by densities and infective rates of the principal vector, *Culex pipiens pallens*, and numbers of infective larvae of *D. immitis* in the vector. Roles of some factors influencing the transmission frequency of *D. immitis* were also evaluated with a simple mathematical model, and it was concluded that the continuation of extensive infection with *D. immitis* in dogs in spite of the presumed decrease of the vector density in recent years is ascribable to the increase of dog density and the increased protection of humans from mosquito bites.

**Key words:** Catalytic model, Critical vector density, *Culex pipiens pallens*, *Dirofilaria immitis*, Transmission dynamics.

*Dirofilaria immitis* is an important parasite of dogs, and its infection is known in humans, too. But little has been studied on the epidemiology of *D. immitis* infection. For this reason, we attempted to analyze the transmission dynamics by using available data in a southwestern part of Japan, and the results obtained are herewith reported.

**PLACES AND METHODS**

The transmission dynamics of *D. immitis* were studied in Nagasaki City and Omura City, both in Nagasaki Prefecture, a southwestern part of Japan. We selected these two

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places, because data of both dogs and vectors were available.

The catalytic model (Muench, 1959) was applied to the age distribution of positive rate for microfilariae of *D. immitis* in dogs (Suenaga et al., 1971, 1974). Using the force of infection obtained by applying the catalytic model, the critical vector density for the disappearance of *D. immitis* was estimated, as in the analysis of onchocerciasis epidemiology (Wada, 1982). Transmission frequencies of *D. immitis* in the two places were calculated by using densities and infective rates of the principal vector, *Culex pipiens pallens*, and numbers of infective larvae of *D. immitis* in the vector reported by Suenaga (1975) and Suenaga and Itoh (1973). Roles of some factors influencing the transmission frequency of *D. immitis* were also evaluated with a simple mathematical model, and the reason was discussed for the continuous infection of dogs in spite of the presumed decrease of the vector density in recent years in Japan.

**APPLICATION OF CATALYTIC MODEL**

Muench (1959) presented several types of the catalytic model to be used in the epidemiology of diseases under different assumptions. Among them, the simple, the reversible and the two-stage model were applied by the method of Muench (1959) to the age distributions of positive rate for microfilariae (mf) of *D. immitis* in dogs reported by Suenaga *et al.* (1971, 1974).

1) The simple model.

If we assume that the force of infection in terms of the number of effective contacts per individual per unit time is constant irrespective of age, then we have

\[
\frac{dy}{dt} = a(1-y) \quad (1)
\]

where *y* is the mf positive rate at age *t*, and *a* is a constant showing the force of infection. "Effective contact" used here means a contact sufficient to produce mf if the subject is susceptible. On the condition that *y* = 0 when *t* = 0, it is expressed in another form as

\[
y = 1 - e^{-at} \quad (2)
\]

This equation describes the expected change of a group of dogs starting entirely negative for mf at birth and exposed to continuous infection at a constant rate of *a* effective contacts per individual per unit time. Here the force of infection, *a*, is measured in terms of the number of effective contacts per individual and not in the number of dogs that have received the contact. In this model, dogs that have become positive for mf do not return to a negative state.

2) The reversible model.

This model assumes that two forces act on a population of dogs in opposite directions simultaneously both at a constant rate; one is a force of infection (*a*) and the other a force of reversion from positive to negative state for mf (*b*). The equation is

\[
\frac{dy}{dt} = a(1-y) - by \quad (3)
\]

When *y* = 0 at *t* = 0, it becomes

\[
y = a(1-e^{-(a+b)t}/(a+b)) \quad (4)
\]
Fig. 1. Age distribution of positive rate for microfilariae of *D. immitis* in dogs in Nagasaki, 1968, with theoretical curves by simple, reversible and two-stage catalytic models. Data of dog infection are from Suenaga *et al.* (1971).

Fig. 2. Age distribution of positive rate for microfilariae of *D. immitis* in dogs in Omura, 1973, with theoretical curves by simple, reversible and two-stage catalytic models. Data of dog infection are from Suenaga *et al.* (1974).
Any sort of protective immunity is involved in this model, because the rate of becoming positive is equal for those dogs that have lost the evidence of infection and for those that have no experience of infection.

3) The two-stage model.

The assumption of this model is that a dog that has once become positive for mf and reverted negative never becomes positive again. If we denote by x the fraction of the population that has ever become positive for mf, and by z the fraction that, once becoming positive, has lost all mf, then \( y = x - z \) is the remainder that still has mf. Letting \( a \) be the rate at which \( x \) is formed (force of infection), and \( b \) the rate at which \( x \) loses mf and changes to \( z \) (force of reversion), we have

\[
\frac{dy}{dt} = a(1-x) - by \tag{5}
\]

of which general solution, if \( y = 0 \) when \( t = 0 \), is

\[
y = \frac{a(e^{-bt} - e^{-at})}{a-b} \quad (a \neq b)
\]

\[
y = ate^{-at} \quad (a = b) \tag{6}
\]

The constant \( b \) is similar to that in the reversible model, but, in this model, produces an irreversible change. The two-stage model assumes the presence of complete protective immunity.

The results of applying the three types of the catalytic model to the age distribution of positive rate for mf in dogs in Nagasaki City and Omura City are shown in Fig. 1 and 2. It is apparent that both the reversible and the two-stage model were well fitted for the age distribution of positive rate, but the fitness of the simple model was not good.

Table 1 gives the constants in the three catalytic models applied to the age distribution of positive rate. The constant \( a \) representing the force of infection was different in the models depending on the underlying assumptions, but smaller, in each model, in Nagasaki with the microfilaria positive rate of 0.291 than in Omura with the rate of 0.432. The constant \( b \), which is the force of reversion from positive to negative state for microfilariae, should be equal in the two places in each of the reversible and the two-stage model. The value was, however, slightly larger in Nagasaki than in Omura, the reason of which was not clear.

The reversible model assumes the absence of any protective immunity and the

<table>
<thead>
<tr>
<th>Table 1. Constants obtained by applying simple, reversible and two-stage catalytic models to the age distribution of positive rate for microfilariae of <em>Dirofilaria immitis</em> in dogs in Nagasaki and Omura</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagasaki</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>simple</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>reversible</td>
</tr>
<tr>
<td>two-stage</td>
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</tbody>
</table>
two-stage model does the presence of complete protective immunity. The direct evidence was not available as to which assumption is valid in the infection with *D. immitis* in dogs. It seems certain that some immune mechanism acts in dogs to protect the reinfection (Hayasaki, 1986), and in the case of human filariasis, the general shapes of age-prevalence and age-density curves for microfilariae indicate that protective immune responses do occur after many years of exposure (WHO, 1984). Therefore, the two-stage model was conveniently used in theoretical analyses in the present paper.

**FORCE OF INFECTON AND MICROFILARIA POSITIVE RATE**

The relation between the force of infection and the microfilaria positive rate in dog populations was obtained by a similar method as described in Wada (1982). If the microfilaria positive rate *y* at age *t* is given by Equation (6) of the two-stage catalytic model, the positive rate for all dogs (the oldest age is 12 years), *y*₀, can be obtained by

\[
y_0 = \int_0^{12} a(e^{-at} - e^{-bt})(a-b)dt/12
\]

\[
= \left(\frac{(a - ae^{-12b})b - (1 - e^{-12a})}{12(a-b)}\right) (a+b)
\]

\[
y_0 = \int_0^{12} ate^{-at}dt/12
\]

\[
= \left\{\frac{1 - (12a + 1)e^{-12a}}{12a}\right\} (a=b) \quad \text{........(7)}
\]

This is the theoretical positive rate of all dogs expressed by the force of infection and the force of reversion.

In Nagasaki the observed microfilaria positive rate was 0.291 and the theoretical rate calculated by Equation (7) from two constants given in Table 1 was 0.319, and in

![Fig. 3. Theoretical relation between the force of infection (a) and the microfilaria positive rate of dogs (y₀) based on two-stage catalytic model when b=0.07.](image-url)
Omura the observed rate was 0.432 and the theoretical one 0.497. The slight deviation between observed and theoretical rates is ascribable chiefly to unequal numbers of dogs examined for microfilariae in age groups. The number of dogs in any age group is considered to be equal in Equation (7), but more dogs in younger age groups were usually examined.

The force of reversion $b$ in Table 1 was 0.092 in Nagasaki and 0.050 in Omura. Even if 0.07 (mean of the two) is used as the value of $b$, the theoretical value by Equation (7) does not greatly change, 0.347 versus 0.319 in Nagasaki and 0.458 versus 0.497 in Omura. Therefore, the force of reversion $b$ was regarded as 0.07 for simplicity in the following theoretical consideration.

Fig. 3 shows the theoretical relation between the force of infection $a$ and the microfilaria positive rate of all dogs $y_0$, when the force of reversion $b$ is 0.07. The relation clearly indicates that when the force of infection decreases, the positive rate acceleratedly decreases.

**CRITICAL VECTOR DENSITY**

By a similar method in the analysis of onchocerciasis epidemiology in Wada (1982), the critical vector density for maintaining *D. immitis* in the dog population was obtained. If the force of infection $a$ is assumed to be proportional both to the density of vectors and to the microfilaria positive rate (mf (+) rate) of dogs, then

$$a = p \times (\text{vector density}) \times (\text{mf (+) rate})$$

where $p$ is a proportional constant. Substituting $p \times (\text{vector density})$ with vector density index, we have

![Graph](image.png)

**Fig. 4.** Theoretical relation of the force of infection and the microfilaria positive rate of dogs to the vector density index, based on two-stage catalytic model when $b=0.07$. 
Thus, if \( a \) is given, we can calculate the vector density index with the value of \( (mf (+) rate) \) by Equation (7).

Fig. 4 shows the theoretical relation, based on Equation (7) and (9), of the force of infection \( a \) and the microfilaria positive rate of dogs \( y_0 \) to the vector density index. The force of infection \( a \) decreases nearly linearly with the decrease of vector density index, and becomes 0 when vector density index is 0.216. However, \( mf (+) rate \) must be 0 when the force of infection \( a \) is 0, and accordingly the vector density index in Equation (9) takes an indefinite form. Therefore, 0.216 should be considered as the limit of the vector density index when the force of infection becomes infinitely small. \( Mf (+) rate \) is also 0 when the vector density index is 0.216, and convexly increases with increasing vector density index with the limit of 0.677.

The presence of the critical value for the vector density index, below which \( D. immitis \) does not maintain itself in the dog population, is epidemiologically significant. An attempt will be made to convert the index for the critical vector density to the concrete density in the next section.

**TRANSMISSION FREQUENCY OF \( D. immitis \)**

Letting the transmission period in a year be 180 days (from May to October), annual biting rate (ABR) and annual transmission potential (ATP) were calculated as in Table 2. ABR is defined as the total number of vectors coming to feed on one dog in a year, and ATP as the total number of infective larvae of \( D. immitis \) carried by the vec-

| Table 2. Annual biting rate (ABR) and annual transmission potential (ATP) of the vector (Culex pipiens pallens) of Dirofilaria immitis |
|-------------|-------------|-------------|
|             | Nagasaki    | Omura       | Total       |
| Mf(+) rate of dogs | 690/2370=0.291<sup>2</sup> | 392/908=0.432<sup>3</sup> | 1082/3278=0.330 |
| No. vectors/dog/night | 1098/79=15.57<sup>3</sup> | 143/14=10.21<sup>3</sup> | 1241/93=13.34 |
| Transmission period (days)<sup>3</sup> | 180         | 180         | 180         |
| ABR         | 15.57×180=2803 | 10.21×180=1838 | 13.34×180=2401 |
| Infective rate of vectors | 12/2944=0.0041<sup>4</sup> | 5/863=0.0058<sup>5</sup> | 17/3840=0.0045 |
| No. infective larvae/vector | 27/12=2.3<sup>3</sup> | 10/5=2.0<sup>6</sup> | 37/17=2.2 |
| ATP         | 2803×0.0041×2.3=26.4 | 1838×0.058×2.0=21.3 | 2401×0.0045×2.2=23.77 |

1) from May to October  
2) after Suenaga et al. (1971)  
3) after Suenaga & Itoh (1973)  
4) after Suenaga et al. (1974)  
5) after Suenaga (1975)
tors, from which ABR is calculated (Duke, 1968; Walsh et al. 1978). The main vector in the study areas is *Culex pipiens pallens* (Suenaga, 1975; Suenaga and Itho, 1973). In Nagasaki (mf positive rate of dogs 0.291) and in Omura (0.432), ABR was 2803 and 1838, respectively, and ATP 26.43 and 21.32. Both ABR and ATP were larger in Nagasaki with lower mf positive rate than in Omura. This discrepancy is perhaps due to the fact that the data related to vectors were obtained only at Sakamoto in Nagasaki area and at Nishi-omura in Omura area, while those of the dog infection in the whole area.

Next, an approximate vector density index will be estimated, with the data in Nagasaki and Omura put together, by Equation (9). Since the mean force of infection \((a)\) in Nagasaki and Omura was 0.16 and the mean force of reversion \((b)\) was 0.07 (from Table 1), the microfilaria positive rate was estimated at 0.412 by Equation (7) and the vector density index at 0.388 by Equation (9). The value of 0.388 corresponds to the mean number of vectors per dog per night of 13.34 during the breeding season of vectors from May to October (Table 2). From this relation, we have an estimate for the critical number of vectors for maintaining *D. immitis* as 7.43, corresponding to the critical vector density index of 0.216. Similarly, the critical ABR was estimated at 1337. Thus, it is implied that *D. immitis* would not be maintained in the dog population at vector densities below 7.43 per dog per night during the breeding season, or annual biting rate (ABR) below 1337, if other situation remains unchanged.

The above estimation was based on rather incomplete data available, and further studies will be required to obtain more accurate estimates. The critical vector density of 7.43 per dog per night may be thought to be too high, but the real critical density would not be much lower than this value.

**Consideration on Yearly Changes in Microfilaria Positive Rate**

The heavy infection of dogs with *D. immitis* has been continuously reported in Japan, as in Fig. 5 that chronologically presents infection rates of dogs. As indicated in the previous sections, the high density of vector mosquitoes expects to support the high prevalence of *D. immitis*. But any tendency of decrease in the dog infection was not recognized in spite of presumed reduction in vector density in recent years. Therefore, other factors than vector density were to be considered for the continuous infection in dogs. They must have acted in the direction to increase the prevalence of *D. immitis* in the dog population.

Besides the vector density, there are many factors affecting the transmission of *D. immitis*. Among them, the availability of host animals for vectors to feed on was thought to be important, because it has greatly changed in recent years. The availability depends mainly on the numbers of host animals and the degree of human protection from mosquito bites.

*The number of dogs*

*Cx. pipiens pallens*, the main vector mosquito of *D. immitis*, prefers to feed on
By examination of microfilariae

By dissection of dogs

Fig. 5. Reported infection rates of dogs with *D. immitis* in different years in Japan. Data are from Ohishi (1986).

Fig. 6. Yearly change of the number of registered dogs in Nagasaki City.
humans and dogs. The number of dogs greatly increased in recent years as shown in Fig. 6, while the number of humans only slightly did. Therefore, the effect of the dog density on the prevalence of *D. immitis* was examined.

Supposing that the vector feeds only on humans and dogs, the feeding rate on each host can be calculated under a set of situations. When the number of humans is *e* and that of dogs *f*, and the total number of vectors feeding on humans is *q* and that on dogs *r*, we have the feeding rates of vectors on humans and on dogs as in the below.

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>No. vectors feeding</th>
<th>No. of vectors per individual</th>
<th>Feeding rate of vectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans</td>
<td><em>e</em></td>
<td><em>q</em></td>
<td><em>q/e</em></td>
<td><em>q</em>(q + <em>r</em>)</td>
</tr>
<tr>
<td>Dogs</td>
<td><em>f</em></td>
<td><em>r</em></td>
<td><em>r/f</em></td>
<td><em>r</em>(q + <em>r</em>)</td>
</tr>
<tr>
<td>Total</td>
<td><em>e + f</em></td>
<td><em>q + r</em></td>
<td><em>(q/e + r/f)</em></td>
<td>1</td>
</tr>
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If the number of dogs changes from *f* to *sf* but the total number of vectors remains unchanged, then

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<th>No. vectors feeding</th>
<th>No. of vectors per individual</th>
<th>Feeding rate of vectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans</td>
<td><em>e</em></td>
<td><em>C</em>e*</td>
<td><em>C</em>e/q<em>e</em></td>
<td><em>q</em>(q + <em>sr</em>)</td>
</tr>
<tr>
<td>Dogs</td>
<td><em>sf</em></td>
<td><em>C</em>sf</td>
<td><em>C</em>sf/q</td>
<td><em>sr</em>(q + <em>sr</em>)</td>
</tr>
<tr>
<td>Total</td>
<td><em>e + sf</em></td>
<td><em>q + r</em></td>
<td><em>(q</em>e + rsf)*</td>
<td>1</td>
</tr>
</tbody>
</table>

where *C*=(q + *r*)(q + *sr*). If the number of dogs increases (*s > 1*, accordingly *C < 1*), it is

![Fig. 7. Theoretical relation between the degree of dog density increase (s) and the microfilaria positive rate (y0) based on Equation (7) and (10).](image)
expected that the number of vectors per dog decreases but the feeding rate of vectors on
dogs increases. Letting the force of infection under an initial set of situations be 0.16
(mean in Nagasaki and Omura) for simplicity, we have the new force of infection $A$ when
the number of dogs changes from $f$ to $s/f$
\[
A = 0.16 \times \frac{(C \times r/f \times sr(q + sr))}{(r/f \times r/(q + r))} = 0.16 \times C^2 s
\]
where $C = (q + r) / (q + sr)$. We can calculate the microfilaria positive rate in dogs by
Equation (7), if the force of infection is given.

Fig. 7 represents the relation between $s$ and the microfilarial positive rate $y_0$
calculated with $A$ by equation (10) when $q/r$ is 0.01, 0.1, 1, 10 and 100. When $s=q/r$, $y_0$
has a maximum value. Therefore, when $s$ increases from one (the number of dogs in-
creases from $r$), the microfilaria positive rate $y_0$ decreases if $q/r$ is less than one. This
means that if the total number of mosquitoes feeding on dogs is larger than that on
humans, then the force of infection $A$, and accordingly the microfilaria positive rate also,
decrease with the increasing number of dogs. On the other hand, if $q/r$ is more than one,
the microfilaria positive rate $y_0$ first increases, reaches a maximum, then decreases with
the increase of $s$. The microfilaria positive rate in dogs would usually increase with the in-
crease of the number of dogs, because the number of mosquitoes feeding on dogs is, in
most cases, much smaller than that on humans.

The microfilaria positive rate in each of the divisions of Nagasaki City was plotted
in Fig. 8 against the mean number of dogs per house. The higher microfilaria positive
rate in dogs tended to be found in the divisions with larger mean number of dogs per
house. This seems to support the expectation that if the number of dogs increases, the
microfilaria positive rate would become higher.

The degree of human protection from mosquito bites

Similarly to the case in which the number of dogs was considered, we suppose that
the degree of human protection from mosquito bites becomes higher by $v$ times, that is,
the number of vectors feeding on man changes from $q$ to $wq$ where $w$ is $l/v$, while other
situations remain unchanged. Then we have

Fig. 8. Relation of the rate of dogs positive for microfilariae of $D. immitis$ to the mean number of
dogs per house in each of administrative divisions of Nagasaki City.
<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>No. vectors feeding</th>
<th>No. of vectors per individual</th>
<th>Feeding rate of vectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans</td>
<td>e</td>
<td>wq</td>
<td>wq/e</td>
<td>wq/(wq + r)</td>
</tr>
<tr>
<td>Dogs</td>
<td>f</td>
<td>r</td>
<td>rlf</td>
<td>r/(wq + r)</td>
</tr>
<tr>
<td>Total</td>
<td>e + f</td>
<td>wq + r</td>
<td>wq/e + rlf</td>
<td>1</td>
</tr>
</tbody>
</table>

Letting again the initial force of infection be 0.16 (mean in Nagasaki and Omura) for simplicity, the new force of infection \( B \), when the degree of human protection becomes higher by \( v \) times, is obtained as

\[
B = 0.16 \times \frac{rlf \times r/(wq + r)}{rlf \times r/(q + r)} = 0.16(q + r)/(wq + r) \]

where \( w = l/v \).

Fig. 9. shows the relation between \( v (=l/w) \) and the microfilaria positive rate \( y_0 \) by Equation (7) with \( B \) when \( q/r \) is 0.01, 1 and 100. It is clear that the microfilaria positive rate \( y_0 \) in dogs increases with the higher degree of human protection from mosquito bites. An apparent increase in microfilaria positive rate \( y_0 \) would be expected, since the human protection from mosquito bites has been very much improved and \( q/r \), which is the ratio of the number of vectors feeding on humans to that on dogs, is considered to be generally quite high. Thus, in addition to the increase of dog density, another factor responsible for the continuation of extensive infection of dogs with \( D. immitis \) in recent years seems to be the increased protection of humans from mosquito bites.

In the above, it was shown that the microfilaria positive rate in dogs would vary by the density of dogs and the degree of human protection from mosquito bites. These two factors are liable to differ from place to place, therefore the critical vector density of 7.43, which was obtained in the present paper, could not probably be applied in other areas until detailed studies are made.

Fig. 9. Theoretical relation between the degree of human protection from mosquito bites \( (\nu) \) and the microfilaria positive rate in dogs \( (y_0) \), based on Equation (7) and (11).
REFERENCES


