ORIGINAL CONTRIBUTION

Effect of Changes in Breast-feeding on the Age Distribution of HTLV-I Carriers Using a Mathematical Model

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Based on a mathematical model of human T-cell leukemia virus type I (HTLV-I) transmission, the non-vanishing condition of HTLV-I was derived, and the effect of changes in breast-feeding patterns on the prevalence of HTLV-I was evaluated. The non-vanishing condition was shown to be $a > 1/(1+b)$, where a is the probability of mother-to-child transmission and b is the probability of husband-to-wife transmission. This condition implies that if a is under 0.5, HTLV-I cannot be sustained in populations over a long term. The age-specific prevalences in 1985 were calculated under this model and the assumption of changes in breast-feeding over the period 1925-1985, based on information from many surveys on breast-feeding in Japan. The prevalence increased with age, like the prevalences observed in many populations in Japan. These findings suggest that the probability of mother-to-child transmission had been over 0.5 and was reduced by the spread of compound milk and the shorter duration of breast-feeding in recent years in Japan, and that it has resulted in a decrease in HTLV-I carriers among younger age groups. *J Epidemiol*, 1991; 1: 1-5.

HTLV-I, ATL, breast-feeding, age distribution

Adult T-cell leukemia (ATL) has been shown to be caused by infection of human T-cell leukemia virus type I (HTLV-I)^{1,2}. Since HTLV-I is transmitted in a cell-to-cell mode and its target is the T-cell³, the transmission of HTLV-I is likely to follow the liver transfer of T-cells⁴. The main routes of HTLV-I transmission seem to be mother-to-child through breast-feeding, husband-to-wife and blood-borne transmission⁴⁻⁶.

The probability of transmission via breast-feeding has been reported to be about 0.3⁷⁻⁹. However, if this probability is about 0.3 or less, it has been shown that the prevalence of HTLV-I could not have been sustained in populations until today¹⁰.

In many populations in Japan, the prevalence of HTLV-I has been observed to increase with age¹¹⁻¹³, and no explanation for this has as yet been given¹³.

This paper aims to derive a non-vanishing condition of HTLV-I, and to show that the increase of the prevalence with age can be caused by changes in breast-feeding.

MATERIALS AND METHODS

1. Mathematical model

In the model proposed in Figure 1, the routes of HTLV-I transmission are assumed to be only mother-to-child and husband-to-wife. A carrier mother transmits HTLV-I to her child with a probability, a . A carrier husband transmits it to his wife who is a non-carrier, with a probability, b .

Let P_n be the prevalence in mothers of the n th generation. The prevalence in mothers of the $(n+1)$ th generation can be written as follows,

$$P_{n+1} = aP_n + (1-aP_n)aP_nb. \quad (1)$$

The first term in (1) represents the mother-to-child transmission, and the second term represents the husband-to-wife transmission.

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Figure 1. Mathematical model of HTLV-I transmission. P_n and P_{n+1} are prevalences in mothers of the n th generation and in those of the $(n+1)$ th generation, respectively. a and b are probabilities of mother-to-child and husband-to-wife transmissions, respectively.

2. Non-vanishing condition of HTLV-I

In order to derive a non-vanishing condition of HTLV-I, we consider that the prevalence is stationary, that is, P_n never changes through generations. Let P be the stationary prevalence in mothers. From (1), the relationship among P , a and b can be obtained.

3. Effect of changes in breast-feeding patterns on prevalence

The age-specific prevalences of HTLV-I in 1985 were calculated under the mathematical model in Figure 1 and the following assumptions.

First, consider the relation between the probability of mother-to-child transmission, a , and the total amount of breast milk given to an infant during the period of breast-feeding. The solid and broken lines in Figure 2 represent the amount of breast milk per day in two patterns of breast-feeding. The first pattern (the solid line in Figure 2) is modified from the observed data on breast-feeding in recent years in Japan, and the second pattern (the broken line in Figure 2) is modified from those of several decades ago¹⁴⁾. The ratio of the total amount of breast milk in the first pattern to that in the second pattern is calculated to be about 3:7. If $a=0$ for no breast-feeding, $a=0.3$ for the first pattern, and a is proportional to the total amount of breast milk, a for the second pattern becomes 0.7. It is, therefore, assumed that $a=0.15$ when the total amount of breast milk is less than that

in the first pattern, as its value is the average of a for no breast-feeding and a for the first pattern, that $a=0.5$ when the total amount of breast milk is between that in the first pattern and that in the second pattern, and that $a=0.7$ when the total amount of breast milk is more than that in the second pattern.

Infants are categorized by their total amount of breast milk into 3 groups (the total amount of breast milk is less than that in the first pattern, between that in the first pattern and that in the second pattern, and more than that in the second pattern). Proportions of each of 3 groups of infants to all infants are assumed to be shown in Figure 3 from 1925 to 1985, based on information from many surveys on breast-feeding in Japan¹⁴⁻¹⁶⁾, and are assumed to have been constant before 1925.

Other assumptions are as follows: Males and females get married at the age of 25 years, and a carrier husband quickly transmits HTLV-I to his wife. Children are borne to 25 year old mothers, and a carrier

Figure 2. Amount of breast milk given to an infant per day in the two patterns of breast-feeding.

Figure 3. Proportions of each of 3 groups of infants to all infants from 1925 to 1985. The first pattern and the second pattern are shown in Figure 2.

mother quickly transmits HTLV-I to her children. The prevalence of HTLV-I in mothers was 25% before 1925, since the prevalence in females older than 60 in a population was reported to be about 25% in 1984-85¹⁰. The probability of husband-to-wife transmission, $b=0.68$, as this value was determined by the following non-vanishing condition.

RESULTS

1. Non-vanishing condition of HTLV-I

For example, taking the prevalence in mothers of the baseline generation, $P_0=0.5$, and assuming $a=0.3$ and $b=0.7$, we obtain a prevalence trend through generations in Figure 4. The prevalence in mothers of the first generation, $P_1=0.24$, $P_2=0.12$, and P_n is less than 0.01. In this case, HTLV-I can not be sustained.

Noticing that $P_{n+1}=P_n=P$ in (1), with unchanging prevalence through generations, we obtain

$$b=(1-a)/(a(1-Pa)). \quad (2)$$

The relation among P , a and b in (2) are illustrated in Figure 5. If a given point (a , b) is on the curve with the value of P , P_n converges to P as n increases. For example, putting $a=0.6$ and $b=0.8$, P_n converges to about 30%.

In (2), $P>0$ if and only if

$$a>1/(1+b).$$

This is a non-vanishing condition. Furthermore, since b is 1 or less, $a>0.5$. This condition implies that when a is 0.5 or less, the prevalence decreases towards zero, even if $b=1$, that is, a carrier husband always transmits HTLV-I to his wife.

Figure 4. The prevalence trend in mothers through generations (an example).

2. Effect of changes in breast-feeding patterns on prevalence

As the duration of breast-feeding becomes shorter and the proportion of mothers breast-feeding becomes lower, the averaged probability of mother-to-child transmission decreases. This probability was estimated to be 0.64 in 1925, and 0.3 or less after 1965.

For 1985, the prevalence increases with age (Figure 6). This increase with age was like prevalences observed, for example, in Figure 7¹⁰. In Figure 6, the differences between prevalences with changes in breast-feeding and prevalences without those (— vs. ——— in female, --- vs. in male), represent an effect of changes in breast-feeding on prevalence.

DISCUSSION

1. Non-vanishing condition of HTLV-I

The proposed model does not include the route of blood-borne transmission. The non-vanishing condition of HTLV-I would not be affected by the route of blood-borne transmission, since blood transfusion was never performed in much earlier decades, and screening of donors will prevent most cases of HTLV-I transmission from now on in Japan⁹.

Figure 5. Relations among stationary prevalence (P), probability of mother-to-child transmission (a) and probability of husband-to-wife transmission (b).

Figure 6. Prevalences calculated under the model.

Figure 7. Prevalences observed in a population¹³⁾.

In the present study, it was shown that if the probability of mother-to-child transmission was under 0.5, HTLV-I could not be sustained. However, from recent studies⁷⁻⁹⁾, this probability has been reported to be about 0.3. These findings suggest that this probability had been over 0.5 and was reduced to the above value by some factors in recent years. If not, other unknown important routes of HTLV-I transmission would exist.

2. Effect of changes in breast-feeding patterns on prevalence

The increase of prevalence was partially caused by blood-borne transmission⁴⁾. Differences between prevalences in males and those in females were associated with husband-to-wife transmission⁸⁾. However, the increase of prevalence with age in both sexes could not be caused by only these routes¹³⁾.

The changes in breast-feeding (Figure 3) are not only an impractical assumption, since they are based on information from many surveys on breast-feeding in Japan¹⁴⁻¹⁸⁾. Furthermore, it was reported that the duration of breast-feeding has become shorter by the education of proper duration of breast-feeding for mothers in recent years, and that the use of compound milk has been widely spread from 1950s in Japan¹⁴⁾. Therefore, the changes in breast-feeding of our assumption may reflect on those in most of the Japanese

population. Based on our model, the increase of prevalence with age, which was observed in prevalences in many populations in Japan, was induced by these changes in breast-feeding patterns. The curve of the age-specific prevalences could not be greatly distorted by small changes in other assumptions.

The above discussion suggests that the probability of mother-to-child transmission had been over 0.5 and was reduced by the spread of compound milk and the shorter duration of breast-feeding in recent years as compared to previous years in Japan, and that these resulted in the increasing prevalence with age. Furthermore, without great changes in breast-feeding patterns tending to produce an increase in the probability of mother-to-child transmission, the prevalence of HTLV-I will converge to zero in the future.

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