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REGULAR ARTICLE

Use of a mathematical model to estimate tuberculosis transmission risk in an Internet café

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Abstract

Objective People who live under fragile living conditions may stay overnight in Internet cafés in urban areas. An outbreak of tuberculosis (TB), the routes of which were possibly related to such a facility, has been reported. The purpose of this study was to use a mathematical model to quantify the public health risk of TB infection in such a facility.

Methods The reproduction number for airborne infection in an enclosed space (R_A) was estimated using a Wells–Riley model. First, we estimated R_A for the TB infection based on the report of the TB outbreak in the Internet café. Second, TB infectious dose, number of days of exposure, and air-exchange rate in the facility were varied to estimate the effect of TB risk settings and environmental factors.

Results We assumed that TB patients and 59 susceptible subjects stayed for 150 days in a room where the air-exchange rate was five per hour. Using the estimated median R_A of 44.14, the TB infection rate was 74.6%. This result was similar to the epidemiological report that the TB infection rate among employees in the Internet café was 70%. The median R_A increased linearly as the number of days of exposure increased. The slope of the change in median R_A divided by the change in the number of days of exposure increased exponentially as air-exchange rate decreased; thus air ventilation in a facility may be essential to prevent TB infection.

Conclusions Appropriate air ventilation in facilities such as Internet cafés is needed as part of a TB-control program in metropolitan areas.

Keywords Tuberculosis · Urban area · Internet café · Wells–Riley model · Air ventilation

Introduction

According to a nationwide survey of tuberculosis (TB) [1], the incidence of all forms of TB in Japan was 20.6 per 100,000 in 2006. There has been a gradual decrease from 23.3 per 100,000 in 2004. In terms of new TB patients, 61.5% are older than 60 years, 20.4% are in their forties to fifties, 17% are in their twenties to thirties, and 1.1% are under twenty years old. However, the incidence among subjects in their twenties to thirties was unchanged from 2004 to 2006. New TB cases have been concentrated in urban cities, and the prevalence of TB among disadvantaged and homeless people in metropolitan areas is higher than that in the general population in Japan [2–4].

It was reported that among a group outbreak of TB in Kawasaki city, a 40-year-old construction worker was diagnosed with pulmonary TB and secondary infections had occurred in one of the city's Internet cafés [5]. After tracing the Internet cafés where he often stayed, seven of ten employees in one Internet café tested positive for exposure to TB, and two of the seven infected employees developed TB [5].

In Japan, people who lack a conventional residence stay overnight in various places, including the streets,

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bunkhouses for construction workers, transient hotels, and 24-h public saunas. Such people are referred to as living under fragile living conditions. Many Internet cafés have been built for people to use online services in urban cities, and people with fragile living conditions frequently stay overnight in these Internet cafés [6].

People with fragile living conditions are at high risk of TB infection, and affected individuals may spread the disease in young urban communities. This was considered one reason for the finding that the rate of incidence among younger people was found not to decrease from 2004 to 2006. As the prevalence of drug-resistant TB among the poor urban population increases, multi drug-resistant (MDR) TB may be an especially important risk, and intensive public health intervention will be required [2, 3].

The Wells–Riley mathematical model has been used to estimate airborne TB infection risk in an enclosed space [7–10]. The spread of TB infection in an Internet café used by an unspecified number of people is not clear. In this study, we used the Wells–Riley mathematical model to quantify the risk of infection to supplement epidemiological findings. In addition, we examined the effect of variable TB risk settings and environmental control measures on reduction of the risk of infection.

Methods

To quantify the risk associated with the inhalation of indoor airborne infection microbes, we used a model based on the Wells–Riley equation and estimated the reproduction number for an infectious disease in an enclosed environment (R_A).

Risk models

A quantum is defined by the number of infectious droplet nuclei required to infect 1 − 1/e (63.2%) of susceptible people in an enclosed space at the time when each susceptible person breathes one quantum of infectious droplet nuclei [11]. The quantum for a microorganism (infectious agent) depends on the biological characteristics of the organism and the immunological state of the susceptible people. Thus, a quantum represents the average infectious source strength (or infectious dose) of infectious individuals. Using the quantum generation rate q (quanta per hour, qph) of an infectious person, the probability P of cumulative risk of infection for a susceptible individual during n days is estimated using the Wells–Riley equation as:

$$P = 1 - \{\exp(-Ipqt/Q)\}^n \cong D/S \qquad (1)$$

where D is the number of newly infected cases in the enclosed environment and S is the number of susceptible people in an enclosed space. I is the number of infectious people, p is the breathing rate per person (m^3/h), t is the exposure time (h) per day, and Q is the room ventilation rate (m^3/h) [9]. Q is calculated from $A \times V$, where A is the air-exchange rate by ventilation per hour (/h) and V is the volume of the ventilated space (m^3). Finally, n is the total number of days of exposure. Eq. 1 assumes steady-state exposure conditions. These conditions were chosen assuming: equal host susceptibility, uniform sizes of droplets, uniform ventilation, homogeneous mixing of air, and minimal elimination of infective particles other than by removal by ventilation. The risk of infection was also assumed to be constant during days of exposure.

When $I = 1$ and $S = N - 1$, the reproduction number for an infectious disease in an enclosed environment (R_A) is expressed as follows:

$$R_A = (N - 1) \times P \qquad (2)$$

where R_A is the number of secondary infections that arise when a single original infectious case is introduced to susceptible people in an enclosed environment [12].

Estimating distributions for the quantum generation rate of TB

We obtained the quantum generation rate q by back-calculating from the risk of infection P, using the following expression from the Wells–Riley model:

$$q = -Q/Ipt \times \log(1 - P). \qquad (3)$$

From the epidemiological data of transmission of MDR TB during an 8.75-h airplane flight, Ko et al. [10] reported mean risks of TB infection in a commercial airline of 2.4×10^{-3} (standard deviation, 2.4×10^{-3}), 1.5×10^{-3} (9.3×10^{-3}), and 0.12 (0.10) estimated for quantum generation rates q varying from 2 to 13, and then to 108, respectively. These distributions of the risk of TB infection P(s) were right-skewed and log-normal distributions were assumed. Log-normal distribution with a geometric mean of 0.0017 and a geometric standard deviation of 2.2992 (LN(0.0017, 2.2992)), LN(0.0127, 1.7688), and LN(0.0922, 2.0672) were obtained as TB infection risk distributions for mean TB infection risks, respectively. We calculated three log-normal distributions for quantum generation rate q(s), for which the median ranged from 2.33 to 17.58, and then to 132.30, from TB infection risk distributions and Eq. 3, with values [10] in this commercial airline as shown in Table 1, by Monte Carlo simulation with Crystal Ball software (Decisioneering, Denver, CO, USA). It was reported that a quantum generation rate of 1.25 quanta per hour (qph) represented the infectious dose of chemotherapy-treated TB patients, 13 qph represented that of active TB patients without chemotherapy, and more than 100 qph represented that of highly infectious TB patients who had cavity lung lesions or laryngeal tuberculosis [7, 9].

The goodness of fit of distributions was tested by use of Kolmogorov–Smirnov statistics.

Values for hypothetical scenario and for estimating distributions for R_A of TB infection

We based the hypothetical scenario on information about an outbreak traced to a single Internet café. Table 2 shows the base values and study ranges of the variables used to estimate R_A for TB infection in this Internet café. The total number of occupants was assumed to be 60 because there are 60 booths in the café. As the number of booths was the only information available about the structure of the Internet café, the area and height were assumed to be 330 m^2 and 3.5 m, respectively, on the basis of another Internet café that had the same number of booths [13]. Hence, the volume of the ventilated space V was 1,155 m^3. Q is calculated from $A \times V$, where A is the air-exchange rate by ventilation per hour (/h). An air-exchange rate of five times per hour for guest room accommodation is recommended by the National Institute of Health Science in Japan [14]. A TB patient with symptoms such as productive coughing had stayed overnight at this Internet café for about six months. We assumed the patient and susceptible people stayed together for 10 h overnight each day, and assumed there were up to 150 days of exposure.

Table 1 Variables used to estimate the quantum generation rate

Variable	Value
Volume of shared airspace (V) (m^3)	205[a]
Total exposure time (t) (h)	10
Breathing rate (p) (m^3/h)	0.3[b]
Number of infectious people (I)	1
Outdoor air supply rate (Q) (m^3/h)	4,100

Q is calculated from an air-exchange rate of 20 per hour and the volume of shared airspace V

[a] There were 136 people (N) in the ventilated airspace

[b] From Ref. [10]

Table 2 Variables used to estimate R_A for TB infection in an Internet café

Variable	Value
Number of people in enclosed airspace (N)	60[a]
Volume of shared airspace (V) (m^3)	1155[a]
Total exposure time (t) (h)	10
Breathing rate (p) (m^3/h)	0.3[b]
Number of infectious people (I)	1
Air exchange rate per hour (A/h)	1, 3, 5
Number of days of exposure (n) (days)	1–150

[a] From Ref. [13]

[b] From Ref. [10]

Based on the estimated quantum generation rate and using Eqs. 1 and 2 with the values in Table 2, we quantified R_A for TB infection in the Internet café using a Monte Carlo simulation. The goodness of fit of distributions was tested by use of Kolmogorov–Smirnov statistics.

To estimate the effect of different factors, we changed the quantum generation rate and the number of days of exposure. We also evaluated environmental factors, for example lowering the outdoor air-exchange rate.

Results

Estimated probability distribution of R_A based on the TB outbreak report

We assumed that one affected individual and 59 susceptibles stayed one night (10 h) in a room where the air-exchange rate was five per hour. Using the distributions of the quantum generation rate q, with a median of 17.58, we observed that the estimated probability distribution of R_A for 30 days of exposure fit a gamma distribution that had a median of 14.22, a location parameter of 1.18, a scale parameter of 3.87, and a shape parameter of 3.74132. The estimated probability distribution of R_A for 60 days of exposure was fitted to a beta distribution $B(\alpha, \beta)$ with $\alpha = 3.04057$, $\beta = 1.56254$, and a median of 25.01. The estimated probability distributions of R_A obtained were B(2.50054, 2.78186), which had a median of 33.20 for 90 days of exposure, B(2.76827, 2.01818), which had a median of 39.42 for 120 days of exposure, and B(3.04057, 1.56254), which had a median of 44.14 for 150 days of exposure. Thus, we noted relationships between the medians of estimated probability distributions of R_A and months of exposure (Fig. 1).

Effects of number of days of exposure and air-exchange rate per hour on median of distribution for R_A

Using the distributions of quantum generation rates q(s), with medians of 2.33, 17.58, and 132.30, we observed that the estimated probability distributions of R_A fit log-normal distributions that had medians of 0.43, 0.54, and 4.02, respectively.

We estimated changes in medians of distribution for R_A for consecutive stays with different ventilation conditions for two lower distributions of quantum generation rates. First, we considered the case of active TB patients without chemotherapy (median quantum generation rate, 17.58).

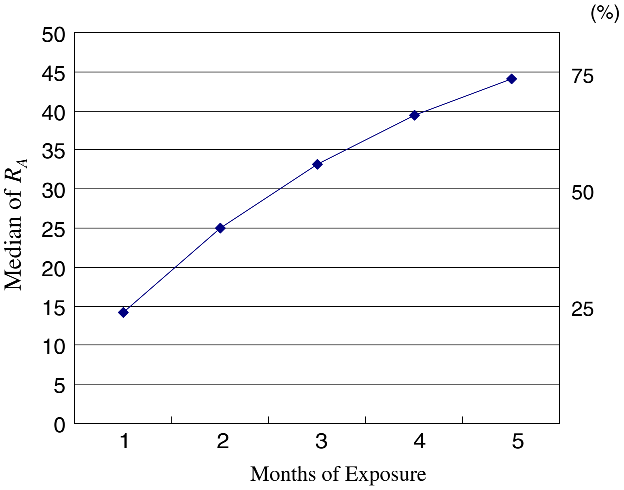

Fig. 1 Relationship between months of exposure and the median of the estimated probability distribution of R_A for the quantum generation rate's distribution with a median of 17.58 quanta per hour

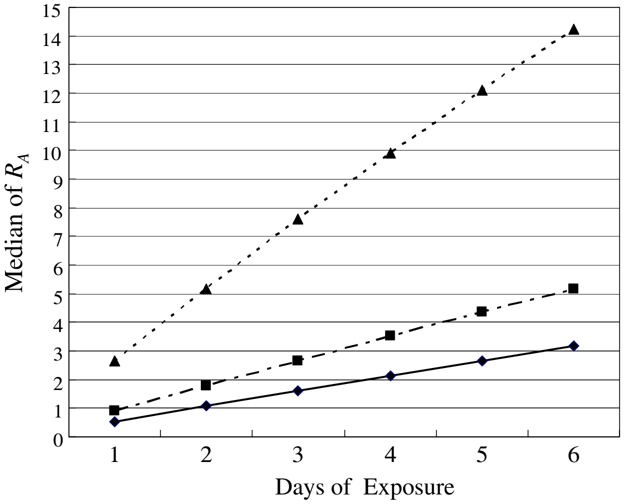

Fig. 2 Relationship between the number of days of exposure and the median of the estimated probability distribution of R_A for the quantum generation rate's distribution with a median of 17.58 quanta per hour. *Filled diamonds* denote five air changes per hour (ACH), *filled squares* denote three ACH, *filled triangles* denote one ACH

For a one-night stay the median R_A was 2.65 if the air-exchange rate was once per hour, whereas the median R_A was less than unity if the air-exchange rate was three or five times per hour (Fig. 2). After a two-day stay, the median R_A exceeded unity, even if the air-exchange rate was three or five times per hour (Fig. 2). We calculated the slopes of the change of the median R_A for a change in number of days of stay (Δmedian R_A/Δdays of exposure) for each air-exchange rate, and investigated the relationships between the slopes and air-exchange rates (Fig. 3). The slope Δmedian R_A/Δdays of exposure increased exponentially as the air-exchange rate per hour decreased.

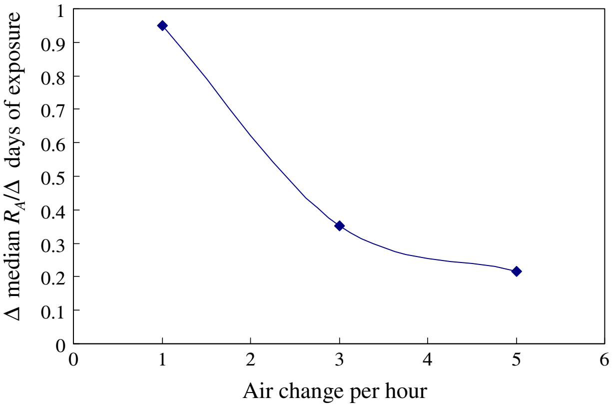

Fig. 3 Relationship between Δmedian R_A/Δdays of exposure and air changes per hour for the quantum generation rate's distribution with a median of 17.58 quanta per hour

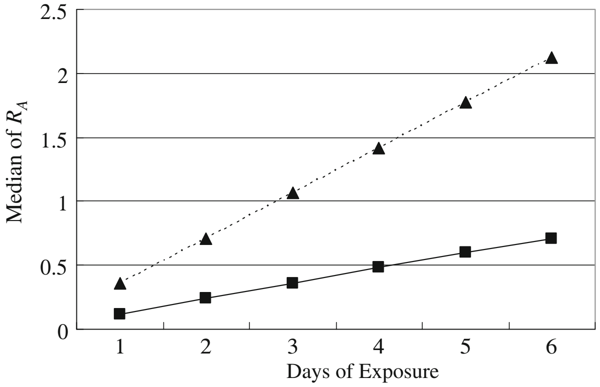

Fig. 4 Relationship between number of days of exposure and the median of the estimated probability distribution of R_A for the quantum generation rate's distribution with a median of 2.33 quanta per hour. *Filled squares* denote three ACH, *filled triangles* denote one ACH

When the median of the quantum generation rate was 2.33, the median R_A was less than unity, even after a six-day stay, if the air-exchange rate was three times per hour (Fig. 4). However, the median R_A exceeded unity after a three-day stay if the air-exchange rate was unity (Fig. 4). As the number of days of exposure increased from 1 to 6, the median of the estimated probability distribution of R_A increased linearly in both distributions of quantum generation rates (Figs. 2, 4).

Discussion

The Ministry of Health and Labor and Welfare conducted a survey of overnight users of an Internet café in an urban area [6]. There were 1,664 participants, and 37.9% used the facility more than three days per week; 7.8% of participants were considered to have fragile living conditions.

People in their twenties accounted for 51.2% of all participants. Among participants with fragile living conditions, those in their twenties accounted for 26.5%, and those in their fifties accounted for 23.1%. This survey showed that Internet cafés were used for Internet use by young people and as a place to sleep for people with fragile living conditions.

People with fragile living conditions have a higher risk of TB infection than the general population [2, 3]. Kizuki et al. [2] investigated the social course of TB patients with fragile living conditions and observed that such patients showed a high rate of interruption of TB treatment. Tamaru [15] summarized recent reports about TB outbreaks by suspected transmission in a facility used by an unspecified number of people, and reported that it was difficult to identify the contact trace in this facility, but molecular epidemiology techniques could detect TB clusters that could not be identified by routine contact investigations. Kinoshita et al. [5] reported a TB outbreak in which people with fragile living conditions were index cases and their routes of infection were possibly related to a facility, such as Internet café, which was used by an unspecified number of young people. As the spread of TB infection in this type of facility is unknown, we used a mathematical model to estimate the risk of TB infection.

There are several reports of use of the Wells–Riley model to estimate the risk of TB infection using epidemiological data [7–10], but this model has limitations, for example assuming steady-state conditions. Rudnick and Milton [16] developed a non-steady-state version of the Wells–Riley model, and this model has been used to estimate airborne viral infection risks in various environments [12, 17]. However, despite its limitations, because we used reported TB infection risks developed using the original Wells–Riley model, we felt the need to use this original model to estimate the risk of infection in an Internet café.

Comparisons between estimated TB infection risk and epidemiological data

Kinoshita et al. [5] reported a TB outbreak in which nine TB patients had contact with each other in four different Internet cafés in a vicinity of about 500 m. In seven of the nine patients the infection was resistant to streptomycin, and *Mycobacterium tuberculosis* strains in five patients showed identical patterns on DNA fingerprinting analysis.

In the case of one Internet café, a single index patient who had been under fragile living conditions since 2000 had symptoms of productive cough from the end of August 2004 to the end of February 2005, when TB was diagnosed and he was admitted to hospital [5]. During this period he had often used this Internet café. After the city's health-care center was informed about this TB patient, ten employees (one full-time, nine part-time) of this Internet café were examined. Results showed that seven of the ten employees had positive TB results, and two of seven infected employees had already developed TB. The public was informed of the outbreak and the possible relationship with an Internet café (the name of the Internet café was not disclosed) was revealed by the health-care center. Eleven users of this Internet café subsequently contacted the health-care center, and six of the eleven tested positive for TB. The rate of TB infection among employees in the Internet café was 70%, which was similar to the estimated TB infection rate of 74.6% for 150 days (five months). The TB infection rate among clients was regarded as higher than the rate 54.5% among contacted clients from the estimated result.

Sensitivity analysis of source strength and ventilation rate

In this study, for one-night stays by affected individuals whose median distributions of quantum generation rates q(s) were 2.33 and 17.58 the estimated probability distributions of R_A had medians less than unity under room ventilation conditions of an air-exchange rate of five times per hour, as recommended by the National Institute of Health Science. For the highly infectious TB patient, whose median distribution of quantum generation rate was 132.30, the median of the estimated probability distribution of R_A was 4.02, and results showed high infectiousness even during a one-night stay (10 h). Kenyon et al. [18] reported that a single index patient, aged 32 years, who had smear-positive and cavitary pulmonary TB, was identified among airplane passengers on an 8.75-h flight. Tuberculin skin tests were performed for 249 passenger and crew contacts on the same flight as this index patient. The results showed that 15 contacts had positive tuberculin skin tests, nine of fifteen contacts had other previous risk factors for TB, and six (including four with conversions) of fifteen contacts had no other risk factors for TB and had been seated in the same cabin section with the index case. The authors insisted that the possibility of transmission of the TB infection was related to proximity to the index case.

Using the Wells–Riley equation, Ko et al. [10] estimated the quantum generation rate of this index case to be 108 qph from the epidemiological data in the above report by Kenyon et al. [18]. The air-exchange rate in the aircraft ranged from six to twenty times per hour based on the manufacturer's report and is higher than our condition of five times per hour. These results suggest our estimate of high infectiousness during a one-night stay (10 h) is probable.

For the lowest distributions of quantum generation rate representing chemotherapy-treated TB patients, the TB infection risk for a one-week stay is low if the air-exchange rate is three times or more per hour. If the air-exchange rate is once per hour, the median of distribution for R_A exceeds unity after a three-day stay, and TB infection risk increases. For distributions of quantum generation rates representing TB patients without chemotherapy treatment, Δmedian R_A/Δdays of exposure increases exponentially as air-exchange rates per hour decrease (Figs. 2, 3). As exposure days increase from one to six, the median of the estimated probability distribution of R_A increases linearly for the two lower distributions of quantum generation rates. From Eq. 2, the median of distribution for R_A decreases in proportion to the decrease in the number of susceptible people in the facilities.

The air conditions in a guest room in a hotel is regulated by the Hotel Business Law, and in the Building Sanitation Law in hotels with a total floor area greater than 3,000 m^2. These laws regulate indoor air conditions needed to maintain air quality, such as levels of carbon monoxide, carbon dioxide, and floating dust. The guidance of the National Institute of Health Science in Japan [14] recommends air-exchange rates of five times per hour for guest-room accommodation, and air-exchange rates of five times per hour satisfied air quality regulated by these laws. Facilities such as Internet cafés are regulated by the Entertainment Business Control Law or Food Sanitation Law, as opposed to the Hotel Business Law. Although no report about indoor air conditions in the Internet café was found, indoor air conditions in parts of the Internet cafés may be worse than those in hotel guest rooms.

Several reports have been published on the relationship between indoor air ventilation and TB outbreaks in Japan. Shigematsu and Minowa [19] reported a TB outbreak in the workplace and showed that CO_2 concentrations in the air increased to as high as 2,000 ppm when the ventilation system was closed. They considered that frequent suspension of the air-conditioning system to conserve energy contributed to insufficient ventilation that could increase the risk of indoor TB transmission. Toyota [20] reported a mass outbreak of TB in a junior high school; the rate of infection was 90.0%, and the attack rate was 30.0% in the same classroom. He also investigated environmental factors related to this outbreak, and, using sulfur hexafluoride, observed that the air-exchange rate ranged from 1.6 to 1.8 times per hour when the doors of the room were closed.

These results suggest poor air conditions contribute to mass outbreaks of TB, and it is highly recommended that air-exchange rates of five times or more per hour be maintained in public facilities to prevent such mass outbreaks. When the air-exchange rate is five times or more per hour, TB infection risk over a several-day stay in a facility such as an Internet café may be decreased. Further investigation of real air conditions in these facilities is needed. Environmental intervention such as improvement in air-exchange rates will be required to prevent airborne infection in facilities such as Internet cafés, because it is difficult to investigate the contact traces of infection in these facilities.

The persistence of new TB cases in urban areas is an important social problem. As this study was based on limited epidemiological data, results are similarly limited. Despite this limitation, it is valuable to investigate social environments that may affect the distribution of TB in urban areas. A chest X-ray-screening program for people with fragile living conditions has been conducted in urban areas, and TB cases have been identified [3, 4]. In addition to TB screening, better air conditions should be regarded as an important aspect of TB-control programs in metropolitan areas.

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