

# RISK OF TUBERCULOSIS INFECTION AMONG CARE WORKERS DURING AN OUTBREAK OF TUBERCULOSIS AT A CARE FACILITY FOR THE ELDERLY

Hiroki YANAGIHARA

**Abstract** [Objectives] Owing to limited evidence, the risk of and factors related to tuberculosis (TB) infection among care workers is not understood. We experienced an outbreak of TB with 2 cases of active TB (positive cultures) and 34 cases of latent TB infection at a care facility for the elderly. Using an epidemiological investigation of the outbreak, this study aimed to investigate the risk of and factors related to TB infection among care workers and to establish a system for TB control in care facilities for the elderly.

[Subjects and Methods] The index patient (80-year-old woman; fever for 1.5 months) was diagnosed with TB [bI3: GAKKAI classification, sputum smear (3+)]. We investigated the contacts of the patient. On the basis of the epidemiological investigation, we conducted a contact examination of close contacts, including those of residents and care workers at the care facility and staff at the medical facility to which the patient was referred. Reviewing this information, we compared both the results of the QuantiFERON®-TB Gold (QFT-GIT) test and the degree of contact in 10 care workers and 7 nurses who had close contact while providing care services to the patient.

[Results] The QFT-GIT test was conducted twice: 3 weeks and 11–12 weeks after the last contact with the patient. The number of care workers who tested positive while providing care services to the patient were 3, 0, and 5 according to the contact time of <20 h, 20 to <40 h, and 40 to <60 h, respectively. In addition, one equivocal result was found in the <20 h group. Equivocal results were noted in 1, 1, and 0 nurses, respectively. Only care workers tested positive using the QFT-GIT test, and one developed active TB. Each of the care workers spent approximately 50 min daily in planned care service to the patient, while each of the nurses spent approximately 20 min for the same. Care workers provided daily care services such as feeding, changing the patient's posture, turning in bed, diaper changing, bathing, and pro-

viding a bed bath, and nurses provided services such as the measurement of vital signs, hydration, administration of medication, and exchange of cooling material for lowering body temperature. In addition, care workers had been in contact with the patient while providing care services before the patient developed fever, and nurses initiated contact with the patient for care after the fever developed. With regards to daily health monitoring, the staff of the care facility had not monitored the patient for fever, loss of appetite, and/or weight loss before the fever became apparent. On the basis of these results, we suggest that the risk of TB infection is higher in care workers than in nurses because they work in close proximity (with body contact) with the patient for a longer period of time during the infectious period, including the asymptomatic period.

To reduce the risk of TB infection in care workers, it is important to establish early detection systems in care facility residents by improving compliance with TB preventive measures, including routinely conducting closer observation of these health conditions.

[Conclusions] The high rate of infection among care workers may have been related to the longer period of close contact while caring for the patient. To reduce such risks, it is important to establish an early detection system for TB preventive measures in care facilities for the elderly.

**Key words:** Care facility for the elderly, Outbreak, Risk of TB infection, Care worker, QuantiFERON®-TB Gold (QFT-GIT), Contact examination

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## Original Article

COMPARISON OF BIOMARKERS OF PULMONARY TUBERCULOSIS ACTIVITY  
— Serum Surfactant Proteins A and D, KL-6, C-Reactive Protein, and Erythrocyte Sedimentation Rate —Yasunori ENOMOTO, Eri HAGIWARA, Shigeru KOMATSU, Ryuichi NISHIHIRA,  
Tomohisa BABA, and Takashi OGURA

**Abstract** [Objective] To evaluate serum surfactant proteins A and D (SP-A and SP-D), KL-6, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) as biomarkers for monitoring the activity of pulmonary tuberculosis.

[Methods] Patients with recently diagnosed and sputum smear-positive pulmonary tuberculosis were consecutively recruited between February and April 2013 at the Kanagawa Cardiovascular and Respiratory Center. Serum levels of SP-A, SP-D, KL-6, and CRP, and ESR were measured twice before treatment initiation and after confirmation of disease improvement (indicated by two consecutive negative smears or one negative sputum culture). The relationship of those biomarkers with disease activity was evaluated by comparing the baseline values with the biological and radiological disease severities and by assessing the changes in those values before and after treatment.

[Results] Twenty-seven patients with pulmonary tuberculosis were enrolled in the study. The median age was 66 years, and the male/female ratio was 19/8 for the entire cohort. The baseline levels of most biomarkers significantly or relatively increased in patients with severe biological and radiological outcomes, which were indicated by findings such as long-term positive sputum culture, and the presence of cavities and

shadows on chest radiographs. A second measurement of these biomarkers was performed after a median treatment period of 56 days. The changes in the median levels for these biomarkers were as follows (before/after treatment): SP-A (ng/mL), 55.3/39.2 ( $p < 0.01$ ); SP-D (ng/mL), 71.5/38.5 ( $p = 0.03$ ); KL-6 (U/mL), 365/374 ( $p = 0.43$ ); CRP (mg/dL), 3.8/0.4 ( $p < 0.01$ ); ESR (mm/hr), 69/46 ( $p = 0.27$ ). After treatment, the levels of SP-A, SP-D, and CRP significantly decreased.

[Conclusion] The levels of SP-A, SP-D, and CRP reflected not only the baseline values but also the chronological disease activity. Therefore, these biomarkers could be useful for the management of pulmonary tuberculosis.

**Key words:** Pulmonary tuberculosis, Surfactant protein A, Surfactant protein D, KL-6, Biomarker

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## PROSPECTIVE ANALYSIS OF ADVERSE REACTIONS WITH LONG-TERM LEVOFLOXACIN USE

Naikakai, Ryoken

**Abstract** [Background] The safety of the long-term use of levofloxacin as an antibiotic has not previously been reported via a prospective study. This lack of evidence acts as a barrier for its use as an anti-tuberculosis drug.

[Method] Cases with long-term levofloxacin use were prospectively followed at member hospitals of Ryoken. The frequency of adverse events is reported.

[Results and discussion] Of 91 total cases, 7 cases were reported to have adverse drug reactions that may or may not have been levofloxacin-related. Of these 7 cases, 5 reported arthralgia and muscle pain that occurred 37–157 days after starting levofloxacin. Of 49 bacillary-positive cases, 1 case died 1 month later, 1 case did not have a culture examination,

and 47 cases showed culture conversion.

[Conclusion] Long-term levofloxacin use is likely to be safe; however, arthralgia should be monitored in these long-term users.

**Key words:** Levofloxacin, Long-term use, Adverse reactions, Tuberculosis, New quinolone

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## OCCURRENCE AND CLINICAL CHARACTERISTICS OF TUBERCULOSIS AMONG HOME MEDICAL CARE PATIENTS

Satoshi UBUKATA, Daisuke JINGU, Takehiro YAJIMA, Makoto SHOJI,  
and Hiroshi TAKAHASHI

**Abstract** [Objective] To clarify the occurrence and clinical characteristics of tuberculosis among home medical care patients, we conducted a retrospective study of patients who received home medical care from our hospital.

[Subjects and Methods] We investigated 502 patients (mean age, 79.5 years) who received home medical care from our hospital between January 2003 and December 2012. The newly notified tuberculosis cases aged  $\geq 70$  years in the general population in Miyagi were defined as the control group. Among the patients receiving home medical care, we evaluated the clinical characteristics of the patients with tuberculosis.

[Results] Four of the 502 patients (0.8%) developed tuberculosis. Using the person-years method, the case rate of tuberculosis was calculated as 298.3 per 100,000 among home medical care patients. Compared with the control group, home medical care patients had a greater incidence of tuberculosis (298.3 vs. 36.06; rate ratio, 8.27; 95% confidence interval, 3.06–22.3;  $p < 0.001$ ). When home medical care patients visited the hospital or were transported there by ambulance,

they were initially often diagnosed with aspiration pneumonia. Moreover, the time interval to the onset of disease from the introduction of home medical care varied among cases (3–192 months).

[Conclusion] Patients receiving home medical care are at high risk of contracting tuberculosis. Therefore, for the medical staff involved in treating home medical care patients, the onset of tuberculosis should be carefully considered in daily medical practice.

**Key words:** *Mycobacterium tuberculosis*, Home medical care, High-risk group, Active case finding

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## Short Report

## COMPARISON OF TESTS RESULTS BETWEEN T-SPOT®.TB AND QuantiFERON®-TB GOLD IN-TUBE IN A CONTACT INVESTIGATION

<sup>1</sup>Haruko MUKOUYAMA, <sup>2</sup>Kazue HIGUCHI, and <sup>2</sup>Nobuyuki HARADA

**Abstract** [Background] We compared T-SPOT®.TB (T-SPOT) and QuantiFERON-TB Gold In-Tube (QFT-GIT) test results in a contact investigation.

[Subjects and Methods] The index case was a male lecturer at a vocational school in Tokyo. Chest X-ray examinations and T-SPOT tests were performed on all 397 contacts, and QFT-GIT was performed on a subset of these contact subjects.

[Results] Chest X-ray examination showed no evidence of tuberculosis in any subjects. Among 389 contacts that underwent T-SPOT testing, 5 showed a positive reaction, 3 showed borderline reactions (1 positive borderline and 2 negative borderline), and 381 were negative. Among 56 contacts tested using both QFT-GIT and T-SPOT, 4 were positive, 1 was borderline, and 51 were negative by QFT-GIT. By T-SPOT, 2 contacts were positive, 1 was borderline positive, and 53 were negative. Preventive chemotherapy was indicated for the 5 positive and 1 borderline positive contacts identified by the T-SPOT test.

[Discussion] Chest X-ray examination and the T-SPOT test did not identify the TB outbreak.

[Conclusion] The majority of contact subjects were negative by both tests, suggesting that both have a high specificity in contact investigations. However, the moderate concordance rate indicates that further testing is necessary to fully evaluate these tests.

**Key words:** IGRA, T-SPOT.TB, QFT-3G, Contact investigation, Latent tuberculosis infection

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## Case Report

## TENOSYNOVITIS CONFIRMED BY MRI DURING ANTI-TUBERCULOUS TREATMENT SUSPECTED DUE TO ISONIAZID

— 2 Case Reports and Literature Review —

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and <sup>2</sup>Haruto SUGIYAMA,

**Abstract** The adverse effects of anti-tuberculosis agents is an important problem for treatment of tuberculosis. We report 2 possible cases of isoniazid-induced tenosynovitis.

Case 1: A 49-year-old man with untreated diabetic mellitus presented with hypesthesia and difficulty grasping with his right hand 1 month after starting treatment of tuberculosis of the lung and pleuritis using isoniazid, rifampicin, ethambutol, and pyrazinamide. His symptoms were due to tenosynovitis, which was detected by magnetic resonance imaging. The clinical course and isoniazid challenge test revealed that the condition was related to isoniazid. After discontinuing isoniazid treatment, his symptoms gradually improved.

Case 2: An 78-year-old man operated on for rectal cancer 3 weeks previously presented with edema and arthralgia of both hands 1 month after starting anti-tuberculosis treatment. His tuberculosis was diagnosed at preoperative screening tests for rectal cancer. Owing to a medical history of gout, pyrazinamide was discontinued. However, his symptoms did not improve. Magnetic resonance imaging revealed findings indicative of tenosynovitis. At the end of anti-tuberculosis treatment, his

symptoms improved slightly within 6 months.

Isoniazid-induced tenosynovitis and arthritis are rare adverse effects. However, they may be underestimated because the severity is variable. We suggest further investigations of the side effects of isoniazid using imaging techniques such as magnetic resonance imaging.

**Key words:** Isoniazid, Tenosynovitis, Complications of bone and joint during antitubercular treatment, MRI

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# IMPORTANCE OF A SYMPTOMATIC VISIT IN TUBERCULOSIS CONTACTS

## — Classification of Secondary Cases —

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**Abstract** [Objectives] In order to improve the appropriateness of contact examinations, we investigated the characteristics of secondary tuberculosis cases.

[Subjects and Methods] We included tuberculosis patients that were located in Kawasaki City between 2008 and 2011. The patients were considered as 2 separate groups: those with tuberculosis following contact with index cases registered in Kawasaki City and those with tuberculosis who were located in Kawasaki City. Secondary cases were defined as subjects who underwent a contact examination and developed active tuberculosis within 2 years from the last contact with the index case. The secondary cases were classified by diagnostic method, time, and sputum smear test results, followed by consideration of improvement measures.

[Results] There were 1196 tuberculosis patients and 6157 subjects who underwent a contact examination. Of these, 35 patients developed tuberculosis secondary to index cases registered in Kawasaki City. These 35 cases were classified by diagnostic methods. Diagnosis occurred during a contact examination in 31 cases and during a symptomatic visit in 4 cases. There were 2 sputum smear-positive patients detected in a contact examination that was conducted  $\geq 6$  months after contact. These 2 cases had a symptomatic cough, but did not visit a medical institution. There were 39 patients with secondary tuberculosis who were located in Kawasaki City. These 39 cases were also classified by diagnostic methods. Diagnosis

occurred during a contact examination in 33 cases and during a symptomatic visit in 6 cases. There were 4 sputum smear-positive patients detected in a contact examination that was conducted  $\geq 6$  months after contact. These 4 cases had a symptomatic cough, but did not visit a medical institution.

[Discussion] Of the secondary cases, a sputum smear-positive state was detected in some of the patients at the time of a contact examination that was conducted  $\geq 6$  months after contact. However, secondary cases should be discovered at a sputum smear-negative stage. Appropriate education regarding the importance of a medical visit at the onset of symptoms could decrease the number of patients that are identified in the sputum smear-positive state during a contact examination that occurs at least 6 months after contact.

**Key words:** Public Health Center, Contacts examination, Symptomatic visit, Secondary cases, Sputum smear-positive

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### — (2) Childhood and Elderly Tuberculosis —

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**Abstract** In 2012, there were 63 newly notified childhood tuberculosis (TB) patients (patients aged 0–14 years) in Japan, corresponding to a notification rate of 0.38 per 100,000. The annual number of notified childhood TB patients was less than 100 in 2006, since then the numbers and rates (per 100,000 population) decreased steadily. Of the 63 patients with childhood TB notified in 2012, 30 (47.6%) were aged 0–4 years, 12 (19.0%) were aged 5–9 years, and 21 (33.3%) were aged 10–14 years. Thus, the proportion of TB patients aged 0–4 years was the highest among children. In 2012, only one patient of TB meningitis and no patient of miliary TB were reported in children. On the point of case detection, similar to percentages reported in previous years, 22 patients (34.9%) were identified at medical institutions and 32 patients (50.8%) were detected by contact investigation of household members.

Since 1999, the notification rates of TB in Japan have been consistently higher among patients aged 85 years and above than among those aged 65–84 years in Japan. The annual rate of reduction in the notification rates of TB patients aged 65 years and above in 2012 (13,307 cases) was 3.3%, compared to 2011 (13,756 cases). The proportion of TB patients aged 65 years and above has consistently increased, reaching up to 62.5% in 2012; notably, the proportion of TB patients aged 80 years and above has increased to 34.0%. The proportion of bacteriologically positive TB patients among pulmonary TB (PTB) patients was higher among those aged 65 years and above than among those aged 15–64 years. The proportion of

PTB patients with only non-respiratory symptoms increased with age, reaching 27.6% among those aged 85 years and above. The proportion of TB patients associated with patient delay of two months or longer was lower among the patients aged 65 years and above than among those aged 15–64 years (14.5% vs. 26.7%), whereas the proportion of TB patients associated with doctor delay of one month or longer was slightly higher among patients aged 65 years and above than among those aged 15–64 years (22.9% vs. 20.2%). Of the newly notified TB patients aged 65 years and above in 2011 whose treatment outcomes were available at the time of reporting, 31.3% died within a year after the initiation of TB treatment; of these, 18.4% died within three months. The proportion of deaths within three months after the initiation of TB treatment among patients aged 65 years and above increased substantially with age from 8.1% in the 65–69 years age group to 31.9% in the 90 years and above age group.

**Key words:** Tuberculosis, Notification rate, Childhood tuberculosis, Elderly tuberculosis, Annual trend

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