

## THE MINIMUM NUMBER OF SPUTUM SMEAR SAMPLES NEEDED FOR THE DIAGNOSIS OF TUBERCULOSIS

Kanako KOBAYASHI, Shuichi YANO, Emiko NISHIKAWA, Shinichi IWAMOTO,  
Mitsuhiro TADA, Toru KADOWAKI, Masahiro KIMURA, and Toshikazu IKEDA

**Abstract** [Objective] To determine whether three sputum examinations with fluorescent staining are necessary to diagnose tuberculosis (TB) in our hospital.

[Patients] From April 2005 to December 2012, 379 TB patients were admitted and received anti-TB therapy in our hospital.

[Methods] A retrospective study was conducted to assess the positivity rates of sputum smears based on three examinations. The positivity rate of first sputum smear and the cumulative smear-positive rates in the second and third were determined. Then, we also determined difference of positivity rates in sputum properties, sampling procedures and cavity formation.

[Results] Of the 379 patients who met the screening criteria, 300 tested positive based on the first sputum smear (79.2%). The positivity rate of the first sputum smears was higher in the purulent sputum group than in the mucous sputum group (91.2% vs. 72.3%).

Cavity formation, and sputum extraction procedures were

not related to the positivity rate of the first sputum smears. In the mucous sputum group, the cumulative smear-positive rate in the second test significantly rose, but did not rise in the third test.

[Conclusions] Three sputum smear examinations were necessary in patients who submitted mucous sputum samples. It is important to get purulent sputum.

**Key words:** Three sputum smear examinations, Fluorescent staining, Positivity rates of sputum smears

Department of Pulmonary Medicine, National Hospital Organization Matsue Medical Center

Correspondence to: Kanako Kobayashi, Department of Pulmonary Medicine, National Hospital Organization Matsue Medical Center, 5-8-31, Agenogi, Matsue-shi, Shimane 690-8556 Japan. (E-mail: kanako.kobayashi@mmedc.jp)

## Original Article

RISK OF TUBERCULOSIS INFECTION AND DISEASE  
AMONG JAPANESE FEMALE NURSES AND MALE DOCTORS  
IN RECENT YEARS

Yuko YAMAUCHI, Yoko NAGATA, Noriko KOBAYASHI, and Toru MORI

**Abstract** [Objectives and Materials] Based on the tuberculosis (TB) surveillance database, the incidence rates of TB infection and active disease among healthcare workers were observed for female nurses and male doctors in 2010 in comparison with those of the general population.

[Results] The relative risk (RR) of active TB among female nurses aged 20–69 years was 4.86 (95% confidence interval: 4.31–5.45) for 2010, which has increased from 2.30 observed in 1987–1997. The RR was highest for nurses aged 20–29 years at 8.84 and declined with age until 3.60 for those aged 50–59 years that was still significantly higher than 1. For male doctors the RR was significantly higher than 1 only for those aged 39 years or younger.

The rates of those who were indicated for treatment of latent TB infection (LTBI) were clearly higher among healthcare workers; for female nurses the RR was 32.7 (95% CI: 30.5–35.0), ranging from the highest level of 62.8 among those aged 20–29 years down to 11.6 for those aged 60–69 years. For male doctors also, the RR was high at 9.7 (7.9–11.7) for 20–69 years, ranging from 14.5 for those aged 20–29 years down to 5.3 for those aged 60–69 years.

[Discussion] TB cases of nurses and doctors were more likely to be detected by the active case finding measures such as periodic screening and contact investigations than cases in the general population, which indicates the current effort of addressing the occupational exposure in the healthcare settings. The high level of risk of TB disease as well as LTBI among healthcare professions and its possibly increasing trend as seen in female nurses warrants further strengthening of monitoring of the problem and overall countermeasures in their workplaces.

**Key words** : Tuberculosis, Incidence rate, Relative risk, Healthcare worker

Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association

Correspondence to: Yuko Yamauchi, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-8533 Japan.  
(E-mail: yamauchi@jata.or.jp)

---

**Original Article**

---

**THE FREQUENCIES AND MANAGEMENT OF ADVERSE REACTIONS  
IN MULTI-DRUG RESISTANT TUBERCULOSIS TREATMENT**

Yuka SASAKI, Takashi YOSHIYAMA, Masao OKUMURA, Kouzo MORIMOTO,  
Maki MIYAMOTO, IRINA, Kouzo YOSHIMORI, Atsuyuki KURASHIMA,  
Hideo OGATA, and Hajime GOTOH

**Abstract** [Objectives] To investigate the adverse reactions of antimicrobial drugs in multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) patients.

[Results] Sixty-six patients with MDR-TB who have been treated from 2010 through 2014 were evaluated in the retrospective analysis. Variety of adverse reactions including psychological reaction, central nervous system toxicity, ophthalmic toxicity, peripheral neurotoxicity, gastrointestinal reactions, hematologic abnormalities, musculoskeletal adverse effects, and endocrine disorder, were observed. However, there was no fatal case due to the adverse reactions of the anti-tuberculosis drugs in this observation.

[Conclusions] Drugs for MDR-TB and XDR-TB treatment are limited and the adverse reactions of drugs for MDR-TB

and XDR-TB are not well-known. Therefore, the treatment may fail due to inappropriate management of adverse events. MDR-TB and XDR-TB should be treated by the experts of the adverse reactions of all anti-tuberculosis drugs.

**Key words** : Tuberculosis, Multidrug-resistant tuberculosis (MDR-TB), Treatment, Adverse reaction

Respiratory Medicine Division, Fukujiji Hospital, Japan Anti-Tuberculosis Association

Correspondence to: Yuka Sasaki, Respiratory Medicine Division, Fukujiji Hospital, Japan Anti-Tuberculosis Association, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-8522 Japan.  
(E-mail: sasakiy@fukujiji.org)

## Original Article

TREATMENT SUPPORT AND TREATMENT OUTCOMES OF  
PULMONARY TUBERCULOSIS IN PATIENTS WITH HIV INFECTION  
IN OSAKA CITY

<sup>1</sup>Kenji MATSUMOTO, <sup>1</sup>Jun KOMUKAI, <sup>1</sup>Yuko TSUDA, <sup>1</sup>Hideya UEDA,  
<sup>1</sup>Maiko ADACHI, <sup>1</sup>Naoko SHIMIZU, <sup>1</sup>Kazumi SAITO, <sup>1</sup>Hidetetsu HIROKAWA,  
and <sup>2</sup>Akira SHIMOUCI

**Abstract** [Objective] To contribute to countermeasures against pulmonary tuberculosis in patients with HIV infection through analyzing and evaluating its treatment outcomes and patient management.

[Methods] The subjects were pulmonary tuberculosis patients newly registered between 2008 and 2014 in whom concomitant HIV infection was detected. For the control, sex- and generation-matched pulmonary tuberculosis patients newly registered in Osaka City between 2012 and 2014 were adopted. On analysis, the  $\chi^2$  test and Fisher's exact test were used, and a significance level below 5% was regarded as significant.

[Results] 1) There were 25 pulmonary tuberculosis patients complicated by HIV. All were male and the mean age was 43.2 years old.

2) The sputum smear positivity rate was 76.0% in the pulmonary tuberculosis patients complicated by HIV and 50.8% in 250 control pulmonary tuberculosis patients, showing a significantly higher rate in the former.

3) Risk factors for the discontinuation of medication for tuberculosis: In the patients complicated by HIV, the following risks of the discontinuation of medication were noted in the order of a decreasing frequency: 'Lack of medication helpers' in 68.0%, 'Side effects' in 48.0%, 'Financial problems' in 32.0%, and 'Liver damage' in 28.0%. Those in the control pulmonary tuberculosis patients were 33.2%, 22.8%, 16.0%, and 11.6%, respectively, showing a significant difference in each factor.

4) The DOTS executing rates were 68.0% and 94.8% in the patients complicated by HIV and control patients, respectively, showing that it was significantly lower in the patients complicated by HIV. On comparison of the treatment

outcomes excluding died, on treatment, transferred out, not evaluated, treatment succeeded in 72.7% in the patients complicated by HIV and 92.9% in the control patients, showing a significantly lower success rate in the patients complicated by HIV. The numbers of risk factors of discontinuation in 16 and 6 patients complicated by HIV in whom treatment succeeded and treatment failed/defaulted were 3.8 and 2.8, respectively, showing that the number was higher in patients with successful treatment, and the DOTS execution rates were 75.0% and 33.3%, respectively, showing a higher rate in the successful treatment cases.

[Conclusion] The treatment outcome was significantly poorer in pulmonary tuberculosis patients complicated by HIV than in the control pulmonary tuberculosis patients. More risk factors for the discontinuation of medication were observed and the DOTS execution rate was lower in the patients complicated by HIV, suggesting that risk assessment for the discontinuation of medication should be appropriately performed, and support for medication should be strengthened.

**Key words:** Pulmonary tuberculosis, HIV, Co-infection, DOTS, Treatment outcome, Risk factors for failed/defaulted

<sup>1</sup>Osaka City Public Health Office, <sup>2</sup>Nishinari Ward Office, Osaka City

Correspondence to: Kenji Matsumoto, Osaka City Public Health Office, 1-2-7-1000, Asahimachi, Abeno-ku, Osaka-shi, Osaka 545-0051 Japan.

(E-mail: ke-matsumoto@city.osaka.lg.jp)

## Original Article

THE POTENTIAL ROLE OF SOCIAL NETWORK ANALYSIS  
IN TUBERCULOSIS CONTACT INVESTIGATION

<sup>1,3</sup>Kiyohiko IZUMI, <sup>1</sup>Lisa KAWATSU, <sup>4</sup>Satoshi MIYAKE, <sup>4</sup>Yu WATANABE,  
<sup>2</sup>Yoshiro MURASE, <sup>1</sup>Kazuhiro UCHIMURA, and <sup>1,3</sup>Akihiro OHKADO

**Abstract** [Aim] To explore the possible role of social network analysis (SNA) in identifying infected contacts and visualizing data in a tuberculosis (TB) contact investigation.

[Method] We analyzed TB contact investigation data from an outbreak in a Japanese language school in Tokyo, Japan, in 20XX. Information on places which the index case and his contacts commonly shared was collected in line with the data collected routinely in contact investigation. Average hours of exposure to the index case were calculated for each contact by using SNA software, and the relationship to the index case via commonly shared places was visualized as a sociogram. Statistical analysis was performed to compare the exposure hours and TB infection statuses between those infected, including active TB and latent TB infection (LTBI), and non-infected contacts.

[Result] The data on the index TB case and 41 contacts, of whom 5 and 10 were diagnosed with active TB and LTBI, were analyzed. Contacts with active TB and LTBI had 12.5 and 11.5 times longer median hours of exposure, which were significantly longer compared to non-infected contacts. The sociogram summarized the network of index TB case, contacts characterized by exposure hours and infection statuses, and

the places shared by the index case and the contacts.

[Discussion] SNA analysis was considered to be useful in prioritizing contacts in a TB contact investigation, in assisting interpretation of indeterminate Interferon-Gamma release assay test results, in estimating places where transmission occurred, and visualizing data accrued in TB contact investigations.

**Key words** : Social-network analysis, Tuberculosis contact investigation, Tuberculosis outbreak

<sup>1</sup>Department of Epidemiology and Clinical Research, <sup>2</sup>Department of Mycobacterium Reference and Research, Research Institute of Tuberculosis, Japan Anti-tuberculosis Association (RIT/JATA); <sup>3</sup>Graduate School of Biomedical Sciences, Nagasaki University; <sup>4</sup>Shinjuku City Public Health Center

Correspondence to: Kiyohiko Izumi, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-8533 Japan.  
(E-mail: kizumi@jata.or.jp)

## A CASE OF SUBPHRENIC ABSCESS WITH PARADOXICAL RESPONSE CAUSED BY *MYCOBACTERIUM TUBERCULOSIS*

<sup>1</sup>Masami YAMADA, <sup>1</sup>Hideaki YAMAKAWA, <sup>1</sup>Masahiro YOSHIDA, <sup>1</sup>Takeo ISHIKAWA,  
<sup>1</sup>Masamichi TAKAGI, and <sup>2</sup>Kazuyoshi KUWANO

**Abstract** A 40-year-old woman was admitted to our hospital with cough and sputum production. A chest computed tomography (CT) scan revealed a diffuse nodular shadow in the upper lung. The patient was diagnosed with pulmonary tuberculosis, based on a positive T-SPOT®.TB test result of peripheral blood and a positive polymerase chain reaction (PCR) test result for *Mycobacterium tuberculosis* in gastric aspirates. *M. tuberculosis* was subsequently isolated from the gastric aspirate specimen. After 2 months of treatment with antituberculous medication, the patient developed a low grade fever and left-sided chest pain. A CT scan revealed a left pleural effusion and a right subphrenic abscess. Tuberculous pleurisy with paradoxical response was diagnosed on the basis of an increased lymphocyte count and increased adenosine deaminase activity in the pleural fluid exudate. A percutaneous ultrasound-guided needle biopsy of the subphrenic abscess was performed. Histological analysis revealed epithelioid cell granulomas with necrosis and PCR for *M. tuberculosis* using puncture needle washing fluid returned

positive results. Based on these findings, a diagnosis of subphrenic abscess with paradoxical response, caused by *M. tuberculosis*, was made. Subphrenic abscess caused by *M. tuberculosis* is an important consideration during antituberculous therapy.

**Key words:** Pulmonary tuberculosis, Paradoxical response, Subphrenic abscess, Tuberculous pleurisy

<sup>1</sup>Department of Internal Medicine, Division of Respiratory Medicine, Jikei University School of Medicine, Kashiwa Hospital, <sup>2</sup>Department of Internal Medicine, Division of Respiratory Medicine, Jikei University School of Medicine

Correspondence to: Masami Yamada, Department of Internal Medicine, Division of Respiratory Medicine, Jikei University School of Medicine, Kashiwa Hospital, 163-1, Kashiwashita, Kashiwa-shi, Chiba 277-8567 Japan.  
(E-mail: masami-y@jikei.ac.jp)

PULMONARY TUBERCULOSIS AND TUBERCULOUS PLEURISY  
COMPLICATED WITH RIFAMPICIN-INDUCED HYPOTHYROIDISM :  
A CASE REPORT

<sup>1,2</sup>Yuto HAMADA, <sup>1</sup>Akiyuki SATO, and <sup>2</sup>Shinji MOTOJIMA

**Abstract** Rifampicin can induce hypothyroidism. We report a case of pulmonary tuberculosis and tuberculous pleurisy that was complicated by rifampicin-induced hypothyroidism. The patient received rifampicin-based tuberculosis treatment and experienced persistent appetite loss, which led us to provide concomitant hypothyroidism treatment.

An 85-year-old woman with no underlying thyroid-related disease presented to her local hospital with a 3-month history of appetite and weight loss. A chest radiograph revealed pleural effusions and infiltrative shadows in the lower fields of both lungs, and we also detected high levels of lymphocytes and adenosine deaminase levels (49.6 IU/l) in the pleural effusion, with positive results from a polymerase chain reaction assay of a sputum sample. Thus, we diagnosed the patient with pulmonary tuberculosis and tuberculous pleurisy, and initiated treatment using isoniazid, rifampicin, ethambutol, and pyrazinamide. Her clinical course was good and her anorexia was improved. However, she subsequently experienced recurrent appetite loss, malaise, and bilateral lower-leg edema. Follow-up laboratory testing revealed that she had developed hypothyroidism. We started treatment using levothyroxine without interrupting the tuberculosis

treatment. The loss of appetite and other thyroid-related symptoms were improved. The patient's thyroid function had been normal at her admission, and there were no findings of Hashimoto's thyroiditis or other thyroid conditions. Based on the clinical course, we conclude that the rifampicin induced the hypothyroidism.

Therefore, rifampicin-induced hypothyroidism should be considered in cases with persistent appetite loss, even if the patient appears to be experiencing anorexia as an adverse drug reaction.

**Key words :** Rifampicin, Adverse reactions, Hypothyroidism, Tuberculosis, Hashimoto's thyroiditis

<sup>1</sup>Department of General Internal Medicine, <sup>2</sup>Department of Rheumatology, Kameda Medical Center

Correspondence to: Yuto Hamada, Department of Respiratory Medicine, Sagamihara National Hospital, 18-1, Sakuradai, Minami-ku, Sagamihara-shi, Kanagawa 252-0392 Japan.  
(E-mail: yutohamada1983@gmail.com)