

## Original Article

## PREDICTIVE FACTORS FOR TREATMENT INCOMPLETION IN ELDERLY PATIENTS WITH NEWLY DIAGNOSED PULMONARY TUBERCULOSIS

Etsu Tsuzuki FUSE, Yuichiro TAKEDA, Emiko TOYODA, Ayako MIKAMI,  
Nobuyuki KOBAYASHI, and Koichiro KUDO

**Abstract** [Background] To identify predictive factors of treatment incompleteness in elderly patients with newly diagnosed pulmonary tuberculosis.

[Materials and Methods] In elderly patients of more than 65-years old and with newly diagnosed pulmonary tuberculosis, a retrospective study was conducted. A total of 88 patients were admitted in International Medical Center of Japan with pulmonary tuberculosis between June 2000 and February 2002. The relationships between several clinical parameters, including patients' performance status (PS) scale proposed by the Eastern Cooperative Oncology Group, laboratory data, or, radiological findings on admission and treatment incompleteness were assessed by univariate and multivariate logistic regression analyses.

[Results] Ten patients could not complete their treatment; including nine patients who died during hospitalization and one who refused tuberculosis treatment. Preliminary analysis indicated that the treatment incompleteness was related with twelve factors including PS. On univariate analyses, 9 factors were associated with incomplete treatment. The best model

was built up by using 5 independent factors, that is, diabetes mellitus, PS, hypoxemia, duration of sleep, drug resistant strain. On multivariate analysis, only the PS was significantly related to treatment incompleteness in elderly patients with pulmonary tuberculosis (odds ratio: 0.41, 95% confidence interval: 0.17–0.98,  $p=0.04$ )

[Conclusions] High PS showed a strong association with treatment incompleteness in elderly patients with pulmonary tuberculosis. The PS is considered to be a useful clinical indicator.

**Key words:** Pulmonary tuberculosis, Elderly patients, Complete treatment, Performance status

Respiratory Department, International Medical Center of Japan

Correspondence to: Etsu Tsuzuki Fuse, Department of Microbiology and Infection, Toho University of Medicine, 5-21-16, Ohmori-nishi, Ohta-ku, Tokyo 143-8540 Japan.

(E-mail: etfusefuse@yahoo.co.jp)

## Review Article

SEVERE ADVERSE REACTIONS AFTER VACCINATION WITH  
JAPANESE BCG VACCINE: A REVIEW

Ichiro TOIDA and Shizuko NAKATA

**Abstract** Japanese BCG vaccine has been admitted by the quality control of World Health Organization (WHO) as the safest BCG vaccine in the world. Even though, BCG, as a live bacterial vaccine, inevitably causes dissemination beyond vaccination site and regional lymph-nodes to various part of the body under certain special conditions.

We tried to review the clinical features and immunological status of the cases in which "severe" adverse reactions had developed after vaccination with Japanese freeze-dried BCG vaccine prepared from BCG substrain Tokyo. "Severe" adverse reaction was arbitrarily defined as the adverse reactions of clinical significance developed beyond vaccination site and regional ipsilateral axillary lymph-nodes. By the extensive search of the literatures, 39 cases were identified since 1951 when vaccination with freeze-dried BCG vaccine became compulsory by the Tuberculosis Prevention Law in Japan. Incidence rate was calculated as 0.0182 cases per 100,000 vaccinations.

Clinical manifestations of bone and joint were reported in 27 cases (multiple sites: 15 cases, single site: 12 cases), abnormalities in chest X-ray in 13 cases, skin manifestations in 17 cases, diseases in other sites or organs in 8 cases. Most of the cases had lesions in multiple organs.

Among these 39 cases, 13 had been diagnosed to have some types of primary immunodeficiency (5 cases: chronic granulomatous disease (CGD); 4 cases: severe combined immunodeficiency (SCID); 4 cases: IFN- $\gamma$  receptor 1 defi-

ciency). Further, unidentified defects in cellular immunity were reported in other 6 cases. Death was reported in 6 cases, but in two cases the causes of death were the infections due to different pathogens, namely, pulmonary abscess due to *Staphylococcus sp.* and bacteremia due to *Pseudomonas aeruginosa*, respectively, and in only one case death was evidenced as due to disseminated BCG infection by autopsy. All of 6 death cases had some type of immunodeficiency.

Apart from fatal cases, outcome of "severe" adverse events were generally favorable and they were successfully treated by anti-tuberculosis therapy with or without surgical treatment for bone and joint lesions.

Because the risk of "severe" adverse reactions is high among those of primary immunodeficiency, so it is advisable to avoid BCG vaccination during the first three months after birth when the detection of immunodeficiency is practically impossible.

**Key words:** BCG vaccination, BCG substrain Tokyo, Adverse reactions, Immunodeficiency

Japan BCG Laboratory

Correspondence to: Ichiro Toida, 660-52, Mizuno, Sayama-shi, Saitama 350-1317 Japan.

(E-mail: kanematsu@tbg.t-com.ne.jp)

————— Case Report —————

A CASE OF LABORATORY CROSS-CONTAMINATION OF *MYCOBACTERIUM TUBERCULOSIS* ON THE BROTH-BASED CULTURE SYSTEM

<sup>1</sup>Koichi WATANABE, <sup>2</sup>Ataru MORIYA, <sup>2</sup>Kenji HAYASHIHARA, <sup>2</sup>Takefumi SAITO,  
<sup>2</sup>Shimao FUKAI, <sup>3</sup>Takio TAKAKU, and <sup>4</sup>Kozo MORIMOTO

**Abstract** We experienced a case of laboratory cross-contamination of *Mycobacterium tuberculosis* on the broth based culture system. These false-positive cultures were confirmed by analysis of DNA fingerprinting, RFLP method, which showed the same pattern in three specimens with that of the first manipulated specimen in our laboratory on that day, out of 7 specimens examined. We found possible several process causing cross-contamination where mixture of the foreign body could occur in buffer or NALC-NaOH. False-positive cultures for *Mycobacterium tuberculosis* may lead to unnecessary, potentially toxic, costly treatment, and changing the treatment strategy. So we must critically interpret a single positive culture, especially by liquid media.

**Key words:** Cross-contamination, Tuberculosis, False-positive, RFLP, Broth based culture

<sup>1</sup>Graduate School of Comprehensive Human Sciences, University of Tsukuba, <sup>2</sup>NHO Ibarakihigashi National Hospital, <sup>3</sup>Department of Pulmonary Medicine, Infection and Oncology, Nippon Medical School, <sup>4</sup>Department of Pulmonary Medicine, Japanese Red Cross Medical Center

Correspondence to: Koichi Watanabe, Graduate School of Comprehensive Human Sciences, University of Tsukuba, 1-1-1, Tennodai, Tsukuba-shi, Ibaraki 305-8574 Japan.  
(E-mail: perowan@taiiku.tsukuba.ac.jp)

————— Case Report —————

A CASE OF MULTI-DRUG RESISTANT PULMONARY TUBERCULOSIS  
WITH BILATERAL CAVITARY LESIONS  
SUCCESSFULLY TREATED BY SURGICAL TREATMENT

<sup>1</sup>Masao OKUMURA, <sup>1</sup>Hideo OGATA, <sup>1</sup>Takashi YOSHIYAMA, <sup>1</sup>Hiroyuki KOKUTOH,  
<sup>1</sup>Eiji TADOKORO, <sup>1</sup>Motoko KUBOTA, <sup>1</sup>Masako UEYAMA, <sup>2</sup>Masako WADA,  
and <sup>3</sup>Yutsuki NAKAJIMA

**Abstract** A case was 38 years old male. He was pointed out abnormal shadow on chest X-ray and complained respiratory infection symptoms. He had not past history of tuberculosis. He was diagnosed as multi-drug resistant tuberculosis (MDR-TB) in a certain hospital and was referred to our hospital to undergo treatment. His drug sensitivity test by Ogawa medium was resistant to all anti-tuberculosis drugs except for kanamycin (KM) and enviomycin (EVM). His chest X-ray revealed large cavities in the right upper field and infiltrations in the right lower field and small cavitory lesions in the left lower field. The right pneumonectomy was done because he took anti-tuberculosis drugs but his sputum examinations continued to be smear and culture positive without improvement of the lesions. After the surgical treatment (right pneumonectomy), he continued anti-tuberculosis drugs therapy and the chest X-ray improved including the collapse

of left lower cavitory lesions. This case was a difficult case to treat because of bilateral cavitory lesions. However he was successfully treated by the surgical treatment.

**Key words:** Multi-drug resistant tuberculosis (MDR-TB), First resistance, Bilateral cavities, Surgical treatment

<sup>1</sup>Department of Respiratory Medicine, Fukujuji Hospital, Japan Anti-Tuberculosis Association (JATA), <sup>2</sup>Research Institute of Tuberculosis, JATA, <sup>3</sup>Thoracic Surgery, Fukujuji Hospital, JATA

Correspondence to: Masao Okumura, Department of Respiratory Medicine, Fukujuji Hospital, JATA, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-0022 Japan.  
(E-mail: okumuram@fukujuji.org)

## Field Activities

INVESTIGATION ON THE CHANGES IN THE HOSPITALIZATION PERIOD AFTER  
THE INDUCTION OF NEW DISCHARGE CRITERIA FOR PULMONARY TUBERCULOSIS

— Utility of Assessment Sheet for Using Clinical Path —

<sup>1</sup>Jun MITSUISHI, <sup>1</sup>Takeko SONODA, <sup>1</sup>Mikiko OSHIMA, <sup>2</sup>Taku NAKAGAWA,  
<sup>2</sup>Yuko SAITOU, and <sup>2</sup>Kenji OGAWA

**Abstract** [Purpose and Methods] The new discharge criteria devised by the National Hospital Organization have three patterns (A, B and other). It was predicted that the hospitalization period would be markedly shortened by the pattern A. In order to judge whether these patterns were adequately applied, we used an assessment sheet. We investigated the adoption rate of the pattern A and the changes in the hospitalization period after its induction.

[Results] There was a low adoption rate for the pattern A; namely 18%, and the main reasons for not following it were severity illness and the presence of complications. Hospitalization for less than 4 weeks was seen in 25%, while it was over 8 weeks in 42%. The average period of hospitalization was shortened by 20 days and the average number of patients per day also decreased.

[Conclusion] Interpretation of discharge criteria is standar-

dized by using the assessment sheet, allowing us to perform smooth induction of a clinical path and guide patients along it. Shortening of hospitalization raises patient turnover and allows more rational management of pulmonary tuberculosis. These results could help to refine the clinical path in the future.

**Key words:** Pulmonary tuberculosis, New discharge criteria, Clinical path, Hospitalization, Assessment sheet of new discharge criteria for TB patients

Department of <sup>1</sup>Nursing, and <sup>2</sup>Pulmonary Medicine, National Hospital Organization Higashi Nagoya National Hospital

Correspondence to: Jun Mitsuishi, Department of Nursing, NHO Higashi Nagoya National Hospital, 5-101, Umemorizaka, Meito-ku, Nagoya-shi, Aichi 465-8602 Japan.

DIAGNOSIS AND TREATMENT OF TUBERCULOSIS OR  
*MYCOBACTERIUM AVIUM-INTRACELLULARE* COMPLEX INFECTION  
IN HIV-INFECTED PATIENTS

Takuma SHIRASAKA

**Abstract** The clinical features of tuberculosis vary according to its CD4 count. With CD4 count  $>350/\mu\text{L}$  pulmonary lesions are “typical” (upper lobe infiltrates  $\pm$  cavitation). With CD4 count  $<50/\mu\text{L}$  extrapulmonary TB is more common, and chest X-rays show lower and middle lobe and miliary infiltrates, usually without cavitation. The treatment of tuberculosis in HIV-infected patients should follow the same principles for persons without HIV infection. Presence of active tuberculosis requires immediate initiation of anti-tbc therapy. The delay of antiretroviral therapy for 4–8 weeks after initiation of tuberculosis treatment is recommended. MAC is a relatively common cause of disseminated infection without pulmonary involvement in patients with AIDS. Preferred regimens contain clarithromycin and EB, and in case of high MAC load or absence of effective antiretroviral therapy rifabutin may be

considered as a third drug. Start antiretroviral therapy simultaneously or within 1–2 weeks. In Japan, an increasing number of HIV infections are reported year after year. So HIV infection should be included in possible diagnosis for atypical Tbc or disseminated MAC infection.

**Key words:** HIV, AIDS, Tuberculosis, MAC infection

AIDS Medical Center, National Hospital Organization Osaka National Hospital

Correspondence to: Takuma Shirasaka, AIDS Medical Center, National Hospital Organization Osaka National Hospital, 2–1–14, Hoenzaka, Chuo-ku, Osaka-shi, Osaka 540–0006 Japan. (E-mail: [sirasaka@onh.go.jp](mailto:sirasaka@onh.go.jp))

————— The 82nd Annual Meeting Symposium —————

## SURGICAL TREATMENT OF MYCOBACTERIOSIS

Chairpersons: <sup>1</sup>Keiji IUCHI and <sup>2</sup>Yutsuki NAKAJIMA

**Abstract** The pulmonary resection plays an important role in the management of tuberculosis, especially MDRTB, or non-tuberculous mycobacteriosis. For the satisfactory outcome, pre- and postoperative chemotherapy is mandatory. On the same time, resected specimens should be examined bacteriologically to evaluate preoperative chemotherapy.

Acute mycobacterial empyema occurs frequently by the perforation of cavitory lesions, especially with pulmonary NTM. The outcome of such acute and destructive diseases is poor in the case of old age over 70y/o. But without surgical intervention, such difficult condition becomes more miserable.

Although mycobacterial mediastinal lymphadenitis, or osteoarthritis are rare tuberculosis-related disease in Japan, we should keep in mind such rare diseases in ordinary practice.

1. Surgical treatment of pulmonary tuberculosis: Naoto IMAMURA, Minoru AOKI, Takao NAKANISHI, Yosuke OTAKE (Nishi-Kobe Medical Center)

Between August 1994 and December 2006, 26 patients underwent 27 pulmonary resections at Nishi-Kobe Medical Center. Almost all patients had drug-resistant pulmonary tuberculosis, 16 of which were multi-drug resistant tuberculosis. All patients received at least 3 susceptible drugs preoperatively and postoperatively. Operative mortality was 0%, and morbidity was 15%. No relapse occurred in 19 follow-up patients. For patients with refractory pulmonary tuberculosis which is localized, and with adequate pulmonary function, surgical treatment combined with chemotherapy will provides a favorable outcome.

2. Surgical treatment of non-tuberculous mycobacteriosis: Motoshi OUCHI, Etsuo NEMOTO, Nobutaka HAYAKAWA, Tsuyoshi GOTOU (Respiratory Surgery, NHO Minami Yokohama National Hospital), Masaya YAMAZATO, Yoko SHINOZAWA, Sumire OOTANI, Hiroshi KAWADA, Mamoru MIYAIRI (Internal Medicine, NHO Minami Yokohama National Hospital), Naoki HASEGAWA (Respiratory Internal Medicine, Keio University)

Eighty-six patients, treated surgically for NTM (non-tuberculous mycobacteriosis), were investigated over 9 years. In all cases, 93.9% of bacteria were eliminated. Bacteria turned negative 77 of 82 cases, excluding 4 cases in which follow-up chemotherapy could not be performed.

3. Surgical treatment for mycobacterial empyema: Hisaichi TANAKA, Keiji IUCHI, Naoko OOSE, Yukio NAKAMURA, Naoto KITAHARA, Masahiro SAKAGUCHI, Akihide MATSUMURA (Department of General Thoracic Surgery,

NHO Kinki-chuo Chest Medical Center)

We made a retrospective analysis of surgical results of 63 cases of mycobacterial empyema which were treated in our institution. The surgical treatment resulted in success in 54 (86%) cases, unsuccess 9 (14%). The most deteriorated local factors related to unsuccess were the existence of bacterium, bronchopleural fistulas and the width of the space of the empyema. In the empyema of such high risk group, the open drainage (the fenestration) which improves the infection of the pleural space and the nutritional condition of patients was followed to the successful curative operation. But in the acute empyema, the reluctant fenestration often cannot be closed or results in death without the improvement of nutritional condition.

4. Diagnosis and treatment of tuberculous mediastinal lymphadenitis without pulmomy lesions: Masazumi WATANABE, Hiroaki KURODA, Masafumi KAWAMURA, Tomoyasu NISHIMURA\*, Naoki HASEGAWA\*, Akitoshi ISHIZAKA\*, Koichi KOBAYASHI (Department of Surgery and Internal Medicine\*, Keio University)

Tuberculous mediastinal lymphadenitis without pulmonary lesions in an adult patient is relatively rare and difficult to diagnose. We have experienced 7 cases (4 males and 3 females, mean age of 43 y/o) of mediastinal tuberculous lymphadenitis that are 2.4% of all tuberculosis. Chest CT scan showed mediastinal mass of central low density area with peripheral rim enhancement in 6 of 7 cases. Diagnosis was confirmed by mediastinoscopy in 2, thoracoscopy in 2 and surgery in 1. Other 2 cases were diagnosed through clinical follow-up. Seven patients were treated by standard anti-tuberculous therapy with 3 or 4 drugs successfully.

5. Tuberculosis of the skeletal system: Kazutaka IZAWA (Department of Orthopaedic Surgery, NHO Toneyama National Hospital)

Presently, osteoarticular tuberculosis is relatively rare in Japan, therefore current generation of doctors is unfamiliar with the clinical manifestation of the disease. Surgery is required when the patient with severe paraplegia, persistent pain or severe disability is not responding after chemotherapy. Debridement, drainage and arthrodesis are commonly indicated and the outcome is satisfactory. For the patients with multi-drug resistant tuberculosis, the role of surgical treatment is quite limited. Surgery only should be considered when the severe symptoms are not controlled by prolonged multi-drug therapy.

**Key words:** Multi-drug resistant tuberculosis, Nontuberculous mycobacteriosis, Empyema, Mediastinal tuberculous lymphadenitis, Tuberculosis of bone and joint

<sup>1</sup>Department of Surgery, National Hospital Organization (NHO) Kinki Chuo Chest Medical Center, <sup>2</sup>Department of

Respiratory Diseases, NHO Tokyo National Hospital

Correspondence to: Keiji Iuchi, Department of Surgery, NHO Kinki Chuo Chest Medical Center, 1180 Nagasone-cho, Kita-ku, Sakai-shi, Osaka 591-8555 Japan.  
(E-mail: [iuchi@kch.hosp.go.jp](mailto:iuchi@kch.hosp.go.jp))



————— The 82nd Annual Meeting Open Symposium for Citizens —————

## TUBERCULOSIS CONTROL IN URBAN AREAS

Chairpersons: <sup>1</sup>Akira SHIMOUCI and <sup>2</sup>Masako OHMORI

**Abstract** Directly Observed Treatment, Short Course (DOTS) in Japan was initiated and is now established for homeless TB patients in urban areas. The experience of this DOTS is assisting the development of DOTS in Japan. However, TB incidence and problems are now concentrated in urban areas. What makes tuberculosis control in urban areas difficult? How can we overcome these problems? In this symposium we reviewed TB control activities and discussed the issues highlighted by four presenters.

1. Trend and evaluation of tuberculosis control program—Kobe city: Riyo FUJIYAMA (Kobe City Public Health Office)

The incidence of TB in Kobe is the second highest in Japan. A 5-year TB control plan was started in 2000, and the second 5-year plan got underway in 2005. Activities are monitored with 24 indicators for evaluation. Kobe City Public Health Office placed special emphasis on DOTS and screening of high-risk groups, and analyzed treatment results reported from all nine public health centers in Kobe city. From 1999 to 2005, the defaulter rate fell from 7% to 1%, and the incidence rate from 57.9 per 100,000 to 34.5.

2. Trend and evaluation of tuberculosis control program—Osaka city: Akira SHIMOUCI (Osaka City Public Health Office)

To reduce the high incidence of TB, DOTS was officially introduced in 2001 as part of a 10-year control plan, 2001–2010. DOTS coverage reached 64% of all pulmonary TB patients in the Airin area (high endemic area) and 68% of all pulmonary smear-positive patients. As a result, the failure or defaulter rate fell from 13.8% in 1998 to 4.9% in 2004. The combined multi-drug resistant rate decreased from 2.6% in 2001 to 0.8% in 2005. Therefore, DOTS has been found to be effective.

3. Current issues regarding tuberculosis among the homeless: Takako OHSAKA (NPO Health Support Osaka, International Buddhist University)

The number and rate of the homeless in Osaka city is the highest in Japan. TB accounts for 10% of deaths among the homeless, many of whom die without treatment. We conducted a chest X-ray screening program for the homeless, which helped to identify TB cases and to complete treatment. These activities have stimulated the initiation of new programs by other organizations such as screening with computed radiography, TB screening at Osaka Social Medical Center, and DOTS by a visiting nurse in Airin. To strengthen such

activities, cooperation between the governments, NPOs, and private organizations is important.

4. Tuberculosis control for foreigners—beyond the scene of medical care: Junpei YAMAMURA (Minatomachi Medical Center)

Some foreigners are discriminated against and suffer prejudiced, and have no access to medical care. Tuberculosis hits them directly in such a situation. Tuberculosis among foreigners as a social illness cannot be solved only by the medical workers. Therefore it is important in curative and preventative care to build confidential relations not only between the patient and the medical worker, but also among other organizations. Medical workers should tackle the problem actively with NGOs that support foreigners.

Moreover, the crackdown on foreigners and detention by the immigration bureau under the Ministry of Justice obstructs the curative and preventative care of foreigners with tuberculosis. The reduction of medical budget by the Ministry of Health, Labour and Welfare leads to a lower quality of medical care. The actions of the central government are a cause of this social illness. Extensive cooperation beyond the medical framework must be built, and demands must be made to the central government continuously.

In addition to the above presenters, five other persons were requested to express their opinions.

Junko MONBAYASHI of Osaka City Public Health Office reported that DOTS conferences have been conducted in 12 TB hospitals to facilitate patient management after discharge from the hospital. A manual for nursing assistance was drawn up to standardize the cooperation between hospital nursing and community nursing. Thanks to both measures, the rate of patients agreeing to start DOTS in the community has increased.

Kazuhide TSUKAMOTO of Kawasaki City Public Health Office experienced a TB outbreak of nine patients covering four cities in a period of one and a half years. All lived around station “K” and had visited a shop that was open 24 hours a day. Some homeless use the shop as a place to sleep. Therefore, it is important to provide knowledge on TB infection and to better ventilate the rooms that are shared by many people.

Sumi KAGURAOKA of Nishi-Shinjuku Public Health Center explained efforts to find cases early through chest X-ray screening upon admission to shelters, a screening program in the street for the homeless, and regular screening at a Japanese language school for foreign students. As patient support, she emphasized the need to consider individual

conditions in collaboration with NPOs, volunteers from the same country, and school staff.

Une IKEGAME of Health Support Sumidagawa reported based on her experience of supports for the homeless that some ward offices do not approve the sole application of medical support under the Poverty Law, and do not approve of staying in a hotel as a condition of applications under the Poverty Law, and instead order the homeless to stay in a public or private dormitory as a condition. However, such circumstances will make treatment fail completely. It was emphasized that individual human rights and the person's will should be respected. It is important to learn from individual experiences to improve the system.

Finally, Nobukatsu ISHIKAWA of the Research Institute of Tuberculosis, JATA summarized that tuberculosis is a social disease and solutions cannot be discussed without considering the social pathological aspect of urban areas. Although the apparent number of TB cases is reducing, difficult problems

to be addressed are increasing. The program of TB needs to be informed to the whole of society. The "STOP TB Partnership" was started as a recent international movement, which emphasizes respect for human beings and social security. It also includes the participation of TB patients themselves. In the urban setting, a Japanese style of urban DOTS should be developed that fully considers the viewpoints of TB patients.

**Key words:** Urban areas, Tuberculosis control, Outbreak of TB infection, Homeless, Foreigners, NPO

<sup>1</sup>Osaka City Public Health Office, <sup>2</sup>Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association

Correspondence to: Masako Ohmori, Research Institute of Tuberculosis, JATA, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-8533 Japan. (E-mail: ohmori@jata.or.jp)