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Current Topics

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DISCUSSION ON EVIDENCE FOR PRINCIPLE OF  
TUBERCULOSIS CONTACT INVESTIGATION

—From the Experience in Osaka City—

<sup>1</sup>Akira SHIMOUCHI, <sup>2</sup>Kenji MATSUMOTO, and <sup>2</sup>Tomomi TATSUMI

**Abstract** Risk factors for tuberculosis transmission from patients to contacts were found to be younger age, presence of cavitory lesion in chest X-ray findings, shedding higher number of organisms, longer duration of respiratory symptoms, longer hours of contact, and smaller space of contact environment. It should be noted that even casual contacts identified by contact investigation developed tuberculosis later on. In the past contact investigation and subsequent latent TB infection (LTBI) treatment, preventive effects of tuberculosis was obvious, although there might be some over-diagnosis of LTBI with tuberculin skin testing (TST). Introduction of interferon- $\gamma$  release assay (IGRA) added to TST seems to increase specificity and reduce over-diagnosis of TB infection. However in case of outbreak investigation in schools, screening by TST is still effective and efficient. Only those case with 30mm or over of

redness (equivalent of 15 mm of induration) of TST were tested with QFT, IGRA. If anyone shows positive QFT, test of QFT would be expanded to the contact with TST of less than 30mm.

**Key words :** Tuberculosis transmissibility, Contact investigation, Tuberculin skin testing, Interferon- $\gamma$  release assay, Latent tuberculosis infection

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## INTERPRETATION OF QFT RESULTS IN SEVERAL CONTACT INVESTIGATIONS

Nobuyuki HARADA

**Abstract** QuantiFERON®TB-2G (QFT-2G) is now widely used for contact investigations, as QFT-2G is not affected by BCG vaccination, whereas the conventional tuberculin skin test (TST) is confounded by BCG vaccination. We applied the QFT-2G tests to numerous contact investigations and found that the majority of contacts who had been supposed to be infected with *M.tuberculosis* (Mtb) based on TST were negative in the QFT-2G tests, strongly suggesting the possibility that the unnecessary preventive chemotherapy was indicated for many TST positive contacts due to BCG vaccination in conventional contact investigations. Although QFT-2G positive results implicate that Mtb in certain active phases presents in the body, when Mtb had been infected cannot be decided by QFT-2G. Therefore, QFT-2G results should be carefully interpreted, especially in elder persons who had been exposed to Mtb in the past in Japan. Furthermore, since there were some active TB cases in QFT-2G negative contacts, attention must

be paid for QFT-2G negative contacts in highly exposed groups. In this paper, I will discuss about current usages of QFT-2G based on our experiences of contact investigations.

**Key words:** QuantiFERON®TB-2G, Contact investigation, Latent tuberculosis infection, Development of active tuberculosis, Tuberculin skin test

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TUBERCULOSIS CONTACT EXAMINATION AND QFT-G TESTING FOR  
THE PREVENTION OF HOSPITAL ACQUIRED INFECTION<sup>1,2</sup>Takashi YOSHIYAMA

**Abstract** Hospital acquired infection mainly occurs at hospitals, not clinics. In Japan, QFT-G is the main tool for the diagnosis of tuberculous infection among health care workers. Contact examinations are basically done for contacts of sputum smear positive TB cases, but infection may occur at fiberbronchoscopy of sputum smear negative TB cases and at the time of irrigation of TB abscess. Therefore, contact examination requires bigger target group than usual contact examinations. Mathematical model analysis of cost effectiveness examination showed that contact examinations at the age of 20s to 40s will be cost saving if it is done for the contacts with the risk of infection of 6% and beneficial for the DALY lost due to TB infection if it is done for the contacts with the risk of infection of 3%. Addition of baseline QFT for the HCWs at the age of 20s requires 100 million yen for the recovery of 1 DALY lost due to hospital acquired TB infection. Also mathematical modeling showed that periodical QFT

testing of HCWs at the age of 20s to 40s will be beneficial for the DALY lost due to TB infection if the annual risk of infection will be around 2% and will be cost saving if the annual risk of infection will be around 8%. Therefore, periodical QFT is recommended for the staff working at the environment with high risk of infection (around 2% per year).

**Key words:** Tuberculosis, Hospital acquired infection, Contact examination, QFT-G

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## DETECTION OF MOLECULAR EPIDEMIOLOGY OF *MYCOBACTERIUM GORDONAE* ISOLATES

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<sup>2</sup>Motohisa TOMITA, <sup>1</sup>Masaji OKADA, and <sup>3</sup>Mitsunori SAKATANI

**Abstract** [Objects] To analyze the molecular epidemiology of *Mycobacterium gordonae* strains from patients and environments in the hospital.

[Subjects] A total of 46 clinical strains were obtained from patients registered at the NHO Kinki-chuo Chest Medical Center and 3 strains from hospital environments.

[Methods] By using genetic data from the 16S rRNA gene and *hsp65*PRA, pulsed-field gel electrophoresis (PFGE) assessment of their intraspecies variability and epidemiology was carried out.

[Results] Strains from six patients and environmental cultures exhibited the different genotypes of 16S rRNA gene sequencing and the *hsp65*PRA type. The PFGE analysis suggested no pseudo-outbreak and showed a polyclonal infection in one patient.

[Conclusion] These findings suggest that we should maintain

effective surveillance of environments in the hospital and continuously perform molecular epidemiological investigations for infection control of *M. gordonae*.

**Key words:** *Mycobacterium gordonae*, 16S rRNA gene sequence, *hsp65*PRA, PFGE, Polyclonal infection

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Review Article

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INTEGRATION OF TUBERCULOSIS CARE INTO GENERAL HOSPITALS  
IN THE UNITED STATES

Kunihiko ITO

**Abstract** [Purpose] In Japan we are now urged to rethink and reform the present ward-centered institutional system of clinical service for tuberculosis (TB). To provide useful information for this rethinking and reform, we performed a literature review of the process of integrating TB service into general hospitals in the US.

[Method] Literature review.

[Result] The process of integrating TB service into general hospitals in USA began around 1970, and continued until around 1980, when it was almost complete. From the experience and opinions of the authors reviewed, the following points were found to be important to successful integration: establishing an efficient outpatient department, maintaining patients' adherence to treatment, using a long-term care facility for TB patients requiring long-term in-hospital care, planning a program for integration of care fully in advance, individualizing the program according to the region, adopting a phased step-by-step program, educating hospital staff and

securing financial support from governments.

[Conclusion] The reform of tuberculosis wards in Japan will occur at the same time as the reform of the country's TB control program, and will provide a good opportunity to improve our program.

**Key words:** Tuberculosis ward, General ward, Tuberculosis bed, Sanatorium, General hospital

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## START OF TB CASE-REGISTRATION AND CASE-MANAGEMENT SYSTEM IN JAPAN

Tadao SHIMAO

**Abstract** TB control in Japan started in 1951 through legislation of TB Control Law, consisting of three major components; mass health examination, vaccination and promotion of adequate methods of treatment for TB cases. Mass health examination was first targeted for younger generation below 30 years of age as it was believed that TB was highly prevalent among them, however, it was expanded to cover whole population based on the results of TB Prevalence Survey in 1953 revealing high prevalence of TB in all age groups except children and low awareness of TB cases.

Methods of treatment for TB were developing rapidly in late 1950s and early 1960s; initially artificial pneumothorax, then surgical collapse treatment such as thoracoplasty, then pulmonary resection, and finally long term combined use of INH, SM and PAS. Up to surgical treatment era, most TB patients earnestly followed doctor's instruction, however, in chemotherapy era, as most symptoms improved rapidly after the initiation of chemotherapy, patients felt as if they were cured, and it had become difficult to maintain high adherence to treatment. Such behavior was found oftener in patients detected in early stage through mass health examinations.

1947, it was legislated for all doctors to report all diagnosed TB cases to an adjacent health center, and the cases are registered at the health center covering his (her) residence, however, standardized formula of registration was not indicated. In accordance with the progress of TB control program, the number of TB registered cases increased, and the need for standardized registration and case-management had become apparent in mid 1950s, and some preliminary trials had been done.

In response to this request, the Ministry of Health and Welfare organized a research group headed by Dr. Misonou K, and the staffs of prefectural health department and enthusiastic staffs working in health centers (HCs), staffs of NIPH (National Institute of Public Health) and RIT (Research Institute of

Tuberculosis) to study how to register TB cases, how to collect information and how to improve patients' adherence to treatment.

Registration index cards were prepared in each HC arranged alphabetically to avoid double register. The formula of registration card was indicated in Fig. 1 and 2. Small hollows were made in the lower part of the card, and registration card container with 45 metal bars in the bottom as shown in Fig. 3 was prepared. By setting 30 cards dislocating one each hollow as shown in Fig. 3, in one card container with 30 rows, altogether 600 registration cards were stored. In most right part of the card, important information such as activity of the case, treatment status, expected time of next home visit, expiring time of public support for TB treatment, etc. are indicated by different color metal signals.

This new system was applied in 216 HCs, about one fourth of all HCs in Japan in 1959, another 200 HCs were added in 1960, and finally from 1961, the new system of registration and case-management started in the whole country after making minor amendments based on experience in 1959 and 1960. Quality of TB case-management improved much after the introduction of new system, and annual statistics not only newly registered TB cases but also on prevalence of active as well as registered cases was available since then, and this was the starting point of TB surveillance system started in 1986.

**Key words:** TB case-registration and case-management system, Reporting of TB cases, TB case registration system, Activity classification

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## TUBERCULOSIS ANNUAL REPORT 2008

### — Series 9. Treatment of TB (2) —

Tuberculosis Surveillance Center, RIT, JATA

**Abstract** The standard treatment for tuberculosis (TB) is the key to its control. Here we report on the statistics of treatment status and the duration of hospitalization/treatment.

The place of initial treatment was observed among newly notified TB patients ( $n=24,760$ ) in 2008. Of those, the proportion receiving treatment in hospital among sputum smear positive pulmonary TB patients was the most (91.7%), including 2.1% hospitalized mainly due to other diseases. The proportion receiving treatment in hospital among bacteriologically negative pulmonary TB cases was the least (25.8%), including 10.3% hospitalized mainly due to other diseases. This proportion of patients receiving treatment in hospital did not differ with age, among sputum smear positive pulmonary TB cases. But, this proportion differed greatly in their age groups (e.g. 9.9% in their 20s, 25.7% in their 50s and 50.0% in their 80s), among bacteriologically negative pulmonary TB cases.

The duration of hospitalization for TB treatment among newly notified cases in 2007 was observed at the end of 2008. The median hospitalization periods were 69 days, 74 days, 45 days, 38 days and 45 days, among new sputum smear positive

pulmonary TB cases, retreatment sputum smear positive pulmonary TB cases, other bacillary positive pulmonary TB cases, bacilli negative pulmonary TB cases and extra-pulmonary TB cases, respectively.

The duration of TB treatment among newly notified cases in 2007 was observed at the end of 2008. The median treatment duration among all forms of TB was 273 days. The longest median treatment duration was 298 days for retreatment sputum smear positive pulmonary TB cases and the shortest was 204 days for bacteriologically negative pulmonary TB cases.

**Key words:** Tuberculosis, Age, Treatment status, Duration of hospitalization, Duration of treatment, INH, RFP

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