

CLUSTERING ANALYSIS OF *MYCOBACTERIUM TUBERCULOSIS* BY USING THE JATA(12)-VNTR SYSTEM FOR MOLECULAR EPIDEMIOLOGICAL SURVEILLANCE OF BROAD AREAS OF JAPAN

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Abstract [Objectives] Japan Anti-Tuberculosis Association (JATA) (12)-variable numbers of tandem repeats (VNTR) is a standard method for genotyping of clinical isolates of *Mycobacterium tuberculosis* in Japan. As a model study for nationwide surveillance, this study aimed to describe the tendency and frequency of genotypes of *M.tuberculosis* in a large number of clinical samples.

[Methods] Clinical isolates of *M.tuberculosis* (n=1,778) were obtained from patients with tuberculosis in 3 areas, i.e., Osaka City, Osaka Prefecture, and Kobe City, during 2007 and 2008. The samples were analyzed using JATA (12)-VNTR. All genotypes were subjected to clustering analysis.

[Results and Discussion] In total, 1,086 (61.1%) isolates showed clustering. The most common clusters were composed of 3 members. Such clusters were considered to reflect either actual transmission or low discriminatory power of JATA (12)-VNTR. Several prevalent JATA(12)-VNTR genotypes formed large clusters and were discussed in relation with epidemiological findings of other studies. The findings of this study will aid in the construction of an effective genotyping-

based surveillance system of *M.tuberculosis*, through improvement of interpretation of VNTR types, observation of certain particular strains in an area, and efficient detection of unidentified outbreaks.

Key words: *Mycobacterium tuberculosis*, VNTR, Molecular epidemiology, Public health, Surveillance, Genotyping, Traceability of transmission

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EVALUATION OF JATA(12)-VARIABLE NUMBER OF TANDEM REPEATS AS A MARKER OF THE SOURCE OF TUBERCULOSIS OUTBREAKS IN OSAKA

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Abstract [Objectives] To evaluate the usefulness of the JATA (12)-variable number of tandem repeats (VNTR) system for identifying the source of *Mycobacterium tuberculosis* outbreaks.

[Design] JATA(12)-VNTR genotyping was performed on *M.tuberculosis* isolates from a total of 206 patients in whom group infection was confirmed by epidemiological studies (“group infection”), as well as from 64 patient clusters in whom group infection was suspected but not confirmed (“non-group infection”). The patients were diagnosed in Osaka Prefecture from April 1999 to December 2011.

[Results] All isolates from the “non-group infection” patients showed a unique VNTR pattern, whereas isolates from 185 (89.9%) “group infection” patients showed a common and group-specific JATA (12)-VNTR pattern. However, single-locus variants were observed in 1 (1.6%) “non-group infection” case and in 21 (10.2%) “group infection” cases.

[Conclusion] Tuberculosis in 248 (91.9%) of the 270 study patients could be correctly identified based on the genotyping

of the isolates by using the JATA (12)-VNTR. If proper attention is paid to the single-locus variant, the JATA (12)-VNTR system would be a useful tool for identification of sources of tuberculosis outbreaks.

Key words: *Mycobacterium tuberculosis*, Variable number of tandem repeats, Tuberculosis outbreak, Group infection

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Original Article

ESTIMATING THE PREVALENCE OF TUBERCULOSIS INFECTION
AMONG HEALTHCARE WORKERS IN OUR HOSPITAL
BY REPEAT QFT-G TESTING

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Abstract [Objective] The QuantiFERON®-TB (QFT) blood test is the major tool for the diagnosis of *Mycobacterium tuberculosis* (TB) infection among healthcare workers (HCWs). We used QFT tests to estimate the prevalence of TB infection among HCWs in our hospital.

[Material and Methods] Between 2003 and 2010, a total of 733 HCWs were enrolled in this study, and the prevalence of TB infection was analyzed according to the HCWs' jobs and work place.

[Results] Among the 152 men and 581 women who were evaluated, 3 female HCWs had a history of TB. Fifty-eight HCWs (8 men and 50 women with a mean age of 56.3 years and 48.4 years, respectively) demonstrated positive QFT tests. The positive rate was 7.9% for all staff members throughout the study period.

The QFT test was positive for 1 HCW who was treated for TB in 1998, and negative and inconclusive for 2 other HCWs treated for TB in 2002. The positive rate for QFT was 16.0% in the TB ward (12/75, 95% confidence interval [CI]: 7.7–24.3%), 9.9% in the other wards (22/222, 95% CI: 7.9–11.9), and 1.1% in the outpatient department (1/91, 95% CI: 0–2.2). According to the job category, the QFT positive rates were as follows: doctors, 4.3% (3/70, 95% CI: 1.9–6.7); nurses, 10.3% (27/263, 95% CI: 8.4–12.2); radiology technicians, 20.0% (3/15, 95% CI: 9.7–30.3); laboratory technicians, 11.4%

(4/35, 95% CI: 6.0–16.8). The positive rate among doctors working in the TB ward was 10.0%, and that for nurses was 24.3%. This indicates that the prevalence of infection among HCWs in the TB ward was significantly higher than that in other work places. A comparison of the results from 2003 through 2007 revealed that for a total of 307 workers, 90.6% and 5.2% remained negative and positive, respectively, while 1.6% converted from negative to positive, and 2.6% from positive to negative.

[Conclusion] The positive rate among HCWs in the TB ward was higher than that in other wards. This is especially remarkable for doctors and nurses working in the TB ward.

Key words: Healthcare workers, Health screening, QFT, Prevalence of tuberculosis infection, QFT use in healthcare workers

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CONTACT INVESTIGATION USING QuantiFERON-TB® Gold TEST TO EVALUATE TB EXPOSURE IN 61 SUBJECTS IN A HOSPITAL SETTING

— (2) Change in QuantiFERON Response during One Year after Exposure —

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Abstract [Objectives & Subjects] The change in IGRA (interferon-gamma release assay, with QuantiFERON-TB® Gold, QFT) responses was followed up for one year in a group of contacts of healthcare workers who had been exposed to tuberculosis (TB) infection for a relatively short period in a hospital. The observation was made of a total of 59 close contacts of the index case, where 16 showed positive QFT-conversion and 7 showed the intermediate response ranging 0.1 to 0.35 IU/mL. Three of the conversion cases developed active TB.

[Results] 67% of the QFT conversions occurred within 2 months of exposure and the others between 2 to 9 months. Those having converted later than 2 months after the exposure showed generally weaker QFT responses than the earlier converters. In response to the treatment to converters (either to latent TB infection or to active TB), 80% of the cases reversed to negative or intermediate. The geometric means of the response values for ESAT-6 and CFP-10 also showed significant decline over the treatment time.

[Discussions] The time profile of responses in the intermediate responders revealed an obviously distinct pattern from that of the negative responders with the values remaining uniformly at very low level throughout, which suggests that

this group includes somehow exceptional responders either with or without infection.

Key words: IGRA, QuantiFERON, Tuberculosis outbreak, Nosocomial infection

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Short Report

IMPACT OF INTRODUCING RIFAMPICIN ON THE TREATMENT OF TUBERCULOSIS DURING THE 1970'S IN JAPAN

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Abstract [Setting] The average duration of tuberculosis chemotherapy in Japan increased year by year throughout the 1960's and reached 49 months by 1973. It then began decreasing slowly in the 1970's and more rapidly after the 1980's.

[Purpose] To clarify the significant factors contributing to the prefectural variation of changes in the average duration of chemotherapy that occurred from 1973 to 1979.

[Method] Multiple regression analysis was conducted with the slopes of the average duration of chemotherapy of tuberculosis in prefectures throughout Japan from 1973 through 1979 as the dependent variable and with parameters related to treatment and patient characteristics of the prefectures as independent variables.

[Results] The variables, including uses of rifampicin, proportion of bacteriologically confirmed patients among newly registered cases, and average duration of chemotherapy as of 1973, contributed significantly to the slope of change in chemotherapy duration of the prefectures; the duration decreased faster in prefectures where there were more bacteriologically confirmed patients, and where the duration had been shorter at

the beginning of the study period.

[Discussion] Short-course chemotherapy had not been established in the study period, but confidence in the potency of antibacterial activity of the new drug seems to have facilitated the departure from unnecessarily long treatment. The recognition of the importance of bacteriology in the clinical practice of tuberculosis worked in the same way against dependence on X-ray findings causing long-term treatment. Also, the prefectures that had been less affected by the long-term treatment could depart faster from it.

Key words: Tuberculosis, Duration of chemotherapy, Rifampicin, Monitoring

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A CASE OF TUBERCULOUS PLEURISY DISTINGUISHED FROM PLEURISY CAUSED BY *MYCOPLASMA* INFECTION

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Abstract We report a case of tuberculous pleurisy that required differentiation from pleurisy caused by *Mycoplasma* infection. A 28-year-old woman presented to a clinic with fever and pain on the left side of her chest. A chest radiograph revealed pleural effusion in the left thorax, and the condition was diagnosed as bacterial pleurisy. The patient was referred to our hospital because of an increase in the pleural effusion despite antibiotic treatment. *Mycoplasma* infection was suspected because the patient was young, the white blood cell count was not elevated, and the result of the ImmunoCard Mycoplasma test (IC) for *Mycoplasma pneumoniae*-specific IgM antibodies was positive. However, the fever persisted even after treatment with azithromycin and pазufloxacin. The left pleural effusion was exudative, with lymphocytosis and high adenosine deaminase (ADA) levels. The results of the QuantiFERON test were positive. Therefore, tuberculous pleurisy was diagnosed, and the effusion subsided after treatment with standard anti-tuberculosis chemotherapy. Although detection of *Mycoplasma* infection using the IC is rapid and simple, the accuracy of this test is poor. The patient was first diagnosed with pleurisy of *Mycoplasma* origin because of a single high-particle agglutination titer of 1 : 320 and because of the

presence of exudative pleural effusion with lymphocytosis and elevated ADA levels, which has been reported in patients with *Mycoplasma* infection. The results of the IC test and the ADA level of the pleural effusion might not be reliable when distinguishing between tuberculous pleurisy and pleurisy caused by *Mycoplasma* infection.

Key words: Tuberculous pleurisy, *Mycoplasma pneumoniae* infection, ImmunoCard Mycoplasma test (IC), Particle agglutination test, Pleural fluid lymphocytosis, ADA levels of pleural effusion

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Field Activities

ON-THE-STREET DOTS FOR A HOMELESS TUBERCULOSIS PATIENT
— Case Report of a Patient Who Had Difficulties with TB Treatment Adherence —

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and ⁶Nobukatsu ISHIKAWA

Abstract [Purpose] A homeless patient with tuberculosis (TB), who had often quit his TB treatment in mid-course and then gone homeless again, succeeded in completing his treatment for over 10 months through on-the-street DOTS (“Bluesky DOTS” is another expression). Based on the analysis of this case, we have discussed how to provide effective countermeasures to non-compliant TB patients.

[Method] An episode of a successful on-the-street DOTS for a 70-year-old homeless man with sputum smear positive pulmonary TB was qualitatively analyzed, with a view toward patient’s empowerment.

[Result] The patient had had human-relations problems in his life, and trouble with medical and welfare service staff. During his hospital admissions, he repeatedly self-discharged or was forced to discharge due to violent behavior against staff. Public health nurses at Shinjuku public health center visited the patient frequently at the hospital, and tried to build a good relationship with the patient from the beginning of the treatment. Following a two and half month interruption of the TB treatment after he disappeared from the hospital, he was discovered staying outside at a canal side in the area, and on-the-street TB treatment was carried out, with good cooperation with the hospital and social welfare office. Directly observed TB medication was given to him by a public health nurse and another health center staff member for 293 days, at the park near his living place. The patient often rejected the medication, particularly when he was hungry, but offering lunch to him was a very effective incentive. Through comprehensive supports to the patient, he gradually changed his attitude, and on his own

came to consider his health and his future.

[Discussion] We have analyzed a successfully treated case of a homeless TB patient who had difficulties in maintaining a social life and had not been cooperative in complying with the medication. The level of independence improved during the course of on-the-street DOTS with incentive and other supports. He became receptive to TB treatment and became self-supportive during the course of DOTS, with food as an incentive. This indicates that on-the-street DOTS was successful not only for the treatment completion but also contributed to empowering the TB patient. This approach of adjusting the service to the patient’s needs fostered a positive relationship with all stakeholders.

Key words: Tuberculosis, Shinjuku City, On-the-street DOTS, Homeless patient, Difficulties in treatment adherence, Empowerment

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Report and Information

TUBERCULOSIS ANNUAL REPORT 2010

— (9) Treatment of Tuberculosis—2 —

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

Among the newly noted TB patients in 2010, sputum-smear positive pulmonary TB patients were the most likely to receive hospital treatment (91.4%); 2.5% of these patients were primarily hospitalized for other diseases. The median duration of hospitalization in newly notified TB cases in 2009 was 73 days for new sputum-smear positive pulmonary TB cases, 75 days for sputum-smear positive pulmonary TB cases undergoing further treatment, 42 days for other bacillary positive pulmonary TB cases, 40.5 days for bacillary negative pulmonary TB cases, and 44 days for extra-pulmonary TB cases.

The duration of TB treatment among newly notified cases in 2009 was assessed at the end of 2010. The median treatment

duration for all forms of TB was 270 days. The longest median treatment duration was 285 days for retreatment of sputum-smear positive pulmonary TB cases, and the shortest duration was 196 days for bacillary-negative pulmonary TB cases.

Key words: Tuberculosis, Age, Treatment status, Duration of hospitalization, Duration of treatment, Isoniazid, Rifampicin

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