

A STUDY ON CLINICO-PATHOLOGICAL FEATURES OF ACTIVE PULMONARY TUBERCULOSIS FOUND AT AUTOPSY IN A GENERAL HOSPITAL

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Abstract [Objectives] To clarify clinico-pathological features of tuberculosis found at autopsy.

[Methods] This study investigates 18 (3.7%) of active pulmonary tuberculosis out of 489 autopsy in Tachikawa Sougo Hospital during the period from 1992 to 2005.

[Results] There were 11 men and 7 women, with a median age of 69.5 years. Tubercle bacilli were proved from sputum in 6, which consisted of 3 with positivity on sputum smear microscopy and culture, and 3 with positivity only on sputum culture. Two were examined, but not diagnosed before death. Three didn't show any positive result despite of repeated sputum tests. The features of the chest radiological findings were: (1) Shadows that present prior tuberculosis (ex: nodules, fibrotic lesion) were found in 9 and ground-glass-opacity in 5. (2) In 6, radiological findings consistent with tuberculosis were not pointed out because shadows such as fibrosis, pleural effusion, or cancer were mixed in the same lung. (3) In 11, main radiological findings were found in atypical segments, when there were some underlying conditions such as the use of corticosteroidal therapy or diabetes mellitus. Four were diagnosed correctly, and treated with anti-tuberculosis drugs. Other 14 were not diagnosed before death and diagnosed wrongly as pneumonia, cancer, or other diseases. Encapsulated caseous nodules were seen in 7, and autopsy confirmed that

12 including these 7 were caused by endogenous reactivation. Miliary tuberculosis was found in 5, caseous pneumonia/bronchitis in 6. One had tuberculous empyema. As to underlying diseases, 8 had malignant disease, 6 had diabetes mellitus and 6 were treated with corticosteroids.

[Conclusion] This study suggests that sputum culture or radiological findings are not sufficient enough to diagnose tuberculosis, especially in compromised host. We emphasize the vital role of treatment for latent tuberculosis for cases with high risk of endogenous reactivation, and it's necessary to make the guideline for the treatment of such latent tuberculosis.

Key words: Autopsy, Active pulmonary tuberculosis, Corticosteroids, Endogenous reactivation, Latent tuberculosis

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Short Report

**SITUATION ANALYSIS OF THE MONITORING OF TUBERCULOSIS
INFECTION AMONG HOSPITAL STAFF**

Kunihiko ITO

Abstract [Purpose] To investigate monitoring of new tuberculosis infection among staff in hospitals running the model-beds for tuberculosis patient care.

[Object & Method] Questionnaires were sent to the hospitals and the responses were analyzed.

[Result] Valid answer sheets were recovered in 51% (38/75). Forty percent of hospitals performed periodic monitoring of new tuberculosis infection among staff. Fifty percent performed only one test for tuberculosis infection on employment but did not perform further periodic tests. Ten percent did not perform specific tests for tuberculosis infection at all. There were very few persons who were prescribed preventive therapy based on test results for tuberculosis infection.

[Conclusion] Less than half of the hospitals performed periodic monitoring of new tuberculosis infection, but there were

few tuberculosis cases among hospital staff. It is necessary to investigate further the efficacy and necessity of periodic monitoring of new tuberculosis infection among hospital staff.

Key words : Tuberculosis, Hospital infection control, TST, QFT-2G

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The 83rd Annual Meeting Invited Lecture

FINDINGS AND ONGOING RESEARCH IN THE MOLECULAR
EPIDEMIOLOGY OF TUBERCULOSIS

Dick van SOOLINGEN and Kristin KREMER

Abstract [Settings] While in The Netherlands the organization of tuberculosis (TB) control in the era of elimination is being discussed, worldwide TB is still a major problem.

[Objectives] To highlight findings and ongoing research in the molecular epidemiology of tuberculosis.

[Findings] In the past decade, many studies have pointed out the significance of the Beijing strains in the worldwide tuberculosis epidemic. In South-East Asia, as well as the former USSR Republics, the Baltic States and South Africa, Beijing strains are emerging and associated with (multi-drug) resistance. Recent research in China has pointed out that the average proportion of Beijing genotype strains in 10 provinces amounts 73%, but varies significantly by region. The highest density was observed in the Beijing region; 93%. Currently, research is focused on the evolutionary development of Beijing strains. Two evolutionary lineages were distinguished and the "modern" lineage seems associated with spread, despite BCG vaccination in Vietnam. A project of the European Union with 11 international partners is trying to disclose the evolutionary adaptation of *M. tuberculosis* in response to vaccination and exposure to anti-tuberculosis drugs. Also in Europe the interest in the Beijing genotype has recently been strongly awakened. While 6–7% of the susceptible isolates are of this genotype, 85% of the MDR-TB transmission in Europe can be attributed to the spread of Beijing strains. Moreover, one cluster of 174 MDR-TB cases has been detected and this re-emphasizes that particular genotypes are capable of gaining poly-resistance without losing fitness. It seems, therefore, important to have more studies on the dynamics in the population structure of *M. tuberculosis* worldwide. In the presentation examples of such studies will be discussed.

Since 1993, IS6110 restriction fragment length polymorphism typing has gained recognition as the gold standard in the molecular epidemiology of tuberculosis. However, although the application of this method has brought significant new insights into the transmission of tuberculosis, it remains

technically demanding and time-consuming. Therefore, recently a new standard typing method, the variable numbers of tandem repeat (VNTR) typing, has been proposed in a publication in the J. Clin. Microbiol. In the Netherlands, a large part of the collection of nearly 15,000 *M. tuberculosis* isolates are currently being retyped with VNTR typing. This is not only meant to evaluate the utility of the new 24 loci VNTR typing, but also to conserve the epidemiological trace of tuberculosis transmission in the past. The first results will be discussed.

The role of non-tuberculous mycobacteria (NTM) in the diagnosis and treatment of tuberculosis-like diseases becomes increasingly important in the era of the HIV/AIDS pandemic. In Zambia it was recently shown that only in 50% of the cases diagnosed by Ziehl-Neelsen microscopy and X-ray, *M. tuberculosis* was isolated in a liquid culture system. In the other cases often only NTM can be cultured. In The Netherlands, particular NTM like *M. avium*, frequently cause lymphadenitis in children. This infection is normally indicated as "bird tuberculosis". However, with IS1245 RFLP typing it was pointed out that the *M. avium* isolates from lymphadenitis cases do not represent the bird type *M. avium* strains, but the *M. avium* strains typically found in humans and slaughtered pigs: *Mycobacterium avium hominissuis*.

Key words: Molecular epidemiology, Beijing genotype, Multidrug-resistant tuberculosis, Surveillance

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TUBERCULOSIS CONTROL TOWARD LOW INCIDENCE SITUATION

Chairpersons : ¹Toshio TAKATORIGE and ²Seiya KATO

Abstract : Incidence of tuberculosis in Japan is steadily decreasing in the past several years in spite of stagnation from 1980's followed by upsurge in late 1990's and declaration of emergency in 1999. In some prefectures, it is already about 11/100,000. In near future, it will happen in many areas and Japan is supposed to be low incidence country in approximately 10 years. In western countries where had been in low incidence situation, re-emergence of TB was happened in 1990's, because of unawareness of TB among general population, weakened health structure for TB control, increase of high risk group such as drug abuse, HIV/AIDS, foreign-born, homeless etc.

In this symposium, panelists who participated study tours to London and Leeds in UK, New York and San Francisco in US, Berlin in Germany and Hague in Netherland discussed current situation and efforts in order to show directions and challenges toward low incidence in Japan.

1. Challenges of TB control under low incidence situation:

Seiya KATO (Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association)

It is estimated that it will take approximately 10 years until the time when Japan become low incidence country, however, it may be influenced by immigrant from high incidence country, HIV/AIDS, high risk population such as alcohol/drug addicts, unawareness on TB in general population and/or retarded control by curtailed budget etc. Experience in low incidence country suggested the challenges toward low incidence situation as follows; 1) Commitment of central government; In US, CDC plays definitely important role in all aspects of TB control throughout the country with a quite large amount of budget which is provided to local governments. In UK, TB control system was reorganized as one of the component for management of health crisis. 2) Maintaining technical expertise; The following should be considered: integration of TB control organization, strengthened technical support from central organization regardless of public or non-public sector, training and/or qualification of experts, network

of the experts. 3) Provision of medical service: it should be considered for reorganization from the aspects of quality of service as well as accessibility from community. 4) Bacteriological surveillance system including drug sensitivity test and genotyping should be established.

2. The health care system for the tuberculosis control in the low incident countries—USA, UK, Germany: Toshio TAKATORIGE (Public Health, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University)

The tuberculosis control in New York City is implemented on Chest centers. Chest centers provide all range of state-of-the-art tuberculosis (TB) services under one roof. All services are provided with free of charge to the patient and confidential. The tuberculosis countermeasure in London is implemented on Chest clinics and TB offices. The TB offices have TB specialist nurses. TB specialist nurses are the important health profession to case management and support in UK. There are public health centers in Germany. The public health center performs the registration and management of the tuberculosis patient, the medical examination of the contact persons. The public health center has a few doctors, social workers and radiologist. As the tuberculosis incidence is decreasing, health manpower and facilities are decreasing. It is necessary to have the chest clinic for tuberculosis control such as New York City in the area where the tuberculosis prevalence is high. The public health centers in the area where the resource for TB health care is scarce, may be necessary to provide medical care service.

3. Medical care to tuberculosis patients under low prevalent situation: Kunihiko ITO (Department of Research, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association)

High quality of clinical care for tuberculosis patients is the most important component for good tuberculosis program. However, in Japan incidence of tuberculosis has been steadily declines, and in the near future low prevalent situation will come. Under low prevalent setting, maintaining of the quality of clinical care for tuberculosis will become more difficult, and therefore we will need some intervention to maintain the quality, such as centralization of tuberculosis care to some special hospitals. By those centralizations, the experience and knowledge could be maintained, but accessibility to the tuberculosis care for patients will be poorer. We must consider the best way to maintain the quality of clinical care for tuberculosis.

4. Effective approaches to tuberculosis high-risk group—How to evaluate and treat high-risk group with tuberculosis

and latent tuberculosis infection in San Francisco, California, USA: Tomoyo NARITA (Children's Medical Service Section, Declining Birth Rate Countermeasures Division, Bureau of Social Welfare and Public Health, Tokyo Metropolitan Government), Michihiko YOSHIDA (Health Service Section, Shinagawa City Health Center, Shinagawa City Government)

Incidence of TB in the San Francisco City is 16.6/100,000, which is 3 times more than that of US. Foreign-born comprise 75% of the cases and other high risks are drug abuse and HIV/AIDS. Early case detection in high-risk groups is a key for TB control, so that screening for TB and LTBI was given high priority by all TB control. The approaches to the TB high-priority subpopulation, such as immigrants, included following points; 1) ensuring quality TB surveillance, 2) thorough and timely evaluations on TB, 3) appropriate treatment, 4) appropriate approaches to cases with diverse cultural and linguistic background, 5) financial and welfare supports, 6) restructuring medical service. To build the future framework for tuberculosis control in Japan, we should consider the tactics as above.

5. Establishment of Pathogen Surveillance System: Satoshi MITARAI (Bacteriology Division, Mycobacterium Reference Centre, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association)

The pathogen surveillance system for *Mycobacterium tuberculosis* will be beneficial to the effective tuberculosis control in Japan. Some other countries where the incidence of tuberculosis is low, the United Kingdom and the Netherlands for example, have an efficient surveillance system. The system will provide the information of anti-tuberculosis drug resistance and molecular epidemiology regularly. The information will be utilized for the evaluation and planning of anti-tuberculosis strategy/program. However, the medical resources in Japan are not well organized at present. It will be necessary to re-organize the possible resource facilities considering the surveillance and reference system.

Key words: Low incidence, Tuberculosis control, Health structure, High risk group, Pathogen surveillance

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