## ----- Original Article -----

### A STUDY ON PULMONARY TUBERCULOSIS RETREATMENT CASES

Yuka SASAKI, Fumio YAMAGISHI, Takenori YAGI, Meiji ITAKURA, Ayako FUJIKAWA, Meiji KUGA, and Tsuyoshi ISHIMARU

**Abstract** [Objective] To investigate the factors leading to the retreatment for tuberculosis.

[Materials] Forty-seven retreatment cases with pulmonary tuberculosis, who were discharged from the National Chiba Higashi Hospital from 2000 to 2002.

[Methods] Data on all retreatment cases were studied as to the condition of the original treatment and factors leading to the retreatment.

[Results] Of the 47 cases, 33 cases received the original treatment in our hospital. Of the 33 cases, 24 cases were relapsed cases and 9 cases were defaulters. Most relapsed cases were male aged 50s and 12 cases (50%) were jobless. As the factors leading to retreatment, the delay in the negative conversion of sputum culture accounted for 11 cases (45.8%) out of 24 cases. No specific factors were found in three cases (12.5%). Among the defaulters, no bias was seen as to age and occupation of cases, but all the cases were male, and they defaulted during the maintenance phase of treatment at the out-patient department.

[Consideration] The delay in the negative conversion of sputum culture was the main factor relating to the relapse. Diabetes mellitus (DM) is one of the factors leading to the

relapse, but many factors were observed in DM patients. Male cases aged 50s had many factors leading to the relapse. An intensive management for out-patients and involvement of welfare department aiming at the completion of treatment for the socially vulnerable groups might be necessary as the measure to prevent defaulting.

[Conclusion] The delay in the negative conversion of sputum culture was the main factor leading to relapse, and intensive management for out-patients aiming at the completion of treatment is necessary to prevent the defaulting.

**Key words**: Relapse, Defaulting, Retreatment, Management of regular drug-taking, Directly observed treatment, short course

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## ----- Original Article -----

# ENVIRONMENTAL FACTORS RELATING TO A MASS OUTBREAK OF TUBERCULOSIS IN A JUNIOR HIGH SCHOOL

#### Makoto TOYOTA

**Abstract** [Objective] To clarify environmental factors relating to a mass outbreak of tuberculosis.

[Methods] A 15-year old girl, a third-grade student of a junior high school (the index case) was found to have smear-positive cavitary pulmonary tuberculosis. Among 718 subjects who underwent contacts investigation, the rates of infection and cases among different exposure groups were compared. The ventilation rate within the room of the junior high school was analyzed using sulfur hexafluoride (SF6) as the tracer gas.

[Results] Up to 56 months after the detection of the index case, a total of 34 tuberculosis patients were newly diagnosed, and 155 persons were subjected to chemoprophylaxis. The rates of infection were 90.0% among homeroom classmates and 60.8% among other classmates, respectively. Out of the subjects who had only indirect contact with the index case, 11 patients were diagnosed. Most of the windows of the building were of the fixed sash type, permitting only low ventilation ranging from about 1.6 to 1.8 room air change per hour. When sliding doors of the room were opened, the SF6 concentration

in the room was rapidly mixed up with that in the passage.

[Conclusion] Low ventilation of the room and overcrowding contributed to the high infection rate among homeroom classmates. Infectious droplet nuclei spread to the passage at recess. The homeroom of the index case was located in front of the building's entrance. The index case used some common rooms of the building. In addition to these environmental factors, other factors, especially the high infectiousness of the index case also contributed to the mass outbreak.

**Key words**: Tuberculosis outbreak, Junior high school, Building, Environmental factor, Ventilation, Sulfer hexafluoride (SF6)

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## ----- Original Article -----

## FLUCTUATION IN THE RATIO BETWEEN DRUG-RESISTANT AND -SUSCEPTIBLE M. TUBERCULOSIS BACILLI WHICH WERE ISOLATED FROM PATIENTS WITH PROLONGED ANTI-TUBERCULOSIS TREATMENT

Hiromi ANO, Tomoshige MATSUMOTO, Hiroko YOSHIDA, Chieko ISHIDA, Nobuko TANIGAWA, Kunimitsu KAWAHARA, Hirokazu TOBA, Tetsuya TAKASHIMA, and Izuo TSUYUGUCHI

**Abstract** [Purpose] In this study, we examined the fluctuation in the ratio between strains of tuberculosis bacilli resistant and susceptible to the anti-tuberculosis drugs.

[Material & method] We selected the cases in which the bacilli acquired drug resistance during the therapy and the cases in which drug resistance was fluctuating during prolonged anti-tuberculosis treatment. We selected the isolates throughout the medication period, and the selected isolates were separated into respective single colonies. Then we measured the minimal inhibitory concentration (MIC) for each colony by microdilution test for *M. tuberculosis* complex, BrothMIC MTB-1 (Kyokuto Pharmaceutical Inc., Tokyo).

[Results] Five patients were eligible for analysis because their medical histories were clearly recorded and drug resistance changed during the course. The MIC of 19 isolates, 202 colonies were measured. Isolates with coexisting drug-resistant and -susceptible colonies were detected in 2 patients. From these results, we considered that the fluctuation in the ratio between drug-resistant and -susceptible bacilli changes

with the progression of anti-tuberculosis medication.

[Conclusion] We showed in this article that the drug-resistant bacilli increased rapidly when the strains acquired the drug resistance during medication, and when the administration of particular anti-tuberculosis drug was stopped, the susceptible bacilli seemed to increase gradually. However, the strain immediately became fully drug-resistant when the particular antibacterial drug was readministered.

**Key words**: *Mycobacterium tuberculosis*, Drug resistance, Colony, Minimal inhibitory concentration, RFLP analysis, Fluctuation in drug-susceptibility

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	<b>Short Report</b>	
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# INFANTS AND CHILDREN WHO DEVELOPED TUBERCULOSIS FOLLOWING CONTACTS INVESTIGATION

Shinya KONDO and Masaki ITO

**Abstract** [Object] Reevaluating the important points in tuberculosis contacts investigation.

[Subject and methods] We retrospectively examined the medical charts of 25 infants and children who developed tuberculosis following contacts investigation.

[Results] In thirteen patients, diagnosis of infection was missed, and three of five infants less than one year old suffered from meningitis or miliary tuberculosis while they were waiting the next examination. Three patients were not indicated preventive treatment despite of induration of 5 mm or more in tuberculin skin test. Other twelve patients including five infants less than one year old were diagnosed to have tuberculosis infection and started preventive therapy, however, tuberculosis developed in 10 patients while taking the medicine, and in two patients probably because of defaulting from taking the medicine.

[Conclusion] These results suggest that the contacts investigation have to be done promptly and be flexible based on age of contacts, evaluation of tuberculin skin test results and radiographic findings in order to reduce the disease further.

**Key words**: Tuberculosis, Contacts investigation, Infants, Dissemination, Preventive therapy, Defaulting

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#### A CASE OF PRIMARY NASOPHARYNGEAL TUBERCULOSIS

## Akiko SHIMADA, Yuichi OSHITA, Takashi KINOSHITA, Toru RIKIMARU, and Hisamichi AIZAWA

**Abstract** [Background] Although the prevalence of nasopharyngeal tuberculosis has decreased after the wide use of anti-tuberculous agents, recently the number of reports with the disease has slightly increased in accordance with advances in the diagnostic tools. A case of nasopharyngeal tuberculosis without any tuberculous lesions in other organs (primary nasopharyngeal tuberculosis) was reported.

[Case report] A 74-year-old female complained of vertigo and cervical masses, and nasopharygolaryngoscopy disclosed a polypoid lesion on her nasopharynx. The biopsy from the mass revealed epithelioid cell granulomas with caseous necrosis and multinucleated giant cells consistent with tuberculosis. Since there were no tuberculous lesions in other organs except cervical lymph nodes in clinical examinations, we diagnosed the case as primary nasopharyngeal tuberculosis with tuberculous cervical lymphadenitis. The nasopharyngeal manifestation disappeared after four months chemotherapy with INH,

#### RFP and EB.

[Discussion] Most reported case of nasopharyngeal tuberculosis were in the young age group. A rare case of old woman complicated with cervical tuberculous lymphadenitis was reported.

**Key words**: Primary nasopharyngeal tuberculosis, Tuberculous lymphadenitis, Old people

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### The 78th Annual Meeting Lunch Time Lecture

### PULMONARY ASPERGILLOMA, DIAGNOSIS AND TREATMENT

Shigeru KOHNO, Tsutomu KOBAYASHI, Hiroshi KAKEYA, and Yoshitsugu MIYAZAKI

Abstract Pulmonary aspergilloma is a saprophytic form of aspergillosis, and the diagnosis is usually based on radiological findings such as thickened cavitary wall and fungus ball, and on positive serum antibody. Up to 58% of the patients with aspergilloma in Japan have medical history of tubeculosis. Serum anti-Aspergillus antigen is almost always positive in aspergilloma patients but aspergillus antigen is usually negative. Massive hemoptysis can be a fatal complication of aspergilloma, and the most common complication was respiratory failure according to our study. Surgical resection is the only promising intervention to cure the aspergilloma, however, low pulmonary function does not allow operation. Antifungal treatment is chosen for those who are out of operation indication, but the efficacy of antifungal treatment against aspergilloma is contravercial.

Some patients with aspergilloma show progressive form, and we define such aspergillosis as CNPA, chronic necrotizing aspergillosis, although the original entity of CNPA by Binder et al. is different. We make a diagnosis of CNPA only if all the following entity meets, 1; progressive shadows in radio-

logical findings regardless of the presence of aspergilloma, 2; have some symptoms such as cough, sputum, hemosputum, hemoptysis or fever, 3; proof of *Aspergillus* attribution by mycological or pathological examination, 4; positive systemic inflammatory reaction, 5; neglect of other etiology of pulmonary diseases. Since CNPA is usually progressive, patients with CNPA should be treated with antifungals.

**Key words**: Pulmonary aspergilloma, Voriconazole, Itraconazole i.v., Liposomal amphotericin-B, Micafungin sodium

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