

Original Article

ADVERSE EFFECT OTHER THAN LIVER DYSFUNCTION IN TREATMENT OF LATENT TUBERCULOUS INFECTION BY ISONIAZID

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Abstract [Purpose] To study the frequency and degree of adverse effect, other than liver dysfunction, of isoniazid (INH) preventive therapy in Japanese people.

[Object and Method] Chart review of Japanese persons who started isoniazid preventive chemotherapy in the two clinics in Tokyo, from 2003/1/1 to 2004/12/31.

[Result] There were 779 cases who did not transiently or completely stop INH preventive therapy because of adverse effect, and 20 cases who stopped INH transiently or completely because of adverse effect other than liver damage (total 799 cases). Of those cases, 153 cases ($153/799=19.1\%$) experienced one or more adverse effect other than liver damage, and 20 cases ($20/799=2.5\%$) of these 153 cases stopped INH transiently (12 cases) or completely (8 cases). For each category of adverse effect, digestive system symptoms were most frequent (5.9%), and then in frequency order, lethargy or easy-fatigability (4.6%), central nervous symptoms (4.5%), skin eruptions (2.6%), acne (2.5%), alcohol intolerance-like symptoms (2.5%), peripheral neuropathy (0.4%), arthralgia or limb pain (0.3%). Adverse effect requir-

ing stopping INH transiently or completely were skin eruption (1.3%), digestive system symptoms (1.1%), central nervous symptoms (0.6%), acne (0.1%). Most of the adverse effect were not serious, and not required hospitalization. In isoniazid (INH) preventive therapy in Japanese people, adverse effect other than liver damage were not infrequent, but most of them are not serious, and do not disturb continuation of preventive therapy in most cases.

Key words: Isoniazid, Treatment of latent tuberculosis infection, Preventive chemotherapy, Adverse effect

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Original Article

NEW CRITERIA FOR DISCHARGE FROM WARD IN PATIENTS WITH PULMONARY TUBERCULOSIS USING MYCOBACTERIA GROWTH INDICATOR TUBE

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and ²Hidenobu MATSUMOTO

Abstract [Objectives] To find a new method to predict the result of the egg based Ogawa medium using the Mycobacterium Growth Indicator Tube (MGIT) system and to evaluate the usefulness of a new discharge criterion that uses the new prediction method for smear positive pulmonary tuberculosis patients.

[Materials and Methods] We compared mycobacterial growth of sputum specimens weekly between the Mycobacterium Growth Indicator Tube (MGIT) and the egg based Ogawa solid media, using a total of 3952 sputum specimens of patients with pulmonary tuberculosis (TB) who underwent chemotherapy in our hospital from September 2001 to March 2006 to find relationship between the results of the two culture methods and to utilize the findings to new discharge criteria of pulmonary TB patients. And we compared the duration of hospitalization between two patients' group: one group using the new discharge criterion, the other the old one.

[Results] We found that if a specimen shows negative culture on the MGIT system within the first two weeks, the same specimen shows negative or scant growth on the Ogawa media in the 8th week. Introducing this fact as a part of new criteria for hospital discharge of patients with pulmonary tuberculosis, the median duration of hospitalization in our hospital was shortened from 121 days to 71 days and no patient showed treatment failure.

[Discussion] We have used the result of sputum culture on Ogawa medium as a standard when we judge infectivity of

patients with pulmonary tuberculosis in Japan, but it was one of the reasons why Japanese pulmonary tuberculosis patients stay long in TB hospital. Using our finding, we can predict the results of Ogawa system six weeks earlier, when a specimen shows negative culture on the MGIT system in the first 2 weeks. After we introduced this fact into new criteria for hospital discharge of patients with pulmonary tuberculosis, the median duration of hospitalization in our hospital was shortened and no patient shows treatment failure until now. We highly recommend the usefulness of the MGIT system (especially when a specimen shows negative growth in the first two weeks) as a reliable method of predicting infectivity of patients with pulmonary tuberculosis and propose that the new TB discharge criterion should be widely confirmed and used in other hospitals.

Key words: Pulmonary tuberculosis, Discharge criteria, MGIT, Ogawa egg medium

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Original Article

TUBERCULOSIS AND ITS CONTROL MEASURES FOR HOMELESS PEOPLE:
IMPLEMENTATION OF CHEST X-RAY EXAMINATION
FOR THREE SUCCESSIVE YEARS

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Abstract [Purpose] To clarify the status of tuberculosis and its control measures for homeless people.

[Object and Methods] Chest X-ray examinations were conducted for 1,309, 1,545, 1,546 homeless people, annually between 2003 and 2005.

[Results] Homeless people with old tuberculous foci accounted for about 30%, and about 2% were judged to need immediate medical treatment. Thirty cases needed treatment in 2005, and thirteen of these twenty cases had shown healed tuberculous shadows at the previous examinations. The annual incidence rate (3/20) of tuberculosis cases among persons with Type IV (inactive) lesions in 857 participants in both 2004 and 2005 was 11.2 times higher than the rate (8/597) among those who did not show chest X-ray abnormalities.

[Conclusion] The annual incidence of tuberculosis among persons with Type IV lesions was higher than those who did not show chest radiographic abnormalities. It is thus necessary to establish prophylactic treatment criteria for persons with

Type IV lesions by using a new method such as QFT.

Key words : Tuberculosis, Homeless people, Chest X-ray examination, DOTS, QFT

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A CASE OF TUBERCULOSIS SHOWING IMMUNE RECONSTITUTION SYNDROME
AFTER THE INITIATION OF ANTIRETROVIRAL THERAPY
FOR HIV INFECTION

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Abstract A 27-year-old man admitted for high fever, wet cough and abnormality on his chest radiograph. He was diagnosed as pulmonary tuberculosis, and started treatment with INH, RFP, EB, and PZA. After other examinations, he was diagnosed as having an acquired immunodeficiency syndrome, too. We gave him zidovudine and lamivudine/abacavir sulfate to treat HIV infection. After starting treatment with anti-tuberculosis drugs his fever alleviated, but after 10 days from the start of anti-HIV drugs, he showed high fever, and abnormality of his chest radiograph exacerbated. We diagnosed him as immune reconstitution syndrome, and gave him prednisolone 30 mg/day. His symptoms improved gradually.

Key words: Acquired immunodeficiency syndrome, Pulmonary tuberculosis, Paradoxical worsening, Immune reconstitution syndrome

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A CASE OF MULTIDRUG-RESISTANT PULMONARY TUBERCULOSIS CURED BY THE REGIMEN INCLUDING THIA CETAZONE

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and ⁴Hideo OGATA

Abstract A 30 years-old-male was referred to our hospital for surgical treatment of multidrug-resistant tuberculosis in April 1998, three years after diagnosis of tuberculosis. All first-line anti-tuberculosis drugs and second-line anti-tuberculosis drugs were resistant on drug susceptibility tests by Ogawa medium. The right upper lobectomy was done because of massive hemoptysis and enlargement of cavitory lesion in June 1998, but this surgical operation was complicated with bronchial fistula and chronic empyema. Open drainage surgical treatment for chronic empyema was done one month after lobectomy. Sputum culture for *M. tuberculosis* converted 4 months after the lobectomy, but bacteriological relapse occurred 17 months after initial operation. The new cavitory lesion on middle left lung field developed and sputum smear and culture were continuously positive. Immunotherapy with interferon- γ via aerosol didn't show any clinical effect. Thiacetazone, sparfloxacin, pyrazinamide, cycloserine was prescribed after 21 months of the initial operation. Four months after changing the regimen sputum smear and culture

converted to negative. Chemotherapy was terminated in June 2003, two years after negative conversion. Three years after the termination of treatment no relapse occurred. We considered thiacetazone was effective in this case, because all of the drugs was companied with thiacetazone were resistant by the drug susceptibility tests and were previously used.

Key words : Multidrug-resistant tuberculosis, Relapse, Thiacetazone, Surgical resection

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LET'S DOTS— EMBODYING THE DESIRE OF NURSING TO HEAL IN DOTS

Chairpersons: ¹Kenichi TAKEUCHI, and ²Keiko KOKUBU

Abstract The purpose of this symposium encompassed (1) determining the extent to which DOTS has spread throughout the country, (2) gaining a deeper understanding of the need for DOTS, and (3) providing a detailed understanding of the methodology behind DOTS. The following reports were made based on case studies presented by a tuberculosis research facility, head of the nursing department at an actual health care institution, public health nurse and various institutions in Miyagi Prefecture.

1. Local DOTS programs have been implemented at public health centers by 37% of 127 local municipalities throughout the country as of 2004, and when those centers currently proceeding with preparations for implementation of these programs are included, roughly 60% of all public health centers are implementing local DOTS programs, representing a roughly three-fold increase over the previous year.

2. In-hospital coordination through conferences provided supports for implementation of in-hospital DOTS programs.

3. In order for public health centers to effectively work with local communities, it is necessary to (1) develop skilled technicians and (2) establish an environment for effective communication between the public health center and related health care institutions.

4. It is necessary for prefectural governments to construct a unified coordination system to enable all public health centers within a prefecture to smoothly coordinate their efforts with health care institutions.

In response to these reports, Dr. Murashima, serving as commentator, summarized the findings into three basic questions from the standpoint of a researcher of regional nursing training. These consisted of: (1) what is the significance of DOTS for those persons it involves, (2) how should results be indicated as a result of nursing embodying its desire to heal in DOTS, and (3) what types of steps should be taken to ensure the proliferation of “favorable case studies”?

Since the effects of providing nursing care for tuberculosis can be verified easily, expectations have been placed on tuberculosis nursing to be able to propagate those effects throughout the nursing community.

Center Director Mori provided an overview of the global strategy of DOTS thus far while emphasizing that the results of current tuberculosis treatment in Japan cannot necessarily be said to be satisfactory, and that a “Japanese DOTS strategy” must be promoted by positioning at the core of tuberculosis countermeasures in Japan.

1. Implementation of a Japanese Version of DOTS: Noriko KOBAYASHI (The Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association)

There is an increasing trend in the number of public health centers implementing DOTS programs. From the standpoint of the training of nurses and public health nurses, there is the impression that hospital DOTS programs are providing the driving force behind regional DOTS programs. Moreover, a larger number of related conferences and cohort study groups are believed to be leading to the providing of higher quality patient services. In the future, it will be necessary to provide support for the services provided by health care nurses in ensuring that patients take their medication while also sharing in those support methods.

2. Implementation of DOTS at Health Care Facilities: Tomoko ABE (Fujita General Hospital)

We began an in-hospital DOTS program at our facility in March 2001. The impetus behind its implementation was when an 80-year-old hospitalized patient for whom about 4 months had passed since being sputum positive requested to stay overnight with his family, the patient’s family found a large amount of medicine with his luggage on the following morning, making us painfully aware of the need to confirm

whether or not hospitalized patients are actually taking their medication.

Important factors enabling us to promote our in-hospital DOTS program smoothly consist of (1) obtaining patients' consent, (2) including the participation of pharmacists in the administration of anti-tuberculosis drugs from the time patients are hospitalized, and (3) having out-patient DOTS supervisory nurses visit patients before they are discharged from the hospital. In addition, as a result of having implemented an out-patient DOTS program, coordination between hospital wards and out-patient services, and between out-patient services and the public health center has improved considerably, making it possible to continue to provide support for ensuring patients take their medication after they have been discharged from the hospital.

On the basis of these findings, it is felt that in order to allow patients who have become familiar with DOTS while in the hospital to continue with their routine of taking medication, it is important to strengthen coordination between health care institutions and public health centers to create a system that enables all participating facilities to provide support for each patient.

3. The Role of Health Care Centers in Promoting DOTS: Mutsuko KONNO (Yamagata Prefectural Murayama Health & Welfare Center)

Following the establishment of a legal basis for DOTS, the responsibility of public health centers engaged in providing therapeutic support in the form of public health services has been clearly defined. Public health centers must strengthen their efforts to enhance systems for providing support for patient medication through respecting patients' rights and coordination with related institutions.

Examples of efforts to be made by public health centers with respect to coordination with health care institutions include aggressively and continuously approaching health care institutions so as to obtain their understanding and cooperation regarding the tuberculosis countermeasures implemented by public health centers, establishing an effective coordination and cooperation system, and identifying the characteristics of patient outbreaks in their area of jurisdiction and their associated high-risk factors through cohort study groups.

In addition, it is also important for public health centers to establish and maintain a satisfactory communications environment with local related institutions even in the absence of outbreaks so as to provide familiar but specialized consultation services while proceeding with accommodations in anticipation of patient outbreaks from a preventive standpoint at all times. In order to accomplish this, it is necessary to further strengthen the important functions of health care centers consisting of the development of capable personnel corresponding to local characteristics and the construction of a network with related institutions.

4. Positioning of DOTS in Tuberculosis Prevention Programs: Yuuko MATSUDA (Miyagi Prefectural Main-Office Department of Health & Welfare)

Miyagi Prefecture is currently facing issues such as a tendency towards a long treatment period, lack of adequate understanding and support for taking medication by public health centers, and tending to have a low treatment success rate as compared with the rest of the country. In addition, DOTS programs are only implemented at some health care institutions handling tuberculosis patients and public health centers, and have not been established uniformly throughout the prefecture.

The Miyagi Prefecture Tuberculosis Prevention Program was enacted in July 1995 with the objective of reducing the prevalence of tuberculosis from the level of 16.2 (per 100,000 people) in 1993 to 12 or less by 2020.

DOTS has been positioned as an important measure for providing appropriate health care for tuberculosis patients.

In the future, local DOTS programs are scheduled to be implemented at all public health centers focusing primarily on patients with positive sputum smears with the aim of promoting DOTS while establishing a coordination system between public health centers, health care institutions and other related institutions.

5. Let's DOTS—Embodying the Desire of Nursing to Heal in DOTS: Sachiyo MURASHIMA (Department of Community Health Nursing, Division of Health Science & Nursing Graduate School of Medicine, The University of Tokyo)

I. The significance of DOTS can be understood from the process of asking related persons what type of significance DOTS has for them. That is, DOTS does not simply involve the dispensing of medication, but rather fulfills the role of supporting the independence of patients.

II. In order to demonstrate benefits gained from the concept of nursing embodying DOTS, it will be necessary to provide positive evidence of those benefits for hospital administrators and ensure that DOTS is deployed in the form of a continuous program.

III. In order to determine the manner in which effective measures should be deployed for ensuring the proliferation of successful case studies, efforts should be made to appeal to the benefits of DOTS through case studies indicating that DOTS contributes to the development of local caregivers through caring for tuberculosis.

Tuberculosis nursing differs from other nursing fields in that the effects are readily visible. Providing nursing care for tuberculosis makes it easier to verify the effects of one's own nursing care. I believe that it will be necessary to involve the desires and objectives of tuberculosis nurses involved in DOTS with those of all nursing professions in order to enhance effectiveness through even greater coordination and cooperation.

6. Expansion of DOTS Japanese Version and its Perspective:
Toru MORI (Leprosy Research Center, National Institute of
Infectious Diseases)

When the condition of tuberculosis treatment is becoming unfavorable year by year in Japan, the expansion of the quality DOTS is badly needed. The DOTS should be the kernel of the Japan's NTP that would be enhanced by the Stop TB Japan Partnership, involving wide variety of related organizations, and all the categories of health-related professions. In this way, Japan could share the global effort toward the Millennium Development Goals following the roadmap by the Stop TB Strategy.

Key words: Nursing, Coordination, DOTS

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APPLICATION AND PROBLEMS OF QuantiFERON®TB-2G FOR TUBERCULOSIS CONTROL PROGRAMS

— (1) Tuberculosis Outbreak in a Cram School —

Keiji FUKAZAWA

Abstract [Objective] The purpose of this study was to evaluate the usefulness of the QuantiFERON®TB-2G (QFT), which is a novel method of detecting tuberculosis (TB) infection, in a case of TB outbreak.

[Subjects and Methods] The index case was a teacher of a cram school in which students received one-to-one lessons. Subjects of the contact investigation were 118 students, 28 teachers, and 47 guardians. At first tuberculin skin test (TST) and QFT were performed only on subjects under 40 years old, but subjects of QFT were extended to the other contacts later.

[Results] The QFT positive rates for students (70.0%) and teachers (56.5%) proved to be high according to the first contact investigation. Total of 46 secondary TB cases have been detected during the past 15 months after the index case had diagnosed as TB. The secondary attack rate for students, teachers, and guardians was 24.6%, 42.9%, and 8.3%, respectively. Ninety-three contacts, who were QFT positive or intermediate, or strong TST reactors, were indicated for chemoprophylaxis. The restriction fragment length polymorphism (RFLP) patterns of isolates from eight patients were identical to those of an isolate from the index case. Both infection and attack rates among students tended to increase in proportion to

the degree of exposure and the frequency of attendance to the school. The youngest among students who developed TB disease was 13 years old and the attack rates were about 30 to 50 percent between 15 and 33 years old.

[Conclusions] It was concluded that the QFT test was very useful for confirming the extent of transmission of TB and for motivating the candidates for chemoprophylaxis to accomplish treatment. However, the QFT test was not helpful for reducing the indication of chemoprophylaxis because the infection rates were very high in our case. Some epidemiological findings about the influence of age factor to the potential of progression to active TB in young people were obtained.

Key words: Tuberculosis outbreak, Cram school, Contact investigation, QuantiFERON®TB-2G, Chemoprophylaxis

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APPLICATION AND PROBLEMS OF QuantiFERON®TB-2G FOR
TUBERCULOSIS CONTROL PROGRAMS

— (2) Clinical Use of QuantiFERON®TB-2G —

Yoshiko KAWABE

Abstract [Background] QuantiFERON®TB-2nd Generation (QFT) is an accurate tool for detecting tuberculosis infection regardless of past history of BCG vaccination. In Japan, QFT test was recognized for diagnostic tool on April 2005, and adopted officially on January 2006. Tuberculosis Society issued Guideline for using QFT-2G on May 2006.

[Purpose] This article describe the usefulness and remarks in clinical use on diagnosis and system for detection of tuberculosis infection among staff in NHO Tokyo Hospital that has 100 beds for tuberculosis.

[Method] (1) QFT test for 403 definite diagnosed tuberculosis patient before tuberculosis treatment or within 7 days chemotherapy in NHO Tokyo Hospital. Seventy-four patients have immunosuppressive diseases such as diabetes mellitus, malignant disease, using corticosteroid or immunosuppressor and HIV+ including overlap diseases. QFT result was analyzed by immunosuppressive diseases and by age for 329 patients who have no immunosuppressive diseases.

(2) For control of tuberculosis infection of staff, QFT test is used in 3 situation. One is baseline QFT for staff who are shifted to tuberculosis ward from non-tuberculosis ward and new employee, 2nd is following up for staff who work at tuberculosis ward, and 3rd is contact investigation for staff who work at non-tuberculosis ward. Tuberculin skin testing and baseline QFT were done for 92 staff on April 2006, 2 were shifted to tuberculosis ward from non-tuberculosis ward and 90 were new employee.

[Result] (1) Among 403 definite diagnosed tuberculosis patient before tuberculosis treatment or within 7 days chemotherapy, QFT positive rate was 78.7%. Among 74 patients who have immunosuppressive diseases such as diabetes mellitus, malignant disease, using corticosteroid or immunosuppressor and HIV+ including overlap diseases, QFT positive rate was 58~70%. Among 329 patients who have no immunosuppressive diseases, QFT positive rate was 88~89% in thirties and forties, 69% in sixties and 63% in nineties.

QFT-2G test for 134 previously treated tuberculosis cases who are not suffered from active tuberculosis, 49 cases (37%) were positive, 27 cases (20%) were intermediate and 58 cases (43%) were negative. Instructive three cases were reviewed. Suspicion of tuberculosis relapse with QFT negative case was *M. avium-intracellulare* disease. Suspicion of *M. avium-intracellulare* disease rather than tuberculosis by X-ray and CT with QFT positive case was tuberculosis. A case with small nodule on CT with QFT positive was adenocarcinoma.

(2) Tuberculin Skin Testing and baseline QFT for 92 staff, 4 were QFT positive. Compared with Tuberculin Skin Testing more than 29 mm in erythema, QFT positive rate was 9% and more than 9 mm in induration, QFT positive rate was 7%. By following up QFT test for staff working at tuberculosis ward, 2 staff, one nurse and one helper, were diagnosed tuberculosis infection. As to contact investigation, one nurse was diagnosed tuberculosis infection.

[Conclusion] Although QFT is a very excellent tool for detecting tuberculosis infection, on clinical diagnosis, it is important to mind that QFT depends on clinical condition especially immunosuppressive diseases, aging and past infection. We cannot diagnose or exclude active tuberculosis by QFT result. This is a useful assistant tool on clinical diagnosis.

Key words : QuantiFERON®TB-2G, Tuberculosis, Tuberculosis infection, Tuberculin Skin Testing, Immunodeficiency, Control of healthcare infection

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