

RESULTS OF REPEATED QFT-2G CHECKINGS AT TWO-YEAR INTERVAL
AND THEIR COMPARISON WITH TST RESULTS
INTRODUCED INTO INFECTION CONTROL PROGRAM FOR STAFFS
WORKING AT A HOSPITAL WITH ISOLATION WARDS FOR TUBERCULOSIS

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Abstract [Objective] In Fukuji Hospital, we have been conducting TST to tuberculosis (TB) non-infected staffs to find new latent TB Infection (LTBI) every year, although almost of them were BCG vaccinated, and the reliability of TST is controversial in BCG vaccinated group. Recently, a new technique, QFT-2G, is evaluated highly to detect TB infection, especially in BCG vaccinated individuals. We examined hospital staffs twice at two-year interval using QFT-2G and TST, and compared these data.

[Material & Method] About four hundreds fifty staffs in Fukuji Hospital with isolation wards for tuberculosis, provided with high level program against nosocomial infection of TB were examined. Almost all of them were BCG vaccinated. Because one fifth to one seventh of them were supposed as TB non-infected, they had been examined with TST to find new LTBI every year. QFT-2G was applied for about 80–85% of staffs twice, 2003 Jan. and 2005 Jan., with each person's consent. We compared the sequential changes of TST reactions and QFT-2G data.

[Results] (1) The positive rate of QFT-2G was approximately 10% in both two-year interval checkings. (2) Two hundreds twelve persons, about half of staffs, were sequentially checked QFT-2G twice at two-year interval. 19 persons were positive at both checkings, 4 converted to negative and 7 converted to positive, suggesting that the rate of new LTBI in staffs would be 3.7% [7/ (212 – 19 – 4)] during 2 years, 1.85% per year by QFT-2G conversion. (3) In comparison with data between TST and QFT-2G, QFT-2G was positive only in 13% of staffs with strongly reactors to TST. More-

over, even in 13 staffs converted by TST reaction to strong positive and highly suspected of new LTBI at two-year interval, there were no positive and positive converted persons based on QFT-2G checkings. Lastly, out of 7 staffs who converted to positive by QFT-2G checkings, only one was tested with TST, and no increase in the intensity of TST was observed.

[Conclusion] The QFT-2G positive rate was about 10% and the new TB infection rate was estimated to be 1.85% per year in staffs of a hospital with TB wards provided with high level programs against nosocomial TB infection. In addition, there are apparent disagreements between the results of QFT-2G and TST reactions, presumably affected by prior BCG vaccination. Therefore we must be cautious to detect new LTBI by ordinary TST in BCG vaccinated group.

Key words : QFT-2G, Tuberculin skin test, Infection control for tuberculosis, Health screenings against nosocomial infection, Tuberculosis infection rate among the hospital staff

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直腸吸収改善を目的として製剤改良したリファンピシン坐剤の検討

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要旨：〔目的〕 Rifampicin (RFP) 坐剤に吸収促進剤および吸収保持剤を配合し血中 RFP 濃度上昇を目的として製剤化した RFP 坐剤の検討を行った。〔対象および方法〕 対象は研究に同意した 3 名のヘルスポランティアとした。RFP 坐剤は 600 mg, 750 mg, 900 mg の RFP に吸収促進剤であるカプリン酸ナトリウム坐剤重量の 3% 前後, 吸収保持剤であるアルギン酸ナトリウムを RFP 含量の 25% 添加した。各坐剤挿入後 2 時間, 6 時間, 10 時間後に採血した血清を検体として血中 RFP 濃度を測定した。〔結果〕 Subject no. 1 においては RFP 600 mg を含有する坐剤で $0.807 \mu\text{g/ml}$, 750 mg で $1.093 \mu\text{g/ml}$, 900 mg で $1.291 \mu\text{g/ml}$ となる RFP の最高血中濃度が得られた。〔考察〕 本邦において RFP 注射剤が使用できないため, RFP 坐剤の製剤的検討が, 治療効果を示すうえでも耐性菌の出現を回避するうえでも重要な課題であった。本研究において RFP 血中濃度が $1 \mu\text{g/ml}$ を超えたことにより治療薬として使用可能であると考えられた。今後, さらに製剤的検討を加えて臨床的な有用性を検討していきたい。

キーワード：肺結核症, リファンピシン, 坐剤, 直腸吸収, カプリン酸ナトリウム, アルギン酸ナトリウム

Original Article

RISK FACTORS FOR SIDE EFFECTS DUE TO THE USE OF ANTITUBERCULOUS DRUGS IN ELDERLY PATIENTS

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Abstract [Purpose] This study was designed to evaluate incidence of clinical risk factors for side effects due to the use of antituberculous drugs.

[Method] We retrospectively analyzed clinical records of 229 elderly patients with tuberculosis treated at our hospital.

[Results] Temporary stop of antituberculous therapy proved to be needed because of side effects in 77 patients (33.6%). Adverse effects leading to drug discontinuation were liver dysfunction (15.7%), gastrointestinal dysfunction (7.0%), and skin rash (5.7%); other effects accounted for discontinuation in 5.2%. Risk factors for liver dysfunction according to Cox proportional hazards regression analysis were complications of HCV infection (hazard ratio or HR, 2.97; 95% confidence interval or CI, 1.20 to 7.38; $p=0.019$); hepato cellular injury present at admission (HR, 3.37; 95% CI, 1.56 to 7.29; $p=0.002$); and dose of isoniazid (per mg/kg, HR, 1.40; 95% CI, 1.05 to 1.85; $p=0.02$). Body mass index was a risk factor for gastrointestinal dysfunction (per kg/m^2 ,

HR, 0.83; 95% CI, 0.70 to 0.98; $p=0.026$).

[Conclusion] Such identification of risk factors for side effects from antituberculous therapy in elderly tuberculosis patients would minimize adverse effects.

Key words: Elderly tuberculosis, Antituberculous drugs, Side effects, Multivariate analysis, Retrospective cohort study

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Original Article

CHARACTERISTICS OF 109 INDEX CASES IN TB OUTBREAK

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Abstract [Objectives] To elucidate characteristics of index cases in TB outbreak.

[Subjects and Methods] The subjects of this retrospective study were 109 index cases in TB outbreak observed in Japan between 2003 and 2005, and reported to the Ministry of Health, Labour and Welfare.

An index case rate (ICR) for a category of patients was defined as following; $ICR = NI/NA$, where *NA*: Number of TB patients in a category A, and *MI*: Number of index cases in category A.

[Results] Of the 109 patients, 20 were female and 89 were male. Smear-positive pulmonary TB patients were 102 in number, and separated to 87 patients with cavitory lesion on a chest X-ray and 15 without cavitory lesion, and the remaining 7 patients were smear-negative and culture-positive pulmonary TB patients. The index case rates were 0.46% for smear-positive cavitory patients, 0.10% for smear-positive non-cavitory patients, and 0.04% for smear-negative culture-positive patients. The differences were highly significant between smear-positive cavitory patients and smear-positive non-cavitory patients, as well as between smear-positive cavitory patients and smear-negative culture-positive patients ($p < 0.001$). In 57 male patients with smear-positive cavitory lesion, the index case rates were significantly different between the thirties and the forties (1.84% vs 0.61%, $p < 0.01$). All patients were grouped by age to a younger group

with 10 to 39 years of age, a middle aged group with 40 to 69 years, and an elder group with 70 years or higher. The index case rates in smear-positive cavitory patients were 2.32% for the male younger group, 0.37% for the male middle group, 0.06% for male elder group, 0.41% for the female younger group, 0.37% for the female middle group, and 0% for female elder group. The differences were highly significant between the male younger group and the male middle group, as well as between the male younger group and the female younger group ($p < 0.001$). The index case rates for smear-positive cavitory patients were significantly higher than non-cavitory patients in two categories; 1.58% versus 0.21% for the younger group ($p < 0.001$), and 0.37% versus 0.11% for the middle aged group ($p < 0.05$).

[Conclusion] These findings suggest that TB outbreak risk is the highest in those patients categorized to be smear-positive, cavitory, younger group, and male.

Key words : TB epidemic, Index case rate, Smear-positive pulmonary TB, Cavitory lesion, Aging, Gender difference

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COMPARISON OF BBL MYCOPREP AND 2%NaOH DECONTAMINATION PROCEDURES FOR MGIT

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Abstract [Objectives] We compared the BBL Mycoprep (Becton Dickinson Japan) and home-made 2%NaOH decontamination procedures by using an equal amount of expectorated sputum in the aerosol-free 30 ml KT centrifuge tube with the rugged inner surface.

[Method] A total of 113 sputum specimens obtained in NHO Kinki-Chuo Chest Medical Center in November 2004 were subjected to two decontamination methods. All specimens were divided into two equal portions after concentrating the sediments processed by semi-kaline protease (SAP), then decontaminated, and inoculated into MGIT. The tubes were incubated at 37°C and monitored for up to forty-second days.

[Results] Comparing these decontamination procedures, the time of the recovery of mycobacteria strains in the 2% NaOH (mean 8 days) was significantly faster than in the BBL Mycoprep (mean 11 days). Of these, 19 specimens (16.9%) processed by the BBL Mycoprep were positive for growth of mycobacteria, and similarly 18 specimens (16.0%) processed by the 2%NaOH ($p>0.5$) were positive. The 19 mycobacteria recovered by the BBL Mycoprep were identified as 14 *M.*

tuberculosis strains and 5 NTM strains. The decontamination rate was 0.9% in 2%NaOH and 6.2% in Mycoprep, however the difference was statistically not significant ($p>0.5$).

[Discussion] We verified that the 2%NaOH was an alternative method suitable for the digestion and decontamination procedure, and 2%NaOH was useful for the isolation and detection of mycobacteria as well.

Key words : MGIT, NALC/NaOH, 2%NaOH, Semi-kaline protease, Decontamination procedure

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Report and Information

**HUMAN RESOURCE CAPACITY BUILDING ON TB LABORATORY WORK
FOR TB CONTROL PROGRAM**

— Through the Experience of International TB Laboratory Training Course for
TB Control at the Research Institute of Tuberculosis, JATA, Japan —

Akiko FUJIKI and Seiya KATO

Abstract The international training course on TB laboratory work for national tuberculosis program (NTP) has been conducted at the Research Institute of Tuberculosis since 1975 funded by Japan International Cooperation Agency in collaboration with WHO Western Pacific Regional Office. The aim of the course is to train key personnel in TB laboratory field for NTP in resource-limited countries.

The course has trained 265 national key personnel in TB laboratory service from 57 resource-limited countries in the last 33 years. The number of participants trained may sound too small in the fight against the large TB problem in resource-limited countries. However, every participant is playing an important role as a core and catalyst for the TB control program in his/her own country when they were back home.

The curriculum is composed of technical aspects on TB examination, mainly sputum microscopy in addition since microscopy service is provided at many centers that are deployed in a widely spread area, the managerial aspect of maintaining quality TB laboratory work at the field laboratory is another component of the curriculum.

Effective teaching methods using materials such as artificial sputum, which is useful for panel slide preparation, and technical manuals with illustrations and pictures of training procedure have been developed through the experience of the course. These manuals are highly appreciated and widely used by the front line TB workers. The course has also contributed to the expansion of EQA (External Quality Assessment) system on AFB microscopy for the improvement of the quality of TB laboratory service of NTP.

The course is well-known for not only having a long history, but also for its unique learning method emphasizing "Participatory Training", particularly for practicum sessions to master the skills on AFB microscopy. The method in

learning AFB microscopy, which was developed by the course, was published as a training manual by IUATLD, RIT and USAID. As it is mentioned, the course has been contributing to human resource capacity building including management of laboratory service to improve NTP in the resource-limited countries.

Currently, expansion of technology transfer on culture examination for drug susceptibility test has been attempted to the resource-limited countries due to the occurrence of MDR-TB (Multi drug-resistant tuberculosis) and XDR-TB (Extensively drug-resistant tuberculosis) cases. However, since sputum smear examination is most effective method of detection of infectious TB, the writers believe it is still a core component of TB control, unless a new diagnostic tool that is practicable and effective in the resource-limited countries is developed. Therefore the course will keep focused on the smear examination as the basic curriculum.

The course is highly appreciated by international experts and it is our responsibility to answer the expectation from them.

Key words: International training, International course for TB laboratory work, Human resource capacity building, Sputum smear examination, TB control, Tuberculosis

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