ことは大きな利点である。診療会では、本文で既述のごとき統一された診療基準で実施しているため医療機関にも協力が得られ初回標準治療の普及も進みつつある。また統合以前には多くみられた菌検査のみならず不必要に始められる再治療も大幅に減少した。菌検査の指導、定期外検診の指導も行っており診療会は保健所と医療機関との橋渡しの役割を果たす努力をしているので患者管理上も大きな成果を上げている。神戸市においても診療会の統合により成果を上げていると報じている6)。全国的には結核の減少に伴い各保健所での診療件数も少なくなっていると推定され、結核専門医も減少している。したがって地域全体で検討し可能な範囲で診療会の統合を考えるべきと思われる。したがって全国の診療会ができたかぎり統一した考え方で運用できればわが国の結核対策に計り知れない利益がもたらされると考えられる。 }

SUGGESTIONS FOR BETTER MANAGEMENT OF THE TUBERCULOSIS ADVISORY COMMITTEE

Kazuhiko KAMEDA

Abstract Since 1951 tuberculosis advisory committee, established according to the tuberculosis control law, has played an important role in improving the quality of tuberculosis control programme in Japan.

The management of tuberculous patients has changed markedly in the past ten years due to advances in chemotherapy and changes in the epidemiological situation of tuberculosis.

In this paper, several suggestions were made on better management of the tuberculosis advisory committee intending to judge cases by unified criteria.

Key words: Tuberculosis advisory committee, Tuberculosis control law, Unified standard

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ISOLATION OF MPB63 IN THE CULTURE FLUID OF MYCOBACTERIUM BOVIS BCG
TOKYO: GENETICAL AND IMMUNOLOGICAL CHARACTERIZATION

Katsuhide KAWAJIRI

Abstract MPT63 is a secretory protein first isolated from a culture fluid of M. tuberculosis H37Rv by Nagai et al. In this study, this protein was isolated from an 8-day-culture fluid (Sauton synthetic medium) of M. bovis BCG Tokyo 172 according to Nagai’s method. It was shown that M. bovis BCG Tokyo 172 secreted this protein in the medium. The mpi63 gene was detected only in the species of M. tuberculosis complex by polymerase chain reaction (PCR) among 40 different mycobacterial species. Therefore, it is appropriate to designate this protein as MPB63 or MPB/T63 from M. bovis BCG, in similar way as other major secretory proteins of Mycobacteria, such as MPB59 and MPB64. Comparison of the nucleotide sequences of the genes encoding MPB63 protein of M. bovis BCG and MPT63 protein of M. tuberculosis showed only single nucleotide difference at the position 474 where thymine (T) in the former was replaced by adenine (A) in the latter. Amino acid sequences of both proteins were completely identical. MPB63 didn’t show delayed-type hypersensitivity (DTH) skin reaction in the sensitized guinea pigs with live or heat-killed M. bovis BCG or heat-killed M. tuberculosis.

However, the measurements of serum IgG antibody titers of active tuberculosis patients by enzyme-linked immunosorbent assay (ELISA) showed 74% sensitivity and 96% specificity compared to healthy subjects. Therefore, MPB63 seems to be a promising candidate as an antigen for serodiagnosis of active tuberculosis.

Key words: MPB63, Secretory protein, Culture fluid, BCG, PCR, ELISA

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CLINICAL EVALUATION ON THE DURATION OF HOSPITALIZATION FOR PATIENTS WITH PULMONARY TUBERCULOSIS

Tetsuro INOUE, Eisaku TANAKA, Kazukiyo OIDA, Yoshio TAGUCHI,
Terufumi KATO, Minoru SAKURAMOTO, Yuji MAEDA, and Ko MANIWA

Abstract In 1996, six-month short course regimen containing PZA was adopted as the standard method of chemotherapy for tuberculosis. According we reevaluated discharge criteria for patients with pulmonary tuberculosis and tried to shorten the duration of hospitalization. We investigated retrospectively the duration of hospitalization for patients with pulmonary tuberculosis who were admitted to the Tenri Hospital.

PZA was used for 23.3% of patients who were admitted during 1992 to 1996 (group A, N=200), and 80.1% of patients who were admitted during 1996 to 2000 (group B, N=234). The time needed to bacterial negative conversion was significantly shortened from 2.5 months in group A to 1.8 months in group B. The mean duration of hospitalization for patients with pulmonary tuberculosis was significantly shortened from 133.8 days in group A to 63.7 days in group B. Moreover, the mean duration of hospitalization for patients with smear positive pulmonary tuberculosis was significantly shortened from 147.5 days in group A to 73.0 days in group B. There was no significant difference between group A and group B as to the rate of adverse reactions, discontinuation of drug taking and recurrence of the disease.

We concluded that the duration of hospitalization for patients with pulmonary tuberculosis could be shortened by applying PZA in the initial phase of tuberculosis chemotherapy.

Key words: Pulmonary tuberculosis, Hospitalization period, Pyrazinamide, PZA

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例の比率は Moore らでは 5.6%、本調査では 11.8% であった。これも再治療例の比率が少ないほど、再治療例の薬剤耐性率が低いことを裏付けていた。

ま と め

近年、結核菌の薬剤耐性率の増加が見受けられている。しかし、当院における最近 8 年間の調査では、耐性率の增加を認めなかった。従来的報告と比較しても、初回治療例で耐性率が増加を認めず、再治療例の比率および薬剤耐性率は低下していた。現在では多剤併用療法が標準化されているが、今回の調査結果から多剤併用療法は結核菌の耐性獲得を誘導しにくいと考えられる。

文 献


TRENDS IN DRUG-RESISTANT TUBERCULOSIS
IN NATIONAL HIGASHISAITAMA HOSPITAL, 1994–2001

Trends in Drug-Resistant Tuberculosis

Abstract  To know the prevalence of resistance to four first-line anti-tuberculosis drugs, we reviewed the results of drug-susceptibility tests of patients with tuberculosis who were admitted to our hospital from 1994 to 2001. Among patients with no prior chemotherapy against tuberculosis, the complete resistance rate was 1.9% for INH, 0.81% for RFP, 5.1% for SM, 0.81% for EB, and 0.32% for multiple drug-resistance (MDR). The acquired resistance rate was 9.7% for INH, 11.5% for RFP, 7.3% for SM, 2.4% for EB, and 6.1% for MDR. There was no significant increase in the prevalence of drug resistance between the first half (1994–1997) and the latter half (1998–2001) of the investigation periods. Compared with the previous reports, our results indicated no increase in the prevalence of drug resistance in tuberculosis patients with no prior treatment and the decrease of prevalence in patients with prior treatment of tuberculosis. A multi-drug regimen consisted of INH, RFP, PZA and EB or SM, which is currently considered as a standard regimen of tuberculosis chemotherapy and used quite widely, does not seem to induce the increase of drug-resistant tuberculosis.

Key words: Drug-resistant tuberculosis, Multiple drug-resistant tuberculosis, Resistance ratio, Primary resistance, Acquired resistance

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Original Article
Abstract We retrospectively evaluated the clinical and laboratory data of children with tuberculous meningitis (TBM) treated at our hospital from 1990 to 1999 to determine the optimal method of diagnosing TBM. The evaluated diagnostic criteria for TBM were as follows: (1) fever and malaise as symptoms of acute/subacute inflammation, (2) positive cerebrospinal fluid and/or gastric aspirate cultures for *Mycobacterium tuberculosis*, (3) pleocytosis of cerebrospinal fluid, and (4) a good response to anti-tuberculous therapy. The data for eleven patients (6 boys, 5 girls) with TBM (mean age, 10.7 months) were reviewed. Three patients (27%) were previously vaccinated with BCG. A known contact with tuberculosis was established at the time of admission in four patients (36%). Symptoms related to tuberculosis appeared on the average 14.8 days before the diagnosis. Three patients (27%) were diagnosed as clinical stage I, three (27%) as stage II, and five (46%) as stage III; all patients had fever (100%). With regard to the cerebrospinal fluid examinations, pleocytosis with mononuclear predominance was noted in all patients but one (91%), and mycobacterial staining was positive in three patients (27%). Tuberculin skin test was positive in four out of 10 patients (40%). Mycobacterial staining of gastric aspirate was positive in four patients (36%). Chest radiological examinations showed a swelling of the mediastinal lymph nodes and/or parenchymal infiltration in all patients (100%). A cranial CT examination demonstrated a basal meningeal enhancement in all patients (100%), hydrocephalus in nine patients (82%), and infarction in eight patients (73%). These results suggest that chest and cranial CT examinations are useful adjunct methods for diagnosis of TBM in infants and young children suffering from meningitis with pleocytosis of the cerebrospinal fluid and mononuclear predominance, in addition to conventional methods such as the tuberculin skin test, plain chest radiography, and staining for mycobacteria in body fluids.

Key words: Tuberculous meningitis, Infant, Cranial Imaging, Basal meningeal enhancement, Chest radiographic study

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Abstract Brief review is made of the interconnections between tuberculosis and poverty and other social factors, with special emphasis on the current Japan's tuberculosis situation. In pre-war Japan, the tuberculosis had apparently an aspect of a socioeconmic problem which led to lively discussions. With the progress in medical technology and control measures after the war, such aspect of the disease has become more masked and difficult to see. Often, it is viewed merely as a problem of a small and special fragment of the population such as homeleses, and its wide and diffuse connections with the society and economy are likely to be overlooked. Studies in tuberculosis, both basic and epidemiological, as well as multidisciplinary, should be further encouraged from such a point of view, in order to lay such interconnections bare, on which the new control strategy should be based.

Key words: Tuberculosis control, Society, Poverty, DOTS, Epidemiology

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MANAGEMENT OF RESPIRATORY FAILURE IN PATIENTS WITH PULMONARY TUBERCULOSIS

Kazuko MACHIDA

Abstract The prognosis is very poor in patients with acute respiratory failure (ARF) due to active pulmonary tuberculosis, especially in those who necessitate mechanical ventilation. The underlining factors of ARF are low nutrition, old age and severity because of patient’s delay and doctor’s delay. So, management consists of two parts, one, early patient detection considering of tuberculosis and early treatment, the other, focused control to high risk groups.

Patients with chronic respiratory failure due to pulmonary tuberculosis sequelae have long insidious period and mainly restrictive, sometimes mixed pulmonary dysfunction. Hypercapnea, pulmonary hypertension and respiratory disorder during sleep are seen in high percentage in them. In acute on chronic failure the principles of therapy are treatment of precipitating factors such as respiratory infection or congestive heart failure, controlled (low flow) oxygen therapy, bronchial hygiene and maintaining adequate pulmonary and circulatory condition. In chronic stage patient education is very important. Management of chronic stage is constructed of nutrition control, long-term oxygen therapy, pharmacological therapy, pulmonary rehabilitation including controlled breathing technique, physical chest therapy and exercise training. Noninvasive positive pressure ventilation is effective on improvement of prognosis in chronic respiratory failure, and on treatment in acute on chronic failure.

Key words: Active pulmonary tuberculosis, Pulmonary tuberculosis sequelae, Respiratory failure, Acute respiratory failure, Chronic respiratory failure, Mechanical ventilation, Long-term oxygen therapy, Noninvasive positive pressure ventilation

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とが重要であり、地域の結核対策の中核機関としての保健所の機能強化が急務である。

追加発言：最近の西欧諸国の結核対策
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西欧では毎年結核担当官国際会議を開催し、患者定義の標準化および感受性検査の精度管理、疫学分析により互いに問題を建設的に批判して対策を推進している。患者の確定診断は培養検査による。治療結果、RFLP解析も重要視している。入院や検査目的と重症患者のためであり、期間は短い。特に隔離しなくても自国民の罹患率が減少し続けていることから、日本の隔離政策の有効性を見直す必要がある。また、罹患率が下がるほど、中央や県レベルに担当官を配置し、国内外で専門家のネットワークを形成する努力をしている。

ま と め

わが国では結核対策の効果が顕著であった時代の制度や方法が、「良き伝統」として社会に定着し、改革議論がタブー視されてきた面がある。本シンポジウムでは、過去の伝統や法的制度の枠組みにとらわれず、各演者からは今後のあるべき姿を概観しながら最新の科学的な evidenceや情報に基づく改訂案が数多く発表された。中でも小・中学生に対するツベルクリン反応検査による健診と BCG 再接種のあり方、ツベルクリン反応検査の測定方法（硬結径の採用）のあり方、および定期胸部健診のあり方など、シンポジウム参加者の関心が高く論議が行われた。伝統的な対策の発展や間引きに関する提案には不安を抱いている参加者も多かったが、提案の背景や根拠に関する理解が深まったと思われる。市町村等が関与する対策の発展に関する提案が多いので、結核対策に対する公的関与の必要性が低下するように誤解される危険がある。しかし、世界的にみるとわが国は結核の「中蓋滞国」であり、DOTS 略の推進など、公的責任の強化すべき対策が多い。厳しい行政改革が進む中で、地方分権時代の結核対策や公的関与のあり方は、今後も検討されるべきであろう。本講演で契機に、新しい時代の結核対策を切り開くための突破口となる研究や実践活動が促進され、専門家集団である日本結核病学会関係者から多くの有効な提案が出されることを期待したい。

--- The 77th Annual Meeting Symposium ---

BREAKTHROUGH FOR TUBERCULOSIS CONTROL PROGRAM IN JAPAN

Chairpersons: 1Nobukatsu ISHIKAWA and 2Tadayuki AHIKO

Abstract  Half a century has past since the frame of the national TB prevention law was legislated in 1951. Many aspects of the law are now unable to meet the changing needs of current TB problems. This symposium aimed to propose a breakthrough to a new national tuberculosis control program in Japan with 5 speakers from various aspects of the program.

1. BCG vaccination: Isamu TAKAMATSU

The effectiveness of primary BCG vaccination is shown by Meta-Analysis to be 70–80% effective against the serious disease, and 50% effective against pulmonary tuberculosis. Under the current epidemiological situation, BCG vaccination should be continued for infants, especially in the urban cities and the surrounding areas. As for the re-vaccination, there is no enough evidence either for positive or negative effect. WHO, however, does not recommend the re-vaccination because of no grounds for the positive effect. Globally many countries take a negative view. We should critically review efficacy and discontinue the on-going re-vaccination program at the earliest, because the demerit of the re-vaccination particularly of skin scars or keloid is larger than its merit if any. The measures for childhood tuberculosis need to shift from mass approach to individual and high risk focused ones.

2. Case-finding: Hidenori MASUYAMA

The case detection rate of the annual mass chest X-ray examination (MMR) has recently dropped so low to 0.0069% as the whole and 0.016% for general inhabitants. We need to discontinue the annual MMR for indiscriminate population. However among the young aged 15–19 years, 29% of the total patients were detected by MMR. For people under 40 years of age, MMR is recommended at the special occasions such as the entrance to college, new job, or new environment. For those aged 40 years or above, MMR is advised as a part of the routine periodical health examination. Special attention needs upon high-risk groups, for them annual MMR is recommended.

3. Treatment program: Motoyasu OKUNO

Standard regimen with 2HRZE(S) / 4HR(E) and DOT particularly for the in-patients should be further promoted unless there are contraindications. The current use of standard regimen is still 55% for the sputum smear positive cases. Most
of the sputum smear patients spend more than 2 months in hospitals in Japan. We have however little study results yet in Japan how or to whom DOT should be applied. For preventing drug resistance, we need to promote studies for effective tuberculosis treatment.

4. Issues for Tuberculosis prevention Law: Tomokazu INAGAKI

Current TB Prevention Law needs revision because of the changing situations in TB epidemiology, medical technology, concept for human rights and decentralized government system. For the revision, following viewpoints are necessary: 1) objective and policy of the law, 2) notification and surveillance system, 3) actions for infectious patients and patient’s rights, 4) control measures for group infection in community and institutions, 5) new control measures to changing epidemiological situation, 6) legal issues for protecting executor of the control measures, 7) flexible control measures to meet local needs, 8) does legal system contribute to TB elimination? 9) to include TB control in ”Infectious Disease Law” or to develop New TB Law?

5. TB control program and decentralization: Tadayuki AHIKO

NTP in Japan has been carried out by the central government throughout the country in the last five decades, and the TB incidence has considerably declined. However, Japan has yet the highest TB incidence among the industrialized nations. Current national surveillance data show that the decrease of TB is stagnating and the difference in the epidemiological features among prefectures has been expanded. The quality of control activities through public health centers has been also deteriorating in many prefectures. It is anticipated that a promotion of decentralized health care systems will be a breakthrough to TB elimination in Japan. However, a strategic plan needs to be developed by each local government under the revised national program, and the plan should be periodically revised based on local surveillance and program evaluation data.

6. TB programs in European countries: Akira SHIMOUCI

An international workshop is held every year for TB coordinators from most European countries to exchange the data and to standardize the criteria. Evaluation of treatment result evaluation and RFLP analysis are also made. Hospitalization of patients is only for examination and care of severe patients, but not for isolation. Despite no isolation policy, TB incidence of indigenous population has steadily decreased in Western Europe. The effectiveness of isolation policy should be also critically reviewed in Japan. As TB incidence decreased, TB coordinator’s posts are secured at national and provincial levels, and their network is strengthened.

**Key words**: TB control program, BCG revaccination, Health examination, DOTS, TB prevention law, Decentralization

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EDUCATION AND TRAINING CONCERNING DIAGNOSIS AND TREATMENT OF TUBERCULOSIS

Chairpersons: 1Ryoichi AMITANI and 1Hirohisa TOGA

Symposium Topics and Presenters:
1. Current status of tuberculosis education in medical schools and future tasks: Shuji KURANE (Fourth Department of Internal Medicine, Nippon Medical School)
2. How to refine the education of tuberculosis in teaching hospitals: suggestion by a physician in a National Chest Hospital: Katsuhiro SUZUKI (Department of Antimicrobial Drug-resistance, Clinical Research Center, National Center Hospital for Chest Diseases)
3. Education of tuberculosis in a general hospital that doesn’t have tuberculosis beds: Yasuo NISHIZAKA (Department of Respiratory Medicine, Osaka Red Cross Hospital)
4. Education of tuberculosis for general practitioners, residents in the section of respiratory medicine and co-medical staff: Masakatsu TAKAHASHI et al. (Department of Respiratory Medicine, National Nanao Hospital)
5. A novel system of tuberculosis education for doctors and co-medical staff organised by a public health center, in association with the outbreaks of tuberculosis infections: Makoto TOYOTA (Kochi City Health Center) et al.

Abstract In Japan the incidence of tuberculosis has not declined so much as predicted for a past few decades and is still much higher compared to that in most western industrialized nations. Among several factors probably related to the high incidence of tuberculosis in our country, effects of decrease in concern and knowledge of medical staff, especially doctors, as well as citizens regarding tuberculosis should not be under-estimated, because they may cause delay in diagnosis and treatment of tuberculosis. In order to resolve the problem, it is urgent to organize an efficient education system in university hospitals and other teaching hospitals concerning the diagnosis and the treatment of tuberculosis. However, there are several disadvantages to the teaching hospitals for tuberculosis education. The number of the teaching hospitals including university hospitals holding tuberculosis beds is gradually decreased, and most tuberculosis patients are hospitalized in some selected hospitals other than university and other teaching hospitals. Consequently, it is easy to surmise that the opportunities and time available for educating medical students and younger doctors concerning tuberculosis has been decreased.

In this symposium, each symposist presented current status of tuberculosis education in university hospitals, national chest hospitals holding tuberculosis beds, teaching hospitals without tuberculosis wards and public health center. They also presented some proposals concerning education and training of tuberculosis management from each different standpoint.

Dr. Kurane from Nippon Medical School outlined the problems of tuberculosis education, and he also referred to the current status of tuberculosis education in medical schools in Japan by analysing the responses to a nationwide questionnaire survey on tuberculosis education sent to 80 medical schools in our country. He emphasized the importance of tuberculosis beds in education and training of younger doctors and co-medical staff regarding tuberculosis management.
Dr. Suzuki from National Center Hospital for Chest Diseases emphasized that university hospitals should possess tuberculosis wards or beds in order to adequately educate medical students and younger doctors regarding the diagnosis and the treatment of tuberculosis, and he also emphasized the importance of establishment of department of infectious diseases in university hospitals to educate specialists of infectious diseases well accustomed to the management of the diseases including tuberculosis.

Dr. Nishizaka from Osaka Red Cross Hospital explained the way of tuberculosis education for doctors and co-medical staff in the teaching general hospital that doesn't have tuberculosis beds. In the hospital tuberculosis education was involved in regular lecture meetings on prevention of nosocomial infections held twice a year. He suggested the importance of tuberculosis education for not only respiratory physicians but doctors of internal medicine, emergency section and otolaryngologists who are likely to be faced with tuberculosis patients.

Dr. Takahashi from National Nanao Hospital holding tuberculosis wards has organized lecture meetings and seminars for educating general practitioners, younger doctors and co-medical staff in hospitals in Ishikawa Prefecture. He collaborated with doctors in a university hospital and in other teaching hospitals to organize the meetings. Each meeting was composed of at least two subjects (combination of tuberculosis and other familiar respiratory diseases) to increase the number of attendants.

Dr. Toyota from Kochi City Health Center presented lecture meetings and seminars on tuberculosis management for educating general practitioners, younger doctors and co-medical staff in hospitals in Kochi Prefecture. The lecture meetings and the seminars are organized by Kochi City Health Center, in association with the outbreaks of tuberculosis infections which were sensationaly informed to the public through mass media.

**Key words**: Tuberculosis education, Tuberculosis wards, University hospital, General hospital without tuberculosis beds, Core curriculum, Public health center

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