

NEWSLETTER FROM KIYOSE



No. 9, September 1995

The Research Institute of Tuberculosis, JATA
3-1-24 Matsuyama, Kiyose-shi, Tokyo 204, Japan

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New Movements in RIT

Dr. Masakazu Aoki, Director

The Research Institute of Tuberculosis has recently started three new epoch-making programmes. They are "International Course on Prevention and Care of AIDS in Asia", "International Collaborative Research Programme on Tuberculosis", and "International Mobile Seminar on Tuberculosis Control, which is held in several countries." All of them are supported by the national budget.

The International AIDS Course was carried out for six weeks from February 12 to March 24, 1995, with 20 participants from Asian countries. Although we have more than 30 years of experience in international training courses for tuberculosis, we have had little experience in the AIDS field. Many lecturers were invited from Japan and overseas including Centers

preventive strategy, giving priorities to surveillance and national prevention strategies for AIDS. The course was highly evaluated by the participants.

The International Collaborative Research Programme mainly consists of two themes; "Epidemiological Study on Tuberculosis" and "Studies on Efficiency of Tuberculosis Treatment". This programme is supported by a new national budget of about 1.2 million US\$. The studies will be carried out exchanging ideas with CDC of U.S.A., WHO, CDC of Thailand and so on.

The International Mobile Seminar will be held in Cambodia and Thailand this year and is now under preparation.



International AIDS Course, 1994

Though tuberculosis continues to be a big domestic problem in Japan, the Research Institute of Tuberculosis intends to expand and strengthen the activities in the field of International

for Disease Control and Prevention in the U.S.A., WHO, CDC of Thailand and so on. The course covered a wide area from basic science to care and

Cooperation, and to have closer friendship with many countries in the world.

The time I spent in Japan is one of the most wonderful times in my life because I met marvelous people from other countries with different ways of thinking and different habits. I could see a lot of things about the "Nihon" style of living, thinking, working entertaining, studying, eating and others. I learned to admire and love Japanese people and Japanese life. Every time I watch news from Japan or about Japan, I want to know all about them. Now Japan is like a part of me and I love all you nice people.



After I came back from Japan, I did not feel good cooperation from the institute I was working for. Too much work, the absence of the missionary community organizations which I had been voluntarily involved in before, and the lack of my own laboratory equipment have not let me continue for the time being in the TB field. Even so sometimes I do a direct smear for TB when it is necessary to confirm the healthy condition of couples who want to adopt children, and I have done it for homeless people I have seen with symptoms.

I have talked with laboratory technologists in charge of the TB control programme in the Regional Health Service, and shared with them the knowledge I got from Japan. I think our programme here is good, but some times is only a "good" programme because the lack of sufficient budget does not let us develop as much as we would like. We use the direct smear like the base of the programme.

The technologists perform 10-20 exams a day; in addition to slides from other districts they review in quality control. Culture tests are also performed, but for identification and sensitivity tests, the positive cultures are sent to the national level.

I am still working in forensic serology, so my TB work is very limited, but I hope I can be involved in health programmes again. Anyway I have put into practice the discipline and the organization which I learned in Japan and I hope I will soon be in a TB control programme.

Please give greetings to all my teachers. I love everybody in Kiyose and I miss Japan a lot. I learned so many things about organization, discipline, and civilization that I would like people in our Latin countries

to know. A nice way to live life is to respect the law, be kind, love peace and try ones best, not fighting, but studying and improving every day.

Ms. Nohora Moritza Diaz T
(Colombia, Laboratory Course 1991)



Being a graduate student of Public Health in Shinshu University School of Medicine, Japan, I had the chance to learn about TB by attending a "Group Training Course in TB Control II" in 1994 at RIT.



It is true that intuition inspires a person to fulfill the desire of expectation. Intuitionally I had an opportunity to be involved in participatory action research (PAR) guided by Dr. N. Ishikawa and Dr. N. Yamada, RIT to improve TB control in Bangladesh.

Through involvement, I realize that PAR is helpful for finding out how a programme is going on in reality with NTP guidelines and locally adjusted systems. Health centres at the PHC level face some constraints regarding DOTS, field workers' participation and regular supervision, monitoring and so on. Through the organization of participatory study meetings, it became clear that many unseen, unknown and unidentified views could be identified. Health personnel can be motivated and committed to recognizing their respective duties through mutual understanding and exchange of opinion.

From the above views, PAR might be considered as the supporting environment for NTP to identify the roots of success, problems and constraints through the involvement of personnel from the top to grass-root level of health care. The process and outcome of such study meetings, based on the concept of learning from experience, could contribute to further improvement of NTP through better proposals.

From external researcher's views, I realize that there should be a trinity (triad bond) relationship among PAR, NTP and health centres with regular feedback systems to improve programmes. I consider it possible that PAR can be included with NTP for better success.

Dr. Abdul Fattah (Bangladesh, Control Course 1994))

About the questionnaire to participants 1990-1994

Takashi Yoshiyama, Int'l Cooperation Dept.

With the newsletter from Kiyose No 8, the section of international training has sent a questionnaire to the ex-participants in the control course and the advanced course 1990-1994. The questions are about the usefulness of the training, requests to the training courses, treatment results in their areas, and opinions about "directly observed treatment". By July 1st, 13 answers were returned and also we got a report of the

achievement of action plan for the control course 1994. With this information, the treatment results in participants' countries are: some high fatality rates in Malawi (Kwanjana 91C and Gonde 92C) and India (Barua 92C Assam in 1993), a very high proportion of transfer-out cases in Thailand (Pethcawan 94C), some satisfactory results from Vietnam (Dochau-Giang 92C), some results which leaves need for improvement in Philippines (Tahir 90C, Binua 92C), Laos (Jayawong 93C) and Yemen (Yassin 93C). We would like to analyze these results when we get further replies.

Response to a request on the cost of SCC in Newsletter No. 8.

Dr. Muherman Harun (Indonesia, Control Course 1967)

The National TB Control Programme (1982-1992)

1. Short Course Chemotherapy with 6 month regimen: 1HRE/5H2R2 for sputum positive cases and
2. Long Course Chemotherapy with 12 month regimen: 1HSE/11H2S2 for sputum negative cases with Rontgenologic pulmonary lesions highly suggestive of active tuberculosis.

Updated National Anti-Tuberculosis Regimens (1994)

1. 2HRZE/4H3R3 for new cases with smear positive cases. The cost of this regimen is Rp92873 or US\$41.28 (regimen 2HRZE/4HR would cost Rp124047 or US\$55.13).
2. 2HRZSE/1HRZE/5H3R3E3 for relapse and failure smear positive cases. The cost is Rp172292 or US\$76.57.
3. 2HRZ/2H3R3 for new cases with smear AFB negative sputum with Rontgenologic pulmonary

lesions highly suggestive of active tuberculosis. The cost is Rp67934 or US\$30.19.

The drugs are generic drugs, provided in blister packs and aimed at patients of 15 years or older. The doses of the anti-tuberculosis drugs are fixed for all patients, presumably with a body weight between 33 and 50kg: INH 300; RMP 450; PZA 1500; EMB 750 and 8M 750mg.

Unit cost per 1000* in US\$

INH	100mg	4.3	PZA	500mg	56.9
INH	300mg	10.2	EM	500mg	55.8
RMP	300mg	154.5	SM	1000mg	206.0

* Price list of generic drugs 1994/1995, US\$1.00 = Rp2250

One Year after the Course

Mr. Somsak Rienthong (Thailand, Laboratory Course 1991)

The following is my progress report on the action plan I made at the end of the course.

Subject: Niacin Test to Identify M.tuberculosis by Microtiter Plate Method.

Material & Method

1. 476 strains of M.tuberculosis were isolated from sputum by sputum swab culture method (WHO Method) and cultured on L-J medium until growth appeared.
2. Extract niacin from L-J medium by adding 1-1.5ml of distilled water onto the media with confluent growth of bacilli.
3. Autoclave them and collect the extracted fluid for niacin test.

Niacin Test Method

Use microtiter plate of 96 wells (U-shape or Flat bottom shape) to compare with tube test (standard) method.

Microtiter Plate Method

Pipette 20 microtiters of the hot water extract, 10% cyanogen bromide and 4% aniline solution of equal volume in each well, mix and let stand for 5 minutes, and read the result. If yellow color shows, positive results.

Tube Test Method

Take 500 microtiters of the extract, 10% cyanogen bromide and 4% aniline solution in equal volume in test tube (12 x 100mm), mix well and let stand for 5 minutes and read the result. Pink or red precipitates show positive results.

The Result

Table 1. Number of strains which were niacin-positive by the microtiter plate method and the tube test method.

Number of Strains	Niacin Positive	
	Tube Test	Microtiter Plate Test
476	467	460

Table 2. Sensitivity, specificity, PPV and NPV value of Niacin test by microtiter plate method.

		Tube Test		
		+	-	
ELISA	+	460	0	460
	-	7	9	16
		467	9	476
Sensitivity = 98.7%		PPV = 100 %		
Specificity = 100 %		NPV = 54.5%		

Discussion

A new niacin test method using a microtiter plate was compared with the standard method using test tubes. Sensitivity and specificity by the new method were 98.7% and 100% respectively. Only seven strains of 476 strains tested were positive by the test tube method but negative by the plate method. Because the volume of hot-water extract in the well of the plate was 25 times less than in a test tube, the concentration of niacin in the extract was low, so the plate method may have given a false-negative result. If niacin were extracted with a smaller amount of water, say 0.5ml, instead of 1.0-1.5ml, the sensitivity of the new method might be improved.

Conclusion

- 1) Use the microtiter plate test for the screening of M.tuberculosis. If negative, test again by test tube for confirmation.
- 2) The microtiter plate method is a good modification for the Niacin test, saving the reagent and minimizing contact with toxic substances like cyanogen bromide and aniline.

DOT as a Way to Secure the Cure

Dr. Nobukatsu Ishikawa

DOT is currently used as a keyword to a successful TB programme. It is "Directly Observed Therapy", meaning originally 'each dose of medication is given under supervision or under a health worker's observation'. The concept of DOT has been developed mainly in the USA as a method of ensuring patient drug taking.

DOT Increases Cure Rate

DOT is a strengthened type of supervised therapy and its effectiveness has been demonstrated in many studies; namely DOT increases the cure rate. Only introducing SCC without a strengthened case-holding system is hazardous and creates many drug-resistant cases.

Basic Principles

The basic principles of a DOT programme are given as below by the American Lung Association:

The health care provider

- 1) observes the patients swallowing medicine,
- 2) offers incentives to encourage adherence,
- 3) establishes efficient clinical systems for scheduling appointments, keeping records, and providing pharmacy services,
- 4) works with a team to assist each patient in completing treatment,
- 5) provides effective education to patients and key people for the patients, and so on.

A successful DOT programme recommends that:

- 6) the staff must recognize DOT as their standard of care and convey this with confidence to patients,
- 7) the patient and care-provider must mutually agree on the time and location to be convenient,
- 8) sometimes the staff may designate another person to watch the patient take the medications; patient's family members are not recommended because of emotional ties, but other responsible persons in the community or work place can give DOT,
- 9) the staff needs to be trained to conduct DOT service as creatively and flexibly as possible according to the patient needs.

How Is DOT Possible ?

There are practical difficulties and obstacles in conducting DOT, particularly in many of the developing countries. Firstly, the service provider may need more staff members to look after each patient; obviously the patient has to visit a clinic or treatment place more frequently than before. Each country and area therefore needs to develop a most suitable method for using DOT according to its basic principles. Some countries have already shown a successful application.

From Bangladesh Experience

Currently in Bangladesh, DOT has been widely introduced to over 30 districts under World Bank and WHO assistance. After one year, most of the districts achieved the considerably high cure rate of nearly 80%. There were various methods in applying DOT.

For example:

- 1) one third of the patients came to a district hospital or a subcenter every day,
- 2) another one-third came to the hospital twice weekly and took home medicines for other days to be supervised by someone in the community,
- 3) the last one-third came to the hospital once a week and took home medicines for the other days to be supervised in the community.

The doctor in charge, the health worker and the patient decided the most convenient way.

DOT as a Goal

What was different in Bangladesh after DOT was used ?

First was the secure drug supply. Second was the motivation of the staff and patients through discussing the importance and responsibility for drug taking. The frequency of drug collection or hospital visit seems to be important. Weekly collection of medication at the hospital under the DOT scheme resulted in a much better cure rate than the previously used monthly drug collection. To conduct DOT in its strict sense is not easy, it is a useful strategy worth aiming toward.

DOT as National Policy

DOT is not possible by motivation alone. The government commitment to make it a national policy, securing the necessary drug supply and manpower is a prerequisite.

DOTS by WHO

WHO has currently taken DOT into their global strategy, based on the review of successful programmes in Tanzania, New York City, China and other areas. WHO strongly advocates DOTS (directly observed treatment, short course) as the most effective method to control TB by curing patients,

stopping the spread of the disease and preventing the multi-resistant TB. ('Stop TB at the Source' :WHO report on the tuberculosis epidemic, 1995)

Let us have further debate on the use of DOTS and gather experiences in making a global combat against TB successful.

Recommended reference:

- 1) WHO: Stop TB at the Source (see next page)
- 2) CDC (USA): Improving Patient Adherence to TB Treatment

*CDC, Division of TB Elimination
Atlanta, Georgia, USA
CDC Information Service
Fax: 1 (404) 332-4565*

OUR ACTIVITIES

Library

Our library's major objectives are:

To quickly and comprehensively collect information in the field of tuberculosis and related areas on a worldwide scale.

We have at present:

- Books (about 15,300 titles)
- Foreign journals (160 titles)
- Japanese journals (380 titles)
- Publications of WHO
- Reprints
- Conference proceedings



Four titles of literature searching (CD-ROM version);

- 1) MEDLINE; National Library of Medicine (OVID)
- 2) CURRENT CONTENTS; ISI -Life Science (OVID)
- 3) CURRENT CONTENTS; ISI -Clinical Medicine (OVID)
- 4) IGAKU-CHUOU-ZASSHI (ICHUSHI) CD-ROM.

To construct a database.

Since 1986, our library computerizes a large amount of information, using a personal computer for cataloging and classification.

In April 1994, RIT library was accepted for accessing the National Center for Scientific Information System, Cataloging System (NACSIS-CAT). It is operated by the Ministry of Education, and is a system for on-line shared cataloging. It produces a union catalog for the NACSIS-IR searching system and the NACSIS-ILL interlibrary loan system.

The NACSIS-CAT database consists of bibliographic records made from Japan/Marc and TRC-MARC and is created by member libraries. NACSIS-CAT is growing since the system started in 1984.

To provide users with services:

- Literature Searching Services: short searches may be run by course participants with the help of the library staff.
- References Services;
- Photocopying Services;
- Public Reading;
- Weekly Contents Sheet Services;
- Interlibrary Loan Services;

The library has been making efforts to learn various new technologies for advanced and effective information services to respond to its users' needs.

We hope all course participants will use the library, during their stay in Kiyose.

Ms. Yoshiko Kazami



Stop TB at the Source (WHO/TB/95.183)

Published by WHO
7 Swiss Franc per copy

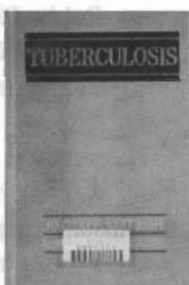
In the last Newsletter from Kiyose, we introduced "TB, a Global Emergency" by WHO. This year WHO has published "Stop TB at the Source" with its subtitle "WHO Report on the Tuberculosis Epidemic 1995". This edition includes little new information about the TB epidemic in the world but does include more practical methods to combat TB. DOTS is the directly observed treatment, short course. How to apply the idea of DOTS in each country. How to improve TB control with the tension and enthusiasm concerning the global burden and its unique solution - DOT. These WHO reports are good for advocacy and also call for enthusiasm for the combat.



Tuberculosis : Clinical Management and New Challenges

Edited by Milton D. Rossman, Rob Roy MacGregor McCraw-Hill, INC. Health Professions Division, 1995
hard cover, ISBN 0-07-053950-2

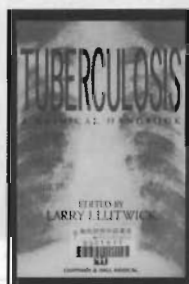
As was introduced in Newsletter from Kiyose No. 7, several books were published recently about TB, all written by several authors then edited. This book is very compact. As written in the preface this book is a "handy straightforward guide through all areas for the practicing physician wishing to be abreast of the newest information and most current recommendations regarding the diagnosis and management of this ageless foe of humanity".



Tuberculosis : A Clinical Handbook

Edited by Larry I. Lutwick
Chapman & Hall Medical (2-6 Boundary Row, London SE1 8HN, UK) 1995
378 pages, soft cover, ISBN 0-412-60740-9

Also listed here is this book for clinicians. For example, if you look at the details about specimen collection for extrapulmonary cases, you can understand that this book is very practical. It is a soft-covered book and easy to bring.



Tuberculosis : pathogenesis, protection and control

Edited by Barry R. Bloom
ASM Press (American Society for Microbiology, 1325 Massachusetts Avenue, N.W. Washington, DC 2005, USA) 1994
637 pages, hard cover, ISBN 1-55581-072-1

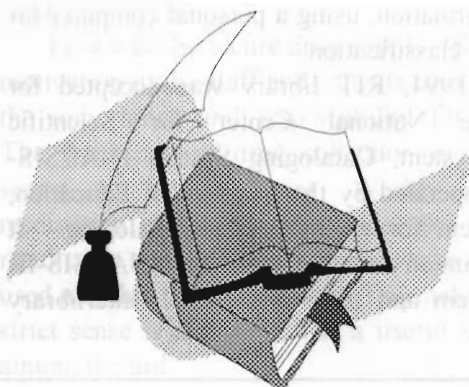
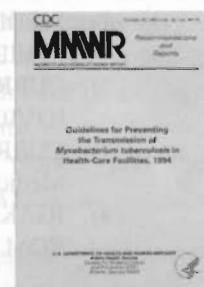
This is a comprehensive book mainly oriented to the basic science of tuberculosis. The main topics discussed are "Animal Models of Tuberculosis", "Generics of Mycobacterium Tuberculosis", "Physiology of Mycobacterium Tuberculosis", "Immunology and Pathology of Tuberculosis", "New Approaches to Prevention and Treatment of Tuberculosis" and the last topic includes molecular epidemiology and new drugs.



Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Facilities, 1994 (MMWR, Vol.43/No.RR-13)

U.S. Department of Health and Human Services, Public Health Services, CDC, Atlanta, Georgia

Since it is too advanced, this book may not be applicable to most developing countries. But it can be useful as a reference book to persons working in a central level of laboratory and research laboratory. Copies of the book can be purchased from: Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325. (202)783-3238.



JICA TB Project in Nepal

Dr. Ryoko Komatsu

The Kingdom of Nepal lies between two big countries, China and India. Its population is approximately 20 million, 52% of which is under 20 years old. The country has 5 regions and 75 districts.



At the Health Post

→ JICA conducted the Western Public Health Project from 1973 to 1985 in Pokhara, which is well known as a city with beautiful mountains and lakes. That project's main component was tuberculosis control, because TB was still a major public health problem in Nepal at that time. Based on that project JICA started the Nepal-Japan Technical Cooperation Project for the National Tuberculosis Programme in 1987. This Project was mainly aimed at establishing a responsible organization for NTP. In accordance with this purpose, the National Tuberculosis Center (NTC) in Thimi, Bhaktapur and Western Regional Tuberculosis Center (RTC) in Pokhara, Kaski were constructed by an aid grant from the Japanese Government in 1989.

→ Through this project, not only JICA experts but also concerned staff of HMG/N were trained at the RIT, Tokyo, Japan. Recently, staff members of international NGO's conducting the TB Project in rural Nepal also participated in the training course at RIT. In this sense the JICA TB Project in Nepal has been mostly operated by the RIT course participants.

This project terminated April 16th, 1994 and its main achievement was establishment of NTC as a top agency of the country with regard to tuberculosis control. It showed short course chemotherapy could be effective and feasible in the existing health care system in Nepal. According to these achievements, Project Phase II was started July 5th, 1994. Of the six experts engaged in this project, two medical

doctors from RIT, one laboratory technologist and one public health nurse were trained at RIT.

→ The new project has two major purposes. One is to improve the organizational and functional aspects of NTP through the PHC structure. The other is to improve the treatment results of tuberculosis cases in a model area in the Western Region so as to be duplicable in other districts. Thanks to the effort by Dr. Shimao and others, the Japanese Government has decided to donate anti-TB medicines to Nepal in order to ensure and assist the TB control activity. Furthermore, Drs. Aoki, Mori and Ishikawa are members of the domestic committee of the project and are supporting the project. In this way, many RIT doctors, laboratory technologists and Public Health Nurses are involved.

→ I would like to express my gratitude to all the helpful people who join with Nepalese people for improving the TB situation. We shouldn't miss this good opportunity and should give the priority to NTP. We of course face the various difficulties of a long decision-making process, a lack of budget, frequent transfer of counterparts, and political instability, etc. But we must be patient and flexible to adapt ourselves to whatever circumstance and keep our physical and mental condition well.

→ After finishing the baseline survey, we will try to confirm the will of the concerned staff and carefully keep in mind the government regulations and policy for carrying out the Project. Finally, I must report that a new training session has just started and SCC will be implemented in the Western Region from July 1995.

Namaste !



My Life in Cebu

Dr Masashi Suchi

Hello, how are all of you ex-participants? I graduated from the TB Control Course in 1985. Time goes fast. It is 10 years already. Within these 10 years, I have experienced so much in my private life and in my job as well.

I am now in Cebu, Philippines. I moved from Tokai University to RIT in 1992. Then I joined JICA Philippines Public Health Development Project as Chief Adviser. The project was started in September 1992. I have been working on the project from its beginning. This job is my second experience as a JICA long term expert, having worked at the Yemen Tuberculosis Control Project from 1986 to 1988 for two years and half. Cebu is very famous as a beach resort. Since these islands are just four hours by direct flight, many Japanese tourists vacation here. All of my friends are envious that Cebu is a nice place for marine sports and vacationing on a beautiful beach. I think so, too. However, I am not at the beach every day but am working for tuberculosis control in one of the world's epidemic countries. However, I enjoy the beautiful beach with my family on holidays specially when doctors of RIT visit our project.



My family attending the wedding ceremony

My biggest change in these 10 years is that I married and became the father of two daughters. Tokuko is four years old and Satoko is three. They speak mainly in Japanese but sometimes in English or Cebuano, the local language. We parents cannot understand their conversations with our home helpers. Anyhow, they are enjoying life in Cebu without any serious diseases except ascariasis. Many people speaks to us in the Cebuano language because we are sun-tanned very well. We call Tokuko TOKO. But TOKO in Cebuano means "a big lizard" which cries "Tokko, Tokko, Tokko.....". Every night, we are troubled with Toko's noisy cry.

We will go back to Japan in August. I do not know if this three-year period has been long or not. Anyway, Satoko will go back on her own feet. When she came to Cebu, she was just a baby held in my wife's arms. I hope to see you again somewhere.

Obituary

Her Imperial Highness Princess Chichibu passed away on 25th August 1995 at the age of 85.

Princess Chichibu had been the Patroness of the Japan Anti-TB Association for over a half century since its beginning in 1939.

An article regarding Princess Chichibu will appear in the next issue.

Letter from Dr. Fox

Dear Dr. Aoki,

I was very pleased to receive your Newsletter No. 8 April 1995.

Although retired I like to keep in touch with colleagues and groups with whom I had close contact.

The photos too are of particular interest since I sometimes forget a name but you provide a name and a photo and cover a number of people from a wide international group as well.

Princess Akishino has been of great interest world wide and I'm glad you have such an important Patroness.

My best greetings to the staff members who were always so helpful to me when I used to visit.

With my warmest regards to you and your colleagues,

Dr. Wallace Fox

Staff News

Welcome:

Mr. Ikuo Togawa (Head, Administration Dept.)
 Dr. Nobuyuki Harada (Chief, Biochemistry Div.)
 Mr. Hiroyuki Hisanaga (Chief, Administration Dept.)
 Mr. Yutaka Hoshino (Radiological Tech. Training Div.)
 Dr. K. Osuga (International Cooperation Dept.)

Farewell:

Mr. H. Ishii (Head, Administration Dept., retired)
 Ms. E. Tanaka (Administration Dept., retired)
 Ms. T. Kanashima (Administration Dept., retired)

Your news and voices are always welcome!

NEWSLETTER FROM KIYOSE

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