TB Control under Universal Health Coverage
The Experience of a Rapid Decline of TB in Post-war Japan

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The End TB strategy aims to dramatically reduce TB in order to achieve a TB free world. The milestones for 2025 are 75% reduction of TB deaths and 50% reduction of TB incidence compared with 2015. This means the annual decline of incidence should be 10% to reach the rate under 10/100,000 in 2025, and this can be possible with the maximized application of current service programs and back-ups by universal health coverage (UHC) and social protection.

TB control and UHC are complementary to each other. To accelerate ‘End TB’, UHC should be strengthened as a basis for wide and effective programme implementation. UHC is strengthened through the TB control programme as a good individual programme including all aspects of disease control and prevention.

Japan experienced a 10% decline of TB mortality and incidence after World War II when the country was still economically underdeveloped, which is worth analyzing and can be shared with current developing countries. The effect had multi-dimensional causes rather than being caused by any single factor.
Professor Takemi, Member of the House of Councilors of Japan, Gave a Lecture at RIT in the International TB Training Course

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Professor Keizo Takemi, Member of the House of Councilors of Japan, The Liberal Democratic Party’s Special Committee on International Health Strategy, Member of the UN’s High-Level Commission on Health Employment and Economic Growth, JCIE Chair, and the Global Health Working Group for the 2016 G7 Summit, gave a lecture at RIT on 6th June 2016 on JICA’s Knowledge Co-Creation Program: “Ending TB in the era of Universal Health Coverage,” which was conducted by RIT. This course was revised in 2016 and lectures covered not only TB control but also Universal Health Coverage (UHC). One of the main aims was to share the knowledge of Japan’s UHC. RIT asked Professor Takemi to give a lecture and he kindly accepted.

His lecture was about the background of achieving UHC in Japan and its international expansion. The lecture title was “Universal Health Coverage and Japan’s Experience” and included 2 topics: “Evidence-based policy making and goal setting” and “Lessons from Japan’s experience”. In the contents of “History of Public Health Insurance in Japan”, his explanation started from the “Health Insurance Law” of 1922 through the issues surrounding sustaining this insurance via achieving UHC in 1961. He used a variety of graphs depicting financial factors, population, life expectancy at birth, vital statistics and so on. In his lecture, he said that Japan’s achievement of UHC was based on a variety of factors like the National Health Insurance Law, economic growth, population growth, and disease control, among others. He summarised that UHC was part of a comprehensive policy package including economic growth and the establishment of a social safety net, contributing to income redistribution and the stabilization of society and politics.

He also insisted upon sustaining UHC. After achieving UHC, people face the difficulty of sustaining UHC. In Japan the stagnation of economic growth and aging of the population are key factors contributing to this difficulty. He showed that the aging population is not only in Japan but also in Asian countries such as South Korea, Singapore, Thailand, China and Sri Lanka. He taught that one of the solutions is increasing healthy elderly, and that Japan’s experience can be useful to other countries.

His lecture was very informative and helpful for understanding UHC in Japan. The course participants learned a lot.

He kindly agreed to release his lecture handouts on the RIT website. If you need more information please access the address below:
http://www.jata.or.jp/english/centre.html
TB-LAMP; A New Nucleic Acid Amplification Test for the Detection of Tuberculosis as a Point of Care Test

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TB-LAMP is a simple nucleic acid amplification system developed by Eiken Co. Ltd. in Japan in 2012. The amplification system is based on the LAMP (loop-mediated isothermal amplification) technique invented by Dr. Notomi in 2000. It is normally used in combination with the PURE (procedure for ultra-rapid extraction) nucleic acid extraction/purification system, and fully operated manually. It requires only a simple heating device and the electricity required is minimal. The final positive amplification result is indicated by fluorescent light under blue LED, and can be identified by the operator’s naked eye. The test can be operated using only 60 µl of purulent sputum directly, and it takes less than one hour to obtain the final result. TB-LAMP with PURE is the most simple and easy manual nucleic acid amplification test now available in the world.

When the operator wants to use the TB-LAMP test, the technician has to prepare the PURE kit, TB-LAMP kit, and LF-160 heating device. LF-160 can incubate the PURE sample tube and TB-LAMP reaction tube at 95 °C and 67 °C for 5 min and 40 min, respectively and automatically. The operator should take 60 µl of the purulent part of the sputum specimen directly using the exclusive and disposable micropipette (attached to the PURE kit), which is specially designed for easy handling of purulent and viscous sputum. The operator puts the specimen into the PURE heating tube directly and closes the cap. The PURE heating tube contains blue solution which can kill the TB bacilli and extract DNA during 5 min of incubation with LF-160. The bottom of the PURE heating tube has a screw-like shape and can be directly connected to the PURE absorbent tube, which can purify the DNA extract by mixing with absorbent powder in the tube. After mixing, the injection cap is connected to the bottom of the absorbent tube (which has a screw-like shape). When the operator squeezes the absorbent tube, the extracted DNA solution comes from the injection cap. Approximately 30 µl of the solution is directly put into the TB-LAMP reaction tube (there are two lines on the side of the tube to indicate the appropriate amount). The TB-LAMP tube contains dried reaction reagent inside the cap of the tube, and after closing the cap, the solution is mixed well with the reagent by inverting the tube. After two minutes of mixing, the solution is bottomed and the tube is incubated in LF-160 for 40 min at 67 °C automatically. After incubation, the tube is checked under blue LED light (attached to LF-160) for the development of green fluorescent light. If the operator recognizes green light, it shows a positive result, and indicates the existence of TB bacilli in the specimen.

The World Health Organisation has recently endorsed the TB-LAMP as a TB diagnostic kit and developed policy guidance. It says TB-LAMP is: rapid and requires less than one hour to perform, more sensitive than smear microscopy, may also be useful for differential diagnosis of NTM, does not require sophisticated instrumentation, and training is similar to the amount of training for smear microscopy. Now the Eiken company is taking orders, and the cost for one test will be around seven euros. Concessional prices for the public sector are available in 145 countries. TB-LAMP detects the presence of Mycobacterium tuberculosis complex (MTC), therefore it should not replace Xpert MTB/RIF, which simultaneously detects MTC and rifampicin resistance. TB-LAMP will become a plausible alternative in settings where Xpert MTB/RIF cannot be implemented. Then, TB-LAMP may be a replacement test for smear microscopy in settings with low prevalence of HIV and low prevalence of drug resistance. Unfortunately, it is still unclear whether TB-LAMP has additional diagnostic value over smear microscopy for the detection of TB in persons living with HIV. In addition, other specimen types (e.g. urine, serum, plasma, CSF or other body fluids) have not been adequately evaluated and therefore are not currently recommended for use with the assay. Like Xpert MTB/RIF, TB-LAMP is a nucleic acid amplification test, so the tests are not used for the follow-up of the TB patients in treatment. Adoption of the TB-LAMP test does not eliminate the need for sputum smear microscopy, which should still be used for monitoring treatment of TB patients.

The sensitivity of TB-LAMP in smear-positive/culture-positive and smear-negative/culture-positive specimens are 98.2% (95% CI 94.9–99.4) and 55.6% (95% CI 43.4–68.0), respectively. It is really clear that the sensitivity is more than smear microscopy examination. TB-LAMP has emerged as a real point of care test which will be able to work at peripheral settings even in developing countries. Extensive use of TB-LAMP for further detection of smear-negative presumptive TB cases will be expected with its high sensitivity.
What Brought about a 10% Annual Decline in Tuberculosis Notification in Japan?

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Japan experienced a 10% annual reduction in tuberculosis (TB) notifications from 1965 to 1978, such that the notification rates from 320.9 per 100,000 population level in 1965 went down to 70.0 in 1978 (Fig.1). It was one of the largest TB notification reductions globally (Fig.2). Why did this happen in Japan? What can we learn from this to accelerate TB notification reduction in the world?

As one of the first steps, we tried to brainstorm retrospectively what happened then and what kind of potential contributing factors existed among the RIT staff concerned. We gathered existing data through websites, books, and other documents, and interviewed key informants like Dr. Tadao Shimao, an advisor to JATA in 2016. The preliminary results were presented at the 41st UNION World Conference on Lung Health in Liverpool, UK in November 2016 as one of the 4 presentations at a workshop, “What brought about a 10 percent annual decline in TB incidence? Lessons learnt from Japan, Western Europe, and North America” [1].

Recognizing that it is fairly difficult to establish cause-and-effect relationships between the potential contributing factors and the steep TB notification reduction, we roughly described what happened then, focusing on 4 aspects, 1) TB control activities, 2) medical system infrastructures, 3) policy, law, and research, and 4) other factors such as the social welfare mechanism and human resource development.

TB control law was drastically modified in 1951, just 6 years after the end of World War II, stipulating that all infectious TB patients needed to be hospitalized. This law facilitated an increase in the number of admitted TB patients, backed-up by the rapid increase of TB beds nationwide. This may have prevented further TB transmission among close contacts during the era without strong chemotherapy. Mass vaccination with BCG was introduced in 1942 and financial assistance through a tax for annual health check-ups and BCG vaccination started in 1953. In combination with the introduction of freeze-dried BCG vaccine, BCG vaccination was applied quite extensively, e.g., all people under 30 years old were targeted for annual health check-ups with tuberculin skin testing (TST), and BCG vaccinated if TST negative until the middle of the 1970’s. Isoniazid Preventive Therapy (IPT) was also introduced nationwide in 1957, targeting children under 3 years old with recent TB infection. General practitioners were involved in the tuberculosis control system from the very beginning of the establishment of TB control in Japan, i.e., public-private mix has been one of the norms in Japan. Surgical interventions like selective thoracoplasty and artificial pneumothorax were extensively applied until the 1970’s before chemotherapy became the main mode of TB treatment. Chemotherapy, two drug combination of either SM, PAS, Tbl,
or INH in the early stage was introduced in the late 1940's, followed by three drug combination of SM, PAS and INH since the late 1950's. RFP combination regimen was introduced in the 1970's and expanded nationwide in the 1980's.

The TB control law enacted in 1951 has been frequently revised in response to the advance in TB diagnosis, treatment, and research such as nationwide TB prevalence surveys. This law provided a framework of TB control nationwide. As a result of the application of this law, with the approval of a TB advisory committee at public health centers, a public subsidy was given to medical facilities where physicians made TB diagnosis. So, the public subsidy on TB diagnosis and treatment would not be paid to medical facilities without the approval of the TB advisory committee. This mechanism has worked as a kind of quality assurance mechanism for TB diagnosis and treatment. The national health insurance system was established in 1961 in parallel with the establishment of the TB control law that stipulated full coverage of the medical expense of the admission fee for TB patients in hospital. This meant that virtually no out-of-pocket payment (OOP) was made, at least for the admission fee, starting in 1951.

As one of the social security mechanisms, an allowance for the sick and wounded that compensated two-thirds amount of the salary during sick leave for a period of 1.5 years, helped TB patients financially beginning in 1948. In addition, public assistance started in 1950 to provide assistance to cover minimum living requirements for people in economic difficulty.

JATA has been playing a very important role in TB human resource development in Japan. JATA started training courses for nurses and radiological technologists in 1946 followed by those for physicians from 1948. These training courses have been continuing until the present day, ever since the national government started providing funding to JATA in order to conduct the TB training courses.

In summary, our senior TB experts implemented all possible interventions at that time, through engaging all health care providers to combat this extremely serious health hazard, TB, in concert with a kind of quality assurance mechanism for TB diagnosis and patient care with minimum OOP. Human resource development has been reinforced through persistent running of the training courses. Finally, they were very eager to conduct researches to invent new tools to tackle TB, such as freeze-dried BCG, and to conduct TB prevalence surveys for seeking better TB control. All of the above-mentioned factors may have contributed to the rapid reduction of TB notification in Japan.

[References]

Voices from RIT Alumni

The First RIT Course Student

Thavisakdi Bamrungrakul
President, The Anti-Tuberculosis Association of Thailand
(1963 TB Control)

It is an honor to be invited to write a few sentences on the TB Control International Course at RIT. I was among the first RIT TB Control students in 1963. I can say that I learned not only basic TB control but also some Japanese culture and traditions. I have met world class TB experts that RIT invited as guest speakers. It did inspire me very much to work with determination on TB control in Thailand after coming back to Thailand. I was a TB manager in Thailand for many years and after my retirement as a government officer (TB Control Director, MOPH), I had been working with The Anti-Tuberculosis Association of Thailand and am currently working as the President of this association. For me, this course was very useful for building basic knowledge in TB control both in terms of epidemiology and case management. It should be continued for the benefit of doctors who work in TB control.

Dr Thavisakdi (center, back row)
It has been an honor to be invited as a facilitator while working as an associate researcher in the National Center for TB Control and Prevention, China CDC, Beijing, China. I participated in the training course “Stop TB Action Training Course” in 2012. The training course was not only a good chance to learn TB control knowledge, but also an exchange platform in which we had much time to communicate with others from different countries and learn about their different cultures. At the end of the training course, everyone had become good friends, and it was like a warm family. And, I still keep in contact with some participants.

After the course, I made some contributions to TB control in China, and some research results were published in international journals. The research focused on TB spatial clustering distribution and TB infection control, which was one part of my daily work. I think that’s why the RIT team invited me as a facilitator this year. And I was proud to have my role shift from a participant to a facilitator.

As a facilitator, I liked to share our experiences of TB control in China with other participants. I felt so happy if our experience could be used to help other countries to stop the TB epidemic. There are two things in particular that I gained through my training course in 2012, which are used in my daily work as well. Firstly, the knowledge and skills in project management was one useful way of thinking to find the key problems and solutions in our daily work. Second, the writing course helped me very much in writing the manuscript and publication. These two points were used in my daily work and I unreservedly shared the experience with the participants in 2016. I hope the experience can help them to inspire their daily work and make a big contribution.

I spent a very good time with other participants, sharing the experience of my daily work and knowledge from the previous course. It was a short 3 days as a facilitator. However, it was a good platform that the RIT team gave a chance to communicate with other participants and reported my work to the teachers in RIT. I would like to extend my gratitude to RIT and JICA for affording me this visit and extending continued warm hospitality. I will do my best to use the knowledge and skills that I gained from the course in my daily work and make more contributions to TB control.
Learning comes in different forms which can be from the academy, life’s teaching, through self-discovery or from wisdom of another individual. Learning is a never-ending process from the moment you are born until the day you cease to exist. People evolve through time as they acquire additional knowledge and how they apply what they have learned, not minding the risk and eventual effects of it if only you are brave enough to get out of your so-called “comfort zone”.

Typically, I was living within my “comfort zone”, confined in a four-cornered biocontainment all my life, doing tests, and final diagnosis which have given me contentment and satisfaction. That was my routine. That was me.

However, the training course in Tuberculosis Laboratory Management for Achievement of MDG’s was a step forward in my professional career as it has educated me on the global fight against tuberculosis employing various state of the art technologies and research and development on top of the conventional method which is still the gold standard in its detection. My passion for TB has increased because it has provided me different insights on how the TB program is being implemented from third world countries to more progressive countries during interactions with my co-participants from this training.

Apart from the technical aspects of the training, I have developed friendship with my co-participants and sensei. I have learned so much about their cultures and traditions. Together we explored and discovered the wonders of Japan. Our sensei have taught us the culture, tradition, norms and language of Japan during our sessions. We were even blooming all over the city. We really enjoyed a good life there with participants from many different cultures. We played football, ran, learned how to cook, how to separate garbage, and took turns cleaning and using our shared kitchen.

I am encouraging those who may have the opportunity to attend similar trainings abroad to enjoy the place, appreciate its culture, collect memories and take thousands of pictures which you will be taking home with you to cherish and to hold. Nobody can ever take these away from you.

It was my great opportunity to get a chance to join the course “Ending TB in the Era of Universal Health Coverage 2016” which was funded by JICA and organized by RIT. Many activities conducted during this course, including workshops, group discussions, presentations, tutoring sessions, etc., trained us how to analyze problems and perform “think-do-present” operational research. We gained presentation skills, and also improved our speaking and listening in various situations. We are now confident to stand in front of the class discussing or sharing our opinions. We learned to accept the differences between each of us. It was a good chance to broaden our minds when we shared experiences with participants from various countries.

The unforgettable field trip to Osaka, Airin area was an impressive experience which demonstrated the real difficult situation of how to work with TB patients there. It also showed the great effort of all staffs trying to help homeless people and TB patients as much as they can. We also visited the comprehensive medical examination center at Osaka Anti-tuberculosis Association. We got a chance to learn about many tests for health during the visit.

Other than the knowledge we gained, we all had the great honor and the highest privilege to meet Her Imperial Highness Princess Akishino, patroness of JATA. I believe that it was a very special and remarkable moment for all of us.

During the 2-month period, we stayed at RIT in Kiyose city, which is a peaceful city with lots of trees, and the weather was great. When the course started, beautiful Hydrangeas were blooming all over the city. We really enjoyed a good life there with participants from many different cultures. We played football, ran, learned how to cook, how to separate garbage, and took turns cleaning and using our shared kitchen. Finally, we formed really good friendships. We were also taken really good care of by a Japanese mama, Takarai san, who always helped us during our stay. I appreciated all of those valuable and unforgettable moments. What a memorable time for all of us.

We all appreciated and realized how dedicated the people around us were. They all played a vital role in assisting and supporting us to complete the course successfully.

I would like to extend my deep gratitude to all the people involved for their kind dedication, for the time we’ve shared, and for the good friendship we made. I am certain that all of these things will help us to forge our future path in our countries.

We promise to do our best. Given all the effort and many lessons learned, I am confident that all participants will make valuable contributions to their own countries. Thank you very much once again.
Japan Anti-Tuberculosis Association is going to host the 6th Conference of International Union Against Tuberculosis and Lung Disease Asia Pacific Region, which will be held during the season of Beautiful Spring in conjunction with World TB Day, March 22–25, 2017 at Tokyo International Forum.

The theme of this conference is “TB Free Asia Pacific – Accelerate. Steps toward Healthier Lungs”, which is in accordance with the End TB strategy. It should also impact lung health issues other than TB. Furthermore, the new strategy, in line with universal health coverage, will significantly benefit health services in general.

The recent changes in the clinical and epidemiological picture of TB and other lung diseases have been remarkable; i.e., rapid aging of TB patients, socioeconomically marginalized people, increasing attention to TB in children, claims for wider use of advanced technologies, and the tobacco problem as a basic human rights issue.

Themes of the plenaries and lectures are as follows:

- Contribution of Japan in global tuberculosis control
- Post-2015 Global strategy in WPRO
- Prevalence survey
- Research agenda in TB
- Inmate immunity
- TB/HIV issues in Asia
- Addressing social determinants

A total of 18 symposia with regard to the following issues are scheduled:

Components of current strategy

- TB Surveillance
- MDR TB: Epidemiology/Management
- Pediatric TB: Epidemiology & Prevention
- Progress in universal health coverage in Asia Pacific countries
- Patient-centered TB care and support
- Ensuring TB control policy: legislation/political commitment

- Asia Pacific’s women’s group activity (open to the public)
- Pharmacovigilance and side effect management
- TB case finding in high-risk people
- TB prevention and care for immigrants in the Asia Pacific Region
- Strengthening contact investigation
- LTBI treatment: Expectations and feasibility
- Place of IGRA in TB control
- TB in elderly and immune compromised host
- Current status on development of new technology
- Perspectives in TB vaccine
- Current status of molecular epidemiology in Asia
- New drugs, New treatment
- Enhancing TB diagnostics (together with Japanese Society for Tuberculosis)
- Host factor, genetics and biomarkers

There will be several sessions other than TB: smoking cessation, threat of pandemic of viral infections, COPD/Rehabilitation, lung cancer, pulmonary fibrosis, pneumonia, NTM and asthma.

There will be workshops on health ethics, programmatic management of MDRTB, TB diagnostic network strengthening and Modeling TB Transmission.

The Post-graduate course will be on writing scientific papers, use of literature databases and Cochrane collaboration and introduction to Molecular epidemiology of TB.

It is expected that there will be some satellite sessions. Visit the web site and register for APRC2017 http://www.aprc2017.jp/

We would expect a lot of alumni members of the international training courses of RIT not only from Asia Pacific Region but also other regions of the world.