The Third Nikkei Asian Conference on Communicable Disease
Tokyo Communicable Diseases Statement 2016

Introduction

As economic globalization advances, Japan is becoming inextricably linked at all levels—including the economic, social, and cultural—with the rest of the world, and most particularly with Asia. As is clear from the emergence of the Zika virus, a new outbreak of the Ebola virus, and global multidrug-resistant (MDR) communicable disease epidemics, the threat posed by our health by communicable diseases has moved to the foreground as a major issue both domestically and abroad. At the Kyushu Okinawa Summit held in July 2007, Japan launched the Okinawa Infectious Diseases Initiative, calling for global partnership in the fight against communicable diseases. The first Nikkei Asian Conference on Communicable Disease (NACCD) in 2014 as well as the second Conference in 2015, were also held in Okinawa, and on April 22–23, 2016, key figures working in the area of communicable diseases in the public and private sectors as well as government and academia gathered from more than 10 countries to take part in the Third Nikkei Asian Conference in Tokyo. Participants reaffirmed the necessity and the efficacy of addressing health-threatening communicable diseases through public-private partnership (P3).

The conference also confirmed progress with and issues arising from (1) a P3 initiative for packaging and disseminating Japanese medicines and diagnostic tools to Asia that was proposed by the Tuberculosis Working Group under the Asian Medical Innovation Consortium (AMIC) formed at the recommendation of the Second NACCD held in January last year, and (2) Ebola countermeasures being pursued in Guinea, West Africa that again package Japanese medicines and diagnostic tools. Participants also discussed possibilities for new P3-based action on communicable diseases using Japanese technologies and services, and agreed on The Third Nikkei Asian Conference on Communicable Disease: Tokyo Communicable Diseases Statement 2016. Combating MDR communicable diseases is also slated for discussion at the G7 Ise-Shima Summit next month, with concern over communicable diseases growing. The Tokyo Communicable Diseases Statement will be widely communicated not only in Japan but throughout Asia and the rest of the world. Leveraging the deeper international understanding achieved accordingly, it will be incumbent upon Japan to demonstrate even stronger commitment to the international community through measures to combat communicable diseases.

I. Report on Progress with Japan's P3 Communicable Disease Programs since the Second NACCD

Last year, a draft P3 MDR tuberculosis initiative developed through deliberations at the AMIC Tuberculosis Working Group was presented to the Prime Minister's Office and the relevant government ministries and agencies. A P3 program is also underway in Japan in relation to the Ebola virus as discussed at the Second NACCD. Progress with and issues arising from these two initiatives were reported as follows.

Tuberculosis

1. AMIC Tuberculosis Working Group P3 Initiative: Proposal made to Prime Minister's Office

A P3 MDR tuberculosis (MDR-TB) initiative was proposed at the AMIC Tuberculosis Working Group for providing MDR tubercular bacteria diagnostic tools and medicines as a package, engaging in empirical research in those Asian countries with tuberculosis incidence, and assisting them in eliminating tuberculosis. The plan was to implement the initiative on the basis of close partnership among the Japanese government; the governments, medical institutions and universities of the targeted Asian countries; and Japanese private enterprises, medical institutions such as the Japan Anti-Tuberculosis Association, and universities.

More specifically, with assistance from the Japanese government and the cooperation of the targeted Asian countries, tubercular patients would be screened using a simple, high-precision genetic test (TB-LAMP, Eiken Chemical Co.) in place of a sputum examination using a microscope, boosting the diagnostic rate for tubercular patients. A MDR genetic test (Genoscholar, Nipro Corporation) would then be used to produce a definite diagnosis of MDR-TB. In accordance with these diagnoses, the first new MDR-TB drug to be approved in Japan and Europe in 40 years (delamanid, Otsuka Pharmaceutical Co., Ltd.) would be prescribed as appropriate to boost the curative effect and reduce the occurrence of MDR bacteria, helping to control MDR-TB in the targeted countries.

2. Progress since Proposal to the Prime Minister's Office

Since appealing to the Prime Minister's Office and the relevant government ministries and agencies, P3 projects have begun at various levels.

In Afghanistan, where the most progress has been made, TB-LAMP is already in use, and arrangements are currently being made to have Genoscholar included within the scope of government procurement. As of FY2016, TB-LAMP, Genoscholar and delamanid will be utilized in Phase 3 (2015–2018) of the Tuberculosis Control Project, a technical cooperation project between the Japan International Cooperation Agency (JICA) and Afghanistan. As a new drug, delamanid is currently going through Afghanistan's drug approval process. As part of grant aid for Afghanistan, Japan also implemented the Project for the Supply of Anti-TB Medicines and Laboratory Consumables and the Development of Drug Management Systems in Afghanistan over November 2014–
May 2015 and built the Afghan-Japan Communicable Disease Hospital (completed in August 2013). Further work will be implemented in conjunction with these two existing initiatives.

In the Philippines, a program for the dissemination of a new TB diagnostic algorithm based on Japanese technologies (TB-LAMP and Genoscholar) that was adopted in February 2016 has now been launched as a JICA Collaboration Program with the Private Sector for Disseminating Japanese Technologies. JICA is in the process of dispatching healthcare policy advisors to the Philippines, and consultations were held on January 21, 2016 between the Philippines' Undersecretary of Health and the local Japanese embassy and JICA office. The next stage will entail considerations on the provision of delamanid, etc. On February 29, 2016, a joint public-private field survey was conducted by Japan's Ministry of Health, Labour and Welfare (MHLW),

JICA, Otsuka Pharmaceutical, Nipro, Eiken Chemical, and the Japan Anti-Tuberculosis Association, with project preparations moving forward.

In Indonesia too, two JICA Collaboration Programs with the Private Sector for Disseminating Japanese Technologies are currently underway: one promoting the dissemination of a system supporting the medication compliance of tubercular patients (delamanid), adopted in July 2015, and the other promoting the dissemination of tuberculosis diagnosis kits (Genoscholar), adopted the same month.

In Myanmar, consultations have begun on the use of delamanid, TB-LAMP, and Genoscholar, etc., while Japan is also looking at introducing these technologies into Vietnam and other countries.

In addition, Japan has begun exploring collaboration with the United States Agency for International Development (USAID), which is also combatting tuberculosis through P3 programs.

Ebola

1. Ebola Plan since the Second NACCD

Following the Ebola outbreak in West Africa in 2014, a three-year project funded by a MHLW scientific research grant was launched on novel strains of influenza and other emerging and re-emerging communicable diseases at St Luke's International University as of FY2014. Upon receiving a request for assistance from the government of affected Guinea and a joint research request from the French National Institute of Health and Medical Research (INSERM), Japan immediately launched its first P3 project.

The project entails supplying LAMP-based diagnostic drugs and tools developed in Japan for the Ebola virus (RT-LAMP, developed by Toshiba Medical Systems Corporation and Nagasaki University) and conducting empirical tests in Guinea, as well as engaging in clinical research on the efficacy of Favipiravir (Fujifilm Holdings Corporation, Toyama Chemical Co., Ltd.), an influenza drug with a new mechanism of action, in treating Ebola. Favipiravir is an inhibitor of RNA polymerase that is necessary for RNA virus proliferation, and it was hoped that it would also be efficacious against Ebola. However, adding this new indication required adjusting the actual dosage and demonstrating the drug's efficacy.

2. Progress since the Second NACCD

In December 2014, a proof-of-concept experiment (the JIKI clinical trial) was conducted with the cooperation of INSERM, NGOs such as Médecins Sans Frontières, and the Guinean government in order to plan clinical research demonstrating the efficacy and safety of Favipiravir in treating Ebola. The outcome of the JIKI trial, which analyzed the results of treating 126 patients with the drug, was ultimately published in the March 1, 2016 issue of PLOS Medicine. Important information was gleaned in terms of planning further clinical trials, such as that the drug should be given to moderately rather than seriously infected patients, and that the frequency of kidney damage and the amount of Ebola virus found in the bloodstream can be used as prognostic biomarkers.

On the diagnostic front, in April 2015, in response to a request from the Guinean government, RT-LAMP, 3,000 specimens, and three diagnostic devices were passed on to Guinea via Japan's Ministry of Foreign Affairs. A research team funded by an MHLW scientific research grant sent personnel out to Guinea to implement a human resource development (HRD) program in relation to RT-LAMP diagnostics and examinations.

Based on these P3 results, on October 5, 2015, the French Prime Minister, who was in Japan at the time, signed a Collaborative Agreement to Enhance R&D on Ebola Virus Diseases (EVD) with St. Luke's International University President Tsuguya Fukui in the Prime Minister's Office, widening the scope of activity to pursue joint research on combating Ebola, cooperation in the comprehensive analysis of results, and joint empirical research and HRD cooperation on communicable disease countermeasures in Africa. Data from the JIKI trial is currently being analyzed, while research is underway on the pharmacokinetics of Favipiravir and the according optimal prescription, with the results progressively reflected in JIKI trial follow-up research. Research using animal models has now also begun toward developing an injectable solution and identifying the optimal combined therapy.

Kyowa Hakko Kirin Co., Ltd., which was part of the MHLW scientific grant research team, is conducting screening research on antibodies neutralizing Ebola, while Toray Industries is developing infection-protective garments, etc., and conducting empirical research in Guinea.

II. New Challenges and Solutions to Them

Discussion at the Third NACCD revealed challenges that should be addressed toward further enhancing and expanding P3.

Tuberculosis

Closer partnership is required in supplying the targeted countries with TB-LAMP, Genoscholar and delamanid as an MDR-TB package. Delivery of this MDR-TB package has been imperfect under Japan's current assistance regime, and more public-private partnership and coordination are needed. The AMIC Tuberculosis Working Group must pursuer close public-private information exchange and cooperation. Consideration also needs to be given to expanding the scope of those countries (four at present) targeted by P3 programs. HRD assistance should be given in countries where empirical experiments are conducted, as well as assistance in developing guidelines for the treatment of communicable diseases.

Efforts should be made to have the results of empirical experiments published in academic journals, etc., deepen the understanding of international institutions, and have information garnered from research results listed in WHO recommendations and treatment guidelines. Lobbying needs to be strengthened towards those international institutions handling procurement in order to have TB-LAMP, Genoscholar, and delamanid supplied to TB high-burden countries.

At the same time, the relevant Japanese companies should work harder to reduce costs in order to supply products to developing countries at a cheaper price. They must also not neglect to develop

drug resistance diagnostics for more drugs and MDR-TB drugs with new mechanisms of action. The Japanese government should also examine ways to assist this R&D.

Ebola

Clinical trials on RT-LAMP need to be properly concluded, information based on the results of that research supplied to the WHO and other relevant institutions in Japan and abroad, and consideration given to having the information listed in Ebola guidelines, deploying diagnostic devices and stockpiling diagnostic agents to deal with further outbreaks.

Information on Favipiravir needs to be provided in Japan and overseas, including analysis of the data from the JIKI trial and follow-up research results. Based on the JIKI trial results a plan should be drawn up for clinical trials that prove the efficacy and safety of Favipiravir. An injection form should also be developed premised on hospital treatment, and the effects in terms of preventing Ebola infection demonstrated using animal models. Based on that clinical research and experiment results, consideration must be given to emergency use when outbreaks occur and to clinical trials on adding a new Ebola indication. In terms of immediate tasks, the Guinean government has requested that the drug be provided to address the new Ebola outbreak which began in March.

Internationally, biodefense and counter bio-terrorism responses are being deployed to deal with highly-virulent viruses. The Japanese government should recognize the importance of having the means to protect the country and discuss the establishment of national stockpiles, etc., while also bearing in mind the possible spread of such viruses to Asian countries.

Other

Communicable diseases were discussed at last year's G7, and are also on the agenda for this year's Ise-Shima Summit. Last year, antimicrobial resistance (AMR) was addressed as an area of growing international concern, and in April 2016, the Japanese government too released an AMR Action Plan. AMR therefore needs to be added to items for discussion at the next NAACD.

P3

Based on deliberations at the Third NACCD, the following steps need to be actioned in order to further enhance P3 on communicable diseases.

A. Begin preparations for the establishment of a new clinical research center in Asia, taking into consideration cultural and ethical aspects.
B. Look at enhancing the development of human resources able to operate at overseas clinical research centers for communicable diseases, and at partnership with PMDA.
C. Build a drug and diagnostic agent approval system for Japan in conjunction with other Asian countries and expedite investigations for approval of new indications.
D. Promote the development of human resources able to share information and negotiate with international institutions such as the WHO, the Global Fund and Gavi, the Vaccine Alliance.
E. Enhance and expand communicable disease research hubs in Japan.
F. Develop long-term P3 mechanisms.

G. Promote the establishment of venture businesses that will accelerate the commercialization of medical innovations.
H. Strengthen partnerships with the WHO and other UN and international institutions (assistance for listing in recommendations and treatment guidelines).
I. Strengthen partnership with NGOs (promoting empirical experiments, etc.)
J. Develop innovative and ongoing fund procurement mechanisms.
K. Further develop commodity procurement mechanisms, including stockpiling.
L. Use Japan's experience to assist in enhancing medical and public hygiene systems, communicable disease countermeasures and surveillance included (universal health coverage).
M. Promote participation in P3 by companies from other areas such as logistics and ICT that will contribute to combating communicable diseases.
N. Strengthen collaboration with the government's Conference for Government-Private Sector Partnership on Combating Communicable Diseases in Developing Countries.

New Technology Seeds

New seed-level technologies developed in Japan with the potential to contribute to combating communicable diseases in Asia were announced at the Third NACCD, attracting expressions of strong expectation from other Asian countries. The technologies will now need to be carefully evaluated, companies and institutions invited to participate in consortia for promoting communicable disease countermeasures, and considerations undertaken toward drawing up these projects as new P3 initiatives.

A. A new hepatitis vaccine and a new influenza vaccine based on a vaccinia virus vector (Tokyo Metropolitan Institute of Medical Science)
B. A malaria diagnostic device (Sysmex Corporation), malaria vaccine (Osaka University) and treatment drug (Eisai Co., Ltd.)
C. Drugs treating infections caused by multi drug resistant (MDR) bacteria (Shionogi & Co., Ltd.), vaccines treating and preventing the occurrence of the same (Daiichi-Sanko Co., Ltd.)
D. Tuberculosis vaccine (National Institutes of Biomedical Innovation, Health and Nutrition)
E. New indications for Favipiravir beyond Ebola (Toyama University, Fujifilm Holdings Corporation, Toyama Chemical Co., Ltd.)
F. Technologies and services for combating communicable diseases, refrigerators, logistics, sterilization services, ICT, etc.

Subsequent progress with the above technologies will be reported as appropriate at the Fourth Nikkei Asian Conference on Communicable Disease.

III. Conclusion

The Third Nikkei Asian Conference on Communicable Disease affirmed that concrete results are beginning to emerge from P3 initiatives combating communicable diseases. It was confirmed that initiatives have been formed for addressing MDR-TB and Ebola, with concrete steps beginning to be taken, and results emerging in some areas. Participants also affirmed that a diverse range of seed-level technologies contributing to combating communicable disease in Asia are being developed by Japanese companies and research institutes.

At the same time, there are still many issues to address in further developing P3 initiatives. HRD and building networks among the various stakeholders in and beyond Japan are particularly pressing tasks.

On April 21, 2016, the Japanese government launched the Conference for Government-Private Sector Partnership on Combating Communicable Diseases in Developing Countries, comprising representatives from the relevant ministries and agencies, private firms and related associations, etc. The aim is for the public and private sectors to work together to contribute to international efforts to combat communicable disease, with the Conference to develop specific policies for deploying Japanese innovations in developing countries.

In relation to the strategies agreed at the Third NACCD, proposals need to be presented to the above Conference particularly on themes that require a national-level approach to finding solutions.

Regarding the NACCD, it would be important for AMIC, which was established by the Second NACCD, to provide ongoing and progressive assistance to P3 initiatives, and for NACCD to engage in further efforts in conjunction with government initiatives such as the above. They further agreed on the need to hold a Fourth Nikkei Asian Conference on Communicable Disease.