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Priority Research and Development Area for Emerging/Reemerging Infectious Disease Control—An Expert Questionnaire Survey in Japan

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Abstract

Since long, Japan has addressed infectious disease control through regulatory and scientific frameworks. Due partly to the outbreaks of H1N1 pandemic (2009) and Ebola virus disease (2014), Japan has tried to strengthen research and development (R&D), focusing on emerging/reemerging infectious diseases through “The Healthcare Policy”. In order to contribute to such a national strategy, the Science and Technology Foresight Center of the National Institute of Science and Technology Policy conducted an expert questionnaire survey on the direction of R&D for emerging/reemerging infectious disease control in September 2014. The survey revealed that among experts, R&D for emerging/reemerging infectious disease control is considered to be very important but vulnerable to tough international competition. Moreover, topics that should receive priority included those related to HIV/AIDS, drug-resistant infections, and influenza. Finally, it was suggested that recent information technology (IT) development such as big data analytics had potential for being applied to the emerging/reemerging infectious disease field. Although the survey has several limitations, such results may contribute to designing and supporting a setting of concrete R&D programs in Japan and other countries.

1. Introduction

Emerging/reemerging infectious diseases have become a major global public health concern, exemplified by the 2009 pandemic H1N1 influenza, the outbreaks of Ebola virus disease in 2014, and a multidrug-resistant tuberculosis epidemic. In Japan, dengue fever has become problematic for the first time for more than 60 years. Brown [1] and Woodworth et al. [2] reported that emerging infectious diseases have been occurring at an unprecedented rate of one or more per year in human populations since the 1970s. Given this situation, Japan has since long addressed emerging/reemerging infectious disease control through regulatory and scientific frameworks, consisting of legislation, such as the “Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients with Infections” (the Infectious Diseases Control Law: Law No. 114, latest amendment: Law No. 115, 2014), and various research and development (R&D) programs [3]. Additionally, Japan has enhanced its international contribution to

infectious disease control by, for instance, developing the Japan Initiative for Global Research Network on Infectious Diseases (J-GRID), launched by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) in 2010. In this network, ten Japanese research institutions have established nine collaborative Research Centers in nine Asian and African countries, where Japanese researchers are stationed, performing collaborative research [4].

Since 2014, the Japanese government has tried to strengthen healthcare R&D programs through the “Healthcare Policy” (stipulated by the Cabinet on July 22, 2014), which is a new national 5-year healthcare strategy (foreseeing the next 10 years) that includes emerging/reemerging infectious diseases [5]. The goal of the policy is to realize the most advanced medical technologies and services as a pioneer challenge solver and further extend the health expectancy as an ultra-aging society ahead of other

countries. In order to management R&D in this strategy, the Japanese government launched the Japan Agency for Medical Research and Development (AMED) on April 1, 2015 [6].

Under the “Healthcare Policy”, emerging/reemerging infectious diseases have been considered as one of the priority disease areas [7]. AMED has managed R&D to develop therapeutic drugs, diagnostic tests, and vaccines based on key performance indicators (KPIs) in 2015, 2020 and 2030 (Figure 1). In view of the KPIs, around 2020, R&D will focus on the development of drugs and diagnostic methods against influenza, dengue fever, diarrheal diseases, and drug-resistant bacterial infections. Japan sustained an outbreak of dengue fever in 2014; such an outbreak had not been reported for more than 60 years in the country. Such reemerging infectious disease and possible emerging infectious diseases have been targeted under the “Healthcare Policy” in Japan.

Key performance indicators to be achieved by around 2020

- Identify drug target sites based on whole-genome databases obtained for pathogens (influenza, dengue fever, infectious diarrhea, drug-resistant bacteria) and develop and put new rapid diagnosis methods into practical application
- Conduct non-clinical and clinical trials of a norovirus vaccine and a nasal influenza vaccine, and apply for pharmaceutical approval for these

Key performance indicators to be achieved by 2030

- Develop new vaccines (E.g. versatile influenza vaccines)
- Develop new antibiotics and antivirals, etc.
- Eradicate/eliminate infectious diseases such as polio and measles, working in partnership with the WHO and various other countries

Key performance indicators to be achieved by 2050 in the case of tuberculosis

- Eradicate/eliminate tuberculosis, working in partnership with the WHO and various other countries

Figure 1. Key performance indicators related to emerging/reemerging infectious disease control of the “Healthcare Policy”.

In order to contribute to such a national strategy, the Science and Technology Foresight Center of the National Institute of Science and Technology Policy (STFC) conducted an expert questionnaire survey in September 2014. In the survey, R&D priority area for emerging/reemerging infectious disease control was demonstrated from the perspective of experts. This paper discusses the result of survey. I hope this paper provides valuable information to design concrete R&D programs for not only in Japan but other countries.

2. Materials & Methods

2.1. Background of the Expert Questionnaire Survey

Questionnaire surveys are useful for involving people who may not be able to meet, provide some anonymity for individual responders, and avoid the social pressure that can exist within groups to confirm [8]. For the purpose of contributing to policy making processes in science and

technology, STFC has taken advantage of such characteristics in the questionnaire survey. STFC has collected the opinion of a large number of experts by the questionnaire survey for more than 40 years [9].

2.2. Setting up Survey Questions by an Expert Panel

STFC organized an expert panel for setting up survey questions about emerging/reemerging infectious disease control. The expert panel comprised eleven Japanese individuals and they were mainly invited from universities and national institutes in Japan. Referring to the KPIs of the “Healthcare Policy”, the expert panel extracted R&D topics that were considered to be key technologies and to be important in 2020 to 2050 in Japan. The R&D topics were thoroughly based on the expert judgement of the panel, because key technologies in the coming three decades could not be grasped in a rigorous manner. Additionally the topics were set up under assumption of an extension of current

national R&D programs.

Subsequently the expert panel established survey items for each R&D topic, considering R&D characteristics.

2.3. Conducting Web-based Expert Questionnaire Survey

In order to collect responses rapidly and analyze a large number of responses, a web-based expert questionnaire survey about the R&D topics was conducted. Candidates who would join the questionnaire survey were listed based on recommendations from the expert panel. Criteria for expert recommendations were that the person had knowledge of infectious diseases or could supervise research and development in not only biomedical field but also others. The reason why such supervisors were also selected was that they could judge recent transdisciplinary R&D for emerging/reemerging infectious disease control.

The candidates were invited to participate in the web-based expert questionnaire survey via e-mail. Only the candidate who consented to participate in the survey became

a responder. The period of the survey was during September 1 to September 30, 2014.

3. Results and Discussion

3.1. Responders

Ninety-sixth Japanese people were recruited for the questionnaire survey. They belonged to various organizations such as universities (49 persons), public and private research institutes (14 persons), companies (23 persons), medical institutions (6 persons), governmental agencies (3 persons), and academic society (1 person).

3.2. R&D Topics and Survey Items

Twelve R&D topics were extracted by the expert panel (see Table 1 “Topics”). Some of the R&D topics refer to legislations and infrastructure development (including animal welfare), which are not technologies but likely to influence technological development or to be influenced by technology.

Table 1. Twelve R&D topics and scores of their characteristics.

Topics	Importance	Uncertainty	Non-continuity	Morality
Curative treatment for chronic viral infections (e.g., HIV/AIDS, chronic hepatitis, etc.).	3.50	2.87	2.51	2.92
Technology to rapidly prepare neutralizing antibodies for new pathogens and then mass produce them.	3.50	2.79	2.67	2.35
A quantitative prediction and evaluation system that comprehensively takes into account environmental, pathogenic, and host factors to determine the impact of emerging infectious diseases on humans (i.e., virulence or the potential to cause a global epidemic).	3.48	2.78	2.63	2.73
A prediction and alert system for infectious disease epidemics based on a comprehensive infectious disease surveillance system that utilizes medical data such as electronic medical record, test results, and prescription records along with various types of web data.	3.48	2.25	2.15	2.95
A system to control the development and spread of drug-resistant infectious diseases (including both science-based technologies such as pharmaceuticals and social-based technologies such as a new approach to infection control).	3.47	2.63	2.30	2.59
Technology for the isolation and identification of unknown pathogens by utilizing a pathogen database. (Note: The pathogen database would be a comprehensive database of information about genes and proteins of pathogens infecting both humans and animals.)	3.46	2.36	2.29	2.69
Influenza vaccines that can provide lifelong protection against infection through only a few vaccinations regardless of viral antigenic variation.	3.43	3.27	2.97	2.71
Methods to test the effectiveness and side effects of therapeutic agents being developed for infectious diseases using cells derived from stem cells such as iPS cells as an alternative to using animal models.	3.41	2.79	2.72	2.62
Ultra-lightweight sensors that can be used in contaminated areas and aircrafts to quickly detect and determine the presence or absence of a particular infectious disease, the infectiousness of an infected person to others, and the susceptibility of non-infected people to the disease.	3.33	2.81	2.62	2.78
An efficient development and supply system for diagnostic methods, vaccines, and pharmaceuticals against infectious diseases in which social willingness to invest is low due to low incidence or other reasons (e.g., drug resistant bacteria, neglected tropical diseases, etc.).	3.32	2.85	2.46	2.81
Disinfection technology that can be used for anything including living bodies (e.g., mucous membranes) and capable of sterilization regardless of the target object, including spores.	3.28	2.72	2.61	2.50
A real-time simulation system that supports the formulation of strategies (both medical interventions and non-medical interventions to encourage awareness or behavior modification) to respond to emerging infectious diseases where the rapid development of vaccines and pharmaceuticals is difficult.	3.18	2.86	2.63	2.95

Scores are calculated by an average of the indices of each topic.

Twelve R&D topics are listed according to the score of “importance”.

Additionally four survey items for each R&D topic were set by the panel, consisting of R&D characteristics such as “Importance”, “Uncertainty”, “Non-continuity”, and “Morality”. The definitions of four survey items are shown in Table 2.

Table 2. Survey items for all R&D topics.

Survey item	Definition	Choice
Importance	Overall importance as seen from both sides of science and technology and society	4; very high
Uncertainty	Stochastic elements in the process of research and development that can often lead to risk. Research and development results that cannot be predicted in advance.	3; high
Non-continuity	Research and development results that are not in the current extension and cause a market destruction and innovation	2; low
Morality	Ethics in research and development which is necessary to consider the social acceptance.	1; very low

3.3. Key R&D Topics Demonstrated by the Expert Questionnaire Survey

Twelve R&D topics were characterized based on the four survey items. The responses regarding the survey items of each R&D topic were scored as “very high,” “high,” “low,” or “very low.” These four scores were indexed as score 4 (corresponding to “very high”), score 3 (“high”), score 2 (“low”), score 1 (“very low”) (Table 2).

According to types of emerging/reemerging infectious diseases, HIV/AIDS, chronic hepatitis, and drug-resistant infectious diseases are considered to be more important in Japan (Table 1, the score of “Importance” is from 3.50 to 3.47). Influenza is also considered important because the related topic scored 3.43, a close behind. Since the topic related to influenza was also shown to have the highest scores in the cases of “Uncertainty” and “Non-continuity”, it was considered to have a relatively high risk of R&D but a potential of innovation.

Similar to other developed countries, the above diseases are of high concern in Japan taking the recent trends in outbreaks and political approach into account. With regard to HIV/AIDS, the recent trend in outbreaks may have an influence on the responses. In 2013, 1,106 HIV carriers and 484 AIDS patients were newly reported [10]. The number of HIV carriers has been more than 1,000 since 2007 and the number of 1,106 carriers (prevalence) reported in 2013 is the second-worst in Japan. Although the number of HIV carriers/AIDS patients is lower in Japan compared with other countries, as far as the transition of HIV carriers, HIV/AIDS is considered to be an important disease in the country. Looking at drug-resistant infectious diseases and influenza, the domestic and international political approach may also affect the responses. In the case of drug-resistant infectious diseases, the Science Council of Japan issued a joint statement with G8 summit countries and academies of the related countries intended to the G8 summit in June 2013 (Drug Resistance in Infectious Agents—A Global Threat to Humanity” [11]). Concerning influenza, the Cabinet Secretariat developed the “National Action Plan for Pandemic Influenza and New Infectious Diseases” and associated guidelines in June 2013 [12]. Generally, these backgrounds may lead to the high importance of topics related to HIV/AIDS, drug-resistant infectious diseases, and influenza in Japan.

Regarding technology, the important topics are “Technology to rapidly prepare neutralizing antibodies for new pathogens and then mass produce them,” “A quantitative prediction and evaluation system that comprehensively takes into account environmental, pathogenic, and host factors to determine the impact of emerging infectious diseases on humans (i.e.,

virulence or the potential to cause a global epidemic),” “A prediction and alert system for infectious disease epidemics based on a comprehensive infectious disease surveillance systems that utilize medical data such as electronic medical record (EMR) system data, test results, and prescription records along with various types of web data,” “Technology for the isolation and identification of unknown pathogens by utilizing a pathogen database (Note: The pathogen database would be a comprehensive database of information about genes and proteins of pathogens infecting both humans and animals),” and “Methods to test the effectiveness and side effects of therapeutic agents being developed for infectious diseases using cells derived from stem cells such as induced pluripotent stem cells (iPS cells) as an alternative to using animal models” (the score of “Importance” is from 3.50 to 3.41). Particularly test methods using stem cells were considered to have a high potential of innovation (the second highest score in the case of “Non-continuity”). Out of these five important topics, three topics have to do with enormous quantities of data (two topics regarding prediction, evaluation, and alert systems, and pathogen databases). This result demonstrates that recent information technology (IT) development such as big data analytics have the potential to be applied to the emerging/reemerging infectious disease field. On the other hand, the three topics related to IT had relatively high scores in the case of “Morality” (the score of “Morality” is from 2.95 to 2.69). This result shows the importance of personal information protection in the process of collecting, organizing and analyzing large sets of data.

3.4. Limitations of the Expert Questionnaire Survey

This expert questionnaire survey could demonstrate the key R&D topics for emerging/reemerging infectious disease control, however it should be improved methodologically in several viewpoints. Firstly, twelve R&D topics in the emerging/reemerging infectious disease area are considered as representative topics; however, with twelve topics only, it was not possible to cover the entire range of the area. On the other hand, many R&D topics are considered to be a burden on responders. Taking one thing with another, R&D topics should be set with satisfactory balance between the scope of survey and the burden on responders. Secondly, the number of responders varied among organization sectors. This is because only the responders who agreed to participate in the survey were recruited. A listing of more candidates might be effective to reduce a variation in the number of responders among sectors. Thirdly, only Japanese persons participated in this survey. Since emerging/reemerging infectious diseases have

become a major global public health concern, international expert questionnaire survey is needed in the future.

4. Conclusions

This paper discussed R&D priority areas for emerging/reemerging infectious disease control on the basis of the expert questionnaire survey conducted in September 2014. The R&D topics related to HIV/AIDS, drug-resistant infectious diseases, and influenza was discussed. It was also demonstrated that the recent IT development such as big data analytics had potential for being applied to the emerging/reemerging infectious disease field. Although the survey should be improved methodologically, such result may contribute to designing and supporting a setting of concrete R&D programs in Japan and other countries.

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