AMR Alliance Japan

POLICY BRIEF

Enabling the further and active use of screening methods for the detection of antimicrobial resistance, and rapid diagnostic technology

Executive summary

- Antimicrobials are sometimes prescribed for patients who do not need them. Rapid diagnostic technology can shorten time needed for identification and susceptibility testing, making it possible to tell who should and should not receive antimicrobials.
- In Japan, a lack of resources and personnel prevents the uptake of rapid diagnostic technology
- Greater investment is needed in research and development of new technology, as well as increased support for adopting rapid diagnostic technology in medical facilities

Introduction

While many people throughout the world do not have access to antimicrobials, a certain level of antimicrobials are prescribed needlessly to patients who do not need them. A study found that 43% of antibiotics are inappropriately prescribed in the US. [1]

To guide the proper use of antimicrobials, doctors may implement screening. Screening is a means to identify patients with antimicrobial resistant infections. By determining the etiology of a patient's infectious disease, doctors can prescribe antimicrobials only when they are effective. However, in some cases, it may take time to obtain screening results even though immediate treatment is needed. Therefore, in many cases, doctors rely on "empirical" diagnoses – prescribing antimicrobials based on experience in the absence of complete information. While "empirical" diagnosis is needed, it is less precise, and antimicrobials may be inappropriately prescribed. [2]

Rapid diagnostic technology helps doctors identify the nature of infection in days and improve diagnostic accuracy. Rapid diagnostic technology allows for real-time information on whether an infection is either viral or bacterial and can recommend the best line of treatment. These technologies include "point-of-care" (medical facility tests) and "walk-away" tests (home tests).[3] Examples of tests for AMR organisms include pathogen culture and identification, drug susceptibility tests, nucleic acid amplification tests, antimicrobial resistance gene (ARG) tests, and AMR rapid diagnosis kits.

As well as reducing the unnecessary use of antimicrobials, rapid diagnostic technologies support the active surveillance of AMR. Active surveillance is when healthcare providers proactively collect information on AMR on a rolling basis. While active surveillance tends to be more comprehensive, it is costly and labor intensive. Rapid diagnostic technology can help lower costs and the time that active surveillance requires.

Background of the Issue: Japan

Japan is in the fortunate position to have access to a wide range of rapid diagnostic technologies. However, a shortage of infectious disease specialists and lack of resources prevents the spread of such technology. Moreover, limited investment into the research and development of rapid diagnostic technologies has slowed down innovation.

In Japan, the uneven distribution of resources among prefectures has led to differences in the availability of rapid diagnostic technology and the capacity for AMR screening. While in-house clinical microbiological laboratories have been important in the

detection of AMR bacteria, examination in medical institutions has been unprofitable.[4] Therefore, some hospitals may outsource such testing or rely exclusively on phenotypic testing without utilizing alternative types of rapid diagnostic technologies, such as genetic testing and epidemiological testing. Moreover, testing costs for novel diagnostic technologies (i.e. tests to identify the presence of ESBLs or CREs) are not covered under the Japanese insurance system and are paid for by individual medical facilities. Consequently, the use of genetic testing is lower in Japan compared to that of the US.

In Japan, innovations in rapid diagnostic technologies have been slowing as a result of limited investment.[5] Between 2007 and 2018, Japan ranked fourth in the number of patents filed for point-of-care diagnostics for pathogens and infectious disease, behind the US, UK, and Europe. However, during this decade, there has been a downward trend in the number of patents filed in Japan. Therefore, greater investment is needed for Japan to lead the innovation for rapid diagnostic technologies.

Stakeholders and Countermeasures: Japan

Stakeholder	Countermeasure
Ministry of Health, Labour, and Welfare	• National Action Plan on Antimicrobial Resistance (AMR) 2016-2020 - highlighted the need to improve rapid diagnostic technologies, ensure the availability of examination systems, conduct research on microbial examination systems, and explore the possibility of introducing new technologies and equipment in public and animal health laboratories. [6]
Central Government	• G20 Osaka Summit (2019) - Japan led the initiative to recognize the importance of developing rapid diagnostics as part of the recommended $10 billion for strengthening AMR global infrastructure. [7] • G20 Okayama Health Ministers' Meeting (2019) - Japan reiterated its mission to enhance rapid dialogistic technology by promoting the access and training of health and veterinary workers. [8]
Japan Agency for Medical Research and Development (AMED)	• Emerging and re-emerging infectious disease control project – support the development of diagnostic technology for infectious diseases. [9]
Public-academic partnerships	• Faculty at Nagasaki University and Tokyo Medical and Dental University, with the support of AMED, are working to develop and strengthen rapid diagnostic technology. [10]
Private sector	• Becton Dickinson and Company Japan – develop new rapid diagnostic technology as well as increasing awareness about the benefits of utilizing such technology. [11]

Background of the Issue: Global

Antimicrobial use has been rapidly rising worldwide, and between 2000 and 2015, global antimicrobial consumption increased by 65% from 21.1 to 34.8 billion Defined Daily Doses (DDDs).[12] * However, a certain level of antimicrobials are prescribed needlessly to patients who do not need them. In the US, between 2007-2009, compared to the 13 million people annually who receive antibiotics when needed, 27 million people receive antibiotics unnecessarily.[2] In the UK, according to Public Health England, about 1 in 5 antibiotics were prescribed inappropriately in 2018. [13]

Rapid diagnostic technology can help to address this issue by identifying which patients require antimicrobials. In recent years, the world has seen the development of novel genetic, molecular, epidemiologic tools for diagnosing infections. Currently, among AMR Industry Alliance members, 15 diagnostic technologies are in development, with companies actively engaged in research and development.[14] The global rapid diagnostic kit market is expected to reach US$28.8 billion by 2023 from US$18.7 billion in 2017.[14] However, between 2013 and 2015, the number of patents filed for rapid diagnostic technology has declined, and research on point-of-care (POC) tests appears to be limited to a few countries.[5] For example, 61% of all patent families (450 families) related to POC for antibiotics come from the US.

In addition to the discovery of new technologies, mechanisms are needed to the ensure the efficient and effective uptake of rapid diagnostic technology. The Joint Initiative Programme on Antimicrobial Resistance (JPIAMR) promotes a "mix-and-match" method, which highlights the need to take into account the opinions and requirements of end users and the importance of remaining technologically flexible to meet future demands. [15] This method will require multi-sectoral collaboration between point-of-care testing innovators, health providers, and the general public.

Stakeholders and Countermeasures: Global

Stakeholder	Countermeasure
National Institutes of Health (US)	• Antimicrobial Resistance Diagnostic Challenge - a $20 million federal prize competition that seeks innovative, rapid point-of-care laboratory diagnostic tests. [16]
National Endowment for Science, Technology and Arts (UK)	• Longitude Prize - a £10 million prize fund that rewards a team of researchers to develop a point-of-care diagnostic test that will conserve antibiotics for future generations. [17]

*Defined Daily Doses – assumed average maintenance dose per day for a drug used for its main indication in adults

Stakeholder	Countermeasure
Joint Initiative Programme on Antimicrobial Resistance (JPIAMR)	• *AMR Dx Global - a multi-sectoral, multi-stakeholder network that brings together partners from 18 countries including international organizations like WHO, Foundation for Innovative New Diagnostics (FIND), The African Medical and Research Foundation (AMREF), and Infection Control Africa Network (ICAN). In 2019, AMR Dx Global published a survey on the current level of training, teaching, and awareness regarding AMR diagnostics. AMR Dx Global has also mapped available teaching and training resources for AMR diagnostics.* [18]
National Institutes of Health (NIH), Human and Health Services (HHS)	• *The Antimicrobial Resistance Diagnostic Challenge: A prize competition for the development rapid point-of-care laboratory diagnostic tests. Visby Medical Inc. received US$19 million for a rapid diagnostic for gonorrhea.* [20]
Regulatory-based initiatives	• *Federal Drug Agency (US)* ▸ "Transparency initiative" – report on eight initiatives to make FDA's compliance and enforcement data more accessible and user-friendly. [19] ▸ "pre-submission" (pre-SUB) process - manufactures in cutting-edge technology can submit an informal pre-SUB process to navigate protocols and requirements of the regulatory pathway. [19]

AMR Alliance Japan Recommendations

- The Government should consider revising the medical fee system to fund the following AMR countermeasures.
  - The spread of AMR screening tests and rapid diagnostic technology, which allow for accurate judgements about AMR, enabling the effective prescription or halting of antimicrobials.
  - The promotion of training initiatives that can help medical facilities find the personnel to operate AMR screening tests, microorganism 5 identification tests, and susceptibility tests (including genetic screening tests).
  - Measures to appropriately cover the costs of tests that are currently borne by individual medical facilities (e.g. tests to identify the presence of ESBLs or CREs).
  - Measures to make it possible to run multiple susceptibility tests in cases in which AMR is suspected.
- In revising the medical fee system, the Government should clarify regulations related to the dispatch of specialized staff and the installation of testing devices in order to resolve problems related to the lack of laboratory personnel and testing technology at medical facilities. Furthermore, the Government should make the submission of test data mandatory for medical facilities selected as important to the domestic AMR surveillance system.

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