National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Collaborative projects between the People's Republic of China and the Netherlands
Progress and future of public health activities within MoU's

Within the framework of a Memorandum of Understanding (MoU) drawn up between the Ministry of Health of the People's Republic of China and the Ministry of Health, Welfare and Sport in the Netherlands, the Dutch National Institute for Public Health and the Environment (RIVM), has been engaged in bilateral collaboration. Although the Netherlands and China differ substantially in size, geography and culture, the collaborative projects have improved mutual knowledge and expertise in several fields of the health domain. These projects contribute to an improved level of scientific understanding and better methodologies, and ultimately will result in health promotion and disease prevention in both countries. We believe that global health problems require global solutions. In this brochure we present the projects undertaken by RIVM within the framework of the MoU.

The CARSS delegation at the former official entrance of RIVM

Antimicrobial resistance

Antimicrobial resistance (AMR) is a growing threat to global public health. To deal with AMR, the Netherlands has chosen an integrated approach involving all the domains in which human health is threatened by antibiotic-resistant bacteria: healthcare, animals, food and environment, also referred to as the One Health approach. As resistant bacteria do not respect international borders, the Netherlands considers international cooperation a priority when dealing with AMR. The Dutch are striving to put the One Health approach on the international agenda. A crucial component of the One Health approach, and one of RIVM's main expertises, is active surveillance, which is key for effective control strategies and information-based policy.

Recent activities

In April 2016, a delegation of the ChinaAntimicrobial Resistance Surveillance System (CARSS) visited the Centre for Infectious Disease Control at RIVM. As a follow up to visits in previous years, the goal of the 2016 visit was to exchange experience and expertise on the technical aspects of setting up and maintaining a national AMR surveillance system.

As a result of the meeting held in April, RIVM was invited to give a presentation on Antimicrobial Resistance Surveillance and Control in Humans in the Netherlands at the 13th National Conference on the Clinical Pharmacology of Antimicrobial Agents (13th NCCPAA) and at the 1st National

The CARSS delegation visiting a microbiology laboratory in a Dutch hospital

Conference on Antimicrobial Resistance Surveillance (1st NCARS) in Beijing on 1-3rd July.

In September 2016, as a follow up to a visit made by four RIVM AMR experts to China in September 2015, RIVM and the Chinese Center for Disease Control and Prevention (China CDC) organised a Second SINO-Dutch Conference on the Epidemiology and Control of Antibiotic Resistance- One Health Surveillance in Beijing. Participants from different sectors involved in AMR research, surveillance and control attended the workshop.

Also in September 2016, RIVM participated in the Sino-Dutch Forum of Antibiotic Use and Resistance Containment co-organised by the Netherlands Consulate General and the Shanghai Health Development Research Centre in Shanghai.

Future plans

In addition to continuing the current knowledge exchange, the Dutch Ministry of Health, Welfare and Sport and RIVM are currently exploring the possibilities of extending the collaboration on AMR with China by working together on a regional One Health project. This project should lead to the creation of a sustainable structure in a Chinese region in which the systematic collection of multisector data (such as on AMR prevalence and spread and antibiotic use in humans, animals and the environment) could lead to information-guided action to reduce the prevalence of AMR.

Second SINO-Dutch Conference on the Epidemiology and Control of Antibiotic Resistance- One Health Surveillance

Syndromic Infectious Disease Surveillance

In the past three years, China and the Netherlands have set up a successful collaboration centred on three topics: **early warning of infectious diseases, mortality monitoring, and using data from emergency medical services for surveillance.** Project partners China CDC, RIVM, Maastricht University, and Beijing CDC have achieved a solid baseline analysis of each country's surveillance systems and early warning structures. Furthermore they have also conducted a joint first exploration of mortality data and will jointly explore the use of emergency medical services data (EMS) for surveillance.

The introduction and spread of diseases and vectors, such as mosquitos, is driven by travel, trade and climate change. Research carried out by China and the Netherlands emphasises the cross-border dimension which is beneficial in strengthening our surveillance in a globalised world.

Prof. Qiyong Liu, China CDC, Vector Biology and Control department, National Institute for Communicable Disease Control and Prevention, China CDC

Activities

Three successful workshops were conducted, one per year (two in China, one in the Netherlands, in 2015, which was also attended by the Counsellor for Health, Welfare and Sports from the Dutch Embassy. The workshops included presentations, discussions of plans and results of joint research and site visits (to national and regional CDC's and public health agencies). All the partners considered the workshops highly successful as there was much dialogue and a high level of engagement.

Future plans

We wish to extend the MoU 'Assessing and responding to outbreaks and potential threats: syndromic infectious disease surveillance in China and the Netherlands' to build further on this knowledge. We would like to perform an in-depth study of the surveillance of potential future threats, such as unexplained pneumonia. We will explore collaboration on arbovirus surveillance and continue collaboration on the analysis of the interactions between climate and infectious diseases on mortality. Furthermore, we will continue to explore the added-value of emergency medical services data (such as '120' in China and '112' in the Netherlands) for surveillance purposes.

Continuation of the collaboration is very much welcomed by all partners (China CDC, RIVM and Maastricht University) and will additionally be supported by Beijing regional CDC.

Project partners China CDC, RIVM and Maastricht University

Collaboration on tuberculosis control

Tuberculosis is the most deadly infectious disease worldwide. The incidence is declining, but only very slowly. One of the major problems, in Europe and China, as well as in other parts of the world, is the increasingly common failure of most available tuberculosis drugs to cure tuberculosis due to the development and spread of resistant variants of its causative agent Mycobacterium tuberculosis.

The ongoing collaboration between China and the Netherlands established almost 10 years ago addresses this mutual problem as one of its key components. At CDC China in Beijing, a PhD study is being conducted on the evolutionary development of M. tuberculosis in China, in which RIVM is participating. This is of mutual interest, as the 'Beijing' genotype of M. tuberculosis, first described by RIVM in 1995, is not only the driving force behind the resistance problem in Europe, but also in Asia.

The project has not been confined to the Beijing region, nor limited to RIVM researchers. In previous years, staff members working in different disciplines in TB control in the Netherlands have attended workshops in Beijing, Ghangzou, Heilongjiang, Shangdong, and Zhangjiang, and Chengdu in which opportunities were identified to optimise the diagnosis and treatment of (resistant) tuberculosis. Several of these workshops included practical sessions, in which e.g. modern LED-operated microscopy, DNA techniques for the detection of resistance, as well as biosafety in a tuberculosis laboratory were brought to the attention of the audience.

Activities

Over the last years, several visits were made to Chengdu, the capital city of the Sichuan province with nearly 90 million residents. Local enthusiasm and commitment from our Chinese colleagues resulted in the creation of concrete plans for working on the optimisation of several aspects of TB control by combining the implementation of modern techniques, e.g. on the detection of resistance in M. tuberculosis, with research on the extent and nature of the tuberculosis problem in the province.

In addition, other ambitious activities have been introduced via this collaboration, such as the surveillance of TB, DNA fingerprinting of M. tuberculosis, drug resistance testing, optimisation of treatment, etc.

Such activities are expected to result in a sustainable tuberculosis control programme with the critical mass needed to impact on disease control throughout the Sichuan province.

Currently, three PhD candidates from Chengdu have been identified to work on this major infectious disease that is still diagnosed in around one million Chinese residents per year.

Working visit to Chengdu.

Meatborne Toxoplasmosis

Toxoplasma gondii (T. gondii) is a prevalent foodborne pathogen which causes a high disease burden worldwide. Pregnant women and immune-compromised patients are especially at risk of having a severe outcome of infection. Meat products, in particular pork and mutton, are regarded as important sources of infections in humans. In order to develop effective prevention strategies, information on the relative importance of different sources of human infection needs to be known.

At RIVM, a quantitative risk assessment (QMRA) model to predict the human toxoplasmosis incidence from meat products has been developed. This model will also be used to provide more insight into meatborne transmission in China.

Activities

A one-year joint project between RIVM, Jilin University and the China National Center for Food Safety Risk Assessment, Key Laboratory of China Food Safety Risk Assessment (CFSA), financed by the Royal Dutch Academy of Science (KNAW) and the MoU-budget was initiated in February 2016. The project aims to quantify and compare the risks of T. gondii infection via different meat products in China and the Netherlands by using the QMRA model. This information can be used to identify gaps in data resources and eventually to develop an evidence-based public health policy. Outcomes of this project include the development of a work plan, familiarisation with the structure of the QMRA and what data is needed for the QMRA model and the collection of Chinese data for model input parameters in China. This was done by a junior scientist on an exchange with China.

In July 2016, RIVM made a working visit to collaborative partners at the Institute of Zoonosis of Jilin University and the National Institute of Risk Assessment (CFSA) in Beijing. The working visit was very useful in establishing the collaboration and starting the collection of human consumption data in China in collaboration with the National Risk Assessment Institute.

Currently, the junior scientist is analysing the prevalence data of T. gondii in meat-produced animals and humans. Together with the collected human consumption data, the next step of this project is to run the QMRA model with Chinese data and compare the results to the Dutch outcomes.

It is a successful collaboration as all partners are very willing to continue

working in the field of microbial risk assessment for foodborne pathogens. One of the success factors of this

Joke van der Giessen (RIVM) and Jenny Deng (Chinese junior scientist) on a working visit in China

collaboration is the Chinese junior scientist who works at both RIVM in the Netherland and in China. She has proven to be a good intermediary between China and RIVM. It is our ambition to continue and extend the studies on foodborne diseases and risk assessment with China in a PhD setting for the Chinese scientist at RIVM.

Activities

In March 2016, a work plan and familiarisation with the Dutch GMRA model was completed and a Chinese junior scientist was trained at the University of Florida.

Chinese data on the prevalence of T. gondii infection in livestock species and humans were collected.
In June-July 2016 a working visit was

made to collaborative partners in China. A collaborative agreement to share and analyse the human consumption data was prepared and approved by the CSFA, the Institute of Zoonosis, Jilin University and RIVM.

In September 2016 preparation and running of the QMRA model will start. Chinese data will be analysed using the QMRA model at RIVM.

Future plans

In 2017, preparations will start for a scientific publication to report the QMRA of meatborne Toxoplasmosis in China and the Netherlands.

Joke van der Giessen working visit China

Seroprevalence of emerging zoonotic viruses

The surveillance of emerging viruses is primarily based on the molecular detection of viruses. With this technique, only acute infections can be detected. With serological surveillance, previous infections can also be identified. This way, the circulation of emerging viruses can be mapped more accurately.

For the Netherlands, the availability of a validated serological multiplex assay for a large number of emerging zoonotic viruses will benefit the preparedness and response to emerging viruses. Considering the growing passenger traffic, rapid surveillance tools will become increasingly important.

The Center for Disease Control and Prevention (CDC) Zhejiang, Wageningen Bioveterinary Research and RIVM are partners in the project Seroprevalence of Emerging Zoonotic Viruses. The project aims to improve methods of surveillance of emerging zoonotic viruses. For this, a so-called antigen micro-array, which has been developed by RIVM, will be used. With this micro-array the antibody response against multiple viruses can be detected in a single serum sample.

The project started at the beginning of 2016. The viruses to be included in the antigen micro-array have been selected and RIVM is currently developing the antigen tests for these viruses.

Future plans
In 2017, the developed antigen micro-array will be validated and Chinese researchers will visit RIVM to take part in a training programme on the use of the micro-array. Subsequently, Dutch project members will visit the CDC Zhejiang to transfer the antigen micro-array technology. Once the test is developed, validated and transferred to China, a pilot sero-surveillance project will start in China. The aim is to fully implement the sero-surveillance programme in 2018.

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