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Laboratory biosafety in China: past, present, and future

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ABSTRACT

The launch of the new journal, Biosafety and Health, presents me with a unique opportunity to recount the progress of laboratory biosafety (LB) in China and my contribution to this area over the past 30 years. Since the severe acute respiratory syndrome epidemic in 2003, China has constructed a primary network of high-level biosafety laboratories at different levels and established an expert team on LB. Furthermore, a series of LB management documents, including laws, regulations, standards, and guidelines, have been developed and published. This gradually maturing LB system has played a pivotal role in emerging infectious disease control and prevention, as well as in research, which in turn contributes to public health. In recent years, international collaboration between China and other countries has also been accelerated. Despite these achievements, we are still facing many challenges and opportunities in the field of LB. Sustainable LB development requires the joint efforts of the entire society and continuous international cooperation to safeguard global public health.

I began my career in infectious disease control and prevention in the 1980s after I graduated from Peking Medical University. In the early 1990s, as the director of the Technical Guidance Office of the Chinese Academy of Preventive Medicine, I participated in the accreditation of the first batch of biosafety level 3 (BSL-3) laboratories for HIV research in China. In the meantime, I held a concurrent position in the Infectious Disease Supervision and Management Office of the Ministry of Health of China. During the severe acute respiratory syndrome (SARS) epidemic, as a deputy leader of the Field Supervision Group, I was entrusted with the mission at the critical and tough moment to fight against this significant pathogen along with my colleagues. I would like to use the word “dedication” to describe the generation of experts who initiated the laboratory biosafety (LB) project in China. After an incident of laboratory exposure of SARS-CoV in 2004, I was asked to set up the first Office of Laboratory Management of the Chinese Center for Disease Control and Prevention (China CDC). The core responsibility of this office was to establish and improve the LB management system of the China CDC. A series of our pioneering efforts have changed the scattered and disordered condition of laboratories into a comprehensive, centralized, standardized, and scientific LB management system in the China CDC, and later, all over the country. Since then, under the supervision of the Chinese Government and through the joint efforts of experts from different institutions, China has made great achievements in LB.

1. Overview of LB achievements in China

As LB is closely related to infectious disease control and prevention, the preservation of microorganisms, and the application of biotechnology, high-level biosafety laboratories and microbial resource preservation platforms are essential parts of the national biosafety infrastructure. The outbreak of SARS in 2003 wreaked havoc on the society and economy of China, but a silver lining of the outbreak was that it also initiated the construction of China's LB system. Since then, China has made remarkable advancements in the development of high-level biosafety laboratories and supervision systems for these laboratories, as well as corresponding international collaborations [1]. Currently, China has raised biological safety and security, of which LB is a crucial part, to the height of national strategy.

1.1. Establishment of a primary network of high-level biosafety laboratories

High-level biosafety laboratories are the basic supporting platform for public health, scientific research, technical production, and national biosecurity. As of May 2019, a series of high-level biosafety laboratories have been established nationwide, covering certain provinces, autonomous regions and municipalities directly under the central government. As China's first BSL-4 laboratory put into operation, Wuhan National Biosafety Laboratory conducts studies on highly pathogenic viruses. Since January 2018, the laboratory has been in operation for global scientists who wish to conduct scientific experiments on BSL-4 pathogens. In the near future, Wuhan BSL-4 Laboratory will serve as the national research and development center for the prevention and control of emerging infectious diseases, the culture collection center of microorganism and viruses and a WHO reference Laboratory for Infectious Diseases [2]. Meanwhile, low-level

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pathogenic infectious agents are tested, identified, and isolated in a large number of BSL-2 laboratories all over the country.

1.2. Achievement in preservation and utilization of biological resources

Biological resources, including bacteria and viruses, are vital strategic resources for disease control and scientific research. Therefore, a preservation platform is a key component of LB. After a laboratory leak incident of SARS in 2004, the former Ministry of Health of China initiated the construction of preservation laboratories for high-level pathogens such as SARS, coronavirus, and pandemic influenza virus. Samples previously preserved by provincial research institutions and medical institutions were transferred to designated national institutions for storage [3]. In 2013, the National Health and Family Planning Commission issued a plan for the construction of collection centers for human-borne pathogenic microorganisms and viruses (2013–2018). This plan encompasses six national-level culture collection centers, 27 laboratories, and at least one provincial culture collection center for each province. To date, accreditation has been completed for all of the six national-level culture collection centers. In addition, to integrate national expert teams and technical forces, the Biological Resource Management and Utilization Branch of the Chinese Preventive Medicine Association was established in 2018 with the objective of promoting the development of biological resources.

1.3. The training and development of LB professional teams

In 2005, the first LB textbook in China was published under the guidance of the former Ministry of Health of China, and then, the National LB Teacher Training Program was launched. One thousand or so teachers completed the training and served as the first group of LB instructors across the country. Since 2006, health administrative departments and laboratories at different levels have offered their own LB training programs. In 2008, the China CDC published a video titled “LB of Pathogenic Microorganisms,” which was used for large-scale video training at various disease control institutions in China. Laboratory staffs were required to take training annually at their own institutions to ensure that they were competent to perform LB-related work. Over the past 15 years, a total of nearly 100,000 personnel have undergone this training, and these well-trained specialists have played a pivotal role in LB.

1.4. Establishment and development of LB management documents

In November 2004, the State Council of China promulgated and implemented the Management Regulations on LB of Pathogenic Microorganisms (Order No. 424 of the State Council) [4]. Since then, the vast majority of health administrative departments, the CDCs at different levels, universities, and scientific and research institutions have established LB management departments, allocated special funds, and designated staff to take charge of LB. China has built a six-level LB management framework consisting of biosafety laboratories, institutions with biosafety laboratories, relevant authorities, and regional, provincial, and national health administrative agencies. The management departments at all levels are linked together to form a highly efficient management system.

China has also developed a series of LB-related laws, regulations, standards, and guidelines to cover the entire chain of LB, ranging from experimental activities to transport and preservation of microorganisms. In addition, some provincial health agencies have set up their own regulations on LB management, including laboratory registration, internal transport of microorganisms, and emergency plans for biosafety incidents, mainly focusing on non-highly pathogenic microorganisms in BSL-2 laboratories.

1.5. High-level LB and infectious disease control and prevention

Manipulation of highly pathogenic microorganisms should be performed in high-level biosafety laboratories, namely BSL-3 or BSL-4 laboratories. The establishment and improvement of LB system provide the fundamental support for successful responses to disease control and prevention. Since 2003, China has successfully dealt with human infections of swine streptococcus, pandemic H1N1 influenza, the H7N9 avian influenza epidemic, and imported cases of Middle East respiratory syndrome, Zika virus disease, yellow fever, and Rift Valley fever, etc [5,6]. Meanwhile, high-level biosafety laboratories have also played a significant role in surveillance and basic research on these pathogens. In addition, the success of a series of large-scale events held in China, such as the 2008 Summer Olympic Games, has proven the effectiveness of China's LB system. After 15 years of development, the LB system in China can be viewed as a successful example for the prevention and control of infectious diseases worldwide.

1.6. International collaboration

During the Ebola outbreak in West Africa in 2014, the insufficient detection abilities of local laboratories seriously restricted the early control of the Ebola epidemic. China sent a mobile BSL-3 laboratory to Sierra Leone and then constructed a fixed BSL-3 laboratory there. From breaking ground to completion, China's first overseas BSL-3 laboratory was built in only 87 days with all parts and equipment made in China. This project reflects the ethos of “China speed, China quality” and received high recognition from the WHO and the Ministry of Health of Sierra Leone. Since its initial operation on March 11, 2015, tens of thousands of suspected Ebola clinical samples have been tested in this laboratory, which played a critical role in the infectious disease surveillance system of Sierra Leone. Meanwhile, the overall operation of this laboratory is stable without any biosafety incidents to date, demonstrating China's excellent capabilities in LB and infectious disease control and prevention. Moreover, we have trained a number of LB professionals with LB work experience for Sierra Leone.

Chinese LB specialists have established extensive international partnerships with well-known organizations and institutions, including the WHO, Asia-Pacific Biosafety Association (A-PBA), European Biosafety Association (EBSA), and American Biological Safety Association International (ABSA). It is worth mentioning that in 2018, the 13th A-PBA Biosafety Conference was successfully held in Beijing. Through academic conferences, training, and assessments, we have enhanced our exchanges and collaborations with these organizations. In the future, China will continue to strengthen its ties with other countries in the field of LB and advocate the “One Health” concept [7].

2. Challenges

Obviously, China has made significant progress in LB over recent decades, especially in the past 16 years. However, with the rapid development of biomedical technology, there are still many challenges that we need to overcome.

First, the number of high-level biosafety laboratories in China is not sufficient. More than 60 BSL-4 laboratories have been established in developed countries, and all of these BSL-4 laboratories have the full range of capacity to handle highly pathogenic microbes. In China, however, only one BSL-4 laboratory is fully operational. Although a number of BSL-3 laboratories have been set up in the last decade, the distribution of these laboratories is not well balanced across the country, with more located in the eastern and middle regions than the western areas of China.

Second, the LB management system in China still needs to be improved. The disease control and prevention centers at different levels (national, provincial, city, and county) have a relatively complete, independent management system for LB, covering personnel training, supervision, and inspection. However, the overall level of biosafety management, including pathogen preservation systems in universities, hospitals, and academic institutions, should be enhanced. In particular, a comprehensive system of legal and regulatory standards is lacking for BSL-2 laboratories in China.

In addition, we do not have enough well-trained and experienced LB specialists. Although professional LB teams have been established in the disease control and prevention centers in China, experienced LB staffs in

universities, hospitals, and research institutes across the country are seriously insufficient.

Moreover, compared to developed countries, China is still in the beginning stages of LB development. Our innovation capacity is relatively weak, and some key techniques and products do not have independent intellectual property rights. Similarly, the research and development of LB techniques and equipment fell behind some western countries. The design and reliability of our LB system also lacks acute evaluation criteria and schemes.

3. Perspectives

With the accelerated development of biotechnology and the continuous threats from emerging and re-emerging infectious diseases, LB should receive much more attention [8]. Administrative staff at all levels of management and laboratory technical personnel must raise their awareness and enhance their sense of responsibility. In view of national security strategies, we must re-examine and adjust all aspects of biosafety, including management structures, human resources, and technical systems.

There is a pressing need to improve the regulatory standards system. In particular, policy research units and administrative departments should work together to propose necessary and prompt revisions of regulatory measures for biosafety, providing support and guidance for the development of synthetic biology, gene editing, and biological resource preservation and utilization. Moreover, biosafety laws are urgently needed.

By gradually increasing the number of high-level biosafety laboratories, a technical platform based on the LB network should be established to respond to potential public health emergencies. The Chinese government has planned to build an additional five to seven BSL-4 laboratories in accordance with the principle of appropriate regional distribution, complete functions, and outstanding features. In addition, to make full use of the existing BSL-3 laboratories, a new batch of BSL-3 laboratories (including mobile laboratories) will be constructed to achieve the goal of at least one BSL-3 laboratory in each province. Moreover, a nationwide network for the preservation of pathogenic microbes, including bacteria and viruses, and the development of relevant professional teams also suggest a significant direction in the field of disease control and prevention.

Currently, China has no national association for biosafety, but several biosafety-related branches were set up within some other national associations. To raise public awareness of LB and to promote domestic and international collaborations on biosafety, we need to establish a national association of biosafety that will integrate resources and elevate LB to a new level in China. In addition, the professional competence and sense of responsibility of laboratory staff are important foundations for LB. The training of LB professionals should be strengthened, which in turn will provide motivation for the sustainable development of LB in China.

LB is a long-term and systematic project. In the past 30 years, my colleagues and I have been working tirelessly for the development of LB in China. At present, we are trying to integrate a global perspective and a global security vision with the career we love and to make greater contributions to our global biosafety and biosecurity.

Conflict of interest statement

The author declares that there is no conflict of interest.

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