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Short Communication

Biosafety and biosecurity

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ABSTRACT

With the profound changes in the international security situation, the progression of globalization, and the continuous advancement of biotechnology, the risks and challenges posed by major infectious diseases and bioterrorism to the international community are also increasing. Biosafety, therefore, presents new opportunities for international cooperation and global governance. The world has become more integrated and now shares a common destiny in terms of biosafety. In the face of the current risks and challenges, the international community must work together to avert threats, advance mutual interests, and safeguard global biosecurity. In the context of the current situation regarding biosafety and biosecurity, we conducted the present analysis, and present here some appropriate countermeasures.

1. Introduction

In a broad sense, biosafety, and biosecurity (hereafter collectively referred to as "biosafety") refer to a nation's ability to respond effectively to biological threats and related factors. This requires a nation to maintain and protect its own safety and interests. Such requirements include the prevention and control of major emerging infectious diseases, defensive action against biological weapon attacks, the prevention of bioterrorism attacks, the prevention of biotechnology abuse, the protection of laboratory biosafety, the protection of special biological resources, and the prevention of invasion by alien organisms.

The necessity for biosafety is greater than that at any other time in history, spatiotemporal factors are broader than ever before, and internal and external factors are more complicated than those seen in the past. In the present article, we have discussed the key aspects of biosafety technology, the risks and challenges facing biosafety, and some solutions to these problems.

2. Key areas of biosafety technology

Since the beginning of the 21st century, the rapidly developing field of biotechnology has become integrated with many disciplines such as nanotechnology, information technology, precision electronics, optoelectronic engineering, and micromanufacturing. This has completely changed the mode of research adopted by traditional life sciences, and has promoted the development and maturation of biosafety technology. Biosecurity defense requires systematic engineering, which involves monitoring and warning, detection traceability, prevention and control, diagnosis and treatment, emergency measures, and other technical aspects.

2.1. Monitoring and warning

Real-time monitoring and warning of biological risk is the first step towards biosafety defense. Multimodal spectral analysis techniques are appropriate for short- and long-distance biological detection, field investigation, and rapid detection in the field. Intelligent big data analysis technology can enable the mining and utilization of biosecurity's big data and establish the full-dimensional assessment, and highly sensitive identification and prediction of biosecurity risks.

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2.2. Detection traceability

Climate change and population flow have direct effects on microbial diversity and pathogen transmission, so the traceable detection of pathogens is very important. Biological nanometer technology and biosensor technology have emerged at the right moment. Continuous improvements in biological detection and recognition, and the rapid, sensitive, and specific identification of pathogens have enabled rapid preliminary screening and early warning.

2.3. Prevention and control

The most effective means of preventing and controlling infectious diseases is immunization. Synthetic biology, gene editing technology—represented by CRISPR/Cas9, which is highly efficient at genetically transforming species—and the rapid synthesis of newly emerging infectious pathogens, have great potential in the development of emergency vaccines and new drugs.

2.4. Diagnosis and treatment

Bio-omics includes genomics, proteomics, transcriptomics, metabolomics, glyco-omics, and epigenomics. Relying on high-throughput sequencing and mass spectrometry, bio-omics reveals the mysteries of life, ranging from gene coding to the emergence of life, and comprehensively supports disease prevention, diagnosis, and treatment.

2.5. Emergency measures

Virtual simulation technology plays an important supporting role in rapid response, efficient disposal, and decision management, and is the frontier of biosecurity defense. It applies highly integrated, automated, and intelligent model algorithms, and integrated technology products to multi-dimensional hazard assessment. This enables rapid and accurate quantitative risk assessment, and reshapes the whole process of event occurrence, development, and evolution into disaster. It also establishes a strategic and tactical training technology platform for biological defense and enables interactive and visual drilling in the whole process of biological defense.

3. The risks and challenges of biosafety

Biosafety is a major emerging aspect of global security, and involves many fields such as health, agriculture, science and technology, education, and the military. It concerns such aspects as concealment, sudden onset, diffusion, spillover, and destructive impact, and is an integral part of national security.

3.1. Emerging infectious diseases

Infectious diseases do not respect national borders. With the changing global ecological environment, and increasing international communication, the sudden emergence and spread of infectious diseases are becoming more frequent. More than 40 new infectious diseases have appeared in the past 30 years.

In July 2003, severe acute respiratory syndrome coronavirus (SARS-CoV) emerged in China, and subsequently spread across the globe. In China alone, 5327 people became infected, 349 died, and nearly half of the survivors had somatic complications, ischemic necrosis, hypoadrenocortical dysfunction, or mental disorders.[13]

In March 2013, a new subtype of influenza virus A, H7N9, was discovered in eastern China. Of the 469 laboratory-confirmed cases, 182 died (a mortality rate of 38.9%). Simultaneously, the H1N1 swine flu virus began to spread in South America and was subsequently reported in China, eventually resulting in 128,033 laboratory-confirmed cases (805 deaths). Vaccination is key to fighting seasonal influenza and reducing the burden of disease. However, owing to the variability of influenza viruses, traditional vaccines do not provide effective immunity to evolutionary strains.[7]

In 1976, Ebola was first discovered in Central Africa. Ebola hemorrhagic fever has been rampant in West Africa since 2014; it has spread rapidly to South America and Europe and is almost out of control. As of August 2015, the worst-affected countries are Guinea, Liberia, and Sierra Leone, with a total of 280,005 cases and 11,287 deaths (40.3% mortality), which has caused global panic.[1] Ebola virus causes a strong inflammatory response, destroys the host's immune response, and causes multiple organ disorder syndrome.[6] Ebola remains a priority disease for the World Health Organization (WHO) owing to the risk of relapse it poses, and the lack of effective vaccines and antiviral drugs to combat it.[8]

In May 2015, the first case of Middle East respiratory syndrome (MERS) was reported in Guangdong, China. Nipah virus in Southeast Asia and Hendra virus in Australia are also import risk factors. If they spread, these infectious diseases will pose a considerable threat to global health.

3.2. Biological weapons and bioterrorism threats

Bioterrorism is the use of pathogenic bacteria, viruses, and toxins in military operations for the purpose of causing infection, morbidity, and mortality in humans, animals, or plants, and endangering social stability and national security. To cause disease quickly in a specific population, biological warfare agents that are often highly pathogenic and infectious may be used. Such agents include *Bacillus anthracis*, *Brucella* spp., *Clostridium botulinum*, *Yersinia pestis*, *Francisella tularensis*, Tula virus, and Ebola virus.

Biological weapons have been used many times in warfare throughout history. The Biological Weapons Convention entered into force in March 1975. However, the Convention lacks an effective means of verification, and does not prohibit the development of biological weapons for defensive purposes. Since the September 11 attacks in 2001 and the subsequent anthrax event in the United States, bioterrorism has become a real threat. Bioterrorist attacks are a constant treat throughout the modern world, and are gradually increasing in frequency. For example, a restaurant in the United States was the target of a bioterrorism attack involving contaminated salads, which resulted in the infection of at least 750 people with typhoid fever; botulinum toxin-contaminated beverages poisoned 63 people in a US base, and 50 people died; and a cult organization has planned a "suicide attack" using the Ebola virus.

The invisibility, diversity, and speed of action of biological weapons make early diagnosis and medical identification difficult.[1] Moreover, the harmful effects of biological weapons have strong situational dependence. Different pathogens, different attack methods, different social and natural environments, and other conditions result in different paths of risk evolution and different risk levels, which increases the difficulty of national biological defense. New requirements have been put forward for national biological defense capabilities such as emergency personnel, emergency supplies, medicines and vaccines, treatment equipment, monitoring and early warning systems, and on-site disposal, recovery, and reconstruction.

3.3. Misuse of biotechnology

While the rapid development of life sciences and biotechnologies such as synthetic biology, reverse genetics, viral engineering, and various advances in histology have benefited human society, their misuse, abuse, and misapplication pose potential threats to human health and the environment. Biological pathogens can be artificially modified to enhance their toxicity, drug resistance, environmental stability, genetic characteristics, and immunogenicity. Such modifications can even result in "gain-of-function mutations" in which the altered gene product has a new molecular function or a new pattern of gene expression. Gain-of-function mutations are almost always dominant or semi-dominant. Once spread from the laboratory, genetically engineered microorganisms (GEMs) may have direct or indirect effects on the external environment.[12] In 2011, scientists in the Netherlands and the United States developed an H5N1 avian influenza virus with human-to-human transmission capacity through targeted transformation. Studies suggest that influenza hemagglutinin (HA) is the main barrier to interspecific transmission. The H5N1 subtype prefers to identify the Siaαi and 3Gal receptors of poultry airway epithelial cells, which are specific for poultry receptor binding.[4] Although it can spread from birds to humans, it is difficult for the virus to spread through the respiratory tract. One research team found that only five point mutations or four gene re-assortments allowed the virus HA to break through the interspecies barrier.[11]

The successful transformation of the H5N1 subtype of avian influenza virus was an important milestone in influenza virus research, and is highly significant to the direction of evolution of the epidemic strain. However, such biotechnological breakthroughs have both favorable and unfavorable consequences: they pose a major threat to human survival and global biosecurity as well as providing early warning of outbreaks.

There is another aspect to the misuse of biotechnology: cutting-edge dual-purpose biotechnology such as synthetic biology and CRISPR/Cas9. Anyone who is sufficiently motivated could synthesize the gene for a toxin or even an entire viral genome using readily available reagents, and without a specialized synthesizer (Minshull et al., 2012). In 2017, Tonix Pharmaceuticals announced that they had synthesized a potential smallpox-preventing vaccine—a live form of the horsepox virus (HPXV) that has a vaccine activity in mice. However, the safety concerns for existing smallpox-preventing vaccines outweigh the potential benefits of immunizing first responders or the general public.

3.4. Alien species invasion

With economic integration and globalization, an increasing number of invasive alien species are being introduced into China through various channels. Moreover, these species are breeding, spreading, and replacing local species at an unprecedented rate; this is destroying the diversity of local species and the original ecological balance, seriously threatening the safety of national plant resources.[3] To date, more than 600 harmful alien species have invaded China, of which more than 100 occur over large areas and are seriously dangerous and harmful. According to statistics, in 2009, the number of pests intercepted at Chinese ports reached 200,000 batches, including more than 3200 species, which was 3.1 times the number discovered in 2002, and which represents an increase of more than 20% per year.

3.5. Biological accident disclosure

Laboratory infections not only endanger the health of laboratory staff, but may also cause the accidental leakage of organisms. This may cause an epidemic in the area surrounding the laboratory, which may endanger the health and safety of the general population, and may even have a serious global impact on public health.

In 1979, a major bio-facilities accident at Sverdlovsk, in what was then the Soviet Union, led to the death of at least 66 people from inhaled anthrax; it remains the largest anthrax outbreak in human history.[9] In 2004, laboratory personnel in China were infected with SARS, which was spread by the infected people, resulting in new infections in many places. In 2007, the British Institute of Animal Health allowed a virus to leak from a damaged sewage system, causing an outbreak of foot-and-mouth disease in nearby farms. In 2009, a researcher died after becoming infected with plague bacillus at the University of Chicago Medical School. Between 2004 and 2010, the US Centers for Disease Control and Prevention reported a total of 727 incidents of theft, loss, and leakage of biological media, including 639 leaks, most of which were Biosafety Level 3 (BSL-3) incidents. In 2010, untested goats were used in a "Live Goat? Anatomy Experiment" at the College of Animal Medicine of a university in China, resulting in 28 people in 5 classes (27 students and 1 teacher) becoming infected with brucellosis. Unexpected disasters can occur in the event of a bio-accident leak, especially from a high-level biosafety laboratory.

3.6. Super-resistant bacteria

Penicillin was introduced in the 1940s, marking the beginning of a new era in the treatment of infectious diseases. Since then, many new antimicrobials have been developed to effectively prevent and control infectious diseases. However, human health has been seriously threatened in recent years owing to the emergence and dissemination of multidrug-resistant bacteria and new strains of resistant bacteria.

WHO first issued a global antibiotic resistance report in 2014. The report showed that methicillin-resistant *Staphylococcus aureus*, carbapenem-resistant *Klebsiella pneumoniae*, and third-class cephalosporin-resistant *Neisseria gonorrhoeae* have spread throughout the world, which suggests that standard antibiotics are becoming ineffective.

Antimicrobial resistance (AMR) has also had a negative economic impact on global health systems. The treatment of infections caused by almost all resistant strains is more expensive than the treatment of sensitive strains. According to statistics from the American National Health Center and the Centers for Disease Control and Prevention, approximately 230,000 people die from infections caused by resistant strains every year, and the treatment of such strains costs the US healthcare system approximately $200 trillion. Moreover, the consequent loss of productivity amounts to approximately $35 billion. In December 2014, a work report published by the UK government predicted that the global gross domestic product (GDP) would be reduced by 2–3.5% by 2050 because of resistant bacteria, and that the health of millions of people would be threatened every year.

4. Solutions

4.1. Improve global biosafety defense capability

Biosafety is closely interlinked and interacting among countries. The 2001 white powder anthrax spore terrorist incident in the USA, the 2003 SARS outbreak, the 2009 global H1N1 pandemic, and the 2014 Ebola outbreak in West Africa have made people realize the importance of a joint effort to strengthen global biosafety. To achieve this goal, biologists should uphold the standard of win-win cooperation and promote the building of a global biosafety community.

4.2. Establish and improve a biosafety monitoring network

Biosafety supervision requires the collection and analysis of information to provide an early warning for natural or externally transmitted infectious diseases. It is necessary to strengthen biosafety monitoring, develop a biosafety resource platform, participate in global cooperation in various fields including the prevention and control of major newly emergent infectious diseases, and draft standards and guidelines for medical services and centers that are capable of responding to international emergencies.

4.3. Improve monitoring and early warning systems for infectious diseases

Within the context of globalization, continuous population growth, the concentration of megacities, and the development of air transport markets have led to the continuous evolution and transmission of infectious diseases. In response to emerging infectious diseases, the primary task is to: "identify the pathogen, identify the outbreak and identify the source." Increasing basic research on the pathogenesis of new diseases is the key to discovering their causes and to establishing rapid real-time pathogen identification technology. Moreover, increasing surveillance and early warning strategies to safeguard against epidemics, establishing and improving global new pathogen monitoring systems, improving and optimizing the surveillance of global epidemic-causing diseases transmitted by wild animals, and promoting the investigation of major unknown pathogens in wild animals will support the response to emerging infectious diseases and reduce the impact of outbreaks.

4.4. Improve the identification, prevention, and control of bioterrorist pathogens

A wide range of biological warfare agents are designed to attack a target, but also to infect healthcare workers and the public, causing rapid panic in the population. It is worth noting that emerging infectious diseases and genetically modified strains can also be used for bioterrorism, and there are no specific drugs or vaccines to treat most of these pathogens, which exposes medical institutions to more complex scenarios and challenges. In response to bioterrorism, it is necessary to establish pathogen detection technology and a bioterrorism pathogen database, strengthen risk assessment and early warning strategies to counteract bioterrorism activities, and improve bioterrorist pathogen inspection and detection. It is also necessary to establish a diagnostic reagent supply base and a national vaccine drug reserve, and to increase dual-use biotechnology research to minimize the impact of bioterrorism.

4.5. Improve the management of biotechnology applications

Biotechnologies have benefited people, but their misuse is potentially threatening to human health. It is important for governments to strengthen the management of biotechnology, especially gene synthesis technology. Gene synthesis companies should not produce or edit genes that match any sequence on a list of restricted sequences compiled by the relevant experts, without an official permit. Implementing a sane regulation and enforcement policy regarding gene synthesis will avoid the possibility that synthesized genes can be used to cause harm (Minshull et al., 2012).

4.6. Improve technological platforms for controlling invasive alien species

The invasion of alien species is considered the most serious challenge to people, biodiversity, and the environment of the 21st century. Therefore, a platform for the active prevention and control of invasive alien organisms, a database of invasive alien species, and early warning and detection technologies to counteract invasions are required. Such strategies will curb the spread and transmission of harmful organisms in biological systems, prevent agricultural production that encourages invasive species, and ensure biodiversity and ecological security. The ability to cope with invasion, dissemination, and harm from alien organisms should be comprehensively enhanced.

4.7. Increase research into the mechanisms underlying the evolution and transmission of drug-resistant strains

Multidrug-resistant bacteria pose a growing threat to global public health. There are more than 10 million new cases of tuberculosis each year, of which 600,000 are caused by multidrug-resistant *Mycobacterium tuberculosis* strains that are resistant to first-line drugs such as rifampicin and isoniazid. Mutations in efflux pump genes, transporters, cell wall biosynthesis genes, and virulence genes may contribute to the development of drug-resistant phenotypes and the transmission of resistance. Research into the evolutionary mechanisms underlying drug-resistant strains plays a crucial role in preventing their spread. Moreover, strengthening the management of antimicrobials is the key to preventing further drug resistance and spread of disease.

Conflict of interest

None.

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Further reading

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