Front. Agr. Sci. Eng. 2014, 1(2): 96–103
DOI: 10.15302/J-FASE-2014030

REVIEW

Prevention and control of zoonoses at their source: from the Chinese perspective

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Abstract Zoonoses are a significant public health concern and cause considerable socioeconomic problems globally. The emergence of severe acute respiratory syndrome (SARS), highly pathogenic avian influenza (HPAI), and Ebola virus disease (EVD) has had a significant effect on the national economy and public health in China, and other countries. This review analyzed zoonotic disease issues faced by China, and the main factors contributing to the risk of zoonotic disease. The Chinese government has devised new strategies and has taken measures to deal with the challenges of these diseases, and the prevention and control of zoonoses at their source. A strategy that is suited to China's national conditions, is proposed.

Keywords zoonosis, prevention and control, joint prevention and control

1 Introduction

Zoonoses are diseases that can be transmitted between humans and animals. Almost all types of pathogens, including viruses, bacteria, parasites, fungi, spirochetes, mycoplasma and chlamydia, can cause zoonoses, and more than 800 pathogens have been shown to transfer between humans and vertebrates, with more than 73% of infectious diseases in humans originating from animals [1,2].

Economic globalization not only contributes to globalization of capital, technology, labor, and commodities, but also promotes the globalization of emerging infectious diseases [2]. China is a major contributor to the spread and control of infectious diseases in the world. For example, the first case of severe acute respiratory syndrome (SARS) arose in 2002 in Guangdong, China, and was transmitted to Hong Kong, and then to other countries [3,4]. The goose/Guangdong/1/1996 H5N1 virus found in a goose farm in southern China in 1996 is considered the precursor of the currently circulating highly pathogenic avian influenza (HPAI) H5N1 viruses in more than 60 countries [5,6]. The current Ebola virus disease (EVD) outbreak began in Guinea in March 2014, and now involves in Guinea, Liberia, Nigeria, and Sierra Leone. By 13 August, 2014, a total of 2127 cases, including 1145 deaths, had been reported by the World Health Organization (WHO). This is currently the largest EVD outbreak ever recorded. Fruit bats likely carry Ebola virus, with humans infected by close contact with infected body fluids. Human-to-human transmission occurs only by close contact with infected body fluids. The Ebola outbreak in West Africa constitutes an extraordinary event, and a public health risk to other countries [7]. These diseases have a negative impact on economic development and human health in both developing and industrialized countries [8,9]. In this review, we summarize the major zoonotic disease issues, contributing factors, control strategies and measures, and propose the prevention and control of zoonosis at their source, a strategy that is suited to China's national conditions.

2 Zoonotic disease issues faced by China

In the past 20 years, zoonotic diseases have produced a bleak situation in China. Ancient zoonoses continue to occur, new zoonoses are appearing and the risk of new diseases from abroad is increasing. Zoonoses pose a serious threat to human health, animal survival, the development of the livestock industry, food safety and biosecurity [10–13]. Meanwhile, global warming, globalization, changes in farming methods, accelerating urbanization, the destruction of the environment, close contact between humans and animals, and the abuse of biotechnology are increasing the risk of zoonoses [2].

Received May 20, 2014; accepted July 17, 2014

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2.1 Resurgence of ancient zoonoses

Rabies, brucellosis and plague are epidemic and increasingly prevalent in certain areas of China, and hemorrhagic fever, dengue fever, leishmaniasis and hydatid disease have caused significant morbidity and mortality in Xinjiang. Schistosomiasis and tuberculosis are epidemic and potentially very dangerous.

Rabies was first described about 2400 years ago, and there are 35000–50000 deaths every year worldwide [14]. One Asian dies of rabies every 15 min, and 50% of the victims are children under 15 years of age who experience a mortality rate of up to 100% [15]. In China, there is an annual incidence of approximately 3000 fatal cases [16,17].

Plague, also known as “kala-azar”, first appeared about 1400 year ago. This disease has a mortality rate of 30%–100% and has cumulatively killed as many as 150 million people [18]. Plague occurred in India in 2003 [18]. Currently, plague has entered an active phase worldwide, with high incidences in Asia, Africa and America [20–22]. In China, this disease mainly occurs in Yunnan and the Qinghai-Tibetan Plateau, with a higher incidence in summer and autumn due to hunting and rodent breeding activities [23,24]. According to China’s Ministry of Health, 254 cases occurred in 2000 and 22 cases occurred in 2004, including nine fatal cases. An epidemic of human plague occurred in Zhongba County, Xigaze Region, Tibet in 2005, with five people affected, two of whom died [25]. One fatal case of human plague occurred in Sichuan in 2012 [26].

China is one of the 22 countries with a high incidence of tuberculosis (TB) [27]. Currently, there are approximately five million cases of TB, and prevalence in China is ranked second in the world. Approximately 1.3 million new cases are diagnosed annually, and up to 150000 patients die each year from the disease [27]. In 2011, WHO announced that drug-resistant TB (XDR-TB), for which no treatment is currently available, has been found in 45 countries [28,29].

The incidence of human and animal brucellosis increased 100-fold from 329 cases in 2001 to 35816 in 2009. According to the Report on National Notifiable Infectious Diseases released by the National Health and Family Planning Commission of China, 2992 cases of brucellosis occurred in February of 2014. In total, 160 million cases of schistosomiasis have been reported worldwide. By the end of 2010, schistosomiasis was epidemic in 453 of the counties, cities and districts of China, with 325800 patients affected [30,31]. In February, 2014, 415 cases of trematodiasis were reported in China. In the areas of China where echinococcosis is endemic, the average annual prevalence of this disease is over 1%. It is primarily found in the pastoral and farming/pastoral regions of seven provinces and autonomous regions, including Inner Mongolia, Sichuan, Tibet, Gansu, Qinghai, Ningxia and Xinjiang, with 66 million patients at risk [32,33].

2.2 Successive emergence of new zoonoses

In the past 20 years, new zoonoses have emerged worldwide (Table 1). Bovine spongiform encephalopathy, scrapie, avian influenza (H7 subtypes), Nipah disease, West Nile virus and Rift Valley fever are the key zoonoses requiring prevention efforts.

Since 2002, the H5N1 highly pathogenic avian influenza virus has evolved from infecting only birds to infecting mammals and humans [34,35]. According to a report from WHO, a total of 649 cases (including 385 fatal cases) had occurred worldwide by 9 January, 2014. One fatal case has

Table 1 Important new zoonoses that have emerged in the world in recent years

Disease	Pathogen	Year	Countries/Regions
Ebola virus disease	Ebola virus	2014	Guinea, Liberia, Nigeria, and Sierra Leone
H7N9 avian influenza	H7N9 A influenza virus	2013	Canada and China
Middle East respiratory syndrome	New coronavirus	2012	Kuwait, Oman, Qatar, Saudi Arabia and Spain
E. coli infection	O104: H4 bacteria	2011	Denmark, Germany, Poland, Switzerland, the UK and the United States
Schmallenberg virus infection	Schmallenberg virus	2011	Belgium, France, Germany, Italy, Luxembourg, Netherlands and the UK
H1N1 A Influenza	H1N1 A influenza virus	2009	China, Japan, Mexico and the United States
SARS	SARS coronavirus	2002	32 countries including Canada, China, Singapore, Vietnam, et al.
West Nile virus	West Nile Virus	1999	Africa, Australia, Greece, Israel, Romania, United States, Middle East, West Asia and Venezuela
Highly pathogenic avian influenza	H5N1 A influenza virus	1997	Worldwide
Nipah virus encephalitis	Nipah virus	1994	Bangladesh, India, Malaysia and Singapore
Brazilian hemorrhagic fever	Sabia virus	1994	Brazil, the United States, and other South American countries
Bolivian hemorrhagic fever	Machoupo virus	1994	Agua Kerala Bolivia, Las Mocas, Youtiaoer and Yue Teer
Hantavirus pulmonary syndrome	Hantavirus	1993	The United States

occurred in Canada, and the mortality rate associated with this disease is nearly 60%. Forty-five cases, and 30 deaths have occurred in China. Existing experimental data have shown that H5N1 viruses with three to five mutated amino acids could be spread in aerosols to mammals.

In 2003, the SARS coronavirus crossed the species barrier and spread from wild animals to humans, infecting 8422 people worldwide. Of these, 916 died, resulting in a mortality rate of 10.9%. A total of 32 countries and regions were affected, causing huge economic losses and widespread social panic [36].

In 2009, a mutant H1N1 influenza virus (a complex recombinant of swine, poultry and human influenza viruses) began to spread. By 27 November 2009, at least 7826 people had died from this disease worldwide. In mainland China, a total of 54927 confirmed cases of H1N1 and 16 deaths were reported in 31 provinces and autonomous regions [37].

In 2013, the H7N9 avian influenza virus first began to infect people in eastern coastal areas of China, including Shanghai, Jiangsu, Zhejiang, Beijing, Henan, Shandong, Anhui, Jiangxi, Hunan, Guangdong, Fujian and Taiwan. By March 2014, a total of 379 cases of human infection of H7N9, including 80 fatal cases, were reported in China, with an associated mortality rate of 21%. According to the Chinese Ministry of Agriculture, the H7N9 avian influenza cost the livestock industry 80 billion RMB [38].

2.3 Continuing threats of foreign zoonoses

As a consequence of frequent international travel, livestock trading and the migration of migratory birds, the major zoonoses that have not yet occurred in China, including the Hendra, Nipah and West Nile viruses and mad cow disease could enter China at any time (Table 1).

In recent years, mad cow disease (bovine spongiform encephalopathy) from the UK and other European countries has appeared in Japan, Korea, Hong Kong, Taiwan and other countries near China [39–41]. Hang-Nipah encephalitis, first reported in Australia in 1994, appeared in Malaysia in 1998 and then in Bangladesh in 2001, with continuing outbreaks in recent years and an associated mortality rate as high as 74%. Rift Valley fever has also continued to spread, with epidemics occurring since 2006 in Kenya, Madagascar, Somalia, Sudan, and Tanzania [42].

West Nile virus first occurred in 1937 in the West Nile Basin of Uganda. The mortality rate associated with this disease has been 3%–5%. In 1999, the West Nile virus occurred in the Western Hemisphere, with the first reported case in New York. By 2004, the West Nile virus had spread throughout the United States, and 5387 cases and 243 deaths were reported in 2012 [43]. In recent years, this disease has continued to occur in Russia and India. Antibodies to this virus have been detected in birds in Xinjiang, China.

Ebola virus disease (formerly known as Ebola hemorrhagic fever) is considered to be one of the most acutely potent infectious diseases, with a mortality rate of 25%–90%. There is no treatment for this disease and no known methods of preventing its occurrence [44,45]. In 1976, this disease appeared for the first time in the Republic of Zaire (now known as the Democratic Republic of the Congo), and a further eight reported outbreaks have occurred there since. In 2011, one case of Ebola virus infection was reported in Uganda. By the end of 2012, 32 people had been infected and 22 people had died. It is noteworthy that Ebola virus disease was originally endemic only in Africa. However, one case occurred in the Philippines in 2009. By November 2012, a total of 2382 people had been infected worldwide, and 1586 people had died. In March 2014, WHO was notified of an outbreak of Ebola in Guinea. The outbreak began in Guinea in December 2013 but was not detected until March 2014, after which it spread to Liberia, Sierra Leone, and Nigeria, and over 1000 people had died of this disease by the end of August in West Africa [46,47].

Middle East respiratory syndrome is an acute respiratory infection caused by a novel coronavirus. In June 2012, a 60-year-old Saudi man was infected with the virus and died in the Netherlands [48]. In September 2012, a Qatari man seeking medical treatment in the UK was diagnosed with this disease [49]. Since September 2012, a total of 178 cases of Middle East Respiratory Syndrome confirmed by a coronavirus infection test had been reported worldwide, including 75 fatal cases [50,51].

2.4 Impact on food safety

Zoonoses represent another important pathway by which the transmission of foodborne diseases can occur. According to the WHO, one third of the population in developed countries is affected by foodborne diseases each year, and over 1.5 million people worldwide die annually from diarrhea-related diseases induced by foodborne pathogens, most of which are considered to be zoonotic.

In recent years, meat, eggs, milk and other animal food products have been contaminated in China and other countries, and 70% of the documented cases were caused by pathogenic pathogens. Data from the Chinese Center for Disease Control and Prevention showed that 506 episodes of food poisoning occurred in China in 2007. One hundred and fifty nine of these cases involved 7790 people and were caused by pathogenic microorganisms. According to the bulletin of the General Office of the Ministry of Health, 174 public health emergencies related to food poisoning were reported in 2012 in China with 6685 people affected and 146 deaths. A total of 56 cases involving 3749 people with 16 deaths were caused by pathogenic microorganisms. Currently, brucellosis and tuberculosis have become the most important pathogens associated with food security in developing countries.

2.5 Increased risk of bioterrorism

Bioterrorism is the deliberate or threatened use of biological factors (including viruses, bacteria, fungi and biological toxins) that can cause death or disease in humans, animals or plants, to pressure governments, civilian authorities or other agencies to achieve political or social objectives [52]. Since the September 11 attacks in the United State, potent pathogens have become important potential weapons, and terrorists have repeatedly attempted to launch bio-terrorist attacks.

In 2001, *Bacillus anthracis* powder was mailed to institutions in the United States resulting in 16 confirmed infections, five suspected infections and five deaths. On 17 April 2013, a mail screening agency outside of the White House intercepted mail addressed to President Barack Obama containing a suspicious substance. According to representatives of the Federal Bureau of Investigation (FBI), this suspicious package contained ricin.

In China, bioterrorism has become a real threat. On the eve of the Beijing Olympics, the East Turkistan separatist activists attempted to use botulinum toxins to launch a terrorist attack. Around the time of the 60th National Anniversary, the “Xingjiang Acupuncture Incident” caused widespread social panic and rioting [53].

The list of international verified biological weapons includes 58 types of potential biological agents, 28 of which are zoonotic pathogens. The outbreak of SARS, the spread of avian influenza and super pathogens, current research on artificial bacteria and artificially modified viruses and biosecurity issues are of increasing concern.

3 Main factors increasing the risk of zoonotic disease

3.1 Global warming increases the occurrence of insect-borne zoonoses

The continuing degradation of the ecological environment has become an important factor in the spread of various infectious diseases. Global warming allows many pathogens and hosts to be more active, as the destruction of river ecosystems boosts the reproductive rate of mosquitoes, leading to significant changes in the distribution and ecology of populations of pathogens, vectors and animal hosts. With increasing density of insect vectors and intermediate hosts, the breeding and reproduction season is extended, and the occurrence and prevalence of the disease has expanded and continues to expand [2].

Deforestation, the development of human settlements and mining are important factors that promote the transmission of vampire bat rabies to humans in the Amazon basin. The destruction of the bat’s habitat led to an outbreak of Nipah disease in Malaysia. The arenavirus from South America is also a new pathogen associated with the development of new human settlements. The emergence of Lyme disease in the United States is related to deforestation and the return of ticks and other insect vectors.

The destruction of forest ecosystems, the shrinking of wildlife habitats and the disrupted wildlife food chain has forced wild animals to migrate from the depths of the forest to the edge of the forest, increasing their chance of coming into contact with humans, domestic animals and insect vectors. Desertification and a rapid increase in the number of marmots are the major causes of the ongoing plague epidemic in Qinghai Province, China. Environmental pollution has produced a large variation in the range of pathogens. The emergence of multi-drug resistant super bacteria is a consequence of continued pollution of the environment with antibiotics.

3.2 Globalization increases the risk of the spread of zoonoses

With the development of globalization, convenient and accessible modern means of transport allow cross-border transportation of animals and animal products from different countries and regions. However, inadequate inspection and quarantine regimes can lead to a failure to prevent the spread of diseases, increasing the risk of transmission of zoonotic diseases by long-distance transport.

In recent years, international travel has grown by more than 10%, and revenue from tourism in just two African countries, Kenya and Tanzania, is approximately $500 million every year. However, insufficient numbers of health personnel involved in eco-tourism have increased the possibility of the spread of zoonoses. In this context, a regional epidemic can rapidly become a global epidemic, and an epidemic occurring in one country can rapidly spread to other countries.

3.3 Changes in rearing methods affect the spread of zoonoses

With economic and social development, livestock industries in many developing countries are in transition. The increase in the number and types of animals reared for food production and the widespread application of artificial feed and pharmaceutical chemicals promotes stress-induced mutations of pathogenic microorganisms, thus favoring the spread of zoonoses.

Since the reform of the agricultural market in China began in the mid-1980s, livestock production has accelerated, intensified and industrialized. However, various rearing models, including the self-sufficient backyard poultry model and different intensive models will continue to exist for a long period of time. Most backyard rearing households have deficient production facilities, extensive feeding conditions and poor management. In backyard rearing, the shed and the house are connected, and people often live in the same area as their animals. Consequently, animal diseases pose a threat to human health. Meanwhile, the development of production and management is not synchronized. Livestock production in China has reached or exceeded the levels found in certain developed countries or regions. However, the management of these facilities does not match that of developed countries, resulting in high morbidity and mortality, and resultant difficulties in preventing and controlling zoonotic diseases. Moreover, the overuse of antibiotics in animal feed has promoted bacterial resistance.

3.4 Urbanization enhances the opportunity for the spread of zoonoses

With the acceleration of urbanization, the size of the urban population has rapidly increased. The practice of local slaughter, cold chain transportation and cold meat consumption is still common, and its many disadvantages and traditions are difficult to change. The trade and transportation of livestock across the country occurs frequently, increasing opportunities for the spread of zoonoses.

The annual international trading volume of live wildlife consists of approximately 40000 primates, four million birds, 670000 reptiles and 350 million tropical fish. The SARS outbreak was caused by the hunting of wild animals. The outbreak of plague in Qinghai in July 2009 was closely associated with the hunting of local marmots.

In China, certain populations consume live animals and wildlife. Therefore, live animal markets for livestock and wild animals will continue for the foreseeable future. However, the management of live animal markets is inadequate. The unlawful slaughter of animals in certain areas has become extensive, making these regions a significant source for the spread of zoonoses. The prevalence of avian influenza and anthrax in China is closely related to the live poultry trade and illegal slaughter of cattle and sheep.

3.5 Disruption of the environment affects the spread of diseases with natural foci

In nature, diseases that occur within a population of wild animals have natural foci, and are usually spread only among animals. However, people can be infected when entering these areas. The geographical area where the disease is found is the natural focus region. In these regions, natural conditions ensure the survival of the animal source of infection and the propagation and cycling of the pathogen in animals. Foci with small ranges or individual foci are defined as epidemic sites, whereas foci with large ranges or several foci connected to one area are known as epidemic regions. Because of the different habitats and diverse environments of wild animals, pathogens found in these animals (e.g., parasites, bacteria, chlamydia and viruses) are extremely complex. Ecological destruction, changes in the environment and climate, rapid population growth, the over-exploitation of natural resources and deforestation are major causes of the spread of wildlife pathogens to humans. The destruction of wildlife habitats disrupts the food chain, forcing animals to migrate from the depths of the forest to the edge of the forest for food, which increases their risk of coming into contact with humans, domestic animals and insect vectors and promotes the emergence of new zoonoses. It has been estimated that 61% of 1415 confirmed human infectious diseases are zoonotic [54]. Of the 335 infectious diseases occurred between 1940 and 2004, 60.3% are of animal origin and 71.8% of these diseases first occurred in wild animals, including Hendra, highly pathogenic avian influenza, mad cow disease, monkeypox, Nipah, West Nile virus, SARS, and Type A influenza, most spread from animals to humans.

3.6 Pets have become an important source of zoonoses

Domestic animals and humans have coexisted for a long time. In addition to traditional species such as dogs and cats, wild animals such as monkeys, rats, lizards and snakes have become common pets. However, inadequate monitoring of these pets for zoonoses, insufficient immunization, and close contact between people and pets have greatly increased the risk of the spread of zoonoses to humans. The spread of zoonoses from pets to humans is not uncommon. For example, rabies is often transmitted to humans by dogs or cats. Cat scratch disease caused by Bartonella occurs when a human is bitten or scratched by a cat, and toxoplasmosis is closely related to contact with cats. Monkeypox, which is similar to smallpox, emerged in the midwest of the United States and is transmitted by pet prairie dogs.

4 Control strategies and measures

The Chinese national medium- and long-term plan for animal epidemic prevention (2012–2020) noted that the control of zoonoses should focus on management of the diseases at their source and integrated control [55]. China should follow a similar strategy to prevent the occurrence and development of zoonoses and establish a disease prevention mechanism to prevent human disease in animals [55]. Starting at the animal source, we should enhance our awareness, strengthen management, improve regulation and rely on science to prevent and control zoonotic diseases.

4.1 Enhance awareness and prevent and control at the source

The primary duty of veterinarians has changed from controlling significant traditional animal diseases to strengthening management, improving laws and regulations and preventing and controlling animal diseases to promote the health of animals and humans and ensure food safety. Currently, two misunderstandings are widespread. First is the belief that the prevention and control of animal disease is the responsibility of the agricultural department only. The agricultural department primarily deals with the safety of animal husbandry. However, the prevention of zoonotic diseases also relates to public health, human health and the global economy. Second is the mistaken belief that zoonotic diseases and veterinary medicine are two independent divisions of science. Therefore, it is recommended that awareness of animal disease be enhanced, that the prevention of human diseases in animals be established and that the prevention and control of zoonoses occur at their source.

4.2 Improve regulations and commit to preventing and controlling zoonoses by law

To prevent and control zoonoses at their source, it is recommended to further study, develop, supplement and improve the relevant laws and regulations. For example, laws and regulations can be improved by referring to the International Animal Health Code and general international practices. The epidemic reporting system of the Ministries of Health and Agriculture should be improved. The prevention and control of zoonoses should be ensured from a legal perspective.

4.3 Improve mechanisms and strengthen management

The prevention and control of zoonoses is a systematic project that requires unified management by the government and the cooperation of multiple sectors, disciplines and systems. The regulatory functions related to animal health and animal-derived food safety are scattered throughout many departments, including the Ministry of Health, the Ministry of Agriculture, the State Forestry Administration and the State Administration of Quality Supervision. These institutions must be centrally managed to establish an efficient general health epidemic prevention system that is integrated with human medicine and veterinary medicine. Training of qualified personnel in relevant departments must also be strengthened. Especially for the currently EVD outbreak in West Africa, we should be prepared for the infectious disease import, including the reservation of appropriate human and material resources.

4.4 Strengthen relevant research for scientific prevention and control

Top-level research on zoonoses should be conducted at the national level to promote the application of advanced and practical scientific and technological achievements. In basic research, studies of pathogen ecology and warning models should be conducted. Studies should also be conducted on basic scientific problems such as the cause of high variability in viruses, the mechanisms of cross-species transmission and multiple drug resistance, virus-host interaction and the traceability of pathogens. Research on diagnostic techniques should focus on the development of rapid and high-throughput diagnostic reagents. Research on vaccines should focus on the development of new low-cost and efficient vaccines, such as oral vaccines and virus-like particle-based vaccines. Ebola virus eVP24 counters cell-intrinsic innate immunity by selectively targeting PY-STAT1 nuclear import while leaving the transport of other cargo that may be required for viral replication unaffected [56]. Mechanism analysis of VP24 provides a new way to fight against the virus. New technologies based on protecting agents and adjuvants should also be supported. Finally, biosecurity should be enhanced. The patterns and characteristics of zoonoses should be studied, the source of infection should be eliminated, the transmission of diseases should be interrupted, populations of susceptible hosts should be controlled, surveillance measures should be strengthened and the emergence and recurrence of new zoonoses and the importation of foreign zoonoses should be strictly prevented.

Acknowledgements This work was supported by Consulting Research Project of the Chinese Academy of Engineering (NY3-2014), the National Key Technologies R&D Program (2013BAD12B04), Governmental Public Welfare Research Special Funds for Agriculture (201303042 and 201103032) and the National High Technology Research and Development Program of China (2012AA022006).

Compliance with ethics guidelines Songtao Yang, Yuwei Gao, Jun Qian, Quan Liu, Xuexing Zheng, Hualei Wang, Zhiping Xia and Xianzhu Xia declare that they have no conflict of interest or financial conflicts to disclose.

This article is a review and does not contain any studies with human or animal subjects performed by any of the authors.

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