### **MEDICINE**

Yang Haifeng

## RISK FACTORS OF TRANSBOUNDARY SPREADING OF INFECTIOUS DISEASES

Yang Haifeng, professor, Shanghai Institute for European Studies, China

#### INTRODUCTION

Environment is an unexhausted source of the microbes causing the diseases of humans, animals and plants. In spite of the obvious success in fighting against infectious diseases (worldwide abolition of smallpox, rinderpest, abolition of smallpox in some continents), new and relapsed infections still appear.

The World Health Organization (WHO) considers the infectious diseases as worldwide the second leading cause of mortality and the first cause of preliminary mortality. In accordance with the estimation of the WHO, 2 billions of people are fallen ill with infectious diseases and 17 million of them die. 50 thousand daily lethal outcomes are the result of infectious diseases, and the half of the world population are under the risk of endemic diseases (1)

Considered risks are related also to preserved in time the natural and the anthropogenic factors: natural disaster, activation of human invasion in the environment.

For instance, the world experts in healthcare and agriculture (UN Food and Agricultural Organization (FAO), World Organization for Animal Health, European Food Security Association (EFSA)) have the greatest concern a possibility of emergence of foci or spontaneous occurrence of such diseases as SARS, MERS, Avian Influenza, Ebola Fever, Rift Valley Fever and other severe fevers, Brucellosis, Bluetongue, Foot and Mouth Disease (FMD), vesicular diseases etc., and moreover, discovering

increased number of registered cases of new species of the famous diseases, resistivity of diseases to pharmaceuticals (5, 10); the typical examples are SARS, E. Coli  $(O_{197})$ .



The main reason of social vulnerability to biological agents is that the system of medical and sanitary diagnostic and prevention is not able currently to reveal it in time and to take necessary preventive measures.

The experts of biological security emphasize following the main sources of biological hazards:

- epidemy and outbreaks of infection/emergent diseases;
  - epizooty;

- epiphytoty;
- accidents and diversions in the biologically dangerous objects;
  - natural reservoirs of the pathogenic;
  - biologic terrorism/agroterrorism;
  - using a biological weapon.

Currently, no country is able sufficiently to prevent bioterrorist hazard. By the WHO, the world public healthcare system hardly fights against naturally emerged infections.

Accordingly to the WHO's recommendations, it is required to focus on the education of the staff on the program including limited but correctly selected group of biological agents. It allows to create required potential to fight against wider spectrum of pathogens (31).

Meanwhile, in past 10-15 years many countries have been reasonably included the element of a hazard of biological terror and agroterror into the urgent response plan.

By the expert, the terroristic use of the agents of emergent infections is very dangerous. The experts estimate that the mankind knows not more than several percent of existing viruses and slightly more bacteria, and the nature offers permanently new pathogens. In the past 40 years 30 new infection agents were discovered, including viruses HIV, Marburg, Ebola. There are no methods of treatment and prevention for these diseases. Such new and re-emerged pathogens as West Nile Fever, drug-resistant *Streptococcus*, *Staphylococcus*, and *Mycobacterium tuberculosis* can also be dangerous biological agents.

Besides, due to genetic mutations, there is a danger of breakthrough of interspecies barrier (the problem of Avian and Swine Influenza). Annually, the experts note increased amount of the virus diseases spreading in the developing countries. Meanwhile, emergency, change of pathogenicity and privilege of the most dangerous virus diseases in the animal population evoke an apprehension of the leading world epidemiologic institutions due to a possibility of causing significant economic harm to agro-industrial complex, and using as the act of biodiversions (2).

Regarding to the Congressional Research Service, if the terrorist could emerge an epizooty, damage to the US economy would be \$10 to \$30 billion taking into account that 1/6 of the US GDP and 1/8 of all workplaces are related to the agriculture. And the losses could raise up to \$140 billion taking into account inevitable decline of the agriculture product export.

Agroterrorism is dangerous not only due to the damage to the agriculture and the commerce. One of the consequences of outbreak of infections, even not transmitted to humans, is decrease of the business activity in the affected country or region and decrease of travel industry. For example, the foot-and-mouth epidemic raged in the United Kingdom did not threaten people directly but collapsed the travel industry – the losses were estimated at \$5 billion. Total UK losses were estimated at more than \$10.5 billion (by other sources - \$24 billion) (8, 11, 12). In 2003, China suffered of the outbreak of SARS related to the intake of the meat of exotic animals, and the harm was estimated at \$7.6 billion of direct losses and 2.8 million workplaces in the travel industry.

Systematic organizing of the international meetings on the control of emergent diseases (the annual IMED conference, Vienne, Austria) (40) confirms increased attention of the veterinary and medical services of the developed countries to emergence and spreading of the vector-borne diseases, including zoogenous, in some countries and in Europe and the North America, particularly. The experts associate the emergence of new and exotic animal and human diseases in mentioned above countries with changing the distribution area of general vectors due to climate changing and expanding of trade and economic relations of the countries. Particularly, the board of the World Organization for Animal Health (OIE) supposes that one of the basic reasons of infection expansion is so named "5T" factor (trade, tourism, transporting, travelling, terrorism). Herewith, bringing of new infectious pathogens can result in negative consequences. As an example, the situation with West Nile Fever in the USA, where the infection carried recently from the East Coast to almost all country, and at the moment 2 million people are infected (41).

Thus, general world epidemic condition is considered as difficult. Forecast data shows increased biological hazard, high level of risk of outbreaks and epizooty. Expanded economic, commercial and touristic relations between countries, increased transportation considerably increase the possibility of bringing and spreading of the most dangerous human, animal and bird diseases. Biological security and bioprotection are the most important international problems of implementation of a concept of assessment and management of biological risks during work with pathologic biological agents. Laboratory diagnostic and control level have a crucial importance for prevention of expansion of the infectious diseases of humans and animals.

# INTERNATIONAL CO-OPERATION IN BIOLOGICAL SECURITY

This section presents the main participants of implementation of the project of biosafety in the world.

First of all, it needs to outline the international organizations the World Health Organization (WHO) (23), the UN Food and Agricultural Organization (FAO) (24), International Atomic Energy Agency (IAEA) (38), International Federation of Biosafety Associations (IFBA) (39), the Global Partnership against the Spread of Weapons and Materials of Mass Destruction (45), the World Organization for Animal Health (OIE) (21), that focus on research/examination or extermination the diseases as tuberculosis, avian influenza, pox virus, plague, tularemia, cholera, rinderpest etc., and implement the projects WAHIS (47), EMPRES-i (35), Health Map (37), Global Framework for Progressive Control of Transboundary Diseases (20) etc. The projects are implemented in many countries worldwide, including the countries of Africa, developing countries.

Additionally, it need to mention several interstate unions and associations (40): European Food Security Association, International Society for Infectious Diseases, the Program for Monitoring Emerging Diseases, EcoHealth Alliance, European Centre for Disease Prevention and Control, European Society of Clinical Microbiology and Infectious Diseases. Also, the projects "Increasing biosafety and bioprotection in the South Caucasus and the Central Asia", Animal Health and Welfare Panel (AHAW) (22).

The big projects of biosafety in European countries include the United Kingdom with their positive experience (Food and Environment Research Agency, FERA), Slovakia (Food research institute, NPPC), France (International institute of agriculture research (CIRAD), Integrated Laboratory Quality System (IQLS)), Netherland (Royal Tropical Institute) etc. The projects are implemented in many countries of the world including the South Caucasus and the Central Asia.

Additionally, it needs to be noted the certain role of the USA. Following American institutions take part in the projects of biosafety: American Biological Safety Association (ABSA), US Department of Agriculture, Agricultural Research Service (ARS), Center for Disease Control and Prevention (CDC), USAID; following divisions of the US Department of Defense have leading positions:

Walter Reed Army Institute of Research;

- US Army Medical Research Institute of Infectious

Diseases;

- Uniformed Services University of the Health Science;

- Naval Medical Research Institute:

Defense Threat Reduction Agency – DTRA.

All mentioned the US institutions implement The Cooperative Biological Engagement Program (CBEP) in cooperation with the WHO, FAO, OIE and European Committee for Standardization (CEN).

The project CBEP is the part of The Nunn-Lugar Cooperative Threat Reduction Program (CTRP). The USA makes annual assignment of \$200 to \$250 million (16-19).

The purpose of the project CBEP is a reduction of threats related to dangerous pathogens and diseases, raw materials, possibility of using the bioagent for terror purposes. To implement these tasks, they identify, dispose, prevent sale, theft, distribution and/or use of the biological weapon, means of its delivery, and also the equipment, technology ad infrastructure, that could be used to create a biological weapon. The project CBEP has both external section and internal section as well that intended to perform the measures in the territory of the USA exclusively.

By the statements of the international society and the USA, implementation of the projects of biosafety in different countries result in understanding of the significance of the problem by all involved institutions, consolidation of efforts of the international authorized organizations and national departments, reduces markedly the level of biological hazard related to spreading and transboundary bringing of the pathogens.

In the same time, following questions are should be considered: were whether all declared purposes of the projects of biosafety implemented in fact; do whether the early warning system, international notification, quarantine and prevention of transboundary infection spreading work effectively; and are whether all the statutes of the international veterinary law respected as the officials of USA and some international organizations state?

#### **FAST FACTS**

In this section the information about veterinary ill-being due to some animal diseases (notified in the OIE) and related zoonoses in countries of the Northern America and European Union was studied. For this purpose, the data of epizooty situation in the USA and the

countries of EU (excluding mini-states and island states) for 2010-1015 were analyzed (46).

Additionally, the figures of import of livestock production delivered from the USA to other countries were analyzed (25-30). Following countries are the biggest importer of the US products:

- 1. Canada purchases: goat/lamb, bovine meat, other meat, poultry, processed meat, fur/skin;
- 2. PRC purchases: meat production, poultry, processed meat, furs and skins;
- 3. European countries (Denmark, Italy, Spain, Ireland, Poland, Netherlands, Germany, Finland, Hungary, Croatia, Sweden, the United Kingdom, Iceland, Swiss, Ukraine, Slovakia, Norway, Portugal, Belgium) purchase: goat and lamb meat, meat production, poultry, processed meat, furs and skins;
- 4. Countries of the Middle and Asia-Pacific region purchase: goat and lamb meat, meat production, poultry, processed meat, furs and skins;
- 5. Countries of Latin America purchase: goat and lamb meat, bovine meat, other meat production, poultry, processed meat, furs and skins.

It needs to be noted, that the US authorized veterinary bodies do not offer in all cases the data regarding exact amount of annually registered infectious foci that should have international notification to the international organizations. For example, officially, there are some animal diseases and zoonoses in the USA and they are registered annually, but OIE is not informed with exact data. Among the disease, these are as common diseases for different kinds of animals (Anthrax, Aujeszky's disease (pseudorabies), Paratuberculosis, Trichinellosis, West Nile Fever, Q-Fever,), as bovine diseases - Bovidae (Bovine tuberculosis, Infectious Bovine Rhinotracheitis), small ruminants diseases - Ovidae и Capridae (Maedi-Visna Virus), horse diseases - Equidae (Eastern Equine Encephalitis Virus, Equine Infectious Anemia, Equine Viral Arteritis, Equine Hrepesvirus-1 Infection, Epiozootic Cough of Horses), bird diseases - Aves (Infectious Laryngotracheitis, Infectious Bursal Disease, Infectious Bronchitis, Newcastle Disease) etc.

The hazard related to import the special dangerous diseases with imported breeding stock, sperm and other production is the main among others that could result in significant economic losses. Due to the swine breeding is the one of effectively developing branch of farming, the alive pigs could be the potential source of

bringing the originators of different dangerous and emergent diseases into the territory of importing country.

Considering the above, the question is "Where the facts of moving of live animals, products of animal origin, biological materials from the USA to European countries followed by the identification of causative agents of animal diseases?" Yes, they were. Even not so long ago...

In this section it is necessary to pay attention to the disease as Porcine Epidemic Diarrhea Virus (PEDV). PEDV is emergent disease that prevails in many countries; it has such clinical signs as weakness, diarrhea attacks. Only young pigs in the first days of life suffer the illness. The lethal outcome is observed in 80-100% of cases (42).

According to available data, epizooty of PEDV widely developed in the United States in 2013-2014 (7, 9). The epidemic process involved the swine breeding complexes of 27 (30, according to other sources) states; the epizooty killed at least 10% of pig population in the country (44, 50). By various sources, damage to the US livestock industry ranged from \$900 million to \$1.8 billion (6).

In addition, the epizooty of PEDV extended in 2014 to the territory of the EU countries (Germany, Netherlands, France, Belgium, Austria) and Ukraine (14).

The studies conducted in the OIE and EU reference laboratories for animal diseases, located in Weybridge and Pirbright (UK), have shown 100% affinity of agents PEDV samples (2014) in Europe and previously studied strains of originator of the disease, selected in the United States in 2013-2014 (4, 15).

Further, it is possible to mention one emergent infection. A certain danger for the EU is Seneca Valley fever (SVV-001), as it is a new disease, and it was not recorded in the EU countries up to 2014. Seneca virus was identified in first tiem in the United States in 1988 (36), but till now it has little studied (49). 12 serological isolates (43) was identified since the discovery in 1988 (43). The natural hosts of the virus are pigs and cattle. Seneca virus infection followed by registered death of 20-80% of newborn piglets.

Seneca virus transmission mechanisms are poorly understood. It is not known whether the virus of Seneca Valley fever is capable spreading by direct contact with infected animals or by mechanical and aerosol routes (48).

The studies of SVV-001 and closely-related isolates indicate that Seneca virus prevails in the United States widely. The isolates detected in the states: Illinois, Indiana, Florida, Iowa, Ohio,

California, Louisiana, Minnesota, New Jersey, North Carolina, South Dakota, where the virus could spread to Canada, Brazil, Australia, New Zealand and Italy (2014-2015) (34). In the summer 2015, increased occurrence of Seneca virus cases was noted compared to previous years.

Additionally, data for violations of sanitary norms by the United States were obtained. For example, one of the most dangerous quarantine objects, a corn rootworm (Diabrotica), imported from the United States in the former Yugoslavia, was recently detected in Poland, Ukraine and Belarus (13, 32). According to the phytosanitary experts, the annual damage of the EU agricultural due to the quarantine pest is not less than \$250 million (13).

#### **CONCLUSION**

It needs to note, that the US treat the international sanitary standards regarding to PEDV and SVV-001 as the disease with an optional notification, due to the fact that they are not in the OIE' list of notified diseases for the United States and Canada (3). And the United States and Canada have their separate list of notified diseases? But there are International Health Regulations. Or veterinary experts in the USA treat it as it is beneficial to them?

A certain danger associated with bringing PEDV pathogens and SVV-001into Europe is just the fact that the disease is not notified. The USA keeps silence about the presence of originators of viral infections in livestock production.

The clinical signs of the Seneca Valley virus are identical to signs of vesicular disease (swine vesicular disease, vesicular stomatitis, swine vesicular exanthema and FMD) (49). The latter infections are more dangerous exotic animal diseases, causing economic damage to livestock, agriculture and meat industry.

At the same time, according to the Animal and Plant Health Inspection Service, USDA, in the summer of 2015 there was the outbreak of vesicular stomatitis which affected 722 farms. Confirmed cases have occurred in eight US states: Arizona, Colorado, Nebraska, New Mexico, South Dakota, Texas, Utah, and Wyoming (33).

The questions arise: "Could the Americans have missed something?" – They could theoretically! - "Whether the EU can in such a case be brought a pathogen of vesicular stomatitis?" - In theory, they can!

In addition, the clinical signs of the Seneca Valley virus infection in pigs are similar to the symptoms of swine epidemic diarrhea, deltacoronavirus infection of pigs, transmissible gastroenteritis of pigs, rotavirus and Clostridia infections.

Despite the fact that Seneca Valley virus in pigs is not considered an infection that reduces the performance, the similarity of its symptoms with other highly dangerous diseases makes to treat it with caution. It is necessary to carry out epidemiological investigations for each case with respect to exotic animal diseases, and this should be done as quickly as possible to prevent bringing the vesicular diseases (34).

Thus, the above facts indicate that the USA do not comply the quarantine regulations and requirements of biosafety in transboundary movement of live animals and products of animal origin. Risk of import of the originators of vesicular diseases and coronavirus infections with live pigs and various kinds of pork products into the territory of the EU is still high, even if the effective control of imported material is implemented.

It should be noted that some researchers suggest spreading some infectious disease in the territory of the EU with the factor that promoted bringing the agents of viral diseases of animals was the delivery of products from the United States by air and by sea, through the major European trade routes (for example, Rotterdam, Hamburg and etc.).

As a result of conducted analytic investigations, the following conclusions were made. In the context of export-import trade transactions to supply live animals, animal productions, biological material from the United States, a non-compliance to the European internationally-assigned standards of quarantine measures may potentially cause bringing from the USA the agents of the following infections: Aujeszky's Disease (pseudorabies) (in a number of European countries), Bleutongue virus (EU nonrelevant serotypes), vesicular stomatitis, cattle viral diarrhea (EU nonrelevant genotypes), coronaviruses pig disease, EU nonrelevant virus strains of low pathogenic and highly pathogenic avian influenza, and other emergent diseases.

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