

Commentary

Emerging Zoonoses: the “One Health Approach”

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Zoonoses represent a public health risk recently pointed out by the spreading of previously unknown human infectious diseases emerging from animal reservoirs such as severe acute respiratory syndrome and avian influenza caused by *H5N1*-virus. These outbreaks have shown that animal breeding activities can pose a significant public health risk. Until now, the risk of zoonoses has probably been underestimated, particularly in occupational settings. The emergence or re-emergence of bacterial (*Mycobacterium bovis* and *Brucella spp*) or viral (*hepatitis E virus*) infections shows that zoonoses should be considered as emerging risks in agricultural and animal breeding and should be addressed by specific preventive interventions. Close cooperation and interaction between veterinarians, occupational health physicians and public health operators is necessary, for a worldwide strategy to expand interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment. This is what the One Health Approach was intended to be.

Key Words: Biological risk, Agriculture, Zoonoses, Emerging and reemerging zoonoses

According to the World Health Organization (WHO, <http://www.who.int/topics/zoonoses/en/>), a zoonoses can be defined as “any disease or infection caused by all types of agents (bacteria, parasites, fungi, viruses and unconventional agents) transmissible from vertebrate animals to humans and *vice-versa*”. During recent decades, the public health risk represented by zoonoses was suggested by the onset of outbreaks and epidemics of previously unknown human infectious diseases that emerged from animal reservoirs such as Ebola virus, West Nile virus, Nipah virus, Hanta virus, Creutzfeldt-Jakob disease.

More recently, severe acute respiratory syndrome (SARS), highly pathogenic avian influenza (HPAI) viruses [1] have shown that biological agents and animal breeding activities can pose a significant public health risk, because several animal infectious diseases are not only endemic but also epidemic-prone, such as leptospirosis, brucellosis and rabies [2]. Therefore, these agents can potentially cause epidemics at any time. In this light, we can affirm that the risk of zoonoses, particularly in occupational settings, has been probably underestimated in past years. This has been highlighted by epidemics that originated from the animal breeding sector, and, in some cases, from specific and identified animal breeding and feeding modalities.

The example of HPAI clearly shows that any emerging disease may rapidly, for several reasons, become endemic, causing a public health concern. Therefore, emerging and re-emerging diseases represent priorities for prevention and the creation of an early warning system that is specifically targeted

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Table 1. Factors affecting infectious disease emergence

Factor	Specific factor	Disease emergence
Ecological changes	• Climate change • Changes in water ecosystems • Deforestation/reforestation • Flood/drought • Famine	• Rift Valley fever • Argentine haemorrhagic fever, Hantaan or Korean haemorrhagic fever • Hantavirus pulmonary syndrome in the southwestern United States of America
Human behavior international travel and commerce	• War • Population migration (movement from rural areas to cities) • Economic impoverishment • Urban decay • Factors in human behaviour (such as the commercial sex trade, outdoor recreation and activities...) • Worldwide movement of goods and people • Air travel	• HIV and other sexually transmitted diseases • Dengue • Rat-borne hantaviruses • Introduction of cholera into South America, dissemination of O139 (non-O1) cholera bacteria (via ships)
Technology and industry Developments (food)	• Globalization of food supplies • Changes in food processing and packaging	• Food production processes: haemolytic uraemic syndrome certain <i>Escherichia coli</i> strains from cattle contaminating meat and other food products), bovine spongiform encephalopathy, Nipah virus (pigs), avian influenza, severe acute respiratory syndrome (probably)
Technology and industry Developments (health care)	• New medical devices • Organ or tissue transplantation • Drugs causing immunosuppression • Widespread use of antibiotics	• Ebola • HIV • Creutzfeldt-Jakob
Microbial adaptation and change	• Microbial evolution as a response to selection in the environment	• 'Antigenic drift' in influenza virus • Possibly genetic changes in severe acute respiratory syndrome, coronavirus in humans • Development of antimicrobial resistance (HIV, antibiotic resistance in numerous bacterial species, multi-drug-resistant tuberculosis, chloroquine-resistant malaria)
Breakdown of the host's defenses	• Immunodepression • Immunodeficiency resulting from HIV infection	• <i>Mycobacterium bovis</i> • <i>Listeria monocytogenes</i> in humans
Breakdown in public health or control measures	• Lack of or inadequate sanitation and vector control measures	• Tuberculosis (mainly in the United States of America) • Cholera in refugee camps in Africa, resurgence of diphtheria in the former Soviet republic and Eastern Europe in the 1990s

HIV: human immunodeficiency virus.

at predicting the risk of an epidemic or at least at detecting early signs of its onset.

Prevention is based on knowledge, but very often the processes by which zoonoses emerge and re-emerge are complex and poorly understood [3], mainly because a single event, or a chain of events, that promote the emergence of a disease and/or its evolution into an endemic disease, often vary on a case by case basis, and are affected by several factors such as genetic evolution, environmental conditions, climate changes affecting the vector's distribution, demographic changes, movement of animals, etc. [4]. Predicting which zoonotic diseases may

emerge, or become endemic, is extremely difficult due to the multifactorial and constantly evolving nature of the risk factors involved (Table 1), with the exception of vector-borne infections, whose onset, due to their correlation with environmental factors, can be, in some aspects, anticipated [5].

The size of the problem is significant: according to Cunningham [6], about 61% of the several diseases attributable to human pathogens are zoonotic. Since an emerging zoonoses is a disease that is newly recognized or newly evolved, or that has occurred previously but shows an increase in incidence or in geographical expansion, host or vector range, it is evident

that these diseases might not be easily recognized at their first manifestation, and might be public health risks, as confirmed by epidemiological data suggesting that about 75% of emerging infectious diseases are zoonotic, and originate mainly from wildlife [7].

Based on the above considerations, it can be easily argued that the list of more than 200 zoonoses known, in some cases for many centuries, might be increased by the number of the new emerging and re-emerging ones. Each emergence or re-emergence may pose a public health risk that deserves particular attention from the public systems of research and prevention. Several human occupations require contact with animals and some selected workers' subgroups are particularly exposed to the zoonotic risk. Such risk should be considered and addressed in risk assessment and management activities. Among occupational groups at risk are workers in contact with living animals such as veterinarians, animal farmers, zoo workers, fishermen, fish farmers, hunters, animal trainers, animal sanctuary workers, animal cruelty inspectors; workers in contact with animal carcasses and products (slaughtermen, butchers, meat inspectors, fishmongers, food industry and catering workers); workers who have laboratory exposure to infectious specimens (medical laboratory workers, animal researchers...); and finally workers who have environmental exposure such as agricultural workers, forestry workers, sewage workers or outdoor activity instructors, guides, and park keepers.

In this paper we have selected specific examples of animal infectious diseases that are transmissible to humans and the related causal factors, not with the aim of doing an exhaustive review, but with the aim of identifying cases exemplifying the current situation.

In some cases, at the basis of the disease's emergence, there are increases in the density of animal or wildlife populations associated with intensive breeding methods for domestic animals, and proximity with human and animal populations caused by growth of the human settlements [8]. Examples diseases are *Mycobacterium bovis* (*M. Bovis*), *Brucella spp.* or *Francisella tularensis*' infection in cattle breeders.

In developing countries, as reported by Kock et al. [9] in Africa, the close contact between human and livestock populations have led to major health problems, and in particular to the creation of a cycle of degradation and disease affecting especially traditional pastoral systems with a close physical association between people, livestock, and wild animals. An example is the recent outbreaks of *M. bovis* in wildlife in Kruger National Park, whose onset originated from an infected cattle herd [10].

As for new viral pathogens with animal origins, *hepatitis*

E virus (HEV) is responsible for many sporadic waterborne cases and epidemics around the world, as confirmed by the case of the Cruise Ship "Aurora", which took place in in 2008 [11]. HEV infection may be asymptomatic in industrialized countries, where it can be considered quite rare, with a tendency toward an increase, possibly mediated by migration flows from endemic countries [12]. Consumption of raw meat of infected animals, in particular pigs, as well as occupations involving contact with pigs or biologic pig materials have been identified as possible routes of transmission. Different studies have shown that in swine workers the prevalence of subjects with detectable serum anti HEV immunoglobulin G (IgG) is higher than in general population [13], but data regarding seroprevalence might be affected by the different kits used for the analysis, showing significant variability in levels of sensitivity. Therefore, the real incidence of HEV infection in the general population and among workers cannot be estimated yet and further research is needed. Collecting this information is also particularly important because HEV might have a dramatic impact on human health, and in particular in pregnant women. During a HEV outbreak among a group of displaced persons in Darfur, Sudan, 253 HEV cases were recorded in a 6-month period. Among them, 61 were pregnant women, and in this subgroup 19 (31.1%) died from the infection.

Regarding ecological factors, it seems that a milder climate due to global climatic change may be followed by an increase in the areas of distribution of major disease vectors, i.e., ticks and mosquitoes, together with an increase in areas already colonized, in the number of vectors. Moreover, milder climatic conditions prolong the seasonal period of activity of vectors and hence the period in which pathogen transmission can take place. An increased number of vectors in areas where wild and cash animals are currently present increases the possibility of transmission of wild animal diseases to domestic animals and bring wild animal biological agents to agricultural settlements, places where the presence of the risk is not anticipated and therefore not addressed by any preventive intervention. Specific examples of the association between climate changes and zoonoses are the recent emergence of arthropod-borne infections like the tick-borne encephalitis virus (TBEV) group of *encephalitis*, *Lyme borreliosis* and *Coxiella burnetii*, the agent of Q fever, infections and anaplasmoses [14]. It is easily arguable that these diseases might pose a risk to agricultural workers.

An ecological factor having a significant impact on biological risk is represented by the fast degradation of the natural environment and, in particular, deforestation affecting developing countries. In fact, deforestation forces wildlife species to move to new areas, sometimes into suburban zones, increasing

the possibilities of contact with humans, cash animals and pets [15], with a risk of transmission of wildlife infections to these animals and possibly to humans. A similar impact on public health is due to human behavior, and in particular to animal population or repopulation strategies based on the introduction of selected animal species in specific areas for promoting fauna diversity or for hunting purposes [16]. In line with the health problems related to species migration or introduction in new areas, there is species translocation among continents, often accompanied by the movement of infectious agents, which may lead to unexpected exchanges of genetic material. For example, it seems that in the 1980s, a commensal *E. coli* of the human intestine acquired an aggravated pathogenic capacity becoming verocytotoxic (*E. coli* O157:H7), due to an exchange of genetic material with a bacteria from the *Shigella* genus.

Environmental pollution may expose wildlife species to infectious agents that can be disseminated. Open-air landfill sites, manure dispersal and, more recently, the attitude of some breeders of wasting in the environment without costs, the carcasses of the animals sacrificed in as preventive measure against bovine spongiform encephalopathy diffusion, represented very good opportunities for foxes, stray dogs, prey birds as well as marauders, especially seagulls, to pick up and disperse pathogenic agents, such as enterobacteria, mycobacteria, brucellas and other biological agents [17].

Mycobacterial infection is still a prevalent problem in cow breeding enterprises, as demonstrated by several reported outbreaks such as, the recent ones of *M. bovis* observed in the region of Lombardy (Italy) with a report of 37 cases from 2006-2008 (Table 2). Taking into account that the Mycobacterial infection can be transmitted to humans, these data clearly demonstrate that *M. bovis* is still an occupational problem in developed countries.

Zoonoses are also suspected to bring about an increased risk of cancer, as suggested by some epidemiological data signifying that veterinarians, meat inspectors and slaughterhouse

workers experience an increased risk of myelolymphoproliferative disorders attributed, by epidemiological studies carried out in the eighties, to contact with animal oncoviruses [18]. The data still needs to be confirmed, but we note that a potential exposure to zoonotic viruses is present in the agricultural environment. Examples of these viruses are herpes, a causal factor of Marek's disease in poultry, Avian Leukosis, and papilloma in cattle. Moreover, the rapid expansion of information on retroviruses indicates that other zoonoses viruses will be identified. Identification of the Bovine Leukemia virus as the etiologic agent of the adult form of bovine Lymphosarcoma has also been made. Other viruses to be addressed by research belong to the genera Alpharetrovirus, Betaretrovirus, Gammaretrovirus, and Deltaretrovirus. All of them have been identified as causes of malignant diseases in animals. The Jaagsiekte Sheep Retrovirus and Enzootic Nasal Tumor Virus also deserve attention [19].

The idea that slaughterhouse workers should be considered as a group particularly at risk has been presented in the recent report of an outbreak of peripheral neuropathy observed in pig abattoirs [20]. Between November 2006 and May 2008, two swine abattoirs from Minnesota and Indiana were affected by a subacute neurological syndrome. The two workers had an occupational exposure to aerosolised porcine brain. The neurological disorder described seems to have an autoimmune origin in response to multiple aerosolised porcine brain tissue antigens; the pattern of nerve involvement suggests a vulnerability of nerve roots and terminals where the blood-nerve barrier is most permeable.

In some countries, the re-emergence of bacterial zoonoses may be due to a lack of surveillance or a lack of appropriate control measures by public services [21]. This can involve an occupational issue. It can be easily assumed that when agricultural workers are not involved in health surveillance protocols, or existing health surveillance protocols do not take into account biological agents, the risk of zoonoses is higher. Occu-

Table 2. Tuberculosis outbreaks in the region of Lombardy (from 2006 to 2008)

Year	Outbreaks (n)	Place of detection	Origin of infection	Type of putting down	<i>M. bovis</i> isolation	Outbreak type
2006	14	12 slaughterhouse 2 farm	13 unknown 1 introduction	5 stamping out 9 selective	13/14	All closed
2007	11	10 slaughterhouse 1 farm	11 unknown	5 stamping out 6 selective	11/11	All closed
2008	12	10 slaughterhouse 2 farm	11 unknown 1 correlation	1 stamping out 4 selective	12/12	All closed

M. bovis: *Mycobacterium bovis*, selective: only affected animals put down, stamping out: all animals of the livestock farm put down, All closed: outbreaks restricted to the place of onset.

pational risk also increases when governments lack resources to enforce hygiene or security standards in slaughterhouses or shelters, leading to an increase in cases of brucellosis, Q-fever or anthrax among workers during certain periods or in specific countries.

Finally, it must be taken into account that most occupational risks are reported in agriculture, an area where under-reporting of occupational diseases is well known. This includes occupational zoonoses, and can lead to underestimation of the real burden of disease attributable to biological risk in agriculture. Agriculture represents a good model to explain this trend. In fact, the agricultural sector is characterized by small size and family-run enterprises. This leads to a difficult evaluation of the exposures and a lack of health surveillance of the workers. The experience of our center, the International Center For Rural Health, fully supports this claim. For example, a case of “Milker’s Nodule” was observed in a young cow milker. The man came to our attention through a medical examination performed as part of a program of periodical health surveillance at the workplace. During the patient’s examination, a 1×1 cm papule at the 4th finger of the right hand, characterized by light rose-yellowish color, surrounded by an erythematous area was noticed. The patient told us that he and his colleagues had already suffered from the same symptom several times, and was well aware that the disease comes from cows. Therefore, after a consultation with the veterinarian in charge of the breeding farm, we knew that an epidemic of the cow parapox infection was present at the farm. In collaboration with the veterinarian, we diagnosed the parapox virus lesion (“Cow Milker’s Nodule”) (Fig. 1). The lesion disappeared spontaneously, as anticipated, but the preventive intervention by us and the veterinarian avoided any further infection in animals and/or workers. This example shows that some zoonotic diseases can actually be transmitted from animals to workers, and *vice versa*, and that the ability to detect early signals is fundamental in prevention. In this case, the signal was not detected early [22].

Another interesting finding of our center comes from

the evaluation of the immune system function in cow and pig breeders. The study showed a statistically significant increase in serum concentrations of tumor necrosis factor (TNF)- α , interleukin (IL)-8 and IL-10 and total serum proteins compared to non-breeders, suggesting a condition of immune activation in animal breeders, which might be indicative of contact with different biological agents [personal unpublished data].

Based on our experience and on a literature review, zoonoses should be considered as an emerging risk in agriculture and animal breeding and should be addressed by specific preventive interventions, in particular, by an early and accurate detection of new outbreaks of epidemic diseases, including emerging zoonoses. The ability to understand the underlying causes of the emergence of diseases and the ecology of the agents and their hosts is urgently needed. Fulfilling these needs is the only way to support an effective prevention or a rapid containment of possible emerging events.

The only promising approach to adequately tackle the problem is the creation, of adequate systems for early detection warnings, to interpret them and to prepare adequate control measures. Since health risks in agriculture and animal breeding affects animals, workers and consumers, and prevention involves several different disciplines, it is evident that a holistic approach is needed, in which all the factors of prevention in agriculture are involved.

In this light, the concept, defined as the “One Medicine” by Schwabe [23], has seen an unprecedented revival in the last decade and has evolved towards “One Health” conceptual thinking, emphasizing epidemiology and public health [24].

This approach is the key to defeating emerging and re-emerging zoonoses at the interface between the health of humans, animals and the ecosystem. It supports and legitimizes improved cooperation between animal, public and environmental health. It also gives rise to a new call for the strengthening of animal and human health systems, without which diseases cannot be controlled or defeated [25].

Regarding the collaboration between different disciplines,

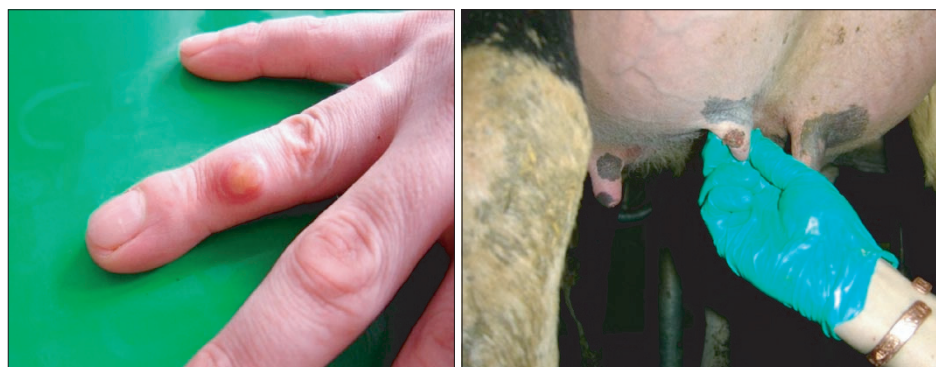


Fig. 1. Pseudopoxvirus infection in human and in cows. The diagnosis was reached in close collaboration with the agricultural enterprise veterinarian.

it is important to mention Rudolf Virchow (1821-1902), the German physician and pathologist, who, in the last century said that “between animal and human medicine there are no dividing lines-nor should there be. The object is different but the experience obtained constitutes the basis of all medicine” [26]. Virchow was not only the founder of (or ‘father of’) comparative medicine but he also coined the term “zoonoses”.

Today there is still no generally accepted definition of One Health. The American Veterinary Medical Association (AVMA), Food and Agriculture Organisation (FAO), Office International des Epizooties (OIE), WHO, the United Nations Children’s Fund (UNICEF), and The World Bank in their “Strategic Framework on One Health” established in 2008 that One Health is: the collaborative efforts of multiple disciplines working locally, nationally and globally to attain optimal health for people, animals and environment [27]. However, this definition has not been unanimously accepted, as some consider that it is too broad since it includes environmental health.

In conclusion, what is important to highlight is that the “One Health” concept is a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment. However, the “One Health Approach” remains little known outside of special sectors and institutions concerned with infectious diseases and especially zoonoses.

National and regional public health sectors should give priority to surveillance systems and enhanced diagnostics regarding emerging pathogens. A broad collaboration among clinicians, public health workers, veterinary medicine and veterinary public health officials is necessary for prompt response strategies ensuring the prevention and management of such infections [28]. Moreover, developed countries should invest in the establishment and strengthening of surveillance systems in resource-limited countries, considering the international significance of emerging zoonoses. Based on the new international health regulations, emphasis should be to build the appropriate awareness and response capacity in all countries and on promoting interdisciplinary collaboration and coordination. Integrating the early warning systems of international organizations should be undertaken to facilitate the detection of outbreaks of communicable diseases of international public health importance [6]. Finally, the reduction of zoonotic risks in farms should be a priority in order to improve the overall health of humans and animals. To achieve this purpose a close cooperation and interaction between veterinarians, occupational health physicians and public health operators is necessary.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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