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Title: Reducing hazards for humans from animals: emerging and re-emerging zoonoses

Short running head: Reduce zoonosis hazards for humans from animals

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Abstract

Pathogens able to infect more than one host, more than one taxonomic order and wild hosts, present all a higher relative risk of (re-)emergence. A long environmental persistence gives pathogens a more selective advantage. In case of emerging and re-emerging zoonoses, the infection prevalence in animals and exposure determines the incidence of human cases. The human exposure to zoonotic agents depends on lifestyle and occupation (e.g., veterinarians and farmers are more at risk for livestock zoonoses). Raising awareness, providing information on prevention and the application of biosecurity are essential. Moreover, a substantial decline in the incidence of human disease implies the prevention, the control or the elimination of zoonoses from the animal compartments. The only way to prevent health hazards is to adapt the existing systems of health governance at world, regional, national and local levels in a harmonised and coordinated manner. To achieve such a goal, the One Health strategy was recently developed to expand interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment between veterinary, human medical, public health professionals and stakeholders.

Keywords: Zoonosis, Emerging disease, Re-emerging disease, Human, Animal, Prevention, Control, Biosecurity

The aim of this short review is to present how to reduce hazards for humans from animals, especially for emerging and re-emerging zoonoses. For this purpose, factors of (re-)emergence were presented followed by some considerations concerning the role of the animal compartment in the decrease of human cases of zoonoses, the biosecurity and education programs.

Case definitions

The most appropriate definition of a zoonosis seems to be the one suggested by Teufel specifying that ‘zoonotic agents are infectious [transmissible] agents which are not only confined to one host but which can cause an infection [infestation] (with or without clinical disease) in several hosts including humans’ (Teufel et Hammer, 1999). On the other hand, all diseases affecting animals and humans are not strictly zoonotic but could be qualified as common: both animals and man generally contract the infection from the same sources (soil, water, invertebrate animals and plants), however, animals do not play an essential role in the life cycle of the etiologic agent, but may contribute in varying degrees to the distribution and actual transmission of infections (Acha et Szyfres, 2005). According to the World Organization for Animal Health (OIE), 75% of the emerging diseases find their origin in domestic or wild animals, which prompts for a close collaboration between animal and public health authorities[1]. To achieve such a goal, the One Health strategy was recently developed to expand interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment[2]. Such collaborations are particularly evident when considering zoonoses.

[1] http://www.oie.int/eng/edito/en_edito_avr09.htm
[2] http://www.onehealthinitiative.com/mission.php

Emerging infectious animal diseases (EIDs) have taken a growing importance these last decades because some of them are zoonoses (Saegerman et al. 2011). Several definitions of an emerging disease coexist (e.g. Pattison, 1998; Center for disease control and prevention, 1998; Brown, 2001; Morse, 2004) but with a common denominator (Saegerman et al., 2007). An emerging disease is a disease of which the true incidence increases in a significant way in a given population, in a given area and during a given period, in comparison with the usual epidemiological situation of this disease (Toma et Thiry, 1999).

Factors of (re-)emergence

The increase in true incidence is due to several factors such as the evolution or the modification of a pathogenic agent or an existing parasite, which results in a change of host, of vector, of pathogenicity or strain (Morse, 1995). Specific social, ecological, climatic, environmental or demographic factors contribute to the emergence of a disease (Wittmann et al., 2001; Morse, 2004; Slingenbergh et al., 2004; Weiss ans McMichael, 2004), but it is difficult to establish a ranking of causes and of mechanisms (Rodhain, 2003). However, pathogens able to infect more than one host (which, for human diseases, includes all zoonoses), more than one taxonomic order, and pathogens infecting wildlife hosts, all have a higher relative risk of emergence than pathogens with more restricted host ranges (Cleaveland et al. 2001). Moreover, pathogens resisting a long time in the environment have a more selective advantage.

The world is confronted with new epidemiological risks because of, among other factors, climatic changes, human demographics and behaviour, economic development and land use (e.g. the increasing demand for arable land and pastures and the development of urban and peri-urban animal production), poverty and social inequality, and events related to globalisation of trade in animals and animal products (**Table I**) (Saegerman et al., 2011).

There is some evidence supporting the impact of climate change on the occurrence, distribution and prevalence of livestock diseases (e.g. Woolhouse and Gowtage-Sequeria, 2005; Purse et al., 2005; Woolhouse, 2008; Gale et al., 2009). However, when trying to disentangle the effect of climate change and other possible causes of disease upsurge, it is often the case that social and economic factors, including trade and travel, play a much more important role (e.g. Simulo et al., 2007 and 2008). It is therefore inappropriate to use only climate-based models to predict the incidence of a future disease (Reiter, 2008). In fact, understanding the mechanisms that underlie newly emerging and re-emerging infectious zoonoses is one of the most difficult scientific problems society must face today (King, 2008), despite the fact that different models designed to help understanding this phenomenon have been developed in recent years, e.g. a model of ecological continuum between host and pathogen (**Figure 1**) (Daszak et al., 2000), a model improving clinical detection of rare events (Saegerman et al., 2003) and a convergence model of zoonotic diseases (King, 2004).

If we want indicators of risk, and a system to monitor how such indicators change over time, we need to construct quantitative models relating risk factors (temperature, land cover, human behaviour, etc.) to outcomes (disease case numbers). Therefore, we need a good understanding of the epidemiological processes at the origin of introduction, installation and spread of diseases. We need disease surveillance systems with a high sensitivity for the detection of suspect cases, and a high specificity for diagnosis. We also need prioritization of diseases affecting food-producing animals, wildlife, pets and novel pets, including zoonoses (e.g., Humblet et al., 2012; Martin et al., 2012).

Stakeholders involved in animal health and disease surveillance must be aware of these issues. Therefore, training courses must be adapted to prepare veterinary, human medical, public health professionals and stakeholders to play their role in disease prevention, control and surveillance.

Pathogens of humans and domestic animals

In their review, Cleaveland and collaborators identified 56.5% (N = 800) as being zoonotic, after listing 1,415 pathogens infecting humans and their domestic mammals (**Table II**) (Cleaveland et al., 2001). A previous study focusing on recorded events of EIDs highlighted that 60.3% of these diseases were indeed zoonoses (Jones et al., 2008).

In the group of zoonotic pathogens, it is of major importance to consider both emerging agents (e.g. SARS, Nipah virus, hantavirosis, new variant Creutzfeldt-Jakob disease) and re-emerging diseases (e.g. rabies, bovine brucellosis and bovine tuberculosis).

RNA viruses are more likely to emerge than DNA viruses mostly because they present a higher mutation rate (nucleotide substitution) and are more easily transmissible across species and orders (Cleaveland et al., 2001 and 2007).

The temporal evolution of EIDs suggests they will preferentially be vector-borne diseases (e.g. tick-borne encephalitis, West Nile fever) and pathogens resistant to classical treatments (e.g., Methicillin-resistant *Staphylococcus aureus*) (Jones et al., 2008). The majority of EIDs events originate in wildlife because of inter-species transmission (e.g. Lassa fever, Ebola, SARS) and are increasing significantly over time (Jones et al., 2008; Merianos, 2007; Marston et al., 2012). Although they can arise anywhere in the world, the promiscuity between humans and animals is one of the main risk factors (King , 2008). In addition, some EIDs may also emerge in old (leptospirosis, leishmaniosis) and new companion animals (tularaemia, monkey poxvirosis) (e.g. Avashia et al., 2004; Azad, 2004).

Emerging infectious animal diseases represent health, as well socio-economic, international, biological, partnership and media challenges. There is thus a need to develop new educational programmes, new disciplines and new research themes in epidemiology, microbiology and infectiology of EIDs. Moreover, the problem being global, these solutions must be adapted to various ecological and socio-economic contexts, including those found in less developed countries. Veterinary, agronomic and medical know-how are resources and assets required to take up these challenges.

Reducing hazards for humans from animals

A growing public interest exists in the prevention and control of new pest and disease introductions (Waage and Mumford, 2008). For example, many EIDs related to wildlife are caused by highly pathogenic agents (e.g. haemorrhagic fevers like Ebola and Marburg, encephalitis like Nipah) (Merianos, 2007). Preventing the occurrence of such diseases requires higher levels of biosecurity, and thus, appropriate training in medical and veterinary schools and universities, but also general information for all people and precautions to minimize the risk of zoonotic diseases. The reduction of hazards must imply collaborations between the main actors involved in animal as well as human health.

Several actions can be taken and should be carried on in parallel:

- The collection and dissemination of information;
- The use of general precaution;
- The improvement of biosecurity;
- The prevention and control;
- The heatlh governance (One Health approach).

Collecting and disseminating information

Numerous websites allow gathering information on human diseases and/or animal diseases and zoonoses. They provide data on ongoing disease events or periodic summaries of disease statuses around the world (compiling information on morbidity and mortality rates). An overview of pertinent websites is presented in **Table III**. Their data are easily accessible (free of charge) and should be disseminated. The frequent consultation of such sources of information allows being updated on the evolving situation of EIDs, which is crucial from a prevention point of view.

Using general precaution

General precautions to minimize the risk of zoonotic diseases are listed in **Table IV**. Furthermore, some categories of persons are particularly at risk regarding emerging, and especially re-emerging diseases: YOPI's, stating for Young, Old, Pregnant and Immunodeficient. Additional precautions should be taken by persons with weakened or compromised immune systems. For example, several diseases have recently seen their incidence considerably increase among immunodeficient individuals, e.g. tuberculosis *(*Kasprowicz et al., 2011*)*, cryptosporidiosis (O'Connor et al., 2011) and parasitic infections (Lloyd-Smith et al., 2008).

Some EIDs are related to an occupational exposure, e.g. Q fever among veterinarians (Bosnjak et al., 2010) or hantavirosis in employees of forest industries (Crowcroft et al., 1999). Professionals at risk must be advised and should take precautions to reduce the risk linked to their exposure. The constantly increasing contacts with nature (and water), within the frameworks of recreational activities, represent a risk for contracting infectious diseases related to wildlife. For example, the incidence of leptospirosis contracted through recreational exposure has considerably increased in the recent years (Monahan et al., 2009). In order to reduce the risk of illness, knowledge of potential risks before engaging in any risky activity is important.

Improve biosecurity

The international definition of biosecurity in the domain of animal health is quite broad (World Organization for Animal Helath, 2008): Biosecurity is the implementation of measures that reduce the risk of introduction (bio-exclusion) and spread of disease agents (bio-containment); it requires the adoption of a set of attitudes and behaviours by people to reduce risk in all activities involving domestic, captive exotic and wild birds and their products.

Recently, such biosecurity approach was implemented at the Faculty of Veterinary Medicine (University of Liege) (http://www.fmv.biosecurity.ulg.ac.be). It allows also all actors of the Faculty and its clinics to protect themselves against the risk of bio-contamination but also favour the protection of environment (management of biological waste) (**Figure 2**).

Biosecurity includes different activities, such as education programme, vaccination, quarantine, surveillance, slaughtering, indemnification, cleaning and disinfection, each needing detailed explanations on the concept, design and implementation.

Any recommended biosecurity measure must consider the socio-economic realities of those who will implement it. In terms of epidemics, spread matters as much as the initial disease introduction and local installation. Biosecurity is one of the key pillars in slowing disease spread. Each measure must be practical and sustainable for all stakeholders – producers, traders, intermediaries and service providers and all those pursuing activities that may contribute to the dissemination of pathogens (Food and Agricultural Organisation, 2008). The fundamental principles of biosecurity are the following:

- Biosecurity is about reducing the risk of introduction and spread of infection;
- Actions of people are fundamental in applying biosecurity;
- Biosecurity consists of three major stages – segregation, cleaning and disinfection – segregation being the most effective and disinfection the least effective.

In addition, a greater focus on international cooperation to deal with threats at source and a commitment to refocus biosecurity on building resilience to invasion into agrosystems rather than building walls around them are recommended (Waage and Mumford, 2008). The information, awareness and training should begin at each school or university involved in the training of veterinary, human medical, public health professionals and stakeholders (e.g. Colorado State University, 2008).

Prevention and control

The prevention of zoonotic agents relies on a series of measures and behaviours aiming at reducing the risk of disease introduction and spread. According to the pathogen involved, several approaches could be applied, alone or together, such as:

- Awareness campaigns addressed to animal and human health professionals, but also to professionals at risk and the general public, as were mentioned above the increasing interactions between humans and wildlife through recreational activities (Heyman and Saegerman, 2009);
- (Continuing) education for veterinary practitioners, human medical, public health professionals;
- Vaccination of animals at risk (e.g. vaccination of pets against rabies, to prevent the risk of human contamination) or humans at risk (e.g. vaccination of humans against influenza);
- For zoonotic agents, to act on the animal compartment with the view of reducing the incidence of human cases (e.g. bovine brucellosis or bovine tuberculosis) (Saegerman et al., 2010; Ron-Román et al., 2012; Allix-Béguec et al., 2011).

Controlling zoonoses can require the implementation of drastic measures such as the culling or euthanasia of infected animals (e.g. stamping out in a tuberculosis-infected cattle herd, or euthanasia of a rabid dog), the control of animal movements to prevent the spread of infectious agents (e.g. in case of H5N1 avian influenza) or the quarantine of infected facilities, etc.

The prevention and control of zoonoses also implies the communication between animal health and human health professionals. Once a zoonosis is diagnosed in a patient, animal health authorities should be advised rapidly in order to implement the appropriate measures at the animal level. Inversely, any outbreak of a zoonotic disease should be notified as well to human health professionals. Such bilateral transmission of information is crucial and falls within the scope of the 'One Health' concept.

British scientists recently developed an algorithm for early qualitative public health risk assessment to guide risk management (Palmer et al., 2005). **Figure 3** illustrates the methodology applied, which relied on the categorization of the evidence of zoonotic potential into 4 levels. Indeed, in case of an EID event, there is rarely sufficient evidence to make a risk assessment of its zoonotic potential (Palmer et al., 2005).

Health governance

'Global health governance' refers to 'the use of formal and informal institutions, rules, and processes by states, intergovernmental organizations, and non-state actors to deal with challenges to health that require cross-border collective action to address effectively' (Fidler, 2010). The control of emerging and re-emerging infectious diseases requires coordination between national and international authorities; the ability to respond reflects the capacity of a governing system (Prescott, 2007). In the last 20 years, several health crises have revealed the inadequacy of global national health governance. For example, one of the concerns raised during the H1N1 pandemics was the access to vaccines. The failure to prevent HIV/AIDS pandemics and the appearance of antimicrobial resistance also raised the question of global health governance effectiveness (Fidler, 2010).

There is a strong need for increasing the implementation of collective actions for the prevention of emerging and re-emerging zoonotic diseases. One should militate in favour of a strengthening of programmes already in place. Strategies of health governance to face the emergence or re-emergence of zoonotic diseases should be clear and elaborated within the scope of the ‘One Health’ concept, in a concerted action between all partners.

Conclusion and recommendations

Zoonotic diseases create a strong relationship between human and animal health. Wildlife is the main cradle of zoonotic EIDs and would thus deserve additional attention in terms of surveillance, to ensure an early detection of (re)emerging zoonotic events, a potential threat for domestic animal and human health. The awareness of target publics is crucial also in order to reduce the risk for human health.

As detailed above, factors of (re-)emergence are predominantly linked to human activities. From this point of view, biosecurity is one of the key points to ensure the control and prevention of zoonotic (re-)emerging diseases, by reducing the risk of introduction in a free country or the risk of dissemination in case of a disease event. It is necessary, not only to implement biosecurity rules, but above all, it is primordial to ensure they are correctly and strictly applied. Education to the importance of respecting biosecurity measures should be encouraged for all actors involved in animal health.

The recent emergences of zoonoses, such as Q fever and West Nile fever in Europe, and the re-emergence of well-known diseases, such as echinococcosis or bovine tuberculosis also in Europe, have highlighted the need to reassess teaching objectives and contents for the prevention and control of OIE-listed diseases, wildlife diseases and rare events. The amount of subjects increases each year but it is not possible to increase accordingly the time allocated to teaching trainee veterinarians and medical doctors on all these diseases. Therefore, it is crucial for veterinarians and medical doctors to acquire and adopt an adequate mode of understanding of new diseases. Earlier clinical diagnosis, new concepts in infectiology, better skills in entomology, ecology, integrated ecosystem health, epidemiology and risk analysis must be covered. Teaching engineering (e.g. e-learning, skills of evidence-based (veterinary) medicine through case-based disease study or focus-group), and dissemination must be improved (Saegerman et al., 2011 and 2012).

At last, a better communication between human and veterinary health professionals would facilitate an early detection of re(emerging) zoonotic events, or in the animal compartment in case of human disease, or among people in case of animal disease. The reduction of the risk related to (re-)emerging zoonoses passes by an increased collaboration between animal health stakeholders and human health authorities, not only locally, but also at national, regional and international levels.

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Table I. Main factors influencing the emergence of animal diseases according to the period of time (Planté, 2008)

Factor	**2007**	**2017**	**2027**
International travel and commerce	↑	↑↑	↑↑↑
Climate change and weather	↑	↑↑	↑↑↑
Economic development and land use	↑	↑↑	↑↑↑
Poverty and social inequality	↑	↑↑	↑↑↑
Human demographics and behaviour	↑	↑↑	↑↑↑
Breakdown of public health measures	↑	↑	↑
Changing ecosystems	↑	↑	↑
Intent of harm	↑	↑	↑
Lack of political will	↑	↑	↑
Microbial adaptation and change	↑	↑	↑
Technology and industry	↑	↑	↑
War and famine	↑	↑	↑

Table II. Important animal host categories for human and emerging human zoonoses* (Cleaveland et al., 2001)

Host categories	Number of zoonotic diseases (Total=800)	Number of emerging zoonotic diseases (Total=125)
Ungulates	315 (39.3%)	72 (57.6%)
Carnivores	344 (43.0%)	64 (51.2%)
Primates	103 (12.9%)	31 (24.8%)
Rodents	180 (22.5%)	43 (34.4%)
Marine mammals	41 (5.1%)	6 (4.8%)
Bats	15 (1.9%)	6 (4.8%)
Non-mammalian host (include birds)	109 (13.6%)	30 (24.0%)
Birds	82 (10.3%)	23 (18.4%)

Legend: * Host range detailed represents minimums as full host range for many pathogens may not be known. Diseases for which the animal hosts were completely unknown were excluded (n=72 diseases and 8 emerging diseases).

Table III. Overview of some main web sources of information on human and animal infectious diseases and zoonoses

Source of information		**Type of information provided**	**Web Link**
OIE (WAHIS/WAHID)	World Organization for Animal Health (Information system/Information database)	Information per country on the status of listed animal diseases and zoonoses (outbreaks, etc.), control measures implemented per country, etc. Terrestrial Code and Manual	http://www.oie.int/en/
CDC	Centers for Disease Control and Prevention	Information on human diseases and zoonoses	http://www.cdc.gov/
EFSA	European Food Safety Authority	Information on risk assessment regarding food and feed safety (animal diseases and zoonoses)	http://www.efsa.europa.eu/
ECDC	European Centre for Disease Prevention and Control	Information on human and animal diseases, and zoonoses	http://ecdc.europa.eu/en/Pages/home.aspx

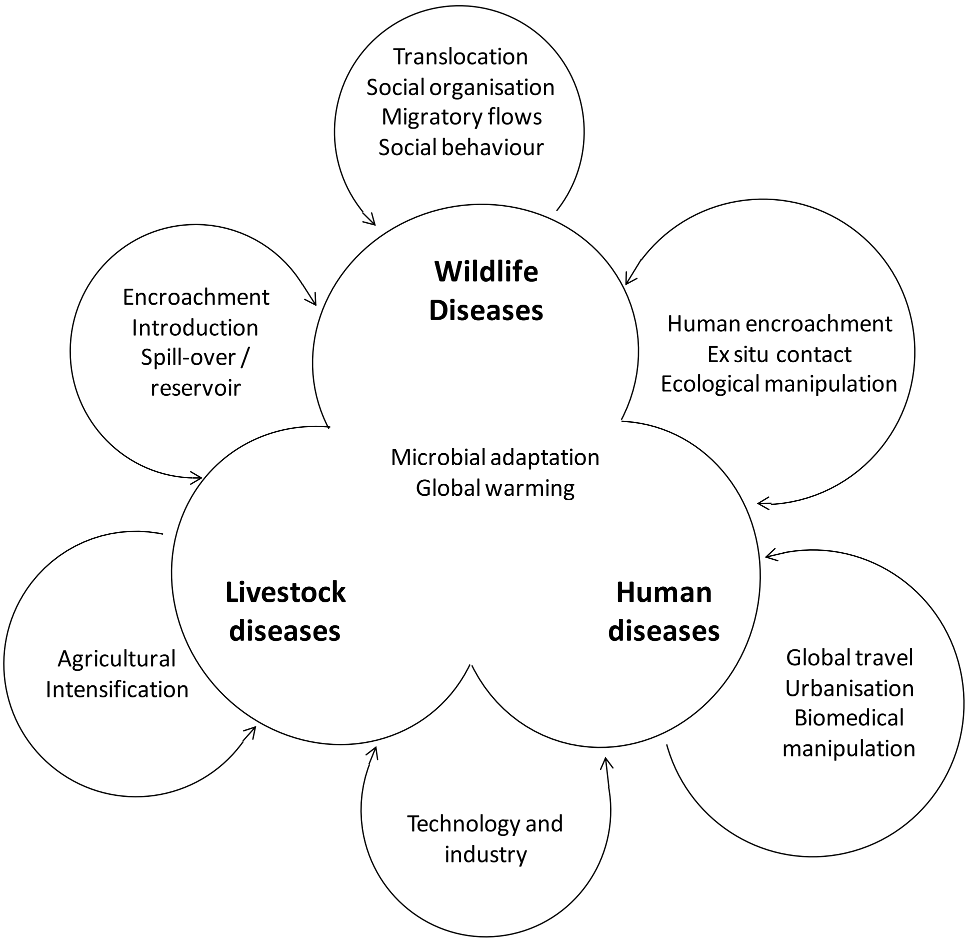
ISID	International Society for Infectious Diseases	E-mail alerts on human and animal disease events in the world (ProMED-mail)	http://www.promedmail.org/
CSFPH (Iowa State University)	Center for Food Security and Public Health	Information on animal diseases and zoonoses (technical factsheets)	http://www.cfsph.iastate.edu/
HealthMap	Children's Hospital Boston	Information on the current global status of human and animal infectious diseases as well as zoonoses worldwide through an automated process (gathered from different sources)	http://www.healthmap.org/en/

Table IV. General precautions to minimize the risk of zoonotic diseases (Center for Food Security and Public Health, 2008).

Hand washing and hygiene ▪ Hand washing is one of the most effective ways to prevent the spread of disease ▪ Use warm water and soap for a minimum of 20 seconds ▪ Antimicrobial hand gels can be effective when hands are not visibly dirty ▪ Wash your hands often ▪ Supervise children to ensure proper hand washing ▪ Avoid direct contact with animal faeces ▪ Clean and disinfect areas accessed by pets
Personal protection while outdoors ▪ Avoid contact with animals or waterfowl ▪ Avoid insect vectors (e.g., ticks and mosquitoes) ▪ Use vector control measures around your home
Food safety ▪ Handle and prepare foods safely ▪ Promptly wash any kitchen utensils, or surfaces that have been in contact with raw meat or eggs
Children and animals ▪ Children, especially those 5 years old and younger, should always be supervised while interacting with animals.
Pet health ▪ Keeping pets healthy can minimize zoonotic diseases ▪ Do not allow pets to interact with wildlife

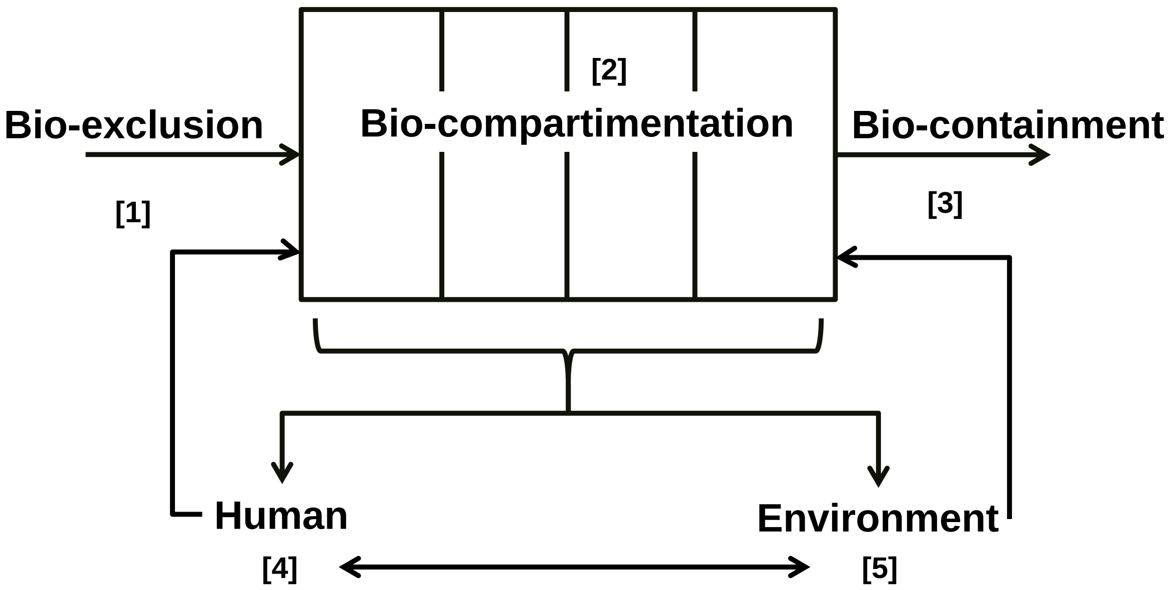
- Do not allow your animal to eat other animal's faeces
- Do not feed raw or undercooked meats to your pet-feed a high-quality commercial pet food

Figure 1. Interactions with zoonotic pathogens within a host-parasite continuum between wildlife, domestic animal, and human populations (Daszak et al., 2000)



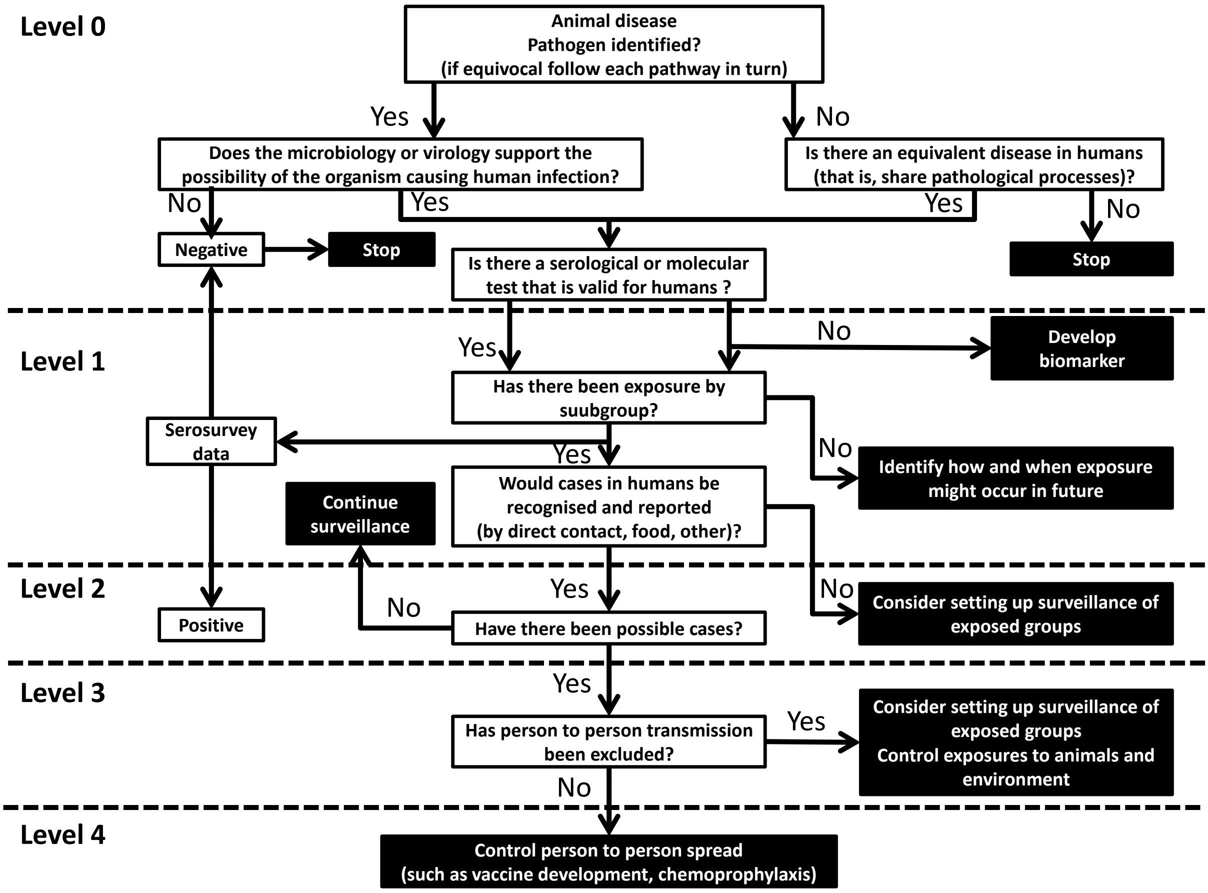
Legend: The host-parasite ecological continuum (here parasites include viruses and parasitic prokaryotes). Most emerging diseases exist within a host and parasite continuum between wildlife, domestic animal, and human populations. Few diseases affect exclusively only one group, and the complex relations between host populations set the scene for disease emergence. Arrows denote some of the key factors driving disease emergence.

Figure 2. Biosecurity principles in animal facility



Legend: All the stages specified in the figure above are part of a biosecurity approach and contribute to the reduction of the risk of introduction and spread of infectious agents: [1] To limit the risk of introduction (bio-exclusion); [2] To limit the spread of the pathogen within the same facility, e.g. by isolating excreting animals (bio-compartimentation); [3] To limit the spread of the disease agent outside the facility (inter-herd transmission) (bio-containment); [4] To prevent the risk of human bio-contamination; [5] To prevent any environmental bio-contamination and persistence of the pathogen. Human can contaminate animals as well (e.g., *Mycobacterium bovis* [Fritsche et al., 2004]). Animals can be re-infected by the contaminated environment, which is especially true for pathogens presenting a long environmental persistence such as *Bacillus anthracis* (Hugh-Jones and Blackburn, 2009) or *Mycobacterium bovis* (Kelly et al., 1978) when ecological conditions are optimal.

Figure 3. Template for qualitative risk assessment of zoonotic potential of animal diseases (Palmer et al., 2005)



Legend: levels 1 to 4 are levels of confidence of risk of zoonotic transmission of animal diseases; Level 1 = Not zoonotic, Level 2 = potentially zoonotic, level 3 = confirmed as zoonotic (human cases reported, but no transmission person to person) and level 4 = confirmed as zoonotic (person to person transmission not excluded).