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Articulation agriculture, public health and environment for the management of risks associated with the food production in the Americas:

Institutional experience for preventing zoonoses and emerging diseases

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SUMMARY

Most emerging infectious diseases are zoonotic and zones of emergence are more likely to be in the tropics, which includes most of Central and South America. Major progresses have been accomplished in the control of zoonotic diseases in these countries, including a 95% decrease in cases of dog and human rabies cases of canine origin over the last 25 years or a significant reduction of cystic echinococcosis. However, many challenges are still present with the large increase in human population and human migration, uncontrolled urbanization, deforestation, encroachment of human populations in wildlife habitat and economic difficulties encountered in many remote rural areas. Such issues are associated with the emergence and identification of new viral (i.e. arenaviruses, arboviruses, hantaviruses, myxoviruses, paramyxoviruses) and bacterial (i.e. Rickettsiae, Bartonellae) zoonotic pathogens. Furthermore, practices such as the wide use of antibiotics for humans and animals, bushmeat consumption, ownership of exotic pets or even blood and organ donations can also favor the emergence of new pathogens. Therefore, it is crucial that local, national, regional and international collaborations between the public sector (i.e. human and animal health, environmental agencies) and the private sector be re-enforced under the guidance of international institutions which warrant the quality of diagnostic tests, surveillance methods and emergency responses to outbreaks. An extensive and innovative education program aiming at local populations living in the poorest areas need to be among the health priorities in order to reduce the risks of exposure to wildlife zoonoses, domestic and exotic pet transmitted zoonoses and food-borne zoonoses.

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INTRODUCTION

Most emerging infectious diseases (EID) are zoonotic, as an estimated 75% of these EIDs are of zoonotic nature (Taylor et al., 2001). Despite their recognition in many developed countries, emerging zoonoses are largely originating in the tropics. Emerging infectious disease origins are significantly correlated with socio-economic, environmental and ecological factors (Jones et al., 2008). Analysis of EID events over the last 40 years provides a basis for identifying regions where new EIDs are most likely to originate (emerging disease 'hotspots'). Particularly, there is a substantial risk of wildlife zoonotic and vector-borne EIDs originating at lower latitudes where reporting effort is low.

The burden of emerging zoonoses on human health and on national and international trade and economy is considerable and has been estimated to exceed 120 US$ billion between 1995 and 2008 (Cascio et al., 2011). According to the World Bank, the direct cost of zoonoses over the last decade has been estimated to be more than $20 billion with over $200 billion indirect losses to affected economies as a whole (Narrod et al., 2012). For example, the emergence of SARS in Asia in 2002-2003 was estimated to have a cost US$ 18 billion in Gross Domestic Product (GDP) in nominal terms (about US$ 2 million per person infected by the SARS virus) and almost US$ 60 billion in overall demand and business revenues, corresponding to about a 2% decline of the regional GDP (Greger, 2007). Similarly, the cost of the BSE epidemic that impacted largely the United Kingdom and Europe, but also several other countries, has been estimated to be more than US$ 5 billion for the UK economy (Cascio et al., 2011; Greger, 2007). The economic burden of cystic echinococcosis, a parasitic zoonosis of major concern in several Latin American countries, has an impact worldwide of 1.2 billion US$ on human health only and a substantial global burden estimated at over 1 million DALYs per year (Brunetti et al., 2011). In Peru, cystic echinococcosis (CE) constitutes an important public health problem with a total estimated yearly cost of human CE of almost 2.5 million US$ (95% CI:1,1-4.8 million) and close to 4 million US$ for direct and indirect livestock-associated costs (Moro et al., 2011). An estimated 1.139 (95% CI: 861-1,489) DALYs (surgical CE-associated disability adjusted life years) were also lost due to surgical cases of CE (Moro et al., 2011). In South America, it was estimated that the viscera of 2 million cattle and 3.5 million sheep are condemned every year, and that the cost of such condemnation (1999) amounts to US$ 6.3 million in Argentina and US$ 2.5 million in Chile (Battelli, 2009). The cost of the plague outbreak (526 human cases notified) in Cajamarca, Peru, in 1994 raised to more than 2.3 million US$ (Modesto et al., 2002). Food-borne diseases are also extremely costly and their importance being better recognized in Latin America. Health experts estimate that the yearly cost of all food-borne diseases in the USA is US$ 5 to 6 billion in direct medical expenses and lost productivity. Infections with the bacteria *Salmonella* alone account for $1 billion yearly in direct and indirect medical costs (CDC).

ANTECEDENTS

Latin America has been impacted by many zoonotic diseases, as most of Latin American countries are located between the tropics, where biological diversity and presence of many insect vectors favor the presence and maintenance of zoonotic pathogens. Similarly, population increase -recently estimated at 580 million including 195 million living in poverty (Schneider et al., 2011) -, deforestation and encroachment in new habitats have led to the spread and emergence of zoonotic diseases. Urbanization is also associated with new modes of food supply delivery and large scale distribution of food products, which can lead to large food-borne outbreaks, such as salmonellosis or campylobacteriosis.

CURRENT SITUATION

If progress has been made in combating specific zoonoses, such as dog rabies, brucellosis, bovine tuberculosis or Chagas disease, emergence of new risks have appeared, such as hantavirus infection, arenavirus infections (Guanarito virus, Sabia virus), or the emergence of visceral leishmaniasis in Brazil and neighboring countries and the spread of West Nile virus to all the Americas. Other well-know zoonotic infections are being under scrutiny, such as plague or echinococcosis, but little is known on the natural pathogens infecting wildlife in many parts of Latin America. Vampire bat rabies, which has been for many year an economical issue in the cattle industry, is on the rise, as the number of human cases is now exceeding the cases related to dog rabies (Schneider et al., 2009). Similarly, the emergence of new wildlife reservoirs of rabies are identified, such as the crab-eating fox (*Cerdocyon thous*) or the marmoset (*Callithrix jacchus*) in Brazil (Favoretto et al., 2006) or insectivorous bat-borne rabies in Chile (Favi et al., 2011). In Brazil, it was shown in the region of Fortaleza (Ceará state) that a close relation exists between humans and their pet marmosets, but these people show minimal knowledge regarding rabies, which represents a greater risk of infection. Of 29 saliva samples collected on pet marmosets, one (3.4%) was positive for direct immunofluorescence test and of the 11 CNS samples, three (27.3%) were positive for rabies (Aguiar et al., 2011). This emerging problem was recently illustrated by the death of a 9 year old boy in March 2012 who was bitten when playing on February 3rd with a pet marmoset and did not have immediate rabies Post exposure treatment (Promed March 14, 2012) . In Chile between 1989 and 2005, out of almost 40,000 samples analyzed, 719 bats, 7 dogs, 7 cats, 1 bovine and 1 human were positive for rabies, showing a significant increase in the proportions of positivity in bats, with predominance of variant 4 between the reservoirs (Favi et al., 2008). These authors properly assessed that "given the complexity of the wild cycle of the rabies in Chile, it is necessary to maintain a program control of rabies, directed to educate people for a responsible possession of domestic animals, due to the risk of rabies transmission from bat to the susceptible species".

New arenaviruses causing hemorrhagic fevers in South and Central America have been discovered, such as the Chapare virus in Bolivia (Delgado et al., 2008). Mayaro virus is another example of an arbovirus endemic to the tropical forests of northern South America and the Amazon Basin, which is emerging with the movement of populations in forested areas (foresters, tourists) (Tesh et al., 1999). Similarly, a new arenavirus was detected from Mexican deer mice (*Peromyscus mexicanus*) captured near the site of a 1967 epidemic of hemorrhagic fever in southern Mexico (Cajimat et al., 2012). The deer mice were infected with a novel Tacaribe serocomplex virus (proposed name Ocozocoautla de Espinosa virus), which is phylogenetically closely related to Tacaribe serocomplex viruses that cause hemorrhagic fever in humans in South America. However, very little is known about vector-borne zoonoses such as rickettsial infections or even *Bartonella* infections other than Carrion disease. Many human cases attributed to *Bartonella bacilliformis* in the Andean countries could be overlooked and caused by other *Bartonella* species, such as *B. rochalimae* which was first identified in an American tourist visiting Peru (Eremeeva et al., 2007) and is highly prevalent in dogs in that country (Diniz et al., 2011).

A major issue with many emerging zoonoses is detection and identification. In many developing countries in Latin America, febrile illnesses, such as dengue viral infections, are common and monopolize the attention of the government health departments. For that reason, even when the conditions of living are similar with children living in proximity to animals such as dogs, cats, opossums, mice, and goats, even with well-documented occurrence of human infections caused by *Rickettsia rickettsii*, Rocky Mountain Spotted Fever (RMSF) is frequently not considered in the differential diagnosis of febrile illnesses (Zavala-Castro et al., 2008). Several spotted fever agents are now reported from Brazil, Colombia, in humans, domestic animals and wildlife (Toledo et al., 2011).

Furthermore, surveillance of animal disease and zoonotic disease in animals is often not legally mandated to the same extent as in humans, particularly in wildlife (Vrbova et al., 2010). This lack of a legal mandate, structured reporting mechanism and funding often means that emerging infectious diseases (EID) surveillance attempting to include animal and human data are challenging to design, interpret and operate. The significant investments being made in EID surveillance makes the evaluation and design of EID surveillance systems of prime importance. In the analysis by Vrbova et al., (2010), most surveillance systems were from North America (40%) and Europe (29%) with very little from South and Central America (Table 1). Most systems (70%) were designed to detect 'known' pathogens, followed by systems targeting both known and unknown pathogens (22%), and the least (8%) for only unknown pathogens. The proportion of systems focusing on unknown pathogens was much higher in North America (45%) than in Europe (20%). The systems primarily examined human data (56%), followed by animal data (25%) with the least evaluating both human and animal data (19%). These authors concluded that:"currently, few human or animal health agencies have an explicit mandate to compare animal and human disease data in a 'one health' manner. Without formal legislation, these 'integrated' surveillance systems will remain in the hands of key motivated individuals, susceptible to disuse or complete collapse if these individuals take on new responsibilities or leave their positions".

Table 1: Emerging zoonoses surveillance systems by continent (n = 221), pathogen(s) under surveillance, type of data collected and number of diseases under surveillance (Vrbova et al., 2010)

	No. systems for known and unknown pathogens (n = 190)			No. systems collecting human and animal data (n = 194)			No. systems collecting one disease versus multi-disease data (n = 216)		Total no. systems included (n = 221)
Continent of system [a]	Only known pathogens	Only unknown pathogens	Both known and unknown pathogens	Human data	Animal data	Human and animal data	One disease	Multi-disease	Total
Africa	8	0	0	4	3	4	7	4	11
Asia	11	1	3	11	0	1	8	8	16
Australia and Oceania	13	0	2	9	4	4	6	12	18
Central and South America	3	0	0	2	0	1	1	2	3
Europe	48	1	11	30	24	7	26	35	63
North America	41	11	23	46	16	15	21	65	88
International [a]	12	2	4	7	2	4	6	14	21
Unknown	0	0	1	0	0	0	0	1	1
Total [b]	136	15	44	109	49	36	75	141	221

[a]Continent of a system was determined by the country in which the system was located, systems spanning more than one country (even on the same continent) were classified as International.

[b]Totals for the systems by pathogen(s) under surveillance, type of data collected and number of diseases under surveillance do not always add to 221 because of missing values.

Some evident successes

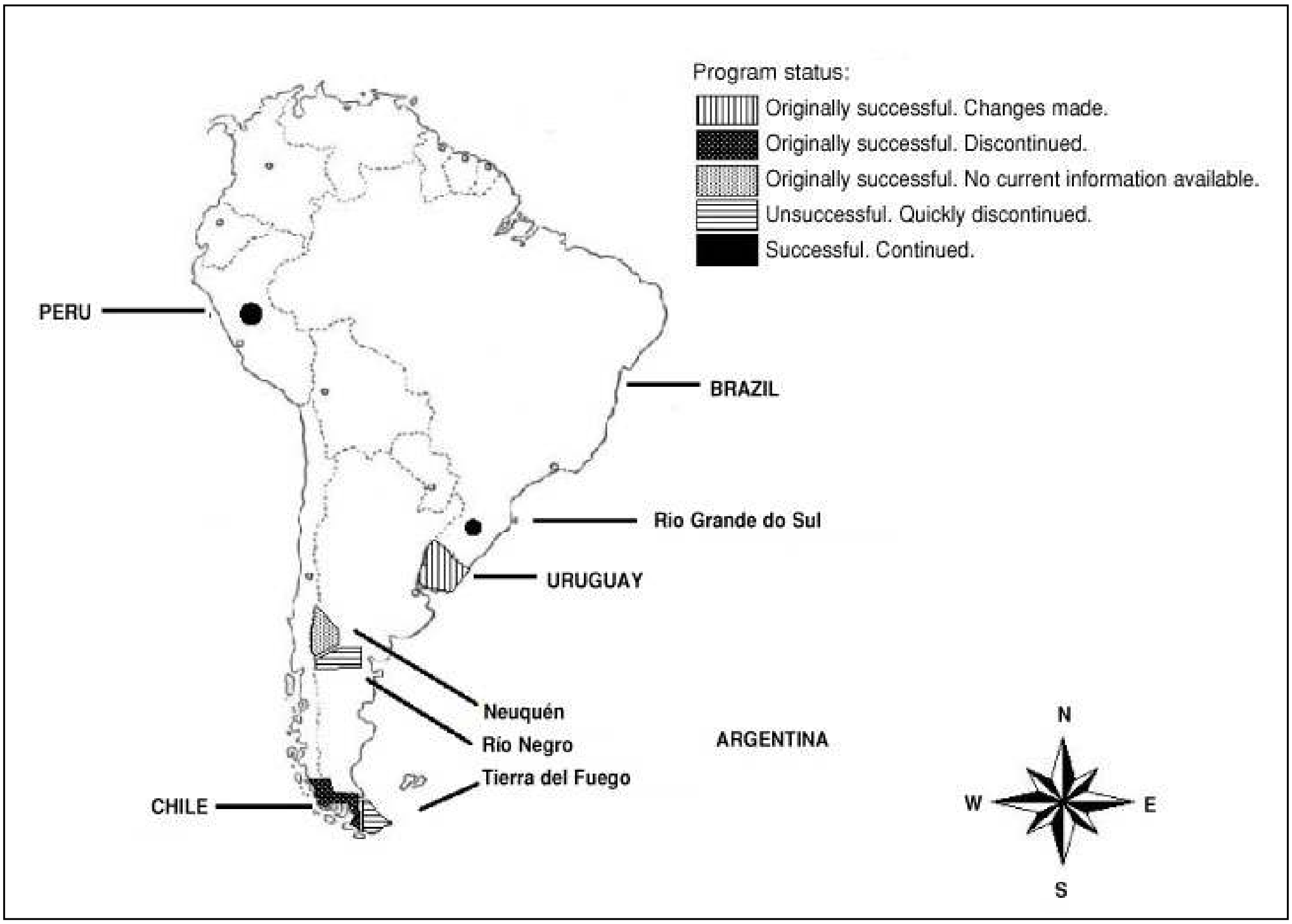
1. Dog rabies control:

In 1983, the countries of the Americas, with support from the Pan American Health Organization (PAHO), pledged to eliminate human rabies transmitted by dogs (Schneider et al., 2007) The goal established was initially limited to major cities, as illustrated by the success of dog rabies control in Lima-Callao in Peru in 1985 (Chomel et al., 1988) and later extended to the entire Region. Since then, through the Regional Program for the Elimination of Human Rabies Transmitted by Dogs, the countries have made great efforts to reach the goal, with remarkable success. Between 1982 and 2011, the number of cases of human and dog rabies was reduced by 93%, from 332 cases to 24 cases. Dog rabies cases alone were reduced from 12,408 in 1982 to 465 cases in 2011, a reduction of 96.3% during the same period. Nearly 42 million dogs are vaccinated annually in Latin America. Most vaccinated animals (75%) are from Brazil (17 million) and Mexico (16 million), with the largest canine populations in Latin America and excellent vaccination coverage (Schneider et al., 2007). Establishing a rabies vaccination day across the whole country, like in Brazil, has been highly successful to reach the immunization goal of at least 70% to 80% of the dog population. Epidemiological surveillance is essential for rabies control in Latin America. However, nearly half of the countries have a fair surveillance system and improvements are still needed in some Andean countries and the Caribbean, especially Bolivia and Haiti, were human rabies transmitted by dogs is still occurring (Schneider et al., 2011), and improvements are needed. It is still worrisome that 55% (57/104) of all human rabies cases related to dog exposure during the recent period 2006-2012 are reported from Haiti and Bolivia. Key components of a succesful control program are based on: 1) proper coordination of the control activities among dog populations (mass vaccination in the shortest period of time possible with coverage of the estimated dog population within a few days to less than a month (average incubation period of rabies in dogs) at a rate above 70%) and surveillance of suspect cases in dogs and other animal species; b) coordination of human bite injuries report and care, with appropriate training of health official for medical care of patients of proper administration of rabies PEP; c) international cooperation between Latin American countries for rabies control and prevention and join programs at shared geographic borders.

2. Control of cystic echinococcosis (CE) in the southern Cone sub-region:

Cystic echinococcosis (CE) is one of the most prevalent zoonoses in Argentina, Brazil, Chile, Peru, and Uruguay. Control programs in South America were originally modeled after programs developed in insular territories, such as Tasmania and New Zealand (Larrieu and Zanini, 2012). The advent and proven effectiveness of praziquantel, plus the experience of insular models, produced high expectations for rapid advances. However, after 30 years of praziquantel use, no endemic area in South America has obtained complete eradication (Figure 1).

Figure 1: Current status of cystic echinococcosis control program in South America, 2010.



Source: Larrieu and Zanini, Rev Panam Salud Publica. 2012;31(1):81-87.

Therefore, a joint program between Argentina, Brazil, Chile and Uruguay under the guidance of PAHO was established in 2001 (RIMSA XII) to promote and strengthen national programs on control of cystic echinococcosis. If successes have been recorded in the detection and reduction of animal infections as well as in the reduction of the number of human cases with approximately 200 notified cases in a dozen South American countries (Larrieu and Zanini, 2012), some of the challenges which are still to be tackled are: to achieve the sustainability of the project, especially in economically challenged rural areas, implementation of technical groups for analysis and assessment at request of the countries, improvement of the regional information systems, to continue training human resources of the control programs and to expand and strengthen the technical cooperation among countries (Irabedra and Salvatella, 2010). Uruguay used to have the highest rate of human hydatidosis in the world until a 5-phase, self-sustaining program was launched in 1990 that brought the number of human surgical cases from 550 prior to the program to 246 in 1999 (Arambulo, 2008).

The over-all prevalence in dogs, the primary source of infection, was reduced from 10.7% in 1991 to 0.74% in 1997. In Chile, between 2001 and 2005, incidence rate was 2.2 per 100,000 inhabitants with higher rates in the regions of Coquimbo, La Araucania and Magallanes (Cortes and Valle, 2010). The hospital discharge rate for the period was 6 per 100.000 inhabitants, with the most affected regions being La Araucania, Aysén and Magallanes. However, confirmed etiology (*E. granulosus*) was reported for less than 60% of the cases, indicating that surveillance needs improvement. Concerted actions from member States and PAHO recommended a plan of action in Peru in 2007, an integrated plan of control and prevention at the Brazil-Uruguay border in 2009, the eradication of CE in Tierra del Fuego in both Chile and Argentina and more recently targeted action in Municipio de Tupiza, Bolivia (Irabedra and Salvatella, 2010).

Certain areas in Argentina have had success with simple and economically viable alternatives. Based primarily on continuous field work supported by the local community, these strategies have significantly decreased transmission to humans. In addition, new possibilities and tools, such as the EG95 vaccine, are being evaluated; as are early detection and treatment of asymptomatic carriers. A major impediment in many areas has been the infrastructure needed to administer praziquantel to dogs in rural areas 8 times per year over numerous years. Such an infrastructure has not been financially or politically sustainable in endemic areas, which tend to be the poorest (Larrieu and Zanini, 2012). It shows, as stated by Brunetti et al. (2011) “that chronic diseases clustering in poor rural areas need intelligent, creative approach, and CE urgently needs operational research incorporating the particularities of resource-poor settings into consideration.” A better education of local population is greatly needed to reduce incidence of CE. For example, in Peru it was found during a survey that most respondents (65%) incorrectly identified the etiologic agent and mode of transmission (Reyes et al., 2010). Therfore, lact of knowledge is likely a major contributor to maintain the endemicity of disease in Peru.

3. Plague outbreak, Peru

Plague was introduced in Peru in 1903 and from the harbors of Callao and Pisco spread in wild rodents across the country and the most recent outbreaks were in the mid 1990s (1993: 610 cases and 1994: 1128 cases). A limited outbreak (17 human cases: 12 bubonic (1 death), 4 pneumonic (2 deaths), 1 septicemic) occurred in 2009 in the Department of La Libertad, which was quickly controlled thanks to updated techniques (better serological and molecular testing) and a good interaction between local field activities and laboratory support at the local and national level. The control measures implemented included insect control in households located in high risk areas, strengthening of disease surveillance and case management, contact tracing, and sensitization of the affected population.

4. Bovine Spongiform Encephalopathy (BSE) prevention

Bovine spongiform encephalopathy is a neurodegenerative disease of cattle caused by prions that was first described in the United Kingdom (UK) in 1986. The BSE epizootic spread into other countries in Europe and Asia through exports of contaminated meat-and-bone meal or infected cattle. The negative effect of such exports means that to implement successful preventive and strategic programmes to safeguard animal health, such programmes must, as a priority, take a regional approach. Global thinking, regional planning and local performance constitute the key factors for the successful control of animal diseases. In South America, initial preventive actions against BSE were adopted in 1989 (van Gelderen et al., 2003). Further measures adopted since then and based on new scientific and technical findings, have led to the demonstration that the region is free of BSE. These early preventive actions have reliably protected the region from importing BSE-infected material. An integral part of the project to determine the BSE status of South America was the training of personnel, the incorporation of technology and the provision of updated information through close relationships with international organisations and prominent international researcher workers. Regional activities aimed at harmonising BSE prevention programmes, producing objective and transparent data on the equivalence of regional BSE status and facilitating regional and international trade have recently been launched. Maintaining the BSE-free status of the region was given high priority by the beef agro-industrial sectors.

5. Food-borne Zoonoses and antimicrobial control and monitoring resistance to antibiotics

At a meeting in Washington DC, USA September 26-30, 2011, a round table was organized on antimicrobial resistance which outlined the importance of the problem in the Member states (WHA51.17). WHO/ PAHO urged the Member States to adopt measures to encourage the appropriate and cost-effective use of antimicrobial agents; to develop measures to prohibit the dispensing of antimicrobial without a prescription or the prescription of a qualified health care professional; to improve practices to prevent the spread of infection and thereby the spread of resistant pathogens. It also urged countries develop sustainable systems to detect antimicrobial-resistant pathogens and monitor volumes and patterns of use of antimicrobial agents and the impact of control measures. In order to do so, WHO/PAHO introduced a policy package that provides the framework for specific interventions: (a) Commit to a comprehensive, financed national plan with accountability and civil society engagement; (b) Strengthen surveillance and laboratory capacity; (c) Ensure uninterrupted access to essential medicines of assured quality; (d) Regulate and promote rational use of medicines, including in animal husbandry, and ensure proper patient care; (e) Enhance infection prevention and control; and (f) Foster innovations and research and development for new tools. Therefore, it is necessary for legislation to be more rigorous in controlling the use of antimicrobial drugs, their prescription in outpatient facilities and the community, length of treatment, and dosage, in addition to having rapid diagnostic kits to support the proper prescription of antimicrobial drugs and encouraging other infection control measures, such as hand washing, surveillance, and rapid post-diagnosis isolation. To date, 12 Latin American and Caribbean countries have taken concrete steps to curtail the growth of antibiotic resistance, mainly through the creation of surveillance systems (http://www.paho.org/english/dpi/Number13_article1_4.htm). Since 1997, PAHO has been working closely with Bolivia, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, and Peru to implement programs for training microbiologists and physicians to tackle the problem. So far, only Chile and Cuba have implemented truly nationwide programs to curb antibiotic resistance. Beginning in 1999, Chilean public health authorities began enforcing local drug-dispensing laws, complementing their efforts with a public information campaign.

In the Americas region, major problems with antimicrobial resistance in humans now include:

- Multi-resistant hospital-acquired infections, which in some countries claim more lives annually than HIV/AIDS, influenza, and traffic accidents combined.
- Community-acquired infections, especially urinary and respiratory infections, that no longer respond to routine antibiotics but require more expensive, wide-spectrum drugs.
- Multidrug-resistant tuberculosis (MDR-TB), which now affects all the countries of the Americas, and extensively drug-resistant TB (XDR-TB), which has been reported in most of the region’s countries and for which there is no effective treatment.
- Growing resistance to ampicillin and trimethoprim/sulfamethoxazole, which were but are no longer effective against dysentery.
- Resistance to chloroquine developed by the malaria parasite *P. falciparum*, thus requiring the use of more expensive treatments.

Some 15% of people with HIV who receive antiretroviral treatment (ART) in the Americas now require second- and third-line drugs, which are as much as 100 times more expensive than first-line drugs. This additional cost threatens the region's goal of providing universal access to ART.
(http://new.paho.org/hq/index.php?option=com_content&task=view&id=5241&Itemid=1926&lang=e):

It is also essential that restriction of use of antimicrobial substances in animal production systems, both in terms of quantity use and type of molecules, be properly implemented and monitored, illustrated by the emergence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) strains in domestic animals and pets. MRSA is a significant pathogen in both human and veterinary medicine. The importance of companion animals as reservoirs of human infections has not been thoroughly investigated. The companion animals of 49 MRSA-infected outpatients (cases) were screened for MRSA carriage, and their bacterial isolates were compared with those of the infected patients using Pulsed-Field Gel Electrophoresis (PFGE) (Ferreira et al., 2011). Rates of MRSA among the companion animals of MRSA-infected patients were compared to rates of MRSA among companion animals of pet guardians attending a "veterinary wellness clinic" (controls). MRSA was isolated from at least one companion animal in 4/49 (8.2%) households of MRSA-infected outpatients vs. none of the pets of the 50 uninfected human controls. Using PFGE, patient-pets MRSA isolates were identical for three pairs and discordant for one pair (suggested MRSA inter-specie transmission p-value=0.1175). These results suggest that companion animals of MRSA-infected patients can be culture-positive for MRSA, representing a potential source of infection or re-infection for humans.

Similarly, an historical review (1950-2002) of emergence of antibiotic resistance of *E. coli* isolates from human and food animal samples was recently performed (Tadesse et al., 2012).

A total of 1,729 *E. coli* isolates (983 from humans, 323 from cattle, 138 from chickens, and 285 from pigs) were tested for susceptibility to 15 antimicrobial drugs. A significant upward trend in resistance was observed for ampicillin ($p<0.001$), sulfonamide ($p<0.001$), and tetracycline ($p<0.001$). Animal strains showed increased resistance to 11/15 antimicrobial agents, including ampicillin ($p<0.001$), sulfonamide ($p<0.01$), and gentamicin ($p<0.001$). Multidrug resistance (≈3 antimicrobial drug classes) in *E. coli* increased from 7.2% during the 1950s to 63.6% during the 2000s. These data describe the evolution of resistance after introduction of new antimicrobial agents into clinical medicine and help explain the range of resistance in modern *E. coli* isolates.

6. <u>Interaction between the Agricultural and Health sectors</u>**:** A highly needed collaboration between the human and agricultural sectors

In order to control and prevent zoonotic diseases which have an impact on both human health and animal production such as bovine brucellosis, bovine tuberculosis or equine encephalitides, joint efforts from the agricultural section and the human health sector are necessary. For example, in Chile herd immunization was a key component of disease control in the regions raising more than 90% of the Chilean cattle. The use of vaccine strain B 19 and later of RB51 allowed to stop the infection within herds, despite the absence of compensation for reactors animals which may stay in infected herds for several months before being destroyed (Lopetequi, 2004). In Argentina, bovine brucellosis is still present, despite numerous efforts made to reduce its impact, especially in the dairy industry (Samartino, 2002). However, there is a need for increasing the awareness of both Ministries of Health and Agriculture regarding to human brucellosis, as collaboration between both these units is essential for the success of any control program. Producers have demonstrated a very strong interest in eradicating animal brucellosis from their herds as evidenced by the decreased incidence of brucellosis in dairy herds. However, the efforts and financial burden that have to be made to reach this accomplishment are too high to be borne by local producers without federal support.

Progress has still to be made towards the control and eradication of bovine tuberculosis (BTB) in many countries in Latin America. For instance, in Ecuador, there is no national BTB control program (Proaño-Pérez et al., 2011). Several factors, including the dairy industry's expansion (preempted by the high demand for milk and its by-products), intensified efforts to increase the cattle population, the presence of M. bovis, and a lack of BTB controls, have caused a rise in BTB prevalence, and consequently, a growing push for the implementation of a national BTB control program. In Chile, the northern part of the country has a medium to high prevalence of BTB and will be categorized as a control zone. In contrast, the southern part, which has a high proportion of the bovine population, has a low prevalence of BTB and will be classified as an eradication zone (Max et al., 2011). Although there have been several past attempts to create a national control and eradication program in Chile, none has been successful. Therefore a national program needs to be implemented, despite the numerous difficulties associated with this program initiation, mostly because of the global economic crisis, difficulties in the milk and meat industry, and social and political issues. In Mexico, human cases of BTB were commonly extrapulmonary and affecting children and associated with consumption of unpasteurized milk (Portillo-Gomez and Sosa-Iglesias, 2010). Efforts to eradicate *M. bovis* in humans in the Americas should therefore be directed at eradicating the disease in cattle, increasing pasteurization of dairy products and providing education about the dangers of consuming unpasteurized dairy products, as suggested by de Kantor et al. (2010).

Enhanced surveillance and vaccination programs for equine is also a key factor for controlling equine encephalitis, especially Venezuelan equine encephalitis. The disease burden of endemic VEE in developing countries remains largely unknown, but recent surveillance suggests that it may represent up to 10% of the dengue burden in neotropical cities, or tens-of-thousands of cases per year throughout Latin America (Aguilar et al., 2011). The potential emergence of epizootic viruses from enzootic progenitors further highlights the need to strengthen surveillance activities, identify mosquito vectors and reservoirs and develop effective strategies to control the disease. As stated by Aguilar et al. (2011)," Perhaps the greatest risk for an increased range and transmission of endemic VEE is the possibility that endemic or epizootic strains could initiate an urban transmission cycle by exploiting the highly efficient vector of dengue virus, *A. aegypti*. which has re-infested most of the neotropics and is a competent vector of a variety of VEEV strains. Furthermore, *Aedes albopictus*, which is present in both tropical and temperate regions, is also an efficient laboratory vector. Thus, human viremia levels after infection with both endemic and epizootic VEEV strains, combined with urban vector susceptibility, could potentially lead to a stable, endemic, urban VEEV cycle that could have devastating public health implications throughout Latin America".

Evaluation and comparison of zoonoses surveillance systems

In the United States, much of the efforts for zoonotic disease surveillance are at the state level with either the state public health department for surveillance of human populations, or state agriculture agencies, for surveillance of domestic animals (Scotch et al., 2011). For human surveillance, many public health departments employ a state public health veterinarian. This individual is trained in veterinary medicine and often epidemiology. Conversely, for domestic animal surveillance, a state department of agriculture often employs a state veterinarian to lead this effort. Each state is different and these appointments are not true for every state.

- Differences exist between state public health veterinarians and state veterinarians regarding the use of electronic databases to store zoonotic disease data, the use of electronic statistical analysis, and attitudes towards Geographic Information Systems (GIS).
- Both state public health veterinarians and state veterinarians indicated using mostly as needed approaches to collaboration including phone and email.
- Use of automated systems to link data was low, yet a high percentage of both groups indicated the importance of sharing data across state agencies.

It was suggested that an informatics solution might be to create a linkage between veterinary and human electronic health records. In addition to pulling diagnostic data, electronic information retrieval of syndromes (e.g. respiratory symptoms) and procedures (e.g. tick removal from pets) might compensate for these discrepancies and increase the amount of cross-agency data sharing. With veterinary national chains such as Banfield Pet Hospitals possessing electronic record systems, this could represent a valuable initiative. For example, A National Companion Animal Surveillance Program (NCASP) was established in the USA at Purdue University to monitor clinical syndromes and diseases using the electronic medical records of >80,000 companion animals visiting >500 Banfield hospitals weekly in 44 states (Glickman et al., 2006). With federal funding (Centers for Disease Control and Prevention), NCASP was initially aiming at syndromic surveillance of Category A agents of bioterrorism and then surveillance was expanded through inclusion of electronic reports

from Antech Diagnostics, a nationwide network of integrated veterinary diagnostic laboratories serving >18,000 private veterinary practices. This program characterizes and displays temporal and spatial patterns of diseases in dogs, cats, and other companion animals. It detects unusual clusters of potential emerging/zoonotic infections and monitors flea and tick activity and can serve at a sentinel system for human exposure to zoonotic pathogens. An integrated system which has been quite successful in the USA is the ArboNET national electronic surveillance network for the detection and reporting of West-Nile virus and other arboviral infections in both humans, animals (horses, birds) and mosquitoes vectors.
(http://www.avma.org/issues/policy/zoonotic_surveillance.asp).

In Canada, Emerging zoonotic disease (EZD) surveillance focuses on detecting both range expansions of known pathogens and the emergence of new pathogens, for which the causative agents, reservoirs or vectors may remain unknown. Suggested EZD surveillance approaches, as proposed in December 2011 by David Roth, from School of Population and Public Health, University of British Columbia in his document "Surveillance for Emerging Infectious Diseases: A Canadian Perspective", include: 1) Syndromic or rapid response surveillance; 2) Information surveillance; 3) Sentinel surveillance and 4) Laboratory surveillance. Perhaps the greatest challenge in EZD surveillance is the lack of a clear case definition or identified causative agent when looking for novel disease emergence. The practical effectiveness of EZD surveillance depends on the strength of relationships between public health, clinical, veterinary, and agricultural personnel. EZD surveillance nationally may be improved by implementing legally mandated data sharing between human and animal health, similar to that found in Quebec.

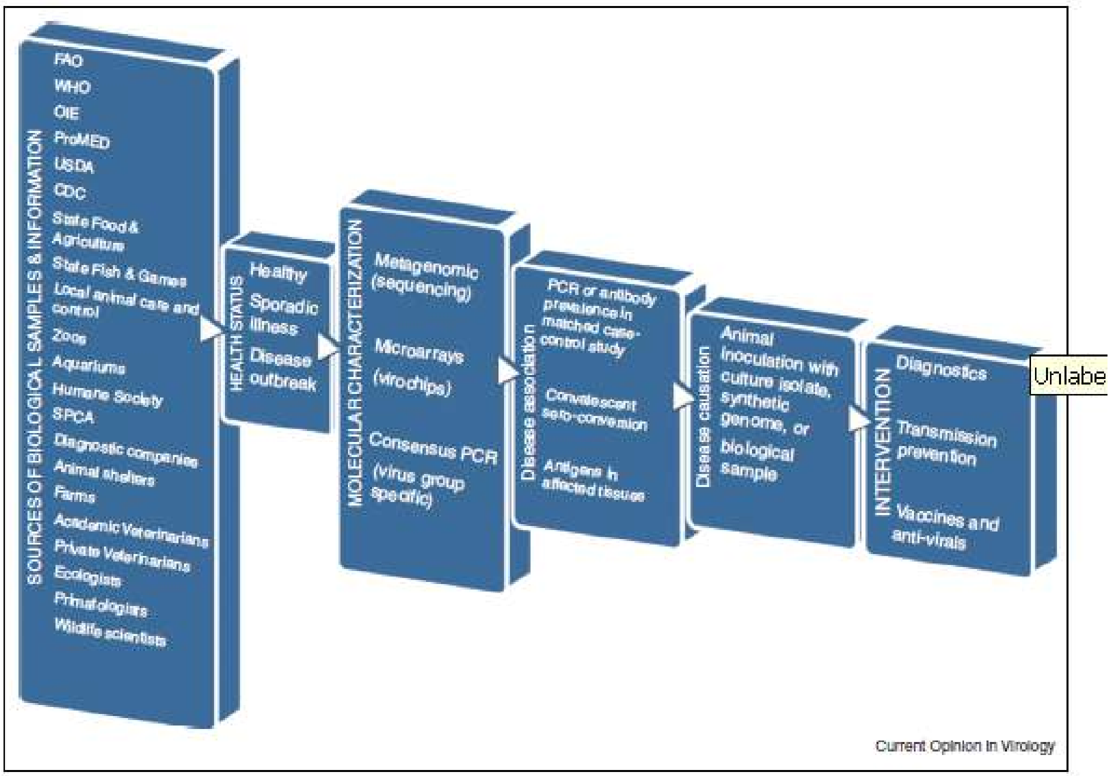
In Quebec, the Directorate of Animal Health and Meat Inspection (DSAIV) has created the **R**éseau d'**A**lerte et d'**I**nformation **ZO**osanitaire (Animal Health Alert and Information Network) which includes regional veterinarians, sentinel networks, zoonotic disease surveillance, and a laboratory network and is mandated to continually monitor Quebec's livestock population health. A single veterinarian represents a regional group and is responsible for epidemiological surveys and biological sampling of potential zoonotic cases. Information on potential zoonoses gathered through these meetings is shared according to a signed agreement between public health authorities and animal health agencies.
(http://www.ncceh.ca/en/practice_policy/ncceh_reviews/surveillance_emerging_infectious_diseases)

Future development and assessment of emerging risks

Several issues are to be faced in regard to emerging zoonoses. Certainly the first one is related to the increase in human population, its urbanization and encroachment in wildlife habitat, leading to exposure of domestic animals and humans to existing or new pathogens (Chomel et al., 2007). Another issue is related to adoption of exotic pets and to consumption of bushmeat. If consumption of bushmeat is not as common in the Americas than in other parts of the world, such as Africa or Asia, it is still an emerging trend associated with further deforestation and access to new territories. Such a risk is clearly illustrated by the recent investigations conducted at international airports both in Europe (Chaber et al., 2010) and in the USA (Smith et al., 2012). Initial findings from samples collected at several US international airports identified parts originating from nonhuman primate (NHP) and rodent species, including baboon, chimpanzee, mangabey, guenon, green monkey, cane rat and rat (Smith et al., 2012). Pathogen screening identified retroviruses (simian foamy virus) and/or herpesviruses (cytomegalovirus and lymphocryptovirus) in the NHP samples. It demonstrates that illegal bushmeat importation into Europe and the United States could act as a conduit for pathogen spread, and suggest that implementation of disease surveillance of the wildlife trade will help facilitate prevention of disease emergence. Another emerging issue which relates to zoonosis transmission is the increasing risk of transmission of these infections through blood donation and organ transplantation, illustrated by the risks associated with Chagas disease in South America, rabies, West Nile virus and Lymphocytic-choriomeningitis virus (Kotton, 2007; Razonable, 2011).

Diagnosing new emerging pathogens of zoonotic potential is also challenging and will require that up-to-date diagnostic methods and tools will also be available to laboratories trough out the world and in developing countries where these pathogens are likely to emerge. As indicated by Delwart (2012), the introduction of molecular methods has greatly simplified the genome characterization of both known and emerging or previously unrecognized viruses. For example, random nucleic acid amplification with or without prior enrichment for viral particles, followed by DNA sequencing (including next generation sequencing) and in silico similarity searches for sequence related to those of known viruses has been highly productive (Delwart). This author also proposed a flow chart of animal virus discovery that involves many partners that have not been commonly involved up to present such as shelters, humane societies, zoological collections (Figure 2) that will help recognition of emerging pathogens. The wide diversity of viruses capable of switching host species highlights the difficulty in predicting from which viral family will emerge the next human viral pandemic. Since the frequency and intensity of viral exposure can also be expected to increase the likelihood of cross-species transmission, the study of viruses in farm or companion animals with extensive contact with both humans and wildlife should also uncover viral species of concern for future zoonoses (Delwart, 2012). Serosurveys for antibodies to these viruses would reveal the extent of their replication in highly exposed humans.

Figure 2: Flow chart of animal virus (and pathogens) discovery, pathogenicity determination and interventions (Delwart, 2012).



Flow chart of animal virus discovery, pathogenicity determination, and interventions.

New approaches to prioritizing zoonoses diseases need to be developed, such as multidisciplinary and evidence based methods. For example, to prioritize 100 animal diseases and zoonoses in Europe, a multicriteria decision-making procedure based on opinions of experts and evidence-based data based on 40 international experts performing intracategory and intercategory weighting of 57 prioritization criteria was used (Humblet et al., 2012). Two methods (deterministic with mean of each weight and probabilistic with distribution functions of weights by using Monte Carlo simulation) were used to calculate a score for each disease, leadind to consecutive ranking. Compared with previous prioritization methods, this procedure was evidence based, included a range of fields and criteria while considering uncertainty, and will be useful for analyzing diseases that affect public health.

In prioritizing surveillance and intervention strategies (especially for vector-borne zoonoses), decision-makers often need to consider spatially explicit information on other important dimensions, such as the regional specificity of public acceptance, population vulnerability, resource availability, intervention effectiveness, and land use (Hongoh et al., 2011). There is a need for a unified strategy for supporting public health decision making that integrates available data for assessing spatially explicit disease risk, with other criteria, to implement effective prevention and control strategies. Multi-criteria decision analysis (MCDA) is a decision support tool that allows for the consideration of diverse quantitative and qualitative criteria using both data-driven and qualitative indicators for evaluating alternative strategies with transparency and stakeholder participation (Table 2) and was proposed by Canadian researchers for managing vector-borne diseases (Hongoh et al., 2011).

Table 2: General steps in a Multi Criteria Decision Analysis (MCDA) process adapted to risk assessment, selection of alternatives and site selection (Hongoh et al., 2011).

Adapting the MCDA methodology for vector-borne disease management

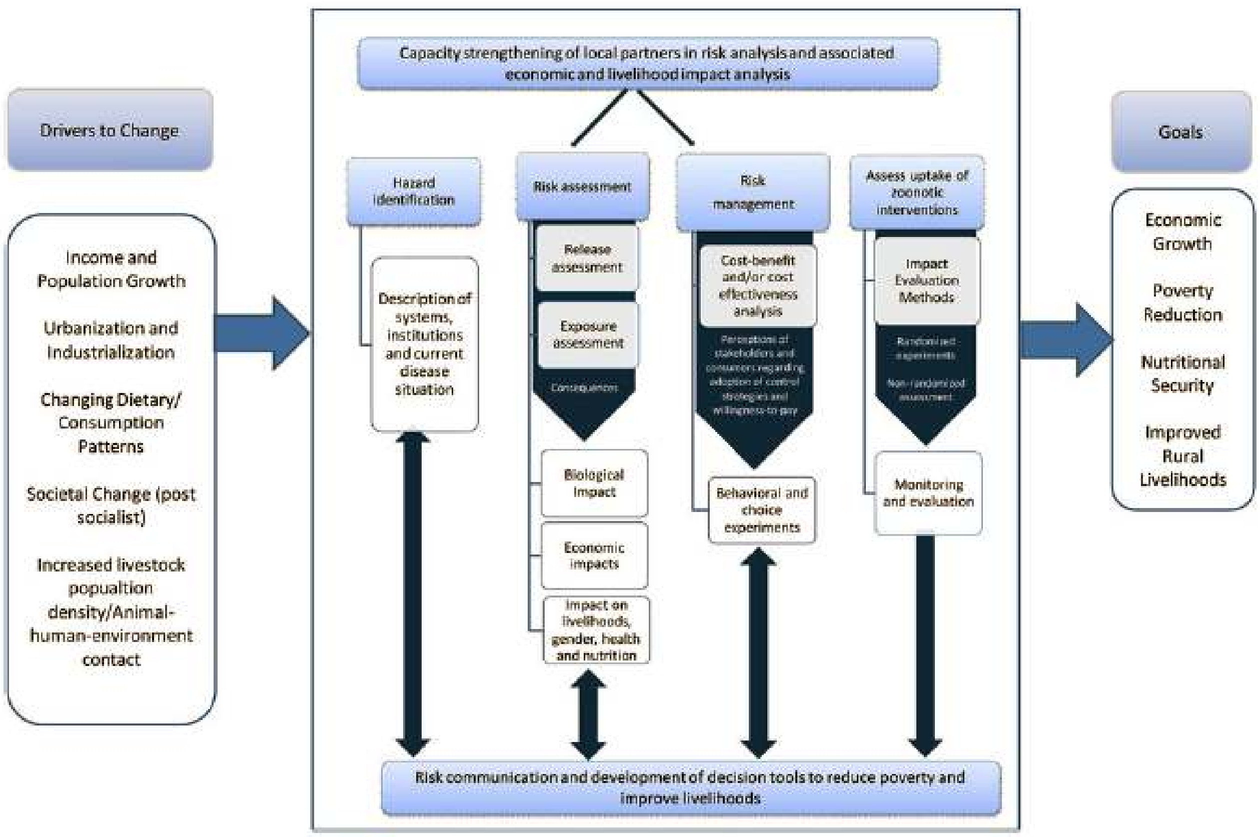
General MCDA steps	Risk Assessment	Selection of Alternatives	Site Selection	Strengths
1. Definition of the problem	What is the distribution of disease risk? E.g. RVF in Africa [17]	What are the spatial effects of alternatives? E.g. vector control	Which sites should we prioritize for preventive action ? E.g. tsetse vector spraying [31]	Implemented by decision-makers, actual questions reflecting the needs of public health authorities are addressed
2. Identification of stakeholders	This step can be run as a single-stakeholder process or as a group process. Stakeholders can include: public administrators, scientific and engineering experts, representatives of civil society or others.			Able to include views from multiple stakeholders (public health, ecologists, private organizations, etc…)
3. Identification of alternatives	Identify risk determinants E.g. Climate, landscape, livestock density, etc…	Identify potential choices & alternatives E.g. vector *vs* landscape management	Identify potential geographical sites E.g. Regions, cities…	Allows comparison between a large range of alternatives
4. Identification of criteria	Examples of vector-borne related criteria could include: human incidence, entomologic risk, adverse effects, public and private costs, impact on habitat and wildlife, human resource needs, organizational changes, delay and duration of effect, social acceptability.			Able to integrate multiple considerations or criteria (economical, environmental, social, burden of disease)
5. Evaluation of alternatives	Calculation of the effects of each alternative on all criteria using current data from the literature, consultations with experts, focus groups and surveys.			Synthesis of current knowledge, using both quantitative and qualitative data
6. Weighting of criteria	Stakeholder determination of the relative importance of all criteria by survey.			Enables exploration of disciplinary, organisational, cultural preferences and values.
7. Decision analysis	Application of MCDA decision rule and analysis of results. E.g. Identification of the best alternatives for surveillance, prevention and control among group of stakeholders			Captures complexity. Exploration and comparison of an alternative's efficiency. Enhances transparency and social acceptability
8. Sensitivity analysis	Simulations of extreme effects on ranking and assessment of the robustness of results.			Allows exploration of the relative importance of criteria and effect on the efficiency ranking of an alternative

Involvement of new partners for the control of zoonoses appears essential to lead to successful programs. For instance, environmental agencies as well as social services need to be fully integrated in zoonotic control programs in order to reach and educate people on the way to improve their resources and reduce the risks of infection. For food safety, HACCP practice should be expended to all sectors of the food chain, which includes street vending in many countries of Latin America. New approaches, especially educational means, need to be devoted to this traditional aspect of food delivery in many urban and peri-urban areas rather than a coercitive approach not compatible with a common lifestyle. A critical issue is that household livelihood or patient-based private costs of diseases is often missing (Narrod et al., 2012). However, such information is necessary for a fair estimate of the cost-benefit analysis.

A proposed framework of risk assessment was suggested by Narrod et al. (2012), linking outputs associated with animal health transmission models, economic impact models and risk analysis to inform the planning of investments through the most promising interventions (Figure 3). This framework allows identifying potentially useful types of analysis to inform decision makers prior to intervention implementation. With such a model, a stepwise approach is proposed including:

1. Estimate the extent of the disease and potential spread;
2. Estimate the cost of zoonotic disease on livelihoods outcomes (income, health and trade), including environmental impacts;
3. Assess the cost-effectiveness of risk management strategies currently employed for reduction of human and animal zoonotic disease exposure risk;
4. Identify factors affecting adoption of zoonotic risk reduction strategies in poor households, the commercial sector and government bodies.

Figure 3: Modified risk analysis framework to enhance reduction of zoonotic burden (Narrod et al., 2012)



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Such assessments must be done cooperatively and synergistically by epidemiologists, veterinarians, physicians, economists, anthropologists and social sciences specialists. However, it requires advanced capacity in epidemiology, economics and mathematical modeling that need to be developed and supported in many developing countries where these capacities are lacking or in their infancy.

Partnership with non-governmental (NGO) associations, philanthropic institutions or foundations become even more a necessity to better integrate targeted actions and projects and make the best use of financial resources.

Many NGO are settled in remote areas which are usually not supported financially by state funds and have a direct access to local populations. They are a major source of information on human and animal health and emergence of diseases. Their role in an early warning system and sentinel system is key to the detection and prevention of emerging zoonoses. Similarly, access to and sharing of data from private diagnostic laboratories and hospitals for humans and animals should be part of an integrated surveillance system for zoonotic infections.

CONCLUSIONS AND ELEMENTS FOR RECOMMENDATIONS

This review shows that major achievements have been accomplished in Latin and Central America in reducing the burden of zoonotic diseases both in human and animal populations. This is particularly true for the control of dog rabies and cystic echinococcosis. However, many challenges are still remaining with the emergence of new zoonotic pathogens, especially viral or bacterial, borne by wildlife reservoirs and possibly transmitted by vectors. As we dispose of new advanced molecular tools to not only isolate but also detect pathogens, new zoonotic agents are and will be regularly identified in the Americas both in their reservoir hosts and accidental victims, such as hantaviruses, *Bartonella* species other than *B. bacilliformis*, new rickettsial organisms, such as *R. felis*.

Therefore, it appears more necessary than ever to dispose of:

1. An appropriate system and network of diagnostic facilities at the local, national and supra-national (regional) levels, disposing of advanced diagnostic tools in order to recognize emerging pathogens. Such facilities need to be connected to national and international references laboratories allowing for continuous training and quality control.

2. An appropriate timely surveillance system able to conduct epidemiological investigations at the animal and human interface and disposing of technological tools for assessing risk levels and for analyzing landscape, climatic and ecological information in an integrative manner. For instance, a hidden Markov model for analysis of frontline veterinary data for emerging zoonotic disease surveillance was developed from data from Sri Lanka (Robertson et al., 2011). Field veterinarians collected data on syndromes and diagnoses using mobile phones. Region-specific weekly average prevalence was estimated for each diagnoses and partitioned into normal and abnormal periods. Visualization of state probabilities was used to indicate areas and times of unusual disease prevalence. The study suggested that hidden Markov modelling is a useful approach for surveillance datasets from novel populations and/or having little historical baselines.

3. An extensive and innovative education program aiming at local populations living in the poorest areas in order to reduce their risks of exposure to wildlife zoonoses (ie. vampire bat rabies), domestic and exotic pet transmitted zoonoses and food-borne zoonoses.

4. A proper legislation and enforcement of the use of antibiotics in animal production, domestic animal care (especially pets) and as growth enhancers. Establishing structural links between health institutions and the private sector will be essential to reach attainable goals in mass antibiotic use reduction.

5. <u>New Strategic alliances</u>: Partnership with non-governmental (NGO) associations, philanthropic institutions or foundations become even more a necessity to better integrate targeted actions and projects and make the best use of financial resources. Many NGO are settled in remote areas which are usually not supported financially by state funds and have a direct access to local populations. They are a major source of information on human and animal health and emergence of diseases. Their role in an early warning system and sentinel system is key to the detection and prevention of emerging zoonoses. Similarly, access to and sharing of data from private diagnostic laboratories and hospitals for humans and animals should be part of an integrated surveillance system for zoonotic infections.

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