

Invited Review

Control and prevention of emerging parasitic zoonoses

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Abstract

Emerging zoonoses have been defined as zoonoses that are newly recognised or newly evolved, or that have occurred previously but show an increase in incidence or expansion in geographical, host or vector range. Among parasitic zoonoses, protozoa are particularly likely to emerge. Control and prevention of emerging parasitic zoonoses are complex tasks that require an integrative and multidisciplinary approach. Reduction of parasite burden is certainly a major objective but cannot be set alone. Therefore, environmental and ecological modifications need to be implemented to reduce not only the parasitic load, but also the risk of parasite transmission. Finally, education and behavioral changes are critical for the success of both control and prevention of these diseases. However, without appropriate financial resources specifically allocated at the local and national levels as well as through international cooperation, control and prevention of these emerging parasitic diseases will not be possible.

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1. Introduction

Zoonoses, which are diseases and infections naturally transmitted between vertebrates animals and humans (W.H.O., Expert Committee on Zoonoses, WHO tech rep., 1951, Ser No. 40), account for most of the diseases that have been reported as “emerging” or re-emerging, as 75% of emerging human pathogens are zoonotic (Woolhouse, 2002). Taylor et al. (2001) identified 1415 species of infectious organisms known to be pathogenic to humans, including 217 viruses and prions, 538 bacteria and rickettsia, 307 fungi, 66 protozoa and 287 helminths. Of these, 868 (61%) were identified as zoonotic and 175 pathogenic species were associated with diseases considered to be ‘emerging’, 132 of those (75%) being zoonotic. In a recent study, Jones et al. (2008) also showed that emerging infectious disease events are dominated by zoonoses

(60.3%) and the majority of those (71.8%) originate in wildlife.

Emerging zoonoses have been defined as zoonoses that are newly recognised or newly evolved, or that have occurred previously but show an increase in incidence or expansion in geographical, host or vector range (Report of the WHO/FAO/OIE joint consultation on emerging zoonotic diseases, WHO, Geneva, May 3–5, 2004). The vast majority of emerging infectious diseases is considered to be either viral or bacterial (Jones et al., 2008). In a systematic literature survey, 87 of 1399 human pathogen species were first reported in humans since 1980. These new species are mainly viruses, having a global distribution and mostly associated with animal reservoirs (Woolhouse and Gaunt, 2007). However, Taylor et al. (2001) noted that protozoa were also particularly likely to emerge, whereas helminths were unlikely to do so. Prevention and control of emerging or re-emerging parasitic zoonoses require a good understanding of the epidemiology of these infections and of the factors for emergence or re-emergence (Chomel, 2003).

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2. Factors associated with emerging or re-emerging parasitic zoonoses

Many factors are associated with emerging infectious diseases. However, emerging infectious disease origins are significantly correlated with socio-economic, environmental and ecological factors, as reported by Jones et al. (2008).

Certainly, for parasitic emerging and re-emerging infections, human encroachment into wildlife habitat or increased wildlife populations that thrive in a human environment are factors that allow such emergence or re-emergence. In North America, human infections by *Baylisascaris procyonis* have been reported in southeastern USA, where such an infection was thought to be rare or absent, as well as in northern California, where a high density of raccoons is sustained by a plentiful food supply made available directly or indirectly by local populations (Polley, 2005). In Western Europe, the apparent recent dispersion of alveolar echinococcosis, caused by *Echinococcus multilocularis*, has been associated with the successful control of rabies in red fox (*Vulpes vulpes*) populations and the increase in anthropogenic food supplies leading to a substantial increase in these populations, also becoming established in urban centres (MacPherson, 2005; Schweiger et al., 2007). As a consequence, human alveolar echinococcosis cases doubled within a 10 years period in Switzerland, following a fourfold increase in the fox population between 1980 and 1995 (Schweiger et al., 2007). In the Netherlands, the *E. multilocularis* infestation load in foxes is increasing in number, as the average worm count increased from 2.6 worms per fox in a 1996 survey to 16.6 worms per fox in a 2003 survey and is spreading northward at a speed of 2.7 km per year (Takumi et al., 2008). In rural environments, wildlife may serve as reservoirs and amplifiers for helminthic zoonoses such as toxocarasis. Red foxes may also play an important role as a source of *Toxocara canis* shedding in the environment, as demonstrated in the Slovak Republic (Antolová et al., 2004). Coprological investigation of 310 red foxes showed an 8.1% prevalence of *T. canis*, with a higher occurrence in animals of rural origin (8.6%) than from suburban environments (5.6%) (Antolová et al., 2004). As the red fox population increases in most of Western Europe, the role of these rural foxes in maintaining the infection and being a source of human contamination should be emphasised.

Modification of natural habitats by human population activities and increased pet populations are also associated with the emergence of parasitic zoonoses such as toxoplasmosis. *Toxoplasma gondii* affects a wide variety of hosts including threatened southern sea otters (*Enhydra lutris nereis*), causing mortality and contributing to the slow rate of population recovery for southern sea otters in California. It was shown that 52% of 305 freshly dead, beachcast sea otters and 38% of 257 live sea otters sampled along the California coast from 1998 to 2004 were infected with *T. gondii* (Conrad et al., 2005). Areas with high *T. gondii*

exposure are predominantly sandy bays near urban centres with freshwater runoff. The most likely source of infection is by infectious, environmentally resistant oocysts that are shed in the feces of felids and transported via freshwater runoff into the marine ecosystem. In developing countries, densely packed housing in shanty towns or slums and inadequate drinking-water supplies, garbage collection services and surface-water drainage systems combine to create favorable habitats for the proliferation of vectors (Knudsen and Slooff, 1992). Increased urbanisation of human populations in the northeastern part of Brazil where people live in poor conditions with a large population of pet dogs has been directly associated with the emergence of visceral leishmaniasis in that part of the world (Taul, 2006).

Climatic changes may also have an important impact on parasitic diseases, zoonotic or not. Small changes in absolute temperatures can have substantial effects on the transmission dynamics of protostrongylid lungworms and muscleworms (species of *Parelaphostrongylus*, *Protostrongylus* and *Umingmakstrongylus*), which cycle among the environment, gastropod intermediate hosts and ungulate definitive hosts in the most northern regions of the globe (Hoberg et al., 2008). Investigations of emerging infectious diseases associated with parasites in northern wildlife show that emergence of parasitic disease is linked to geographic expansion, host switching, resurgence due to climate change and newly recognised parasite species (Hoberg et al., 2008). Similarly, global warming will increase the geographical repartition of sandflies which transmit leishmaniasis or bartonellosis. In a simulation model looking at the potential effect of global warming on the geographic and seasonal distribution of *Phlebotomus papatasi* in southwest Asia, Cross and Hyams (1996) showed that “among 115 weather stations, 71 (62%) would be considered endemic with current temperature conditions; 14 (12%) additional stations could become endemic with an increase of 1 °C; 17 (15%) more with a 3 °C increase; and 12 (10%) more (all but one station) with a 5 °C increase. In addition to increased geographic distribution, seasonality of disease transmission could be extended throughout 12 months of the year in 7 (6%) locations with at least a 3 °C rise in temperature and in 29 (25%) locations with a 5 °C rise”.

Dispersal of infection through blood and organ donations, especially through immigrant donors, is another issue that needs to be considered for prevention of emerging parasitic zoonoses. An up-to-date review of transmission of tropical and geographically restricted infections during solid organ transplant (SOT) was published recently, giving an in-depth review of fungal and parasitic infections associated with SOT (Martín-Dávila et al., 2008). Chagas disease, leishmaniasis and babesiosis cases have been associated with blood donation (Dey and Singh, 2006) and an increased number of cases have been reported recently in the USA for *Trypanosoma cruzi* infection following blood transfusion (MMWR, 2007; Martín-Dávila et al., 2008). In endemic areas, *T. cruzi* is transmitted pri-

marily by triatomine insects (i.e., kissing bugs) but infection also can occur via blood transfusion, congenital transmission, organ transplantation, laboratory incident and ingestion of triatomine-contaminated food or drink. An American Red Cross study identified 32 donations (approximately one in 4655) confirmed positive for *T. cruzi* antibodies (MMWR, 2007). Two cases of acute Chagas disease in heart transplant recipients were reported by two Los Angeles County hospitals in February 2006 (MMWR, 2006). In the USA, one previous report documented *T. cruzi* transmission through SOT, in which three organ recipients were infected (MMWR, 2006). The first report of transfusion-transmitted kala-azar came from China in 1948 (Dey and Singh, 2006). Other reports of transfusion-transmitted visceral leishmaniasis have been reported from France, Sweden, Belgium, United Kingdom, India and Brazil. Although no case of transfusion-transmitted leishmaniasis has been reported from the USA, concern was raised at the time of first Iraq war. The American Association of Blood Banks recommended that individuals who had traveled to or visited Saudi Arabia, Kuwait, Iraq, Oman, Yemen, Qatar, Bahrain or the United Arab Emirates on or after August 1, 1990, should be deferred as donors of transfusable blood components. The number of published cases of leishmaniasis among transplant recipients has quadrupled since the beginning of the 1990s, with most cases observed in patients living in countries of the Mediterranean basin (Antinori et al., 2008). Leishmaniasis is most commonly associated with kidney transplantation (77%) and visceral leishmaniasis (VL) is the most frequently observed clinical presentation. More than 60 cases of VL in solid organ transplant recipients have been described (Martín-Dávila et al., 2008). The risk of transfusion-transmitted babesiosis is higher than usually appreciated and in endemic areas represents a major threat to the blood supply (Cable and Leiby, 2003). Furthermore, the geographic range of *Babesia microti* is expanding; other *Babesia* spp. have been implicated in transfusion transmission in the western USA and the movement of blood donors and donated blood components may result in the appearance of transfusion babesiosis in areas less familiar with these parasites (Cable and Leiby, 2003). Severe infections caused by *Leishmania* spp. and *Cryptosporidium* sp. have emerged in AIDS patients, organ transplant recipients and the elderly. In some areas of Africa, the number of coinfection cases has increased dramatically due to social phenomena such as mass migration and wars. In northwest Ethiopia, up to 30% of all visceral leishmaniasis patients are also infected with HIV. In Asia, coinfections are increasingly being reported in India, which also has the highest global burden of leishmaniasis and a high rate of resistance to antimonial drugs (Alvar et al., 2008).

Travel to exotic locations as well as changes in our feeding habits, including the internationalisation of exotic and trendy cuisine such as consumption of sushi, sashimi or ceviche, also lead to emergence or re-emergence of parasitic diseases such as anisakiasis or gnathostomiasis (Sakanari

and McKerrow, 1989; Del Giudice et al., 2005; MacPherson, 2005; Kleter et al., 2007) or diphyllorhynchiasis (Dupouy-Camet and Peduzzi, 2004). Many cases of diphyllorhynchiasis are reported each year in Finland and Sweden. Over 30 cases have been identified on the Swiss shores of Lago Maggiore since 1990 and 70 cases on the Swiss and French shores of Geneva Lake between 1993 and 2002 (Dupouy-Camet and Peduzzi, 2004). Many Asian countries have developed a major fish-farming industry that can be a source of human infections by parasites. In Vietnam, fish-borne intestinal parasites are an unrecognised food safety risk in a country whose people have a strong tradition of eating raw fish (Trung Dung et al., 2007). Tourism in exotic countries may also expose large numbers of visitors to contaminated food. In China, about 380,000 people are infected with echinococcosis and approximately 50 million are at risk of infection (Garcia et al., 2007; Zhou et al., 2008).

Wars and social upheavals have also been associated with emergence or re-emergence of parasitic zoonoses. As reported by Cuperlovic et al. (2005), prevalence of trichinellosis in domestic animals and humans is high in Bulgaria, Croatia, Montenegro, Romania and Serbia, but moderate in Bosnia and Herzegovina. In Hungary, human trichinellosis has not been reported for many years; but sporadic cases were recorded in swine in recent years. Sporadic human cases of trichinellosis have been reported in Slovenia and Turkey, but not in Greece or Macedonia. The re-emergence of trichinellosis is connected with the changes in the social and political systems in Bulgaria and Romania but also to wars that took place at the end of the 20th century in Croatia, Montenegro and Serbia. Similarly, *Trichinella* outbreaks associated with inadequate meat inspection were reported after 2000 in Lithuania and Latvia where the annual incidence was 0.6 and 0.7–1/100,000 population, respectively ((Vorou et al., 2007). Similarly, a 2003 report of emergent visceral leishmaniasis in an area of civil conflict in Somalia identified high rates of infection. (Beyrer et al., 2007).

3. Control and prevention

Control and prevention of emerging parasitic zoonoses are complex tasks that require an integrative and multidisciplinary approach. Reduction of parasite burden is certainly a major objective but cannot be implemented alone. Therefore, environmental and ecological modifications need to be implemented to reduce not only the parasitic load, but also the risk of parasite transmission. Finally, education and behavioral changes are essential for the success of both control and prevention of these diseases. However, financial resources specifically allocated to prevention and control of emerging parasitic diseases need to be contributed by local and national authorities as well as through international cooperation in order to successfully control and prevent these infections.

3.1. Need for proper financial resources and public health structures

Appropriate financial resources need to be allocated to sustain programs that will reduce the risk of human and animal infestations; often easy solutions exist but are not implemented due to lack of financial support. For example, since the reassessment of parasitic disease burdens by the international health community in the late 1980s and 1990s, the worldwide problem of schistosomiasis seems to have lost priority in the global health agenda (King et al., 2006). Compared with treatment and prevention of more lethal diseases (such as malaria, HIV and tuberculosis), control of schistosomiasis has not been considered such a high priority. This is unfortunate, because 200–300 million people suffer schistosomiasis-related disability on a daily basis (King et al., 2006). Uncontrolled urbanisation, especially in many tropical areas, where parasitic burden is the heaviest, brings its own constraints and limitations for implementation of control programs. Some diseases are being transmitted in urban areas, due to the emergence or reemergence of their vectors, such as dengue, malaria and visceral leishmaniasis (Taulil, 2006). Difficulties in control occur, as it is often easier to apply control measures in rural areas, because there is more population compliance and adherence to parasitic control programs than in urban areas. Therefore the coverage is higher and disease control is better in rural settings. The end of the 20th century has been characterised economically in many developed and developing countries by a major privatisation effort of many public programs associated with a major reduction in the civil servant workforce. Furthermore, the decentralisation of control activities to states and municipalities has been implemented and difficulties occur as these levels of government have insufficient accumulated experience in control of zoonotic diseases. For more effective control, political commitment, multi-sector articulation and rational use of insecticides are required (Taulil, 2006). The World Health Organization (WHO) encourages governments to integrate disease control programs with primary health care, but most such integrated programs operate in developed countries. Integrated approaches include less dependence on pesticides; encouraging changes in human behavior; disseminating health messages; community participation, particularly youth; mobilization of human and financial resources; and proper urban development, e.g., better quality housing, adequate sanitation and drinkable water (Knudsen and slooff, 1992).

3.2. Reduction of parasite burden

In order to better control parasitic emerging zoonoses, reduction in the presence of parasites or their eggs in the environment is critical. The industrialisation of pig production associated with screening measures has considerably reduced the level of infestation by *Trichinella spiralis* in many European countries. However, re-instatement of

free-roaming farming (organic farms) and a high level of infestation in wild boars present new risks which need to be fully assessed by proper education of hunters and appropriate cooking temperature and time of the game before consumption (Dupouy-Camet, 2006). In central and eastern European areas, where *E. multilocularis* is endemic, dogs that have access to rodents should be considered potential hazards for humans (Guillot and Bouree, 2007). A dramatic increase in the prevalence of echinococcosis in foxes in Hokkaido, Japan, associated with invasion of wild foxes into urban areas, infection among pet and stray dogs, and the possibility of spreading the disease to the main island of Japan, pose significant threats to public health. The enforcement of a national reporting system for veterinarians, international collaboration and the establishment of a Forum on Environment and Animals (FEA) are major steps to reduce the disease burden (Kamiya et al., 2006).

3.3. Action on the animal reservoirs and vectors

Integrated actions may be needed to reduce the density of animal reservoirs. Reduction of fox populations by development of contraceptive vaccines is an approach that might be very beneficial to reduce the number of foxes carrying *E. multilocularis*, especially in urban and peri-urban areas, where high densities have been observed recently (Stöhr and Meslin, 1997; Strive et al., 2006; Schweiger et al., 2007).

Rational measures for preventing animal and human infection include pet owner education and regular deworming of dogs and cats (Guillot and Bouree, 2007). Education of pet owners should focus on prevention and will include personal hygiene, clearing up pet feces regularly to reduce environmental contamination and minimizing exposure of children to potentially contaminated environments. Because puppies, kittens, pregnant and nursing animals and hunting dogs are at the highest risk of roundworm or tapeworm infection – and are therefore responsible for most environmental contamination and human disease – antihelminthic treatments are most effective when they are initiated early and target these animal populations. Various guidelines for the treatment and control of parasitic infections in carnivorous pets have been proposed in the USA (by the Centers for Disease Control and Prevention, and the Companion Animal Parasitology Council) and in Europe (by the European Scientific Counsel Companion Animal Parasitology).

For prevention of visceral leishmaniasis, it was shown that distribution of insecticide-treated mosquito nets combined with dissemination of culturally appropriate behavior-change education is likely to be an effective prevention strategy (Kolaczinski et al., 2008). During an epidemic of VL in eastern Sudan, 357,000 insecticide-treated bednets (ITN) were distributed to 155 affected villages between May 1999 and March 2001 (Ritmeijer et al., 2007). An estimated 1060 VL cases were prevented between

June 1999 and January 2001, a mean protective effect of 27%. Although results need to be interpreted with caution, this analysis indicates a potentially strong reduction in VL incidence following a community distribution of ITN. The effectiveness of ITN depends on behavioural factors, which differ between communities.

As indicated by Dantas-Torres and Brandão-Filho (2006), despite the fact that most important aspects of visceral leishmaniasis in Brazil are known, the control of this disease has not yet been achieved. The current control strategies have not been able to prevent geographical expansion, as a rise in the incidence and lethality of VL has been observed. These authors indicated that there is a need not only for a better definition of priority areas, but also for the implementation of a fieldwork monitoring system to the disease surveillance that could permit further evaluation of the control program in areas where VL is endemic. Dog culling for control of VL is still very controversial. As a short-term action, it may reduce the risk of human infection (Costa et al., 2007), but in the long-term it increases the risk of creating a more susceptible population of dogs (Nunes et al., 2008). Therefore, alternative measures such as the wide use of insecticide collars or development of canine vaccines against VL that will prevent carriage of the parasite by dogs are certainly interesting alternatives. In Iran, community-wide application of deltamethrin-impregnated dog collars not only protected domestic dogs from *Leishmania infantum* infections, but also reduced the risk of infection in children (Gavvani et al., 2002). These authors concluded that dog collars could play a role in control of VL and replace controversial dog culling programs in some countries. Similarly, several approaches have been taken to develop canine anti-leishmaniasis vaccines. In a field trial using the naturally excreted/secreted antigens of *Leishmania infantum* promastigotes (LiESAp) in formulation with muramyl dipeptide (MDP) as adjuvant (LiESAp-MDP) vaccine, it was shown that after two completed transmission cycles, the *Leishmania* infection rate was 0.61% (1/165) in vaccinated dogs and 6.86% (12/175) in the placebo group. The efficacy of the vaccine was calculated to be 92% ($P=0.002$) (Lemesre et al., 2007).

3.4. Improved diagnostic tools and broader use of diagnostic tests

Improved methods for detection of parasites in animals or in the environment have a major impact on the possibility of implementing control measures and monitoring their impact. For instance, significant progress has been made in the development of sensitive and specific new techniques for the intra-vitam and post-mortem diagnosis of intestinal *E. multilocularis* infection in definitive hosts, notably the detection of coproantigen by ELISA and of copro-DNA by PCR (Deplazes and Eckert, 2001). Both tests can also be used for the identification of *E. multilocularis* in fecal samples collected in the environment. As reported by Ito

et al. (2006), immunodiagnostic tools are expected to be useful for primary screening of cysticercosis and echinococcosis, and should be combined with confirmation of direct parasitological evidence (morphology or DNA), and imaging techniques for cysts (Ito et al., 2006). Similarly, effective and systematic detection of potential infections for organ donors and blood donors need to be emphasised to prevent the emerging trend of human post-transfusional or post-transplant zoonotic cases (Martín-Dávila et al., 2008).

3.5. Environmental and ecological changes

Studying and monitoring environmental characteristics are key factors to prevent and control many water-borne and vector-borne parasitic zoonoses. For instance, the integrated use of geographical information systems, remote sensing and geostatistics has provided new insights into the ecology and epidemiology of schistosomiasis at a variety of spatial scales (Brooker, 2007). Because large-scale patterns of transmission are influenced by climatic conditions, an increasing number of studies have used remotely sensed environmental data to predict spatial distributions, most recently using Bayesian methods of inference. Such data-driven approaches allow for a more rational implementation of intervention strategies across the African continent. The integration of schistosomiasis control as part of a 'deworming' multi-parasite control initiative offers possible economies-of-scale and economies-of-scope in terms of overall health impact, which are highly attractive for regions afflicted by multiple endemic parasite species (King et al., 2006).

3.6. Human behaviors and education

Changes in human behaviors are certainly among the most difficult challenges. Consumption of raw horse meat was shown to be a major risk factor associated with trichinellosis in both France and Italy since the 1980s (Ancelle, 1998). However, despite early implementation of control measures to reduce such risk, several large outbreaks still occurred (Ancelle, 1998). In recent years, appropriate technical training and quality control appear to have been successful in stopping these outbreaks (Vallée et al., 2007). Similarly, consumption of raw fish has been increasing in many countries and was associated with the re-emergence of clonorchiasis, opisthorchiasis, metorchiasis, (Chai et al., 2005) and anisakis infection (Kleter et al., 2007). Public health professionals play a key role in public education about zoonotic diseases. Surveys have shown that the medical community relies on the veterinary profession for education of the public about zoonoses. As indicated by Grant and Olsen (1999) "physicians believe that veterinarians should be involved in many aspects of zoonotic disease prevention, including patient education". This role needs to be emphasised, but also re-enforced among small animal practitioners. In a survey of Western Canadian small animal practitioners, it was found that only 44% of veterinarians

stated they discussed with all clients the zoonotic risk of animal-derived endoparasites, whereas the remainder discussed it only under particular circumstances or not at all. Therefore, increased educational efforts directed at veterinarians are warranted (Stull et al., 2007).

3.7. International cooperation

Furthermore, the involvement of international agencies and institutions, such as the World Health Organization (WHO), the Food and Agriculture Organization (FAO) and the International Livestock Research Institute, as well as the commitment of policymakers, scientists and field workers, are key means for the sustainable control and prevention of parasitic zoonoses and, hopefully, the eradication of some of those. For example, parasitic zoonoses such as cysticercosis and echinococcosis cause serious human suffering and considerable losses in agricultural and human productivity in many developing and transition countries. Although effective and reliable tools for the diagnosis, prevention and control of parasitic zoonoses are available, their implementation has not always been successful in many countries. This is primarily due to the lack of awareness of the presence or impact of the parasites involved. In addition, the required intersectorial cooperation, resource management and political commitment for their control are weak or absent (Eddi et al., 2006). However, intersectorial collaboration for disease containment, independence of sectorial interests and transparency are critical when managing certain health risks, as mentioned by the WHO (Meslin et al., 2000). The programs from FAO, WHO and the Office International des Epizooties have established a global network of professionals directly involved in zoonotic and food-borne diseases (Eddi et al., 2006). This interagency network provides a basic framework for the spread of information related to the diagnosis, prevention and control of major zoonotic diseases, including emerging or re-emerging parasitic zoonoses.

4. Conclusions

Prevention and control of emerging parasitic zoonoses require a global commitment from not only the different health professionals but also politicians and economists to allocate appropriate funding in order to conduct interactive control programs. Nevertheless, the main task still relies on local populations and requires changes in human behaviors, in making environmental adjustments in our expanding urban society and in better identifying the risks associated with wildlife, as we encroach even more into their already reduced habitat.

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