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Practicality and elements influencing worldwide disposal and conceivable annihilation of rabies on the planet

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Abstract

This article reviews the feasibility of global eradication of rabies and factors affecting eradication of rabies in the world. Effective vaccines are now available against many viruses making eradication a viable proposition. As in the case of smallpox, the following questions should be addressed when the feasibility of eradication of a particular human virus disease is considered. Is the disease worth eradicating? Is there any animal reservoir? Is there a carrier state? Is effective vaccination available? How communicable is the rabies? What level of coverage is required for eradication? What are the possibilities for rabies control in reservoir hosts? Can rabies be controlled in wildlife reservoirs? Can the population density of reservoir hosts be reduced? Can contact between wild dogs and domestic dogs be minimized? Whether a virus disease can be eradicated or not depends on many factors, not least on the will power to implement such a policy. These factors include human (increased human activities and international travel; lack of adequate public awareness, proper surveillance, emergency preparedness planning, solid commitment and resourced initiatives among others); socioeconomic (major ecologic changes, agricultural practices, poverty, increasing demands for meat etc.); animal factors (illegal importation, population increase, migration of dogs, stray animals etc.); and vaccines and vaccination (low vaccination coverage and potent vaccines, vaccine failure, inferior vaccine quality, vaccine shortage, high cost, existence of multiple hosts, reservoir and healthy carriers etc.). Rabies eradication is not feasible because of the extensive factors and the inability to eliminate reservoirs with existing technology. However, elimination of human rabies in urban areas may be possible through different strategies. Vaccination of stray dogs could lead to the eradication of rabies in countries where dog rabies is the sole source of human exposure. Research to design strategies for rabies control globally, is urgently needed. Additional genetic work will help to set priorities for the conservation of populations which may be genetically unique for spread of rabies and other related diseases.

Keywords: Animal factor, continual endemicity, effective vaccines, eradicability, feasibility, human, socioeconomic, vaccination.

HISTORICAL BACKGROUND OF DISEASE ERADICATION

Viruses account for the bulk of infectious diseases. Rabies infection in humans is still a major public health problem, causing upwards of 20,000 deaths per year. Most human deaths from rabies occur in tropical resource-limited countries (Zinsstag et al., 2007). In Africa and Asia, an estimated 24,000 - 70,000 persons die of rabies each year (Knobel et al., 2005) . The domes-tic dog is the main source of exposure and vector for human rabies (Zinsstag et al., 2007). Rabies is acute, progressive, fatal encephalitis caused by viruses in the Family Rhabdoviri-dae, Genus Lyssavirus. Rabies virus is the representative member of the group. Warm-blooded vertebrates are susceptible to experimental infection, but major primary hosts for disease perpetuation encompass bats and mammalian carnivores. The dog is the global reservoir, and important wild carnivores include foxes, raccoons, skunks and mongoose, among others (Rupprecht et al., 2004). Rabies is one of the oldest known diseases of mankind, yet it has been only slightly more than 100 years since Pasteur developed the first vaccine for post-exposure treatment. Since this first crude nerve tissue vaccine, numerous other rabies vaccines for human use have been developed and used with varying degrees of effectiveness and safety.

Attempts to control human rabies and other infectious diseases have a long history: animal and human vaccines provide efficient weapons for prevention. Conta-gious pleuropneumonia of cattle, a disease that had been imported into the United States in 1843, was declared eradicated from the country in 1892, following a 5-year, $2-million campaign to identify and slaughter infected animals (Cockburn, 1961 reviewed by Ginsberg and Woodroffe, 1997). The eventual eradication of smallpox as a result of the use of Jennerian vaccination was predicted by Edward Jenner, as well as by Thomas Jefferson, in the early 19th century. Following the emergence of the germ theory and more systematic approaches to disease control in the mid-19th century, the concept of eradication of a disease first became popular briefly around the turn of the century (MMWR, 1993). The Rockefeller Foundation began campaigns to eradicate hookworm in 1907 and yellow fever in 1915 (MMWR, 1993). Both these campaigns against diseases of humans failed: the hookworm campaign because mass treatment of affected populations with anthelmintic therapy reduced the severity of individual infections but rarely eliminated them and thus did not prevent rapid reinfection and the campaign against yellow fever because of the previously unknown, inaccessible cycle of disease among nonhuman primates living in forests (Andrews and Langmuir, 1963; Soper, 1965 reviewed by Ginsberg and Woodroffe, 1997).

Acceptance of the concept of eradication declined during the late 1920s and early 1930s, after the futility of the eradication of hookworm and yellow fever was recognized (MMWR, 1993) . The concept became popular again in the late 1940s, following the elimination of Anopheles gambiae mosquitoes from Brazil and Egypt, the elimination of malaria from Sardinia, reductions in the prevalence of yaws in Haiti, and the introduction of a stable freeze-dried vaccine against smallpox (Cockburn, 1961; Soper, 1965 reviewed by Ginsberg and Woodroffe, 1997). By 1955, WHO had declared goals of global eradication of yaws and malaria, and in 1958 it adopted the goal of smallpox eradication as well (MMWR, 1993). The yaws campaign failed, partly because persons with inapparent latent cases were not adequately treated, in addition to persons with clinical disease. Many such latent infections relapsed to produce infectious lesions soon after mass treatment teams visited a community. Later, disease-specific control measures were withdrawn prematurely, allowing the infection to reappear in several areas (Hopkins, 1985a reviewed by Ginsberg and Woodroffe, 1997).

The achievement of global smallpox eradication in 1977 and its official certification by WHO in 1980 did not at first bring about the acceptance of the concept of eradication (MMWR, 1993). Concerns were raised that a new eradication effort might detract from efforts to focus attention on the need for developing comprehensive primary health services, rather than focusing on one or two diseases. However, several diseases (e.g., schisto-somiasis, rotavirus diarrhea, brucellosis, and leprosy) that were then being considered as possible targets for global eradication did not have potential for success given the current technology. Several reports and conferences have considered the potential for eradicating other diseases, of which poliomyelitis, mumps, and rubella were among those most frequently cited (Ginsberg and Woodroffe, 1997). Reports in 1980 and 1985 both con-cluded that no other major disease was then a potential candidate to be targeted by a global eradication campaign (Evans, 1985 reviewed by Ginsberg and Woodroffe, 1997). After the concept of eradication was accepted again in the late 1980s, some observers consi-dered a disease to be unsuitable for eradication to the extent that it differed from smallpox or that the intervene-tion against it differed from smallpox vaccine (Hopkins, 1985b reviewed by Ginsberg and Woodroffe, 1997). In this third period of acceptance, WHO has targeted dracunculiasis and poliomyelitis for eradication (MMWR, 1993).

The eradication of smallpox from the world in 1977 proved the feasibility of infectious disease eradication. The International Task Force for Disease Eradication (ITFDE) is assessing the potential for global eradication of other infectious diseases. An important part of the work done by International Task Force for Disease Eradication (ITFDE) was to help identify key impediments to improved prevention and control of the diseases under discussion such as rabies, even if the disease was not considered to have potential as a candidate for eradication. One such "noneradication outcome" was the impetus that the members of the ITFDE gave to initiating a demonstration project to control intestinal parasites among school children in Ghana (MMWR, 1993). The criteria that the International Task Force for Disease Eradication (ITFDE) developed and their conclusions after reviewing more

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than 90 diseases has been previously reported (CDC, 1992a, b; MMWR, 1993).

However, rabies was eradicated from England in 1896 (MMWR, 1993). No indigenous cases of human rabies have occurred in the United Kingdom since 1902, and only 20 cases have been imported into England and Wales since 1946. Person-to-person transmission of rabies is very rare. A theoretic risk of transmission through infected body fluids exists, but the only documentted cases of person-to-person transmission occurred in people who received corneal transplants from donors who died of undiagnosed rabies. The diagnosis can be confirmed during life by detecting rabies virus antigens in corneal impressions or skin biopsies (WHO, 1997). Traditionally, reliance upon long-term, widespread, government-supported programmes aimed at population reduction of animals at risk has been unsuccessful as the sole means of rabies control, based in part upon economical, ecological and ethical grounds. In contrast, immunization of domestic dogs with traditional veterinary vaccines by the parenteral route led to the virtual extinction of canine- transmitted rabies in developed countries. Taken from this basic concept of applied herd immunity, the idea of wildlife vaccination was conceived during the 1960s, and modified-live rabies viruses were used for the experimental oral vaccination of carnivores by the 1970s (Rupprecht et al., 2004).

Effective vaccines are now available against many viruses making eradication a viable proposition. Whether a virus disease can be eradicated or not depends on many factors, not least on the will power to implement such a policy. Many new, emerging and re-emerging diseases of humans are caused by pathogens which originate from animals or products of animal origin. A wide variety of animal species, both domestic and wild, act as reservoirs for these pathogens, which may be viruses, bacteria or parasites. Given the extensive distribution of the animal species affected, the effective surveillance, prevention and control of zoonotic diseases pose a significant challenge. In Africa, such high levels of population immunity are rarely achieved due to a number of reasons. Oral immunization has been shown to be an effective means of inducing high levels of immunity in fox populations in several European countries, and this technique has been mooted as a means of overcoming the logistical problems of delivering injectable rabies vaccines to dogs (Perry and Wandeler, 1993). Dog rabies control relies principally on the mass immunization of dogs in order to achieve population immunity levels sufficient to inhibit rabies transmission (Perry and Wandeler, 1993). Devising an appropriate technology for human rabies immunization includes new regimens of administration, one of which, a revised intramuscular regimen requiring only four doses and three clinic visits, proved highly efficient for postexposure treatment. This article reviews the feasibility of global eradication of rabies and factors affecting eradication of rabies in the world.

CRITERIA AND CONDITIONS FOR ASSESSING ERADICABILITY OF A DISEASE

The criteria and conditions for assessing eradicability of a disease according to MMWR (1993) include: 1) . Scientific Feasibility, 2) Epidemiologic vulnerability (e.g., existence of nonhuman reservoir; ease of spread; natural cyclical decline in prevalence; naturally induced immunity; ease of diagnosis; and duration of any relapse potential), 3) Availability of effective, practical intervention (e.g., vaccine or other primary preventive, curative treatment, and means of eliminating vector). Ideally, intervention should be effective, safe, inexpensive, long-lasting, and easily deployed. 4) Demonstrated feasibility of elimination (e.g., documented elimination from island or other geographic unit), 5) Political Will/Popular Support, 6) Perceived burden of the disease (e.g., extent, deaths, other effects; true burden may not be perceived; the reverse of benefits expected to accrue from eradication; relevance to rich and poor countries), 7) Expected cost of eradication (especially in relation to perceived burden from the disease), 8) Synergy of eradication efforts with other interventions (e.g., potential for added benefits or savings or spin-off effects) and 9) Necessity for eradication rather than control.

Smallpox eradication as a model for global cooperation

The eradication of smallpox serves as a model for global cooperation. It is unlikely that every virus disease is eradicable. Every friend of humanity must look with pleasure on this discovery (smallpox vaccination), by which one evil more is withdrawn from the condition of man; and must contemplate the possibility that future improvements and discoveries may still more and more lessen the catalogue of evils (MMWR, 1993). Smallpox was the first and only virus disease to be completely eradicated. It was eradicated through mass vaccination, and more importantly, the tracing and isolating of known cases and contacts. There were certain features of smallpox which made it a relatively easy target for eradication and this include: 1) Smallpox was a severe disease with significant morbidity and mortality. It had already been eradicated from many developed countries before the WHO campaign began, thus demonstrating the feasibility of global eradication. Eradication would result in significant savings in terms of the cost of vaccination to non-endemic countries. Therefore, the will power was there for eradication. 2) The disease was characteristic and thus easily diagnosed; therefore, there were no cultural or social barriers to case tracing and control. 3) There were no animal reservoirs for smallpox.

4) The incubation period for smallpox was long and infected individuals were infectious after the incubation period. The communicability of smallpox was low. Therefore, people living in the area surrounding a known case of smallpox can be readily protected by vaccination. 5) There was no carrier state and 6) there was only one serotype of virus and an effective vaccine was available which conferred lifelong immunity.

Four factors/conditions enabled the eradication of smallpox: 1) no reservoir of the virus existed except in humans; 2) nearly all persons infected with smallpox had an obvious, characteristic rash and were infectious for a relatively short period; 3) the natural infection conferred lifelong immunity; and 4) a safe, effective (even in newborns), and inexpensive vaccine was available that was also highly stable in tropical environments (Hopkins et al., 1985 reviewed in Ginsberg and Woodroffe, 1997). Any program for the eradication of a particular virus would involve universal vaccination of children, preferably at as young an age as possible. As in the case of smallpox, the following questions should be addressed when the feasibility of eradication of a particular human virus disease is considered.

Is the disease (rabies) worth eradicating?

In the case of severe viral diseases like smallpox and poliomyelitis, the case for eradication is straightforward. However, for milder virus diseases such as chickenpox and mumps, the case for eradication is less straightforward. The priorities would differ between developed and developing countries. The cost-benefit ratio of such an eradication program must be taken into account (Ginsberg and Woodroffe, 1997).

Is there any animal reservoir?

Viruses with a known animal reservoir such as rabies will be very difficult to eradicate. Eradication of the virus would involve eradication of the virus from the animal reservoir as well. This would involve the vaccination of the reservoir. In the case of rabies, eradication from some countries has been achieved by strict quarantine procedures for imported animals and vaccination of pets. However, eradication of rabies from the wildlife would prove to be extremely difficult (Ginsberg and Woodroffe, 1997).

Is there a carrier state?

Viruses which could produce a carrier state or persistent infection in humans such as hepatitis B and the herpes viruses would be very difficult to eradicate unless the carriers could be treated. The possibility that some of these viruses may be vertically transmitted from mother to child by transplacental transmission would confer extra difficulty in terms of eradication (Ginsberg and Woodroffe, 1997).

Is effective vaccination available?

Effective vaccines are now available against some viruses such as rubella, measles and poliomyelitis. These viruses are antigenically stable and are restricted to one or a few serotypes (Ginsberg and Woodroffe, 1997). Other viruses such as influenza A and B are antigenically unstable and the formulation of the vaccine has to be modified annually. These viruses would be almost impossible to eradicate by universal vaccination. Vaccines are still not available against the majority of viruses such as HIV and hepatitis C. In some of the cases, the development of a vaccine is very difficult not because of the multiplicity of serotypes as in the case of rhinoviruses and HIV. In other cases such as in the case of RSV, the development of a vaccine had proved to be very difficult because of other practical difficulties. In the case of RSV, the vaccine would have to be more immunogenic than the natural virus because natural infection does not appear to confer long term immunity.

How communicable is the rabies? What level of coverage is required for eradication?

A 100% coverage rate for vaccine uptake is unlikely to be attainable. However, eradication does not require 100% coverage as herd immunity will impede the transmission of the virus. The coverage rate required for eradication depends mainly on the transmissibility of the virus. Example; smallpox had a low rate of transmission whereas measles had a high rate of transmission. Thus measles is proving difficult to eradicate in countries such as the US even though the vaccine coverage is very good (Ginsberg and Woodroffe, 1997).

IMPETUS FOR ERADICATION OR ELIMINATION OF OTHER DISEASES

Smallpox Eradication Program (SEP)

The 31-year-old success of the Smallpox Eradication Program (SEP) provides an impetus for eradication or elimination of other diseases. A symposium sponsored by the Fogarty International Center of the National Institutes of Health to consider post-SEP possibilities in 1980 identified yaws, measles, and polio as the most likely candidates for eradication (Duffy et al., 1990). In 1986, the the World Health Assembly resolved to "eliminate" Guinea worm disease (Resolution WHA 39.21), the first such resolution since the smallpox campaign; in 1989, the Assembly added the deadline for eradicating Guinea worm disease in "the 1990s" (Resolution 42.29). According to Duffy et al. (1990), Global 2000 and the African Regional Office of WHO have set the informal goal of eradicating Guinea worm disease by 1995. In 1988, the World Health Assembly officially established the goal of eradicating polio by the year 2000 (Resolution WHA 41.28).

Other eradication model for global cooperation

In their discussions, two diseases (Guinea worm disease-dracunculiasis and Poliomyelitis) were judged to be eradicable and three to be candidates (Rabies, yaws and endemic syphilis) for elimination of transmission or of clinical symptoms; three were not considered candidates (measles, tuberculosis and Leprosy-Hansen disease) for eradication at this time. Guinea worm eradication was considered feasiable if the necessary commitment and resources can be mobilized (Duffy et al., 1990). The ITFDE will help publicize efforts and funding needs, and worldwide polio eradication is deemed technically possible by the year 2000; an improved vaccine would facilitate eradication of polio. The ITFDE agreed to write to the heads of state of several nations in the Americas to solicit their support for this hemisphere's goal of eliminating polio by the end of 1990 (Duffy et al., 1990).

Global eradication of measles

Global eradication of measles is not currently feasible because of the high communicability of measles and the suboptimal serologic responses to vaccines administered to young infants. After the ITFDE conference, WHO recommended use of high-titered Edmonsten-Zagreb vaccine beginning at 6 months of age developing countries; however, an improved vaccine is still needed. Global eradication of tuberculosis is not now feasible. Better tools for diagnosis, case-finding, prevention, and treatment need to be developed, and the application of current short-course therapy in developing countries needs to be greatly increased and leprosy (Hansen disease) eradication worldwide is not feasible now (Duffy et al., 1990).

Elimination of blindness

Elimination of blindness caused by onchocerciasis appears feasible through vector control and treatment with ivermectin. Because of the cost, duration, and difficulty of effective larviciding and the absence of a drug to kill the adult worms, eradication of the infection altogether is not now feasible (Duffy et al., 1990).

Eradication of yaws and endemic syphilis

Eradication of yaws and endemic syphilis is not feasible under present conditions. However, elimination of the transmission of these diseases in certain areas appears feasible (Duffy et al., 1990). Tests need to be developed that can reliably distinguish the organisms that cause yaws, endemic syphilis, and pinta from those that cause venereal syphilis (Burke et al., 1985 reviewed by Duffy et al., 1990).

Regional goals of eliminating polio, measles, or neonatal tetanus

Different WHO regions have also established regional goals of eliminating polio, measles, or neonatal tetanus over the next decade, starting with the elimination of polio from the Americas by the end of this year. India and China aim to eliminate leprosy transmission within their borders by the year 2000, and the United States has set a national goal of eliminating tuberculosis by 2010 (defined as an annual case rate of less than one per million population (CDC, 1992a, b).

FACTORS CONTRIBUTING TO DIFFICULTY IN GLOBAL ERADICATION OF RABIES AND CONTINUAL ENDEMITY IN DEVELOPING COUNTRIES OF THE WORLD

Rabies in humans can be prevented by appropriate postexposure prophylaxis and through vaccination of the animal vector, which is not, however, always available and affordable in resource-limited countries (Zinsstag et al., 2007). Infectious pathogens that originate in wild animals have become increasingly important throughout the world in recent decades, as they have had substantial impacts on human health, agricultural production, wildlife-based economies and wildlife conservation (Bengis et al., 2004). Globally, dog-transmitted rabies represents the largest threat to human health. In order to prevent the transmission of rabies in a dog population, it is theoretically necessary to vaccinate a minimum of 60 to 70% of the dogs. Even countries with potentially sufficient resources, however, do not often meet and sustain these rates. One reason for such failure might be that individual dog owners might feel that it is too expensive to vaccinate their pets (Meltzer and Rupprecht, 1998 reviewed by Tamashiro et al., 2007). Risk factors for Rabies including risk behaviours, associated conditions, protective factors, and unrelated factors. However, eradication of rabies from the wildlife would prove to be extremely difficult. Transmission would confer extra diffi-culty in terms of eradication. Whether a virus disease can be eradicated or not depends on many factors (Tamashiro et al., 2007).

Factors that can increase the risk of rabies include: travelling or living in developing countries where rabies is more common, including countries in Africa (Tamashiro et al., 2007). Pathogens can emerge either through introduction into a new population or when the interaction with the vector changes; emergence is also influenced by microbiological adaptation and change, global travel patterns, domestic and wild animal contact and other variants in human ecology and behaviour (Tapper, 2006). Although the discovery of such zoonoses is often related to better diagnostic tools, the leading causes of their emergence are human behavior and modifications to natural habitats (expansion of human populations and their encroachment on wildlife habitat), changes in agricultural practices, and globalization of trade. However, other factors include wildlife trade and translocation, live animal and bush meat markets, consumption of exotic foods, development of ecotourism, access to petting zoos, and ownership of exotic pets (Chomel et al., 2007). Factors such as the size and intensity of infectious foci, the rapidity of spread, difficulty of eradication, etc., will influence these risk factors. However, the main factors that contribute to the increase in the number of cases of rabies and making eradication of rabies in the world difficult include:

Human factors

Meslin et al. (2000) described the direct and indirect implications for public health of emerging zoonoses. Direct implications are defined as the consequences for human health in terms of morbidity and mortality. Indirect implications are defined as the effect of the influence of emerging zoonotic disease on two groups of people, namely: health professionals and the general public (Meslin et al., 2000). Professional assessment of the importance of these diseases influences public health practices and structures, the identification of themes for research and allocation of resources at both national and international levels (Meslin et al., 2000). The perception of the general public regarding the risks involved considerably influences policy-making in the health field. However, other human factors affecting eradication of rabies are:

Sharp and exponential rise of global human activity

Human activities may also be a source of wildlife infection, which could create new reservoirs of human pathogens (Chomel et al., 2007). The emergence of these pathogens (rabies, human immuno deficiency virus/acquired immune deficiency syndrome, influenza A, Ebola virus and severe acute respiratory syndrome) as significant health issues is associated with a range of causal factors, most of them linked to the sharp and exponential rise of global human activity (Bengis et al., 2004). Jebara (2004) described the new challenges that this brings for individual countries and the international community.

Deforestation, development of human habitat, and mining activities

Deforestation, development of human habitat, and mining activities has been suggested as risk factors associated with the reemergence of vampire bat rabies in humans in the Amazon Basin (Chomel et al., 2007). In 2004, 46 persons died of rabies transmitted by vampire bats, mainly in Brazil (22 cases) and Colombia (14 cases); only 20 human cases of rabies were transmitted by dogs in all Latin America (Schneider et al., 2005). A similar trend was again observed for 2005 (Chomel et al., 2007). Such a zoonosis is a good example of deforestation and agricultural development leading to human habitat expansion into natural foci of a viral infection.

Human encroachment on wildlife habitat

The exponential growth of the human population, from 1 billion in 1900 to 6.5 billion in 2006, has led to major ecologic changes and drastic wildlife habitat reduction. Many examples of the emergence or reemergence of zoonoses related to human encroachment on wildlife habitats exist (Chomel et al., 2007). Leading factors for emergence of zoonoses are unbalanced and selective forest exploitation and aggressive agricultural development associated with an exponential increase in the bushmeat trade (Wolfe et al., 2005a; Chomel et al., 2007).

Increasing international travel

Rabies is a fatal disease, and increased international travel is one of the important factors affecting eradication of rabies globally (Shaw et al., 2009). Importation of infectious diseases to new countries is likely to increase among both travellers and immigrants (Fenner et al., 2007). Approximately 80 million people from resource-rich areas worldwide travel to resource-poor countries every year (WTO, 2006) and are exposed to many infections that are no longer prevalent in the countries where they live (Fenner et al., 2007). Moreover, visitors to developing countries are sometimes unaware of the rabies risk posed by dog bites and thus may not seek appropriate medical attention for such bites (Nadin-Davis et al., 2007). The occasional cases of rabies reported in industrialized countries, such as the United Kingdom, are often the result of exposure while travelling in developing countries such as India (Solomon et al., 2005). Arguin et al. (2000) reported that of the 36 cases of human rabies that have occurred in the United States since 1980, 12 (33%) were presumed to have been acquired abroad. Twenty people died of rabies in France between 1970 and 2003 (compared to 55,000 yearly worldwide), 80% on returning from Africa. Dogs were the contaminating animals in 90% of the cases and children were the most common victims (Peigue-Lafeuille et al., 2004). In France, people travelling abroad, particularly to Africa, are warned not to approach unknown animals (especially dogs) or to try to import them, and are advised to comply with vaccinal recommendations for travellers, particularly for toddlers (Peigue-Lafeuille et al., 2004). We should recognizing that humans and animals are part of a global community with frequent travel and translocation, the risks of disease introduction, particularly with sub-clinical or incubating animals, are real and present (Castrodale et al., 2008). In the United States, it is recommended that international travellers likely to come in contact with animals in canine rabies-enzootic areas that lack immediate access to appropriate medical care, including vaccine and rabies immune globulin, should be considered for preexposure prophylaxis (Arguin et al., 2000). However, travelers going to endemic areas need to take precautions (Shaw et al., 2009).

Lack of emergency preparedness planning

Emergency preparedness planning for animal diseases is a relatively new concept that is only now being applied in Africa. Information can be drawn from numerous recent disease epidemics involving rinderpest, contagious bovine pleuropneumonia (CBPP) and Rift Valley fever. These examples clearly demonstrate the shortcomings and value of effective early warning with ensured early reaction in the control of transboundary animal disease events. On a global level, the human health sector lags behind the animal health sector in the assessment of potential threats, although substantive differences exist among countries in the state of national preparedness planning for emerging diseases (Merianos, 2007).

Lack of good laboratory and proper surveillance

Isolation of LBV from terrestrial wildlife in study reported by Markotter et al. (2006a) serves as further confirmation of our lack of understanding of the incidence and host range of lyssaviruses in Africa. Poor surveillance of rabies-related viruses and poor diagnostic capability in most of Africa are large contributors to our lack of information and the obscurity of the African lyssa viruses (Markotter et al., 2006a). The lack of surveillance data on emerging zoonoses from many developing countries means that the burden of human, livestock and wildlife disease is underestimated and opportunities for control interventions thereby limited (Merianos, 2007). Many countries in postcommunist transition face a sharp increase in zoonotic diseases resulting from the breakdown of government-run disease surveillance and control and weak private health and veterinary services (Zinsstag et al., 2007). However, laboratories continue to be sadly behind the times in terms of equipment and skills for diagnosing the emerging pathogens as can be readily observed in developing nation such as Nigeria (Okonko et al., 2008).

Lack of appropriate control methods

Lethal methods of dog population control are even more expensive, and attempting to control rabies by reducing dog populations has not worked for any extended period. Despite the availability of techniques to improve the global rabies situation, limitations in surveillance and epidemiologic investigations impede the institution of such measures (Knobel et al., 2005). In industrialized countries, diagnosis of rabies in animals is achieved by using rabies-specific fluorescein-conjugated antibody to detect viral antigen in brain smears; however, ante-mortem diagnosis in humans must rely on less -invasive methods (Nadin-Davis et al., 2007). The utility of PCR-based methods to detect rabies virus sequences in saliva and other body fluids has been reported, and PCR is being used in many industrialized countries. An additional component of rabies control in such countries is the application of viral typing methods to identify viral variants that circulate in specific host reservoirs; which are lacking in most developing countries (Nadin-Davis et al., 2007).

Lack of solid commitment and internationally resourced initiatives

Little public domain information is available on international coordinated responses to the deliberate introduction of biological pathogens. Terrorist events in the early 21st Century have increased awareness of the risks, but solid commitment and internationally resourced initiatives are still lacking (Lubroth, 2006). However, in many countries, little is known about the real cost of mass vaccination of dogs, and quantitative data are urgently needed to evaluate the cost-effectiveness of different rabies control strategies in resource-limited countries; rabies control strategies in developing countries are currently under review by WHO (Zinsstag et al., 2007).

Inappropriate management

The clinical signs and symptoms of the initial rabies case-patients in Africa may have been altered due to use of traditional medicines. The use of traditional medicines is common in rural settings in Africa and may result in toxicities, including abdominal and psychiatric symptoms and abnormal liver function test results (Luyckx et al., 2004; Cohen et al., 2007) . These medicines could have contributed to the atypical manifestations in some cases. In addition, clinicians may have attributed some of the neurologic symptoms to herbal intoxication (Cohen et al., 2007). "In areas where there is a high prevalence of rabies, such as Africa and Asia, "the Alliance for Rabies Control added, "the need for vaccination has often been overlooked, despite the fact this would cost less than other health care programs," including administering post-exposure rabies immunization to save dog bite victims (Clifton, 2007). In the context of emerging zoonoses, comprehensive risk assessments are needed to identify the animal-human and animal-animal inter-faces where transmission of infectious agents occurs and the feasibility of risk reduction interventions (Merianos, 2007) . Shaw et al. (2009) in a study that examined for those who reported postexposure management to animals while abroad, reported that only 25% of the 459 post-travel records from October 1998 until February 2006 at two travel medicine clinics, in Auckland and Hamilton, received postexposure treatment consistent with WHO guidelines, reflecting inappropriate management abroad (Shaw et al., 2009).

Gross under-diagnosis

The incidence of rabies in many parts of Africa is unknown, but rabies is probably underdiagnosed (Mallewa et al., 2007). Cases of rabies may be incorrectly attributed to other causes of pyrexia and confusion common to rural Africa, including cerebral malaria, bacterial infections, and infection with HIV (Bleck and Rupprecht, 2005 reviewed by Mallewa et al., 2007; Cohen et al., 2007). In a study by Hayman et al. (2008), there were differences in seroprevalence between *E. Gambian us* and *E. helvum* with respect to LBV infection. The underlying cause of the difference in seroprevalence is unclear. Possible explanations include differential susceptibilities to infection; virus–host adaptation; different contact with the virus, including a recent epidemic in the *E. helvum* colony; or different population ecology (Hayman et al., 2008) . No investigations into infections of humans were made during these investigations, but lyssavirus infections in humans in Africa are underdiagnosed (Mallewa et al., 2007; Hayman et al., 2008).

Gross under reporting

Rabies is no doubt underreported and probably misdiagnosed in Nigeria and elsewhere in Africa (Asselbergs, 2007; Fagbo, 2009; Woolf, 2009). According to Ogundipe et al. (1989), in their study the development and efficiency of the animal health information system in Nigeria as well as the completeness and immediacy of data supply by the system for the period between January, 1977 and December, 1984 revealed that the system was found to be characterized by: late, inaccurate and gross under reporting. And these constraints in reporting include inadequate personnel, poor diagnostic and reporting facilities (Okonko et al., 2008).

Poor coordination and cooperation

Because animal disease control, e.g. rabies control and ORV, is the responsibility of each federal state, insufficient cooperation in the planning of vaccination campaigns between neighbouring federal states has also been an important shortcoming (Müller et al., 2005). Preparations for international cooperation in response to disease disasters at the regional or continental levels are poorly coordinated and cooperation is limited, although intergovernmental and international organizations have been advocating for years that emergency responses to infectious disease outbreaks should be planned for and prepared at the national level (Lubroth, 2006).

Lack of knowledge and information

Many countries, especially those with resource constraints and those in sub-Saharan Africa, lack information on the distribution of zoonotic diseases (Zinsstag et al., 2007). Risks for zoonoses are considered negligible compared with those for diseases of higher consequence because the societal consequences of zoonoses are not recognized by the individual sectors. For example, outbreaks of Rift Valley fever in persons in Mauritania were mistakenly identified as yellow fever. However, transmission of zoonoses to humans can already be greatly reduced by health information and behavior. Authorities in Kyrgyzstan, for example, have started an information campaign to reduce brucellosis transmission to small-ruminant herders by encouraging them to wear gloves for lambing and to boil milk before consuming. Interventions in livestock should always be accompanied by mass information, education, and communication programs (Zinsstag et al., 2007).

Lack of risk communication

Lack of risk communication is one of the factors affecting polio eradication especially in Nigeria. Although, the boycott of immunization is no longer in effect, low participation during vaccination may persist reflecting a failure to implement risk communication (Agbeyegbe, 2007). The silence of the government over the alleged report by JNI and widely in the media that the government acknowledged the use of contaminated vaccines but claimed that the contaminated batch had been completely used, could be interpreted as indicative of the accurateness of the report. To address such situations, risk communication is increasingly becoming important in public health (Rudd et al., 2003 reviewed by Agbeyegbe, 2007). Risk communication offers a two-way communication process that presents the expert opinions based on scientific facts to the public, and acknowledges the fears and concerns of the public, seeking to rectify knowledge gaps that foster misrepresentation of risk (Leiss, 2004; Aakko, 2004 reviewed by Agbeyegbe, 2007; Okonko et al., 2009).

Lack of adequate public awareness

Lack of public education campaigns in the developing world (Clifton, 2007) is another factor affecting rabies eradication. Though, public awareness of the human health risks of zoonotic infections has grown in recent years (Heeney, 2006), reliable data on rabies are scarce in many areas of the globe, making it difficult to assess its full impact on human and animal health (Awoyomi et al., 2007). Some steps are being taken. The worldwide communications networks have made inroads with SatelLife and ProMED online services. Physicians in developing nations can consult colleagues, libraries, or data banks for help with puzzling cases. Promising as they are, though, these "electronic conference tables" represent only a small piece of the solution. At present, the networks do not address the underlying causes of new and re-emerging infectious diseases. And they probably can do little to get to the heart of the real issues: educating the public, immunizing the children, improving sanitation, cleaning up the water, housing the homeless, feeding the starving (Hoel and Williams, 1997 reviewed by Okonko et al., 2008).

Lack of motivation

Several studies have documented the costs associated with wildlife-rabies epizootics (Shwiff et al., 2007; Sterner et al., 2009). According to the Alliance for Rabies Control, “the tools for effective rabies control are available. What is lacking are the motivation, commitment and resources to tackle the disease effectively (Clifton, 2007).”

Political instability

In several countries particularly Afganistan and Somalia, part of Parkistan, Sierra Leone, Sudan, Liberia, Congo, and Ethiopia political instability or armed conflicts make vaccination logistically difficult and unpredictable (Okonko et al., 2009). In addition to this internal politics in the 2003 immunization boycott, were ramifications from the international political arena. Anti-western sentiments have increased among Northern Muslims fundamentalist following the September 11, 2001 attacks and America’s war on terrorism. Given the distrust and growing antagonism towards America, the involvement of the West in a program that benefits Muslims was viewed with suspicion (Agbeyegbe, 2007; Okonko et al., 2009).

Conflict-threat of armed militias and forced migration

Other challenges facing vaccination teams included the threat of armed militias that roam the area in search of opportunities to seize control over the local oil resources (Njoku, 2006). With the overwhelming increase in high-intensity local conflicts among political, ethnic, and religious rivals, government-based disease- surveillance systems have little or no chance of success (Okonko et al., 2008). The reintroduction of canine rabies into northern KwaZulu-Natal Province in 1976 followed an influx of refugees from Mozambique (Cohen et al., 2007). The possible contribution of increased immigration into Limpopo Province from Zimbabwe in recent years is difficult to quantify (Oucho, 2006; Cohen et al., 2007).

Cultural and religious beliefs

Cultural and religious beliefs will also contribute to the underreporting of human rabies that may arise from the consumption of infected apparently healthy dogs and cats. The [rabies-related lyssaviruses] Lagos bat and Mokola viruses still remain under-diagnosed in the human populace (Fagbo, 2009; Woolf, 2009). In case of measles and polio viruses, many Nigerians are blaming the outbreak on vaccination efforts; an attitude expert’s fear may ruin previous gains in eradicating vaccine preventable disease in the country (Okonko et al., 2009). Most of the anti-immunization campaigns in Nigeria have been predominantly Muslim north of Nigeria, and a number of Muslim clerics have been quoted in the Nigerian media as claiming that vaccines are dangerous and cause sterility or illness (Adeija, 2007). Cultural and religious objections under vaccinations efforts, resulting in persistently low immunity in the population and consequently, a high incidence of emerging vaccine-derived viruses and reemergence of wild viruses (Okonko et al., 2009). Whereas the undercurrents between Muslims and Christians in Nigeria as well as Western donors may have been sufficient to begin the controversy on the vaccines e.g. polio vaccine, other factors helped to sustain it (Agbeyegbe, 2007).

Ignorance

Factors responsible for the continued endemicity of rabies in Nigeria have been determined in a study by Opaleye et al. (2006). In their study, the knowledge, attitude and practice study among residents of Osun State, Nigeria was reported. In their study among 679 individuals, only 33.4% of the respondents knew rabies could be prevented by vaccination, while 38.7% believed that the infection could be treated with herbs. Of the 387 victims of dog bite, 240 (62%) never sought prophylactic postexposure treatment. Of the 10 people who received postexposure treatment, only one received the appropriate treatment consisting of washing, disinfection of wounds, tetanus toxoid and complete antirabies immunization.

Government negligence

No vaccine is fully safe, perfectly potent and without risk of administering error (Clements et al., 1999 reviewed by Okonko et al., 2009). Deficiencies in national veterinary services have contributed to failures in early detection and response; in many regions investigation and diagnosis services have deteriorated (Rweyemamu et al., 2000). Also, the inability of the Nigerian government to acknowledge the risk involved in vaccination however negligible raises doubt about the sincerity of the government, and positions the boycotts of polio vaccination proponents as a more reliable source of information. The government does not appear to have positioned itself as a credible authority to implement immunization programs (Olugbode, 2007; Okonko et al., 2009).

Government policy

In resource-limited and transitioning countries, many zoonoses are not controlled effectively because adequate policies and funding are lacking (Zinsstag et al., 2007). In Chang et al. (2002) analysis on expenditure reports to estimate the cost of rabies prevention activities. An estimated $13.9 million was spent in New York State in United States to prevent rabies from 1993 to 1998; yet Nigerian government has not seen the need to make such tremendous dedication and policy in the health sector.

Deception

According to Clifton (2007), policymakers in the developing world often seek for their cities the superficially animal-free appearance of a “modern” city that they see in Europe and the U.S., equating this with ridding themselves of rabies. But casual outdoor observation of European and U.S. cities by daylight is deeply deceptive. European and American cities support even more dogs, cats, and wild animals per thousand humans than the cities of the developing world. They have merely achieved a transition from hosting outdoor animals, seen in daytime, to hosting mostly indoor pets and nocturnal wildlife.

Socioeconomic factors

Poverty

Poverty is one other factor. Rabies in humans can be prevented by appropriate postexposure prophylaxis, which is not, however, always available and affordable in resource-limited countries (Zinsstag et al., 2007). Tissue-culture vaccines are expensive and they are not always used in all parts of the world. Industrialized countries have responded rapidly to recent zoonosis outbreaks and contained them well, but many resource-limited and transitioning countries have not been able to respond adequately because they lack human and financial resources and have not sufficiently adapted public health surveillance. In industrialized countries, an important part of successful zoonosis control has been compensating farmers for culled livestock. However, many resource-limited countries would not be able to conduct such programs (Zinsstag et al., 2007).

Hunting with dogs

Hunting activities for the 10 million hunters in Europe generate a financial flux of almost 10 billion euros and 100,000 jobs. Europe is also the world's largest importer of venison (>50,000 tons/year). Similarly, in the United States, hunting activities generate >700,000 jobs (Chomel et al., 2007). The combination of urban demand for bushmeat (a multibillion-dollar business) and greater access to primate habitats provided by logging roads has increased the amount of hunting in Africa, which has increased the frequency of human exposure to primate retroviruses and other disease-causing agents (Chomel et al., 2007). However, urban (dog-mediated) rabies has almost been completely eradicated, except from cases from failed vaccination, increased mortality due to hunting and rabies, dogs and foxes and along their dispersal routes to maximize the effect of vaccination (Eisinger and Thulke, 2008). The viral ecotype that previously had been confined to urban dogs in Texas, variant's occurring in a hunting dog in Alabama in 1993. The last case of rabies in Italy was diagnosed in a fox, sheep and goats kept outdoors; thereby leading to prohibition of hunting with dogs (Eisinger and Thulke, 2008).

Increasing demands for bush meat

Another risk factor related to the emergence of zoonotic diseases from wildlife has been the considerable increase in consumption of bushmeat in many parts of the world, especially Central Africa and the Amazon Basin, where 1 - 3.4 million tons and 67 - 164 million kilograms, respectively, are consumed each year (Karesh et al., 2005 reviewed by Chomel et al., 2007). Similarly, several outbreaks of Ebola virus and other disease-causing agents in western Africa have been associated with consumption of bushmeat, mainly chimpanzees that were found dead (Chomel et al., 2007). Human butchering and consumption of animals potentially infected with rabies and other zoonotic viruses are not limited to Asia (Durosinloun, 2009; Fagbo, 2009; Woolf, 2009). In Africa, the bushmeat trade is generating hundreds of millions of dollars (Karesh et al., 2005 reviewed by Chomel et al., 2007). In the Congo Basin, trade and regional consumption of wild animal meat could reach 4.5 million tons annually; the demand for bushmeat in western and Central Africa could reach up to 4× the demand for bushmeat in the Amazon Basin (Wolfe et al., 2005b; Chomel et al., 2007). However, the fast-growing demand for meat in urban centers in resource-limited countries is leading to the intensification of livestock production systems, especially in periurban areas of these countries (Zinsstag et al., 2007). Because efficient zoonosis surveillance and food safety are lacking, the risk for zoonosis transmission is increasing, particularly in rapidly growing urban centers of resource-limited countries (Steinmann et al., 2005 reviewed in Zinsstag et al., 2007).

Dogs, cats and bats eating

Dogs purchased by restaurants are soon killed for consumption. With the exception of butchers, there would be insufficient time to transmit RABV to other dogs and humans. Until now, persons in China who eat dog meat have not been not considered at risk for rabies because no related infections have been reported (Tao et al., 2009). In Nigeria, dog eating is very common in states such as Plateau, Akwa Ibom, Cross River, Kaduna, Kebbi and Ondo. In fact, dog suya (barbequed dog meat) is sold publicly in the dog eating areas. In some areas such as Jos, only local and seasoned connoisseurs may easily distinguish restaurants where dog and other conventional meats are sold. Cat eating, though not as common as dog eating, can also be encountered, even in cosmopolitan places such as Lagos. While human consumption of bats is also common, there seems to have been little or no local effort (as per the limited information available) to evaluate the risk of rabies transmission (Durosinloun, 2009; Fagbo, 2009; Woolf, 2009).

Major ecologic, environmental and anthropogenic changes of the biosphere

Climatic changes in both East and West Africa were associated with an upsurge of emerging infections such as Rift Valley fever (Rweyemamu et al., 2000). Climatic changes are likely to have a direct impact on the presence and abundance of various pathogens and their vectors, so that with a warming climate exotic diseases may play a role in future UK livestock and wildlife disease management (Böhm et al., 2007). However, the world is experiencing an increase in emergent infections as a result of anthropogenic changes of the biosphere and globalization (Cabello and Cabello, 2008). Global warming unrestricted exploitation of natural resources such as forests and fisheries, urbanization, human migration, and industrialization of animal husbandry cause environmental destruction and fragmentation. These changes of the biosphere favour local emergence of zoonoses from their natural biotopes and their interaction with domestic animals and human populations, favour the dissemination of these zoonotic pathogens worldwide (Cabello and Cabello, 2008).

Globalization of animal trade

Globalization is leading to a rise in the emergence of diseases. The magnitude of the global movement of animals is staggering. In terms of sheer numbers, 37,858,179 individually counted live amphibians, birds, mammals, and reptiles were legally imported to the United States from 163 countries in 2000 - 2004. These imports included Asian macaques, South American rodents, and African great cats (Jenkins et al., 2007; Marano et al., 2007). Abazeed and Cinti (2007) and Swanepoel et al. (2007) reports on rabies and Marburg virus respectively illustrated zoonotic diseases with serious health implications for humans, and both have a common reservoir, the bat. Tumpey (2007) reminded us how globalization has had an impact on the worldwide animal trade. This worldwide movement of animals has increased the potential for the translocation of zoonotic diseases, which pose serious risks to human and animal health (Tumpey, 2007; Marano et al., 2007).

Liberalization of world trade

In the past decades, public health authorities within industrialized countries have been faced with an increasing number of food safety issues. The situation is equally serious in developing countries. The globalization of food (and feed) trade, facilitated by the liberalization of world trade, while offering many benefits and opportunities, also represents new risks (Domenech et al., 2006).

Wildlife trade and translocation

However, other factors include wildlife trade and translocation (Chomel et al., 2007). Wildlife trade provides mechanisms for disease transmission at levels that not only cause human disease outbreaks but also threaten livestock, international trade, rural livelihoods, native wildlife populations, and ecosystem health (Chomel et al., 2007). Worldwide, an estimated 40,000 primates, 4 million birds, 640,000 reptiles, and 350 million tropical fish are traded live each year (Karesh et al., 2005 reviewed by Chomel et al., 2007). International wildlife trade is estimated to be a US $6-billion industry (Check, 2004 reviewed in Chomel et al., 2007). Translocation of wild animals is associated with the spread of several zoonoses (Chomel et al., 2007). Rabies was introduced in the Mid-Atlantic States in the 1970s when hunting pens were repopulated with raccoons trapped in rabies-endemic zones of the southern United States (Chomel et al., 2007). Wild life such as wild deer can feature in the epidemiology of a wide range of livestock and human diseases in the United Kingdom by representing a source of disease via various transmission routes (Böhm et al., 2007). In Eastern Europe, raccoon dogs (*Nyctereutes procyonoides*) are becoming a new reservoir for rabies, in addition to the established red fox reservoir, as raccoon dogs have spread into new habitats from accidental release of animals raised for fur trade (Chomel et al., 2007). Infectious pathogens of wildlife affect not only human health and agricultural production but also wildlife-based economies and wildlife conservation. Zoonotic pathogens that infect domestic animals and wildlife hosts are more likely to emerge (Chomel et al., 2007).

Changes in agricultural practices

The emergence of rabies and its expansion has been directly linked to development of agricultural activities. In the late 1970s and early 1980s, a rabies epidemic occurred in free-ranging greater kudus (*Tragelaphus strepsiceros*) in Namibia (Hubschle, 1988 reviewed by Chomel et al., 2007). The kudu population had increased considerably in response to favourable conditions and human-made environmental changes (Chomel et al., 2007). Suitable conditions for transmission in the kudu population after initial infection by rabid carnivores are provided by the social behavior of kudus, such as browsing on thorny acacia trees and resultant lesions in the kudus' oral cavity, and excretion of relatively high titers of virus in the saliva of infected animals (Chomel et al., 2007). However, reemergence of zoonotic diseases that had been controlled from their domestic animal reservoirs is also of major concern. Wildlife may become new reservoirs of infection and may recontaminate domestic animals (Chomel et al., 2007). Most animal pathogens for which surveillance programs exist relate to farm animals, and few or no programs are specifically aimed at wildlife. Two different but complementary approaches are 1) to monitor the presence of specifically Identified pathogens that have emerged as human pathogens and 2) to investigate in a given wildlife species the presence of known or unknown infectious agents. Furthermore, conservation of habitat biodiversity is critical for preventing emergence of new reservoirs or amplifier species (Chomel et al., 2007).

Topography

This is another important factor affecting eradication of rabies. There are huge numbers of wild animals distributed throughout the world and the diversity of wildlife species is immense (Bengis et al., 2004). According to Bengis et al. (2004), each landscape and habitat has a kaleidoscope of niches supporting an enormous variety of vertebrate and invertebrate species, and each species or taxon supports an even more impressive array of macro- and micro-parasites.

Paving streets

Paving streets tends to eliminate feral pigs, since pigs need mud to wallow in. That tends to leave more habitats to monkeys, if free-roaming dogs disappears mostly macaques in Asia, baboons in Africa. Macaques and baboons do not run from feral cats, bite more often and more dangerously than dogs, are capable of transmitting more deadly diseases to humans than any other animals even though they rarely carry rabies, can outclimb cats, and are often smarter than the public policymakers whose misguided ideas about animal control invite their presence (Clifton, 2007).

Lack of good road network

Of the targeted 29 million children, 4 million reside in impoverished and hard-to-reach settlements across the Niger Delta Region of Nigeria (Njoku, 2006).

Capacity carrying

In effect, mechanization of transport and improvements in urban sanitation reallocated the carrying capacity of the human environment. Instead of supporting dogs and cats who lived directly off of refuse and rodents, the human environment evolved to support dogs and cats who lived on refuse that was processed into pet food, fed to them in human homes. This same reallocation of carrying capacity has occurred in Western Europe, and is occurring now in Eastern Europe, India, China, Ethiopia, and wherever else economic development is transforming former hubs of agrarian commerce into technologically developed modern cities (Clifton, 2007).

Animal factors

Migration of dogs

Also, outbreak of rabies in humans followed an outbreak in domestic dogs. Increasing numbers of human rabies cases in Africa have been attributed to the mobility of human and animal populations (Cohen et al., 2007). Other human-related activities, such as persons migrating with their dogs may also contribute to long-distance spread of rabies. While the majority of reported potential rabies exposures are associated with dog and cat incidents in most places, most rabies exposures have been derived from rabid wildlife (Roseveare et al., 2009). Can contact between wild dogs and domestic dogs be minimized? According to Ginsberg and Woodroffe (1997), this would depend upon local peoples' need for domestic dogs. More research is needed to determine whether domestic dogs' movements could be restricted by, for example, requiring that owned dogs be collared, that dogs be tied up at night, and shooting unaccompanied dogs (Wu et al., 2009) . However, the animal population itself does not pose a rabies threat (Wu et al., 2009). Subsequently, international commerce, human and animal migration and travel, favour the dissemination of these zoonotic pathogens worldwide (Cabello and Cabello, 2008).

Migration of stray animals

According to Roseveare et al. (2009), stray cats were most frequently rabid among domestic animals. This underscores the need for improvement of wildlife rabies control and the reduction of interactions of domestic animals, including cats, with wildlife. Can contact between wild life and stray animals be minimized?

Migration of wildlife

Most emerging infectious diseases are zoonotic; wildlife constitutes a large and often unknown reservoir. Wildlife reservoirs of classical and emerging zoonoses persist in many countries and substantially slow control efforts for livestock (Smith et al., 2006). Though, wildlife is a major source of income, either directly for consumptive or productive use value or indirectly for touristic and scientific values. For instance, worldwide, deer farming has been developing dramatically. In New Zealand, 2 million farmed deer, half of the world's farmed deer population, generate an annual income of NZ $200 million (Chomel et al., 2007). Even in industrialized countries, wildlife-related activities can generate major income. In the United States, the total expenditure for wildlife-related activities was $101 billion in 1996, 1.4% of the national economy; it (wildlife) is now recognized as an important source of emerging human pathogens, including parasites (Polley, 2005). Wildlife can also be a source for reemergence of previously controlled zoo-noses. Although the discovery of such zoonoses is often related to better diagnostic tools, the leading causes of their emergence are human behavior and modifications to natural habitats (expansion of human populations and their encroachment on wildlife habitat), changes in agricultural practices, and globalization of trade (Chomel et al., 2007).

Animal importation

Animals imported for commercial trade represent a substantial risk to human health (Marano et al., 2007). Animals are legally imported into the United States for many reasons. They are used for exhibitions at zoos; scientific education, research, and conservation programs; food and products; and in the case of companion animals, tourism and immigration. Increasingly, however, animals are being imported for a thriving commercial pet trade (Marano et al., 2007) . In many cases the animals that are imported and traded are of species that are considered exotic (here defined as non-native species, animals not traditionally kept as pets, or both). This can be a risky business, as many shipments include a high volume of wild-caught versus captive raised animals. For most of these animals, there are no requirements for zoonotic disease screening either before or after arrival into the United States. There have been anecdotal reports of high rates of death among animals in these shipments (Marano et al., 2007). As a scientist, one might suggest solutions that employ familiar tools, such as post arrival screening of animals with reliable laboratory tests, empirical treatment for known diseases (if such tests and treatments already existed), or quarantine of the animals for an appropriate length of time (Marano et al., 2007). Many of these solutions are not feasible or practical to use on the large volume of animals that are being imported and cannot be employed to prevent new or emerging pathogens or infections. Ultimately, import restrictions may be the only means of preventing introduction of exotic infections (Marano et al., 2007).

Illegal importation of animals

Illegal trade can also be a possible source of human infection (Chomel et al., 2007). Illegal importation of animals still poses a risk of rabies world wide. In March 2007, a puppy reportedly to have been recently imported from India into the United States was found to be positive for rabies by the Alaska Department of Health and Social Services. According to Castrodale et al (2008), this case report highlights several important public health issues. Animal-importation regulations, policies and practices are intended to minimize these risks and should be routinely evaluated and updated as needed in response to occurrences such as detailed in the Castrodale et al (2008) communication. And the illegal trade of exotic wildlife, with promises of considerable financial return in the underground markets, has disastrous implications for many endangered or threatened species (Marano et al., 2007).

Mating activities and dispersal

This is one of the animal factors that contribute to the difficulty in the eradication of rabies. According to Eisinger and Thulke (2008), different transmission patterns of rabies re-emerged out of the set of their model rules, for example the seasonal rabies peaks caused by mating activities and dispersal and the focal spatial pattern of the advancing rabies epidemic. In the study by Eisinger and Thulke (2008), any neighbouring cells of foxes within a distance of up to 3 cells may be infected, with a probability of $0{\cdot}16^1$, $0{\cdot}16^2$ and $0{\cdot}16^3$, respectively, because of mating contacts. There were hardly any infections during dispersal but juvenile foxes dispersing during their incubation period will cause standard transmission after settlement (Eisinger and Thulke, 2008).

Host population increase

As in a classic situation, outbreak of rabies in humans followed an outbreak in domestic dogs of the Africa region (Cohen et al., 2007). Increasing numbers of human rabies cases in Africa have been attributed to increasing numbers in animals (Cohen et al., 2007). Descriptive epidemiologic analysis showed that the increase in domestic dog populations has contributed to rabies epidemics in the 3 provinces in southern China (Wang, 2006). Increases in deer abundance as well as range expansion are likely to exacerbate the potential for disease persistence due to the formation of multi-species deer assemblages, which may act as disease reservoirs (Böhm et al., 2007). In a study by a dog and cat population ecologist John Marbanks in 1947 - 1950 reviewed by Clifton (2007), who estimated that there were only 600,000 street dogs in the already heavily motorized Northeast, but were 3.5 million in the South and 2.3 million in the Midwest, the two most agrarian parts of the U.S. More than 20 years passed before the U.S. dog and cat populations were again studied in depth. By then, in the early 1970s, the U.S. street dog population had disappeared. The feral cat population rose in the absence of street dogs to a peak of about 40 million circa 1990, and then fell with the advent of neuter/return to today's levels of about six million in winter, 12 million in summer (Clifton, 2007) . In the interim, the number of cars and miles driven in the U.S. had tripled.

The pet dog and cat populations rose proportionate to the human population. The pet dog population had increased by just about exactly as much as the street dog population declined. The biomass of dogs and cats relative to human population remained almost the same (Clifton, 2007). A high seroprevalence to LBV in *E. helvum* population may pose a substantial public health risk because *E. helvum* is widely distributed in Africa and a food source in West Africa (Hayman et al., 2008). *E. helvum* resides in high-density populations (hundreds of thousands) and migrates annually, compared with *E. gambianus*, which resides in less dense colonies of tens or hundreds. *E. helvum* commonly forms large colonies in African cities in close proximity to humans and domestic animals and is a food source in West Africa (Hayman et al., 2008).

Neighbourhood contacts

Furthermore, our quest for close contact with wild animals puts us at risk for exposure to zoonoses (Chomel et al., 2007). In the study by Eisinger and Thulke (2008), eight neighbouring cells of foxes have a probability of 16% of getting infected in neighbourhood contacts (adjusted to hunting bag pattern). Infected fox incubates and gets infectious after a time period that is drawn randomly from a negative exponential distribution, with a minimum of 2 weeks and an effective mean of 3·5 weeks. During the following infectious period of 1 week, a fox can transmit the disease using the approach of infection communities or group infection rate. If there is at least one infectious fox in a cell, all other susceptible foxes within the cell become infected in intragroup contacts (Eisinger and Thulke, 2008).

Frequency of consumption of brain (carnivorous animals)

Oral transmission of rabies could be produced in laboratory animals like mice, guinea pigs and hamsters using challenge virus strain (CVS) and 2 strains of street virus. Study of virus pathway following ingestion suggested predominant neural spread to brain and centrifugal spread to non neural organs like heart and kidneys. However it was found that virus dose required for oral infection was relatively very high (Madhusudana and Tripathi, 1990). The role of such a transmission in nature needs to be further evaluated, keeping in view the high dose of virus required for oral infectivity and the frequency of consumption of brain by carnivorous animals.

Consumption of exotic foods

Other factor affecting eradication of rabies includes consumption of exotic foods, development of ecotourism, access to petting zoos, and ownership of exotic pets. Furthermore, our quest for close contact with exotic pets puts us at risk for exposure to zoonoses (Chomel et al., 2007). Industrialized nations' new taste for exotic food has also been linked with various zoonotic pathogens or parasites (Chomel et al., 2007).

Development of ecotourism

One other factor affecting eradication of rabies includes development of ecotourism. For instance, wildlife tourism is among the top exporting activities of Tanzania and Kenya and generates an annual income of approximately half a billion US dollars (Chomel et al., 2007). Adventure travel is the largest growing segment of the leisure travel industry; growth rate has been 10% per year since 1985. This type of travel increases the risk that tourists participating in activities such as safaris, tours, adventure sports, and extreme travel will contact pathogens uncommon in industrialized countries (Chomel et al., 2007). A recent review of a global surveillance network's data set showed different demographic characteristics and different types of travel- related illnesses among immigrant-VFR, traveller-VFR, and tourist travellers (Leder et al., 2006; Fenner et al., 2007). More than 800 million tourist arrivals were registered worldwide in 2005, and an estimated 2% of the world's population lives outside the country of birth. Moreover, because ecotourism is becoming increasingly popular with international travellers, more cases of imported rabies are likely to occur in Europe, North America, and elsewhere in years to come (Fenner et al., 2007). Similarly, the increase of ecotourism, often in primitive settings with limited hygiene, can be associated with the acquisition of zoonotic agents (Chomel et al., 2007). In countries with large migrant populations, improved public health strategies are needed to reach visiting friends and relatives (VFR) travellers (Fenner et al., 2007). Therefore, development of appropriate programs for surveillance and for monitoring emerging diseases in their wildlife reservoirs is essential (Chomel et al., 2007).

Petting zoos

Some other factor affecting eradication of rabies includes access to petting zoos. Petting zoos, where children are allowed to approach and feed captive wildlife and domestic animals, have been linked to several zoonotic outbreaks, including infections caused by rabies (Bender and Shulman, 2004 reviewed in Chomel et al., 2007). More than 25 outbreaks of human infectious diseases associated with visitors to animal exhibits were identified during 1990–2000 (Chomel et al., 2007). Exposure to captive wild animals at circuses or zoos can also be a source of zoonotic infection.

Ownership of exotic pets

Also, one other factor affecting eradication of rabies includes ownership of exotic pets. Exotic pets are also a source of several human infections that vary from severe monkeypox related to pet prairie dogs or lyssaviruses in pet bats to less severe but more common ringworm infections acquired from African pygmy hedgehogs or chinchillas (Chomel et al., 2007). Eight cases of rabies caused by a new rabies virus variant were reported in the state of Ceará, Brazil, from 1991 through 1998. Marmosets (*Callithrix jacchus jacchus*) were determined to be the source of exposure (Chomel et al., 2007). These primates are common pets; most cases occurred in persons who had tried to capture them, and 1 case was transmitted by a pet marmoset. In 1999, encephalitis was diagnosed in an Egyptian rousette bat (*Rousettus egyptiacus*) that had been imported from Belgium and sold in a pet shop in southwestern France. The pet bat was infected with a Lagos bat lyssavirus and resulted in the treatment of 120 exposed persons (Chomel et al., 2007).

Traditional and local food and live animal markets

Traditional and local food markets in many parts of the world can be associated with emergence of new zoonotic diseases. Live animal markets, also known as wet markets, have always been the principal mode of commercialization of poultry and many other animal species. Such markets, quite uncommon in the United States and, until recently, in California, are emerging as a new mode of commercialization within specific ethnic groups for whom this type of trade assures freshness of the product but raises major public health concerns.

However, recent data suggest that civets may be only amplifiers of a natural cycle involving trade and consumption of bats (Chomel et al., 2007).

Persistence of rabies through transplantation

This is another factor that has persisted for so long. On July 1, 2004, CDC reported laboratory confirmation of rabies as the cause of encephalitis in an organ donor and three organ recipients at Baylor University Medical Center (BUMC) in Dallas, Texas. Hospital and public health officials in Alabama, Arkansas, Oklahoma, and Texas initiated public health investigations to identify donor and recipient contacts, assess exposure risks, and provide rabies postexposure prophylaxis (PEP) (CDC, 2004). As of July 9, 2004 PEP had been initiated in approximately 174 (19%) of 916 persons who had been assessed for exposures to the organ recipients or the donor. As a result of its public health investigation, the Arkansas Department of Health determined that the donor had reported being bitten by a bat (CDC, 2004). Srinivasan et al. (2005) reports documented the transmission of rabies virus from an organ donor to multiple recipients and this underscores the challenges of preventing and detecting transmission of unusual patho-gens through transplantation (Srinivasan et al., 2005). In Germany, a recent case of rabies in a person who had visited India remained unidentified until after the patient's death; soft tissue transplantation from this patient resulted in rabies transmission to several organ recipients (Nadin-Davis et al., 2007).

Persistence of rabies in areas with extremely high density of settlements

In Germany, the local increase in the number of rabies cases and the resulting spread of rabies in recent years has been mainly due to the persistence of rabies in areas with an extremely high density of settlements in which ORV is severely hindered. This is a phenomenon that no other country in Europe has been confronted with (Müller et al., 2005). The local increase in the number of rabies cases and the resulting spread of rabies in Germany in recent years are mainly due to increased fox densities (Müller et al., 2005). Rabies reemerges periodically in China because of high dog population density (Wu et al., 2009).

Vaccines and vaccination factors

Vaccines are the basis of the medical and veterinary medical future, the belief being that, if a vaccine can be made to every disease, then all disease can be prevented. This presupposes that 1) disease attacks from outside and has nothing whatsoever to do with the person or animal themselves; 2) that vaccines actually always protect one hundred per cent; and 3) that vaccines themselves are only beneficial and cannot cause harm. None of these are true. There is a growing list of research into and information on the problems that can be caused by vaccines. There has been much debate on the subject of annual pet vaccination, chiefly in response to concerns voiced by pet owners. The veterinary profession is largely unaware of the range of side-effects vaccines can stimulate, and consequently they go unreported. A radical rethink of the vaccination programme is necessary - immunization programmes need not be abandoned, but reassessed.

Human attitudes and errors toward vaccination

In rural areas of Nigeria, nearly every family owns several dogs, most of which are free-roaming, without special diets, and unvaccinated against rabies (to save costs). Sale of these dogs to restaurants can increase a farmer's income (average 12–15 US dollars/dog). Free-roaming and unvaccinated dog populations may increase the likelihood of transprovincial spread of RABVs.

Poor attitude of vaccination record keeping

Quick, decisive action to detect and control novel pathogens, and thereby contain outbreaks and prevent further transmission, is frequently hampered by incomplete or inadequate data about a new or re-emerging pathogen (Tapper, 2006). There is a poor attitude of record keeping among Nigerians as it was practically impossible to obtain the vaccination records. Vaccinees should be educated in all immunization programs to keep their vaccination cards for future reference. Virology Laboratories also should be equipped with adequate test facilities to monitor post vaccination seroconversion among subjects (Ogunjimi, 2008).

Low vaccination coverage (by increasing nonimmune population), including factors contributing to low coverage

The single most important factor affecting eradication of rabies is the failure to immunize domestic dogs, which transmit rabies to humans (Fu, 2008). Descriptive epidemiologic analysis has also shown that low vaccination coverage has contributed to rabies epidemics (Wang, 2006). Mass vaccination of the domestic dog provides the most cost-effective and efficient strategy for controlling canine rabies and hence transmission from dogs to humans (Clifton, 2007). In Zimbabwe, dog rabies cases increased after 1990, after declining vaccination coverage associated with decreased resources and diversion of resources (Cohen et al., 2007). Low vaccination coverage in domestic dogs in Limpopo, South Africa over several years may have led to an accumulation of susceptible animals, which led to the reestablishment of transmission (Cohen et al., 2007). Rabies also reemerges periodically in China because of low vaccination coverage in dogs. Mass vaccination campaigns rather than depopulation of dogs should be a long-term goal for rabies control (Wu et al., 2009).

Lack of ideal cross-reactivity with modern biological

Significantly, less than ideal cross -reactivity with modern biological used for veterinary and public health interventions is a major cause for concern among these emerging viral agents [Duvenhage and Lagos bat viruses] (Nel and Rupprecht, 2007).

High cost of postexposure prophylaxis

Although rabies is preventable, the high cost of postexposure prophylaxis, compounded by the lack of education and awareness about rabies, limits use of postexposure prophylaxis in many developing countries (Nadin-Davis et al., 2007).

Lack of vaccine delivery systems and resources

Outbreak of rabies in humans followed an outbreak in domestic dogs (Cohen et al., 2007). Increasing numbers of human rabies cases in Africa have also been attributed to deteriorating infrastructure and resources for rabies control. Although, the tools for effective rabies control are available, lacking are the delivery systems, public education campaigns and resources to apply these technologies in the developing world (Clifton, 2007). To attempt control, and possibly elimination, of zoonoses, benefits to public health and society need to be demonstrated, particularly in countries with scarce resources (Zinsstag et al., 2007). Zinsstag et al. (2007) in their study presented examples from their work on brucellosis and rabies and demonstrated the circumstances for which zoonosis control would save money for resource-limited countries and likely reduce the occurrence of zoonoses worldwide.

Challenge in testing of vaccine efficacy

It has been suggested that handling stress could have compromised wild dogs' cell-mediated immune response to rabies infection - does vaccination induce a cell-mediated immune response? Cell-mediated immunity can be assayed in the laboratory from blood samples. The ultimate test of vaccine efficacy is challenge with a dose and strain of rabies virus known to be lethal to unvaccinated animals (Ginsberg and Woodroffe, 1997). However, establishing the necessary challenge conditions, followed by carrying out the challenge experiments themselves, would necessitate killing at least 20 - 30 captive wild dogs. The consensus of vets and biologists involved in research on rabies in wild dogs and other carnivores is that challenges would be both unnecessary and unethical - for this reason, applications for government licenses to carry out such experiments would probably be unobtainable (Ginsberg and Woodroffe, 1997). Nevertheless, the experiments suggested above would answer most of the questions that have been raised concerning the efficacy of inactivated rabies vaccines, without the need for carrying out challenge experiments (Ginsberg and Woodroffe, 1997).

Existence of multiple hosts

Sixty-six (66) viruses have been isolated from bats (Calisher et al., 2006). Bats (order Chiroptera, suborders Megachiroptera ["flying foxes"] and Microchiroptera) are abundant, diverse, and geographically widespread. These mammals provide us with resources, but their importance is minimized and many of their populations and species are at risk, even threatened or endangered. Some of their characteristics (food choices, colonial or solitary nature, population structure, ability to fly, seasonal migration and daily movement patterns, torpor and hibernation, life span, roosting behaviours, ability to echolocate, virus susceptibility) make them exquisitely suitable hosts of viruses and other disease agents (Calisher et al., 2006). Bats of certain species are well recognized as being capable of transmitting rabies virus, but recent observations of outbreaks and epidemics of newly recognized human and livestock diseases caused by viruses transmitted by various megachiropteran and microchiropteran bats have drawn attention anew to these remarkable mammals. It is clear that we do not know enough about bat biology; we are doing too little in terms of bat conservation; and there remain a multitude of questions regarding the role of bats in disease emergence (Calisher et al., 2006).

Existence of reservoir host

Most zoonoses are maintained in the animal reservoir but can cross over to humans as a result of different risk factors and behavioural traits. Hence, elimination of zoonoses such as rabies is possible only by interventions that vigorously target animal reservoirs (Zinsstag et al., 2007). Control of most zoonoses usually requires interventions outside the public health sector (Zinsstag et al., 2007). When one considers health from a point of view independent of species, including humans, domestic animals, and wildlife, zoonoses are part of a broader ecologic concept of health systems (Zinsstag et al., 2007). Many new, emerging and re- emerging diseases of humans are caused by pathogens which originate from animals or products of animal origin. A wide variety of animal species, both domestic and wild, act as reservoirs for these pathogens, which may be viruses, bacteria or parasites (Meslin et al., 2000). According to Meslin et al. (2000), given the extensive distribution of the animal species affected, the effective surveillance, prevention and control of zoonotic diseases pose a significant challenge. Bats are listed as protected species across Europe (Stantic-Pavlinic, 2005) . The role that bats have played in the emergence of several new infectious diseases has been under review. Bats have been identified as the reservoir hosts of newly emergent viruses such as Nipah virus, Hendra virus, and severe acute respiratory syndrome-like coronaviruses as well as rabies (Halpin et al., 2007).

Infection and disease in reservoir and spillover hosts determine patterns of infectious agent availability and opportunities for infection, which then govern the process of transmission between susceptible species (Daniels et al., 2007). In the United States, extensive reservoirs of the rabies virus exist in many diverse wild animal species, which continue to pose a serious risk of lethal infection of humans and cause an economic burden exceeding $1 billion annually (Dietzschold and Schnell, 2002). Previous experience with rabies control in foxes in Europe has clearly demonstrated that oral immunization with live vaccines is the only practical approach to eradicate rabies in free-ranging animals. However, unlike Europe where vulpine rabies was the only major reservoir, the Americas harbor a variety of species including raccoons, skunks, coyotes, and bats that serve as the primary reservoirs of rabies. Each of these animal reservoirs carries an antigenically distinct virus variant (Dietzschold and Schnell, 2002).

Existence of healthy carriers

Other authors have suggested that this trend may be caused by a carrier state in healthy dogs that remains undetected (Zhang et al., 2008) . Tao et al. (2009) observed an infection rate of 2.3% in apparently healthy dogs from 15 cities in 3 provinces of China. Previous surveys in regions of high incidence of rabies showed different rates, ranging from 3.9 - 17.9% in dogs. The paper by Ajayi et al., (2006) also indicates a disturbing possibility of transmission of rabies by apparently healthy (free of overt rabies signs) stray dogs. If their observations are confirmed, this, in their words, "signifies a new dimension in the epidemiology of the disease in this environment where the high-risk practices are prevalent (Durosinloun, 2009; Fagbo, 2009; Woolf, 2009)." What's more intriguing epidemiologically and culturally is that the research by Ajayi et al., (2006) was carried out in Maiduguri; the overwhelming Muslim population in the city provides zero economic incentives for dog meat restaurants (Durosinloun, 2009; Fagbo, 2009; Woolf, 2009). However, the dogs were slaughtered in restaurants associated with 2 military barracks in the city (Durosinloun, 2009; Fagbo, 2009; Woolf, 2009).

Long incubation period

During most of the long incubation period of rabies, the virus likely remains close the site of viral entry.

Centripetal spread to the central nervous system and spread within the central nervous system occur by fast axonal transport. Neuronal dysfunction, rather than neuronal death, is responsible for the clinical features and fatal outcome in natural rabies (Jackson, 2003).

Existence of new and other emerging diseases

Polley (2005) discussed the linkages between wildlife, people, zoonotic parasites and the ecosystems in which they co-exist, and revisited definitions for 'emerging' and 're-emerging', and lists zoonotic parasites that can be acquired from wildlife including, for some, estimates of the associated global human health burdens and introduced the concepts of 'parasite webs' and 'parasite flow', provides a context for parasites, relative to other infectious agents, as causes of emerging human disease, and pointing out the drivers of disease emergence and re-emergence, especially changes in biodiversity and climate. *Angiostrongylus cantonensis* in the Caribbean and the southern United States, *Baylisascaris procyonis* in California and Georgia, *Plasmodium knowlesi* in Sarawak, Malaysia, *Human African Trypanosomiasis*, *Sarcoptes scabiei* in carnivores, and Cryptosporidium, Giardia and Toxoplasma in marine ecosystems are presented as examples of wildlife-derived zoonotic parasites of particular recent interest.

New emerging infectious diseases include "severe acute respiratory distress syndrome" (SARS) and avian influenza A H5N1 (Spicuzza et al., 2007). First cases of SARS, induced by a new strain of coronavirus, were described in China in 2002 and by May 2003 8360 cases and 764 deaths were reported by the WHO (Spicuzza et al., 2007) . Avian influenza A H5N1 is another emerging infectious disease transmitted from avian species to humans, without clear evidence of transmission from human to human. The widespread outbreaks of H5N1 avian influenza in 2003-2004 have caused major problems for the poultry industry in many Asian countries. On January 2004 the disease crossed over to humans, for the first time in Vietnam, causing 74 deaths to date (mortality rate of 50%) in southeastern countries (Spicuzza et al., 2007). Unlike SARS, the avian flu occurs in rural areas, where people live in intimate contact with birds, and many of the victims are children < 5 years of age. The World Health Organization has adopted a global action plan to control avian influenza among chickens and ducks and at the same time to limit the threat of a human flu pandemic (Spicuzza et al., 2007).

Inconsistent vaccination and wrong vaccination regime

The local increase in the number of rabies cases and the resulting spread of rabies in recent years has also been attributed to inconsistent vaccination, e.g. missing complementary distribution of baits per hand in non-flying zones (Müller et al., 2005).

Inferior vaccine quality

The inferior quality of the domestically manufactured dog vaccine in China has been documented (Hu et al., 2008). According to Wu et al. (2009), vaccine quality control and mass production, rather than matching, are urgently needed and most important for addressing the current rabies problem in China. Any potent rabies vaccine will protect against rabies.

Vaccine shortage

Vaccine shortages can result from higher-than-expected demand, interruptions in production/supply, or a lack of resources to purchase vaccines (Hinman et al., 2006). Each of these factors has played a role in vaccine shortages especially in the United States during the past 20 years. Since 2000, the United States has experienced an unprecedented series of shortages of vaccines recommended for widespread use against 9 diseases, after more than 15 years without vaccine supply problems. In developing countries, the major cause of vaccine shortages is lack of resources to purchase them. Although there are several steps that could reduce the likelihood of future vaccine shortages, many would take several years to implement. Consequently, we will probably continue to see occasional shortages of vaccines in the United States in the next few years (Hinman et al., 2006).

Vaccine failure

Okoh (1982) reported 10 cases of apparent vaccine failure in Nigeria involving modified live (low egg passage chick embryo) vaccine in use during the study period. In their study, 4 of these cases of infection may actually have been induced by the vaccine. In 1989, Six cases of apparent vaccination failures in rural dogs given modified live virus, chicken embryo origin, low egg passage, Flury-type vaccine, was reported (Okolo,1989). Wiktor et al. (1984) reported that immunization of mice with a rabies vaccine (antigenic value, 10 international units) at a concentration 30-fold high than that necessary for complete protection against homologous challenge with rabies virus was not protective against Mokola infection and that no cross-reactivity between Mokola and rabies viruses was seen with cytotoxic T lymphocytes.

Unavailability of WHO recommended RIG

After severe exposure to suspected rabid animal, WHO recommends a complete vaccine series using a potent effective vaccine that meets WHO criteria, and administration of rabies immunoglobulin (RIG) . RIG is not available globally (Yanagisawa et al., 2008), and is not marketed in Nigeria.

Use of low potency vaccines

When post- exposure prophylaxis are most health sector do not take time to know the sort of rabies vaccine being injected. It is important to know the sort of rabies vaccine injected abroad, because brain-tissue vaccines are less effective in inducing antibody than tissue-culture vaccines.

Safety problem

The currently available modified- live rabies virus vaccines have either safety problems or do not induce sufficient protective immunity in particular wildlife species. Therefore, there is a need for the development of new live rabies virus vaccines that are very safe and highly effective in particular wildlife species (Dietzschold and Schnell, 2002).

Failure to show an adequate antibody titre

In line with study carried out in other countries, Nigeria faces with problem of some vaccinated animals fail to show an antibody titre adequate to meet the requirements of the 0.5 IU/ml minimal threshold level accepted by WHO/OIE. In a study by Jakel et al. (2008) to identify specific risk factors in dogs and cats for post-vaccination rabies antibody titres below 0.5 IU/ml by FAVN test. Data on around 1,200 animals was analyzed. Most animals older than one year had already received more than one rabies vaccination. The influence of breed and sex on antibody titre seems to be insignificant. Young dogs have a high risk of results below 0.5 IU/ml after their first vaccination. This risk can be minimized by the application of a second vaccination and blood sampling according to the manufacturer's recommendations. An important factor for the test outcome might be the virus strain used in the vaccine (Jakel et al., 2008).

In another study in UK by Mansfield et al. (2004), after being vaccinated against rabies some cats and dogs fail to show an antibody titre adequate to meet the requirements of the UK Pet Travel Scheme. To investigate this problem, Mansfield et al. (2004) derived data from 16,073 serum samples submitted to the Veterinary Laboratories Agency for serological testing between 1999 and 2002, 1002 samples submitted to BioBest during March and April 2001, and 1264 samples associated with one make of vaccine submitted to BioBest between June, 2001 and January, 2003, were analyzed. The probability of antibody titre failing to reach at least 0.5 iu/ml was analyzed by logistic regression as a function of the choice of vaccine, the interval between vaccination and sampling, the sex and age of the animal, and its country of origin (Mansfield et al., 2004). In dogs, all these factors, except sex, had highly significant ($P < 0.001$) effects on the test failure rate, and in cats all the factors had a significant effect ($P < 0.05$).

Transboundary and transprovincial spread of RABVs

Transboundary animal diseases pose a serious risk to the world animal agriculture and food security and jeopardize international trade. The world has been facing devastating economic losses from major outbreaks of transboundary animal diseases (TADs) such as foot-and-mouth disease, classical swine fever, rinderpest, peste des petits ruminants (PPR), and Rift Valley fever. Lately the highly pathogenic avian influenza (HPAI) due to H5N1 virus has become an international crisis as all regions around the world can be considered at risk (Domenech et al., 2006). The geographic nature of these rabies foci or groups suggests that dogs are not moving, per se, but that human-related activities may account for these phenomena. Spread of RABVs from high-incidence regions, particularly by the long-distance migration or transprovincial movement of dogs caused by human-related activities, may be one of the causes of recent massive human rabies epidemics (Tao et al., 2009).

Limited number of related vaccine strains

Attenuated tissue culture-adapted and natural street rabies virus (RV) strains differ greatly in their neuroinvasiveness (Faber et al., 2004). A study by Tomori (1980) on wild caught shrews infected with rabies virus strains by the intramuscular, subcutaneous and oral routes suggested a mechanical role in the transmission of rabies. In his study, virus was isolated only from shrews infected with street or wild strains of rabies, but not with vaccine or fixed rabies strains. To identify the elements responsible for the ability of an RV to enter the CNS from a peripheral site and to cause lethal neurological disease, Faber et al. (2004) constructed a full-length cDNA clone of silver-haired bat-associated RV (SHBRV) strain 18 and exchanged the genes encoding RV proteins and genomic sequences of this highly neuroinvasive RV strain with those of a highly attenuated nonneuroinvasive RV vaccine strain (SN0). In their analysis of the recombinant RV (SB0), which was recovered from SHBRV-18 cDNA, they indicated that this RV is phenotypically indistinguishable from WT SHBRV-18. However, characterization of the chimeric viruses revealed that in addition to the RV glycoprotein, which plays a predominant role in the ability of an RV to invade the CNS from a peripheral site, viral elements such as the trailer sequence, the RV polymerase, and the pseudogene contribute to RV neuroinvasiveness (Faber et al., 2004). Faber et al. (2004) analyses also revealed that neuroinvasiveness of an RV correlates inversely with the time necessary for internalization of RV virions and with the capacity of the virus to grow in neuroblastoma cells.

Approximately 57 years ago, Johnson (1952 reviewed by Tao et al., 2009) speculated that RABV strains from Europe were transmitted into China through Hong Kong and Shanghai. The attenuated 3aG strain, which was isolated in Beijing in 1931, and the DRV strain, which was isolated in Jilin Province in 2002, is closely related to group III in a study by Tao et al. (2009). This finding by Tao et al. (2009) implies that a group of viruses that originated in Europe is present in China and is still circulating. The hosts of this group include not only domestic dogs but also other mammals likely infected by rabid dogs (DRV strain) as pointed out by Tao et al. (2009). Alternatively, the similarity among some RABVs circulating in dogs in China and the rest of the world as well as the international vaccine strains (Hu et al., 2008) should motivate health authorities in all over the world to revisit quality standards and adequacy for use of attenuated rabies vaccines to ensure that vaccine-related cases do not occur.

Role of rabies related viruses

According to Shope (1982), five viruses related to rabies occur in Africa. Two of these, Obodhiang from Sudan and kotonkan from Nigeria, were found in insects and are only distantly related to rabies virus. The other three are antigenically more closely related to rabies. Mokola virus was isolated from shrews in Nigeria, Lagos bat virus from fruit bats in Nigeria, and Duvenhage virus from brain of a man bitten by a bat in South Africa. The public health significance of the rabies- related viruses was emphasized in Zimbabwe where in 1981 a rabies-related virus became epizootic in the dog and cat population. It is postulated that the ancestral origin of rabies virus was Africa where the greatest antigenic diversity occurs and that the ancestor may have been an insect virus (Shope, 1982). Identification of the first case of LBV in a mongoose by Markotter et al. (2006a) underscores the need for surveillance of rabies -related viruses and the need for accurate identification of lyssavirus genotypes even if the host involved is normally only associated with RABV.

Spill over

With respect to LBV, Markotter et al. (2006a, b) have recently reported the likely persistence of this virus in pteropid bats in South Africa, which implicates continuous opportunity for spillover into terrestrial species. In determining the extent of risk to human and veterinary public health, it is important to establish the prevalence of LBV not only in bats but also in potential terrestrial animal vectors, to which mongoose species should be added, based on the finding of Markotter et al. (2006a).

Other vaccine related problem

Subsidized post-exposure vaccination is the standard response to rabies in India, China, and much of Africa. Post-exposure vaccination saves thousands of lives annually, despite many failures when dog bite victims fail to seek treatment soon enough, do not complete the full course of injections, or receive fake, expired, or obsolescent vaccines, a problem particularly prevalent in parts of India and China, where post-exposure vaccines are often made by local suppliers, using formulas elsewhere long abandoned (Clifton, 2007) . In summary, however, the most likely cause of the vaccine failures lies in the vaccination protocols used. Each wild dog was given only a single dose of vaccine. However, administration of single doses of inactivated rabies vaccine to wild dogs held in captivity in Tanzania failed to bring about seroconversion, and preliminary vaccine trials in South Africa suggest that two doses must be given in order to achieve and maintain protective antibody levels. Further vaccine trials are urgently needed to determine the best protocol (Ginsberg and Woodroffe, 1997). Suzuki et al. (2008a, b) reported unsatisfactory titre level in their study in comparison with the results from other field investigations with inactivated tissue culture vaccines.

RABIES ERADICATION: HOW FEASIBLE?

Achievement of some or all of these interim milestones will increase support for global eradication of selected diseases (Duffy et al., 1990). Research to design strategies for disease control in wild dogs is also urgently needed. In particular: 1) can vaccines against rabies and canine distemper be delivered to wild dogs in a manner that is safe and effective? 2) Can these diseases be eradicated from their reservoir hosts, protecting wild dogs without vaccinating them directly? Rabies eradication is not feasible because of the extensive and animal and animal reservoirs of the virus and the inability to eliminate those reservoirs with existing technology. However, elimination of human rabies in urban areas may be possible through different strategies. Additional genetic work will help to set priorities for the conservation of populations which may be genetically unique (Ginsberg and Woodroffe, 1997) for spread of rabies and other related diseases.

Possibilities for control in reservoir hosts

In some circumstances, controlling disease in its reservoir hosts could be a better long-term solution than vaccinating wild dogs themselves. For example, rabies control in domestic dogs would protect people and their livestock as well as wild dogs. In other cases, however, it is not always clear that attempts to control disease in other species will provide effective protection for wild dogs (Ginsberg and Woodroffe, 1997). This highlights the need for more research, to address the following questions:

Does the administration of live canine distemper virus and rabies vaccines bring about seroconversion?

According to Ginsberg and Woodroffe (1997), one study, of three litters of pups, found no evidence of seroconversion, while another found that adults given booster vaccinations did seroconvert. These results provide circumstantial evidence that, as suspected for rabies vaccination, more than one dose of vaccine might be needed to achieve and maintain protective antibody levels. In zoos that vaccinate wild dogs against CDV routinely, more studies could be carried out to assess the efficacy of different protocols. As for rabies, it would be useful to know whether multiple doses of vaccine are more effective than a single dose, whether dart-vaccination is as effective as vaccination by hand, and how often boosters must be given (Ginsberg and Woodroffe, 1997).

Can rabies be controlled in wildlife reservoirs?

Domestic dogs are important rabies reservoirs in East Africa, but in southern Africa wild species such as bat-eared foxes and jackals may be more important (Ginsberg and Woodroffe, 1997). Achieving anything approaching adequate vaccination cover in these species would be impossible if vaccines had to be delivered by hand, but oral vaccination is a possible alternative (Ginsberg and Woodroffe, 1997). This method of vaccine delivery has successfully eradicated rabies from red foxes in some parts of Europe and North America. However, although experimental administration of live oral vaccines to black-backed and side-stripe jackals has been shown to confer protection from rabies, the strain used proved highly pathogenic to baboons (Bingham et al. 1995 reviewed in Ginsberg and Woodroffe, 1997). Thus, more (ongoing) research, using other strains, is needed to perfect a method for vaccinating wild canids safely and effectively (Ginsberg and Woodroffe, 1997).

Can the population density of reservoir hosts be reduced?

In principal, reducing the density of reservoir hosts could lead to lower transmission rates and prevent disease from persisting in the population. The practical possibilities of doing this depend upon a number of factors. If the reservoir host was a wildlife species, controlling population size would rarely be possible. For domestic dogs, the possibilities would depend upon local peoples' requirement for those dogs (Ginsberg and Woodroffe, 1997).

Can contact between wild dogs and domestic dogs be minimized?

Again, according to Ginsberg and Woodroffe (1997), this would depend upon local peoples' need for domestic dogs. More research is needed to determine whether domestic dogs' movements could be restricted by, for example, requiring that owned dogs be collared, that dogs be tied up at night, and shooting unaccompanied dogs.

Public health strategy of disease eradication

The public health strategy of disease eradication offers considerable advantages over disease control when eradication is undertaken against appropriate, carefully chosen targets (Duffy et al., 1990). The benefits of eradication are permanent and accrue after a finite cost, whereas the costs of controlling the same disease must be maintained indefinitely. For example, the United States invested $32 million in SEP over a 10- year period; this amount is equivalent to former U.S. costs and expenditures every 3 months for routine vaccination (discontinued in 1971) and management of its complications (Ginsberg and Woodroffe, 1997). The United States government is investing >$50 million annually to maintain its polio-free status and an estimated $25-50 million to keep domestic measles at low level (Hinman et al., 1985 reviewed by Ginsberg and Woodroffe, 1997). These figures do not reflet the cost of vaccination in the private sector or the annual occurrence of vaccine-associated polio (Duffy et al., 1990).

Mobilization for support

A time- limited goal of eradication allows mobilization of support more readily than a control program. An important corollary requirement for global eradication is that unaffected countries will need to provide material assistance where needed, including geographic areas where small residual foci might not otherwise warrant use of scarce national resources (Duffy et al., 1990).

Effective wild dog management

While a great deal of information about wild dog ecology has become available recently, further research will allow more effective wild dog management. Surveys are needed, especially in central Africa, to give a better picture of wild dog distribution. Simple, effective monitoring techniques are needed to track the status of known populations. Long term studies of larger populations should be continued; such studies will identify new threats as they arise, and will also determine wild dog populationsµ ability to recover from natural perturbations, a crucial component of their viability which has not yet been quantified in the field (Ginsberg and Woodroffe, 1997).

Research to design strategies for disease control

In several cases, Ginsberg and Woodroffe (1997) reported that more research would enhance the creation and implementation of effective management strategies. A great deal of research has been carried out on wild dogs recently, so that wildlife managers are now much better equipped to conserve wild dogs than they were ten, or even five years ago. Nevertheless, there are still areas where more information would be extremely valuable. In their study (Ginsberg and Woodroffe, 1997), they summarized researches that would facilitate wild dog conservation. Research to help resolve conflicts between wild dogs and farmers is urgently needed, since persecution represents an extremely serious threat. This must involve work on: 1) the true economic losses caused by wild dog predation on livestock, 2) the circumstances under which wild dogs take livestock, and 3) the degree to which public attitudes reflect a real or perceived assessment of the damage caused. Such information will help to determine the combination of husbandry practices, local legislation, compensation and education needed to allow wild dogs and people to coexist (Ginsberg and Woodroffe, 1997). However, a substantial volume of research is also needed into disease control - it was not until the wild dog study populations disappeared from the Serengeti ecosystem that it became clear just how severe a threat disease could pose to wild dogs. We still cannot determine the best strategy for controlling disease - and at present we are not fully equipped to carry out any of them (Ginsberg and Woodroffe, 1997).

Mass vaccination of domestic dogs and destruction of stray dogs approach

Some developed countries have virtually eliminated rabies in humans by mass vaccination of domestic dogs and destruction of stray dogs (MMWR, 1993). This approach is difficult to apply in rural areas of most developing countries, where animals may not be privately owned, destruction may be unacceptable, and such campaigns may be expensive. Some Latin American countries are conducting successful campaigns in cities, however. Attempts are being made to control rabies in wildlife by development of oral vaccines that can be safely distributed in baits (MMWR, 1993).

New and improved vaccines

Eradication of rabies is not feasible, primarily because of the extensive, varied animal reservoirs of the virus and the inability to eliminate those reservoirs through available technology. It is possible to eliminate human rabies in urban areas, although the costs and benefits of doing so should be considered (MMWR, 1993). A review of the technical feasibility of eradicating other diseases preventable by vaccines currently licensed for civilian use in the United States indicates that measles, hepatitis B, mumps, rubella, and possibly disease caused by *Haemophilus influenzae* type b are potential candidates (Hinman, 1999). From a practical point of view, measles seems most likely to be the next target. Global capacity to undertake eradication is limited, and care must be taken to ensure that a potential measles eradication effort does not impede achievement of polio eradication (Hinman, 1999). Even in the absence of eradication, major improvements in control are both feasible and necessary with existing vaccines. New and improved vaccines may give further possibilities of eradication in the future (Hinman, 1999).

CURRENT SITUATION AND FUTURE TRENDS

Rabies is probably the oldest recorded infection of mankind. Rabies is an enzootic viral disease widespread throughout the world (Sugiyama and Ito, 2007) . Rabies, being a major zoonotic disease, significantly impacts global public health. It is invariably fatal once clinical signs are apparent. The majority of human rabies deaths occur in developing countries (Nagarajan et al., 2008). Although it is a vaccine-preventable disease, the annual number of human deaths caused by rabies is estimated to be 32,000 in Asia (Sugiyama and Ito, 2007). India alone reports more than 50% of the global rabies deaths (Nagarajan et al., 2008). The development of the first rabies vaccine by Pasteur surely had been hoped to eliminate or at least drastically reduce its incidence. To date, the only survivors of the disease have received rabies vaccine before the onset of illness. Many years of research and observations on bait uptake, efficacy, behavioural studies of foxes, reduction and elimination of rabies, population dynamics of foxes following oral vaccination, as well as annual exchanges of researchers' experiences, formed the scientific background for field trials extending over many years. The approach to management of the rabies normally should be palliative (Jackson et al., 2003).

It is a vaccine-preventable disease. Cheap and safe vaccines for animals as well as humans have been developed. No single therapeutic agent is likely to be effective, but a combination of specific therapies could be considered, including rabies vaccine, rabies immunoglobulin (RIG), monoclonal antibodies, ribavirin, interferon-alpha, and ketamine. Corticosteroids were discouraged from use (Jackson et al., 2003). As research advances, new agents may become available in the future for the treatment of human rabies. However, effective rabies prevention in humans with category III bites requires the combined administration of RIG and vaccine (Nagarajan et al., 2008). Vaccination of stray dogs could lead to the eradication of rabies in countries where dog rabies is the sole source of human exposure. The development of safe and effective rabies virus vaccines applied in attractive baits resulted in the first field trials in Switzerland in 1978. Thereafter, technical improvements occurred in vaccine quality and production, including the design of recombinant viruses, as well as in the ease of mass distribution of millions of edible baits over large geographical areas (Rupprecht et al., 2004). Oral vaccination of wildlife with recombinant rabies virus vaccines is beginning to reduce the incidence of rabies among foxes and raccoons. Over the past few decades, extensive oral vaccination programmes focusing upon the red fox, using hand and aerial distribution of vaccine-laden baits, have resulted in the virtual disappearance of rabies in Western Europe. The same dramatic observation held true for southern Ontario (Rupprecht et al., 2004).

The European fox rabies epizootic starting in 1939 at the eastern border of Poland reached Switzerland on March 3, 1967. Rabies spread over large parts of the country until 1977, the year it caused three human deaths (Zanoni et al., 2000). In 1978 the first field trial world-wide for the oral immunization of foxes against rabies was conducted in Switzerland. Initially, the expansion of the vaccination area led to a rapid reduction in rabies cases. However, the 1990s were characterized by a recrudescence of rabies in spite of regular oral immunization of foxes (Zanoni et al., 2000). The last endemic case of rabies was diagnosed in 1996 after an adaptation of the vaccination strategy. During the 1990s in the United States, oral vaccination programmes concentrated upon raccoons, grey foxes, and coyotes, with similar success. For example, raccoon rabies has not spread west of the current focus in the eastern states, grey fox rabies is contained in west central Texas, and no recent cases of rabies have been reported from coyotes away from the Mexican border for several years. Despite the progress observed and the absence of substantive adverse environmental or health effects, oral vaccination is not a panacea, and should be viewed as an important adjunct to traditional prevention and control techniques in human and veterinary medicine (Rupprecht et al., 2004).

However, this goal of eradication has not been achieved because rabies is maintained in many animal reservoirs, including both domestic and wild. There are still many aspects of the pathogenicity of rabies that are unknown. For example, we have no explanation for the long incubation period (up to 6 years). Furthermore, new patterns of rabies infection present a problem for epidemiologists and virologists alike. There are several cases of human rabies in which there was no history of a bite. Despite these continuing problems, there has been tremendous progress in the control of rabies. Local outbreak suppression of rabies among free- ranging wildlife is documented, and regional elimination of particular virus variants among specific, targeted carnivore hosts is demonstrable, but true disease eradication is not achievable at the present time by current techniques (Rupprecht et al., 2004). For example, no practical vaccination methods have been designed for bats. Although lyssaviruses appear in relative compartmentalization between the Chiroptera and Carnivora, major spillover events have been detected from bats to carnivores, and phylogenetic analyses suggest a historical basis for extant viral origins due to interactions between these taxa. Thus, bio-political considerations aside, the possibility for pathogen emergence resulting from transmission by rabid bats with subsequent perpetuation among other animals cannot be discounted easily on any continent, with the possible exception of Antarctica (Rupprecht et al., 2004).

Cell culture rabies vaccines for human use, highly immunogenic and well tolerated, are now used for pre-exposure immunization as well as for post-exposure treatment (Sureau, 1988). Presently available cell culture rabies vaccines induce immunity against the SAD modified live rabies virus used for oral immunization of foxes. They also induce immunity against the newly identified European bat rabies virus (Duvenhage) (Sureau, 1988). The use of the techniques and strategies of oral immunisation of foxes against rabies using SAD B19 can eliminate wildlife rabies among foxes and raccoon dogs, as European experience has shown. The disease then also disappears completely in domestic animals and man. However, the currently available modified- live rabies virus vaccines have either safety problems or do not induce sufficient protective immunity in particular wildlife species. Therefore, there is a need for the development of new live rabies virus vaccines that are very safe and highly effective in particular wildlife species (Dietzschold and Schnell, 2002). Meanwhile, new types of vaccines are being developed by applying gene mani-pulation techniques to rabies virus in order to overcome the disadvantages of current vaccines (Sugiyama and Ito, 2007).

There have been many changes and accomplishments in rabies control and prevention since the first International conference "Rabies in Europe" was held in Kiev on June 15-18, 2005 (Briggs, 2008). Recommendations from the 2005 meeting addressed epidemiology; rabies diagnosis; animal rabies control; human rabies prevention; vaccinology and immunology and bat rabies. Cell culture rabies vaccines have become widely available in developing countries, virtually replacing the inferior and unsafe nerve tissue vaccines. Limitations inherent to the conventional RIG of either equine or human origin have prompted scientists to look for monoclonal antibody-based human RIG as an alternative. Fully human monoclonal antibodies have been found to be safer and equally efficacious than conventional RIG when tested in mice and hamsters (Nagarajan et al., 2008). Clearly, given their biodiversity, distribution, and abundance, novel methods would be necessary to consider meaningful control of rabies in these unique volant mammals (Rupprecht et al., 2004). As suggested by Kuiken et al. (2005), it is time to form "a joint expert working group to design and implement a global animal surveillance system for zoonotic pathogens that gives early warning of pathogen emergence, is closely integrated to public health surveillance and provides opportunities to control such pathogens before they can affect human health, food supply, economics or biodiversity (Chomel et al., 2007)."

Appropriate use of a highly effective vaccine can help eradicate a major disease when humans are the only natural host for the virus, and there is no natural reservoir or intermediate host. During the 1970s, this goal of eradication was achieved for smallpox largely through the use of the live vaccinia virus vaccine and ranks as one of the major public health achievements in all history. Two other viruses have been similarly targeted for eradication, namely poliovirus and measles, and significant progress toward this goal has been made for both viral pathogens. Live virus vaccines have played and continue to play a central role in these current eradication efforts (Graham and Crowe, 2007) . This goal seems more elusive now than ever before because of setbacks from social instability and the threat of bioterrorism, as well as the potential for intentional reintroduction or resurrection of previously eradicated virus pathogens. Therefore, it will be prudent to find ways of maintaining immunity to serious virus pathogens even after eradication of the natural reservoir has been achieved. The new technologies that have improved our ability to identify emerging pathogens and to develop biological for vaccines and therapeutics have also created an intellectual reservoir that is a formidable barrier to true eradication efforts. Elimination of a virus pathogen suggests that epidemic and endemic disease is controlled and that no active cases are present. However, setting the goal of elimination acknowledges the possibility of re-emergence and would include maintenance of active vaccine-induced immunity (Graham and Crowe, 2007).

As a result of the efforts in developing recombinant rhabdoviruses as vaccine vectors and as cytolytic agents, it is likely that clinical trials of genetically engineered rhabdoviruses in humans will take place in the near future. A number of issues need to be considered in the use of such agents, such as their safety for use in humans, as well as the protection of animal populations that may be exposed to such viruses. Nonetheless, the advances in understanding virus replication and pathogenesis should make it feasible to address these issues, so that these viruses that have long been a burden to humanity can instead be a benefit (Lyles and Rupprecht, 2007). Newer approaches in biotechnology may be envisaged some day for eventual extension to bats, as well as more widespread application to global canine rabies remediation in developing countries.

Conclusion

A number of countries throughout the world have been free from rabies for many years; some are reported to have eliminated the disease and in others it has reappeared after variable periods of time. Apart from these minor variations, however, the global distribution of rabies over the last five to ten years appears unchanged and the disease continues to pose both public health and economic problems of varying severity in all continents except Australia and Antarctica. Most of the data presented here are abstracted from the most recent surveys and study by many researchers/authors. According to Turner (1976), the vagaries of international reporting, accurate in some cases and undoubtedly imprecise in others, demand a cautious interpretation of the available data and suggest that the world picture be viewed as an impression rather than as a precise record.

Some challenges and potential solutions to the ability of national governments to adhere to the global health surveillance requirements detailed in the International Health Regulations (IHR) and some practical challenges such as inadequate surveillance and reporting infrastructure and legal enforcement and maintenance of individual human rights has been reviewed by Sturtevant et al. (2007). Among these causal factors affecting rabies eradication are the burgeoning human population, the increased frequency and speed of local and international travel, the increase in human- assisted movement of animals and animal products, changing agricultural practices that favour the transfer of pathogens between wild and domestic animals, and a range of environmental changes that alter the distribution of wild hosts and vectors and thus facilitate the transmission of infectious agents (Bengis et al., 2004). Animals, particularly wild animals, are thought to be the source of >70% of all emerging infections (Kuiken et al., 2005). Leading factors for emergence of zoonoses are unbalanced and selective forest exploitation and aggressive agricultural develop-ment associated with an exponential increase in the bushmeat trade (Wolfe et al., 2005a; Chomel et al., 2007). Similarly, the increase of ecotourism, often in primitive settings with limited hygiene, can be associated with the acquisition of zoonotic agents. Therefore, development of appropriate programs for surveillance and for monitoring emerging diseases in their wildlife reservoirs is essential (Chomel et al., 2007).

According to Chomel et al. (2007), major tasks that should be taken by the international community include better integration and coordination of national surveillance systems in industrialized and developing countries; improved reporting systems and international sharing of information; active surveillance at the interface of rural populations and wildlife habitats, especially where poverty and low income increase risks for pathogen transmission; training of professionals, such as animal scientists, biologists, parasitologists, veterinarians, virologists, zoologists, in wildlife health management; and establishment of collaborative multidisciplinary teams ready to intervene when outbreaks occur. Although debate on the possible negative effect of mass vaccinetion campaigns on routine health services has gone on for decades, Wiysonge et al. (2006) reports points to an overall positive effect. High-quality mass campaigns usually achieve high vaccination coverage because of high-level political commitment and adequate planning and monitoring of vaccination activities (Wiysonge et al., 2006). Any failure of vaccination and PEP should be investigated thoroughly and independently to trace potential errors in the protocol. A national vaccine adverse-event reporting system should be established to track suspected problems for safety and efficacy (Wu et al., 2009). Surveillance should be heightened to monitor efficacy of vaccines in current use in the country. Seroconversion testing after vaccination is not necessary in either humans or animals (Wu et al., 2009).

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