

Rabies: Recent Developments in Prevention and Control in Developing Countries

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Abstract

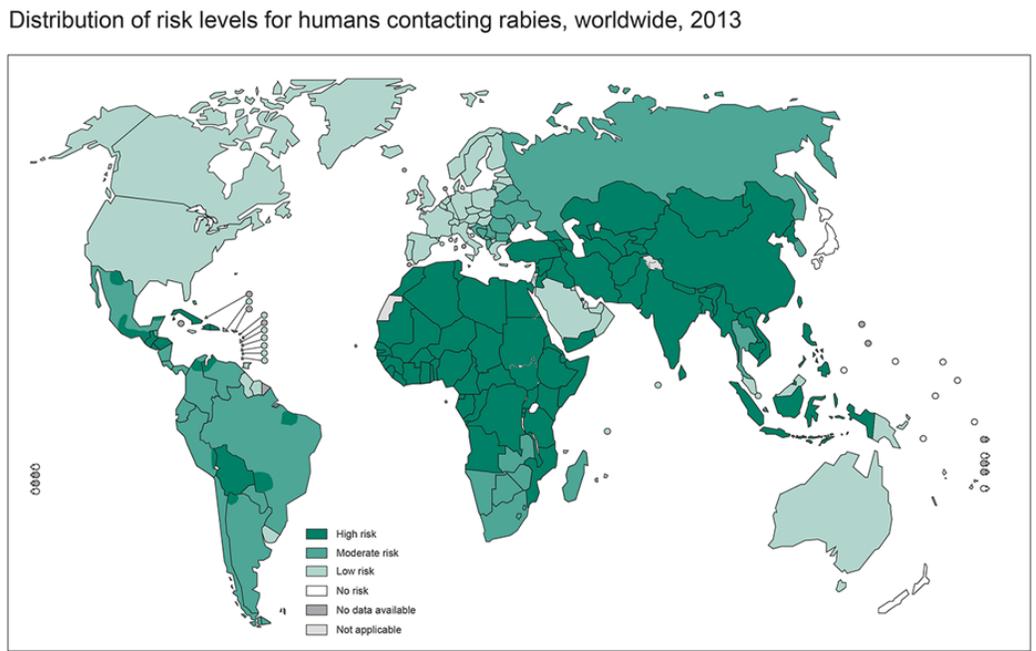
Rabies is a fatal disease of animals and man which infects mammals and has been known to man for thousands of years. Written and pictorial records of rabies date back more than 4000 years and today it is endemic in more than 150 countries around the world (Annex 1). Even though the disease can be prevented, it kills an estimated 59,000 people each year, mostly in the world's poorest and most vulnerable communities. About 40% of the victims are children younger than 15 years living in Asia and Africa. A staggering 99% of human cases are acquired through the bite of an infected dog [1], although some exposures do occur through wild animals like jackals, foxes, wolves and bats that act as viral reservoirs on different continents. At present, although excellent prophylactic vaccines are available for both animals and man, country Governments lack the funds and commitment to launch country wide efforts to prevent and control rabies. Currently, in an effort to prevent and control rabies around the globe, FAO is working with the World Health Organization (WHO), World Organization for Animal Health (OIE) and the Global Alliance for Rabies Control (GARC) to end human deaths from dog-transmitted rabies by 2030, jointly as "United Against Rabies". Dog mediated rabies can be easily prevented and controlled by following a similar but modified strategy used for rinderpest eradication, the first animal disease to be eradicated globally through FAO's excellent global efforts. Looking at past experiences in both animal and human disease control and eradication, the launching of a global campaign with provision of free rabies vaccines (both animal and human), vehicles and equipment (including refrigeration facilities) and technical assistance to Governments of developing countries at virtually no cost, would be the logical step forward in the global efforts to eliminate rabies.

Keywords: Rabies; World Health Organization (WHO); Global Alliance for Rabies Control (GARC)

Introduction

Rabies is a fatal disease of animals and man which infects mammals and has been known to man thousands of years. Written and pictorial records of rabies date back more than 4000 years and today it is endemic in more than 150 countries around the world (Annex 1). Even though the disease can be prevented, it kills an estimated 59,000 people each year, mostly in the world's poorest and most vulnerable communities. About 40% of the victims are children younger than 15 years living in Asia and Africa. A staggering 99% of human cases are acquired through the bite of an infected dog [1], although some exposures do occur through wild animals like jackals, foxes, wolves and bats that act as viral reservoirs on different continents. It is a zoonotic disease caused by RNA viruses where the virus is transmitted to man and other mammals in the saliva of rabid mammals through bites or the aerosol route (e.g. bat caves). After entry to the central nervous system, these viruses cause an acute, progressive encephalomyelitis and after exhibiting typical symptoms, is fatal. Once symptoms appear, dogs usually die within 10 days. Hence it is vital that rabies suspect dogs be quarantined for a minimum of 10 days. The incubation

period usually ranges from 1 to 3 months after exposure but can range from days to years. But there have also been unverified reports of healthy looking dogs in Ethiopia carrying the rabies virus without showing any symptoms. Rabies can be prevented by prophylactic vaccinations in animals and man, avoidance of viral exposure and initiation of prompt medical treatment when exposure does occur. In developing countries, from the point of view of human exposure, control and eradication, the most important animals are domestic and feral dogs. Since 99% of human exposure is from rabid dogs, global vaccination of domestic dogs and dog population management including elimination of stray dogs is the most effective way to prevent and control rabies [2].



Annex 1

Over the past few years, many countries have acted to strengthen rabies control efforts - scaling up dog vaccination programmes, making human biologicals for post-exposure and pre-exposure prophylaxis more accessible, and engaging communities on rabies. Dog-mediated rabies has been eliminated from Western Europe, Canada, the USA, and Japan. Currently 28 of the 35 Latin American countries report no human deaths from dog transmitted rabies. There has been good progress in reducing rabies deaths in countries such as Bangladesh, the Philippines, Sri Lanka, Tanzania, Vietnam, and South Africa, to mention a few. These experiences have generated important collective knowledge on what works and have strengthened both the quality of rabies-related data and the arsenal of tools for the development of rabies-related control programmes, capacity building, education, and surveillance [3].

Epidemiology

Rabies viruses belong to the Lyssavirus genus of the Rhabdoviridae family. The rabies virus was earlier considered to be antigenically unique but after the discovery of the first related virus isolates in Africa, several serotypes, then genotypes and now species have been described, and the genus Lyssavirus was created. Initially the genus was divided into four serotypes: classical rabies virus (RABV); Lagos bat virus (LBV); Mokola virus (MOKV) and Duvenhage virus (DUVV). The isolation of new bat viruses in Europe and Australia, coupled with advances in genetic characterization, has allowed seven genotypes to be initially identified: 1 (RABV) 2 (LBV) 3 (MOKV) 4 (DUVV)

5 European bat lyssavirus type-1 (EBLV-1) 6 European bat lyssavirus type-2 (EBLV-2) 7 Australian bat lyssavirus (ABLV). Each genotype can be subdivided into different strains corresponding to variants circulating among specific vectors and reservoirs. The latest bat lyssavirus isolates in Central Asia have expanded this diversity to 11 distinct virus species. Remarkably, bats are the reservoirs of 10 of the 11 characterized species and are also the sole vectors for 9 of these species. Only the classical rabies virus RABV involves terrestrial vectors (chiefly carnivores) but the animal reservoir for the MOKV species has not yet been clearly ascertained. Only the RABV species is distributed virtually worldwide. The other species have a smaller geographical range. Bat lyssa viruses have been isolated in many species of insectivorous, fruit-eating and hematophagous bats throughout the world. A total of 1,116 bat species have been identified worldwide or 20.6 % of all currently known mammal species. Insectivorous bats are present in virtually every region of the globe [4].

Impact of rabies on lives and livelihoods in developing countries

Rabies has a significant impact on people's lives and livelihoods, particularly in developing countries in Africa, Asia and Latin America where rabies control in animals lags behind developed nations mainly due to lack of funding. In most developing nations, rabies is a widespread, neglected and under-reported zoonosis which is 100% fatal in untreated humans and animals, causing a significant social and economic burden in many countries. The poor and marginalized communities are most heavily impacted as they often cannot afford treatment or transport for medical treatment. In most developing countries animal vaccines are available but it is more difficult to find vaccines for humans. Even when vaccines are available, they may have questionable potency due to inadequate refrigeration facilities and unreliable power supplies. When livestock die from rabies, households lose important food sources, as well as assets for farming and transportation. Livestock become infected with rabies most commonly through dog or wild animal bites, including bats. It is important to remember that dogs play a number of important roles in people's lives, directly linked to livelihoods and food security. Dogs are used for hunting, herding livestock and guarding property but are often not vaccinated due to some of the above-mentioned factors [1]. Some studies estimate that the number of human deaths due to rabies might be even higher than what is reported by Governments, establishing rabies as the most deadly of all known infectious diseases that can be transmitted by animals. These studies also estimate that the economic impact of rabies is enormous at US\$8.6 billion annually, of which 6% of that is due to livestock losses. Major underreporting of rabies cases in animals and humans remains the main reason for the lack of reliable data on the number of rabies cases and their impact on communities in developing countries [1].

Recent developments

Until recently, the global response to rabies was fragmented and uncoordinated. Now, for the first time, following extensive consultation with affected countries, in an effort to prevent and control rabies around the globe, the Food and Agriculture Organization of the United Nations (FAO) is working with the World Health Organization (WHO), World Organization for Animal Health (OIE) and the Global Alliance for Rabies Control (GARC) to end human deaths from dog-transmitted rabies by 2030, jointly as "United Against Rabies". Zero by 30: the Global strategic plan to end human deaths from dog-mediated rabies by 2030 was prepared following a global call in 2015 to end human rabies deaths by 2030. The plan, finalized in consultation with relevant global, regional and country stakeholders, builds on the current international momentum to eliminate rabies. In alignment with the United Nations Sustainable Development Goals and health for all, Zero by 30 advocates for investment to strengthen human and animal health systems and save lives. The partners have jointly launched the Zero by 30 Global Strategic Plan outlining a comprehensive strategy to provide global coordination that will support countries in their efforts, through three key objectives: 1) Efficiently preventing and responding to rabies by improving awareness and education, reducing rabies risk through dog vaccinations and improving access to healthcare medicines and vaccines for populations at risk 2) Generating, innovating and measuring impact by ensuring adherence to proven effective guidelines for rabies control and encouraging the use of technologies in surveillance to monitor progress towards elimination by 2030 3) Sustaining commitment and resources by demonstrating the impact of activities completed as part of the United Against Rabies collaboration in national, regional and global rabies elimination programmes to ensure continued stakeholder engagement at all levels and sustained financing to reach the "Zero by 30" goal [1]. The Global Strategic Plan set three objectives for affected countries, development partners, and key stakeholders: (1) to effectively

use vaccines, medicines, tools, and technologies that will stop dog rabies transmission and reduce the risk of human rabies deaths; (2) to generate evidence-based guidance and high-quality data to measure impact and inform policy decisions; and (3) to harness multi-stakeholder engagement to sustain commitment and resources.

The new rabies-focused partnership - known as United Against Rabies - provides a platform to mobilise resources and leverage existing tools and expertise in a coordinated way. It is fully aligned with the priorities of the Tripartite Memorandum of Understanding signed in May 2018, between WHO, the FAO and the OIE. Through that agreement, the three organisations are intensifying their collaboration to combat critical health risks at the human-animal-environment interface - i.e. challenges that require a genuine One Health approach launched some years ago.

To achieve the 2030 dog-mediated rabies elimination goal, the global rabies response needs to be placed on a sustainable footing over the next 5 years. This requires a phased, multipronged strategy in all affected countries, based on close coordination between the human and veterinary sectors and the public. It requires engaging communities and (animal and human) health workers to build awareness of the problem and prevent bite exposures; to prevent transmission by managing dog populations and ensure herd immunity through free dog vaccinations; and to provide free post-exposure prophylaxis and care for exposed victims. Implementation of recent new guidance from WHO on accelerated human vaccination schedules (including accelerated dose and cost-saving options for pre-exposure and post-exposure) and of OIE's international standards for rabies diagnosis, vaccination, and control in animals will increase feasibility and simplify programmatic delivery, allowing countries to move forwards with the implementation of the Global Strategic Plan. The implementation of the Global strategic plan to end human deaths from dog-mediated rabies by 2030, will also will move affected countries a significant step closer to achieving Sustainable Development Goals 1, 2 and 3 (SDG 1, 2 and 3).

Recommendation for pre and post exposure vaccinations

Animals

In developing countries, due to the presence of numerous wild carnivores and various unknown variables, it is highly recommended that only killed rabies vaccines be used in prophylactic vaccination of animals whether domestic or wild (Shanthikumar, 2019). In this regard, it should be noted that SAD (Street Alabama Dufferin) strain related vaccine-induced rabies cases following ingestion of baits with modified live vaccine were described first in Switzerland and more recently in foxes and other wild carnivores in Austria, Germany, Slovenia and Canada (FAO, OIE, WHO Reports).

Dogs and cats

It is recommended that the first dose of killed rabies vaccine to dogs and cats should be given at 12 weeks of age and then every year (annually).

Human

Recently CDC, USA has put forward new recommendations for the administration of rabies vaccines in humans. The new recommendations update previous recommendations of the Advisory Committee on Immunization Practices (ACIP) for post exposure prophylaxis (PEP) to prevent human rabies. Previously, ACIP recommended a five (5) dose rabies vaccination regimen with human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV). These new recommendations reduce the number of vaccine doses to four (4) doses. The reduction in doses recommended for PEP was based in part on evidence from rabies virus pathogenesis data, experimental animal work, clinical studies, and epidemiologic surveillance. These studies indicated that 4 vaccine doses in combination with rabies immune globulin (RIG) elicited adequate immune responses and that a fifth dose of vaccine did not contribute to more favorable outcomes. For persons previously unvaccinated with rabies vaccine, the reduced regimen of four (4) 1-ml doses of HDCV or PCECV should be administered intramuscularly. The first dose of the 4-dose course should be administered as soon as possible after exposure (day 0). Additional doses then should be administered on days 3, 7 and 14 after the first vaccination. ACIP recommendations for the use of RIG remain

unchanged. For persons who previously received a complete vaccination series (pre- or post exposure prophylaxis) with a cell-culture vaccine or who previously had a documented adequate rabies virus-neutralizing antibody titer following vaccination with noncell-culture vaccine, the recommendation for a 2-dose PEP vaccination series has not changed. Similarly, the number of doses recommended for persons with altered immuno-competence has not changed; for such persons, PEP should continue to comprise a 5-dose vaccination regimen with 1 dose of RIG. Recommendations for pre-exposure prophylaxis also remain unchanged, with 3 doses of vaccine administered on days 0, 7, and 21 or 28. Prompt rabies PEP combining wound care, infiltration of RIG into and around the wound, and multiple doses of rabies cell-culture vaccine continue to be highly effective in preventing human rabies [5-7].

Summary of steps for post exposure prophylaxis in humans

1. Thoroughly wash the wound with soap and water for at least 15 minutes.
2. Administer rabies immunoglobulin (if available) at wound sites, thoroughly infiltrating the wound and the area around the wound sites.
3. Administer 1 ml of human rabies vaccine intramuscularly (IM) on day 0, day 3, day 7 and day 14. In developing countries, due to various variables, a 5th dose on day 28 may be considered (Shanthikumar, 2019).

Pre-exposure prophylaxis in humans

3 doses (1 ml) on days 0, 3 and 7.

Conclusion

Eradication strategy towards “zero 30”

Past experiences in animal and human disease control and eradication efforts indicate that the following can go a long way to improve the chances of success of the current global campaign and help pave the way for a rabies free world:

- Launch of a global rabies vaccination campaign (similar to the FAO Rinderpest campaigns) and the Global commemoration of “World Rabies Day” on 28th September annually.
- Extensive global community education on the dangers of rabies and the need for vaccination of dogs and cats.
- Free universal vaccination of dogs and cats, control of feral animals, dog population management and provision of free rabies vaccination tags in all developing nations (in some developing countries even when rabies vaccines are free, local authorities charge a fee separately for rabies vaccination tags).
- To achieve the above, there is a need for the provision of free vaccines, vehicles, equipment, financial assistance, etc. to developing country Governments so that free animal and human vaccines (and free diagnostic services) can be provided efficiently to communities.

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