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ABSTRACT

During their sixth annual meeting held in Manila (Philippines), the Asian Rabies Expert Bureau (AREB) reviewed the implementation of programs for rabies prevention, control, and elimination in Asia. AREB members strongly support a "one health" approach for controlling rabies, combining increased public awareness, community involvement, pre-exposure prophylaxis (PrEP) programs for children living in endemic areas, improved dog bite management and improved access to post-exposure prophylaxis (PEP) for exposed persons, as well as extended dog vaccination. They called for stronger PrEP recommendations for children living at risk of rabies exposure and clear, simplified PEP regimens utilizing modern WHO pre-qualified vaccines and, in case of category III exposures, appropriate administration of rabies immunoglobulin (RIG) or, hopefully, monoclonal antibody combinations in the future. They renewed their support for World Rabies Day, one of the best opportunities to increase advocacy for rabies control.

1. Introduction

Since its creation in 2004, the Asian Rabies Expert Bureau (AREB) has met annually to review recent progress in human rabies prevention, to explore new and alternative strategies and methods for reducing the rabies burden, and to establish common initiatives and increase advocacy for rabies control in Asia [1–4]. In 2008, AREB conducted a multicentre, multi-country survey of patients seeking rabies post-exposure prophylaxis in rabies prevention centers. The survey included more than 4300 subjects from eight Asian countries and confirmed the urgent need to increase rabies awareness in human populations exposed to the daily risk of contracting rabies, so that they seek appropriate care without delay in case of animal bite [5]. The AREB has attained international recognition and was invited to participate in the Partners for Rabies Prevention Group and other working groups. It was invited to present its achievements to other major international organizations working to alleviate the global burden of rabies (the 2nd Rabies in Asia conference—RIACON 2009, Hanoi, Viet Nam, September 9–11, 2009 and the 20th International Conference on Rabies in the Americas—RITA, Quebec, Canada, October 19–23, 2009). In 2009, The Philippines was selected as host country for the 6th meeting of the Asian Rabies Expert Bureau. The meeting was held in Metro Manila.

2. The Philippines at the forefront of the fight against rabies

Every year, rabies kills an estimated 55,000 people worldwide, the majority (57%) of these deaths occur in Asia [6]. With 250 human rabies deaths reported in 2008, rabies is considered a major public health problem in the Philippines. At least one-third of these deaths occurred in children under 15 years of age and, as elsewhere in Asia, most rabies victims were infected by dogs. 190,000 animal bites were reported to the National Center for Disease Prevention and Control (NCDPC) in 2008, 50% of the bite victims were children.

One highlight of the Manila meeting was the enthusiastic acknowledgment of the commitment made by the Philippines government to supporting rabies control efforts. Dr Yolanda Oliveros, Director IV, NCDPC, Department of Health (DOH), stressed that the country had strengthened its National Rabies Prevention and Control Program by enacting the "Anti-Rabies Act" of 2007, which supports the rabies program, with the aim of eliminating rabies throughout the Philippines by 2020. She also mentioned that several pilot projects had already been initiated.

Three ongoing pilot projects were reviewed during the AREB meeting; two of them in Visayas, one in the province of Camarines Sur.

2.1. For a rabies-free Visayas

The rabies-free Visayas project was launched recently. Visayas is one of the three island groups in the Philippines (the other two being Luzon and Mindanao). Almost one-third of the total cases of human rabies in the Philippines occur in this region, which has a population in excess of 17 million (19% of the Philippine population). The project, coordinated by WHO and funded by the Bill & Melinda Gates Foundation, is conducted through the collaborative efforts of the Department of Health, the Department of Agriculture, and local governmental units. It aims to prevent human rabies through the control and eventual elimination of canine rabies. The main strategy of the project is based on community participation and relies on increasing dog vaccination coverage while concomitantly optimizing management of humans exposed to rabies. The project also includes promotion of local community involvement in understanding 'responsible pet ownership' as well as increased education on how to prevent rabies.

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2.2. The Bohol rabies prevention and eradication program

In Bohol (one of the Visayas islands, with a total population of 1.4 million), the Rabies Prevention and Eradication Program is already in progress. This 4-year project (2007–2010) is supported by the national government and the Bohol Provincial Government, the Alliance for Rabies Control and a private Swiss foundation. Bohol was the first region in recent years to successfully utilize a "one health approach" to prevent and control rabies in the Philippines. A survey of progress to date indicates that specific education about how to prevent rabies has been successfully integrated in the elementary school curriculum; 71% of the dogs in the province have been vaccinated; and 85% of the households are aware of activities related to dog rabies control. As a result of the implementation of the program, no human rabies case was reported in Bohol in 2009, whereas approximately 10 human deaths were reported annually before the program was initiated.

2.3. Pre-exposure vaccination for children living in the province of Camarines Sur

Children playing outdoors are particularly vulnerable to dog bites due to their close proximity with dogs living in their neighborhood and also because children often exhibit provocative behavior around animals, particularly dogs. Children are less intimidating to animals, due to their small stature, and they are less able to defend themselves or escape when attacked. As a result, they are more prone to facial attacks and multiple bites on the head and neck—the most severe type of exposure with the shortest incubation period. Additionally, children are less likely to report animal exposures, such as licks or scratches from dogs and cats, to their parents. These are the main reasons why there is a higher burden of rabies in children. Administering pre-exposure prophylaxis (PrEP) to children living in areas where dog rabies is enzootic can help prevent a fatal outcome by protecting them against unreported exposures to rabies virus, and also from potential failures associated with post-exposure prophylaxis (PEP) due to delayed or incomplete PEP. According to the current WHO recommendations, only two additional doses of rabies vaccine are necessary, in case of an exposure to rabies, for protection of those who previously received a complete pre- or post-exposure immunization course, and, most importantly, no rabies immunoglobulin administration is required.

A rabies PrEP pilot program for school children is currently under way in the province of Camarines Sur, located in the Bicol Region in Luzon. The program was initiated in the municipality of Cabusao, where canine rabies is endemic and the incidence of dog bites and rabies deaths in children is particularly high. The program, which is part of the Philippines National Rabies Elimination Plan, integrates education on rabies prevention in the elementary school curriculum; it includes increased dog vaccination coverage and improved access to PEP, in addition to PrEP in school children. Three years after its implementation, the success of the pilot project is evidenced by the fact that 77% of dogs have been vaccinated and no human rabies deaths have been recorded in Cabusao for the last two years. The program is currently being expanded to include the adjacent municipalities.

3. The benefit of PrEP in children

AREB members agreed that the results of the program currently implemented in Camarines Sur, in addition to the published results of the clinical trials conducted in Thailand [7] and in India [8], have demonstrated that administration of PrEP in school children is a safe and feasible strategy, which brings significant benefit to the community by preventing deaths in children who otherwise may have died from this horrific disease. Considering that protecting vulnerable children from rabies is a public health duty, AREB members strongly recommend PrEP for children living in areas where canine rabies is enzootic. Rabies PrEP is widely recommended for travellers staying only for a limited time in rabies endemic areas; it is only right that the same level of protection should be given to children who live in canine rabies endemic areas and are at higher and constant risk of exposure.

AREB members proposed support for a new comprehensive demonstration project of PrEP vaccination in school children, to be implemented in the Philippines in early 2010. The aims of the project are to complement current experience, to confirm the feasibility of PrEP vaccination, to evaluate the efficacy of PrEP in preventing rabies in children who live in areas where dog rabies has not been eliminated, and to estimate the health and economic impact of the PrEP strategy.

Administration of PrEP to infants is an alternative approach to vaccinating school age children and has the advantage that protection begins at an earlier age. Clinical trials conducted in Thailand [9] and in Viet Nam [10,11] have shown that rabies vaccine can be safely and effectively administered at the same time as routine pediatric vaccines, e.g.: the Japanese encephalitis vaccine [9], or the combination vaccine against diphtheria, tetanus, pertussis, and poliomyelitis (DTP-IPV) [10,11]. Integration of rabies vaccine into the Expanded Program of Immunization (EPI) would facilitate access to the targeted population and minimize operational costs. AREB members thus recommended that demonstration projects should be conducted to evaluate the feasibility of introducing rabies vaccination into the EPI in countries where the risk of rabies is high.

PrEP implementation is not intended to eliminate the need for management of rabies exposure, nor to compromise vaccine availability for PEP. AREB members agreed that PrEP programs must be coupled with complementary strategies aiming at increasing dog vaccination coverage, raising public awareness and education, and increasing access to and compliance with PEP.

In Thailand, the number of human rabies deaths decreased from 200–300 in the early 1980s to the present level of less than 20 annually—this is thanks to outstanding management of dog bite victims and the use of modern cell-culture vaccines. However, rabies is not yet controlled in the dog population in Thailand [12] as 500,000 bite victims still required rabies PEP in 2008. Consequently, large-scale PrEP immunization of children has been advocated to further reduce the number of rabies deaths, but financial barriers have hindered its implementation until now. Cost-effectiveness studies have shown that childhood immunization programs increase the initial total annual expense of immunization (PrEP and PEP), but the cost gradually decreases, and in the long term would be equal to that of PEP without pre-exposure childhood immunization [13]. Another cost-analysis study showed that the total expense would reach equilibrium after 15 years and that the time required to reach breaking point can be shortened proportionally to successful implementation of dog population control measures.

AREB members agree that cost-effectiveness studies as well as studies on the real burden of rabies on public health could be helpful for decision making with respect to PrEP introduction. They request WHO to strongly recommend PrEP vaccination for children living in areas where dog rabies is enzootic as this would support the efforts of affected countries to raise funds for PrEP implementation from national and international organizations.

4. Monoclonal antibodies under development for an increased accessibility of rabies immunoglobulin

Administration of rabies immunoglobulin (RIG) is necessary for the success of PEP in cases of severe exposure (WHO category III