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NOVEMBER 2011 • Issue 25

The newsletter of The Global Alliance for Rabies Control

EDITORIAL

With the end of the year almost upon us, it seems like a good opportunity to let all of you know what we have accomplished by working together in 2011 and to take a look at what we hope to achieve in 2012. Time has passed so quickly since the Global Alliance launched World Rabies Day over five years ago, but clearly this initiative has changed the world of rabies and continues to serve as an excellent platform for individuals and countries to focus more attention on programs aimed at preventing rabies (www.worldrabiesday.org). We have managed to create a large network of public health professionals located in various locations around the world that are willing to share experiences and, where possible, resources to help in the fight against rabies. We have seen countries begin rabies prevention programs that would never have even considering to do so a few years ago. Through the Partners for Rabies Prevention, we have developed a freely accessible on-line resource that provides step by step strategic assistance for countries and individuals that want to make a difference in the rabies situation in their country. Thanks to Dr Katie Hampson and the University of Glasgow team, we are in the final stages of completing an overview of the global burden of rabies. This will be critical in helping to provide more information on the disease burden. Through collaboration and partnerships with many individuals and international organizations, we have launched community-based programs that empower local citizens to take responsibility for sustainable rabies prevention efforts in their own areas (www.globalrabiescontrol.org).

Where are we headed in 2012 and beyond? We continue to focus on improving awareness about how to prevent rabies in humans and how to improve rabies prevention in pets through vaccination and education. We want to accomplish this by adapting and extending the Bohol project into new areas in both Africa and Asia. We aim to adapt some of our current school-based educational programs for 'non-traditional' educational programs, specifically in areas where a large percentage of the population does not have regular access to schools. Additionally, we want to expand our very successful Webinar based educational system to provide information above and beyond the participants in 83 countries that we have already reached. Finally, from the entire team of the Global Alliance want to wish all of you Happy Holidays and we look forward to working together in 2012.

Deborah J Briggs, Executive Director Global Alliance for Rabies Control

NEWS FROM GARC AND WRD

WRD in Madagascar

This year, World Rabies Day was celebrated for the first time in Madagascar, with the focus on raising public awareness of rabies. The Institut Pasteur of Madagascar partnered with Sanofi Pasteur to hold a press conference headed by the secretary general of the Ministry of Health. Presentations on the current state of rabies management and anti-rabies treatment in Madagascar were given, a documentary film from Sanofi Pasteur was shown, and awareness sessions for journalists from TV, radio and print media were also held.



In addition a new rabies treatment centre was opened in the

District of Mandritsara. This area has around 50 dog bite cases per month, but is almost 1000km from the capital and previously the closest treatment centre was over 200km away. The new centre was opened on WRD, and technical training of the personel was carried out so that they now have current knowledge on rabies epidemiology, reporting procedures for rabies, the administration of rabies vaccines, how to establish a committee to fight against rabies, raise community awareness and what to do in the case of a rabies epidemic in the district.

Contributed by Dr Ramahefalalao Emilie Fara II of the Pasteur Institute of Madagascar.

The Alliance is a registered charity in the UK and a 501(c)(3) organization in the US

RABID BYTES The Global Alliance for Rabies Control

CARe Project now Underway in Philippines

The Global Alliance's Children Against Rabies (CARe) Project in El Nido, Philippines will protect children, save lives and gather valuable data on the impact of education as a rabies control measure.



Children have always been at particular risk from rabies – in part, because they have not yet learnt to be cautious around animals that are behaving oddly. School education programs are an effective way to address that. And, when children go home and tell their families what they have learnt, the knowledge spreads through the wider community.

This project covers over five thousand school age children in all 27 public elementary schools of the El Nido Municipality. All participating children are given pre-exposure immunization, to protect them should they be exposed to rabies.

During the course of the project, the schools teach the children about the disease, including: how rabies is transmitted, how to avoid exposure, what to do if bitten or scratched, and the society-

wide benefits of good pet stewardship. A record is kept of the incidence of dog bites in participating children. Analysis of this data will show us just how effective education is at protecting children from exposure to rabies. We will compare our results with data collected before the intervention, to fully understand the health and cost benefits. And, we will also assess the best way to collect information about dog-bite incidence.

Millions of people living in rabies endemic countries don't know how to protect themselves from the disease nor, know what to do if they come into contact with a rabid animal. Folklore and misinformation are rife. Through this project we aim to provide hard evidence of education as a simple and cost effective way to save lives.





Rabies Awareness Poster Distributed in Latin America on WRD

This year, World Rabies Day went far beyond the immediate networks of rabies prevention. On World Rabies Day, this poster was distributed electronically by the Association of Mexican Cavers to 2142 cavers throughout Latin America. It also reached 1457 virologists and 52 rabies specialists throughout the region, as well as veterinary technicians in Mexico, who in turn passed it on to their own contacts. The message asks cavers to be respectful of bats and their habitats, and to be aware that if bats are infected with rabies, they can transmit the disease to humans.

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World Rabies Day Webinar a Huge Success!

On Sept 21-22, 2011 an estimated 600,000 viewers from 83 countries joined the 2nd Annual World Rabies Day Webinar. During the 16-hour event, 28 speakers from 13 different countries discussed topics such as canine rabies elimination; human rabies surveillance, prevention and intervention; wildlife rabies control; information and education campaigns and building sustainable programs. At many locations around the world, numerous viewers gathered at one computer to listen and participate in the global educational initiative designed to reach populations living at daily risk to rabies. To further increase participation, many locations utilized their own technology to transmit the live broadcast to others within their countries. The two day Webinar was recorded and has been viewed over 100 times in 35 countries. If you missed the live Webinar broadcast and would like to view the recordings, please go to: http://webinar.worldrabiesday.org.

On the first day of the Webinar (Sept 21), the program concentrated on presentations and involvement from Asia, the Middle East, Europe and Africa. In order to attract participation from the eastern hemisphere and reach communities most burdened with rabies, the Webinar began at 12am-midnight EDT (New York) and ended at 8am EDT (New York). Administering the Webinar during this time frame allowed for the highest level of participation

around the world. Presentations included [among others] Dr Stella Lapiz discussing the Bohol Rabies Project; Dr Katie Hampson highlighting knowledge gaps in the global rabies burden; and Dr Kira Christian talking about how CDC's Global Disease Detection Team supports international rabies outbreak investigations.

On day two (Sept 22), the Webinar focused on capturing participation from audiences in North America, Latin America and the Caribbean Regions. Running from 9am-5pm EDT (New York), the Webinar featured presentations in English and Spanish. During this Webinar Dr Kis Robertson presented on a community intervention and resulting free online training to reduce misadministration of PEP; Dr Julie Sinclair discussed the risk for introduction of rabies via importation of dogs; and Jordona Kirby provided



Dr Atalvin Zhiva listens to a WRD Webinar in Albania while at work

a comprehensive overview of wildlife rabies surveillance and control. Dr Francois Meslin concluded the two day Webinar event with an overview on the "Role of WHO in Rabies Prevention and Control".

When looking at viewers' job titles as part of our evaluation, we found that the World Rabies Day Webinar was truly a One Health effort with participation from veterinarians, medical doctors, occupational and public health nurses, students, professors, scientists, researchers, consultants, laboratorians, health educators, industry executives, environmental health specialists, animal control staff and wildlife officers. 83% of survey respondents cited the Webinar as being informative and or useful and 97% stated they would attend a future Webinar. When asked about technical difficulties, 21% reported experiencing connection issues. However, more than 90% of these were end-user issues such as local connection issues, firewall/blocked website and not having an audio input device.

With more than 20 topics recommended for future Webinars and phenomenal participation in both the 2010 and 2011 Webinars, we hope to host even more Webinars throughout 2012. If you would like to suggest a topic for a Webinar in your country, please contact <u>peter.costa@worldrabiesday.org</u>. On behalf of the coordinating team, we would like to thank everyone who helped make the 2nd Annual World Rabies Day Webinar a huge success!

Contributed by Peter Costa, co-ordinator of the WRD campaign and the WRD webinars.

WRD Vaccination Clinic

Banfield Pet Hospital of Lilburn, Georgia held a rabies vaccination clinic for World Rabies Day. They raised almost \$1000 in just 6 hours, with the money raised split between the Banfield Charitable Trust Fund (that enables people who would otherwise struggle to care for their pets) and GARC. Educational materials on World Rabies Day and from Banfield's Smarthelp database were also available, and the feedback was very positive, with many clients asking if they would do the event again next year. This type of event and joint fundraising is a great way to make the connection between rabies control at home and overseas, as well as raising money for good causes.



News from the Community

CL184 - A Combination of Human Monoclonal Antibodies for Post-Exposure Prophylaxis of Rabies

Human or Equine plasma derived polyclonal Rabies Immune Globulin (HRIG or ERIG) supplies are limited globally, hence, WHO category III exposures requiring Post-exposure Prophylaxis (PEP) are often treated with vaccine alone rather than the recommended vaccine plus RIG. This shortage has been recognized by WHO and <u>the recommendation</u> to make progressive switch to monoclonal antibodies (mAbs) has been confirmed. Crucell took this recommendation and started their discovery program in 2003 to develop a combination of two fully human mAbs, CR57 and CR4098. A joint development partnership with sanofi Pasteur was implemented in 2007. Each mAb is directed against a distinct nonoverlapping epitope on the rabies virus (RV) glycoprotein. The mAb



combination, CL184, has been developed to <u>ensure coverage</u> against diverse RV isolates and both components are needed to do so.

The use of human mAbs has several advantages over current standard of care, HRIGs or ERIGs. First of all, they can be produced in large quantities sufficient to meet the demand in endemic areas. Second, the mAbs can be produced in a consistent manner under highly controlled conditions. Third, they have a consistent potency with a high specific activity. Fourth, CL184 is formulated much more concentrated allowing to inject, in a higher percentage of rabies exposures, all mAbs into the wound area where the rabies virus is located as recommended by ACIP, avoiding to have to inject the remaining of the dose in a distant site.

To date, CL184 has been evaluated in healthy subjects in four different <u>clinical trials</u> conducted in the US, India, and the Philippines. These studies have demonstrated a good safety profile and also showed that similar serum neutralizing titers were reached in combination with rabies vaccine when compared to human RIG plus rabies vaccine. We are excited in November 2011 another Phase IIb trial in India will start with sanofi Pasteur support to generate additional safety and efficacy data on CL184. In the meantime, we are preparing for Phase III efficacy testing in individuals with confirmed exposures to assess CL184 efficacy in a human PEP setting. Data from these clinical studies will allow us to move toward licensing of CL184 and to make it available to the people in need in rabies enzootic areas.

To ensure global coverage of RV by CL184, we have implemented a wide epidemiological surveillance program. Although previously we had shown <u>full coverage</u> of a global panel of representative RV strains, we wanted to further expand this evaluation due to the heterogeneity in the RV glycoprotein sequence observed in natural field RV isolates. Within our surveillance network, our main areas of attention are USA, China, India, and the Philippines. For each area, we have a collaborating center that is responsible for sample collection, rabies confirmation, and RV glycoprotein sequencing. The RV glycoprotein sequence data is used in a statistical algorithm to determine representative RV isolates in a given RV sequence cluster that we then test for in vitro neutralization by CL184. For this we have developed a new assay specifically designed to assess the neutralizing capacity of CL184 against primary field RV isolates directly without any laboratory manipulations. This prevents potential introduction of mutations during virus amplification as needed for use in RFFIT. To date, we have collected close to 600 RV isolates from the different regions. The program is most advanced in the US where we have collected 200 RV and tested 74 representative RV isolates all of which were efficiently neutralized by CL184.

We anticipate this program will run at least for the next years to come to generate sufficient CL184 neutralization data against RV isolates from different areas in order to enhance the statistical certainty of global RV coverage by CL184 and detect any new RV variant that can emerge in enzootic areas.

Contributed by Dr Wilfred Marissen, Project Director of the Rabies Antibody Combination project, Crucell. There is more information on this project available on the <u>Crucell website</u>. The latest clinical trial data has been published in <u>Vaccine (2008)</u>.

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Rabies and RITA in Puerto Rico



The 22nd Rabies in the Americas (RITA) meeting was recently held in San Juan, the capital of Puerto Rico, with a blend of informative presentations, interesting workshops and enjoyable social activities. Several special presentations and two workshops gave participants an understanding of the special features of rabies in the Caribbean. Mongooses were introduced to several Caribbean islands in a misguided attempt to control rat populations. Now there are an estimated 2 million mongooses on Puerto Rico, with up to 2% infected with rabies (about 80% of rabies cases). Around 25 people

are exposed to suspected rabid mongooses every day, with about 2/day requiring PEP treatment. The mongoose is now present on many Caribbean islands, with Cuba, Dominican Republic, Grenada, and Haiti also having to deal with mongoose rabies. Many of the islands, including Puerto Rico, also struggle with large free-roaming dog populations that can transmit rabies. Translocation of dogs and mongooses that are unknowingly infected with rabies to new areas in the Caribbean remains a real risk.

Mongoose rabies control options were reviewed by Dr Dennis Slate (USDA wildlife services, USA) who concluded that oral vaccination of mongooses against rabies was the most feasible means to eliminate the virus. As mongooses are generalist feeders, baiting is relatively easy and at least one vaccine is known to be effective (though not registered for use) in mongooses. However, mongoose densities can be very high, and bait distribution needs to be planned to avoid non-target species (eg rats and cats) eating them instead. Combining vaccination with injectable contraceptives would be even more effective, as but more research is needed before this is an option. Many of the necessary surveillance, mapping and modelling tools are already in place, and in Puerto Rico, local support is mounting for rabies elimination. Results of a study on mongoose population densities at two



sites in Puerto Rico was presented by Kurt VerCauteren (USDA wildlife services, USA), with baiting strategy design in mind. The data from capture-mark-release and camera trap techniques suggest around 50 mongooses/km².

Dr. Andres Velasco (CDC, USA) presented genetic data on dog-mongoose rabies virus variants from the Caribbean region, collected to better understand the transmission of mongoose rabies. Analyses suggest that in Puerto Rico, both dogs and mongooses play an important role in virus maintenance, with dogs implicated in the longer distance spread. Elimination attempts need to consider both hosts, and possibly also feral cat populations, in their design. Canine rabies cases in Latin America and the Caribbean have been reduced from around 15,000 in the early 1980s to just 268 in 2010, due to a huge international collaboration directed at canine vaccination, the provision of PEP and surveillance. Dr Hugo Tamayo (PAHO) presented the current status, with foci of infection remaining in a few countries, including Cuba and Haiti in the Caribbean. The goal of elimination of canine rabies is very close, but all countries need to remain engaged in the elimination programme.

Rabies transmitted from bats has not been documented in Puerto Rico, although little testing has been carried out. Dr Amy Turmelle (CDC) presented a study on the potential for northern spread of vampire bats from Latin America, based on predicted global warming trends, bat dispersal behavior and geographic barriers. Currently there are vampire bats in the Caribbean only on Trinidad, despite suitable habitat and temperatures elsewhere, suggesting that the ocean forms a barrier to migration. However, islands such as Cuba and Grenada, both close to the mainland, are at risk of chance introductions. This is substantiated by genetic evidence presented by Dr Janine Seetahal, a veterinary officer in Trinidad and Tobago. Her data suggested that rabies virus infected bats flew across the 7 mile stretch of ocean from Venezuela into Trinidad, and caused outbreaks of paralytic rabies in cattle there.

Two workshops also gave participants an opportunity to experience the beautiful Puerto Rican countryside. Participants in one workshop visited the El Yunque rainforest in the east, to see the ongoing mongoose density assessment study and also to perform dRIT testing, a tool commonly used out in the field in surveillance programs. Participants in the second workshop trekked out westwards, to visit one of many limestone cave systems where they were treated to the sight of some of the 300,000 resident bats emerging at dusk, trying to avoid the jaws of the small Puerto Rican boa as they gathered above the cave mouth to capture them (pictured).

Summarised by Louise Taylor. The next RITA meeting will be held in October 2012 in Sao Paulo, Brazil.

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Rabies Vaccination Compliance Through Community-Based Approaches in Kenya

Kisumu district, with its capital Kisumu city, is situated along the shores of Lake Victoria, Western Kenya. About sixty percent of the population live in semi-rural low income villages and domestic dogs are frequently kept, mainly for security purposes. In 2009, Kisumu district Hospital received an alarmingly high number (1623) of patients with dog bite injuries. The hospital had no rabies vaccines for post-exposure prophylaxis (PEP) and the patients had to buy the vaccine from local chemists at very high prices (USD 95). Dogs in this community are rarely vaccinated and turn out for previous dog vaccination campaigns organised by the veterinary department have been very poor. Hence there was concern about dog bite victims contracting rabies, and seven suspect human rabies cases were reported following dog bites in 2009.

In January 2010, the Veterinary department was called upon by the District disease control committee to start a rabies control and responsible dog ownership program. Dogs were rarely restrained and it was common to see many free-roaming dogs in the peri-urban market centres. In order to improve the situation, the Vet department employed a "community-based approach". Inadequate information sharing between the public health department, the district Veterinary office (DVO) and hospital cases was identified as a weakness in rabies surveillance activity. An arrangement was therefore put in place between the veterinary and human health departments that a dog bite register be opened at the Kisumu district hospital. Any person visiting the hospital with a dog bite injury would also be told to report to the DVO.

The DVO conducted a census to estimate the dog population in villages through a household survey, enlisting the services of the village elders and the assistant chiefs. The village elders used a simple proforma to collect the dog data in



Peter Omemo speaks to a man bringing his dog for vaccination

the households under their jurisdiction. The survey included information on the number of dogs per household, their sex, age, and vaccination status. The results indicated that over 90% (14,000) of dogs in the district had homes or owners, and that only about 7% of the owned-dog population had been vaccinated against rabies in the past 12 months. Following these findings the DVO devised a two part approach; community education on rabies control, and application of the law to enforce dog vaccination and responsible dog ownership. The veterinary team headed by Mr. Omemo conducted a series of meetings with the village elders to raise awareness on the risks associated with dog bites, rabies vaccination against rabies and the role the village elders could play in community policing of irresponsible dog ownership.

In September 2010, the month of World Rabies Day, Mr. Omemo was given free air time by a local community FM radio station to discuss dog bite injuries and rabies in the community. The talk show was on air for four months and created a huge impact on case reporting of suspected rabid dog bites to the veterinary office. The main concern of the people who report dog bite injury to the district veterinary office was how to get rabies PEP following the advice given during the talk shows.

The DVO came up with an arbitration process within the provision of the Kenyan law (the Rabies Act, cap 365) to make the owners of the offending unvaccinated dogs meet the cost of rabies PEP for the victims. This approach was made possible because village elders were able to trace the households owning the offending dogs. The arbitration strategy enabled the dog owners to understand the risks associated with bites from their unvaccinated dogs. Such dogs usually disappear from home after getting infected with the rabies virus. Dog owners opted to meet the cost of PEP rather than get charged in a court of law, for a possible two offences, failure to vaccinate their dogs under the Rabies Act (cap 365) and criminal negligence under the Kenya Penal code subsection 243(b).

Between April 2010 and April 2011, a total of 72 cases were successfully arbitrated and the owners of the dogs met the cost of treatments. The village elders were requested to assist in community policing of unvaccinated dogs in their respective villages. The strategy led to a higher response by dog-owners seeking dog vaccination from the vet department. However, the vet department did not have enough vaccine to meet this new demand. They approached Kenya Medical Research Institute (KEMRI) for a donation. Dr Eric Ogola , a veterinarian at KEMRI/CDC liaised with other partners including Dr Sarah Cleveland and Intervet who donated 4000 doses of rabies vaccine through the KEMRI/CDC program in Kisumu. This facilitated community vaccination of dogs. The DVO also benefits from logistical and epidemiological support from the Centres for Disease Control (CDC) through the intersectoral collaboration.

By the end of October 2011, 6,457 (49% of) village dogs had been vaccinated, surpassing the tally of the previous three years campaign in the district. This achievement was driven by the multi-sectoral approach (mass media, village elders, arbitration efforts and the rabies Act) applied by the Veterinary team. The results demonstrate that community-based approaches to rabies control should include effective communications strategies, collaborations and application of existing laws as a feasible way of achieving rabies vaccination compliance and responsible dog ownership in rural communities.

Contributed by Peter Omemo [MPH (Epidemiology & Popln.Hlth), Bsc (Env.Hlth), Dip.(Animal Hlth.), Dip.(Env. Res.Mgt.), Cert. GIS]. He is currently working with the veterinary department (VPH) in Kisumu district, Kenya. He is exploring the application of community –based models to achieve sustainable rabies prevention and control.

Global Surveys on Rabies in Progress

At the recent Rabies in the Americas (RITA) meeting in Puerto Rico, updates on the progress of two ongoing research surveys were presented: one on the availability of rabies biologicals for travelers and another on the reassessment of the global burden of rabies.

Dr Emily Jentes, of the Traveller's Health Branch of the US's Centers for Disease Control and Prevention, presented preliminary results of a short web based survey designed to assess the global availability of human rabies vaccine (RV) and anti-Rabies ImmunoGlobulins (RIG) to travellers. The results from 300 respondents based in travel medicine and other rabies clinics worldwide were analysed. These provided data from 58 countries, most commonly North America (47%), Western Europe (16%), Australia/Pacific (10%), East Asia (5%), and Southern Africa (4%). Most clinics administered postexposure prophylaxis (PEP) very rarely in 2010 (median of 2 patients), but some treated more than 30,000.

Overall, 44% of the respondents stated that patients with animal exposures seldom or never presented with adequately cleansed wounds. RIG was always accessible for 58% of respondents in North America, 64% in Western Europe, 68% in Australia/Pacific, and 38% in East Asia. RV was always accessible for 72% of respondents in North America, 79% in Western Europe, 100% in Australia/Pacific, and 92% in East Asia. Across all regions, about a third of respondents felt that the cost of both RV and RIG was too high. More in depth regional analyses will be conducted next and the final results will be published.

The second study was presented by Dr Katie Hampson of the University of Glasgow, UK at the Partners for Rabies Control (PRP) meeting just prior to RITA. This is a large survey using several datasources to reassess the global burden of rabies. Online surveys ask Veterinary, Public Health and Laboratory experts connected with rabies work in their countries for detailed information such as the numbers of reported human and animal cases, how much under-reporting they think may be occuring, the number of people seeking PEP each year, how far patients have to travel for PEP and how often it is available to them, the number of dogs vaccinated each year, the percentage of dogs and other animals that are vaccinated. In an effort to assess the economic impact of rabies and rabies control, questions about the costs of animal vaccination programmes and PEP provision are also included.

Data from international databases is being used for human population estimates and other relevant published data are also being used. The data are being used to set the parameters of a probability model which estimates both the burden of disease in terms of numbers of human deaths and the years of life lost due to the disease and also through a linked economic model, the economic impacts such as livestock losses and the cost to PEP provision and animal vaccination programmes. A cluster-based approach is being used, grouping together countries within regions where rabies epidemiology and development indices are similar. This approach should allow gaps in the data to be filled as accurately as possible with estimates based on the rabies burden in similar countries.

Data collection, validation and analysis is ongoing, and several significant gaps in the available information were pointed out. However, very preliminary results suggest that the current burden of rabies is around 70,000 human deaths per year, with an worldwide economic impact of about \$4 billion each year. Further critical validation of these data are necessary and input from country public health experts is welcome. Please contact louise.taylor@ rabiescontrol.net

Summarised from the abstracts and presentations by Louise Taylor of GARC. There is more information about the reassessment of the global burden of rabies on the <u>PRP section</u> of the GARC website.

Upcoming Conferences

The 3rd Rabies in Asia Conference (RIACON) will be held November 28-30th, 2011 in Colombo, Sri Lanka. For programme details and to register please go to www.rabiesinasia.org/3riacon-2011.html

The International Congress on Canine Practice will be held in Bikaner, Rajasthan, India on 9-11th February 2012. Further details can be obtained from www.intcaninecongress12.com or by emailing intcaninecongress12.com or by emailing www.intcaninecongress12.com or by emailing intcaninecongress12.com or by emailing intcaninecongress12.com or by emailing www.intcaninecongress12.com or by email or by email.com

The editor of the Alliance newsletter is Louise Taylor, and typesetting is by Pete Else. If you have news items or information about rabies, please contact Louise at louise.taylor@rabiescontrol.net. For further information on the Alliance's work see www.rabiescontrol.net.