



RABID BYTES

The Newsletter of
The Alliance for Rabies Control

Issue 9 September 2008

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Editorial

With the second World Rabies Day (WRD) almost upon us, there seems no end to the incredible enthusiasm that continues to build across the world in support of rabies prevention and education activities. In only 2 years, the Alliance's community has held rabies awareness events in more than 74 countries, with media outreach that reached more than 54 million people worldwide. We have initiated and funded 6 rabies education and control programs across the world, helped set up the 'Partnership for Rabies Prevention', and ignited rabies control discussions at international levels.

This could only have been accomplished through global teamwork. The success is due to *everyone* who invested time and energy into doing something to prevent the devastation caused by rabies. The Alliance considers all of you working to prevent rabies in your own communities as a part of our global team. Between us, we are fluent in every language that is needed to get our messages distributed into rabies endemic countries, we have the talents needed to

increase rabies awareness and we are located exactly where we need to be. Together, we are the most powerful team that the world has ever seen taking rabies awareness to the next level! In this day of electronic communication, you can be in touch with the rest of the Alliance Rabies Team in the time it takes to write an email.

With all of this in place we can be assured that we have the right network needed to accomplish even greater goals in the upcoming years as we focus on expanding WRD events into year long rabies prevention activities. As we look forward toward what we want to accomplish in the upcoming years, let us take time to congratulate all of our fellow team members for their efforts during the past two years that have contributed to the prevention of thousands of unnecessary rabies deaths.

Best wishes for a successful WRD and we look forward to hearing more about your rabies prevention activities throughout the upcoming year.

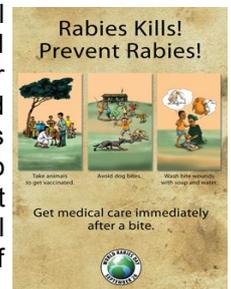
Dr Deborah Briggs, Executive Director of The Alliance

September 28th is World Rabies Day!

With less than two weeks to go, World Rabies Day (WRD) events are flooding-in! To date, we have received event reports from over 50 countries. Last year, veterinary and medical schools around the world embraced WRD and energized the "One Health-One Medicine" community. This year is no exception, with events already planned at over 40 schools, the student community is once again leading the way. Numerous countries such as Japan, Korea, Mozambique, the Netherlands, Saudi Arabia and others that did not report an event last year are coming on-board and notifying us of their events for WRD 2008. We are very excited to work with these countries and any country planning an event by providing materials and resources to help spread the rabies prevention message. So far, we have received enquiries from over 180 countries. This year we will also see many private companies world-wide conducting workforce awareness programs for their employees. This is a very easy way for corporations to get involved, engage their employees and provide vital education about rabies prevention. We also have numerous events being organized this year by the armed forces, such as the 5K Run for Rabies Awareness planned at Andrews Air Force Base (Maryland, USA).



The WRD Team is very pleased to again be coordinating educational poster outreach to Africa. Thanks to the extraordinary support of dedicated global partners such as the University of Pretoria (South Africa), School for Global Animal Health at Washington State University, and the Food and Agricultural Organization of the United Nations (FAO), over 10,000 rabies prevention posters will be distributed in English, French and Portuguese to more than 20 countries throughout Africa. Posters are also available without text, allowing recipients to create their own prevention messages in any local language or dialect. The posters will be delivered to areas in great need of rabies education and are a major outreach component of the 2008 campaign.



With WRD right around the corner, we encourage everyone to feature their event on the WRD web site by filling-out the online form available at: www.worldrabiesday.org/EN/Events/2008_World_Rabies_day_event.html. Having your event listed on the WRD web site is helpful for people seeking local events and an excellent way to promote your agency's involvement! **Remember also that as we move to a year round campaign, events can be held at anytime of the year.** Additionally, if you have educational materials that you would like to share through worldrabiesday.org, we would be delighted to receive those items and add them to our Education Bank.

Following WRD, we hope that all event coordinators will help us evaluate the success of the 2008 campaign by filling-out a short survey and sending us high resolution photos from their events. Last year we received hundreds of excellent photos from all over the world that were used in presentations, on the WRD web site and even in picture calendars. We look welcome these submissions as pictures can truly capture the magnitude of World Rabies Day. The survey will be available after WRD and any pictures can be emailed to Peter Costa (peter.costa@worldrabiesday.org).

North American Vet Students Do It Again

This article is an update on behalf of the Student Chapters of the American Veterinary Medical Association (US and Caribbean) and veterinary medical students at University of Saskatchewan, University of Guelph, Université de Montréal, University of Prince Edward Island, and the inaugural class at University of Calgary in Canada

The achievements of the first World Rabies Day were substantial and beyond all reasonable expectation. The Student Chapters of the American Veterinary Medical Association and other veterinary student bodies were a major driving force behind many events in 2007, and raised funds which when matched by Veterinarians Without Borders/Vétérinaires Sans Frontières, Canada and supplemented by a private donation have enable the Alliance to fund 5 rabies control projects (see more detailed article in issue 8). This year, the Canadian Veterinary colleges, including a brand new college in Calgary have really increased their involvement. The local actions of the veterinary students are having a global impact and are priming the pump for the local, national, and international outreach now underway for WRD 2008.

In support of the veterinary student activities and with direct support from new corporate partners (Intervet/Schering-Plough, Bayer Animal Health, Nestlé Purina, Fort Dodge Animal Health), the Kansas State University College of Veterinary Medicine is providing specially designed T-shirts to all 36 Colleges and programs of veterinary Medicine in North America and the Caribbean. All 36 Universities are listed on the front of the T-shirt to invite collaboration not only among but also within the Universities so that involvement of medical, nursing, Masters in Public Health, ecology, undergraduate, and other interested students may be maximized towards the concept of "One World, One Medicine, One Health."

Once again, the American Veterinary Medical Association is demonstrating its support of the veterinary students through their generous donation of rabies prevention brochures for each student chapter. Two corporate partners, Merial and Fort Dodge, are donating rabies vaccine to the veterinary students who are planning rabies vaccination clinics with the support of their faculty members. A number of the rabies vaccination clinics will be held in under-served communities in the localities near the student campuses, such as the ones by University of Lincoln-Nebraska/Iowa, Cummings School of Veterinary Medicine, Tufts University, and North Carolina State University College of Veterinary Medicine.

There is keen competition among the veterinary students in regard to 2008 World Rabies Day events as the winner of the individual essay contest this year will be awarded a "CDC experience" consisting of a specially tailored two-weeks at the prestigious, cutting-edge health institution that is recognized nationally and internationally and where over 200 veterinarians are engaged daily in a broad range of public health specialties. And we look forward to awarding the 2009 Merial-sponsored symposium for the highest student body participation. Our long term hope is that by increasing medical and veterinary student involvement across the world, and linking them together, a stronger and more effective WRD campaign will follow. The students are demonstrating "One Health in action" and indeed, as Professor Dzikwi from Ahmadu Bello University says, we are **"Working together to Make Rabies History."**

Contributed by Cathleen A Hanlon, David Dreesen, Mylissia Stukey, Peter J Costa, James Hackworth and other key members of the team.

Rabies elimination in Bohol

The Alliance is pleased to announce that it is the recipient of a three year financial award from a private Swiss Foundation to help support a canine rabies elimination project in Bohol, Philippines. The Philippines ranks among the top ten countries worldwide for the continued presence of human rabies with a disease incidence of 2.46%. Bohol, an island in the Philippines, has the second highest incidence of human rabies in the nation.

However, Bohol is committed to protecting the lives of their population against the scourge of rabies. In 2007, they launched the first Bohol provincial rabies summit wherein members of the Department of Health, Education, Finance and Agriculture met with WHO, ARC and other international experts to discuss strategic methods to eliminate rabies on the island; they established an interactive *Provincial Rabies Prevention And Eradication Council* to serve as the liaison between international experts, the provincial oversight board and local management teams; they have revised municipal rabies ordinances, increased the provincial budgetary support to hire additional field workers, sought and received in kind donations of human rabies vaccines; they have developed and published the Bohol Rabies Eradication Manual, developed educational material for all levels of the government and the general public, integrated rabies prevention facts into all levels of the school curriculum; and are in the process of establishing additional animal bite centers in high risk zones.

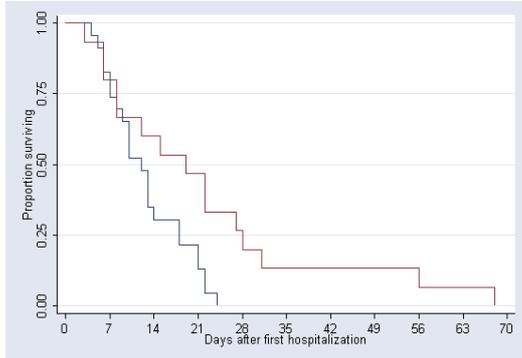
These recent steps provide solid evidence that the entire island of Bohol is committed to eliminating the unnecessary tragedy of rabies. Due to their committed effort to eliminate the unnecessary tragedy of rabies in their province, the Alliance and the private Swiss Foundation are both pleased to announce this new partnership and will be providing technical expertise and financial assistance to help them reach their goal of a 'canine rabies-free island'. As we move forward together during the next 36 months of this commitment, we look forward to further project updates and will continue to keep our readers updated as to our progress!

Dr Deborah Briggs, Executive Director of The Alliance

The Treatment of Human Rabies

Dr Rodney Willoughby of the Medical College of Wisconsin shares his experiences of developing the Milwaukee Protocol;

“Despite the long odds, physicians remain willing to treat rabies in select patients, and there are signs of sunny days ahead. We maintain an updated Milwaukee Protocol (MP) and registry at www.mcw.edu/rabies. For full



transparency and “open science”, we count all attempts, independent of quality, and update the protocol with new information even before academic publication. We are retrospectively aware of 15 attempts. Only three met assumptions of natural immunity, reversible medical complications, and use of recommended drugs, yet one reason for optimism is the markedly improved survival curve using MP anywhere in the world when compared to contemporary controls managed at centers in Europe and North America (Figure, showing MP in red, controls in blue). The figure is reminiscent of early treatments of childhood leukemia and congenital heart disease in previous decades. Further optimism follows introduction of MP version 2. Of the first 3 attempts, we have one case active at 36 days and another who died of malnutrition-related complications during early neurological recovery.

It is essential to develop animal models to advance rabies care, but funding is difficult and veterinary schools uninterested. Nevertheless, we have many preliminary observations on human rabies physiology:

(1) Dysautonomia in rabies is highly problematic, but can be managed with ketamine and deep sedation. (2) Generalized basilar artery spasm occurs early in rabies and correlates with onset of coma or seizures. (3) Later, arteriolar spasm may be severe and is associated with a loss of brain volume, EEG activity, and increase in CSF protein without loss of BBB permeability. (4) Both vascular complications are potentially managed by calcium-channel blockers or magnesium sulfate given prophylactically. (5) High levels of quinolinic acid are found in spinal fluid (CSF) early on, while levels of tetrahydrobiopterin (BH4) and BH4-dependent neurotransmitters (dopamine, serotonin, etc.) decline. (6) Replacement of BH4 increases dopamine and serotonin metabolism. (7) The natural immune response to rabies develops by day 12 of symptoms, but is delayed by use of ribavirin and barbiturates. Early use of these drugs is discouraged. (8) Cerebral edema may complicate the advent of rabies neutralizing antibodies in CSF. (9) Cerebral edema is very sensitive to serum sodium concentration. (10) Recovery of neurological function occurs piecemeal, without clear neuro-anatomical correlates: recovery of corneal reflexes precedes vestibular or auditory recovery; recovery of motor reflexes precedes voluntary motion; legs precede arms.

Rabies care is prolonged, and requires meticulous care and unwavering responsibility by one lead physician. The disease trajectory is similar to that of traumatic brain injury, acute demyelinating polyneuropathy (Guillain Barre Landry or Miller Fisher syndromes), or tetanus. Units capable of handling these diseases are equipped for rabies care. Plans for rehabilitation must be addressed preemptively.”

The Importance of Rabies Education

Rabies remains a neglected and enigmatic disease, for which there is no proven/effective treatment once symptoms develop. However, it is preventable, and modern cell culture vaccines are both safe and effective. Nevertheless, there continue to be approximately 55,000 deaths annually, about half in children less than 15 years old, in developing countries where such resources are too expensive or unavailable. Consequently, much current effort focuses on education about vaccinating pets and livestock, avoiding stray/sick/wild animals, and thorough cleansing of wounds with soap and water immediately after a potential bite exposure.

World Rabies Day (WRD) efforts have provided great impetus to the notion of ‘Make Rabies History’, and the resulting 2008 educational grants to China, Vietnam, Kenya, Peru and Guatemala have added substance to these efforts. In addition the 2007 WRD vaccination of 600,000 animals was a great initial step toward prevention.

In the USA, which is not endemic for canine rabies, most concern rests with wild life, and more recently feral felines. There continues to be an epizootic of rabies in raccoons and skunks along the Atlantic coast, and there is concern that this might spread westward. In 2007, there were only two human rabies cases reported in North America, in Alberta and Minnesota (both from bat bites with no follow-up until rabies developed). The only known unvaccinated rabies survivor lives in Wisconsin, and the reason for her recovery remains enigmatic. She is in college in her home town, mentally normal, but has some problems with coordination and minor speech problems. This has helped strengthen local interest in rabies prevention.

The need for continuing education of both health professionals and the public is apparent, based on programs conducted for several public and health professional groups, both during 2007 and 2008. (see Mad Dogs and Englishmen and World Rabies Day articles referenced in the Education Bank Section of the WRD web site: www.worldrabiesday.org). All too often, I hear the phrase, ‘Gee, I didn’t know that’ when discussing rabies prevention, especially when talking about rabies in bats and kittens. This phrase is echoed throughout our planet, and needs to be changed to ‘Mom, I learned about protecting our family against rabies at school today. We need to have our pets vaccinated, and avoid stray, wild or sick animals!’ This message of prevention and hope must resound to all people everywhere and remain the foundation of our efforts until vaccines become available and affordable everywhere they are needed. And remember ‘There are no passengers on spaceship earth. We are all crew!’

Contributed by Robert E. Dedmon, MD MPH FACP FACOEM, of the Medical College of Wisconsin, Milwaukee, USA and a member of the Alliance’s WRD team who has lead many rabies educational outreach programs in the USA.

The Reality of Rabies in Pakistan

It happened in June this year: 45 year old Hameed was returning home from work at dusk. He had just got off the bus and turned into a dusty lane towards his house when he felt a gnaw in the calf of his right leg. As he turned round to look, he was face to face with a menacing dog that leapt at him. Hameed punched the dog which fell, got up and with bared teeth, dug its claws into his victim's face. Hameed bled copiously from a cut lip, dabbed it with the end of his shirt and headed home. The dog disappeared into a side lane. At home his wife applied powdered red chillies into the leg and lip wounds and took him to a city hospital an hour away where the face and leg were washed. He was given an injection of rabies vaccine, tetanus and a prescription for an antibiotic. Next morning he had a swollen lip which improved over the next few days. He promptly forgot to get the remaining injections and continued with his daily work.

Six weeks to the day the man ran a fever, headache and began sweating. His throat hurt on swallowing. A local doctor recorded his blood pressure as "extremely high", and sent him to a hospital. He was given pills to swallow, at which point he said he could not. He avoided the sight of water. His old aunt, watching him, cackled "you know, in my days we were told that a person who was bitten by a mad dog avoided drinking water." And that is when Hameed realized the gravity of her ominous words.

That afternoon I got called to the Emergency Room at Indus Hospital to see this man with "suspected rabies". He had unmistakable hydrophobia and aerophobia and he was sweating profusely from every pore in his body into his soaked clothes. He told me himself in between throat spasms of his misadventure with the vicious dog. The bite wounds were no longer visible. Hameed was doomed to die, as indeed he did 4 hours later in an isolation room in our hospital.

Had his bite wounds been washed with soap and water immediately to remove the dog saliva, had he received rabies immune globulin (RIG) into the bite wounds and the vaccine series of 5 injections into the arm, Hameed would have been alive, taking care of his wife and five children.

Witnessing yet another horrific rabies death has only reaffirmed my determination that the message for rabies prevention will reach far and wide on World Rabies Day.

Contributed by Dr. Naseem Salahuddin, President of Rabies in Asia (Pakistan Chapter).

The RIA Pakistan Chapter Foundation and Infectious Disease Society of Pakistan are enthusiastically preparing for World Rabies Day 2008 at the Indus Hospital, Karachi, with hundreds of students and parents invited. Informative videos, posters and flyers will be shown, and kites, T shirts, caps, balloons, and buttons given away. The children will present educational songs and skits related to animal care. Fifty senior school students and a tv personality have volunteered to help, and companies have donated 1,000 packets of nutritious breakfast biscuits and milk cartons. Radio, television and newspapers will report.



Opened in 2004, this clinic functions out of the Civil Hospital Karachi where 30-40 new dog bite victims report every day.

Human Rabies Vaccine Production in Asia – part 1 of 2

In this first of two parts, Dr Noel Miranda (of [xxxx](#), Philippines) reviews recent changes in rabies vaccine production in Asia. In our next issue, he will address issues of quality, cost and potential improvements. [It is based on work commissioned for a consultation meeting of the WHO Biologicals Expert Committee.](#)

Human vaccine production capacities of Asian countries have improved greatly. Rabies vaccine supplies come from a mix of private and public manufacturers in several Asian countries and are mainly for domestic use but some manufacturers have the potential to export vaccines. Both private and public vaccine manufacturers in Asia are exerting extra efforts to meet stricter government registration requirements as countries adhere to international and regional GMP (Good Manufacturing Practice) standards and vie for WHO pre-qualification. The National Regulatory Authority (NRA) in most countries generally enforces their local GMP standards- which tend to be more strict and demanding to the producers. The procedure for approval of newly introduced vaccines is very much in place, involving the conduct of complete pre-clinical and clinical testing and establishing lot consistency prior to approval for marketing. Most countries have functional NRAs/ National Control Laboratories (NCLs), which provide overall control on vaccine production process and final product quality. Exceptionally, a few countries still lack the capacities to perform rigid laboratory testing.

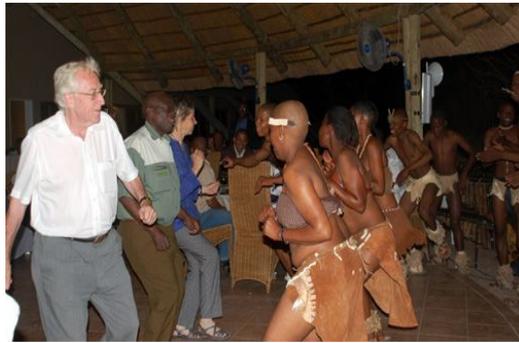
Demand and Supply: Human rabies vaccine manufacturers are growing in number most markedly in China and India with more than 15 manufacturers serving a combined population of more than 2 billion with an estimated demand for rabies vaccines of about 30 million doses or about 6 million full-course treatments [per year?](#) The vaccine production levels typically range from 100,000 doses to 10 million doses per year (for cell-based production facilities), with some producers in China and India upgrading their capacities to produce more than 10 million doses per year.

Vaccine types: China and India discontinued the production of nerve-tissue origin (NTO) vaccines in 2001, and Vietnam stopped producing the suckling-mouse brain vaccine, which has been in use over 30 years, in 2005. It now imports cell-line based vaccines in naked vials, and they have also modernized their main vaccine manufacturing plant (GMP compliant) located in Hanoi. Myanmar is still producing the sheep-brain (Semple) vaccine from more than 40 years ago, but they too have shown the strong desire to shift to cell-line-based vaccines. All these manufacturers follow the WHO standard requirements, as well as refer to USP requirements. There are essentially 5 types of modern vaccines, according to substrate, that are produced mainly in China and India, namely the Primary Hamster Kidney (PHK) cell, Vero cell, Human diploid cell (MRC-5), Embryonated duck egg and Chick-embryo cell. Of these, the Vero cell is the only continuous (animal) cell line. All these vaccine types undergo concentration and purification processes either by zonal centrifugation or tangential filtration and gel chromatography. The virus strains being used include the PV (Pasteur Institute Paris or CDC) and PM (Wistar Institute), and in China they also use their locally-derived strains. Vaccine preparations are either liquid or freeze-dried single-dose (0.5 or 1.0 ml) in glass vials, and are administered according to the Essen regimen.

The 9th SEARG Meeting in Gaborone, Botswana

The Botswana College of Agriculture hosted the 9th meeting of the Southern and Eastern African Rabies Group (SEARG) in Gaborone, 25-28th August 2008. This very successful event was the result of a joint effort by the Botswana Ministry of Agriculture, and the dynamic research team from the University of Pretoria headed by Professor Louis Nel and Dr Wanda Markotter, with funding from Sanofi Pasteur, Intervet and Merial. The meeting began with a welcome reception, a banquet and an impressive performance by a Gaborone music group. Nearly 100 delegates attended, presenting reports and sharing their experiences with rabies from over 20 countries around the world.

The scope of the meeting was wide, with topics including the development of new diagnostics, treatment of human exposures, molecular epidemiology, vaccine and birth control technologies, mathematical models, national and regional control initiatives and country reports. The entertainment schedule was similarly packed, with a cultural tour, traditional music and dance (and impressive audience participation!), and visits to a local game reserve and the No. 1 Ladies' Opera House – a venture supported by Alexander McCall Smith, the patron of the Alliance for Rabies Control!



Dancing and festivities during the meeting

Many countries described similar challenges including limited resources, poor infrastructure, lack of trained personnel and inadequate facilities for surveillance and diagnosis. The prevalence of these ingrained problems suggests that there is much work to be done to improve the rabies situation in the region. Nevertheless, the conclusions from the meeting were optimistic and a number of potentially exciting prospects were reported. For instance, Kevin Le Roux described the ups and downs of rabies control in KwaZulu-Natal over the last 2 decades, and how those experiences have been galvanised into a strengthened plan for future efforts. Professor Debbie Briggs gave an account of recent interest expressed by the Global Alliance

Vaccine Initiative in supporting the distribution and accessibility of human rabies vaccines – a massive opportunity for many SEARG countries. The attendance of Anastasia Pantelias, representing the Bill and Melinda Gates Foundation, was also a clear indication of developing interest in rabies control among international agencies.

A notable feature from the meeting was the growing recognition of rabies as a truly international problem – several presenters showed genetic and epidemiological evidence of rabies circulating between countries illustrating how the disease pays no attention to political boundaries. Hopefully this recognition will translate into coordinated control; already FAO is developing initiatives for collaborative cross-border control programmes within the Southern African Development Countries region. Dr Hevré Bourhy provided an update on the recently established Africa Rabies Expert Bureau: www.afroreb.info, a similar initiative to SEARG bringing together countries from Francophone Africa. Interestingly, AfroREB was more heavily represented by the medical sector, whereas typically more veterinarians attend SEARG meetings suggesting that both groups can potentially learn from one another to develop a truly integrated approach for rabies control on the continent.

Clearly there is much to do, but the impressive showing at this meeting suggests that important steps are being taken and that we should anticipate good progress at the next SEARG meeting planned for 2010 in Mozambique.

Contributed by Dr Katie Hampson, a [Henry Wellcome xxxxx](#) at University of Sheffield, UK. A full account of the meeting will soon be available on the SEARG website (www.searg.info).

?vaccine shortage bit?

Upcoming Meetings

The 19th annual **RITA meeting** will be held from September 28 – October 3, 2008 at the Centers for Disease Control and Prevention in Atlanta, Georgia, USA. Further details are available at www.rabiesintheamericas.org

AUCTION STUFF

Pakistan meeting?

The editor of the ARC newsletter is Louise Taylor who can be contacted at louise.taylor@rabiescontrol.net. If you have any news items or information of interest to those wanting to reduce the burden of suffering of rabies, then please contact Louise. For further information about rabies and The Alliance for Rabies Control see www.rabiescontrol.net.