

# **Report of the Second Meeting of the Middle East and Eastern Europe Rabies Expert Bureau (MEEREB) Paris, France, June 5-8, 2012**

## **Rabies experts call for a regional initiative for rabies elimination in Eastern Europe and Middle East**

### **1. Introduction**

Human rabies transmitted by dogs can be and should be eliminated from the region. This is the resolution taken by a group of rabies experts from the Middle East and Eastern European countries. They met in Paris (5-8 June 2012) with colleagues from the Institut Pasteur and from the Global Alliance for Rabies Control (GARC).

These experts are members of the Middle East and Eastern European Rabies Expert Bureau (MEEREB), an informal network of 'rabies champions' that was established in 2010, during a conference in Istanbul (June 2010). Two 'new' countries joined MEEREB: Romania and Kazakhstan. During their 3 day meeting in Paris, they discussed the rabies situation in their respective countries, its evolution, the problems encountered and the solutions.

### **2. The Global Alliance for Rabies Control (GARC): projects and achievements**

As Deborah Briggs (Executive Director, Global Alliance for Rabies Control) reminded the participants, rabies prevention requires intersectoral support. "Intersectoral" means more than human and animal vaccination. Building a successful rabies prevention and control strategy requires uniting global human/animal/education health communities. Education, advocacy and communication are powerful tools for rabies prevention programs.

Founded in 2006, the Global Alliance (GARC) initiated a global rabies network for rabies prevention, bringing together public health professionals, creating partnerships with several organizations and governments throughout the world, developing new communications tools, and establishing community actions. Since 2006, the Alliance has helped educate millions of people about rabies, is coordinating educational projects in 6 countries and has created 2 successful programs: World Rabies Day and the Partners for Rabies Prevention Group.

The World Rabies Day (WRD) which takes place annually on September 28th, was launched in 2007 and was the first global initiative to increase rabies awareness. It began as a single day of action and has evolved into a year-round initiative to mobilize governments to support rabies prevention programs. It is now included on the United Nations website of annual health days, and is supported by international health agencies, rabies experts, NGOs, private and public organizations, and local champions working to improve rabies prevention in their own communities. The global participation continues to grow each year and to date at least 135 countries have supported WRD by hosting one

or multiple events. More than 150 schools of public health, veterinary and medical colleges have hosted one or more 'rabies-awareness' events, and over 500 000 visitors have logged onto the website to download free educational material and modules. Since September 2007, > 8 million animals have been vaccinated and 200 million people have been educated. New animal vaccination programs are being launched in rabies endemic countries, educational programs are being promoted and global community networks are being established.

In 2008, the "*Partners for Rabies Control*" (PRP) was established to serve as a platform for private and public institutions to come together to discuss problems, find solutions and share resources. It includes all prominent international health organizations (GARC, CDC, FAO, OIE, WHO, PAHO, Animal welfare, Universities, Funders etc.) and the Global Alliance acts as the secretariat of the group. PRP has been very productive: the Blueprint for canine rabies elimination and human rabies prevention has been produced, and a second part of the Blueprint on rabies elimination in wildlife is under completion. In addition, a re-evaluation of the rabies global burden is expected to be published before the end of the year.

*The Blueprint* has been translated into several languages and can be downloaded from the Internet. It includes all of the practical advice and resources necessary for rabies control workers to implement effective control strategies in their areas (<http://www.rabiesblueprint.com>).

**Re-evaluation of the rabies global burden:** The false perception that rabies impacts on society are low is due to case under-reporting and limited awareness of the disease burden. The last estimate of the burden of rabies was published in 2005, in the WHO Bulletin. This study, published by Knobel *et al.*, considered only dog transmitted rabies in African and Asian countries. Now the PRP is focusing on conducting a more inclusive analysis of the true cost of rabies globally.

Preliminary results suggest that the current burden of rabies is around 70 000 human deaths per year, with an annual worldwide economic impact of about \$4 billion (human prophylaxis: \$500 million; dog vaccination: \$160 million; livestock losses: \$800 million). Further critical validation of these data is ongoing.

GARC is involved in several pilot projects for rabies prevention:

**Adopt a village:** The Alliance is a partner in the "Adopt a Village" program in India, aimed at reducing the incidence of human and animal rabies through improved educational awareness and mass vaccination of dogs. Pre-exposure vaccination of school children and other risk groups using intradermal vaccination is also in progress.

**The Bohol Project:** The Alliance, together with several partners including the Government of Bohol; a private Swiss Foundation, and the University of Texas, Health Science Center at Houston, is helping to support a canine rabies elimination project on the island of Bohol in the Philippines. The project brings together educators, physicians, veterinarians, government officials, community leaders and the general public, and thousands of village-based volunteers and teachers. Access to post-exposure prophylaxis (PEP) has been increased through the establishment of new PEP clinics and expanded training of health care workers. Children are taught about rabies in school and then share this knowledge with their families. Seventy per cent (70%) of dogs have been vaccinated and registered. Finally, 4 379 people throughout the island have received training to monitor human exposures and suspect cases, and their presence encourages the responsibility of dog owners.

No rabies deaths have been reported on Bohol since October 2008, whereas, in the 2 years prior to the implementation of this program, there were 10 human cases of rabies per year.

The Bohol program has been built to be self-sustainable so that when the funding from the Global Alliance and other NGOs is no longer provided, the program will continue.

The rabies project has been expanded in the Philippines to El Norte and Sorsogon; it is being replicated in Nias, Indonesia, and adapted to projects in Chad (Africa). The educational component has been adapted to Tanzania (Africa).

**The CARE Project:** This project concerns a prospective observational assessment of the impact of implementing a rabies prevention educational program in elementary school children of El Nido Island in The Philippines, a very rural area with a high incidence of rabies exposure. The project is conducted in collaboration with The Philippines Ministry of Health, El Nido Municipality, and Sanofi Pasteur. In addition to education in rabies, children have received pre-exposure prophylaxis.

**Rabies educator concept:** GARC has developed a program to train lay-persons in basic rabies prevention education with the dual purpose of ensuring the delivery of standard, accurate and evidence-based information on rabies prevention, and increasing the international capacity for rabies education efforts in a sustainable and community-led manner.

Much has been done during the last few years. However, there is still much to do. There is a need for new tools, among which a combined vaccination for dog population control and protection against rabies; improved global and national surveillance; shorter pre-exposure regimens for remote populations at risk; impact models that assess strategic interventions; and evaluation of novel strategies and methods to ensure sustainability to prevent reintroduction.

“... if *One Health*\* is not able to work with rabies, it is not going to be able to work for any disease”.  
Dr Bernard Vallat, Director General OIE at the *Conference for elimination of rabies at the source* - Seoul S Korea Sept 9, 2011

### **3. Persistence of antibodies after rabies vaccination (Noël Tordo)**

Rabies outbreaks caused by vampire bats are a regular threat in the Amazonian region. In May-June 2005, 15 human deaths, mostly children, were reported in a rural community in Augusto Correa (Pará, Brazil). Of the 55 000 people dispersed over a large territory along the Amazon estuary, 3 500 subjects aged from 2 to 60 years received purified Vero cell rabies vaccine (PVRV) for post- or pre-exposure prophylaxis. The persistence of anti-rabies antibodies in vaccinees from this community at repeated risk of vampire bat bites was monitored for 3 years following vaccination (years 2 to 4).

---

\*The One Health concept is a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment. The synergism achieved will advance health care for the 21st century and beyond by accelerating biomedical research discoveries, enhancing public health efficacy, expeditiously expanding the scientific knowledge base, and improving medical education and clinical care. When properly implemented, it will help protect and save untold millions of lives in our present and future generations. Ref: The One Health Initiative: <http://www.onehealthinitiative.com/about.php>

Anti-RABV neutralizing antibodies (VNABs) levels were evaluated by RFFIT, FAVN, and Platelia ELISA using the PV and CVS reference strains as well as a vampire bat strain. All subjects with VNAB levels <0.5 IU(EU)/mL were boosted. From a total of 507 subjects included in 2007, 450 (89%) were still available 2 years later for follow-up, despite relatively high isolation, dispersion, and the nomadic way of life of this community. During the surveillance period, 24 subjects (5%) were re-exposed through bites of dogs (17), bats (2), monkeys (2) or cats (3). The results of the study demonstrated persistence of VNABs in the vast majority of vaccinees. The proportion of patients with WHO minimum “seroprotective” levels of VNABs ( $\geq 0.5$  IU/mL) remained remarkably stable in 2007 (87.7%) and 2008 (87.6%). RFFIT (or FAVN) and ELISA methods were 88% concordant with good statistical significance. However, the GMT value in the global population measured by ELISA (not by RFFIT) increased between 2007 (1.02 EU/mL) and 2008 (1.27 EU/mL), an observation which has been under scrutiny in 2009. Globally, females showed slightly higher GMTs than males. In both sexes, 41–60 years old subjects showed significantly lower GMT (0.5 IU/mL) and seroprotection rate (60%) compared to other age groups. A hundred serum samples were selected randomly each year to evaluate the concordance of RFFIT results using the PV strain versus local vampire bat strain. In addition, this study demonstrated no interference between anti-malaria treatment and PVRV immunogenicity.

#### **4. Rabies situation in MEEREB countries**

Some of the MEEREB countries such as Croatia and Serbia have not recorded human deaths from rabies for more than 30 years. However, persistence of rabies in wildlife (foxes) requires constant surveillance and maintenance of a high level of vigilance and public health interventions in order to prevent human rabies cases. Oral vaccination campaigns for foxes that are being conducted in Croatia and Serbia as well as in Romania with the support of the European Union could, in the near future, lead to fox rabies elimination in these countries. However reintroduction is always possible from neighbouring countries where rabies is endemic.

In the other MEEREB countries represented at the meeting, rabies is present not only in wildlife but also in dogs, which increases the risk of transmission to humans. In fact, human cases still do occur in these countries (see Table).

Human rabies, number of animal bites (admission for PEP) and PEP administered are notifiable in all countries present at the MEEREB meeting. In Romania, however, although all Rabies Centers report to regional public health authorities on a monthly basis, national statistics are not publicly available. In all other MEEREB member countries, national figures permit to closely follow-up the evolution of local situation. In countries where the incidence of human rabies did not exceed 0.15 per million inhabitants during the last 3 years, the incidence of reported bites and PEP remained stable. In the two countries where the incidence of human rabies is the highest, Kazakhstan and Georgia (0.37-0.87 and 0.67-1.37 per 1 million inhabitants, respectively), the mean PEP incidence increase rate was of over 15%. In 2011, 0.4% of Kazakh population received PEP. In Georgia, PEP incidence reached 0.9% - the highest known PEP incidence in the world, and 2-50 times higher than in other MEEREB countries.

All these countries use cell culture vaccines through intramuscular administration, according to the 5-dose (Essen) or 6-dose regimen, or the 4-dose Zagreb regimen. Rabies Immune Globulins of equine origin (ERIG) are locally produced in Croatia, Serbia and Ukraine.

**Table 1. Rabies epidemiology and management in the 7 countries represented at MEEREB**

		<b>Croatia</b>	<b>Georgia</b>	<b>Iran</b>	<b>Kazakhstan</b>	<b>Romania</b>	<b>Serbia</b>	<b>Turkey</b>	<b>Ukraine</b>
Reservoir and vector (vector only)		Red fox (Dog, cat)	Dog, cat, (jackal, wolf)	Dog, wolf, fox, jackal	Dog, cat	Dog, fox	Red fox (Dog, cat)	Dog, fox, jackal, (cat)	Cat, dog, fox
Human population	2011	4 290 000	4 470 000	74 700 000	16 400 000	21 900 000	7 500 000	74 700 000	45 700 000
Number of human rabies cases	2011	0	3	6	8	0	0	0	6
		0	0.67	0.08	0.49	0	0	0	0.13
	2010	0	5	4	6	2	0	1	3
incidence per million		0	1.12	0.05	0.37	0.09	0	0.01	0.07
	2009	0	6	2	14	1	0	2	6
		0	1.37	0.03	0.87	0.05	0	0.03	0.13
Approx. incidence of reported bites (per million)	2011	1 245	11 260	1 700	4 130	n/a	1 750	2 100	2 050
	2010	1 200	8 300	1 600	3 700	n/a	1 450	2 000	2 000
Number of reported PEP	2011	1 442	41 605	128 829	67 384	n/a	1 350	142 333	19 660
	2010	1 453	30 381	120 525	58 727	n/a	1 673	138 022	19 366
	2009	1 750	28 055	130 531	57 061	n/a	1 609	178 250	21 000
Incidence of PEP (per million)	2011	340	9 300	1 700	4 110	n/a	180	1 900	430
	2010	340	6 800	1 600	3 600	n/a	220	1 850	420
	2009	390	6 100	1 700	3 500	n/a	220	2 290	460
Average % of reported bite victims receiving PEP		28%	82%	99,8%	98,3%	n/a	15%	90%	21%
Number of centers providing PEP		21	74	300	250	41	27	State hospitals	29

#### **4.1. Romania**

In European Union countries, Romania has the highest number of wild animals infected with rabies, mainly foxes and wolves. In last three years, the overall number of rabid animals has started to decrease following some regional campaigns of oral vaccination in wildlife. Recently the European Union endorsed a 10-year program (2012-2022) for Surveillance, Control and Eradication of Rabies throughout Romania. One aspect of the program is the oral vaccination of the entire fox population which would be repeated twice a year. This vaccination campaign would, it is hoped, also benefit the wild dog populations in rural areas. Romania has a high number of stray dogs and cats. In Bucharest alone, the number of stray dogs is estimated at approximately 50 000. Even if in national reports stray dogs account for only 8-12% of laboratory confirmed animal rabies cases (40-50 rabid dogs are found yearly compared to 250-400 rabid foxes), they are far more dangerous due to their proximity to humans.

In the last decade, one case of human rabies was reported, on average, every year in Romania. Although in 2011, no cases of human rabies were reported, there was already one case in February 2012: a 5-year old girl was bitten by a stray dog. The investigation is on-going to define why she had not received PEP, for in Romania the law requires all doctors to direct an exposed person to the Rabies Center for PEP. In each of the 41 counties there is a specialized rabies center found in a regional hospital, within the Infectious Diseases Department, where PEP is delivered free of charge through the Essen regimen, or more rarely, the Zagreb scheme, with ERIG if needed. In Bucharest alone, about 12 000 people receive PEP every year. National statistics on animal bites and number of administered PEP are not publicly available.

#### **4.2. Kazakhstan**

Different species of wild and domestic animals are rabies hosts in Kazakhstan. Identified natural foci of rabies have a tendency to expand into new areas, and currently rabies is enzootic in over 20% area of the country. Cattle and other domestic herbivores account for over 2/3 of the approximately 200 laboratory confirmed animal rabies cases, followed by dogs and cats, whereas wild rabid animals are rarely detected.

Over the last 5 years, 44 human rabies cases were registered, mainly in rural areas, the majority of which were due to dog bites. In 2010-2011, the incidence of human rabies, and PEP, in Kazakhstan, was the second highest (after Georgia) among MEEREB countries.

The majority of exposures occurred as a result of contact with dogs (88%) and cats (8%). Rabies PEP, using Russian hamster kidney vaccine and Russian ERIG, is available free of charge in 250 public rabies prevention centers spread throughout the country. In private health centers, WHO pre-qualified vaccines and HRIG are also available. Monitoring of volumes and effectiveness of prophylaxis and control measures are carried out at the regional and national levels.

### **4.3. Georgia**

Georgia remains at the top of the list with the highest reported incidence of human rabies among MEEREB members. In this country with a population of only 4.5 million people, rabies killed on average 10 people per year between 1996 and 2010. However, since then, the number of human rabies reported annually has been steadily declining reaching 3 human deaths in 2011, a level not seen for 20 years, but still the highest in the MEEREB zone. Almost all human rabies cases are caused by stray dogs or unvaccinated pets. Publicizing human rabies deaths in the media and in numerous communication campaigns has, over the past ten years, contributed to a five-fold increase in the number of admissions to health care centers following suspected exposure to potentially rabid animal. As a consequence, the incidence of PEP in Georgia is approaching 1%, which is much higher than in any other country with known data, and can open discussion for the introduction of universal rabies Pre-exposure vaccination (PrEP) in childhood immunizations.

### **4.4. Ukraine**

While all other MEEREB countries report yearly between 50 (Serbia) to 470 (Romania) animal rabies cases, in Ukraine alone 1 430 animals were confirmed rabid in 2011, and 1 854 animals in 2010. This reflects a slight improvement of the situation, as between 2005 and 2010 an average of 2 000 animals (with a peak at 2 932 cases in 2007), mainly foxes (39.5%), cats (24.1%) and dogs (19%) but also cattle and other domestic herbivores (10.7%) were tested positive. A recent molecular genetics study of street rabies virus isolates, undertaken at the Institute of Veterinary Medicine of the National Academy of Agricultural Sciences, divided street rabies virus isolates into two genetic clusters. Animal challenge showed that the effective dose of rabies vaccines varied up to 30% according to the cluster.

With three to six annual human cases, caused by mainly by dogs and cats (rarely foxes) - the incidence of human rabies remains high, in the range of 0.07-0.13 per million people. The major problem here is lack of awareness, especially in rural areas.

Although close to 20 000 people seek medical attention after a suspected bite, only one in five actually qualifies for the rabies PEP; this is due to a risk assessment system, similar to the one existing in countries such as Croatia and Serbia, where rabies is well controlled in domestic animals.

### **4.5. Iran**

In 2011, 297 animals were confirmed rabid in Iran. Although rabies was most frequently found in cattle, dogs and foxes remain the main vectors in transmitting the disease to humans. Rabies continues to kill 2-6 persons every year, but these deaths are not sufficiently publicized to constitute a warning for subsequently exposed persons. Many people, especially in rural areas, do not have sufficient knowledge about rabies prophylaxis and do not seek medical attention after an exposure to a suspected animal. A new project evaluating public awareness concerning animal bites is being implemented in seven Northern provinces of Iran. In addition, the project provides dog vaccination in the rural areas (about 400 000 dogs vaccinated yearly), allows for the evaluation of the population of owned dogs, and proposes measures for stray dog population management.

#### **4.6. Turkey**

In 2008-2010, due to the emergence of fox rabies in the Aegean region and the observed sustained spill over from dogs to wildlife, Turkey benefited from the EU-funded oral vaccination strategy project targeting eliminating fox-mediated rabies cases in ORV areas within 3 years. In effect, in 2009-2010, there was a significant decrease in the number of animal rabies; however, since the end of the project, fox rabies re-emerged in previous ORV areas with the result that the 2011 figures were similar to those from 2007 to 2008. In addition, the vaccinated area was too small; as a consequence, rabies has spread further inland.

Turkey has a similar population, incidence of PEP and number of reported animal cases as does Iran, but a lower number of human rabies deaths. A national program for the control and eradication of human and animal rabies has been adopted since 1987, and the directive for Rabies Prevention and Control was updated in 2005. Since 2006, an average of one human rabies case is notified every year; however, no cases were notified in 2011. Recently, two studies evaluated knowledge and practices in management of rabies exposures among physicians in Turkey. The results suggest that regular education of physicians regarding important and relevant data in prevention and control of rabies combined with large scale communication for the general population may contribute to the elimination of human rabies.

#### **4.7. Croatia**

There is no urban rabies in Croatia, but it continuously persists in wildlife. The total number of rabid foxes is decreasing due to an oral vaccination campaign started in 2010 (14 years after the end of the previous national ORV program) and planned to run at least 5 consecutive years. In 2010, 3 691 foxes were examined for rabies and 589 (16.0%) were found positive; in 2011, among 3 561 foxes examined, 325 were found positive (9.1%). According to a national rabies control program supported by the ministry of Agriculture, Fisheries and Rural Development, all dogs older than 3 months are subject to a yearly mandatory rabies vaccination.

A national rabies control program, supported by the Ministry of Agriculture, Fisheries and Rural Development, includes several strategies:

- A systematic monitoring and surveillance program covering the whole territory of Croatia;
- Mandatory registration of dogs (through a "Lyssacan-electronic" software);
- Mandatory, yearly rabies vaccination of dogs;
- Recommendation of rabies vaccination of cats and ferrets;
- If required by the epidemiological situation - the Minister of Agriculture, Fisheries and Rural Development may also mandate vaccination of other species of animals against rabies.

Each year about 5 000 animal bite victims seek medical attention; among them approximately 1 400 receive PEP. PEP is administered at 21 county public health centers which are located throughout the Republic of Croatia; but when all the cities and towns which are dependent on these county public health centers, are included, this number grows to over 80. Severely bitten patients are taken care of in county hospitals, clinics and hospital centers. The last case of human rabies acquired in Croatia was recorded in 1964. Since then, there were 2 imported cases of human rabies in 1989 and in 1995.

#### 4.8. Serbia

In Serbia, foxes are the main reservoir of rabies, with an occasional spill-over on dogs and cats. In 2009, 181 cases of animal rabies were reported (136 in foxes, 15 in dogs, 23 in cats and 7 in other animals). With the support of the European Union, the oral vaccination (ORV) of foxes was launched in 2010, resulting in a progressive reduction of animal cases in 2010 and 2011 (104 and 46 cases, respectively). Along with the ORV a widespread campaign of rabies awareness among health professionals, veterinarians, and the general public took place.

Serbia is the best example of efficacious collaboration between human and animal health sector. As each animal case is detected, an alert is immediately disseminated to human rabies prevention centers. About 1 400 bite victims (mainly from dogs and cats) receive PEP each year, free of charge, in one of the 27 animal bite centers (Epidemiology Departments of Institutes of Public Health and Infectiology Departments of regional hospitals) scattered throughout the country. Since 1980, there has been no human rabies in Serbia.

### 5. Requirements to conduct a rabies elimination program

MEEREB participants discussed requirements to conduct a successful rabies elimination program (see box).

Although in all MEEREB countries a legal framework for rabies control exists, most often rabies elimination is not considered as a public health priority.

In several countries pet dog vaccination is mandatory, but in practice no sanction is applied for owners who do not vaccinate their dogs.

Uncontrolled stray dog population continues to pose a problem especially in Iran, Turkey and Romania. While Iran is organizing large scale dog elimination campaigns, in Romania killing of stray animals is prohibited. Humane dog population management, including dog sterilization, requires expertise, organization and funding.

Implementation of oral vaccination campaigns for foxes depends on the funding from the European

Commission. ORV programs are being carried out in Croatia, Serbia and more recently in Romania.

#### Minimum requirements to conduct a rabies elimination program

##### Political

- Understand what is required to eliminate rabies in the specific area
- Government support for the short & long term
- A regulatory and legal framework
- Local champions
- Community engagement
- Support of humane dog population management
- Reasonable focus and support for animal welfare

##### Operational activities

- Ability for animal and human public health officials to work together
- Capacity to increase access to PEP
- Ability to vaccinate the equivalent of 70% of dogs
- Capacity to increase mass communication, education and awareness
- Capacity for emergency response (outbreaks)

##### Science

- Data management system including an evaluation of the project
- Dog population/ecology studies
- Adequate access to diagnostic facilities
- Adequate monitoring & surveillance including molecular epidemiology

Turkey also recently benefited from a European-funded ORV program; however, only a limited area was concerned and rabies re-emerged once the program had terminated.

In Middle Eastern and East-European countries, bite victims have good access to PEP, delivered free of charge in public rabies prevention centers. The population, especially in the urban areas, is more or less aware about the risk of rabies. Nevertheless, improved mass communication and publicizing of rabies deaths could contribute to a better reporting of animal bites. Children are at high risk of rabies but, with the exception of Kazakhstan, schools do not play a role in rabies education. Implementation of rabies awareness courses in school curriculums, as has been recently done in several areas in Asia, will contribute to better rabies control.

MEEREB members are local champions in the fight against rabies. They actively contribute to rabies prevention in their respective countries; organize press conferences, educational workshops for health professionals and for journalists, and participate in World Rabies Day manifestations and in GARC surveys.

National rabies figures from Croatia, Romania, Serbia, Turkey and Ukraine are reported in the Rabies Bulletin Europe. Whereas the number of laboratory proven rabid animals published in Rabies Bulletin is consistent with official national figures provided by MEEREB members, it was found that human rabies cases are often underreported. This underlines the importance of better communication between human and animal sector in rabies prevention.

Georgia, Iran and Kazakhstan belong to the Middle East zone and are not listed in Rabies Bulletin Europe. However, all these countries have a well-developed human and animal rabies notification system. As rabies does not stop at the borders, it would be useful to extend this Rabies Bulletin to other countries willing to participate.

In conclusion, although some rabies control measures are already in place, there is still a significant disparity among the MEEREB countries as to each country's response to its rabies situation. Furthermore, some of the conditions for successful rabies elimination programs (as presented by Deborah Briggs) are not met. MEEREB members agreed that reinforced intersectoral collaboration and "One Health approach" are the keys for successful rabies control.

## **6. Rabies prophylaxis in international travelers**

As long as canine rabies still exists in many parts of the world, travelers to regions where rabies is enzootic are exposed to the risk. Most of the time, they are not informed of the danger, and they often do not seek pre-travel advice.

According to Gautret *et al.* [Vaccine 2012], 22 cases of rabies were reported in tourists, expatriates and migrant travelers over the last decade, including three cases following short-term travel of no more than two weeks. Malerczyk *et al.* [2011] found a total of 42 human deaths from rabies reported in Europe, the United States, and Japan between 1990 and 2010; all of these victims were assumed to have contracted the rabies infection abroad. Of these imported human rabies cases, 36 (86%) were reported in clinical literature, 5 (12%) via personal communication, and 1 case (2%)

via ProMed. Among the 39 reports for whom the animal cause of rabies was known, 37 patients (95%) had had contact with a dog or puppy. One patient reported contact with a fox and one with a member of an unknown insectivorous bat species. The most common continent of rabies origin was Asia (n = 19), followed by Africa (n = 14); in contrast, only eight cases were contracted in the Americas, and of those, seven were from the United States [Malerczyk *et al.*, 2011]. More recently, the death from rabies of a woman in her 50s was reported by ProMed. She had been bitten by a puppy while on holiday in India 9 weeks before the onset of disease. It was not mentioned whether or not she looked for any treatment in India. Another ProMed report mentioned a rabies case in a 40-year old resident of Italy, bitten by an aggressive dog in India. Although he immediately underwent PEP consisting of four vaccine injections (on day 0, 3, 6 and 14), RIG was not administered and the patient died.

All travelers must be made aware of the necessity for medical treatment following contact with a potentially rabid animal, which could be life-saving.

Healthcare providers should be trained for advising travelers, and those who seek advice at travel clinics or at their general practitioner should be informed about the risk of contracting rabies and the very high mortality rate. Travelers who do not routinely seek medical advice could also be reached through travel agencies or the media.

Travelers who are victims of animal bites abroad have to face the problems such as language barriers or the need to modify pre-planned travel itinerary. When transferred to local rabies prevention centers, they often do not trust the local healthcare professionals and want to contact their general practitioner (GP) before receiving PEP. Yet difficulties in reaching them may delay the initiation of PEP. Furthermore, bite victims may receive inaccurate advice from GP in their home country, especially when this country is rabies-free. A study carried out in Sri Lanka and presented during the AREB meeting that took place in Thailand in December 2011 showed that less than 10% of tourists were able to communicate with their country general practitioner before initiating treatment – mainly because of the time difference between Sri Lanka and their home country. Less than 7% of GPs responded to e-mails. Some bite victims did not come back to the local prevention center; it is unknown whether their PEP was pursued appropriately elsewhere.

The World Health Organization (WHO) recommends pre-exposure prophylaxis, even if the duration of travel is short, for travelers planning a visit to a country or area at risk, especially if the area to be visited is far from major urban centers and appropriate care (including the availability of post-exposure rabies prophylaxis) cannot be assured [WHO 2012]. Pre-exposure prophylaxis recipients require a reduced course of vaccine, and no immunoglobulin, if exposed to rabies. Vaccination also reduces the risk of contracting rabies due to inappropriate management abroad. Evidence suggests that many travelers and health-care providers are not aware of these recommendations.

Doctors usually recommend pre-exposure vaccination only to long-term travelers expecting to spend extensive time outdoors or to expatriates. This approach may be questionable, as analysis of the cases clearly demonstrates that even travelers on short stays can die from rabies if prophylactic measures are omitted or are administered too late following exposure. Immediate access to appropriate medical

care should be highlighted, and pre-exposure vaccination should be recommended if there is likelihood that state-of-the-art post-exposure prophylaxis will not be available [Malerczyk *et al.*, 2011]. Detailed rabies distribution maps and information on the availability of rabies biologicals would be very helpful in order to identify those travelers who need pre-travel vaccination.

Travelers are also confronted with the issue of starting PEP (or PrEP) in one country, and having to complete it in another one, where available vaccines and vaccination regimens may be different. According to WHO, interchangeability of modern rabies vaccine is not recommended, neither is the change in vaccination route or regimen.

Real life cases illustrating these issues were presented and discussed: the case of a traveler starting PrEP shortly before travel and having to continue in another country, and the case of a patient from Romania who started PEP after he was bitten in his own country. He was to travel to Asia and did not want to cancel his trip, and needed to receive the last two shots to complete his vaccination schedule. What to do if the same vaccine as the one initially used is not available in another country? What can be used in replacement?

It was agreed that it would be helpful to establish a network of clinical experts in rabies and travel medicine, and to make available on the Internet a global database of rabies prevention centers, with their contact details (address, telephone number, opening hours, languages spoken), the type of vaccine available, the availability of immunoglobulin, and the vaccination protocol applied. Such a network would help travel health advisers to better assess the risk and decide whether or not a PrEP should be proposed to travelers; and to give the travelers reliable information about where to seek care in their destination country in the case of a potentially rabid animal-related injury.

This could be done through joining other initiatives or projects such as TravelRabNet to be developed by the European Travel Medicine Network (EuroTravNet), or through the website of the Global Alliance for Rabies Control. Information on the rabies prevention centers in some of the MEEREB countries has already been sent to EuroTravNet.

## **7. Conclusions**

Success stories in Latin America, Western Europe, in some Asian countries, as well as in Croatia and Serbia prove that elimination of human rabies is achievable in the MEEREB region. It requires political willingness and cooperation of all stakeholders, including Ministries of Health and of Agriculture; adequate management of animal bites through PEP using appropriate rabies immunobiologicals; pre-exposure prophylaxis for populations at high risk of rabies exposure; animal vaccination; and humane control of stray dog populations.

MEEREB members call for a regional initiative for rabies elimination in Eastern Europe and Middle East. They are confident that the elimination of human rabies of canine origin can be achieved in the region through intersectorial cooperation and a One Health approach, and that campaigns for rabies elimination will have significant benefit for public health, including strengthening the structure for control of other zoonoses.