OPINION

Fighting Rabies in Eastern Europe, the Middle East and Central Asia - Experts Call for a Regional Initiative for Rabies Elimination

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Impacts

- The article reports data on rabies epidemiology reported by MEEREB members. These data are available at the country level, but have not been published elsewhere.
- Rabies does not stop at national borders; public and animal health activities intended to achieve human rabies elimination need to be coordinated among neighbouring countries. Plans need to be made for including additional countries in this group.
- Meeting participants called for a regional initiative for rabies elimination to be achieved through inter-sectoral cooperation and a 'One Health' approach for expanding interdisciplinary collaborations and communications for humans, animals and the environment.

Keywords:

Rabies; zoonosis; rabies control; public health programmes

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Summary

MEEREB is an informal network of rabies experts from the Middle East, Eastern Europe and Central Asia, seeking to eliminate rabies from the region. They met for the second time to review the current rabies situation, both globally and in their respective countries, highlighting current rabies control problems and potential solutions. Success stories in Latin America, in 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 post-exposure prophylaxis; preexposure prophylaxis for populations at high risk of rabies exposure, animal vaccination and humane control of stray dog populations. MEEREB members called for a regional initiative for rabies elimination in Eastern Europe and the Middle East. They are confident that the elimination of human rabies of canine origin can be achieved in the region through adopting 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.

Introduction

The Middle East and Eastern European Rabies Expert Bureau (MEEREB), established in 2010, is a network of 'rabies champions' working to increase collaboration in rabies prevention and control at the local-, regional- and global levels. The report of the first MEEREB meeting was published by Aylan et al. (2011). This year, the MEEREB group was expanded with the participation of representatives from Kazakhstan and Romania. The content of this review is based on joint discussions at a meeting in June 2012 together with colleagues from the Institut Pasteur in Paris, France and from the Global Alliance for Rabies Control (GARC). Rabies is a major zoonosis with the heaviest burden in Asia and Africa (Knobel et al., 2005). Human rabies occurs rarely in most of the MEEREB countries thanks to post-exposure prophylaxis (PEP), but it remains a public health threat in the region because of the persistence of rabies in domestic- and wild animal reservoirs (Matouch, 2008; Seimenis, 2008). Progress in elimination of rabies has been complicated in some countries by lack of effective animal vaccination and control programmes and public health education as well as under-diagnosis, underreporting, and the economic burden of PEP (WHO-OIE, 2008). At this meeting, the participants updated the rabies situation and ongoing rabies control problems in their respective countries, highlighting potential solutions. The presentations focused on the burden of human urban and rural rabies, and discussed animal rabies in each country from a public health perspective.

Rabies in the MEEREB Countries

Croatia and Serbia have not recorded any deaths from human rabies in more than 30 years. The persistence of rabies in wildlife, primarily foxes, requires constant surveillance and public health interventions to prevent human rabies cases. Oral rabies vaccination (ORV) campaigns for foxes, the main reservoir in Croatia, Serbia and Romania, are now being conducted with the support of the European Union. It could lead to the elimination of fox rabies in those countries, but re-introduction from neighbouring countries where rabies is endemic is possible. In other ME-EREB countries, rabies is present not only in wildlife but also in dogs, which increases the risk of transmission to humans. In fact, human cases were reported in four of the MEEREB countries in 2011. The most recent available epidemiological data from each country was presented by meeting participants and is summarized in Table 1.

¹MEEREB founding countries are: Croatia, Egypt, Georgia, Iran, Serbia, Turkey and Ukraine. Egypt was not represented at the second MEEREB meeting.

Human rabies cases, the number of animal bites (i.e. admissions for PEP) and courses of PEP administered are notifiable in all MEEREB countries. The epidemiological updates on human rabies presented at this meeting derive from reports of suspected human rabies exposure. Data on animal rabies infection are limited to the number of rabies positive animals among rabies suspected animals tested at the national level. In any case, these numbers do not reflect the real rabies epidemiology in animals, but only indicate, for public health use, which species are the most frequently found rabid in the country and may be considered as potential source of human exposures. It is expected that more complete data on animal rabies in the MEEREB countries will be presented in future meetings. In Romania, however, although all rabies centres report to regional public health authorities on a monthly basis, national statistics are not publicly available. In the other MEEREB member countries, public reporting allows close monitoring of the 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 has remained stable. In the two countries with the highest annual incidence of human rabies, Kazakhstan and Georgia (0.37-0.87 and 0.67-1.37 per 1 million inhabitants, respectively), the mean increase in annual PEP incidence over the same period was greater than 15%. In 2011, 0.4% of the Kazakh population received PEP. These figures however contain the total number of PEP that was initiated at the beginning of treatment, and only a quarter of these were completed (Georgia). Three quarters of the number of PEP were stopped after the 10-day-observation period of the dogs and cats. Otherwise, it would be the highest known rate of PEP administration in the world, and 2 to 50 times higher than in other MEEREB countries. All these countries use cell culture vaccines administered by intramuscular injection following the 5-dose (Essen) or 6-dose regimen, or the 4-dose Zagreb regimen. Rabies Immune Globulin of equine origin (ERIG) is produced in Ukraine, and Rabies Immune Globulin of human origin (HRIG) in Croatia and Serbia.

Romania

Among the European Union countries, Romania has the highest number of wild animals infected with rabies, mainly foxes and wolves (Johnson et al., 2008; Herman et al., 2009). The number of rabid animals has decreased following regional oral vaccination campaigns conducted in the past 3 years. Recently the European Union endorsed a 10-year programme (2012–2022) for surveillance, control and eradication of rabies throughout Romania (EC, 2012). One aspect of the programme is the oral vaccination of the entire fox population, which would be repeated twice a

Table 1. Rabies epidemiology and management in eight MEEREB countries*

| - | 1 | | | | | | | |
|---------------------------------------|--------------------|---------------------------------|---------------------------|-------------------------|-------------|-----------------------|--------------------------------|---------------|
| | Croatia | Georgia | Iran | Kazakhstan | Romania | Serbia | Turkey | Ukraine |
| Reservoir and vector (Main vector) | Red fox (Dog, Cat) | Dog, Jackal, Wolf (Dog, Cat) | Dog, Wolf, Fox, Jackal | Wolf, Fox (Dog, Cat) | Dog, Fox | Red Fox (Dog, Cat) | Dog, Fox, Jackal (Dog, 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 |
| Human rabies cases (N) | | | | | | | | |
| Incidence (per million) | | | | | | | | |
| 2011 | 0 | κ | 9 | ∞ | 0 | 0 | 0 | 9 |
| | 0 | 0.67 | 0.08 | 0.49 | 0 | 0 | 0 | 0.13 |
| 2010 | 0 | 2 | 4 | 9 | 2 | 0 | 1 | M |
| | 0 | 1.12 | 0.05 | 0.37 | 0.09 | 0 | 0.01 | 0.07 |
| 2009 | 0 | 9 | 2 | 14 | _ | 0 | 2 | 9 |
| | 0 | 1.37 | 0.03 | 0.87 | 0.05 | 0 | 0.03 | 0.13 |
| Incidence of reported | | | | | | | | |
| bites (per million) | | | | | | | | |
| 2011 | 1245 | 11 260 | 1700 | 4130 | A A N | 1750 | 2100 | 2050 |
| 2010 | 1200 | 8300 | 1600 | 3700 | AN | 1450 | 2000 | 2000 |
| Number of reported PEP | | | | | | | | |
| 2011 | 1442 | 41 605 | 128 829 | 67 384 | AN | 1350 | 142 333 | 19 660 |
| 2010 | 1453 | 30 381 | 120 525 | 58 727 | AN | 1673 | 138 022 | 19 366 |
| 2009 | 1750 | 28 055 | 130 531 | 57 061 | AN | 1609 | 178 250 | 21 000 |
| Incidence of PEP | | | | | | | | |
| (per million) | | | | | | | | |
| 2011 | 340 | 9300 | 1700 | 4110 | ΑN | 180 | 1900 | 430 |
| 2010 | 340 | 0089 | 1600 | 3600 | Ϋ́ | 220 | 1850 | 420 |
| 2009 | 390 | 6100 | 1700 | 3500 | AN | 220 | 2290 | 460 |
| Bite victims receiving PEP (%)† | | | | | | | | |
| 2011 | 28 | 82 | 8'66 | 98,3 | Ϋ́ | 15 | 06 | 21 |
| Centres providing PEP (V) | 21 | 74 | 300 | 250 | 41 | 27 | State hospitals | 29 |
| | | | | | | | | Ī |

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^{*}The data in this table were communicated by MEEREB members during the meeting.
†All reported victims who required PEP received it. The way in which the need for PEP is determined in each country (if presented at this meeting) is discussed in the text of the report. NA, not available.

year. Romania has a high number of free roaming dogs and cats, and some in rural areas might benefit from oral vaccination. In Bucharest alone, the number of free roaming dogs is estimated at approximately 50 000. It is not clear how many of these dogs are actually owned and accessible for parenteral vaccination. Unvaccinated dogs account for only 8–12% of laboratory confirmed animal rabies cases (i.e. 40–50 rabid dogs are found yearly, compared to 250–400 rabid foxes), but are far more epidemiologically significant because of their proximity to humans (Herman et al., 2009).

In the last decade, an average of one case of human rabies was reported every year in Romania. No cases of human rabies were reported in 2011, but one was reported in February 2012, a 5-year-old girl bitten by a stray dog. An investigation is ongoing to determine why she did not receive PEP, for in Romania the law requires all doctors to direct an exposed person to a rabies centre for PEP. In each of the 41 counties in Romania, there is a specialized rabies centre in a regional hospital where PEP is delivered free of charge. The Essen regimen, or more rarely, the Zagreb scheme is followed, with ERIG if needed. In Bucharest alone, about 12 000 people receive PEP every year. National statistics on animal bites and the number of administered PEP are reported but are not publicly available. Not all human rabies cases are reported to the Rabies Bulletin Europe, for example in 2009 at least one, and in 2010 two human rabies cases occurred in Romania (locally reported), none of them were quoted in the Rabies Bulletin Europe. The necessity of reporting of rabies cases by all countries was emphasized.

Kazakhstan

Rabies is enzootic in more than 20% of the area of Kazakhstan. A number of wild and domestic animal species are rabies hosts, and natural foci of rabies have a tendency to expand into new areas. Rabid wild animals are rarely detected; cattle and other domestic herbivores account for over two-thirds of the approximately 200 laboratory confirmed animal rabies cases, followed by dogs and cats. A total of 44 human rabies cases were reported in the past 5 years. Most occurred in rural areas and were caused by dog bites. In 2010 and 2011, the incidences of human rabies and PEP administration in Kazakhstan were the second highest among MEEREB countries after Georgia. The majority of exposures resulted from contact with dogs (40 cases, 91.4%) and cats (3 cases, 6.4%), with one case caused by a fox (2.2%).

Rabies PEP using ERIG and hamster kidney vaccine produced in Russia is available free of charge in 250 public rabies prevention centres located throughout the country. WHO pre-qualified vaccines and HRIG are also available in

private health centres. Monitoring of the numbers of PEP courses and effectiveness of prophylaxis and control measures is carried out at both regional and national levels.

Georgia

Georgia, with a population of only 4.5 million people, has the highest reported incidence of human rabies among MEEREB members. Between 1996 and 2010, rabies has killed an average of 10 people per year. Since then, the number of human rabies cases reported annually has declined, with three human deaths in 2011, the lowest number in 20 years. Almost all human rabies cases were caused by stray dogs or unvaccinated pets (Imnadze et al., 2008).

Publicizing human rabies deaths in the media and in numerous public health communication campaigns has, over the past 10 years, contributed to a 5-fold increase in the number of admissions to healthcare centres following suspected exposure to potentially rabid animals. Consequently, the number of new admissions for PEP each year in Georgia is approaching 1% of the population, which is much higher than in any other country with known data. The high risk of rabies has prompted discussion of the potential benefit of universal rabies pre-exposure vaccination (PrEP) in childhood immunizations.

Ukraine

While other MEEREB countries report from 50 (Serbia) to 470 (Romania) animal rabies cases annually, 1430 animals were confirmed rabid in Ukraine in 2011, and 1854 in 2010. Between 2005 and 2010, an average of 2000 rabid animals were reported (with a peak of 2932 cases in 2007). Most cases were in foxes (39.5%), cats (24.1%) and dogs (19%), but cattle and other domestic herbivores (10.7%) were also involved.

With three to six annual human cases caused mainly by dogs and cats, the incidence of human rabies remains high, in the range of 0.07–0.13 per million people. The major obstacle to rabies prevention is lack of awareness, especially in rural areas. Although every year approximately 20 000 people seek medical attention in Ukraine after a bite, only one in five actually requires rabies PEP. This results from a risk assessment system similar to that existing in countries such as Croatia and Serbia, where rabies is well controlled in domestic animals.

Iran

In 2011, rabies was confirmed in 297 animals. Although rabies was most frequently found in cattle, dogs and wolves remain the main vectors in transmitting the disease to humans (Janani et al., 2008). Rabies kills two to six persons

every year, but these deaths are not sufficiently publicized to serve as a warning for subsequently exposed persons. Many people, especially in rural areas, are not aware of the need for or availability of rabies prophylaxis and do not seek medical attention following exposure to a suspected animal. A new project evaluating public awareness of the risk from animal bites is being implemented in seven provinces of northern Iran. It includes vaccination of about 400 000 dogs in rural areas yearly. Furthermore, the project allows for the evaluation of the population of owned dogs, and proposes measures for management of the free roaming dog population.

Turkey

In Turkey, dogs are the primary host species of rabies, but fox rabies emerged in the Aegean region in the late 1990s as a spillover from dogs to wildlife (Johnson et al., 2006; Vos et al., 2009). Following continued annual increases in the number of cases, an EU-funded 3-year-ORV project targeting elimination of fox rabies began in 2008 (Vos et al., 2009; Un et al., 2012). The number of fox rabies cases had decreased significantly by 2009–2010. However, fox rabies re-emerged in previous ORV areas after the end of the project and spread inland, so that the 2011 figures were similar to those from 2007 to 2008 (Un et al., 2012).

Turkey has a similar population size, incidence of PEP and number of reported animal cases as does Iran, but has a lower number of human rabies deaths. A national programme for the control and eradication of human and animal rabies was implemented in 1987, and the directive for Rabies Prevention and Control was updated in 2005. Since 2002, an average of one human rabies case is reported every year (Buzgan et al., 2009); however, no cases were reported in 2011. Recently, two studies evaluated knowledge and practices in management of rabies exposures among physi-

cians in Turkey (Gönen et al., 2011; Koruk et al., 2011). The results suggest that ongoing education of physicians on prevention and control of rabies combined with large-scale communication to the general population are needed for success in the elimination of human rabies.

Croatia

There is no urban rabies in Croatia, but it persists in wildlife. The total number of rabid foxes is decreasing because of an ORV campaign that began in 2010, 14 years after the end of the previous national campaign. It is scheduled to continue annually for at least five consecutive years. In 2010, 3691 foxes were examined for rabies and 589 (16.0%) were found positive; in 2011, among 3561 foxes examined, 325 were found positive (9.1%). According to a comprehensive national rabies control programme supported by the Ministry of Agriculture, Fisheries and Rural Development, (MAFRD), registration and a yearly rabies vaccination are mandatory for all dogs older than 3 months. This control programme also includes systematic rabies monitoring and surveillance covering the whole territory of Croatia and a recommendation for vaccination of cats and ferrets. If required by the epidemiological situation, the MAFRD may also mandate vaccination of other animal species against rabies.

Each year in Croatia, about 5000 animal bite victims seek medical attention, and approximately 1400 of them require PEP. PEP is administered at primarily 21 county public health centres, but is also available at approximately 60 additional county hospitals, municipal clinics and hospital centres. Each bite and post-exposure treatment is reported to a public health service epidemiologist. The last case of human rabies acquired in Croatia was recorded in 1964. Since then, there have been two imported cases, one in 1989 and the other in 1995.

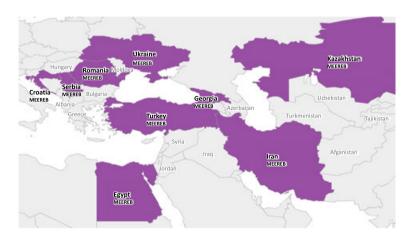


Fig. 1. Middle East and Eastern Europe zone – current reach of MEEREB network.

Serbia

In Serbia, foxes are the main reservoir of rabies, with occasional confirmed cases in 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). The oral vaccination of foxes, launched in 2010 with the support of the European Union, resulted in a progressive reduction in animal cases to 104 in 2010 and 46 in 2011. Coincident with ORV, a widespread campaign of rabies awareness among health professionals, veterinarians and the general public began.

Rabies control in Serbia is an example of effective collaboration between the human and animal health sectors. As each animal case is detected, an alert is immediately sent to the human rabies prevention centres. About 1400 bite victims (mainly from dogs and cats) require PEP each year, given free of charge at one of 27 animal bite centres in the Epidemiology Departments of the Institutes of Public Health and the Departments of Infective Diseases at regional hospitals located throughout the country. Since 1980, there have been no human rabies cases in Serbia.

Discussion

Although a legal framework for rabies control exists in all MEEREB countries, rabies elimination is generally not considered as a public health priority. In several countries, vaccination of pet dogs is mandatory, but in practice, penalties are not assessed for owners who do not vaccinate their dogs. Uncontrolled, free roaming dog populations continue to pose a problem especially in Iran, Turkey and Romania. While Iran is organizing large-scale stray dog elimination campaigns, killing of stray animals is prohibited in Romania. Humane management of dog populations, including sterilization, requires expertise, organization and funding. Oral vaccination programmes for wildlife are underway in Croatia, Serbia and more recently in Romania, but implementation of ORV campaigns depends on funding from the European Commission. Turkey recently benefited from a European-funded ORV programme; however, only a limited area was involved, and rabies re-emerged once the programme ended.

In the MEEREB countries, bite victims have good access to PEP provided free of charge in public rabies prevention centres. Urban populations are more or less aware of the risk of rabies. Nevertheless, improved mass communication and publicizing of rabies deaths would 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 curricula, as recently implemented in several Asian countries, would contribute to better rabies control.

Table 2. Minimum requirements to conduct a successful rabies elimination programme

Political

Understand what is required to eliminate rabies in the specific area Government support for the short-term and long-term

A regulatory and legal framework

Local champions

Community engagement

Support of humane dog population management

Reasonable focus and support for animal welfare

Operationa

Ability of 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)

Scientific

Data management system including an evaluation of the project

Dog population/ecology studies

Adequate access to diagnostic facilities

Adequate monitoring and surveillance including molecular epidemiology

National rabies figures from Croatia, Romania, Serbia, Turkey and Ukraine are reported in the Rabies Bulletin Europe of the WHO (http://www.who-rabies-bulletin.org). Although the number of laboratory proven rabid animals published in the Bulletin is consistent with official national figures provided by MEEREB members, human rabies cases are often underreported. This underlines the need of better communication between the human and animal health sectors in rabies prevention, and better reporting of national cases to global organizations. Georgia, Iran and Kazakhstan are not in Europe and are not listed in the Rabies Bulletin Europe. However, they have well-developed human and animal rabies notification systems. As rabies does not stop at national borders, it would be useful to extend the WHO Rabies Bulletin to other countries that are willing to participate.

Finally, although some rabies control measures are already in place, there are still significant disparities among the individual MEEREB country responses to their rabies situation. Furthermore, some of the conditions for successful rabies elimination programmes are not being met by all countries (Table 2; reviewed in Lembo et al., 2011; Lembo and Partners for Rabies Prevention, 2012). MEEREB members agreed that reinforced inter-sectoral collaboration and a 'One Health'² approach are the keys for successful rabies

²The 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 aim is to accelerate biomedical research, enhance public health, expand the scientific knowledge base, improve medical education, and clinical care. The One Health Initiative: http://www.onehealthinitiative.com/about.php.

control. Prevention and prophylaxis of human rabies are available in each MEEREB country; information on the number of human rabies cases, bites and PEP regimens administered is available in each. Additional progress towards elimination of human rabies is dependent on region-wide achievement of rabies control in domestic dogs, including strays and free roaming dogs with unapparent owners (Lembo et al., 2011). Rabies control in wild animal reservoirs must also be achieved. In this regard, MEEREB would evolve from a 'collaboration' to a 'working group', adding stakeholders from agriculture, wildlife biology, veterinary medicine and other relevant disciplines to the current public health and epidemiology experts, to allow a more comprehensive approach (i.e. enhanced public awareness, human rabies prevention, canine rabies elimination, wildlife rabies control) (Lembo et al., 2011; Lembo and Partners for Rabies Prevention, 2012). The additional expertise on wild animal reservoirs and viral strains in the member countries would be needed to develop interventions beyond control of human rabies and rabies in domestic animals, for example eradication versus elimination.

Currently MEEREB is geographically discontinuous (Fig. 1). As rabies does not respect national boundaries, this leads to the question of how to expand and coordinate efforts to eliminate rabies in additional countries in the region. Specifically, which countries would need to be involved to achieve a goal of regional rabies elimination. Also, given their particular epidemiological situations, how would the programmes needed in those countries compare to those in the current member countries. Ultimately, the working group would identify gaps in the current political, operational, public and animal health situation, agree on country strategies, identify partners to provide the needed expertise, and then implement a programme and monitor its progress (Lembo et al., 2011).

Conclusions

Elimination of human rabies 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 free roaming dog populations. Success stories in Latin America, in Western Europe, in some Asian countries, as well as in Croatia and Serbia demonstrate that elimination of human rabies is achievable in the entire ME-EREB region. The 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 can be achieved in the region through inter-sectoral cooperation, and that campaigns for rabies elimination will

have significant benefit for public health, including strengthening the structure for control of other zoonoses.

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