Epidemiol. Infect. (2014), **142**, 1486–1494. © Cambridge University Press 2013
doi:10.1017/S0950268813002392

Challenges facing human rabies control: the Lebanese experience

A. BIZRI[1], A. ALAWIEH[2], N. GHOSN[3], A. BERRY[4] AND U. MUSHARRAFIEH[1,5]*

[1] *Division of Infectious Diseases, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon*
[2] *Faculty of Medicine, American University of Beirut, Beirut, Lebanon*
[3] *Epidemiological Surveillance Department, Ministry of Public Health, Beirut, Lebanon*
[4] *Communicable Diseases Department, Ministry of Public Health, Beirut, Lebanon*
[5] *Department of Family Medicine, American University of Beirut Medical Center, Beirut, Lebanon*

Received 18 May 2013; Final revision 12 August 2013; Accepted 30 August 2013; first published online 25 September 2013

SUMMARY

Rabies is one of the most important zoonotic infections worldwide. The burden of the disease continues to be significant in countries in the Middle East where the most important vector is stray dogs. Control efforts are hindered by lack of awareness and incomplete post-exposure prophylaxis. The aim of this article is to re-assess the situation of rabies in Lebanon and compare it to other Middle Eastern countries. Eight cases of rabies and 5280 incidents of animal bites to humans were reported to the Lebanese Ministry of Public Health between 2001 and 2012. Dogs were the only vector of infection and were responsible for most reported animal bites to humans. An average of 3·2 doses of vaccine per bite was administered as post-exposure prophylaxis. The status of human and canine rabies control, the risks associated with children's behaviour and the hazards of secondary wild reservoirs are discussed. Our data illustrates the importance of prevention through vector control, public awareness and education, and timely administration of active and passive immunization, as well as the significance of regional cooperation and monitoring the circulation of viral variants in wild animals.

Key words: Rabies (human), virology.

INTRODUCTION

Rabies is a fatal disease of antiquity with the highest case-fatality rate of all infectious diseases, accounting for over 55 000 deaths annually [1]. One person dies from rabies every 10–15 min and around 300 are exposed [2, 3]. According to the global burden of disease report revised in 2013, rabies accounted for the loss of 1462 disability-adjusted life years in 2010 compared to 3234 in 1990 [4]. Even though this may suggest a decrease in the rabies burden worldwide, rabies continues to be one of the most important viral zoonoses given its widespread distribution, public health concerns, veterinary implications, and economic consequences [2]. Each year, more than 10 million people, many of whom are unvaccinated, endure protracted anxiety after exposure to animals with suspected rabies [5]. Despite this anxiety, rabies ignorance is a major public health problem that

* Author for correspondence: U. Musharrafieh, M.D., Associate Professor, Department of Family Medicine, Clinical Associate, Infectious Disease Division, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon. (Email: ali.alawieh1@gmail.com)

requires educating both the public and health professionals [1, 2, 6].

Rabies is an acute, progressive, viral encephalitis with poorly understood pathogenesis and a predictable fatal outcome [7]. Rabies infection is eminently preventable despite the absence of any treatment for the disease. Controlling the infection in dogs is the best measure of prevention, yet this is still not achieved in many developing countries, contributing to the higher incidence of rabies [8, 9]. A major contributor to the absence of canine rabies control in these countries is the lack of competent measures taken by relevant authorities. Other measures for rabies prevention include rabies post-exposure prophylaxis (PEP) with rabies vaccine and immunoglobulin. Most humans die of rabies because of inappropriate, delayed or lack of PEP administration [10]. According to a World Health Organization (WHO) report, post-exposure rabies prophylaxis prevents about 272 000 deaths each year in Asia and Africa [11].

Worldwide, rabies is spread by various warm-blooded mammalian species, such as red foxes in North America, Europe and Eurasia, skunks in North America, raccoons in USA, mongooses in the Caribbean Islands and South Africa, jackals in Africa, and vampire bats in Southern and Central America [12]. Dogs are the main source of human infection in the Middle East, while cats constitute the second most important source. Wild animals, the most important vector in the developed world, are less important in Middle Eastern countries. Infection of cattle, sheep, goats, camels, and donkeys, although rare, is also potentially possible. Around 300 human cases of rabies are reported annually in the Middle East region [13, 14]. Certain countries of the region are facing increasing problems due to wildlife rabies, such as Saudi Arabia, Oman, Yemen, Israel, Iran, and Turkey [14].

Animal rabies is known to be endemic in countries bordering Lebanon, mainly Syria and Israel [15, 16]. Between 2004 and 2007, the biological and molecular characterization of the rabies isolates by David *et al.* showed stray dogs to be the main animal reservoir in Northern Israel [17]. Fifty-seven percent of confirmed rabies isolates between 2001 and 2007 were in dogs compared to 43% confirmed isolates in other wild and domestic animals [17].

Human rabies is a reportable disease in Lebanon. Few reports were published about the burden of rabies in the country and the public attitude towards it [18–20]. The last major report about the burden of rabies in Lebanon was published in 2000. A total of eight cases of human rabies were reported to the Lebanese Ministry of Public Health (LMOPH) between 1991 and 1999 together with an annual average of 184 animal bites to humans between 1991 and 1996. Dogs were the only vector of human disease in that report and the most commonly reported cause of animal bites to humans [19].

In this study, we aim to revisit the status of rabies infection and exposure in Lebanon as reported to health authorities and compare it to studies from other countries. We also evaluate available rabies surveillance, control and preventative measures.

METHODS

Rabies record collection

Records from the American University of Beirut Medical Center (AUBMC), the major medical center in Lebanon, together with records from the LMOPH were reviewed between 2001 and 2012. Records before 2001 were excluded as they were reviewed by our team in a previous study [19].

Documented cases of rabies were reviewed for their setting of occurrence, demographics, source of infection, and mode of management.

Collection of animal bite data

Data about animal bites to humans occurring between 2001 and 2012 along with data on PEP and vaccine administration to individuals exposed to bites were also reviewed from the records of the LMOPH Epidemiological Surveillance Unit in terms of age, location and offending animal. The number of vaccines per animal bite was calculated as an approximate measure of rabies PEP adequacy as the majority of animals reported during that period were not followed, necessitating four doses of vaccine per bite. Data on the number of incomplete PEP is not available.

Statistical analysis

To assess the change in reported rabies exposure, collected data for the period 2001–2012 was compared to that reported between 1991 and 1999. The means of annual animal bites to humans reported in each period was compared using unpaired t tests.

https://doi.org/10.1017/S0950268813002392 Published online by Cambridge University Press

Table 1. *Reported human rabies cases in Lebanon between 2001 and 2012*

Year reported	2001	2001	2002	2002	2004	2010	2010	2012
Sex	Male	Female	Male	Male	Male	Male	Female	Male
Region	North	North	Bekaa	Bekaa	Bekaa	North	Bekaa	Beirut
Age group, yr	5–9	40–59	20–39	⩾60	0–4	20–39	⩾60	40–59
Vector	Dog	Dog	Dog	Dog	Dog	Dog	Dog	Dog
Contact type	Bite	Bite	Bite	Bite	Bite	Bite	Bite	Bite

Modified from the Lebanese Ministry of Public Health website (www.moph.gov.lb).

Table 2. *Total number of animal bites to humans and number of exposed people*

Year Reported	Bites				Vaccine (Verorab)	
	Domestic dogs	Stray dogs	Other animals*	Total	Total distributed	Vaccines per bite
2001	237 (54%)	167 (38%)	32 (7%)	436	780	1·8
2002	221 (51%)	181 (42%)	30 (7%)	432	1655	3·8
2003	234 (52%)	182 (40%)	36 (8%)	452	1397	3·1
2004	353 (58%)	204 (34%)	50 (8%)	607	2028	3·3
2005	304 (61%)	140 (28%)	51 (10%)	495	1168	2·4
2006	321 (67%)	29 (6%)	131 (27%)†	481	1570	3·3
2007	224 (57%)	133 (34%)	35 (9%)	392	1170	3
2008	261 (52%)	211 (42%)	30 (6%)	502	1265	2·5
2009	261 (53%)	213 (43%)	20 (4%)	494	1780	3·6
2010	188 (50%)	165 (44%)	26 (7%)	379	847	2·2
2011	175 (52%)	143 (42%)	21 (6%)	339	1223	3·6
2012	125 (46%)	133 (49%)	13 (5%)	271	1421	5·2
Total	2904 (55%)	1901 (36%)	475 (9%)	5280	16322	n.a.
Annual average	242	158	39	440	1360	3·15

Modified from the Lebanese Ministry of Public Health website (www.moph.gov.lb).
n.a., Not applicable.
* Cats, wild animals, bats, rodents, and others.
† Peaked levels of other animals in 2006 relative to previous years mainly included wild animals. One possible explanation is the war state in Lebanon where families were homeless or living in camps in rural areas and more exposed to unusual bites.

RESULTS

In total, eight cases of human rabies were reported to LMOPH (Table 1), of which one case only was admitted to AUBMC. Out of the eight cases, seven occurred in the North and Bekaa provinces that are predominantly farming areas close to the Syrian border. Only one case was reported from Beirut, the capital of Lebanon. The vector of infection was invariably a dog bite. The eight cases were distributed in different age groups including children, young adults and the elderly. All the reported cases had an unfortunate fatal outcome. The outcome was assessed based on the clinical picture without pathological confirmation. Presentations were classical including agitation, aggression, drooling, excessive sweating, fever and hallucinations.

A total of 5280 animal bites to humans were reported to LMOPH between 2001 and 2012 with an annual average of 431 bites per year. Table 2 shows the number of people exposed to animal bites and the total number of vaccine doses provided by LMOPH. On average, 3·15 vaccine doses were delivered per animal bite during the study period. The offending animals included domestic and stray dogs as well as cats, rats, monkeys, donkeys, and foxes. Dogs, however, were by far the major offending animal responsible for around 91% of all bites with stray dogs constituting 55% of all bites. The highest incidence of animal bites was in older children and adults. Yet, the incidence in those aged <15 years was marked, with an average of 134 bites per year. With respect to region, the highest incidence of exposure to bites was in the North and Mount

https://doi.org/10.1017/S0950268813002392 Published online by Cambridge University Press

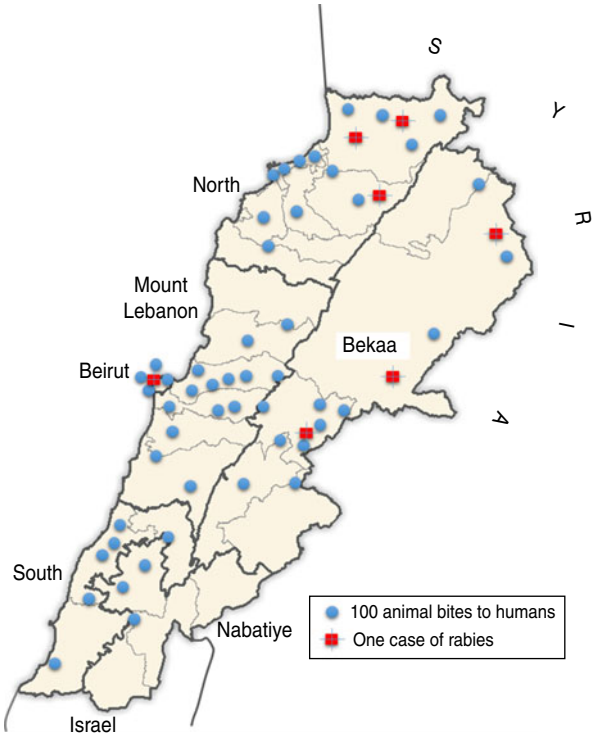

Fig. 1. (*colour online*) Epidemiological map showing the distribution of rabies exposure and cases across the different provinces of Lebanon.

Lebanon despite animals being unprovoked (Fig. 1). Table 3 illustrates the distribution of individuals exposed to bites by age and region.

The comparison of annual animal bites in Lebanon during 2001–2012 to that during the 1990s showed a significantly higher number of reported animal bites in the 2001–2012 period (431 bites per year *vs.* 184, $P < 0{\cdot}0001$).

DISCUSSION

The annual average of animal bites to humans reported to LMOPH between 2001 and 2012 was 440 bites per year, ranging between 271 and 607 bites. This may not reflect the actual number since animal bites are mainly reported when the victim consults a physician who, in turn, suspects a possible rabies risk. The surveillance system of LMOPH is a passive system where physicians in different districts of Lebanon are required to report rabies cases to district authorities who in turn are responsible for reporting to LMOPH as well as the follow-up of suspected animals if possible. Hospitals are also required to report rabies cases to LMOPH directly. However, some cases may go unnoticed by LMOPH if families did not consult a physician or the physician failed to report the exposure, which is quite possible in rural areas where the disease is more prevalent. Active educational campaigns are the best way to enhance the power of surveillance and allow a better evaluation of the rabies burden.

The annual average of vaccine doses distributed during this period was 1360 doses per year with a ratio of 3·15 doses per animal bite. This ratio still lags behind the Centers for Disease Control and Prevention (CDC) recommendation of four doses per bite [21]. The reason for this could be either that there was an incomplete follow-up of victims or that the animal was identified as non-rabid and no further measures were needed. Rabies vaccine is delivered free of charge by LMOPH healthcare centres present in different provinces of Lebanon. In total, eight cases of rabies were reported to LMOPH and were diagnosed on a clinical basis without pathological identification. Vectors in all cases were dogs indicating that human rabies in Lebanon is still secondary to canine rabies as it was in the previous decade [19].

Annually, an average of 0·6 cases of rabies is reported to LMOPH. As with many reportable diseases in Lebanon and worldwide, reported numbers may be an underestimation especially in rural areas with poor awareness and limited access to medical care [20]. The observed annual occurrence in this study is very close to that reported in a previous study by our group between 1990 and 1999 [19] (0·8 cases per year). This may not necessarily reflect stability in disease burden in the country, promoting concerns that this state of balance between near elimination and sporadic emergence of cases may lead to second reservoir species such as foxes or other animals as was the case in Turkey [22]. Such worries seem possible given the presence of similar reservoirs in foxes as reported in Israel, an adjacent country to Lebanon [17]. This is often referred to as rabies 'host switching' and was found to be responsible for the appearance of the virus variants in several wildlife animals such as foxes and skunks originating from dogs and bats in the USA [23, 24]. This emphasizes the need to monitor the circulation of rabies virus variants in different wild animals for the initiation of adequate preventative measures.

Despite this, Lebanon is considered a country with low incidence of rabies compared to other developing countries, especially in Africa and South East Asia [25–27]. One explanation is the limited exposure to rabies reservoirs in Lebanon compared

https://doi.org/10.1017/S0950268813002392 Published online by Cambridge University Press

Table 3. *Distribution of animal bites to humans by location and age*

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Age, yr												
0–4	22	22	14	20	23	15	16	9	13	7	8	9
5–14	121	118	129	166	143	140	92	153	130	96	71	67
15–24	101	89	97	142	108	108	88	105	87	69	82	53
25–44	118	128	124	143	133	120	108	125	139	110	98	80
45–65	44	53	65	96	61	74	58	76	84	60	60	46
>65	29	21	23	39	26	23	29	32	39	35	20	15
n.a.	1	1	0	1	1	1	1	2	2	2	0	1
Region												
North	166	108	90	148	91	133	105	140	122	96	84	35
Bekaa	41	68	90	144	94	91	71	86	81	51	84	16
Nabatiye	26	37	35	31	38	23	18	40	23	42	16	33
South	28	42	48	53	67	54	41	54	56	39	42	25
Mount Lebanon	132	118	136	172	169	144	120	130	162	117	82	80
Beirut	35	57	52	57	33	29	33	46	40	29	25	36
n.a.	8	2	1	2	3	7	4	6	10	5	6	46
Total	436	432	452	607	495	481	392	502	494	379	339	271

Modified from the Lebanese Ministry of Public Health website (www.moph.gov.lb).
n.a., Not assigned.

to those countries. Even though the global burden of rabies is on the decrease [4], the disease continues to be reported in several regions in Europe and the USA [28, 29]. However, many of the reported cases of rabid animals in developed countries, e.g. France, Germany, Italy, Canada and the USA, are believed to be secondary to imported rabid animals [28, 30]. In addition, imported human rabies immigrants and travellers are another concern in those developed countries as reported recently by Carrara *et al*. [31].

In our report, the majority of cases were in adults (six cases) while two cases occurred in children aged <15 years of age (Table 1). A possible explanation may be the fact that children are less likely to go outside and be exposed to animals than adults [32]. This can be inferred from the distribution of animal bites across age groups where the highest numbers occurred in the adult group (Table 3). Although, the occurrence of two cases of this fatal and low-prevalence condition is still alarming. A similar picture can be deduced from our previous report published in Lebanon [19]. On the contrary, studies in high-prevalence areas, especially Africa, indicate that the majority of rabies cases were in children. More than half of the deaths from rabies in Africa involve children raising serious concerns about childhood rabies prevention and control in these areas [33].

With regard to geographical distribution, all but one of the reported cases was from the North and Bekaa provinces (Fig. 1, Table 1). The remaining case was from Beirut. The outcome of all the reported cases was fatal, secondary to the lack of available treatment for this disease, emphasizing the crucial role of rabies prevention.

The socioeconomic conditions in a country and the residential area (rural *vs*. urban) besides age and occupation are influential factors on the epidemiological features of animal bites [34]. In the present study, animal bites were most frequently reported in the 20–60 years age group. Similar to our results, the study of Gautret *et al*. on the epidemiology of dog-related injuries in Marseille, France revealed a mean age of 32 years for affected people [35]. This was not, however, the case in Kerman Province, Iran, where animal bites were more common in younger age groups (10–19 years) [34]. Although less than adults, the incidence of animal bites in children is uncomfortably high with an average of 134 bites per year (31% of average annual bites). It was suggested that children may trigger an attack by a dog through provocative playful actions. Even behaviours not regarded as provocative may be interpreted by a dog as an invasion of territory and may incite an attack. This is important in view of the way children behave around dogs especially if dogs live in the same household or community [36]. Children who have been bitten or scratched by suspect rabid dogs may not tell their parents or guardians, especially if they have

https://doi.org/10.1017/S0950268813002392 Published online by Cambridge University Press

been instructed not to approach animals that are not their own pets [37, 38]. Dzikwi *et al*. studied the effect of educating Nigerian children about rabies on rabies exposure. The study revealed that properly educating children about rabies can result in these children avoiding dogs [39].

The annual animal bite counts in Lebanon reported in this study was much higher than that reported in the previous decade (431 *vs*. 184 bites per year; $P=0{\cdot}0001$) [19]. This may seem to reflect a deterioration of animal control strategies in the country resulting in an increased exposure to rabies through animal bites. However, it can also imply advancement in the reporting and surveillance system at LMOPH.

Dog bites constitute 91% of all bites to humans in Lebanon; therefore, dog control, especially stray dogs, is a major avenue for prevention. Stray dogs are those that are not under the direct control of an owner either because they have no owner or because the owner has not restricted them from roaming freely. Domestic dogs are those that are under direct control and restraint by their owners. Other animals, including wild animals, account for 8% of all bites. This continuous exposure necessitates stronger measures for the control canine rabies in Lebanon as a means of controlling the disease. Control of canine rabies starts with action by the veterinary authorities, i.e. taking responsibility for monitoring and limiting the dog population. Possible measures to be taken include registering domestic dogs and educating owners, capturing stray dogs, controlling dog reproduction, vaccination of non-rabid dogs, humane measures of rabid dog euthanasia, and observation of suspected animals for neurological symptoms or laboratory diagnosis. Several massive canine rabies vaccination programmes were successful in establishing canine rabies immunity in many countries [40]. In the systemic review of Davlin & Vonville of the canine rabies vaccination programmes in the developing world, the majority of the campaigns were capable of accomplishing the WHO-recommended vaccination coverage of $\geqslant 70\%$ [41]. Despite that, countries like China, India and Pakistan where the highest burden of rabies exists did not have any studies reporting such campaigns. Control of canine reproduction is also of importance given the fact that the majority of stray dogs in the developing world are young and short-lived, posing a major limitation to efficiency of dog vaccination campaigns [41].

In Lebanon, attempts to control canine rabies are still inadequate. Canine vaccination is limited to pet dogs in the absence of any governmental vaccination campaigns. In addition, stray dogs to which highest exposure is recorded are not captured, neither are suspected animals followed up after biting humans. Studies pertaining to rabies cases in animals are lacking, and there are no studies that have reported confirmed cases of animal rabies in Lebanon during the study period. However, despite the ability of the Lebanese surveillance system to record cases of human rabies and animal exposure, interventional measures for long-term rabies control are still lagging. Such measures require a competent authority as well as the help of non-governmental organizations to have a good surveillance and interventional system that can control the rabid canine population and its possible wildlife interactions. Such measures should be applied at a national level in order to ensure long-term reduction of rabies reservoirs by limiting rabies infection in dogs and its transmission to humans as well as other animals. Consequences of the lack of interventional measures as well as the absence of follow-up of offending animals also include the inappropriate administration of PEP and rabies immunoglobulin resulting in shortage of supplies at different locations. This problem is shared in many countries of the developing world where canine rabies is the major contributor to human rabies cases [40].

The low level of reported bites in animals other than dogs may be due to poor awareness of the potential risk of rabies transmission through these animals. Despite the fact that dogs are known as the most common source of rabies transmission to humans throughout the world, especially in Asia, Latin America, and Africa [17], bites by other animals should also be addressed in control programmes and awareness campaigns.

A closer look at the distribution of animal bites revealed the highest cluster was in Mount Lebanon where no cases of rabies were reported. However, seven out of eight cases were from remote rural areas in the country. These findings cannot be attributed to greater numbers of wildlife in that area as the distribution of wild *vs*. domestic bites was comparable in both areas (data not shown).

One possibility is the movement of infected stray dogs into Northern Lebanon across the borders resulting in a spillover, especially from Syria which has a higher incidence than Lebanon with 24 reported fatal cases between 1997 and 2002 [42]. Spillover from neighbouring countries like Syria, Lebanon and Turkey was reported to contribute to an outbreak of

rabies in Northern Israel in 2009. This was based on biological and molecular characterization of the rabies strains isolated that revealed the stray dogs as the main animal reservoir [17]. This highlights the need for regional cooperation to ensure the best rabies control measures in neighbouring countries. However, this can be complicated in regions of political and economic instability with shifting governmental priorities [43]. For instance, Hatch *et al.* reported increased rabies and a need for massive rabies vaccination during the civil war in Sierra Leone [44]. The unstable political situation in the region, mainly in countries bordering Lebanon, adds further challenges to efforts aiming at controlling wildlife and urban rabies infection.

Another reason for increased incidence of rabies in the North and Bekaa provinces is the lower adherence to PEP by affected patients in rural areas compared to Mount Lebanon. This may be due to the lack of awareness about the disease and the need for PEP, as well as difficulty in accessing centres where PEP is provided.

Death from human rabies results from the lack of awareness and the untimely administration of PEP along with the failure to follow WHO recommendations on wound washing and vaccination [45, 46]. Wasay *et al.* [47] evaluated the public knowledge regarding predisposing factors, fatality and prevention of tetanus and rabies and the attitudes towards vaccination and PEP in Pakistan. Most of the participants were not aware of the fatality of these diseases and the importance and affordability of vaccination in case of dog bites and minor trauma. In that study, only 11% of 1201 persons bitten by dogs received some kind of vaccine or PEP. In Lebanon, a study was conducted by Saad & Ghosn [20] to assess knowledge, attitudes and practices towards rabies in two major towns in the North and Bekaa provinces (Zagharta and Baalback); 80% of 196 participants reported having no or little information about PEP, despite the fact that the majority of respondents had heard about rabies. This lack of awareness might explain the cluster of rabies cases in these areas.

Despite the low level of awareness towards rabies PEP in rural areas of Lebanon, there is an improvement in the delivery of vaccines after bite exposure at the national level. This is illustrated by an increase in the vaccine/bite ratio from 2·25 doses per bite between 1990 and 1999 to 3·15 doses per bite between 2001 and 2012. This recent ratio is very close to the newest CDC recommendation of delivering four doses/bite [21]. In contrast to Lebanon, where the majority of human victims of suspected animal bites receive the full PEP course, many developing countries still lag behind. Almost 10% of human rabies cases in India received incomplete PEP vaccination [48], and 47% of patients started on PEP in the Ivory Coast failed to complete the course of injections [49]. Interestingly, many of the developed countries are facing the problem of PEP overuse and lack of monitoring of PEP administration as reported in the USA by Christian *et al.* [50].

CONCLUSION

Rabies control remains elusive in both the developing and developed world. The variability in rabies epidemiology in different regions adds to the challenges that face efforts to prevent and eradicate the disease.

The stable incidence of the disease in a country should not be reassuring due to the host-switching ability of the virus and its circulation in different species of wild animals. Dogs remain the most important vector in the developing world compared to wild animals in the developed world. Children are a major high-risk group for acquiring the disease mainly in developing counties. The high incidence of dog bites in the young age group (up to age 15 years) is a cause for concern worldwide. Public awareness is of tremendous importance and disseminating information about all relevant aspects of the disease is essential. Such information should also be included in school curricula and school awareness programmes targeting pediatric age groups.

The ability of animals to cross borders, the reports of imported cases from many countries, and the higher incidence of rabies in border areas such as in Lebanon emphasize the importance of regional cooperation. Cooperative efforts can be impeded by political instability experienced in many regions including the Middle East.

The capacity of national surveillance systems to evolve and cope with the increased risks of exposure is of enormous importance given the future challenges of rabies control. PEP including timely and adequate vaccination and administration of rabies immunoglobulin remains the cornerstone for prevention of the infection and its fatal outcome in the exposed.

Monitoring viral circulation in the various hosts, control of canine rabies in the developing world, regional cooperation, raising public awareness mainly

https://doi.org/10.1017/S0950268813002392 Published online by Cambridge University Press

in children, and timely administration of PEP are essential for decreasing the rabies burden worldwide.

DECLARATION OF INTEREST

None.

REFERENCES

1. **Hemachudha T, Laothamatas J, Rupprecht CE.** Human rabies: a disease of complex neuropathogenetic mechanisms and diagnostic challenges. *Lancet Neurology* 2002; **1**: 101–109.
2. **Rupprecht CE, Hanlon CA, Hemachudha T.** Rabies re-examined. *Lancet Infectious Diseases* 2002; **2**: 327–343.
3. **CDC.** How can you prevent rabies in people? Centers for Disease Control and Prevention, 2011.
4. **Murray CJ, *et al.*** Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380**: 2197–2223.
5. **Meslin F, Stohr K.** Prospects for immunization against rabies in developing countries. In: *Rabies Control in Asia*. Paris: Elsevier, 1997, pp. 15–18.
6. **Dodet B, *et al.*** Rabies awareness in eight Asian countries. *Vaccine* 2008; **26**: 6344–6348.
7. **Jackson A.** Advances in our understanding of the pathogenesis of rabies. *International Journal of Infectious Diseases* 2012; **16**: e330.
8. **Knobel DL, *et al.*** Re-evaluating the burden of rabies in Africa and Asia. *Bulletin of the World Health Organization* 2005; **83**: 360–368.
9. **Wilde H, *et al.*** Rabies control in south and southeast Asia. *Vaccine* 2005; **23**: 2284–2289.
10. **Senior K.** Global rabies elimination: are we stepping up to the challenge? *Lancet Infectious Diseases* 2012; **12**: 366–367.
11. **WHO.** Current strategies for human rabies pre and post-exposure prophylaxis. World Health Organization, 2010.
12. **Chomel BB.** The modern epidemiological aspects of rabies in the world. *Comparative Immunology, Microbiology and Infectious Diseases* 1993; **16**: 11–20.
13. **Aylan O, *et al.*** Report of the first meeting of the middle East and eastern europe rabies expert bureau, Istanbul, Turkey (8–9 June 2010). *Advances in Preventive Medicine* 2011; **2011**: 812515.
14. **Seimenis A.** The rabies situation in the Middle East. *Developments in Biologicals* 2008; **131**: 43–53.
15. **RABNET.** Strengthening international surveillance of human and animal rabies Health Section of the Secretariat of the League of Nations. *Weekly Epidemiological Record* 1998; **73**: 254–256.
16. **WHO.** Surveillance WHODoCD, Response. World Survey of Rabies No. 35: for the year 1999: World Health Organization, 2002.
17. **David D, *et al.*** Emergence of dog rabies in the northern region of Israel. *Epidemiology and Infection* 2009; **137**: 544–548.
18. **Akkoca N, *et al.*** Rabies in Turkey, Cyprus, Syria and Lebanon. In: King AA, ed. *Historical Perspective of Rabies in Europe and the Mediterranean Basin: A Testament to Rabies*, Paris, France: World Organization for Animal Health (OIE), 2004, pp. 157–69.
19. **Bizri AR, *et al.*** Human rabies in Lebanon: lessons for control. *Epidemiology and Infection* 2000; **125**: 175–179.
20. **Saad R, Ghosn N.** P2–539 Rabies: knowledge, attitude and practice survey in Baalbeck and Zgharta districts-Lebanon 2010. *Journal of Epidemiology and Community Health* 2011; **65** (Suppl. 1): A370–A.
21. **CDC.** Rabies vaccine. Centers for Disease Control and Prevention, 2011.
22. **Johnson N, *et al.*** Rabies epidemiology and control in Turkey: past and present. *Epidemiology and Infection* 2010; **138**: 305.
23. **Velasco-Villa A, *et al.*** Enzootic rabies elimination from dogs and reemergence in wild terrestrial carnivores, United States. *Emerging Infectious Diseases* 2008; **14**: 1849–1854.
24. **Leslie MJ, *et al.*** Bat-associated rabies virus in Skunks. *Emerging Infectious Diseases* 2006; **12**: 1274–1277.
25. **Horton DL, *et al.*** Rabies in Iraq: trends in human cases 2001–2010 and characterisation of animal rabies strains from Baghdad. *PLoS Neglected Tropical Diseases* 2013; **7**: e2075.
26. **Hossain M, *et al.*** Human rabies in rural Bangladesh. *Epidemiology and Infection* 2012; **140**: 1964–1971.
27. **Munang'andu HM, *et al.*** Rabies status in Zambia for the period 1985–2004. *Zoonoses and Public Health* 2011; **58**: 21–27.
28. **Johnson N, *et al.*** Imported rabies, European Union and Switzerland, 2001–2010. *Emerging Infectious Diseases* 2011; **17**: 753–754.
29. **Vercauteren K, *et al.*** Rabies in North America: a model of the one health approach. USDA National Wildlife Research Centre – Staff Publications, Paper 1202, 2012.
30. **Blanton JD, *et al.*** Rabies surveillance in the United States during 2011. *Journal of the American Veterinary Medical Association* 2012; **241**: 712–722.
31. **Carrara P, *et al.*** Imported human rabies cases worldwide, 1990–2012. *PLoS Neglected Tropical Diseases* 2013; **7**: e2209.
32. **Senauer A.** Children and nature network research and studies. *Expert Opinion on Biological Therapy*, 2007.
33. **Liu Q, Ertl HC.** Preventative childhood vaccination to rabies. *Expert Opinion on Biological Therapy* 2012; **12**: 1067–1075.
34. **Eslamifar A, *et al.*** Animal bites in Tehran, Iran. *Archives of Iranian Medicine* 2008; **11**: 200–202.
35. **Gautret P,** *et al.* Epidemiology of urban dog-related injuries requiring rabies post-exposure prophylaxis in Marseille, France. *International Journal of Infectious Diseases* 2013; **17**: e164–e167.
36. **WHO.** Expert consultation on rabies. World Health Organization Technical Report Series, 2005, pp. 1–88.

37. **Bhanganada K, *et al.*** Dog-bite injuries at a Bangkok teaching hospital. *Acta Tropica* 1993; **55**: 249–255.
38. **Cleaveland S, *et al.*** A dog rabies vaccination campaign in rural Africa: impact on the incidence of dog rabies and human dog-bite injuries. *Vaccine* 2003; **21**: 1965–1973.
39. **Dzikwi AA, Ibrahim AS, Umoh JU.** Knowledge, attitude and practice about rabies among children receiving formal and informal education in Samaru, Zaria, Nigeria. *Global Journal of Health Science* 2012; **4**: 132–139.
40. **Franka R, *et al.*** Current and future tools for global canine rabies elimination. *Antiviral Research* 2013; **100**: 220–225.
41. **Davlin SL, Vonville HM.** Canine rabies vaccination and domestic dog population characteristics in the developing world: a systematic review. *Vaccine* 2012; **30**: 3492–3502.
42. **Seimenis A, Morelli D, Mantovani A.** Zoonoses in the Mediterranean region. *Annali dell'Istituto superiore di sanita* 2006; **42**: 437–445.
43. **Rupprecht C, *et al.*** Can rabies be eradicated? *Developments in Biologicals* 2008; **131**: 95–121.
44. **Hatch C, Sneddon J, Jalloh G.** A descriptive study of urban rabies during the civil war in Sierra Leone: 1995–2001. *Tropical Animal Health and Production* 2004; **36**: 321–324.
45. **Hemachudha T, *et al.*** Additional reports of failure to respond to treatment after rabies exposure in Thailand. *Clinical Infectious Diseases* 1999; **28**: 143–144.
46. **Wilde H.** Failures of post-exposure rabies prophylaxis. *Vaccine* 2007; **25**: 7605–7609.
47. **Wasay M, *et al.*** Knowledge and attitudes about tetanus and rabies: a population-based survey from Karachi, Pakistan. *Journal of the Pakistan Medical Association* 2012; **62**: 378.
48. **Sudarshan MK, *et al.*** Assessing the burden of human rabies in India: results of a national multi-center epidemiological survey. *International Journal of Infectious Diseases* 2007; **11**: 29–35.
49. **Tiembre I, *et al.*** Adherence to rabies vaccine treatment for people exposed to rabies in Abidjan (Cote d' Ivoire) [in French]. *Santé publique* 2009; **21**: 595–603.
50. **Christian KA, *et al.*** Epidemiology of rabies post-exposure prophylaxis – United States of America, 2006–2008. *Vaccine* 2009; **27**: 7156–7161.