

Translocation of Rabies Virus in Israel by Cattle: A Threat for the Public Health

David, D.,* Dveres, N., Yakobson, B.A. and Davidson, I.

Kimron Veterinary Institute, Bet Dagan 50250, POB 12, Israel.

* Corresponding Author: Dr. D. David, Tel :+972-506241984, Fax: +972-3-9681721. Email: davidd@int.gov.il

ABSTRACT

Rabies is endemic in Israel, the only country in the Middle East that implements a nation-wide anti-rabies campaign. However, between 2002 and 2013 about 32 rabies virus isolates belonging to genetic variant V1 were recovered within Israel. The present study describes for the first time the translocation of the rabies virus strain, fox V1, by infected cattle born on "Tzfon HaGolan dairy farm" located in Kibbutz Ortal on the Golan Heights to two farms situated in the western Yezre'el Valley, emphasizing that cattle may serve also a source of human rabies infection.

Keywords: Rabies; Cattle; Translocation; Diagnosis; Post exposure vaccination.

INTRODUCTION

Rabies virus is a member of the Rhabdoviridae, genus Lyssavirus. All mammals are susceptible to rabies infection. Rabies is enzootic throughout the Middle East, including Israel. Rabies is also a serious enzootic disease in Jordan, Syria, Lebanon and Iran and Irak where stray dogs maintain rabies virus in circulation, with frequent spillover to wildlife, including jackals, squirrels, stone-martens, foxes, wolves and infection of domestic animals and human (1, 2, 3, 4, 5, 6).

Since 1979, red foxes (*Vulpes vulpes*) have become the most important reservoir of rabies virus in Israel (7). An oral vaccination (ORV) program directed at wild animals has been implemented since 1998 in northern Israel (8). In 2004 the program was extended and it currently covers all the territories controlled by Israel and the Palestinian Authority. Israel is the only country in the Middle East that implements ORV program. To insure its success, extensive rabies surveillance along Israel's borders is carried out. Despite the efficacy of the ORV in controlling fox rabies in north Israel, a new outbreak occurred in 2004 in this region, in which stray dogs (*Canis familiaris*) were shown to be main reservoir and transmitter of genetic variant V7 (9, 10).

Molecular epidemiological studies of rabies in Israel between 1993 and 1998 revealed four fox strain genetic lineages (V1-V4), were distributed within four geographical regions (11). Molecular analysis of rabies isolates on the borders of Israel and neighboring countries revealed the presence of three genetic variants V5, V6 and V7 (12). Due to the ORV program, fox rabies genetic variants V1 and V2 specific to northern Israel region were eliminated in 2003, while fox strain genetic variants V3 and V4 enzootic to central and southern of Israel were eliminated by 2005 (9).

However, incursions of fox rabies variant infected animals persisted across Israel's borders. Between 2002 to 2013 about 32 isolates of fox rabies virus belonging to the genetic variant V1, were detected within Israel and its neighboring countries.

All mammals are susceptible to rabies virus. Bovine rabies has a direct economic impact (13) on the livestock industry and represents a public health threat in rabies endemic area. In Israel between the years 1996-2014, 104 rabies cases were reported in cattle, most of them on the borders with neighboring countries.

Recently two human rabies mortalities, one in Iran and

the second in Brazil were reported from human handling rabies infected livestock (14, 15). The two veterinarians involved were not vaccinated against rabies and did not received post exposure prophylaxis.

There are several examples of long distance transmission translocation of rabies virus by human mediated animal movements and trade. Recently there was a number of reported translocations of infected bovine from Romania to Croatia (16), and in Ohio, USA (17). Translocation of dog rabies from northern Israel to Jerusalem (18) and to the center of the country was also reported (19).

In the present report, we describe for the first time rabies translocation by infected cattle from a dairy herd on the Golan Heights to two farms located in the western part of the Yezre'el Valley, as well as a rabies infected case in cattle in Israel. In addition to the economic damage caused to the dairy industry by rabies infection, the zoonotic aspects are discussed.

CASE REPORT

On September 29, 2013, two 11 weeks old calves one from a village Bet Zaid and the other from a village, Kfar Yehushua in the western Yezre'el valley showed clinical signs of change in behavior, salivation, difficulty in swallowing, vocalization and recumbence. Rabies was suspected and the two calves were diagnosed rabies positive by direct immunofluorescence assay (DFA) on the brain tissue, at the Israeli National Rabies Laboratory, Kimron Veterinary Institute (KVI), Bet Dagan, Israel.

In addition on November 1st 2013, two more calves, one 8 months old, from Kibbutz Ortal, and the second from Kfar Yehushua were rabies positive by DFA (Fig. 1).

A case investigation revealed that on August 26, a Jackal had entered an orchard near the Kibbutz Ortal it was shot and the carcass sent to National Rabies Laboratory (20). The Ortal dairy farm is one of the largest and most modern in Israel. Male calves are sold at a few weeks of age to other

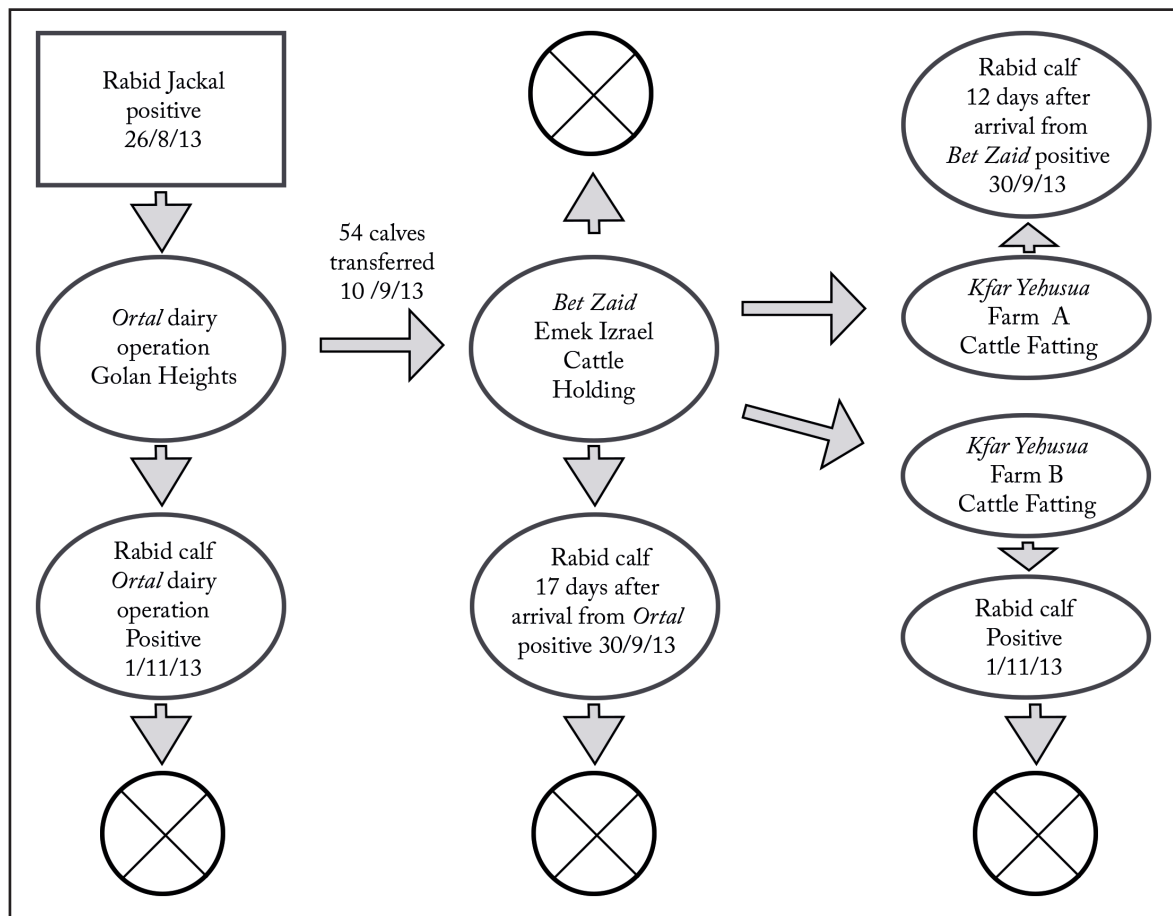


Figure 1: Succession of events following entry of a rabid jackal into Kibbutz Ortal dairy farm.

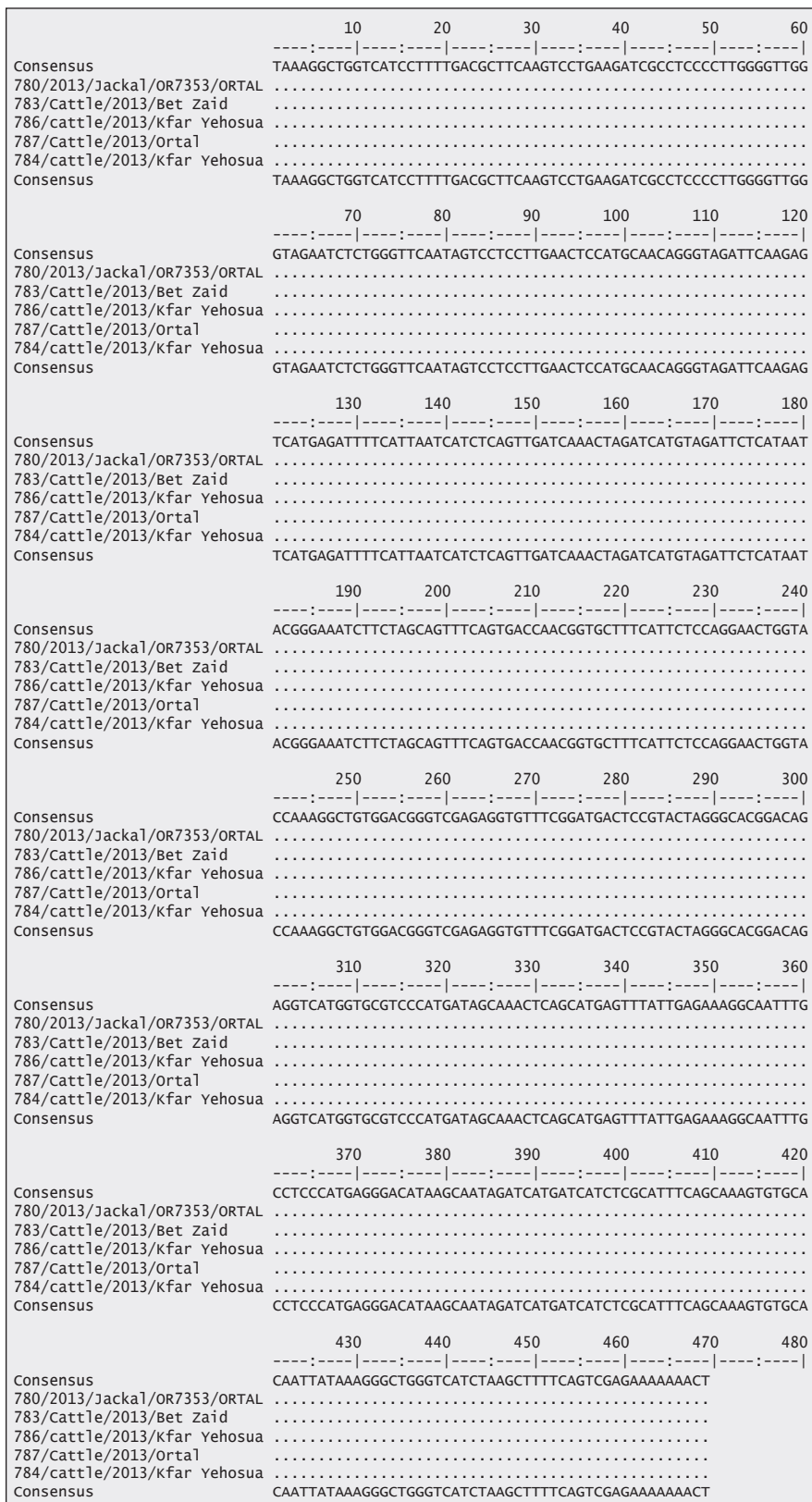


Figure 2: Comparison of 469 base pairs of the G-L intergenic fragments from the sequences of the four calves and the Jackal isolates.

locations throughout Israel for fattening. A group of 54 rabies unvaccinated calves was transported from Kibbutz Ortal on September 10, 2013 to a cattle holding farm in Bet Zaid and then distributed to several farms in Kfar Yehoshua.

Four calves and the jackal were diagnosed rabies positive by DFA. Diagnosis was confirmed by virus isolation in tissue culture, and its inoculation into suckling mice (21). Reverse transcriptase – PCR and direct sequencing were applied to a 469 base-pair (bp) G-L intergenic region fragment (19). A phylogenetic tree was constructed by the neighbor-joining method, with the distance calculated using the Kimura-2 parameter with the computer program MEGA, version 4.1 (22). The reliability of the phylogenetic groupings was evaluated using bootstrapping with 1000 replicates.

The molecular analysis showed that the viral sequence obtained from the 4 calves and the Jackal belonged to the V1 genetic variant (Fig.2). Following the diagnosis of rabies, post-exposure vaccination was administered to a group of 12 people, who had come into contact with the three calves and the jackal (Fig. 3).

DISCUSSION

Rabies is endemic in Israel and since 2004 stray dogs were found to be the main reservoir and transmitter (7, 10). However the ORV program of wildlife eliminated the fox rabies variants V1 to V4 from almost all rural areas in Israel. Nevertheless, there is still incursion of fox genetic variants V1 across the borders with neighboring countries. The genetic variant V1 caused mortality of 11 cattle, 2 sheep and 2 horses during the last 12 year on the border but was never detected in the Yezre'el valley region (Fig. 3).

Based on molecular and epidemio-

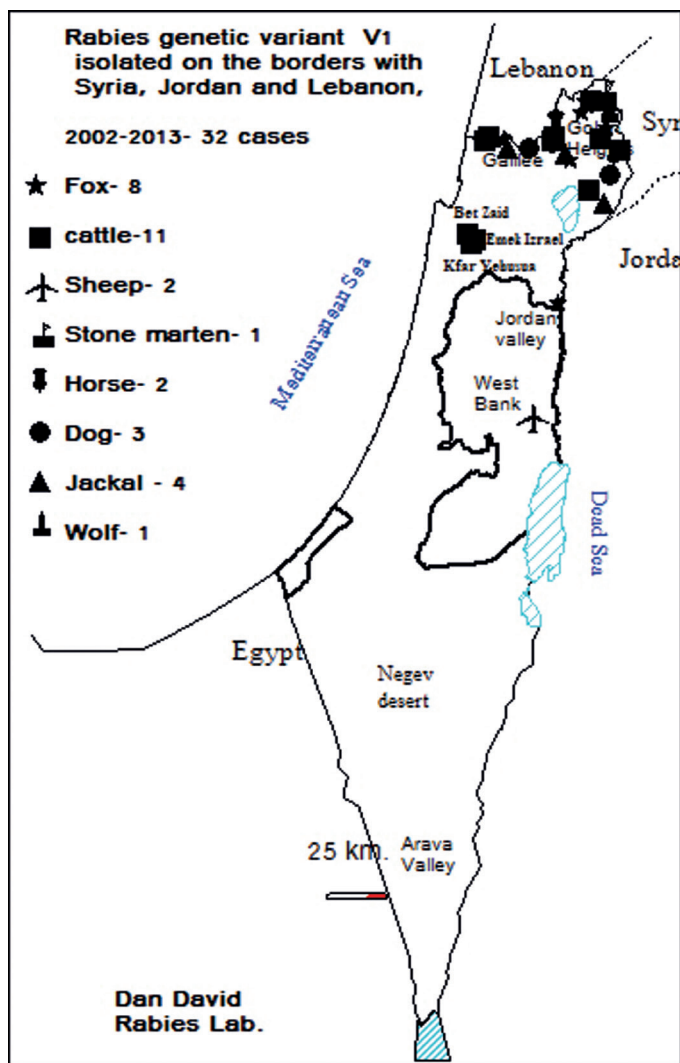


Figure 3: Map of Israel showing the area of northern Israel where 32 rabies virus belonging to the VI genetic variants were isolated during 2002 through 2012 on the borders with neighbors countries; the three positive calves isolated in Emek Yezre'el the Jackal and the fourth calf in Kibbutz Ortal.

logical analysis the 4 calves reported here were most likely bitten by the rabid Jackal. We therefore assumed that the calves were infected by the rabid jackal that had entered Kibbutz Ortal. This notion is supported by the chain of events described above and the identical molecular findings in the infected calves and Jackal.

The incubation period of rabies virus in cattle varies from 20 to 165 days (23). In our case the period of incubation was between 1 to 3.5 months. Various sanitary measures were implemented in Ortal and two farms in Emek Yezre'el as a result of this case: quarantine of cattle at the Ortal dairy farm

and quarantine and vaccination of all the calves at the two farms in Emek Yezre'el.

Vaccination of cattle is not mandatory in Israel however, this case illustrates the importance of the current recommendation of the Israeli Veterinary Services and Animal Health to vaccinate cattle in rabies areas, where a high risk exists of rabies-infected wildlife penetrating its borders.

ACKNOWLEDGEMENTS

The authors thank the veterinary officer of Afula district, for his help. The authors are indebted Dr. Abed Hamaysi for providing information about the cases.

REFERENCES

- Horton, D.L., Ismail, M. Z., Siryan, E.S., Wali A.R.A., Ab-Dulla H.E., Wise E., Voller K., Harkess, G., Marston, D.A., McElhinney, L.M., Abbas, S.F. and Fooks, A.R. Rabies in Iraq: Trend in human cases 2001-2010 and characterization of animal rabies strains from Bagdad. PLOS Neg. Trop. Dis. 7:e2075, 2013.
- Johnson, N., Black, C., Smith J., Un, H, McElhinney, L.M., Aylan, O. and Fooks, A. R.: Rabies emergence among foxes in Turkey J. Wildl. Dis. 2003; 39: 262-270, 2003.
- Al-Qudah, K.M., Al-Rawashdeh, O.F., Abdul-Majeed, M. and Al-Ani, F.K.: An epidemiological investigation of rabies in Jordan. Acta. Vet. (Beogr) 47: 129-134, 1997.
- Bizri, A.R., Alawieh, A., Ghason, N. and Musharrafeh, U. Challenge facing human rabies control: The Lebanese experience. Epidemiol. Infect. 125: 1-9, 2013.
- Nadin-Davis, S.A., Simani, S., Armstrong, J., Fayaz, A. and Wandeler, A.I.: Molecular and antigenic characterization of rabies viruses from Iran identifies variants with distinct epidemiological origins. Epidemiol. Infect 131:777-790, 2003.
- Faizee, M., Hailat N.Q., Ababneh, M.M., Hananeh W.M. and Muhaidat, A. Pathological, immunological and molecular diagnosis of rabies in clinically suspected animals of different species using four detection technique in Jordan. Transbound. Emerg. Dis. 59:154-164, 2012.
- Shimshony, A. Epidemiology of emerging zoonoses in Israel. Emerg Infect Dis. 3, 229-238. 1997.
- Yakobson, B.A., King, R.J., Amir, S., Dveres, N., Sheichat, N., Rotenberg, D., Mildenberg, Z., and David, D. (2005). Rabies vaccination programme for red fox (*Vulpes vulpes*) and Golden Jackals (*Canis aureus*) in Israel (1999-2004). Dev Biol. 125,133-140.
- David, D., Dveres, N., Yakobson, B.A. and Davidson, I.: Emergence of dog rabies in the northern region of Israel. Epidemiol. Infect. 137:544-548, 2009.
- David, D. and Yakobson B. A.: Dogs serve as reservoir and transmit rabies in Israel. Is history repeating itself? Isr. J. Vet. Med. 66:3-8. Review, 2011.
- David, D., Hughes, G.J, Yakobson, B.A., Davidson, I., Hu, N.H., Ayalon, O., Kuzmin, I.V. and Rupprecht, C.E.: Identification of novel canine rabies virus clades in the Middle East and North Africa. J. Gen. Virol. 88: 967-98, 2007.

12. David, D., Yakobson, B.A., Smith, J.S. and Stram, Y.: Molecular epidemiology of rabies virus isolates from Israel and other Middle and Near Eastern countries. *J. Clin. Microbiol.* 38, 755-762. 2000.
13. Vos, A., Un, H., Hampson, K., De Balogh, K., Aylan, O., Freuling, C.M., Muller, T., Fooks, A.R. and Johnson, N.: Bovine rabies in Turkey: patterns of infection and implications for costs and control. *Epidemiol. Infect.* 2013.
14. Simani, S., Fayaz, A., Rahimi, P., Eslami, N., Howeizi, N. and Biglari, P.: Six fatal cases of classical rabies virus without biting incidents, Iran 1990-2010. *J. Clin. Virol.* 54:251-254, 2012.
15. Brito, M.G., Chamone, T.L., Silva, F.J., Wada, M. Y., Miranda, A.L., Castilho, J.G., Carrieri, M.L., Kotait, I. and Lemos, F.L.: Antemortem diagnosis of human rabies in a veterinarian infected when handling a herbivore in Minas Gerais, Brazil. *Rev. Inst. Med. Trop. Sao Paulo*, 53:39-44, 2011.
16. Lojki, I., Bedekovic, T., Cac, Z., Lemo N. and Cvetnic, Z.: Clinical rabies in cattle imported into Croatia. *Vet. Rec.* 172: 22-23, 2013.
17. Chipman, R.B., Cozzens, T.M., Swiff, S.A., Biswas, R., Plumely, J., O'Quin, J., Algeo, T.P., Rupprecht, C.E. and Slate, D.: Costs of raccoon rabies incidents in cattle herds in Hampshire county, west Virginia, and Guernsey County, Ohio. *JAVMA* 243:1561-1567, 2013.
18. David, D., Dveres, N., Davidson, I., Yagil, J., Dvorkin, Z. and Oved, Z.: Geographic Translocation of Dog Rabies by Tourism. *Israel. J. Vet. Med.* 67: 139-142. 2012.
19. David, D., Yakobson, B.A., Gershkovich, L. and Gayer, S.: Tracing the movement of an Israeli dog by viral analysis. *Vet. Rec.* 155: 496-497, 2004.
20. ProMed, 2013. Rabies Animal – Israel (03): North bovine, Jackal, human exposure. Archive Number: 20131002.1980716. 3 October 2013.
21. David, D., Yakobson, B.A., Rotenberg, D., Dveres, N., Davidson, I. and Stram, Y.: Rabies virus detection by RT-PCR in decomposed naturally infected brains. *Vet. Microbiol.* 87: 111-118, 2002.
22. Kumar, S., Tamura, K. and Nei, M.: Integrated Software for molecular evolutionary genetics analysis and sequence alignment briefings in *Bioinformatics* 5, 150-163, 2004.
23. Hudson, L.C., Weinstock, D., Jordan, T. and Bold-Fletcher, N.O.: Clinical feature of experimentally induced rabies in cattle and sheep. *J. Vet. Med.* 43:85-95, 1996.