

Old diseases for new nightmares: distemper strikes back in Italy

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Summary

This article analyses the distemper outbreak that affected the population of Apennine wolves (*Canis lupus*) in Italy during 2013. Distemper, as rabies, is a well-known viral infectious disease that concerns the canine population worldwide and represents a threat for wild species too. Implementation of vaccination and legislation for compulsory vaccination strategies should be achieved in areas with endangered wild species.

Vecchie malattie per nuovi incubi: il cimurro colpisce ancora

Parole chiave

Abruzzo,
Cane,
Cimurro,
Italia,
Lupo appenninico,
Vaccinazione.

Riassunto

L'articolo descrive il focolaio di cimurro che, nel corso del 2013, ha coinvolto la popolazione di lupo appenninico (*Canis lupus*) presente principalmente nel Parco Nazionale d'Abruzzo, Lazio e Molise. Il cimurro, al pari della rabbia, è una malattia virale estremamente nota per la sua patogenicità nei confronti della popolazione canina mondiale e rappresenta una seria minaccia per i carnivori selvatici a rischio di estinzione. In relazione a quanto riportato è auspicabile un miglioramento delle strategie vaccinali attualmente in vigore che preveda l'obbligatorietà della vaccinazione dei cani domestici presenti in prossimità di aree con animali selvatici suscettibili alla malattia.

Throughout its history mankind has been fascinated and scared at the same time by novelties. The printing revolution, nuclear power, television, space race and the Internet offer all good examples of novel tools or achievements that definitely improved our life style and which, all at once, posed the need for new forms of control and management. Similarly, the emergence of novel pathogens and diseases such as avian and swine flu, severe acute respiratory syndrome (SARS), mad cow disease (BSE), West Nile disease (WNV), Middle east respiratory syndrome (MERS) and the entire complex of microorganisms involved in food-borne illnesses, attracted the global attention upon new biological threats and upon the pursuing of innovative prevention strategies. A vast amount of money has been invested worldwide to study and face novel diseases that in the majority of cases have their biological reservoir in wild and domestic animals. The One World One Health program, whose philosophy promotes collaboration and sharing expertise between the several actors operating at

the human-animal-environment interface, offers in this case a paradigmatic example. Although the research on these emerging pathogens gave brilliant outcomes in terms of control and prevention, ancient diseases affecting humans and animals still do exist. We should keep in mind that only 2 (viral) diseases have been so far eradicated from earth: smallpox in humans and rinderpest in cattle (Mariner *et al.* 2012), while several other well-known pathogens still circulate. Rabies, for instance, still kills humans. This is an ancient disease well-known to man since ever, it is probably one of the oldest disease ever recorded. The word rabies comes from the Sanskrit 'rabhas' which means 'acting ferociously'. The Greek used to call this tremendous infection *Lyssa* which stays for 'mad, furious'. Preventive strategies were taken already at the time of Babylon: biting dog responsible for rabies transmission to a man resulted into a heavy fine for its owner (Dunlop and Williams 1996). To these days rabies is still a major threat for public health, and governments should

implement measures to prevent its diffusion. In fact, rabies occurs in more than 150 countries and nearly 60,000 people die every year because of it, mostly in Asia and Africa (Knobel *et al.* 2005). According to the World Health Organization (WHO)¹, 40% of people who are bitten by suspect rabid animals are children under 15 years of age and dogs represent the source of the vast majority of human rabies deaths. Fortunately, an effective vaccine to prevent rabies does exist for both humans and dogs. As stray and unvaccinated dogs are the primary source of rabies for man, strong intervention to fight feral dogs, mass vaccination of both dogs and humans and upgrading the availability of post-exposure prophylaxis (PEP) must be implemented and pursued in developing countries.

Besides rabies, many other infectious diseases of domestic animals keep causing headaches to veterinarian and diagnosticians. One of these is a disease called distemper, which affects primarily dogs. Rabies and distemper share some common grounds: dogs are recognized as the main reservoir of both diseases and they are both related to wildlife. However, the impact on public opinion is quite different, as the global attention usually devoted to rabies becomes worthless when it comes to distemper, whose importance remains confined on a regional scale and to animal health. However the 2 diseases might be connected when considered from the preventive approach point of view. Besides dogs, distemper affects a large number of carnivores as well, both in captivity and the wild, and it is transmitted mainly through direct contact. Distemper is a well-known disease too, in the past it was known as *Distemper* in the UK, *morve* or *maladie des chains* in France and *Hundestaupe* or *Hundeseuche* in Germany. It is not documented from ancient times as rabies, as it is believed to have invaded Europe much more recently, being it imported from Peru into Spain during the 17th century (Blancou 2004). In 1764, distemper made the first appearance in Italy and since then it has been responsible for epidemics within the domestic dog population. This is a highly contagious and severe systemic disease frequently involving the respiratory, gastrointestinal and nervous systems caused by canine distemper virus (CDV). It is very similar to measles virus of humans and rinderpest virus of ruminants; indeed they all belong to the *Morbillivirus* genus that forms a serologically closely related group within the family *Paramixoviridae* (Appel 1987, Barrett 1999, Martella *et al.* 2008). To better represent the evolution of the currently circulating CDV strains, a cluster classification has

been proposed based upon the genetic relatedness of the haemagglutinin (H) encoding gene. When an unprotected dog becomes infected with distemper virus, it is doomed to succumb in the large majority of cases. It is therefore an important pathogen to deal with, especially if we consider that during the last 3 decades, a large number of CDV detection in free-living and captive wild animals has been reported. Thus, CDV represents an important conservation threat too. Renovate attention upon CDV arose in Italy during winter/spring 2013, as an epizootic occurred in dogs in the Abruzzo and Apulia regions (Di Sabatino *et al.* 2014). Interestingly, the novel CDV outbreak caused for the first time an epizootic among the population of Apennine wolves (*Canis lupus*) living mainly in the area of the National Park of Abruzzo, Lazio and Molise (PNALM) and in other wild species including foxes (*Vulpes vulpes*) and badgers (*Meles meles*).

Phylogenetic analysis conducted using H gene sequences revealed that the strains involved in the distemper outbreak of Apennine wolves cluster in the Arctic lineage of CDV. Strains belonging to this lineage were demonstrated for the first time to cause disease in wildlife animals. Previous studies proved that at least 3 CDV lineages were circulating in Italy including Europe-1, Europe Wildlife and Arctic lineages. Europe-1 lineage is commonly found in domestic dogs all-over European countries; Europe Wildlife lineage encloses CDV strains detected in wild animals and domestic dogs in Hungary. Unlike Europe-1 and Europe Wildlife, CDV strains of the Arctic lineage were detected only in domestic dogs in Italy, Hungary and North America. They are called Arctic as they were firstly identified in the susceptible population of the Arctic ecosystem. Therefore, the presence of this lineage in wolves definitely represents a novelty. Though, which was the source of infection for wolves and why CDV spread so rapidly affecting a large number of animals? To answer this question we should consider a plethora of factors including:

- a. several cases of clinical distemper in unvaccinated domestic dogs were reported to the veterinary authorities;
- b. the number of naïve dogs was extremely high meaning that vaccination was not carried out properly in the previous years;
- c. the presence of wolves nearby villages, urban roads and farms is a common finding in the Abruzzo region; in addition transhumance with shepherd dogs is commonly practiced in proximity of places where wildlife exists, scenario that likely enhances the risk of direct contact between dogs and wolves;
- d. exceptional delay of the spring season.

¹ WHO. 2013. WHO Expert Consultation on Rabies. Second report. *World Health Organ Tech Rep Ser*, **982**, 1-139, http://www.fao.org/fileadmin/templates/faovn/files/Administration/ECTAD/Rabbies_report.pdf.

We were able to trace distemper back to summer 2012 in dogs, prior to the epizootics in wolves, and molecular investigation revealed that CDV strains of the Arctic lineage were behind it. Thus, this scenario suggests a spillover of virus from dogs to wolves. The virus spread extensively as the population immunity was very low, while this can be reasonable and acceptable within the wildlife population, this is not a suitable explanation for the domestic dogs, which need to be vaccinated and protected. Only in this way the population immunity is high enough to keep CDV infection under control, so that only sporadic cases may occur. Although the high genetic variation of the H gene raises interrogatives regarding the efficacy of the CDV strains currently used for the attenuated vaccines production (Martella *et al.* 2006), vaccination remains the compulsory preventive measure for dogs. As for rabies, vaccination has been shown to be highly effective, and for CDV, long lasting if carried out properly.

Thus, in order to prevent future and potential devastating distemper outbreaks in the wild population, vaccination strategies should be implemented particularly among the dogs living in rural areas and dogs housed in local kennels. The main concern during the 2013 distemper outbreak was the possibility of CDV transmission to the Marsican brown bear (*Ursus arctos marsicanus*). Approximately, 40 bears (95% CI: 37-52%) live in the PNALM and CDV was previously shown serologically to circulate in the Marsican brown bear of the park (Marsilio *et al.* 1997). Since the Arctic lineage represents a new viral introduction into a naïve ecosystem, it is not possible to rule out that the virus may mutate and potentially increase the chances of expanding its host range to include the bear and cause clinical disease. In this respect, fighting the uncontrolled trading of low cost pets from Eastern Europe and to feral dogs will be

instrumental to control the spread of the disease. Furthermore the implementation of surveillance/vaccination strategies and further studies, regarding antigenic mapping of CDV strains circulating in the susceptible population, are warranted in order to prevent the loss of endangered wild species and vaccine breakthrough events.

In conclusion, in the era of genome manipulation by reverse genetics and next generation sequencing, in the era in which we are able to identify single amino acids to be crucial for pathogenesis and virulence, in the era of recombinant vaccines, humans and animals still suffer from old diseases which cause awful deaths in the case of rabies or conservation threat in distemper infection. Effective vaccines exist, nonetheless these diseases still keep killing. Why is this happening? There is only one simple answer: human habits. Human habits including poor planning strategies are responsible for it. Massive preventive strategies against rabies must be implemented and sustained in poor countries and compulsive vaccination in domestic and shepherd dogs against distemper must be made compelling by law in areas where endangered wild species live. While indigent population cannot afford the vaccine cost (from 7–20 USD in most low-income countries) or PEP (in high throughput clinics use of intradermic regimens can reduce costs to just 60 USD/death averted), the international community must implement strategies aimed to reduce the excessive number of children infected with rabies (Hampson *et al.* 2008). Rabies can only be eliminated through intervention in the animal reservoir (Hampson *et al.* 2009) and this is likely to be the most cost-effective way of averting human rabies deaths in the long-term (Zinsstag *et al.* 2009). It is then clear that veterinarians must occupy a central role in the management of such important infectious diseases with an obvious animal origin.

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