

Monitoring for the possible introduction of Crimean-Congo haemorrhagic fever virus in Italy based on tick sampling on migratory birds and serological survey of sheep flocks

1. Introduction

Crimean-Congo haemorrhagic fever (CCHF) is one of the most widespread tick-borne diseases, with human cases occurring in Africa, Asia, Eastern Europe and the Middle East (EFSA, 2010). It is considered “emerging” at a global scale (Messina et al., 2015) and evidence of this is that CCHF autochthonous human cases were recently reported for the first time in September 2016, in Western Europe (ECDC, 2016), several thousand kilometres westward respect to the nearest endemic areas. CCHF is caused by a virus (CCHFV) of the *Orthonairovirus* genus, family *Bunyaviridae*, which is transmitted by several tick species of the *Ixodidae* family, especially those of the *Hyalomma* genus (Horak et al., 2001). *Hyalomma* spp. are two-host ticks, moulting from larva to nymphs while attached to their first host, a small mammal or a ground dwelling bird (Randolph and Rogers, 2007). The ticks can remain attached to the primary host for a maximum of 26 days, which in the case of migratory birds, allows them to be transported even over long distances (Hillyard, 1996) that is a well-documented occurrence in many European countries (Molin et al., 2011; Jameson et al., 2012; Mancini et al., 2013). The species *Hyalomma marginatum* is considered in Europe as the most relevant CCHFV vector (Hoogstraal, 1979) and infection in tick populations is maintained by both trans-stadial and trans-ovarial transmission. Humans are infected either through tick bites or due to direct contact with infected blood of a mammalian host (Gale et al., 2011).

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CCHFV antibodies were detected in many wild and domestic animals, such as European hare (*Lepus europaeus*), house mouse (*Mus musculus*), cow, goat, sheep, donkey, horse, and pig (Nalca and Whitehouse, 2007). Although CCHF in livestock is generally subclinical, domestic ruminants may become reservoirs because of virus transmission from feeding adult ticks in rural environments which poses a high human health risk due to possible direct transmission (Ozkol, 2000; Gale et al., 2010). Despite this, they can act as sentinels for the arrival and/or circulation of CCHFV especially in non-endemic areas (EFSA, 2010). In fact, by the time CCHF human cases are diagnosed, this would represent the tip of an iceberg with underlying ongoing enzootic cycles that more or less involve different mammal host species, as stated by Randolph and Ergonul (2008).

CCHFV can spread over long distances and potentially be introduced in new areas, transported by vectors attached to migratory birds flying thousands of kilometres during their spring migration from current endemic areas such as in those south of the Sahara, Greece and Turkey (Karti et al., 2004; Papa et al., 2008). Several bird species breeding during summer in Europe fly back in autumn south of Sahara. It is estimated that 2.1 billion song and near passerine birds arrive each spring in Europe (Hahn et al., 2009). On these bases, the risk of CCHFV introduction by this route is considered possible for many countries of Western Europe (Gale et al., 2010) in which naïve populations of the vector are already present (Mild et al., 2010). In view of this, several European countries are in constant alert of the possible arrival of CCHFV, albeit many authors in the last years have downsized the effective CCHFV risk introduction via migratory birds carrying infected ticks (EFSA, 2010; Gale et al., 2010; Gale et al., 2011; Estrada Peña et al., 2011). In most parts of Europe, where *H. marginatum* is permanently resident, spring temperatures are not sufficiently high for nymphs arriving on migratory birds to moult into adults (Gray et al., 2009). Moreover, Gale et al. (2011) defined that the probability of arrival in Europe of an infected nymph on a migratory bird is 10^{-4} , even if the author does not relate this data to a time interval. Therefore, every spring the probability of an infected nymph arriving on a bird is very low i.e., 1:10000. Nevertheless, introduction of CCHFV infected ticks from Africa through this route was considered the possible explanation of virus recovery in Turkey in 2002 (Leblebicioglu et al., 2014) and in Spain in 2010 and 2016 (Estrada Peña et al., 2012; ECDC, 2016). Moreover, due to the continuing climatic changes occurring even in the Mediterranean, this region could become permissive for bird transported infected nymphs of the

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genus *Hyalomma*, to moult on arrival into adults ([Gray et al., 2009](#)) which would then potentially infect their mammal hosts with CCHFV.

Adult ticks carried on imported livestock ([Jameson and Medlock, 2009](#)) could represent another introductory route of CCHFV into European states; as a matter of fact, thousands of meat horses are annually imported from Eastern Europe to Italy.

In this scenario, an innovative approach was adopted to monitor CCHFV introduction and circulation in Italy, targeting two epidemiological phases of the virus:

1)

introduction: monitored by tick sampling on migratory birds to evaluate the arrival of potential CCHFV vectors in Italy from endemic areas of Africa and Eastern Europe. This would provide data on the relative prevalence of *Hyalomma* spp. on migratory birds arriving from endemic areas, considered a prerequisite for assessing the probability of infected ticks entering a country ([Gale et al., 2010](#)), as strongly advised by [Jameson et al. \(2012\)](#) for areas with resident *Hyalomma* populations;

2)

circulation: monitored by a serological survey conducted on sheep flocks aimed at detecting CCHFV circulation in coastal areas of Latium and Tuscany, regions of Central Italy, where migratory birds stop over and where the tick vector is present. Indeed, the serological CCHFV monitoring of susceptible animal populations is considered as a valid indicator for the spread of the virus in a territory ([Schuster et al., 2016](#)).

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Prova ad suggerire dei possibili miglioramenti per l'introduzione di quest'articolo scientifico.

Puoi utilizzare le seguenti domande per analizzare il testo e proporre quindi dei suggerimenti:

- Sono state fornite al lettore adeguate informazioni riguardo le tematiche/l'oggetto dello studio?
 - o La malattia è stata descritta molto brevemente, mancano info riguardo i meccanismi d'infezione (come avviene il ciclo? es. Quali zecche sono implicate? Quali specie domestiche sono sensibili? Non viene detto che è una zoonosi -> l'uomo è un ospite)
 - o epidemiologici (la malattia dove è diffusa? Ci sono stati casi nelle aree di interesse?)
- Sono state fornite adeguate informazioni riguardo le conoscenze finora disponibili sull'argomento?
 - o Mancano le references in molti casi..
 - o Mancano molti dati quantitativi (probabilità di introduzione?)
- Sono state fornite adeguate informazioni riguardo la problematica sottoposta ad indagine?
 - o La problematica è tutto sommato chiara: sembra che la probabilità di introduzione in Europa del CCHFV sia bassa ma non è chiaro se possa arrivare in Italia
- Lo scopo dello studio è stato adeguatamente dichiarato?
 - o Sì ma è molto stringato... valutare l'introduzione e la circolazione: che significa?