

CENTENARY REVIEW

Impact of ticks and tick-borne diseases on agriculture and human populations in Europe

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INTRODUCTION

Ticks are considered in Europe to be the most important arthropod group responsible for vector-borne diseases in humans, while in the tropics mosquitoes take over this position with ticks being the second most important. Over the last decade, vector-borne diseases have proliferated within Southern Europe (Blue tongue and West Nile viruses, both mosquito-borne diseases) while human ehrlichiosis (a tick-borne disease) has increased dramatically in Eastern Europe.

Human and animal health problems related to ticks have been known for a long time. A century ago, this journal published, in its first issue, a paper on the importance of ticks in the UK (Wheler 1905) and retrospective studies proved that *Borrelia burgdorferi* s.l. (the Lyme Disease agent) had been in the UK since at least 1897 (Hubbard *et al.* 1998). With changing climatic conditions, it is likely that tick populations, and tick-borne diseases, will assume a growing importance in the future.

Ticks are not only blood feeders but they are also able to inject pathogens (bacteria, viruses, protozoa) or toxins while taking a blood meal. This review will focus on the impact of ticks and tick-borne diseases (TBD) on livestock, wildlife, pets and human populations, highlighting recent changes in the epidemiological characteristics of some TBD in Europe. Readers interested in other ectoparasites are referred to a recent review from Colebrook & Wall (2004).

TICK ECOLOGY

Ticks are arthropods (*Acari*: *Ixodida*: *Ixodidae*, *Argasidae*) closely related to the mite group. They are obligatory blood feeders and are divided usually into two groups: the *Ixodidae* (hard-shell ticks) and the *Argasidae* (soft ticks). Larvae will hatch from eggs

and, after feeding, will moult into nymphs and then, after another meal, will become either a male or a female adult tick. Some tick species spend their entire life cycle on the same host while others will change hosts for each meal. They can starve for months and will seek and attack hosts if they can sense them around. Typically they will wait at the top of a grass leaf and will jump onto a potential host. Like other blood feeders, they need to prevent the host immune system from clotting the blood after they have pierced the host blood vessels. They expel anti-coagulant products and, like mosquitoes, some local anaesthetics. For a review on the immune mechanisms involved during tick feeding, see Wikel (1996). However ticks will feed during a period of days while mosquitoes will take their meal in a matter of minutes.

Ixodes ricinus needs to have a special place in this review as it is the most problematic tick in Europe. *Ixodes ricinus* is a three-host tick and therefore will feed three times on different hosts; mainly rodents as a larvae and bigger animals (and sometimes unfortunately humans) at nymph and adult stages.

TICK-BORNE DISEASES IN EUROPE

Many tick-borne diseases are now present in different parts of Europe and, due to companion animal, livestock and human movements becoming easier because of the enlargement of the European Union, it is important to know the situation in neighbouring countries. The major tick-borne diseases in Europe are Human Granulocytic ehrlichiosis (HGE), Human monocytic ehrlichiosis (HME), babesiosis, theileriosis, tularaemia, Lyme disease, tick paralysis, Mediterranean spotted fever, African swine fever and tick-borne encephalitis (TBE) (Criado-Fornelio *et al.* 2003a; Amiel *et al.* 2004).

Ixodes ricinus is the major tick in Europe in terms of the number of diseases which can be carried and transmitted. In Scandinavia it is the commonest

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tick for *Anaplasma phagocytophilum* (HGE agent) and for Lyme disease (*Borrelia burgdorferi* s.l. agent), also well-known in Scotland. For a review on Lyme disease see Stanek & Strle (2003). It is also the vector of human babesiosis in France and tick-borne encephalitis in many Eastern European countries.

Rickettsia helvetica has been found in *I. ricinus* in Sweden with, as a proportion, 0.228 of Swedish military recruits training in an endemic area showing a four-fold increase in IgG titres after their training (Nilsson *et al.* 2005). This pathogen was also found in Danish patients (0.125) and in 0.04 of the ticks in the region (Nielsen *et al.* 2004).

HGE prevalence in Spanish *I. ricinus* ticks was between 0 and 0.25, and between 0.004 and 0.667 in adults and nymphs, respectively (Oteo *et al.* 2001).

INCIDENCE IN LIVESTOCK

Pigs in Southern Europe (mainly Spain and Portugal) are known to be exposed to African swine fever which can be transmitted by *Ornithodoros* (*Argasidae*) ticks. Horses are also exposed to piroplasmosis (attributable to *Theileria equi* and *Babesia caballi*) (see Criado-Fornelio *et al.* 2004) and also *Rickettsia rickettsii* and *Ehrlichia equi* (the latter being a member of the *Anaplasma phagocytophilum* cluster and also a zoonotic disease).

Cattle in Southern Europe are exposed to Theileriosis (*Theileria annulata* being the most pathogenic while *T. buffeli* is endemic in southern Italy) and up to five different tick-borne pathogens were found in carrier cattle in Italy (Georges *et al.* 2001).

Babesiosis is linked to a few *Babesia* species. Bovine babesiosis is a world-wide disease with around 400 million cattle at risk (Wright & Riddles 1989). *Babesia bigemina* and *Babesia bovis* (Hofmann-Lehmann *et al.* 2004) are important in tropical and subtropical countries with *Babesia divergens* being most important in Northern Europe. *Babesia divergens*, which was first described in British cattle (M'Fadyean & Stockman 1911), is also a zoonotic disease. The incidence of cattle babesiosis in France is around 0.004 (L'Hostis *et al.* 1995) and *B. divergens* has been isolated up to 9 months after an acute infection in some animals (Malandrin *et al.* 2004).

Timing to assess TBD incidence in cattle is very important, as some tick species can spread after the summer, and cattle babesiosis in Sicily mainly appears at the end of the summer when the *Ixodes ricinus* tick populations are also increasing (Georges *et al.* 2001).

Small ruminants also have their share of diseases transmitted by ticks such as Louping ill, Lyme disease (Ogden *et al.* 1997) anaplasmosis (*Anaplasma phagocytophilum* group) observed throughout Europe (Ogden *et al.* 2002b). Sheep, for instance, have been

well-known to be used by ticks such as *Ixodes ricinus* which feed on them to sustain their life cycle (Ogden *et al.* 2002c). Furthermore, the density of ticks on sheep can influence the immune reaction of the host and change the transmission characteristics of *Anaplasma phagocytophilum* from sheep to ticks (Ogden *et al.* 2002a). In Greece, evidence has been found of *Theileria ovis*, *Babesia ovis*, *B. motasi* and *B. crassa* infecting sheep and goats (Papadopoulos *et al.* 1996).

For a review on tick-borne hemoparasites in ruminants see Uilenberg (1995).

INCIDENCE ON WILDLIFE

Some wildlife animals are known to be dead-end hosts for tick-borne pathogens, meaning that they cannot transmit these to other ticks or other animals. This, in fact, reduces the risk of outbreaks and applies for the HGE agent in pheasants (e.g. Ogden *et al.* 1998). On the other hand, squirrels, pheasants, wild mice and bank voles are known to be reservoirs for Lyme disease (Craine *et al.* 1997; Korenberg *et al.* 2002; Hacinova *et al.* 2003), while anaplasmosis-positive ticks have been found on foxes (Sreter *et al.* 2004), European wild boar and Iberian red deer (de la Fuente *et al.* 2004). A recent study, tracking the host DNA in ticks to know on which host they had fed, highlighted the behaviour of some tick species and how they could pick up tick-borne pathogens such as *Borrelia afzelii*, *B. burgdorferi* s.s., *B. garinii*, *B. valaisiana* or *Anaplasma phagocytophilum* (Pichon *et al.* 2003).

'PET PASSPORT'

Even the recent UK 'pet passport' scheme has shown that ticks are still a real problem in Europe, as acaricide treatment is still a requirement for this scheme (with deworming). Dogs can be infected with babesiosis (*Babesia canis*, *B. microti*, *B. gibsoni*), ehrlichiosis (*E. canis*), anaplasmosis (*A. platys*) and rickettsiosis (*R. conorii*). Studies have also shown that dogs could be exposed to Lyme disease (May *et al.* 1991).

A few *Babesia* species have been isolated from dogs such as *B. canis* (Criado-Fornelio *et al.* 2003b), *B. gibsoni* (Criado-Fornelio *et al.* 2003c). The same authors also described, surprisingly, the presence of *Theileria equi* (well known in horses) in a Spanish dog (Criado-Fornelio *et al.* 2003b, 2004). A recent survey in Hungary showed the six main Ixodid ticks found on dogs (Foldvari & Farkas 2005).

HUMAN RISKS

A few mainly zoonotic tick-borne diseases in humans in Europe are epidemiologically important. For a

review paper on *Babesia divergens* see Zintl *et al.* (2003). Zoonotic babesiosis is widespread in Central Europe (Hunfeld & Brade 2004). A new *Babesia* species has been found in Italian and Austrian patients, which is not related to *B. divergens* (Herwaldt *et al.* 2003). More important is the rise of tick-borne encephalitis and human ehrlichiosis. TBE cases have increased dramatically in the last few decades and are well known in Eastern Europe, with a sharp rise in the 1990s and incidences as high as 15.7 and 13.6/100 000 inhabitants in Latvia and Slovenia, respectively. An International Scientific Working Group on TBE shows a membership of more than 0.5 from the new EU Member States. Human granulocytic ehrlichiosis (HGE), due to *Anaplasma phagocytophilum*, is in fact a multi-host pathogen known also as *Ehrlichia equi* in horses, *Ehrlichia phagocytophila* in cattle and small ruminants. The new taxonomy is now regrouping all these names under the *Anaplasma phagocytophilum* cluster.

In UK studies, farm workers showed a seroprevalence for Lyme disease, HME and HGE of 0.002; 0.002 and 0.15, respectively (Thomas *et al.* 1998). For these patients, there was not always a report of tick bites associated with this serology.

A study on forest workers in the region of Mid-Eastern Poland found that 0.457, 0.045 and 0.009 of the female, male and nymph ticks were PCR positive for *Anaplasma phagocytophilum*, with 0.206 of the forest workers showing a seroprevalence for this disease; furthermore 0.846 of this seroprevalent group also showed seroprevalence for anti-*Borrelia burgdorferi* antibodies (Tomasiewicz *et al.* 2004). Co-infection between *A. phagocytophilum* and *Borrelia burgdorferi* was also observed in an Italian study in 0.016 of forest workers (with 0.057 of these workers at risk showing antibodies against HGE, while the control group showed only a seroprevalence of 0.009) (Santino *et al.* 2004). TBE and HGE were also found in the same patient in Slovenia (Lotric-Furlan *et al.* 2005) and Ehrlichia and Lyme disease was found in the same Swedish patient (Bjoersdorff *et al.* 1999). HGE is also documented in Slovenia (Lotric-Furlan *et al.* 2003). For a review on TBD transmitted to humans, see Perez-Eid (2004).

CONTROL

There are two different approaches to control of TBD; either by controlling the tick proliferation or by treating against the transmitted pathogens. To eradicate ticks, the main control approach is by using acaricide products. However in a few years the EU will have banned some of these products and colleagues have reported acaricide resistance in ticks now for several years. Some interesting results were obtained by developing a vaccine against the

ticks, by inducing antibodies against the tick gut. Thus, when these arthropods blood feed they also ingest antibodies which can, with a complementary cellular response, attack the tick gut wall and lead to internal bleeding after the ticks have been feeding (Willadsen 2001). Good results have been obtained with vaccines raised against the *Boophilus microplus* tick which, unfortunately, is of little relevance in Europe. Against tick-borne pathogens, vaccination and/or the use of chemoprophylaxy can help to treat infected animals.

DIAGNOSTICS

Although some diagnostic tests are still using cell culture or smears (blood, lymph nodes, tick salivary glands), the majority are now using serological (detection of antibodies in the host) or molecular biology methods (detection of the pathogen DNA in the host sample). Surprisingly, sometimes authors are contrasting results from the two methods when they do not detect the same thing and are not focusing on the same infection time frame. Serological tests, being based on antibodies (which should be species-specific if possible to avoid cross-reactivity), will not give a positive reaction on the day of the infection as the host immune system needs a few weeks to produce these antibodies. An Immunoblot based on *Borrelia afzelli* antigen, used in a protein profile exposed to patient serum, showed a specificity of 0.96 for Estonian patients (Kisand *et al.* 2004). Serological studies in Croatia (Topolovec *et al.* 2003) claimed to find antibodies in patients against HGE, HME, Mediterranean spotted fever, Rocky Mountain spotted fever, murine typhus and *Borrelia burgdorferi*. However, it was also suggested that some results could be due to cross-reactivity between *Rickettsia typhi* (murine typhus agent) and *Rickettsia slovaca*.

On the other hand molecular biology techniques such as PCR (polymerase chain reaction, able to amplify artificially a DNA fragment thought to exist only in the pathogen) will reveal whether on the day of the test the host carries the DNA of the pathogen. Once again it is also important to mention that the presence of the pathogen DNA is not a proof that the pathogen is alive. Currently scientists are targeting increasingly the RNA, which is another nucleic acid but which, in contrast to the DNA, does not survive very long after the death of the parasite. For a review of molecular techniques used to detect tick-borne pathogens see Sparagano *et al.* (1999). Multiplex and simultaneous methods such as the reverse line blot hybridization have now been validated for different TBD; in dogs (Sparagano *et al.* 2003), in small ruminants (Bekker *et al.* 2002) and in cattle (Georges *et al.* 2001).

CONCLUSION

In some European countries the high incidence of tick-borne diseases in ticks, small mammals and deer does not match the small number of patients diagnosed with these diseases, for instance HGE. It has been pointed out that practitioners are not always aware of clinical symptoms related to tick-bite and TBD (Strle 2004).

Climatic changes have been associated with new vector-borne diseases arriving in Southern Europe (West Nile and Blue tongue viruses both transmitted by mosquitoes), with tick density increasing as demonstrated by the two-fold increase of TBE in the Czech republic after 1993 (Daniel *et al.* 2004).

The European Union will ban some acaricide products in the next few years, making tick control more difficult. The entry of new EU member countries, with higher national incidences of tick-borne diseases, could lead to the spread of TBD as

Border Inspection Posts (BPIs) have now been abolished between the 25 EU countries. New control methods are needed, and anti-tick vaccines have given good results in reduction of the tick burden on livestock animals, but to date for tick species from the tropics only.

The emergence or re-emergence of some vector-borne pathogens in Europe highlights the greater danger of outbreaks of these diseases in the near future, which could affect livestock, companion animals, wildlife or human populations. Recent publications have shown that *Argas arboreus* (*Argasidae* tick) could be involved in the transmission of the West Nile virus in Israel (Mumcuoglu *et al.* 2005) and that *Rhipicephalus sanguineus* (*Ixodidae* tick) could be a vector for canine visceral leishmaniasis (Coutinho *et al.* 2005).

It is to be hoped that the newly created European Centre for Disease Control (ECDC) will carefully monitor such diseases.

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