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INVITED REVIEW

Major tick-borne parasitic diseases of animals: A frame of references in Turkey

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Öz

Sevinc F, Xuan X. Hayvanların kene kaynaklı başlıca paraziter hastalıkları: Türkiye'de bu konuda yapılan çalışmalara genel bakış.

Abstract

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Keneler vasıtasıyla bulaşan paraziter hastalıklar dünya genelinde, özellikle dünyanın tropikal ve sup-tropikal iklim kuşağında yer alan bölgelerinde hayvancılığın gelişmesini ciddi boyutlarda kısıtlamaktadır. Ilıman ve sup-tropikal iklimin özelliklerine sahip olan Türkiye'nin toprak yapısı, iklim şartları ve mera kaynakları hayvansal tarım için uygun olup, bu durum aynı zamanda ülkenin hemen her bölgesinde parazitlerin konak ve vektörlerle olan ilişkilerinin devamlılığını destekler niteliktedir. Doğu ve Güneydoğu Anadolu bölgelerinde komşu ülkelerle olan coğrafik temas nedeniyle hayvan hareketleri ile ilgili düzenlemeler sınırlı olarak yapılmaktadır. Türkiye'de çiftlik hayvanlarının sayısı her geçen yıl azalma eğilimi göstermekle birlikte, tarımsal gayri safi milli hasılanın yaklaşık yüzde otuzu çiftlik hayvancılığı sektöründen elde edilmektedir. Çoğunlukla geleneksel metotlarla varlığını devam ettiren çiftlik hayvancılığında hayvanlar sıklıkla kene enfestasyonlarına maruz kalırlar. Bu nedenle Türkiye, kenelerle nakledilen paraziter hastalıklar yönüyle endemik bir ülkedir. Bu hastalıklar özellikle ruminantlarda hayvan sağlığı ve ülke ekonomisi üzerinde büyük etkiye sahiptir. Ekonomik önemi büyük olan başlıca kene kaynaklı paraziter hastalıklar; theileriosis, babesiosis ve anaplasmosisdir. Çiftlik hayvanlarında en sık karşılaşılan kan paraziti türleri ise *Theileria annulata, Anaplasma marginale, Babesia bigemina, B. ovis, B. equi* ve *B. caballi*'dir. Kan paraziti hastalıklarının kontrolünde yapılan uygulamalar genel olarak hastaların tedavisi ve kene mücadelesinden ibarettir. Aşı uygulaması sadece sığırlarda *T. annulata*'nın neden olduğu tropikal theileriosise karşı yapılmaktadır. Bu derleme Türkiye'de hayvanlarda kene kaynaklı paraziter hastalıklar konusunda yapılan epidemiyolojik çalışmaları bir araya toplayarak, bu hastalıkların Türkiye'deki durumu hakkında bilgi sunmak amacıyla hazırlanmıştır.

Anahtar kelimeler: Türkiye, kenelerle bulaşan hastalıklar, evcil hayvanlar

Tick-borne parasitic diseases constrain animal production throughout the world, mostly in tropical and subtropical regions. The topography, climate and pasture resources of Turkey which has the characteristics of temperate and subtropical climates are suitable for animal agriculture, and are favorable for the maintenance of the parasite-host-vector relationships in almost all regions of the country. The geographic situation limits the regulations on animal movements in the Eastern and Southeastern regions due to close contact with the neighbor countries. Turkey has a strong foundation for livestock resources. Approximately 30 percent of the agricultural gross domestic product is from livestock sector. Tick-borne parasitic diseases are endemic throughout the country, and have a great importance on economy and animal health, especially in ruminants. The major economically important tick-borne parasitic diseases of animals are theileriosis and babesiosis caused by protozoa, and anaplasmosis caused by rickettsiae. The most widespread hemoparasitic agents are *Theileria annulata, Anaplasma marginale, Babesia bigemina, B. ovis, B. equi* and *B. caballi.* The control of these diseases is mainly based on the treatment of sick animals and tick-control measurements. Vaccination is available for only tropical theileriosis caused by *T. annulata.* In this work, we reviewed the articles published in the national and international journals to collect the epidemiological data on the major tick-borne parasitic diseases of animals in Turkey.

Keywords: Turkey, tick-borne parasitic diseases, domestic animals.

Introduction

Turkey, located in the northern hemisphere between the 36° and 42° northern parallels and the 26° and 45° eastern meridians, has an important strategic location in the Mediterranean region, with her position like a land bridge between Europe and Asia continents. The topography, climate and forage resources of Turkey make her a very suitable ground for animal agriculture. The climate shows the features of the temperate and subtropical climates which exhibit favorable conditions for maintenance of the parasite-host-vector relationships. The regulations of animal movements are limited in the Eastern and Southeastern regions due to close contact with the neighbor countries geographically.

Management system is mostly extensive and traditional in ruminants. Most of the ruminants are usually grazed on pastures during the long period of a year, usually from early spring to late autumn. The traditional farms are mostly localized in the eastern regions. The new more specialized farms have commonly been established in the western regions. In recent years, although the government is granting various subsidies to sustain the sector, the traditional farming is decreasing due to high feed costs and restrictions in the access to pasture on common lands (Turkish Agriculture Industry Report 2010). All these factors associated on the geographical and climatic conditions, and animal management systems make the animals possible to exposure to various diseases.

Turkey's economy consists of modern industry, trade and agriculture sector. Because of the suitable climatic and geographical conditions, and rich soil sources, agriculture is one of the leading sectors in the Turkey's economy. Though the agriculture sector tends to decrease after the 1980s, it is still an important part of the economy. Turkey has a strong foundation for the livestock resources, and the share of livestock sector in the agricultural gross domestic product is around 30%. The main livestock products are poultry, beef and veal in Turkey. Small ruminants are the main livestock resource, with the highest share with a population of over 41 million in the total number of animals. The number of sheep constitutes 55.5% of the total number of animals; cattle 25.2%, goats 18.5% and buffalo 0.9%. Registered horses are only in the jockey clubs and state stud farms. In the data reported by the State Institute of Statistics in 2014, the numbers of horses were 131,497 (TurkStat 2015, Turkish Agriculture Industry Report 2010). The number of dogs is unknown because the dog registration is not compulsory, but it is thought that there are large numbers of stray dogs.

Tick-borne diseases cause major health and management problems in the farming sectors in the African, Asian and Latin American countries localized in the tropical and subtropical regions of the world. Turkey's geographical and climatic conditions and animal management systems encourage the occurrence of ticks and tick-borne diseases. The studies show that Turkey is an endemic country for tick-borne parasitic diseases. In Turkey, several tick-borne diseases including theileriosis, babesiosis, anaplasmosis, ehrlichiosis and hepatozoonosis have been recorded in domestic animals. In this review, the epidemiological studies conducted on the frequent tick-borne parasitic diseases including theileriosis, babesiosis and anaplasmosis are reviewed to state the importance of these diseases on animal health.

Ticks and Tick-Borne Diseases in Turkey

Until the present, thirty-two tick species in ten genera, including *Hyalomma, Rhipicephalus, Boophilus, Haemaphysalis, Dermacentor, Argas, Ornithodoros, Ixodes, Amblyomma* and *Otobius*, were identified in Turkey. The first six genera are most widespread throughout the country. The most common tick species are *Rhipicephalus (Boophilus) annulatus, R. sanguineus, R. bursa, R. turanicus, Hyalomma anatolicum anatolicum, H. anatolicum excavatum, H. marginatum, Haemaphysalis parva, H. punctata, H. sulcata* and *Dermacentor niveus*. The seasonal fluctuation of ticks depends on the tick genus, and it is spring, summer and autumn for *Rhipicephalus* and *Hyalomma* species; autumn, winter and spring for *Hemaphysalis, Dermacentor, Ixodes* and *Ornithodoros* species. The rate of tick infested-animals is usually higher than 20% of the animals in a herd (Aydin and Bakirci 2007, Ica et al 2007a, Ica et al 2007b, Sayin et al 1997a, Sayin et al 1997b, Sayin et al 2003a). Theileriosis, babesiosis and anaplasmosis have been well-recognized tick-borne parasitic diseases of animals for many years, and are still the most important diseases affecting livestock. Though the literature sources are not good enough to estimate the real size of the infections, the huge amount of the disease-specific drugs consumed in the pharmaceutical stores during the disease seasons in every year show the importance of these diseases on the animal health and economy.

Theileriosis

Bovine theileriosis

Among a number of *Theileria* species that infect cattle, *Theileria parva* and *T. annulata* are the most pathogenic and economically important species. In Turkey, the main tick-borne parasitic disease of cattle is tropical theileriosis caused by *Theileria annulata*. The disease causes high morbidity and mortality in cattle throughout the country. *T. annulata* is transmitted by ticks of the genus *Hyalomma*. Principal vector species are *Hyalomma detritum* and *H. anatolicum* anatolicum. The other *Hyalomma* species including *H. anatolicum excavatum, H. dromedarii*, and *H. marginatum marginatum* can also transmit *T. annulata*. Benign *Theileria* species *T. mutans* and *T. sergenti/buffeli/orientalis* were reported in cattle in different regions of Turkey (Aktas et al 2006a, Altay et al

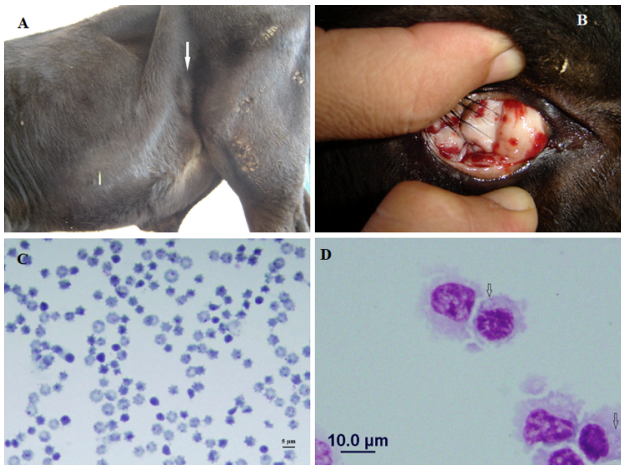

Figure 1. The signs of tropical theileriosis caused by *Theileria annulata*.
A: Swollen sub-iliac lymph node, B: Petechial hemorrhages in the eye mucosa, C. Pyroplasmic forms of *T. annulata* on the Giemsa-stained thin blood smears, D: Schizont forms in lymphoid cells. The pictures were taken from the clinical cases detected in the clinics of Faculty of Veterinary Medicine, Selcuk University.

2007b, Altay et al 2007c, Altay et al 2008b, Cicek et al 2009, Inci et al 2007, Sayin et al 2004).

Tropical theileriosis is more serious in pure breeds than those of domestic and cross-bred animals. The imported and unvaccinated cattle are most susceptible against to *T. annulata* infection, with mortality rates of more than 70%, while in cross-bred among indigenous cattle lesser than 45% (Inci et al 2007, Sayin et al 2003a). The disease is usually seasonal, being prevalent from May to September, with peaks in July. Acute theileriosis is characterized by fever, enlarged lymph nodes, petechial hemorrhages on mucosal membranes, anemia, decreased milk production, labored respiration, abortion, and death (Figure 1).

The combination of buparvaquon and oxytetracycline has currently been used drugs to treat the sick animals. The effectiveness of the treatment depends on the early diagnosis. In the cases of the parasitemia level is higher than 20%, anti-inflammatory and hematinic drugs have also been added to the treatment regime to support treatment. Blood transfusions are being necessary in very anemic animals. The disease control has been achieved with a live attenuated *T. annulata* schizont cell-culture vaccine produced by Ministry of Agriculture since 1982 (Sayin et al 1990, Sayin et al 1997a, Sayin et al 2003a, Sayin et al 2004, Sayin et al 2004), however some clinical reactions and death cases due to the disease were reported in the vaccinated cattle (Aysul et al 2008, Inci et al 2002).

Under the field conditions, the major important factors affecting the severity of clinical infections are animal breed, vaccination status and management system. In an epidemiologic study conducted in the Cappadocia area which is comprising the major part of the Central Anatolia Region, a total of 554 cattle, 62% of which was vaccinated against tropical theileriosis, were followed up for the occurrences of clinical theileriosis from 1999 April to 2001 November including the three disease seasons. The results revealed that the morbidity and mortality rates were higher in unvaccinated animals than the vaccinated ones, in grazed animals than the semi-grazed ones, and in the pure breeds than the cross or local breeds. The number of acute cases was 156 (27.61%), and 86 of them died suffering from tropical theileriosis. The total economic losses because of the infection were estimated as $598,133 USD during the survey in the Cappadocia area (Inci et al 2007).

The diagnosis of theileriosis is based on microscopic examination of thin-blood and lymph smears. *T. annulata* piroplasm forms have been detected at the rates ranging from 2.3 to 60.5% of cattle by microscopic examination of Giemsa-stained blood smears in different parts of Turkey (Dumanli et al 2005, Inci et al 2007, Inci et al 2008). The serological surveys performed by Indirect Fluorescent Antibody test (IFAT) showed that the sero-positivity rate of *T. annulata* infection was ranging from 10 to 90%. The PCR and RLB analysis revealed that the prevalence of *T. annulata* varied between 18.1 and 61.2% in cattle and 12.6 and 46.9% in tick samples (Vatansever and Nalbantoglu 2002, Dumanli et al 2005, Aktas et al 2004, Aktas et al 2006a, Ica et al 2007a, Ica et al 2007b, Sevgili et al 2010). Most of the studies are usually performed in the Eastern and Central Anatolia Regions of Turkey, with high prevalence rates of Theileria infections. The results from the Black Sea Region, which is localized on the north of Turkey, show that the prevalence of hemoparasites was lower than those of above regions (Altay et al 2008b).

The epidemiological data on the tick vectors of bovine theileriosis was obtained from the studies conducted under the field and laboratory conditions. Inci et al (2008) determined *T. annulata* infection at the rate of 17.49% in the salivary glands of vector tick *H. a. anatolicum* by microscopic examination. Sayin et al (2003b) investigated the development stages of *T. annulata* in four *Hyalomma ticks (H. a. anatolicum, H. a. excavatum, H. detritum and H. m. marginatum)* fed on the experimentally infected calves with *T. annulata*, and they examined the roles of the tick species and sex on the intensity of *T. annulata* infection in tick salivary glands. The infection rates were almost equally high in all tick species. The mean intensity of the infection was higher in females than male ticks. Aktas et al (2004) investigated the prevalence and intensity of Theileria infections in *Hyalomma* ticks collected from shelters and the cattle reared by using traditional management system in the eastern part of Turkey. The results showed that 44% of cattle were infested with four *Hyalomma* species. *H. a. anatolicum* was dominant tick species with a percentage of 63.1%, and the other tick species were *H. a. excavatum, H. detritum* and *H. m. marginatum* with the percentages of 23.8%, 11.7% and 0.6%, respectively. The infection rate was highest in *H. a. anatolicum.* The ticks collected from

cattle and shelters had infection rates of 12.6% and 46.9%, respectively. Female ticks collected from cattle showed a higher prevalence rate than male ticks, but the difference between the infection rates of female and male ticks collected from shelters was not significant. The mean intensity of infection was higher in female ticks collected from both cattle and shelters. In another study conducted in Central Anatolia region (Ica et al 2007b), 39 percent of cattle infested with the tick speies including *Boophilus (Rhipicephalus) annulatus, Hyalomma marginatum marginatum* and *Rhipicephalus turanicus,* and 27.9% of 42 tick pools were positive for the haemoparasites including *B. bigemina, T. annulata* and *Babesia* spp. The most prevalent tick species was *Boophilus annulatus*, and the most prevalent hemoparasite was *B. bigemina* followed by *T. annulata.*

Ovine theileriosis

A large number of Theileria species are found in small ruminants. Many of them are non-pathogenic such as *T. ovis, T. separata* and *T. recondita*. The most important *Theileria* species that cause mortality in sheep are *T. lestoquardi, T. lowenshuni* and *T. uilenbergi*. These pathogenic species cause malignant theileriosis which ends with death, while the others cause low or non-pathogenic theileriosis in sheep and goats (Friedhoff 1997, Ahmed et al 2006). *Theileria ovis* is the most prevalent *Theileria* species of small ruminants in Turkey. *T. lestoquardi* and *T. recondita* were found, but any clinical infection has not been documented (Sayin et al 1990, Sayin et al 1997c). Recently, *Theileria* spp. MK, a new strain in Turkey, was described in sheep and goats (Altay et al 2007a, Altay et al 2007b, Altay et al 2008a). The results of epidemiologic studies conducted in different geographical regions of Turkey show that the prevalence of *T. ovis* is varying between the rates of 18.4 to 67.96% in sheep, and the infection rate of goats was 12.36% (Inci et al 2003, Aktas et al 2005c, Altay et al 2005, Altay et al 2007a, Altay et al 2007b, Sayin et al 2009, Inci et al 2010). *Rhipicephalus bursa* plays an important role as a natural vector of *T. ovis* (Inci et al 2003, Aktas et al 2006b). In a comparison to the bovine theileriosis, ovine theileriosis has slight effect on animal health in Turkey.

Babesiosis

Babesiosis is a protozoan disease caused by *Babesia* species in a lot of domestic and wild animals and humans. The disease is endemic, especially in ruminants in tropical and subtropical countries. In Turkey, with respect to the number of clinical infections and death cases, ovine babesiosis has considerably economic and health importance in the livestock industry.

Bovine babesiosis

Babesia species in cattle are *Babesia bovis, B. bigemina, B. divergens* and *B. major*. These parasites are transmitted by the tick species in the genus *Boophilus, Rhipicephalus* and *Ixodes.* In Turkey, most of the bovine *Babesia* cases are due to *B. bigemina* (Sevinc et al 2001, Sevinc et al 2005, Inci et al 2002, Ica et al 2007a). It is usually transmitted by the tick vectors, *Boophilus microplus* and *Rhipicephalus (Boophilus) annulatus*. During the acute babesial infection, the host becomes severely ill. Typically, the infected host suffers from high fever, severe anemia, hemoglobinuria, lethargy, and inappetence. Parasitemia may reach a rate of 50-100%. In the severe cases death occurs following hypothermia, accompanied by uremia with icterus. The mortality rate of acute babesiosis is frequently high. The major post-mortem findings include icterus on the connective tissues, and internal and external mucosae, the enlarged bladder containing haemoglobinuric urine, and jaundice in liver (Figure 2).

Imidocarb dipropionate is currently used anti-babesial drug to treat sick animals (Sevinc et al 2007). The control of bovine babesiosis has been achieved by live attenuated vaccines in many parts of the world, and a single vaccination provides long-lasting protective immunity in cattle (de Waal and Combrink 2006, Alvarez et al 2004, Bock et al 2004, de Vos and Bock 2000, Pipano 1995). However, there is no available vaccine against bovine babesiosis in Turkey (Sayin et al 1997c, Sevinc et al 2005). In Turkey *B. bovis, B. bigemina* and *B. divergens* were detected by microscopic and serological methods while *B. major* by PCR (Aktas et al 2001). The prevalence of *B. bigemina* is ranging from 0.6 to 53.07% depending on the different geographical regions (Sevinc et al 2001, Inci et al 2002, Ica et al 2007a, Ekici and Sevinc 2009, Sevgili et al 2010). Within the haemoparasites detected in vector ticks, B. bigemina was reported as a dominant species in the central part of the country. The most prevalent tick species was *Boophilus annulatus* with the percentage of 26.37% fol-

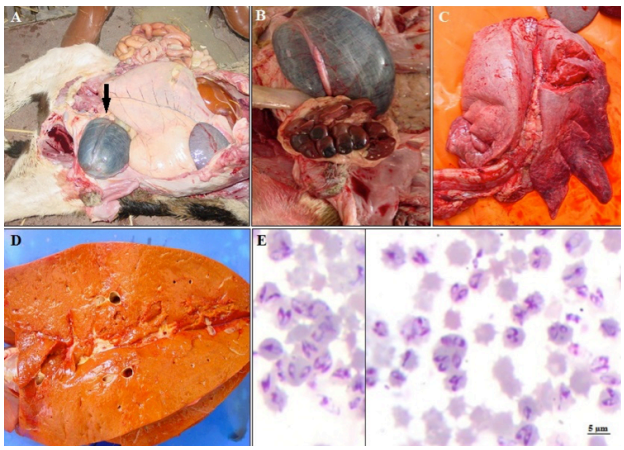

Figure 2. The signs of *Babesia bigemina* infection. Post-mortem findings of babesiosis; enlarged urinary bladder filled with dark colored urine (A), kidney degeneration (B), lung edema (C), jaundice in liver (D), intra-erythrocytic merozoites on the Giemsa-stained blood smears (E). The pictures are taken from a clinical case detected in a calf who was severely infected with *B. bigemina* and died despite intensive treatment in the Faculty of Veterinary Medicine, Selcuk University.

Figure 3. The signs of *Babesia ovis* infection. The visual damages on some organs in necropsy; haemoglobinuria which is the most noticeable clinical sign of acute infection (A, B), anaemia (C), lung edema (D), jaundice in liver (E), petechial hemorrhages in heart (F), kidney degeneration (G), and intra-erythrocytic merozoites on the Giemsa-stained blood smears (H).

lowed by *H. m. marginatum* with 21.12% and *Rh. turanicus* with 18.7% (Ica et al 2007b). Reports on cattle babesiosis have been regularly received by the veterinary practitioners during the disease seasons. However, the data is not enough to assess the number of the cases and to predict its economic impact in the livestock industry because of the lacking case recording system.

Ovine babesiosis

The disease is caused by the tick-borne apicomplexan parasites *Babesia ovis, B. motasi, B. crassa* and *B. foliata. B. ovis* is the most important *Babesia* species infecting small ruminants in Europe, Africa, Asia, and the Far East. The geographic distribution of *Babesia* species shows parallelism with that of their tick vectors, which are mainly *Rhipicephalus* species in tropical and subtropical regions (Yeruham et al 1985, Yeruham et al 1998a, Yeruham et al 1998b, Kuttler 1988, Razmi et al 2003, Uilenberg 2006, Ahmed et al 2006, Shayan et al 2007, Ranjbar et al 2012, Fakhar et al 2012). Babesiosis is the principal tick-borne disease of small ruminants which are the main livestock species in Turkey. Ovine babesiosis is an acute disease that causes clinical signs such as fever, hemolytic anemia, hemoglobinuria and icterus in small ruminants (Figure 3). The disease occurs as single cases or mostly outbreaks in Turkey (Sevinc et al 2013b).

In Turkey, sheep are the main livestock resource, and it constitutes 55.5% of the total livestock (TurkStat 2015). Small ruminants are mostly raised under the traditional systems. The sheep, grazing on pastures from spring until late autumn, are usually exposed to ticks. *Rhipicephalus* spp. is the common vector of the disease in Turkey. Therefore, babesiosis as a season dependent disease is observed from April to October every year, most commonly in June and July (Sayin et al 1997a, Sayin et al 1997b, Aydin and Bakirci 2007, Altay et al 2008a, Sevinc et al 2013b). Babesia ovis is highly pathogenic *Babesia* species of sheep, and the clinical cases are usually severe. In the acute cases, pancytopenia characterized by anemia, thrombocytopenia and leukopenia occurs in the blood picture of sick animals (Yeruham et al 1985, Yeruham et al 1998a, Yeruham et al 1998b, Kuttler 1988, Uilenberg 2006, Sevinc et al 2013b). Untreated cases usually end up in death of sick animals. Some animals may die despite treatment due to severe infection. Many recurrences may also occur after treatment period in the sick animals treated with anti-babesial drug. Even though acute infected animals were treated with specific drug, compensation of the abnormalities in the hematological picture takes a long time (Sevinc et al 2013b). The serological surveys show that the serum samples collected from randomly selected animals have had *B. ovis*-specific antibodies with the percentage of sheep ranging from 32 to 80% (Duzgun et al 1991, Sevinc and Dik 1996, Dumanli et al 1997, Sayin et al 1997a, Aktas et al 2001, Emre et al 2001, Cicek et al 2004, Ekici et al 2012). Prediction about the current actual intensity of the clinical cases is difficult because of the absence of case recording system. However, the results of a follow-up study in Konya province located in the central area of Turkey show the importance of ovine babesiosis. During June and July months in 2011, a total of 122 acute clinical cases (%) were identified in only two sheep flocks, and 15 of them died despite intensive treatment (Sevinc et al 2013b).

The current control of ovine babesiosis is based only on chemotherapy and limited tick control measures. Imidocarb dipropinate has prophylactic effectiveness, as well as its therapeutic effect on ovine babesiosis (Sevinc et al 2007), so huge amount of drug has been used in every year. There is no immunoprophylactic method to control ovine babesiosis. The authorities suggest that despite some disadvantages, the attenuated parasites should be used for the immunization of small and large ruminants against tick-borne diseases unless non-living parasite vaccines are available (Ahmed et al 2002, de Waal and Combrink 2006, Seitzer and Ahmed 2008). One of the most common methods of reducing the virulence of *B. bovis* involves the rapid passages of the virulent strain through susceptible splenectomized calves. The literature gives scant attention to the immunoprophylaxis of *B. ovis* infection.

No information is available regarding how many passages are necessary to attenuate a virulent *B. ovis* strain. In a previous study performed by Yeruham et al (1998c), it was unable to conduct more than three successive passages of *B. ovis* in splenectomized lambs because the third passage lamb had a very low level of parasitemia with no reduction in the virulence. In a preliminary study (Sevinc et al 2014), rapid blood passages were performed to reduce the virulence of *B. ovis* in the 13 susceptible splenectomized lambs. The results of the

study showed that the virulence of *B. ovis* was not eliminated after 12 successive passages. For this reason, further passages or alternative attenuation methods may be necessary to attenuate the virulent strain of *B. ovis.*

The diagnosis of acute babesiosis is based on the clinical signs of the disease and on the demonstration of the parasites in the erythrocytes in Giemsa-stained blood films by microscopy. Microscopic and clinical examinations come up short on diagnosis of subclinical infections. The subclinically infected animals have been determined by the immunological and molecular methods (Bose et al 1995, Georges et al 2001, Bock et al 2004). For the immunodiagnosis of *B. ovis*, a synthetically derived bovine *B. bovis* antigen has been used in enzyme-linked immunosorbent assay (ELISA) to detect anti-*B. ovis* antibodies (Duzgun et al 1991, Emre et al 2001, Sevinc and Dik 1996, Cicek et al 2004). IFAT is also being used in a few laboratories (Wright 1990, Sevinc et al 2007, Ekici et al 2012). IFAT has some disadvantages such as being subjective, time consuming, exhausting and need for experienced personnel. The immunoreactive proteins of some *Babesia* species have commonly been used as diagnostic antigens in the diagnosis of equine, bovine and canine babesiosis (Ikadai et al 2000, Boonchit et al 2002, Huang et al 2003, Zhou et al 2007). It has been determined the presence of the five *B. ovis*-specific immunoreactive proteins in a latest study, however, with regard to the purification of these proteins and their possible usages as diagnostic proteins, further studies are required (Sevinc et al 2013a). Immunoreactive recombinant proteins have significant importance as the antigen sources in quantitative assays and the vaccine candidates in the prevention of diseases. On the producing of recombinant proteins of *B. ovis,* the results of a new study are showing that a secreted protein 1 of *Babesia ovis* (rBoSA1) seems to be a promising diagnostic antigen which is usable for the development of serological assays for the diagnosis of ovine babesiosis (Sevinc et al 2015).

The urgent measures to control ovine babesiosis must be taken into consideration. For implementation of effective control strategies, there is a need to develop diagnostic methods which are specific, sensitive, cost-effective and suitable for use in the field. In addition, an available vaccine would reduce the losses in outbreaks of the disease; therefore, the development of vaccines is crucial.

Equine babesiosis

Equine babesiosis is prevalent and has the potential risks for the horse breeding and racing industry in Turkey where international races continue with increasing interest. The most of epidemiologic studies on equine babesiosis has been performed to estimate the prevalence of the infections. The results of the studies show that *T. equi* is more prevalent than *B. caballi.* According to the studies based on microscopic diagnosis, the prevalence rate of equine babesiosis is varying between 0 to 58.18% (Inci 1997, 2002, Akkan et al 2003, Kurt 2005, Balkaya and Erdogmus 2006). The serological studies performed by ELISA, IFAT and complement fixation test (CFT) showed that the occurrence of *T. equi* varied between 12.8 and 64.5% and *B. caballi* between 0 and 34.6% (Akkan et al 2003, Kurt 2005, Balkaya and Erdogmus 2006, Oncel et al 2007, Acici et al 2008, Sevinc et al 2008, Karatepe et al 2009, Sari et al 2010). The prevalence rates of *T. equi* and *B. caballi* in the show/sport horses have been found 7% and 3% by PCR, respectively (Guclu and Karaer 2007). The results of a comparative study showed that *T. equi* and *B. caballi* infections were higher in racehorses than stud-horses (Sevinc et al 2008). Some studies indicate that the occurrence of equine babesiosis differs depending on the geographical regions. Akkan et al (2003) detected that equine babesiosis was more prevalent in the Eastern border of Turkey compare to the other regions, with the high positivity rates of 69.9% and 58.18% by IFAT and microscopy, respectively. This situation was associated with the lack of regulations on animal movements through the border line. Very little information is available on the tick vectors of equine babesiosis in Turkey. According to the limited number of study, the tick species *H. marginatum, H. detritum, R. bursa* and *R. turanicus* were found on the horses infected with the equine *Babesia* species (Inci 1997, 2002, Akkan et al 2003, Acici et al 2008). In terms of epidemiology, most of these reports are not enough to elucidate the tick vector species of the disease.

Canine babesiosis

The epidemiological aspect of canine babesiosis in Turkey is unknown. Although tick-borne pathogens of pets are of economic significance in many industrialized countries (Jongejan and Uilenberg 2004), there are only a few case reports that show the presence of *B. canis* and *B. gibsoni* in dogs in Turkey (Gülanber et al 2006, Aysul et al 2013, Gokce et al 2013). In a study on investigating *Babesia* species in 493 dogs, the only one *Babesia* species, *Babesia canis vogeli* was detected in small number of dogs with the rate of 3.8% by RLB (Aysul 2006).

Anaplasmosis

The genus Anaplasma consists of six species, which include *Anaplasma marginale, A. centrale, A. bovis, A. ovis* that are pathogens for ruminants, *A. platys* for canines and *A. phagocytophilum* for human and domestic animals. *A. phagocytophilum* has a broad host spectrum which includes ruminants, horses, dogs, humans and wild animals. The main vectors of the *Anaplasma* species are ticks, especially the genera *Ixodes, Dermacentor, Rhipicephalus* and *Amblyomma* (Dumler et al 2005). Direct transfer of *A. marginale*-infected erythrocytes from carrier animals to the susceptible animals by biting arthropods and iatrogenically can result in transmission of the

disease. In Turkey, *Anaplasma marginale* infections are endemic. Most of the animals represent a situation of reservoirs.

Bovine anaplasmosis

Bovine anaplasmosis is the most prevalent tick-borne disease of cattle caused by *Anaplasma marginale* which causes a hemolytic disease in cattle in tropical and subtropical areas of the world. It can be fatal in susceptible cattle and be partially responsible for the high rate of mortality observed in the affected herd. The symptoms of clinical disease are fever, anemia, icterus, weight loss, abortion, lethargy and often death in animals older than 2 years. The animals older than 2 years of age are usually affected by a per-acute fatal form of the disease. Calves from immune mothers receive temporary protection from the colostrum which prevents anaplasmosis. This protection lasts about 3 months, and in most cases, is followed by an age resistance, which lasts until the animals are about 9 to 12 months old. Recovered animals from acute anaplasmosis remain persistently infected for life and serve as reservoirs of infection for transmission, and thus, they contribute markedly to the spread of anaplasmosis (Ristic 1977, Kocan et al 2000, Tassi et al 2002).

Acute anaplasmosis is diagnosed by microscopy seeing the organisms of approximately 0.5-1.0 µm located peripherally in the erythrocytes on the stained blood smears (Figure 4). During the acute stage, anemia develops within 1 to 2 days, and a sharp falling of hematocrit reflects the severity of infection. Following recovery from acute disease, the animals remain persistently infected. During the persistent infection, infected erythrocytes are not always detectable in stained blood smears, and thus, the diagnosis is usually made using a variety of serologic tests for the detection of specific antibodies. Serologic diagnosis is commonly by competetive ELISA (cELISA). It was reported that cELISA was positive in calves acutely infected with *A. marginale* before or concomitantly with the development of rickettsemia, and that the antibodies were detectable in sera from persistently infected cattle inoculated as long as 6 years previously (Knowles et al 1996).

Bovine anaplasmosis has been reported in almost all regions of Turkey (Ozcan 1961, Goksu K, 1970, Mimioglu et al 1971, Tuzer 1981, Birdane et al 2006). Most of cattle represent the carrier state. In the carrier animals, clinical infections may occur as a result of immunosuppression that is usually related with transportation, pregnancy and high milk yield. Death cases due to acute anaplasmosis have been recorded in both private and government dairy cattle farms (unpublished data) in Turkey. Birdane et al (2006) reported the fatal *Anaplasma marginale* infections in a dairy cattle herd located in the Interior Aegean Region of Turkey. In the herd, 55.35% and 34.11% of the 645 animals were determined as positive by cELISA and microscopic examination, respectively, and 15 cows died due to per-acute *A. marginale* infection. It was

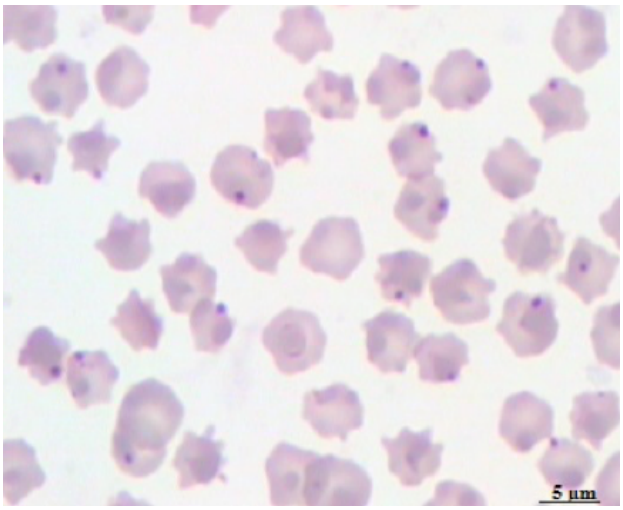

Figure 4. Photomicrograph of a blood smear from *A. marginale*-infected cattle.

noticed that the clinical infections were significantly associated with the ages of the animals. The general microscopic and serologic surveillance in the herd showed that all ages of cattle except 9-12 months of age infected with *A. marginale.* However, the severity of illness and percentage of deaths increased with age. The 15 dead animals were at the age of two or above. Seropositive calves under 9 months of age did not exhibit any clinical signs of acute anaplasmosis.

Tetracyclines and imidocarb dipropionate are the drugs of choices for treating acute disease. Considering the degree of reduction in packed cell volume (PCV), supportive therapy and blood transfusion may be added to the treatment regimen. However, in some per-acute cases, death occurs despite all treatment approaches.

Ovine anaplasmosis

A. ovis infection in sheep and goats is usually asymptomatic. Anemia occasionally becomes severe. The signs similar to those seen in *A. marginale* infection of cattle usually develop in the event of immunosuppression in sheep. The clinical and subclinical *A. ovis* infections were reported in small ruminants by microscopic examination in a few studies (Ozcan 1961, Goksu 1967, Sayin et al 1997a). Until 2005, there was no report showing the presence of *A. phagocytophilum* in sheep in Turkey. In parallel with the emergence of tick-borne diseases in humans in recent years, this agent that is thought to be zoonotic was determined in domestic animals and ticks (Unver et al 2005, Gokce et al 2008, Aktas et al 2009, Aktas et al 2010, Aktas et al 2011). Further studies are needed for epidemiological information on the ovine anaplasmosis.

Conclusions

Theileriosis, babesiosis and anaplasmosis are the most prevalent tick-borne infections causing severe economic losses in livestock sector. These infections have been well-

recognized by the farmers and veterinarians. In Turkey, the principle tick-borne pathogens are *T. annulata, A. marginale* and *B. bigemina* in the bovines, *B. ovis* in the ovines, and *B. equi* and *B. caballi* in the equines. Due to these infectious agents, acute clinical symptoms develop quickly, and the sick animals can die in a short time. These diseases can occur as mixed infections, and they are often complicated by other diseases, so diagnosis and treatment is difficult. Effective drugs are available to cure all these diseases. Cure rates increase in early diagnosis, and supportive therapy is mostly essential in addition to the primer treatment regimen. Acute infections can be identified using microscopic examination of the Giemsa-stained blood or organ smears, but carrier animals are difficult to detect by this method. IFAT has been used for many years to detect the carrier animals for *Theileria* and *Babesia* species. A competitive ELISA using a recombinant antigen termed rMSP5 and MSP5-specific monoclonal antibody has currently been used for detection of *Anaplasma*-infected animals. Under the field conditions, veterinary practitioners usually treat the sick animals according to their own clinical diagnostic skills and experience. PCR-based tests have also been used for detection of *Theileria, Babesia* and *Anaplasma* infections. These methods are valuable research tools for specific studies, but they are costly and laborious for examination of large number of samples, and they also are of little value to the practitioners. There is a necessity to develop diagnostic methods which are specific and sensitive, and practical to use even under the field conditions.

In Turkey, most of the studies have been conducted to determine the prevalence of the diseases. In terms of the host-parasite-vector interactions and risk factors, further studies are necessary. Moreover, the studies have usually been planned in the Central and Eastern Anatolia Regions, whereas Turkey has a wide land area of 783.577 km2, so there is necessity to the surveys representing the whole country.

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