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ANAPLASMOSIS IN ANIMALS

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ABSTRACT

Anaplasmosis is a vector-borne, infectious and non-contagious disease. The disease is caused by various pathogens of the genus *Anaplasma*. The different species cause different types of anaplasmosis depending on which cells that are infected in the mammalian host. Anaplasmosis has a wide host range, including humans, and it is distributed worldwide. The zoonotic potential of some species is of great importance in regards to public health concerns. This review presents information about anaplasmosis in animals and its prevalence in Europe, and other countries in the world.

Key words: anaplasmosis; infectious disease; re-emerging; vector-borne disease; zoonosis

INTRODUCTION

Anaplasmosis is caused by bacteria of the genus *Anaplasma*, order *Rickettsiales* which was formed after a merging of the families *Anaplasmataceae* and *Rickettsiaceae* [17]. *Anaplasma* spp. contains several individual species including: *Anaplasma phagocytophilum, Anaplasma platys, Anaplasma marginale, Anaplasma bovis, Anaplasma ovis*, and *Anaplasma centrale*. A newly discovered species which has not yet been officially recognized as a separate species is named *Anaplasma capra* [45]. The zoonotic potential of the bacteria is of great importance in consideration of public health concerns [30]. Anaplasmosis is a vector-borne disease which is usually transmitted by ticks, but other mechanisms do also exist [50].

Bacteria in the *Anaplasma* spp. are obligate intracellular pathogens found inside vacuoles in the cytoplasm of the infected eukaryotic host cells. The mammalian host cells that become infected are variable depending on the species of *Anaplasma* spp., and includes granulocytes, erythrocytes, endothelial cells and platelets. The bacteria differ from other gram-negative bacteria by not having a cell wall which make them sensitive to mechanical stress. They are enveloped, but lack thickening of the leaflets and are without peptidoglycan layers or lipopolysaccharides (LPS) [30]. The bacteria replicate inside the host cell, forming microcolonies called morulae [45].

Anaplasma phagocytophilum is the causative agent of granulocytic anaplasmosis in horses, humans, canines and felines. In ruminants the disease is known as tick-borne fever [3]. *Anaplasma platys* cause infectious cyclic thrombocytopenia in dogs mainly. Individual cases have also been found in cats, humans and cattle. Although different strains of *Anaplasma platys* with variable pathogenicity have been detected [64], it is considered as a canine pathogen [30, 45]. *Anaplasma marginale* cause the "classical" anaplasmosis called erythrocytic anaplasmosis in ruminants [45]. It is the cause of economic losses in the cattle industry. *Anaplasma bovis, Anaplasma ovis* and *Anaplasma centrale* are closely related to *Anaplasma marginale*, but typically cause a milder disease [1, 59]. *Anaplasma capra* has been detected as an emerging bacterium which infects ruminants and humans [39]. S e o et al. [59] states that if this bacterium is determined to be pathogenic to humans and other animals, it may be an essential health risk.

Anaplasma spp. are commonly transmitted through ticks. The different *Anaplasma* spp. have different tick species for transmission. The most common genus of ticks that function as vectors is *Ixodes* spp. Other species include *Dermacentor* spp., *Rhipicephalus* spp., *Hyalomma* spp., and *Haemaphysalis* spp. [45]. For the tick to be infected and be able to transmit the pathogen, the tick needs to live in a habitat where there are mammals present that can serve as reservoirs for the *Anaplasma* spp. [18]. Biological transmission by ticks is the most common way of transmission of *Anaplasma* spp. In general, transmission of *A. phagocytophilum* by ticks starts within a few hours after attachment but establishment of infections was observed only when ticks attached for greater than 48 hours [26]. Furthermore, other mechanisms such as mechanically by biting flies and by blood-contaminated fomites, have also been recorded in *A. phagocytophilum* and *A. marginale* [37, 63]. The wide variety of reservoir hosts of *Anaplasma* spp. varies with the species and the geographical location, but typically include wild ruminant species [42, 71]. Migrating birds that can carry long-range ticks may have an essential role in the spreading of the pathogen [66, 67].

The incubation period is in the range from 5 to 14 days. The clinical signs of diseases caused by *Anaplasma* spp. show a lot of similarities across the different species and infected hosts, although there are some variations both in what type of signs that occur, and in the degree of severity of the clinical signs. Diseases caused by *Anaplasma* spp. commonly cause non-specific febrile illness in the infected mammalian host. Acutely infected animals lose condition. The next most described clinical signs are distal limb oedema, a reluctance to move, inappetence, decreasing of milk production, loss of coordination and breathlessness. Ruminants that are infected with *Anaplasma* spp. tend to develop more severe disease. Death from infection by *Anaplasma* spp. has the highest occurrence in infected ruminants that develop a progressive disease [5, 37, 54]. In addition, ruminants become persistent carriers and reservoirs for *Anaplasma* spp. [42]. Horses, dogs, cats, and humans rarely succumb to the disease. In most cases, the diseases are self-limiting [58, 64]. The severity of clinical signs tends to increase with the age of mammalian host infected with *Anaplasma* spp. [42, 58, 63]. The most common laboratory findings in diseases caused by *Anaplasma* spp. are thrombocytopenia, leukopenia, and anaemia [30]. When the pathogen comes in contact with the eukaryotic host cells, the pathogen adheres to the surface of the cell. It enters the cell by endocytosis and forms vacuoles within the cytoplasm of the host cells. Once inside the cells, they begin to replicate by binary fission after which the specific morulae is formed [30].

The epizootic history of the patient together with the clinical signs and laboratory findings is essential in confirming infection by *Anaplasma* spp. [18, 30]. The microscopic detection of the morulae in infected cells by Giemsa or Wright's staining is a fast and cost-effective diagnostic tool; PCR, IFA and ELISA are also commonly used [1, 30, 67].

Treatment of individuals with diseases caused by *Anaplasma* spp. depends on the severity. In individuals where the disease is commonly self-limiting, and the clinical signs are mild, the patient is usually left without any specific treatment. If the disease is more progressive, the typical treatment is antibiotics [1, 30, 63, 67]. One should also have in mind that the intensive use of antibiotics increases the chance of microorganisms becoming resistant to treatment by antibiotics [37]. The most important preventive measure to avoid infection and spreading of *Anaplasma* spp. is tick control [1]. There are no current vaccines that are available against *Anaplasma* spp. except for *Anaplasma marginale* [36, 65]. There have been some thoughts that recovery from the disease caused by *A. phagocytophilum* can provide immunity, but the period of protection is variable [1].

The aim of this study was to describe anaplasmosis in animals. This includes describing the different *Anaplasma* spp. with their characteristics, how they affect their host and their distribution worldwide. More cases have been reported during the latest years. This increase can be due to more transportation, climate changes and overall more research on the topic.

OCCURRENCE OF *ANAPLASMA* SPP. IN EUROPE

Anaplasmosis was detected in many European countries in various animal species with the prevalences ranging from 1.09 % to 97.9 % (Table 1). The variability of the prevalences could be due to the specific geographical area. High prevalence may be in association with the region having suitable environment for ticks, with appropriate vegetation and high mammalian host densities. The tick species *I. ricinus* is the main tick species in Europe, as well as a main vector for *Anaplasma phagocytophilum* transmission. Although in Europe several of the *Anaplasma* spp. are present and they vary in prevalence between the geographical areas, *Anaplasma phagocytophilum* was the most detected subspecies. However, the reason may also be the focus on this species due to its zoonotic potential. It has been identified in domestic species such as dogs, small mammals and horses but also in a variety of wild ruminants, as well as humans [54]. Ruminants have also been affected across Europe. *A. phagocytophilum, A. marginale* and *A. ovis* has been detected in Mediterranean countries, Central Europe and Sweden.

In general, higher prevalences seems to be in wildlife animals which could suggest the important role of wildlife as the possible reservoir. The prevalence may also vary with the different ecotypes or strains as showed in the study by J a h f a r i et al. [34]. As climates and habitats are changing, so does the distribution and movement of these wildlife species and the ticks with them. Norway function as a northern limit to the tick distribution due to the colder climate. In recent years there have been reports about the limit of ticks being pushed further north [54]. Tick-borne diseases such as anaplasmosis has been reported most frequently along the coast of Norway where there are high densities of ticks [31]. In Norway anaplasmosis is listed as a C-disease in a ranging system of infectious diseases so there is no need to report the disease [40, 41, 63]. The variation in prevalence across Europe may be explained in association with a few main factors like variation in tick density, and density of vertebrate hosts. Furthermore, the disease is not reportable, meaning there is no database on the occurrences. It also presents with non-specific signs which can lead to it being overlooked. And in addition there has been a lack of attention to the disease, as it is not common to test for it, and there is a lack of specific diagnostic methods [24].

OCCURRENCE OF *ANAPLASMA* SPP. IN OTHER COUNTRIES

Anaplasmosis has spread throughout the world (Table 2). Other than Europe, anaplasmosis has been found in America, Africa, Asia, and Australia [1]. In the USA, the disease caused by *A. phagocytophilum* in humans is needed to be reported. The CDC shows an increase in reports from 2000 until 2017 [9]. Similarly, a significantly increasing trend for *A. phagocytophilum* seroprevalence in the canine population was recently observed by D e w a g e et al. [15] in the eastern USA. Furthermore, cats, cattle, rabbits and small mammal were investigated for the presence of *Anaplasma* spp.

New studies show a higher geographical range of the ticks with a corresponding increased number of cases of human granulocytic anaplasmosis in Canada. Although anaplasmosis is now considered as endemic only in several areas in Canada [11], U m i n s k i et al. [66] suggested that the disease should be made reportable. In Central and South America, *A. platys* in canines have been more frequent than in North America [30]. In recent years, there have been also more reports on *Anaplasmosis* spp. in South America [16, 48].

In Africa and the Middle East most of the *Anaplasma* spp. have been detected. However, mostly ruminants and ticks have been studied, especially in North Africa. Other domestic species, such as horses, dogs, and also humans have not been studied as much. This interest in studying ruminants may be due to the importance of livestock in the economy in these areas. The *Anaplasma* spp. that are studied include: *A. marginale, A. ovis, A. bovis*, and *A. platys*. Only small amount of information about *A. phagocytophilum* and its distribution in this area exist [8]. In Tunisia, studies there have been conducted on cattle with sev-

Table 1. The prevalence of *Anaplasma* spp. in various animal host species in selected European countries
AO —*A. ovis*; AP —*A. phagocytophilum*

Country	Anaplasma species	Host species	No. tested	Prevalence [%]	Source
Austria	AP	Cattle	140 081	3.60	[6]
Czech Republic	AP	Cattle	55	5.45	[14, 33, 53]
		Sheep	109	1.09	
		Horse	40	5.00	
			96	73.00	
Hungary	AP	Dog	1305	7.90	[23, 32]
		Fallow deer	33	72.70	
		Red deer	48	97.90	
		Roe deer	65	60.00	
		Mouflons	16	6.30	
		Wild boars	17	39.20	
Germany	AP	Dog	111	43.20	[35, 38]
			522	43.00	
Italy	AP	Horse	20	15.00	[3, 19, 20, 21, 51]
			135	17.03	
			160	25.62	
			479	15.03	
		Fallow deer	67	46.26	
		Red deer	52	46.15	
		Cattle	137	16.78	
		Sheep	102	12.74	
		Goats	72	4.16	
		Dog	1232	8.76	
			40	7.50	
Norway	AP	Moose	111	70.00	[43, 54, 62]
		Red deer	141	94.00	
			37	81.10	
		Roe deer	28	82.00	
			104	88.10	
Poland	AP	Horse	76	1.3	[60]
Slovakia	AP	Sheep	202	16.16	[14]
	AO	Sheep	202	32.67	
		Goat	12	58.30	
Spain	AP	Cattle	456	3.07	[4]
		Sheep	389	0.51	
		Goat	207	0.48	
		Horse	46	6.52	
Sweden	AP	Sheep	20	45.00	[29]

Table 2. The prevalence of *Anaplasma* spp. in various animal host species in selected countries of the world
AB—*A. bovis*; AC—*A. centrale*; ACa—*A. capra*; AM—*A. marginale*; AO—*A. ovis*; AP—*A. phagocytophilum*; ASp—*A.* spp.

Country	Anaplasma species.	Host species	No. tested	Prevalence [%]	Source
Brazil	AP	Horse	98	17.40	[16, 47, 55, 56]
			91	12.00	
			97	11.34	
			20	65.00	
China	AB	Dog	243	4.10	[12, 52, 70, 71]
		Sheep	435	24.40	
	ACa	Sheep	435	18.20	
		Sheep	1453	8.90	
		Goat	943	9.40	
	AO	Dog	243	6.20	
		Sheep	435	5.70	
	AP	Sheep	49	42.90	
		Goat	91	38.50	
		Yak	158	32.30	
		Cattle yak	20	35.00	
		Dog	243	0.40	
		Sheep	435	28.00	
Iran	AB	Cattle	150	2.66	[46, 72]
	AM, AO	Sheep + goat	370	27.50	
Canada	AP	Dog	86 251	0.19	[57, 68]
		Horse	376	0.53	
Malaysia	AM	Cattle	1045	72.60	[49]
Mexico	ASp	Dog	1706	9.90	[44, 48]
	AP	White-tailed deer	25	20.00	
		Mazama deer	4	50.00	
Mongolia	AO	Sheep	1179	69.00	[22]
		Goat	871	71.30	
Nicaragua	ASp	Dog	329	28.60	[61]
Niger	AO	Sheep	33	69.70	[13]
South Korea	AP	Cat	33	18.20	[10, 59]
		Horse	92	2.20	
		Cattle	129	0.80	
	ACa	Cattle	1219	1.00	
Tunisia	AM	Cattle	232	25.40	[7, 42]
			328	24.70	
	AC		232	15.10	
	AB		232	3.90	
	AP		328	0.60	
Turkey	AO	Sheep + goat	343	60.00	[73]
USA	AP	Small mammal	2121	15.24	[2, 25, 27, 69]
		Rabbits	41	7.32	
		Cats	175	9.70	
	AB	Rabbits	41	36.58	
	AM	Cattle	247	21.86	

eral *Anaplasma* spp. including: *A. marginale, A. centrale, A. bovis*, and *A. phagocytophilum* [7, 42]. Several studies on sheep and goats have been conducted as well. Also, in Turkey, Iran and Niger, the breeding of small ruminants has significant economic importance. In these countries, *A. ovis* and *A. marginale* were detected in sheep and goat with variable prevalences [13, 72, 73].

In Asia and Australia, there has been more reports in recent years. China has reported several different *Anaplasma* spp. including the newly detected *Anaplasma capra*. *A. capra* has been detected in humans, sheep, and goats in China and in cattle in South Korea. The tick species *Ixodes persulcatus* is thought to be a possible vector for *A. capra* [39, 52, 59, 71]. *A. phagocytophilum, A. ovis, A. bovis*, and *A. capra* have been studied on several occasions across China. These *Anaplasma* spp. have been discovered in multiple host species [12, 52, 70, 71]. They have been detected mainly in ruminants, probably due to the high impact of livestock production, but the occurrence of *Anaplasma* spp. were also investigated in dogs. Studies that were done on sheep, goat, and cattle in Mongolia and Malaysia show a relatively high prevalence of *A. marginale* [22, 49]. In Australia, the only detected *Anaplasma* spp. has been on the strains of *A. marginale, A. centrale*, and *A. platys*, which have been introduced to the country by imported animals. However, they recently detected a unique *A. bovis* strains in native Australian ticks. This is genetically different from other variants worldwide [28].

CONCLUSIONS

Anaplasmosis is a disease caused by the bacteria of the *Anaplasma* genus. They affect a variety of host species with varying prevalences around the world. The explanation for the variability can be the size of the population tested, the density of ticks and reservoir hosts which usually depend on the geographical area and climate, and the different strains of *Anaplasma* spp. that are present. To fully understand how this is all connected and to be able to conduct proper preventive measures, more research is needed on anaplasmosis caused by the different *Anaplasma* spp.

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