Climate change related (re)emerging diseases in cattle in the Netherlands

The possible use of natural (plant) substances in an integrated approach

A. van de Aa and M. Groot

WAGENINGEN
UNIVERSITY & RESEARCH

Climate change related (re)emerging diseases in cattle in the Netherlands

The possible use of natural (plant) substances in an integrated approach

A. van de Aa and M. Groot

This research has been carried out by Wageningen Food Safety Research, institute within the legal entity Wageningen Research Foundation subsidised by the Dutch Ministry of Agriculture, Nature and Food Quality (project number KB-35-007-002).

Wageningen, November 2021

WFSR report 2021.017

Van der Aa, A. and M. Groot, 2021. *Climate change related (re)emerging diseases in cattle in the Netherlands; The possible use of natural (plant) substances in an integrated approach.* Wageningen, Wageningen Food Safety Research, WFSR report 2021.017. 30 pp.; 2 fig.; 2 tab.; 83 ref.

Project number: 1297384401
BAS-code: KB-35-007-002
Project title: Nature-based solutions
Project leader: M. Groot

This report can be downloaded for free at https://doi.org/10.18174/556961 or at www.wur.eu/food-safety-research (under WFSR publications).

P.O. Box 230, 6700 AE Wageningen, The Netherlands, T +31 (0)317 48 02 56, E info.wfsr@wur.nl, www.wur.eu/food-safety-research. WFSR is part of Wageningen University & Research.

WFSR report 2021.017

Distribution list:
- Annemarie Groot
- Marjolein Sterk
- Ronald Zom
- Wijnand Sukkel
- Lotte Caarls

Contents

Summary

This literature review report was composed in the framework of the KB project: Nature-based solutions (NBS) climate resilient and circular food systems within the topic Nature-based solutions & Food + Biodiversity.

The goal of this report is to give a short overview on emerging diseases due to climate change in cattle and possible natural interventions such as the use of natural substances. The method used for composing this rapport was a short literature inventory of scientific and publicly available information.

This report focuses on the emergence and re-emergence of infectious diseases in cattle in the Netherlands within the context of climate change. There are new diseases emerging in different parts of the world and some of them are spreading towards Europe. There are however many diseases that are already prevalent within Europe and which are likely to increase in prevalence in the years to come. Most likely, this forms the biggest current (infectious) threat to cattle health in the context of climate change and (re)emerging (infectious) diseases in the Netherlands.

Some of these diseases are transmitted by vectors and are therefore highly dependent on climatic conditions. Climate change can affect a specific vector, pathogen and/or its host directly which may result in geographic spread and may also influence transmission dynamics. Climate change can also influence and change whole eco-systems which also influences the success or failure of different vectors, pathogens and hosts species.

For cattle, diseases transmitted by vectors are of importance because changes in climate have shown to result in changes in spread and survival of these vectors and the pathogens they carry. The three most important vectors for cattle diseases are ticks, mosquitos and midges. Apart from transmitting disease they can also cause irritation, blood loss and stress, leading to compromised welfare and productivity.

The local ticks of northern Europe are Ixodes spp., which can transmit babesiosis and anaplasmosis. Introduction and establishment of exotic ticks like Hyalomma spp. can potentially further enhance the risk of tick-borne diseases. An exotic tick could introduce a pathogen that causes disease directly, and/or ticks could form a reservoir for (newly) introduced pathogens. Examples are the introduction of theileriosis by Hyalomma ticks.

Bluetongue and Schmallenberg virus, which have extended their spread in recent decades, are transmitted by Culicoides spp. and cause clinical disease which results in e.g. abortion and malformation of calves. Lumpy Skin Disease Virus has also been reported to have spread continuously towards Europe and is transmitted by various (blood sucking) vectors. Rift Valley Fever is an emerging disease transmitted by mosquitos, which also are occur in the Netherlands.

Other diseases that are of importance to the Netherlands and that are changing in distribution or occurrence due to climate change are liver fluke and mycotoxins. An increase in incidence of liver fluke infection has been reported in some European countries which may be due to a combination of a rise in anthelmintic resistance and more favourable climate related conditions. Mycotoxins cause illness and reduced productivity in cattle and may also pose a threat to human health e.g. via milk (products). Climate change could influence the presence of mycotoxins, and when more temperate areas get warmer they might experience a higher mycotoxin burden. Next to the effects of climate change there are a range of other factors that also drive the spread of vector-borne disease, such as live animal transport, trading of animal products, contact with wildlife, globalization, land use, sociodemographic factors and characteristics of the specific vector and pathogen involved.

International collaboration and strategic interdisciplinary monitoring programs using combinations of different modelling techniques and field data are actions performed to predict emerging diseases. An integrated approach is needed in which natural substances could be used– especially because of the resistance in conventional (antiparasitic) drugs.

Resistance to commonly used insecticides can lead to persistence of vectors, but also to residues in the environment which can influence biodiversity and ecosystems. The use of plant-derived products to reduce the burden of vectors can be a promising nature-based solution since they show certain advantages over chemical products. Their complex chemical profile naturally limits resistance forming, they only persist shortly in the environment and are generally speaking of low toxicity in various animal species. The disadvantages in the use of plant-derived products consist in the variation of the chemical substances within a plant due to variation in the circumstances under which a plant is grown. So far most findings are the result of "*in-vitro*" experiments and have been mainly evaluated for the use against ticks.

There is still a lack of knowledge especially with regard to practical application including potential toxicity for the host animal and efficacy *in vivo*. There are very few products available.

With regards to possible higher levels/more prevalent levels of mycotoxins a supply chain based approach (beyond the scope of this report) could again be a part of an integrative approach as well as supporting the animals health via mycotoxin binders and gut health support (beyond the scope of this report).

Some ethnoveterinary applications could form a source of inspiration for possible application methods, however they can be quite labor intensive and might hence be less suitable for application in systems in which bigger numbers of animals are kept. Innovative technologies such as nanotechnology could be worthwhile to be further pursued within this context.

An integrated approach in terms of habitat management to potentially lower parasite burden as well as supporting the animals immune system e.g. via gut health could be further explored to find flexible and reliable approaches suited to different farming systems.

Recommendations

- Intensify international collaboration and develop strategic interdisciplinary monitoring programs using combinations of different modelling techniques and field data;
- Carry out more research into the interaction of vectors/parasites and their habitats (e.g. tree masting) as this could also be used in predictive models for vector-borne disease. Also, knowledge gaps with regard to the vector/parasite itself should be further researched as this could provide new approaches for habitat management and preventive or curative strategies;
- Carry out an in depth literature review of mode of actions of natural substances on *I. ricinus* and *F. hepatica*, toxicity on the host animal and practical application methods as well as efficacy in vivo to identify specific research needs;
- Take into account non-infectious disease such as higher mycotoxin levels in feed and food and their potential to be more prevalent in the future in research; carry out more research where applicable;
- Intensify resistance monitoring of conventional anti-parasitic drugs as well as research into their impact biodiversity on and their persistence in nature;
- Take into account (re)emerging diseases at every stage of agricultural (and nature related) policy making and practical implementations thereof.

1 Introduction

In the light of climate change animal and human health and welfare can be affected by (extreme) weather (e.g. heat stress, acute dangers such as flooding, influence on feed, food and water) and by the emergence and re-emergence of infectious diseases, some of which are transmitted by vectors that are highly dependent on climatic conditions (OIE, 2010; Caminade et al., 2019).

The (re)emergence of (new) vector-borne diseases has been linked to climate change in many different ways. Climate change can affect a specific vector, pathogen or host directly which may result in geographic spread and may also influence transmission dynamics. Climate change can also influence and change whole eco-systems which also influences the success or failure of different vector, pathogen or hosts species (Rocklöv and Dubrow, 2020).

One example is the increase of wild boar populations in Europe which is linked to better food provisions during milder winters (Vetter et al., 2020). Wild boar are a reservoir for many diseases including African Swine Fever in pigs, which is spreading rapidly around the globe (Pollock et al., 2021). The wild boar is also a reservoir for hepatitis E, which causes rising concerns for human health in recent years (Di Cola et al., 2021).

There are many examples that highlight the complexity of emerging diseases. The spread of Bluetongue Virus in cattle was originally driven by the spread of its vector *Culicoides imicola* into southern parts of Europe. In northern Europe the indigenous *Culicoides obsoletus spp* is now playing a major part in the spread of the disease (Gale et al., 2010), showing how indigenous vector species can become vital for the spread of new diseases.

Another example is the spread of lumpy skin disease in cattle. Lumpy Skin Disease Virus can be transmitted by various (blood sucking) vectors such as mosquitoes *(Aedes aegypti*), ticks (*Rhipicephalus* and *Amblyomma* species), stable flies (*Stomoxys calcitrans*) and possibly also the house fly (*Musca domestica*) (Sprygin et al., 2019). Kononov et al. (2020) provide evidence that disease transmission via indirect contact which is not vector dependent (e.g. via a shared trough) is possible, which could also contribute to the persistent spread of lumpy skin disease. This shows the complexity and intertwinement of different factors contributing to the spread of diseases.

Next to the effects of climate change there are a range of other factors that also drive the spread of vector-borne disease, such as live animal transport, trading of animal products, contact to wildlife globalization, land use, sociodemographic factors and characteristics of the specific vector and pathogen involved (Rocklöv and Dubrow, 2020, see also Figure 1).

Resistance to commonly used insecticides plays a role, not only in terms that a vector cannot be eradicated efficiently (and may get the evolutionary advantage of greater capacity), but also that residues in the environment can influence biodiversity and ecosystems (Benelli, 2020; Kumar et al., 2020; Rocklöv and Dubrow, 2020; Caminade et al., 2019).

With regards to surveillance/forecasting of (re)emerging diseases multiple authors argue that good surveillance systems are an absolute necessity, but that practical implementation can prove difficult due to the complexity of the intertwinement of climate change with a lot of other factors (Kumar et al., 2020; Rocklöv and Dubrow; 2020, Springer et al., 2020a; Bartlow et al., 2019; Gale et al., 2010).

Therefore integrated approaches such as integrated surveillance and habitat management systems, vaccines and the use of natural substances to keep vector burden low are researched at the moment (Kumar et al., 2020). Global interdisciplinary collaboration is desirable as many of the emerging diseases are zoonotic with animals being potential reservoirs for disease in humans (Folly et al., 2020; Springer et al., 2020a; Bartlow et al., 2019).

The interactions between factors involved in the transmission, spread and establishment of vector-borne diseases are depicted in Figure 1.

2 Materials and methods

For this short literature inventory Scopus, Google Scholar and PubMed have been searched. The main search terms were "emerging diseases + cattle (+ review)", "vector-borne diseases + cattle (+ review)" and "tick-borne diseases + cattle (+review)". For more general information these terms were used without "cattle". Also individual diseases or vectors and "natural substances + vectors" were used when applicable. In addition websites of official institutions and information available on the internet such as in online farming magazines or brochures were used.

3 Results

3.1 (Re)emerging diseases in cattle

At a global level, cattle play a major role in food systems ranging from pastoral systems and smallholdings to intensively and specialized farming systems. In the Netherlands intensive farming is the predominant way of farming (dairy) cattle. According to the Dutch dairy organization Zuivel NL, the Dutch agri- and food sector contributes with 7% to the Dutch economy of which 1% is contributed by the dairy industry. This makes the Netherlands one of the top producers in dairy in Europe when calculated in kg per capita (Zuivel NL: Dutch Dairy in Figures, 2019).

Any (re)emerging disease will therefore not only have a potential impact on the health and welfare of Dutch cattle (and potentially humans) but also an environmental and economic impact.

Currently the Dutch governmental seeks to make a transition into a circular and sustainable agricultural system with as little negative impact on nature, environment and climate as possible. Healthy soil is seen to be a basis for this approach. The aim is to have less harmful residues in soil and water, and more biodiversity (Realisatieplan Visie LNV: Op weg met nieuw perspectief, 17 juni 2019). Furthermore, the Netherlands have taken an active approach to reduce the use of antibiotics and other resistance prone chemical drugs in the Dutch livestock industry. The use of natural substances together with specific management strategies can form a part of this approach (Groot et al., 2021).

Cattle can potentially play an essential role in this vision on agriculture e.g. in grassland management in nature areas. Management practices such as elevating water levels for managing grassland or the fact that the Dutch Forestry Commission (Staatsbosbeheer) does not allow cattle grazing in nature when treated with chemical drugs for parasites, can also lead to potential health and welfare threats for cattle (and potentially) humans. Massive tick infestations of cattle grazing in such areas have been reported by veterinarians and in a non-scientific study (Rund vaker ziek door teek - Nieuwe Oogst, last accessed on 07.05.2021).

The main vectors for disease transmission are arthropods like mosquitos, midges and ticks. But also species such as flies are known to transmit disease in cattle (Folly et al., 2020; Sprygin et al., 2019).

An extensive overview of surveillance activities and spread of vectors and (human) disease within the EU can be found on the European Centre for Disease Prevention and Control website (https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/vector-net, last accessed 07.05.2021).

3.2 Tick-borne diseases in cattle

Ticks are widely known as carrier of disease for various species. Apart from transmitting disease they can also cause irritation and stress leading to compromised welfare and productivity as well as possible anaemia by blood sucking (Kumar et al., 2020). Within the temperate regions of Europe *Ixodes ricinus* is a common vector of tick-borne disease in domestic and wild animals (inclusive birds) and humans (Wilhelmsson et al., 2021; Springer et al., 2020a).

Protozoan diseases such as babesiosis and bacterial disease like anaplasmosis caused respectively by *Babesia divergens* and *A. phagocytophilum* are transmitted by *Ixodes ricinus* and cause clinical disease in cattle. Co-infections of *B. divergens* and *A. phagocytophilum* in cattle have been described and can potentially enhance the severity of clinical disease (Johnson et al., 2020; Andersson et al., 2017). Co-infections of *B. divergens* and *A. phagocytophilum* in the tick itself have so far not been described

(Johnson et al., 2020). However co-infections with different pathogens including *N. mikurensis* and Babesia spp. have been described in *Ixodes ricinus* ticks (Coipan et al., 2013).

Cattle are also potential reservoir hosts for *A. phagocytophilum* and zoonotic Babesia spp. such as *B. divergens*. Furthermore cattle serve as sentinel host for zoonotic tick-borne encephalitis virus and *Borellia burgdorferi* s.l. (the causative agent of Lyme disease) (Springer et al., 2020a). Tick-borne encephalitis virus can also be transmitted to humans via raw milk (products) (Blomqvist et al., 2021; Dobler et al., 2012).

3.2.1 Babesia

Babesia spp. are protozoan parasites who affect the red blood cells of the infected animal (Springer et al., 2020a). Within Europe *Babesia divergens* is the species which is the most widespread amongst cattle (Azagi et al., 2020; Folly et al., 2020) Between ticks Babesia is transmitted trans-ovarially to the next generation (Folly et al., 2020).

The disease is commonly known as "red water" referring to the cow passing dark urine due to haemolytic anaemia (destruction of erythrocytes). Usually a rapid onset of fever reaching up to 41 °C is seen. Further clinical signs can be quite unspecific such as depression and anorexia. Subclinical presentations such as a rise in temperature or anorexia are described and may be missed. Complications concerning renal, liver and lung functions can result in the death of an infected animal (Folly et al., 2020). If an animal recovers it can become a reservoir as low levels of infection can be persistent in the erythrocytes for years without the animal showing any symptoms. Young animals (< 9 months) are not affected by clinical disease as they demonstrate an innate, age related resistance (Folly et al., 2020; Springer et al., 2020b; Zintl et al., 2003).

B. divergens is also a zoonotic disease. It is mainly a problem in immunocompromised patients (Folly et al., 2020; Gray et al., 2009).

3.2.2 Anaplasma

Anaplasmosis – also known as tick-borne fever or pasture fever – is caused by *Anaplasma phagocytophilum*, a gram-negative bacterium (Dumler et al., 2001).

Clinical symptoms are fever (>40°C), anorexia and drop in milk yield, also abortions can occur (Folly et al., 2020; Springer et al., 2020a). Respiratory stress and secondary infection are also described (Folly et al., 2020). Cattle seem to become persistently (re)infected (Springer et al., 2020a).

A. phagocytophilum is also a zoonotic disease. Affected humans generally show unspecific, febrile, flu like symptoms (Hing et al., 2019).

3.2.3 *Ixodes ricinus* and climate change

Ixodes ricinus depends on a combination of temperature and humidity for its life cycle, with humidity being of great importance (Gray et al., 2021). While generally ticks are mainly active in spring, summer and autumn, milder winters enhance the chance of prolonged tick activity and therefore a prolonged risk of infection with tick-transmitted diseases (Johnson et al., 2020).

Its habitat consists mainly of humid areas such as headlands or unimproved permanent pasture but also forest floor (Folly et al., 2020; Caminade et al., 2019).

I. ricinus is widely spread within Europe with the range expanding into higher altitudes (Caminade et al., 2019; Stünzer et al., 2006) and also further northwards (Caminade et al., 2019). For this expansion climate change is probably a driving factor (Jore et al., 2014, Hvidsten et al., 2020). Infection with diseases transmitted by ticks could hence be more likely in the future (Gilbert et al., 2021).

Gray et al. (2021) describe a current lack in understanding of some mechanisms linked to host choosing behaviour in *I. ricinus. I. ricinus* is host unspecific (>300 species) and the initial contact with a host could well be by chance. More specific mechanisms are likely to become of more relevance during the process of attachment. Within the tick life cycle cattle are an important host for adult female ticks. Large ungulates are seen as the maintenance host which's most important for *I. ricinus* populations.

Obiegala et al. (2021) conducted a study on small mammals as important maintenance hosts for ectoparasites and found that ticks were more prevalent than fleas or mites in the small mammals in urban and forest areas they examined for their studies in Germany.

According to Gray et al. (2021) another open question is if immunity by vaccination against *I. ricinus* could be achieved. So far this has proven difficult due to a variety of bioactive compounds in the tick's saliva. The development of commercially viable vaccines is difficult to achieve (Knorr et al., 2018).

With regards to the adaptability of *I. ricinus* to climate change and the tick's ability to live in changing eco-systems its water regulation system is of importance (Alkishe et al, 2017). Gray et al. (2021) describe a lack in current knowledge regarding the understanding of water regulation in *I. ricinus*. Hermann and Gern (2015) report possible divergences in behaviour and physiological mechanisms between uninfected and infected ticks which could influence the spread of disease in changing environments.

How the abundancy of and disease spread by *I. ricinus* due to climate change will evolve also depends on complex relationships in the tick's eco-system (Hartemink et al. 2021), of which al lot is also not yet fully understood. While generally speaking warmer climate is favourable for *I. Ricinus* (Eberhard et al., 2021), in areas affected by severe droughts possibly less ticks will survive. *I. ricinus* is well suited to survive winters. Dautel et al. (2016) report decreased survival only at air temperatures of -15 °C and without snow cover. While temperature and precipitation are factors generally described in literature as reasons influencing the abundance of *I. ricinus*, Bregnard et al. (2021) describe that masting (when the tree seeds, correlated to weather conditions (Zamorano et al., 2018)) by deciduous trees also influences the abundancy of ticks. Their 15 year study monitored the amount of *I. ricinus* nymphs and adults and their *B. burgdorferi* s.l. infection status. Climate related data and masting of beech trees were monitored. Beech trees don't seed every year. It is described that two years after a masting event the numbers of *I. ricinus* nymphs can increase immensely.

3.2.4 Exotic ticks and disease

Introduction and establishment of exotic ticks can potentially further enhance the risk of tick-borne disease. This can work two ways. An exotic tick could bring in a pathogen that causes disease directly, or ticks could form a reservoir for (newly) introduced pathogens (Folly et al., 2020).

The case of African Swine fever demonstrates how exotic diseases -that are originally transmitted by ticks- can evolve to form a threat to animal health and welfare in Europe. The virus originates in Africa where it is transmitted by ticks of the genus Ornithodoros. Warthogs or other indigenous species generally only suffer from subclinical disease. In domestic pigs the disease has immense health implications with morality rates up to 100% being reported (Folly et al., 2020).

Also migrating birds form a risk with regards to the introduction of (infected) tick species (Folly et al., 2020). Hyalomma species have been reported to be transmitted by birds (Estrada-Peña et al., 2021; Portillo et al., 2021).

So far Northwestern European climate seems to be too cold for Hyalomma spp. to establish themselves. However Folly et al (2020) express their concern about the findings of an adult *H. rufipes* tick on an untraveled horse in the South of England. The tick "could have been introduced as a nymph by migrating birds" (Hansford et al., 2019) which "suggests partial completion of the ticks' lifecycle within the UK".

Hylomma nymphs have also been reported in the Netherlands. Adult ticks are rare but have been reported (2018:1, 2019: 11, 2020:4; one of the ticks has tested positive for *Rickettsia aeschlimannii*). According to the RIVM the hylomma tick is not established in the Netherlands as it is too cold for the ticks to survive winter (RIVM https://www.rivm.nl/tekenbeten-en-lyme/hyalomma-teken, last accessed 07.05.2021).

Hyalomma spp. can transmit Theileria to cattle which can cause clinical theileriosis. Theileria spp. are protozoans closely connected to Babesia. In theileriosis subclinical to lethal infections are described. Acute infections are generally characterized by fever and (immune mediated haemolytic) anaemia, conjunctivitis and loss of stamina (Onyinyechukwu et al., 2020). Bovine theileriosis is mainly reported in Africa, Asia the Middle East and Oceania (Australia and New Zealand). Some forms of theileriosis transmitted by ixodid vectors have been reported in the South and South East of Europe (Greece, Italy, Portugal, Spain, Hungary) and Russia. Hyalomma has been reported as vector in Portugal (Onyinyechukwu et al., 2020).

3.2.5 Monitoring ticks

Wageningen University & Research, RIVM and Nature Today are responsible for Tekenradar (Tick Radar), a website that predicts tick activity in the Netherlands.

3.3 Midge-borne diseases

In Europe the main midge species involved in virus transmission are members of the genus Culicoides, *namely C. obsoletus, C. scoticus, C.dewulfi, C. chiopterus, C. pulicaris*, and *C. punctatus* (Carpenter et al., 2013). Mignotte et al. (2021) highlight de complexity of spread of Culicoides spp. (*C. obsoletus*). They describe an active spread at short distances and a semi-active or passive spread at long distances (e.g. by wind). With regards to the environmental factors that they investigated in their study, only cattle density seems to be of influence. In cattle the Bluetongue and Schmallenberg virus are transmitted by Culicoides spp. and cause clinical disease.

3.3.1 Bluetongue

Bluetongue virus belongs to the Oribiviridae. Clinical symptoms are elevated temperatures, inflammation and erosion of the nasal and oral mucous membranes, inflammation of the coronary band resulting in lameness. Ulceration of the teats has also been reported (Folly et al., 2020). Congenital abnormalities in calves due to transplacental transmission have been described (Williamson et al., 2010).

Möhlmann et al. (2021) used field data (midge catching) combined with a multi-scale modelling approach to substantiate the actual biting activity of midges that transmit Bluetongue virus. They conclude that within Europe during different seasons “95% of naïve herds in western Europe have been at risk of sustained transmission over the last 15 years” (p. 17) (with a variation of transmission intensity in different herds).

3.3.2 Schmallenberg

Schmallenberg virus belongs to the family of Orthobunya-viridae. The main symptoms are abortion and malformation in calves due to an in utero infection. In grown cattle symptoms can be mild. A negative impact on milk production and diarrhoea have been described (Folly et al., 2020).

The spread of Schmallenberg has been reported to be linked to climate change. It is thought that wind played an important role in spreading the disease which was first described in Germany in 2011 and quickly spread across the European continent. Besides some years with limited viral circulation the disease kept reemerging in different countries (Endalew et al., 2019).

3.3.3 Midges and climate change

Warmer climate conditions enhance the spread of southernly midges and also increase the capacity of indigenous species acting as vectors for disease (Caminade et al., 2019). Midges can be moved over long distances by wind (Folly et al., 2020).

3.3.4 Exotic diseases transmitted by midges

In Africa, Asia and Australia outbreaks of bovine ephemeral fever transmitted by Culicoides spp. have been described. The clinical symptoms consist of fever and depression accompanied by discharge from the nose and eyes. Lethal cases have been reported. No cases in Europe have been reported apart from possible outbreaks in Turkey’s European part.

3.4 Mosquito-borne diseases

According to the Dutch National Institute for Public Health and the Environment (RIVM) there are currently around thirty different mosquito species established in the Netherlands. Next to the indigenous species also some exotic species such as the tiger mosquito (*Aedes albopictus*) have been reported. Up to now the Asian tiger mosquito has not been able to establish itself in the Netherlands (RIVM https://www.rivm.nl/muggen, last accessed 07.05.2021).

At the moment there are no major diseases transmitted by mosquitos to cattle within Europe.

Batai virus has been found in cattle in Germany and it is suggested that cattle can act as a host but the hosts don’t seem to be clinically affected. It is reported to cause febrile disease in humans (Hofmann et al., 2015). Mosquitos and climate change Mosquitos are very susceptible to environmental conditions such as precipitation and temperature. They depend on water for their lifecycle and development. Warmer temperatures can aide a shorter developmental cycle and in the case of winters getting milder in northern areas, southern mosquito species have more opportunity to spread into more northerly areas. *Aedes albopticus* and *Aedes aegypti* have spread from Asia to almost everywhere in the world. For both species human activity has been suggested as the main mode of global distribution (Bartlow et al., 2019). Mosquitos are carriers of different viruses (e.g. flavi-viridae) and via migratory birds those could become more established within the EU (Folly et al., 2020). Yanase et al. (2020) also describe mosquito (amongst other vectors) borne arboviridae as an emerging problem in ruminant health in East Asia.

3.4.1 Exotic diseases transmitted by mosquitos

Rift Valley Fever is an emerging disease which causes febrile disease in cattle that can result in hemorrhagic disease and liver failure. There is a high mortality in juvenile animals. It is also a zoonotic disease (Folly et al., 2020). It is mainly found in parts of Africa and the Arabian Peninsula. It is suggested that Rift Valley Fever can be transmitted by over 50 mosquito species (Wichgers et al, 2021). Studies have shown that European mosquito species can be competent vectors for the virus (Vloet et al., 2017). Folly et al. (2020) suggest that trade of live animals with Africa can pose a risk factor for the introduction of the disease into Europe. Dutch health authorities reported in October 2020 that the West Nile virus was detected in the Netherlands in a man, presumably bitten by a mosquito near Utrecht. Moreover researchers from Wageningen University and their colleagues from Leiden University recently caught mosquitoes in the same area and found the West Nile virus in these mosquitoes. Both universities collaborate in the One Health Pact (https://www.wur.nl/en/Research-Results/Research-Institutes/plant-research/show-wpr/First-locally-caused-infection-with-West-Nile-virus-suspected-in-the-Netherlands.htm).

Kroeker et al. (2020) describe the role that wildlife (deer) has in the spread of the disease by forming a reservoir. They tested the susceptibility of North American white tailed deer cell lines to the Rift Valley Fever virus and found them susceptible. This highlights the complexity of viral spread to a non-endemic region (Rolin et al., 2013).

3.5 Other emerging diseases linked to climate change

3.5.1 Liver fluke

Liver fluke (*fasciola hepatica*) is an internal parasite that affects the liver of cattle. It mainly causes reduced growth and milk yield. Its main development is in wet grassland and depending on an intermediate snail host. An increase in incidence of fascioliasis has been reported in some European countries which may be due to a combination of a rise in anthelmintic resistance and more favourable climate related conditions. In the future the transmission season could be lengthened (Caminade et al., 2019, Beesley et al., 2018).

Climate change has also been linked to an increase in *Brachycera* spp. fly populations. They can impact the health of cattle by for example causing skin irritation or acting as vectors for transmitting many different diseases such as viruses (eg Lumpy Skin Disease Virus), bacteria (e.g. *Moraxella bovis*), protozoa (e.g. Trypanosoma spp.) and nematodes (e.g. *Parafilaria bovicola* and *Stephanofilaria stilesi*) (Baldacchino et al., 2018).

Parafiliaria bovicola is described in imported animals in the Netherlands (Borgsteede et al., 2009) but so far not endemic. However an increase in Belgium is reported (Dutch Animal Health Service, https://www.gddiergezondheid.nl/sitecore/content/DAPContact/Home/Dierziektes/Parafilaria?sc_lang=nl, last accessed 07.05.2021).

3.5.2 Lumpy Skin Disease Virus

Lumpy Skin Disease Virus has also been reported to have spread continuously towards Europe (Kononov et al., 2020; Sprygin et al., 2019). Clinical signs are fever, edema and (lumpy) skin lesions (Kononov et al., 2020). Epidemiologically the spread of the disease is not fully understood yet but multiple vectors as well as non-vector related spread are described to play a role in disease epidemiology (Kononov et al., 2020; Sprygin et al., 2019).

3.5.3 Mycotoxins

Mycotoxins cause illness and reduced productivity in cattle (Gonçalves et al., 2010). Mycotoxins also pose a threat to human health e.g. via milk (products) (Min et al., 2021). Russell et al. (2010) argue that climate change could influence the presence of Mycotoxins. If more temperate areas get warmer they might experience a higher mycotoxin burden.

4 Management of emerging diseases with an integrated approach using natural (plant) substances

There is wide consensus that innovative strategies for vector control are needed if we really want to prevent global spread of new vector-borne diseases (Koenraadt et al., 2021). A WHO resolution has been adopted on Global Vector Control Response (GVCR) 2017-2030 (WHO 2017). It outlines roles and responsibilities for both Member States and WHO’s secretariat. The increasing resistance to commonly used anti-parasitic drugs such as acaricides has also been named as one of the problems in (re)emerging diseases (Kumar et al, 2020; Rocklöv and Dubrow, 2020; Caminade et al., 2019).

The use of phytochemicals is one of the approaches to circumvent resistance to insecticides. Kumar et al. (2020) mention the use of “characterized phytoformulations” as one of the possible intervention strategies within an integrated approach to combat *Hyalomma* tick species.

They state that plant-derived products show certain advantages over chemical products. Their complex chemical profile naturally limits resistance forming (see also Benelli (2020)), they only persist shortly in the environment and are generally speaking of low toxicity in other animal species. The summarizing table in publication of Kumar et al. (2020) also highlights that different plant preparations excite different mode of actions. Some act e.g. on the fertility of ticks, egg hatching or larvae while others kill ticks or repel them.

There are also disadvantages in the use of plant-derived products. The active chemical substances within a plant can vary due to the circumstances under which a plant is grown. Exposure to sunlight and high volatility can (amongst others) make the chemical substances within a plant less stable then chemical products.

Also some other disadvantages are named: the necessity to find “activity based marker compounds” for quality assurance, the potentially high costs of product development (toxicity testing) in combination with limited options for intellectual property and a reliable supply of plants.

Benelli et al. (2016) also describe non applied uniformity in research as a critical point in the use of phytogenic substances. This results in difficulties comparing different publications.

Kumar et al. (2020) also mention “biased perception regarding chemical acaricides vis-a-vis phytoformulation” as hurdle in the process of the development of such products.

So far most findings are the result of “*in-vitro*” experiments. In his review Benelli (2020) highlights recent research that describes the mode of action of phytogenic substances in the control of ectoparasites and the development of products that can be used under practical conditions (e.g. stability).

Table 1 *Brief summary of the findings by different authors (Benelli (2020), Kumar et al. (2020), Benelli et al. (2016) and Smolarz et al. (2013)) with regards to the usage of phytochemicals mainly in the use against ticks.*

Literature	Findings	Author(s)
Evaluation of 105 plant families with 365 species against 31 tick species (mainly *R. microplus*)	• Some solvent guided extracts and essential oils (from aerial parts of the plant); concentrations of extracts are provided in article • anti-tick activity up to100% recorded in *R. microplus* (not further specified) • *H. scupense*: 100% inhibition of reproduction is described in the use of essential oils from leaves and flowering tops through hydrodistillation from *Lavendula stoechas, Origanum floribundum* Munby, *Rosmarinus officinalis* and *Thymus capitatus, Eucalyptus camaldulensis, E. globulus Labill* • *H. marginatum*: 100% tick mortality in 3 hrs by use of volatile essential oil collected from aerial part of plant at flowering stage through hydrodistillation of *Saturejathyembra L.* • *H. anatolicum*: 100% failure of egg hatching by using petroleum ether and ethanolic extracts of leaves form of *Guierase negalensis* • Most findings are *in vitro*	Kumar et al. (2020)
Use of predators (pathogens and parasites), bacteria, fungi, spiders, ants, beetles, rodents, birds and other living organisms. 96 commercially listed (33 bacteria, 36 fungi). More are reported.	• Varying results for different developmental stages in different species • Promising *in vitro* results, hardly any *in vivo* data available	Kumar et al. (2020)
Use of 83 plant species from 35 botanical families and their ascaricidal/repellent effect *on Ixodes ricinus, Ixodes persulcatus, Amblyomma cajennense, Haemaphysalis bispinosa, Haemaphysalis longicornis, Hyalomma anatolicum, Hyalomma marginatum rufipes, Rhipicephalus appendiculatus, Rhipicephalus (Boophilus) microplus, Rhipicephalus pulchellus, Rhipicephalus sanguineus* and *Rhipicephalus turanicus* were reported in the selected literature	• Asteraceae (were mentioned in 15% of the selected studies), Fabaceae (9%), Lamiaceae (10%), Meliaceae (5%), Solanaceae (6%) and Verbenaceae (5%)	Benelli et al. (2016)
23 raw materials of 16 plant species (chloroform and methanol extracts) and their toxic effect on *I. ricinus*	• Death of tick within 1 hr: *Helichrysum arenarium (L.)* Moench*., Centaurea cyjanus L., Taraxacum officinale Web., Tanacetum vulgare L., Chelidonium maius L.* and *Armoracia rusticana* Gilib. in the concentrations 0.6; 4.4; 6.1; 6.8; 7.2 and 7.6 mg/mL respectively	Smolarz et al. (2013)
Review on current issues in non-chemical insecticides: • Molecular Targets for Components of Essential Oils in the Insect Nervous System—A Review https://doi.org/10.3390/molecules23010034 • Plant Natural Products for the Control of *Aedes aegypti*: The Main Vector of Important Arboviruses https://doi.org/10.3390/molecules25153484 • Efficacy of *Origanum syriacum* Essential Oil against the Mosquito Vector *Culex quinquefasciatus* and the Gastrointestinal Parasite *Anisakis simplex*, with Insights on	• Research focusing on the development of new formulations (including those relating to nano-objects) to magnify the effectiveness and stability of green insecticides in the field represents key advances • The impact of sub-lethal doses of green insecticides on insect behavior represents a timely challenge for future research	Benelli (2020)

Literature	Findings	Author(s)
Acetylcholinesterase Inhibition https://doi.org/10.3390/molecules24142563 • *Pimpinella anisum* Essential Oil Nano-emulsion Toxicity against *Tribolium castaneum*? Shedding Light on Its Interactions with Aspartate Aminotransferase and Alanine Aminotransferase by Molecular Docking https://doi.org/10.3390/molecules25204841 • Effect of Naringenin and Its Derivatives on the Probing Behavior of *Myzus persicae* (Sulz.) https://doi.org/10.3390/molecules25143185 • Surfactantless Emulsions Containing Eugenol for Imidacloprid Solubilization: Physicochemical Characterization and Toxicity against Insecticide-Resistant *Cimex lectularius* https://doi.org/10.3390/molecules25102290 • Optimal Extraction of *Ocimum basilicum* Essential Oil by Association of Ultrasound and Hydrodistillation and Its Potential as a Biopesticide Against a Major Stored Grains Pest https://doi.org/10.3390/molecules25122781 • Menthol Increases Bendiocarb Efficacy Through Activation of Octopamine Receptors and Protein Kinase A https://doi.org/10.3390/molecules24203775 • Insights on the Larvicidal Mechanism of Action of Fractions and Compounds from Aerial Parts of *Helicteres velutina* K. Schum against *Aedes aegypti L.* https://doi.org/10.3390/molecules25133015 • Insecticidal Toxicities of Three Main Constituents Derived from *Trachyspermum ammi (L.)* Sprague ex Turrill Fruits against the Small Hive Beetles, *Aethina tumida Murray* https://doi.org/10.3390/molecules25051100		

Kumar et al. (2020) also mention possible biological intervention by for example pathogens, ants and birds to keep tick populations under control as a part of an integrative approach. Also here mainly *in vitro* research has been carried out. They describe the use of "predators (pathogens and parasites), bacteria, fungi, spiders, ants, beetles, rodents, birds and other living organisms". Commercially listed species are available. Results for different developmental stages in different species vary. There are promising *in vitro* results, however hardly any *in vivo* data is available.

Tick-transmitted diseases are likely to be on the rise in the years to come and are reported in cattle grazing in a Dutch nature reserve. Table 2 (see below) summarizes some relevant research and practical information regarding possible natural interventions with regards to ticks (with emphasis on *I. ricinus* – the most commonly found tick on cattle in the Netherlands).

Also some information is given on possible natural interventions with regards to liver fluke and mycotoxins as the exposure of cattle in the Netherlands may increase also in the coming years.

Table 2 *Short overview on possible natural interventions with regards to prevention of diseases transmitted by ticks (I. ricinus), including some information on possible natural interventions with regards to liver fluke and mycotoxins (based on Mordvinov et al. (2021), Ibekwe (2019), Machado Pereira da Silva et al. (2020), Cwiklinski et al. (2018), Neijenhuis et al. (2017), Wanzala (2017), Knubben-Schweizer et al. (2015), Rana (2015), Chhabra et al. (2014), https://www.wur.nl/nl/download/stalboekje-melkvee-2016.htm, S. Siegenthaler (2014) thesis, Vetsuisse Faculty, University of Bern, Santos and Fink-Gremmels (2014), Villalba et al. (2014), Wanzala et al. (2012), Toner et al. (2008), Whitlow. and Hagler (2005), Elbertsen (2004), Min et al. (2003)).*

Emerging diseases	Possible natural intervention	Practical information
Tick-borne diseases such as Babesia	- Habitat management (not within the scope of this report): e.g. use of certain plants to repel ticks e.g. *Sambuccus nigra*. - Use "green" tick repellents instead of synthetical ones (see also Table 1). - From a ethnoveterinary perspective there are a lot of promising plants but the in vivo efficacy (especially as part of an integrated system) and safety for the host animal should be further studied. Plants like *Allium sativum* and *Azadirachta indica* are described in ethnoveterinary literature. Nanotechnology in the use of natural products should also be further studied.	- https://www.vkon.nl/projecten-items/natuurlijke-tekenbestrijding/: Ticks can form a serious threat for the health of cattle in a Dutch nature reserve (babesiosis). The amount of ticks in a Dutch nature reserve was very high with neither the conventional or herbal treatment having sufficient effect. The trial got ended after three weeks due to health concerns of the exposed cattle. - https://edepot.wur.nl/115355 (Elbertsen (2004): boiling garlic, putting branches in stables e.g. *Sambuccus nigra*, fly traps, feeding garlic - Practical applications in ethnoveterinary medicine include: burning plants (cattle don't seem to avoid the smoke but to readily put their heads into it), growing certain plants e.g. *Azadirachta indica*, Capsicum spp; making e.g. pastes, concoctions etc. and applying them to the animals; spraying dust e.g. from *Tagetes minuta*.
Liver fluke	- Habitat management (not within the scope of this report): e.g. snail control, rotation systems. - Anthelmintic activity of anti-oxidants (tested on *Opisthorchis felineus*): flavonoids. - Genistein (e.g. from soy) in vitro, *Fasciola hepatica* in genistein at a concentration of 0·27 mg/ml movement stopped after 3 hrs - Use critical steps in host invasion and/or metabolism of liver fluke to develop new vaccines or drugs. Those key points could also be used to develop natural interventions. - Stablebooks: No natural products are available on the market which are safe for animals and humans and kill internal parasites. 2 products are mentioned: Herb-All Force (tested on *Ascaris suum* in pigs and mice: The results suggest that there is a detectable effect on the migration of *A. suum* larvae, recommend for prophylaxis and supportive treatment), TWM Hepatica to support liver and immune function. - Ethnoveterinary medicine: *Fumaria parviflora*: aqueous extract in feed: 120 mg/kg (twice) led to approx. 90% reduction in fecal egg count (day 28), improvement of body condition, more information available for small ruminants. - Tannin rich plants are often mentioned in ethnoveterinary literature against internal parasites.	- https://www.louisbolk.institute/downloads/3259.pdf- (Nijenhuis et al. (2017))-advise practical liver fluke management on farm incl. introduction of tool to measure the liver fluke status on a farm - Practical advice stablebook dairy: A more biodiverse grassland seems to lower the worm burden. - Ethnoveterinary experience: More resilient animals via good quality nutrition and water, pasture management, shelter; tannin-rich plants frequently mentioned.

Emerging diseases	Possible natural intervention	Practical information
	- *Azadirachta indica* and *Cuminum cyminum* are mentioned in ethnoveterinary literature in the context of Fasciola hepatica - Self-medication of ruminants against helminths is reported	
Mycotoxins	- Supply chain management (beyond the scope of this report) - Mycotoxin binders (beyond the scope of this report): e.g. glucomannan	

Figure 2 *Self-treatment of cattle against insects in Ethiopia (from Indigenous veterinary practices of South Omo agro-pastoral communities, T. Mesfin and S. Shiferaw).*

5 Discussion and conclusion

The spread of (re)emerging diseases is complex and difficult to predict. Many authors therefore call for international collaboration and strategic interdisciplinary monitoring programs using combinations of different modelling techniques and field data. They also call for an integrated approach in which natural substances could be of potential usage – especially because of the resistance in conventional (antiparasitic) drugs.

There are new diseases emerging in different parts of the world and some of them are spreading towards Europe. There are however many diseases that are already prevalent within Europe which are likely to increase in prevalence in the years to come. This is most likely the biggest current (infectious) threat to cattle health in the context of climate change and (re)emerging (infectious) diseases in the Netherlands.

In addition to this, emerging diseases do not only form a potential threat to animal welfare by impaired health but can lead to severe animal suffering due to strategic choices made out of fear of disease importation. This was the case for cattle transported from Spain to Turkey on ship. The ship was not allowed to dock because of fear of a spread of Bluetongue Virus. After months at sea the animals died or were euthanized (https://nos.nl/artikel/2370579-koeien-op-geweigerd-middellandse-zee-schip-worden-geruimd).

Many authors describe the transport of live animals as a potential route of disease importation and spread. Countries such as the UK and New Zealand are considering banning or have banned live animal export for slaughter and fattening (https://www.reuters.com/world/uk/uk-ban-live-animal-exports-slaughter-part-welfare-plan-2021-05-11/,https://www.theguardian.com/world/2021/apr/14/new-zealand-to-stop-exporting-livestock-by-sea).

Also, many of the diseases are zoonotic. An increase in animal disease could, therefore, mean a potential increase in human diseases. More research should be carried out into the interaction of vectors and their habitats (e.g. tree masting) as this could also be used in predictive models for vector-borne disease. Also, knowledge gaps with regard to the vector itself should be further researched as this could provide new approaches for habitat management and preventive or curative strategies.

Non-infectious disease such as higher mycotoxin levels in feed and food and their potential to be more prevalent in the future should be taken into account in research and more research should be carried out where applicable. Changing agricultural policies and production systems pose their own unique opportunities for emerging diseases.

More nature-based animal management systems could provide more opportunities for cattle to come in contact with vectors such as ticks or diseases like liver fluke while at the same time those systems could potentially be driving factors for a more sustainable form of agriculture in a changing climate. Soil health and the ability to cope with varying water levels will play an essential role in achieving sustainability of food and water supply for the future.

Therefore, (re)emerging diseases should be taken into account at every stage of agricultural (and nature related) policy making and practical implementations thereof.

There should also be support for international cooperation not only in terms of interdisciplinary surveillance and modelling but also in terms of structured research into the use of natural products as part of an integrated approach.

So far the literature available shows some promising *in-vitro* results (e.g. different modes of actions on different developmental stages, low likelihood of resistance development or impact on biodiversity in plant derived substances) but there is little information available on *in vivo* efficacy and application methods as well as safety for the host animal.

Some ethnoveterinary applications could form a source of inspiration for possible application methods, however they can prove to be quite labor intensive and might hence be less suitable for application in systems in which bigger herds of animals are kept.

An integrated approach in terms of habitat management to potentially lower vector/parasite burden as well as supporting the animals immune system e.g. via gut health could be further explored to find flexible and reliable approaches suited to different farming systems.

Recommendations:

- Intensifying international collaboration and developing strategic interdisciplinary monitoring programs using combinations of different modelling techniques and field data;
- More research should be carried out into the interaction of vectors/parasites and their habitats (e.g. tree masting) as this could also be used in predictive models for vector-borne disease. Also, knowledge gaps with regard to the vector/parasite itself should be further researched as this could provide new approaches for habitat management and preventive or curative strategies;
- A in depth literature review of mode of actions of natural substances on I. ricinus and F. hepatica, toxicity on the host animal and practical application methods as well as efficacy in vivo should be carried out to identify specific research needs;
- Non-infectious disease such as higher mycotoxin levels in feed and food and their potential to be more prevalent in the future should be taken into account in research and more research should be carried out where applicable;
- Resistance monitoring of conventional anti-parasitic drugs as well as research into their impact on biodiversity should be intensified;
- (Re)emerging diseases should be taken in account at every stage of agricultural (and nature related) policy making and practical implementations thereof.

References

Alkishe, A.A., Peterson, A.T., Samy, A.M. 2017. "Climate change influences on the potential geographic distribution of the disease vector tick *Ixodes ricinus*." PLoS ONE 12(12): e0189092.

Andersson, M.O., Víchová, B., Tolf, C., Krzyzanowska, S., Waldenström, J., Karlsson, M.E. 2017. "Co-infection with *Babesia divergens* and *Anaplasma phagocytophilum* in cattle (Bos taurus), Sweden." Ticks Tick Borne Dis. 8:933–5.

Azagi, T., Hoornstra, D., Kremer, K., Hovius, J.W.R., Sprong, H. 2020. "Evaluation of disease causality of rare *Ixodes ricinus*-borne infections in Europe." Pathogens 9:150. doi: 10.3390/pathogens9020150.

Baldacchino, F., Desquesnes, M., Duvallet, G., Lysyk, T., Mihok, S. 2018. In: Garros Claire (ed.), Bouyer Jérémy (ed.), Takken Willem (ed.), Smallegange Renate C. (ed.). Pests and vector-borne diseases in the livestock industry. Wageningen: Wageningen Academic Publishers, p. 55-90. (Ecology and Control of Vector-Borne Diseases, 5); DOI: 10.3920/978-90-8686-863-6_3.

Bartlow, A.W., Manore, C., Xu, C., Kaufeld, K.A., Del Valle, S., Ziemann, A., Fairchild, G. and Fair, J.M. 2019. "Veterinary importance and integrated management of Brachycera flies in dairy farms." Vet. Sci. 6, 40. doi:10.3390/vetsci6020040.

Beesley, N.J., Caminade, C., Charlier, J., Flynn, R.J., Hodgkinson, J.E., Martinez-Moreno, A., Martinez-Valladares, M., Perez, J., Rinaldi, L., Williams, D.J.L. 2018. "Fasciola and fasciolosis in ruminants in Europe: Identifying research needs." Transbound Emerg Dis. 65(Suppl. 1):199–216.

Benelli, G., Pavela, R., Canale, A., Mehlhorn, H. 2016. "Tick repellents and acaricides of botanical origin: a green roadmap to control tick-borne diseases?(Review)." Parasitology Research 115 (7):2545-2560.

Blomqvist, G., Näslund, K., Svensson, L., Beck, C., Valarcher, J. 2021. "Mapping geographical areas at risk for tick-borne encephalitis (TBE) by analysing bulk tank milk from Swedish dairy cattle herds for the presence of TBE virus–specific antibodies." Acta Veterinaria Scandinavica 63 (1):16.

Borgsteede, F.H.M., van Wuijckhuise, L., Peutz, J., Roumen, T., Kock, P. 2009. "Import of *Parafilaria bovicola* in the Netherlands." Veterinary Parasitology 161:146-9.

Bregnard, C., Rais, O., Voordouw, M.J. 2021. "Masting by beech trees predicts the risk of Lyme disease." Parasites Vectors 14:168; https://doi.org/10.1186/s13071-021-04646-0.

Chhabra, M. B., Muraleedharan, K., Pathak, K.M.L. 2014. Medicinal plants as alternative for control of parasites. 3. Arthropods. Indian Journal of Animal Sciences 84 (9): 927–938.

Caminade, C., McIntyre, K.M., Jones, A.E. 2019. "Impact of recent and future climate change on vector-borne diseases." Ann. N.Y. Acad. Sci. 1436:157–173. doi: 10.1111/nyas.13950.

Carpenter, S., Groschup, M.H., Garros, C., Felippe-Bauer, M.L., Purse, B.V. 2013. "Culicoides biting midges, arboviruses and public health in Europe." Antiviral Res. 100:102–13; doi: 10.1016/j.antiviral.2013.07.020.

Coipan, E.C., Jahfari, S., Fonville, M., Maassen, C.B., van der Giessen, J., Takken, W., Takumi, K., Sprong, H. 2013. "Spatiotemporal dynamics of emerging pathogens in questing *Ixodes ricinus*." Frontiers in Cellular and Infection Microbiology 4:36.

Cwiklinski, K., Jewhurst, H., McVeigh, P., Barbour, T., Maule, AG., Tort, J., O'Neill, SM., Robinson, MW., Donnelly, S., Dalton, JP. 2018. Infection by the Helminth Parasite Fasciola hepatica Requires Rapid Regulation of Metabolic, Virulence, and Invasive Factors to Adjust to Its Mammalian Host. Mol Cell Proteomics. 2018 Apr; 17(4): 792–809. doi: 10.1074/mcp.RA117.000445.

Di Cola, G., Fantilli, A.C., Pisano, M.B., Ré, V.E. 2021. "Foodborne transmission of hepatitis A and hepatitis E viruses: A literature review (Review)." International Journal of Food Microbiology 338:108986.

Dobler, G., Gniel, D., Petermann, R., Pfeffer, M. 2012. "Epidemiology and distribution of tick-borne encephalitis." Wien Med Wochenschr. 162:230– 8; doi: 10.1007/s10354-012-0100-5.

Dumler, J.S., Barbet, A.F., Bekker, C.P., Dasch, G.A., Palmer, G.H., Ray, S.C., Rikihisa Y., Rurangirwa F.R. 2001. "Reorganization of genera in the families Rickettsiaceae and Anaplasmatacceae in the order Rickettsiales: unification of some species of Ehrlichia and Anaplasma, Cowdria with Ehrlichia with Neorickettsia, descriptions of six new species combinations and designation of *Ehrlichia equi* and 'HGA agent' as subjective synonyms of *Ehrlichia phagocytophilum*." Int J Syst Evol Micro. 51:2145–65; doi: 10.1099/00207713-51-6-2145.

Dutch Animal Health Service https://www.gddiergezondheid.nl/sitecore/content/DAPContact/Home/Dierziektes/Parafilaria?sc_lang=nl, last accessed 07.05.2021.

Eberhard, F.E., Koch, L.K., Klimpel, S. 2021. "Climate change and vector-borne diseases in Europe." Geographische Rundschau 73 (3): 32-37.

Elbertsen, A. (2004). Parasitaire Infecties in de Biologische Melkveehouderij. https://edepot.wur.nl/115355.

Endalew, A.D., Faburay, B., Wilson, W.C., Richt. J.A. 2019. "Schmallenberg Disease—A Newly Emerged Culicoides-Borne Viral Disease of Ruminants." Viruses 11, 1065; doi:10.3390/v11111065.

Estrada-Peña, A., D'Amico, G., Fernández-Ruiz, N. 2021. "Modelling the potential spread of *Hyalomma marginatum* ticks in Europe by migratory birds." International Journal for Parasitology 51 (1):1-11.

European Center for Disease Prevention and Control. https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/vector-net, last accessed 07.05.2021.

Folly, A.J., Dorey-Robinson, D., Hernández-Triana, H.M., Phipps, L.P., Johnson, N. 2020. "Emerging Threats to Animals in the United Kingdom by Arthropod-Borne Diseases." Front. Vet. Sci. https://doi.org/10.3389/fvets.2020.00020.

Gale, P., Brouwer, A., Raminal, V., Kelly, L., Kosmider, R., Fooks, K.R., Snary, E.L. 2010. "Assessing the impact of climate change on vector-borne viruses in the EU through the elicitation of expert opinion." Epidemiol. Infect. 138:214-225; doi:10.1017/S0950268809990367.

Gilbert, L. 2021. "The Impacts of Climate Change on Ticks and Tick-Borne Disease Risk (Review)." Annual Review of Entomology 66:273-288.

Gonçalves, B.L., Corassin, C.H., Oliveira, C.A.F. 2015. "Mycotoxicoses in dairy cattle: A review." Asian Journal of Animal and Veterinary Advances 10 (11):752-760.

Gray, J., Zintl, A., Hildebrandt, A., Hunfeld, K-P., Weiss, L. 2010. "Zoonotic babesiosis: overview of the disease and novel aspects of pathogen identity." Ticks Tick Borne Dis. 1:3–10; doi: 10.1016/j.ttbdis.2009.11.003.

Gray, J., Kahl, O., Zintl, A. 2021. "What do we still need to know about *Ixodes ricinus*?." Ticks Tick borne Dis. 12 (3): 101682.

Groot, M.J., Berendsen, B.J.A. and Cleton, N.B. 2021. "The next step to further decrease veterinary antibiotic applications: Phytogenic alternatives and effective monitoring; the Dutch approach." Front. Vet. Sci. 8:709750. doi: 10.3389/fvets.2021.709750.

Hansford, K.M., Carter, D., Gillingham, E.L., Hernández-Triana, L.M., Chamberlain, J., Cull, B., Liz McGinley, L., Phipps, L.P., Medlock, J.M. 2019. "*Hyalomma rufipes* on an untravelled horse: Is this the first evidence of Hyalomma nymphs successfully moulting in the United Kingdom." Ticks and Tick Borne Diseases 10:704–8; doi: 10.1016/j.ttbdis.2019.03.003.

Hartemink, N., van Vliet, A.J.H., Gort, G., Gassner, F., Jacobs, F., Fonville, M., Takken, W., Sprong, H. 2021. "Seasonal patterns and spatial variation of *Borrelia burgdorferi* (sensu lato) infections in *Ixodes ricinus* in the Netherlands." Parasites Vectors 14:121; https://doi.org/10.1186/s13071-021-04607-7.

Hermann, C., Gern, L. 2015. "Search for blood or water is influenced by *Borrelia burgdorferi* in *Ixodes ricinus*." Parasit. Vectors 8, 6; https://doi.org/10.1186/s13071- 014-0526-2.

Hing, M., Van Den Bossche, D., Lernout, T., Cochez, C., Pirnay, J.P., Heuninckx, W. 2019. "Prevalence of *Anaplasma phagocytophilum* in humans in Belgium for the period 2013-2016." Acta Clin Belg. 74(4):280-285; doi: 10.1080/17843286.2018.1491928.

Hofmann, M., Wiethölter, A., Blaha, I., Jöst, H., Heinemann, P., Lehmann, M., Miller, T., Cadar, D., Yanase. T, Kley, N., Eiden, M., Groschup, M., Schmidt-Chanasita, J. 2015. "Surveillance of Batai Virus in Bovines from Germany." Clinical and Vaccine Immunology 22(6); DOI:10.1128/CVI.00082-15.

Hvidsten, D., Frafjord, K., Gray, J.S., Henningsson, A.J., Jenkins, A., Kristiansen, B.E., Lager, M., Rognerud, B., Slatsve, A.M., Stordal, F., Stuen, S., Wilhelmsson, P. 2020. "The distribution limit of the common tick, *Ixodes ricinus*, and some associated pathogens in north-western Europe." Ticks Tick Borne Dis. 11:101388; doi: 10.1016/j.ttbdis.2020.101388.

Ibekwe, HA. 2019. In vitro anthelmintic activities of aqueous crude extract of Azadirachta indica on Paramphistomum cervi and Fasciola hepatica. International Journal of Veterinary Sciences and Animal Husbandry 2019; 4(1): 14-18.

Johnson, N., Phipps, L.P., McFadzean, H., Barlow, A.M. 2020. "An outbreak of bovine babesiosis in February, 2019, triggered by above average winter temperatures in southern England and co-infection with *Babesia divergens* and *Anaplasma phagocytophilum*." Parasites Vectors 13:305; https://doi.org/10.1186/s13071-020-04174-3.

Jore, S., Vanwambeke, S.O., Viljugrein, H., Isaksen, K., Kristoffersen, A.B., Woldehiwet, Z., Johansen, B., Brun, E., Brun-Hansen, H., Westermann, S., Larsen, I-L., Ytrehus, B. 2014. "Climate and environmental change drives *Ixodes ricinus* geographical expansion at the northern range margin." Parasit Vectors 7:11; doi: 10.1186/1756-3305-7-11.

Knorr, S., Anguita, J., Cortazar, J.T., Hajdusek, O., Kopacek, P., Trentelman, J.J., Kershaw, O., Hovius, J.W., Nijhof, A.M. 2018. "Preliminary evaluation of tick protein extracts and recombinant ferritin 2 as anti-tick vaccines targeting *Ixodes ricinus* in cattle." Front. Physiol. 9, 1696; https://doi.org/10.3389/fphys.2018.01696.

Knubben-Schweizer, G. and Torgerson, PR. 2015. Bovine fasciolosis: control strategies based on the location of Galba truncatula habitats on farms. Vet Parasitol;208(1-2):77-83. doi: 10.1016/j.vetpar.2014.12.019.

Koenraadt, C.J.M., Spitzen, J and W. Takken (eds). 2021. Innovative strategies for vector control: Progress in the global vector control response. Ecology and control of vector-borne diseases Volume 6. https://www.wageningenacademic.com/doi/epdf/10.3920/978-90-8686-895-7.

Kononov, A., Byadovskaya, O., Wallace, B.D., Prutnikov, P., Pestova, Y., Kononova, S., Nesterov, A., Rusaleev, V., Lozovoy, D., Sprygin, A. 2020. "Non-vector-borne transmission of lumpy skin disease virus." Scientific reports 10:7436; https://doi.org/10.1038/s41598-020-64029.

Kroeker, A.L., Babiuk, S., Pickering, B.S., Richt, J.A., Wilson, W.C. 2020. "Livestock Challenge Models of Rift Valley Fever for Agricultural Vaccine Testing." Front. Vet. Sci. 7:238; https://doi.org/10.3389/fvets.2020.00238.

Kumar, B., Manjunathachar, H.V., Srikanta, G. 2020. "A review on Hyalomma species infestations on human and animals and progress on management strategies." Heliyon 6; https://doi.org/10.1016/j.heliyon.2020.e05675.

Machado Pereira da Silva, MA., Zehetmeyr, FK., Pereira, KM.,Pacheco, BS., Freitag, RA., Berne Pinto, N., Machado, RH., Villarreal, JPV., de Oliveira Hubner, S., Aires Berne, ME., da Silva Nascente, P. 2020. Ovicidal in vitro activity of the fixed oil of Helianthus annus L. and the essential oil of Cuminum cyminum L. against Fasciola hepatica (Linnaeus, 1758). Experimental Parasitology 218; 107984. https://doi.org/10.1016/j.exppara.2020.107984.

Mignotte, A., Garros, C., Dellicour, S., Jacquot, M., Gilbert, M., Gardès, L., Balenghien, T., Duhayon, M., Rakotoarivony, I., de Wavrechin, M., Huber, K. 2021. "High dispersal capacity of *Culicoides obsoletus* (Diptera: Ceratopogonidae), vector of bluetongue and Schmallenberg viruses, revealed by landscape genetic analyses." Parasites Vectors 14:93; https://doi.org/10.1186/s13071-020-04522-3.

Min, L., Fink-Gremmels, J., Li, D., Tong, X., Tang, J., Nan, X., Yu, Z., Chen, W., Wang, G. 2021. "An overview of aflatoxin B1 biotransformation and aflatoxin M1 secretion in lactating dairy cows (Review). Animal Nutrition 7 (1): 42-48.

Min, B.R. and Hart, S.P. 2003. Tannins for Suppression of Internal Parasites. Journal of Animal Science, 81, E102-E109.

Möhlmann, T.W.R., Keeling, M.J., Wennergren, U., Favia, G., Santman-Berends, I., Takken, W., Koenraadt, C.J.M., Brand, S.P.C. 2021. "Biting midge dynamics and bluetongue transmission: a multiscale model linking catch data with climate and disease outbreaks." Scientifc Reports 11:1892; https://doi.org/10.1038/s41598-021-81096-9.

Mordvinov, VA., Ponomarev, DV., Pakharukov, YV., Pakharukova, MY. (2021). Anthelmintic Activity of Antioxidants: In Vitro Effects on the Liver Fluke Opisthorchis felineus. Pathogens 2021, 10, 284. https://doi.org/10.3390/pathogens10030284.

Nieuwe Oogst. https://www.nieuweoogst.nl/nieuws/2019/09/28/rund-vaker-ziek-door-teek. Last accsessed on 07.05.2021.

Neijenhuis, F., Verwer, C., Verkaik, J. 2017. Wat zijn de mogelijkheden om een leverbotinfectie bij melkvee te voorkomen? Wageningen Livestock Research, Louis Bolk Instituut, Rapport 1029.

OIE Conf 2010, 179-186 – 179 – CLIMATE CHANGE AND LINKS TO ANIMAL DISEASES AND ANIMAL PRODUCTION. Walter Oyhantçabal, Edgardo Vitale, Patricia Lagarmilla, Ministry of Livestock, Agriculture and Fisheries of Uruguay.

Obiegala, A., Arnold, L., Pfeffer, M., Kiefer, M., Kiefer, D., Sauter-Louis, C., Silaghi, C. 2021. "Host–parasite interactions of rodent hosts and ectoparasite communities from different habitats." Parasites Vectors 14:112; https://doi.org/10.1186/s13071-021-04615.

Onyinyechukwu, A.A., Shaari, M.R., Md Isa, N.M., Ajat, M., Zamri-Saad, M., Hamzah, H. 2020. "Immunopathology and Advanced Vaccine Technology in Bovine Theileriosis: A Review." Pathogens 9:697 (1-22).

Pollock, L.A., Newton, E.J., Koen, E.L. 2021. "Predicting high-risk areas for African swine fever spread at the wild-domestic pig interface in Ontario." Preventive Veterinary Medicine 191:105341.

Portillo, A., Palomar, A.M., Santibáñez, P., Oteo, J.A. 2021. "Epidemiological aspects of crimean-congo hemorrhagic fever in western Europe: What about the future? (Review)." Microorganisms 9 (3):1-19.

RIVM: https://www.rivm.nl/tekenbeten-en-lyme/hyalomma-teken viewed on 7.05.2021.

Rocklöv, J. and Dubrow, R. 2020. "Climate change: an enduring challenge for vector-borne disease prevention and control." Nature Immunology 21; 479-483; https://doi.org/10.1038/s41590-020-0648-y,

Rolin, A.I., Berrang-Ford, L., Kulkarni, M.A. 2013. "The risk of Rift Valley fever virus introduction and establishment in the United States and European Union." Emerg Microbes Infect. 2:e81; doi: 10.1038/emi.2013.81.

Rana, MAA. 2015. Epidemiology, serology and therapeutic trials of fasciolosis in crossbred cows. Thesis. http://173.208.131.244:9060/xmlui/handle/123456789/7657.

Russell, R., Paterson, M., Lima, N. 2010. "How will climate change affect mycotoxins in food?" Food Research International 43:1902–1914.

Santos, R.R. and Fink-Gremmels, J. 2014. Mycotoxin syndrome in dairy cattle: characterisation and intervention results. World Mycotoxin Journal 7 (3); 357-366(10).

Smolarz, H.D., Jędruch, M., Rzymowska, J., Bajorska, A. 2013. "Acaricidal effect of some plants on *Ixodes ricinus* - A pilot study." Current Issues in Pharmacy and Medical Sciences 26 (2):148-151.

Springer, A., Glass, A., Topp, A.K., Strube, C. 2020a. "Zoonotic Tick-Borne Pathogens in Temperate and Cold Regions of Europe—A Review on the Prevalence in Domestic Animals." Front. Vet. Sci.; https://doi.org/10.3389/fvets.2020.604910.

Springer, A., Höltershinken, M., Lienhart, F., Ermel, S., Rehage, J., Hülskötter, K., Lehmbecker, A., Wohlsein, P., Barutzki, D., Gietl, C., Baumgartner, W., Hoedemaker, M. 2020b. "Emergence and epidemiology of bovine babesiosis due to *Babesia divergens* on a northern German beef production farm." Front Vet Sci. 7:649; doi: 10.3389/fvets.2020.00649.

Sprygin, A., Pestova, Y.A., Wallace, D.B., Tuppurainen, E., Kononov, A.V. 2019. "Transmission of lumpy skin disease virus: A short review." Virus Res. 269:197637; doi: 10.1016/j.virusres.2019.05.015.

Tekenradar: www.tekenradar.nlToner, E., Brennan, G., Wells, K., McGeown, J., & Fairweather, I. (2008). Physiological and morphological effects of genistein against the liver fluke, Fasciola hepatica. Parasitology, 135(10), 1189.

Vetter, S.G., Puskas, Z., Bieber, C., Ruf, T. 2020. "How climate change and wildlife management affect population structure in wild boars." Scientific Reports 10:7298; https://doi.org/10.1038/s41598-020-64216-9.

Villalba, J.J., Miller, J., Ungar, E.D., Landau, S.Y., Glendinning, J.2014. Ruminant self-medication against gastrointestinal nematodes: evidence, mechanism, and origins. Parasite 21: 31. doi: 10.1051/parasite/2014032.

VKON https://www.vkon.nl/projecten-items/natuurlijke-tekenbestrijding viewed on 07.05.2021.

Vloet, R.P.M., Vogels, C.J.M., Koenraadt, G.P., Pijlman, M.E., Gonzales, J.L., van Keulen, L.J.M, Wichgers Schreur P.J., Kortekaas, J. 2017. "Transmission of Rift Valley fever virus from European-breed lambs to *Culex pipiens* mosquitoes. PLoS Negl. Trop. Dis. 11, e0006145; https://doi.org/10.1371/journal.pntd.0006145.

Wanzala, W. (2017). Potential of traditional knowledge of plants in the management of arthropods in livestock industry with focus on (Acari) ticks. Evidence-Based Complementary and Alternative Medicine, 2017. Article ID 8647919, 33 pages. https://doi.org/10.1155/2017/8647919.

Wanzala, W., Takken, W., Mukabana, W. R., Pala, A. O., Hassanali, A. (2012). Ethnoknowledge of Bukusu community on livestock tick prevention and control in Bungoma district, western Kenya. Journal of Ethnopharmacology, 140(2), 298–324. https://doi.org/10.1016/j.jep.2012.01.021.

Wichgers Schreur, P.J., Vloet, R.P.M., Kant, J., van Keulen, L., Gonzales, L.J., Visser, T.M., Koenraadt, C.J.M., Vogels, C.B.F., Kortekaas, J. 2021. "Reproducing the Rift Valley fever virus mosquito lamb mosquito transmission cycle." Scientifc Reports 11:1477; https://doi.org/10.1038/s41598-020-79267-1 Nature Research.

Wilhelmsson, P., Pawełczyk, O., Jaenson, T.G.T., Waldenström, J., Olsen, B., Forsberg, P., Lindgren, P. 2021. "Three Babesia species in *Ixodes ricinus* ticks from migratory birds in Sweden." Parasites and Vectors 14 (1):183.

Williamson, S.M., Scholes, S.F., de B Welchman, D., Dennison, M., Batten, C.A., Williams, D.L., Mertens, P.P.C., Mellor P.S., Darpel K.E. 2010. "Bluetongue virus serotype 8-associated hydrancephaly in two calves in south-eastern England." Vet Rec. 167:216– 8; doi: 10.1136/vr.c3302.

Whitlow, LW. and Hagler, WM. 2005. Mycotoxins in Dairy Cattle: Occurrence, Toxicity, Prevention and Treatment. Proc. Southwest. Nutr. Conf.:124-138.

Yanase, T., Murota, K., Hayama, Y. 2020. "Endemic and Emerging Arboviruses in Domestic Ruminants in East Asia." Front. Vet. Sci. 168; https://doi.org/10.3389/fvets.2020.00168.

Zamorano, J.G., Hokkanen, T., Lehikoinen, A. 2018. "Climate-driven synchrony in seed production of masting deciduous and conifer tree species." Journal of Plant Ecology 11 (2):180-188.

Zintl, A., Mulcahy, G., Skerrett, H.E., Taylor, S.M., Gray, J.S. 2003. "*Babesia divergens*, a bovine blood parasite of veterinary and zoonotic importance." Clin Microbiol Rev. 16:622–36; doi: 10.1128/CMR.16.4.622-6 36.2003.

Wageningen Food Safety Research
P.O. Box 230
6700 AE Wageningen
The Netherlands
T +31 (0)317 48 02 56
www.wur.eu/food-safety-research

WFSR report 2021.017

To explore the potential of nature to improve the quality of life

Wageningen Food Safety Research
P.O. Box 230
6700 AE Wageningen
The Netherlands
T +31 (0)317 48 02 56
www.wur.eu/food-safety-research

WFSR report 2021.017

The mission of Wageningen University & Research is "To explore the potential of nature to improve the quality of life". Under the banner Wageningen University & Research, Wageningen University and the specialised research institutes of the Wageningen Research Foundation have joined forces in contributing to finding solutions to important questions in the domain of healthy food and living environment. With its roughly 30 branches, 6,800 employees (6,000 fte) and 12,900 students, Wageningen University & Research is one of the leading organisations in its domain. The unique Wageningen approach lies in its integrated approach to issues and the collaboration between different disciplines.