DISCONTOOLS

DISEASE CONTROL TOOLS

GAPS AND NEEDS FOR INFECTIOUS DISEASE CONTROL IN ANIMALS

discontools.eu

Editorial

Brussels, 1 September 2020

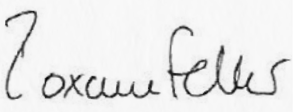
Finally they are here, the DISCONTOOLS Disease Sheets: one-pagers for 53 infectious diseases in animals that summarize the DISease CONtrol TOOLS available, and those we need to improve or secure animal health.

The original plan was to distribute the Disease Sheets during the DISCONTOOLS symposium in Spring 2020 in Brussels. With COVID-19 throwing a spanner in the works, we decided that the dissemination of this information could not wait until the date of the new symposium. Influenced by the lessons learned from COVID-19, the future of animal health and the science to underpin it, is taking new directions and is taking shape now. This will happen among others through the new working programmes under Horizon Europe and through ongoing preparations for a European Partnership in Animal Health and Welfare. Over the past years, many new medicines were marketed in Europe on DISCONTOOLS listed gaps and diseases[1]. However, even more gaps still remain. Worryingly, many companies are finding growing barriers to innovation in animal health, resulting in the tailing off of R&D investment from 10% to 8% of turnover. Also public spending on animal health research tends to decrease globally. Animal health has to compete with many topics and although it is intrinsically linked to many of the pressing societal challenges (e.g. climate change, antimicrobial resistance, animal welfare, prevention and control of pandemics, food security) decision makers seem not yet prepared to match the challenges with research funds[2].

Whereas extended information is available on the DISCONTOOLS website, with the provision of the DISCONTOOLS Disease Sheets, we offer a comprehensible format to support research programme managers and decision makers in focusing on areas that will make a significant advancement in improving animal health and thus also in contributing to the societal challenges. By integrating the identified gaps in the Research Road Maps by the STAR-IDAZ International Research Consortium (IRC) on animal health, this process of developing impactful research programmes is further facilitated. The STAR-IDAZ IRC Research Road Maps structure the gaps in a flow-chart towards target products and identify unfunded areas for a number of priority diseases and cross-cutting topics.

We would like to thank explicitly our experts from academia, government institutions and industry for their selfless contributions in developing the DISCONTOOLS database and Disease Sheets. We invite you to mark 29 April 2021 in your diary as this is when we hope to organize a DISCONTOOLS symposium and discuss the gaps in an old-fashioned way face-to-face. In the meantime, we wish you reading pleasure and hope that the DISCONTOOLS Disease Sheets will make a useful contribution to promote research and innovation leading to improved control tools and key scientific insights in animal health. This will provide many benefits to society as a whole.

Johannes Charlier
DISCONTOOLS Project Manager



Roxane Feller
Secretary General AnimalhealthEurope

[1] Annual Reports European Medicines Agency (2014-2019)

[2] Meeting Report. Pandemic! A one health view of emerging infectious diseases. What veterinary sciences can contribute.

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Please cite this document as: "DISCONTOOLS, 2020. DISCONTOOLS Disease Sheets – Available control tools and needs for infectious disease control in animals, Brussels, 62 pp."

DISCONTOOLS receives funding from a range of national funders of research from Austria, Italy, The Netherlands, Spain, Switzerland and the UK with AnimalhealthEurope providing secretariat support. DISCONTOOLS is part of SIRCAH, the secretariat of the STAR-IDAZ international research consortium on animal health funded by the EU Horizon 2020 research and innovation programme (Grant Agreement N° 727494).

STAR-IDAZ International Research Consortium on Animal Health

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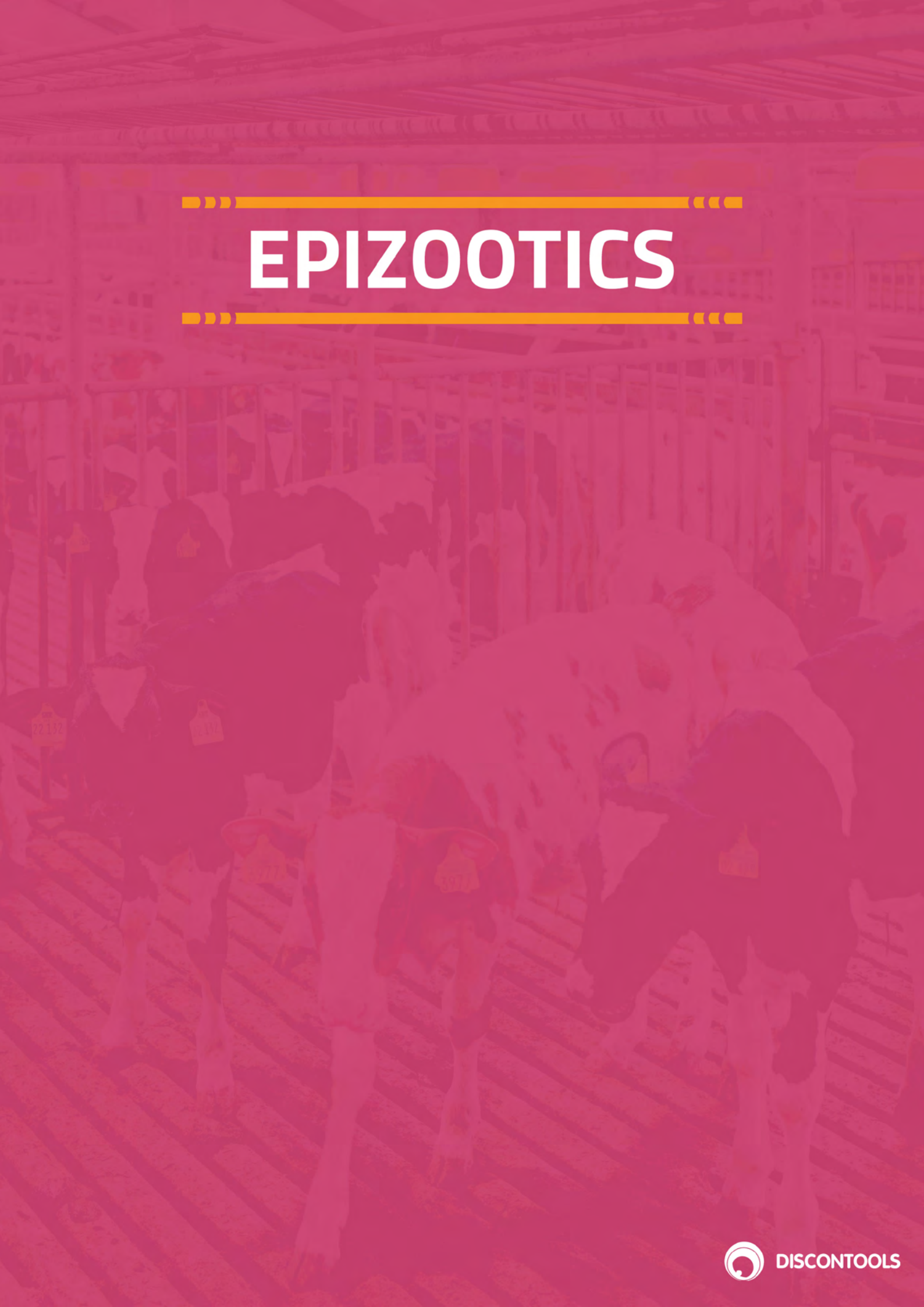
EPIZOOTICS



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African Horse Sickness (AHS)

Disease Profile

AHS is a viral disease with a **major impact on equine populations** which have never experienced the disease. Transmission of AHS virus occurs almost entirely through hematophagous arthropods (*Culicoides* spp.), which act as biological vectors. Mortality rate in horses is 70-95%, in mules it is around 50%, and in donkeys it is limited to 10%. Occasional hosts include elephants, onager, dogs and camels. Zebras and elephants may be infected without showing signs of disease. AHS is endemic in sub-Saharan Africa from where it occasionally spreads to other areas, with outbreaks having occurred in the Near and Middle East, Spain, Portugal and Morocco.

Risk

The major vector of AHS virus, *C. imicola*, occurs in southern Europe and northern spread is expected as global temperatures increase. As **the distribution of C. imicola moves north**, it may bring AHS virus into the range of other Culicoides species that are potentially competent vectors and which are commonly found in northern Europe. Once infected via this 'baton effect', these species may be able to spread the virus over much of Europe. Climate change may also increase vector competence.

What do we have?

Diagnostics: ELISA kits and lateral flow assays for AHS antibody detection are available worldwide

The RT-PCR is a sensitive and rapid method for detecting AHS virus nucleic acids during either the incubation period at the start of an AHS epizootic, or for epidemiological investigations in species where clinical signs may not be apparent.

Once the disease has been confirmed, the virus needs further characterization, primarily the serotype identification. To this aim, beside the virus neutralization test, several molecular tests have been published providing a rapid typing method for AHS virus in biological samples.

Vaccines: There are **no commercially available inactivated or recombinant vaccines** but there are some locally killed vaccines for use in some countries. There is concern about the safety, efficacy (viral variants) and side effects of the live attenuated vaccines. Attenuated vaccines are considered a risk for use in AHS-free countries due to the risk of transmission, reassortment (i.e. exchange of gene segments between vaccine and field strains) and reversion to virulence. No AHS vaccines are currently licensed in the EU.

What do we need?

- Improved knowledge on the pathogenesis, host immune responses and epidemiology of AHS. There is a need to model the possible pathways of introduction and dissemination of the AHS virus in naïve areas.
- Validation and harmonization of diagnostic assays.
- More genome sequencing of AHS virus circulating strains to assess the diagnostic capabilities of the molecular test in use and to investigate the potential for vaccine strains circulation and/or reassortment.
- Authorised and safe vaccines along with tests to differentiate vaccinated from infected horses. The development of cross-protective AHS virus vaccines with a long shelf life and that can provide rapid protection and be differentiated from natural infections during outbreaks is a major priority for research.

Read the full chapter here.

Avian Influenza (AI)

Disease Profile

AI is caused by infection of birds with avian influenza type A viruses (AIV). These viruses occur naturally among wild aquatic birds worldwide and can infect domestic poultry and other bird and animal species. Wild aquatic birds can be infected with AI A viruses in their intestines and respiratory tract, but usually do not get sick. AI viruses are classified into **low (LPAI) and highly pathogenic (HPAI) phenotypes.** HPAI viruses have been eradicated from domesticated poultry in many countries but eradication of HPAI virus on a global scale is not expected as pockets of endemic infection continue to exist. LPAI virus strains are found worldwide. AI infections are widely distributed in aquatic wild bird populations. The majority of infections are acute and asymptomatic. Faecal-oral transmission chains dominate. The environment (surface water, sediments) probably acts as an important factor of virus perpetuation. Incidence of infection is cyclic in the natural hosts and peak values correlate with autumn migration of aquatic wild birds in the northern hemisphere.

Risk

All viruses in general have considerable **genetic flexibility** through point mutations and through exchange of whole genome segments during co-infection of a single host cell with different AI virus. HPAI viruses arise by mutation *de novo*, from LPAI precursor viruses maintained in the natural host reservoir. Influenza viruses circulating in animals pose potential threats to human health. The primary risk factor is direct or indirect exposure to infected live or dead poultry or contaminated environments. Efficient or sustainable human-to-human transmission of avian origin influenza viruses has not yet been reported. Vaccination is an important method for controlling AI but can stimulate antigenic drift if vaccines are not applied properly and under controls. Likewise, without proper **marker systems** it will be difficult to differentiate infection from vaccine responses. Failure of all available vaccines to induce sterile immunity implies risks of silent spread of virus by apparently healthy but infected vaccinated poultry.

What do we have?

Diagnostics are available worldwide but are limited. Technology for characterisation of strains is quite advanced, but sometimes lagging behind in low income countries. The palette of commercially produced and distributed test kits comprises antibody and antigen detection ELISAs, (real time) PCR, rapid antigen detection assays and antigens for serological purposes.

Vaccines: H5, H7, H9 *vaccines* are available. Vaccination of wild birds is not feasible. There are two types of vaccines commercially available at present: inactivated (whole virus) and recombinant vaccines (subunit). Approaches to differentiate infected from vaccinated birds are the use of a heterologous vaccine (vaccine virus with the same H type as the field strain but a different N type) or the use of recombinant subunit vaccines.

Antivirals are effective in AI virus infected poultry but their use is prohibited due to the risk of resistance and hazard thereof for humans.

What do we need?

- Research to fill gaps in relation to pathogenesis, immunology, vaccinology, epidemiology and control.
- Cheap, stable and sensitive tests which allow high-throughput generic and subtype-specific multiplex serological screening.
- Rapid and sensitive methods of assessing infectious status of flocks.
- Easy to apply, single dose, cheap, marker vaccines that induce clinical broad protection and bring virus shedding to a minimum. Further development of recombinant vaccines is required.

Read the full chapter here.

African Swine Fever (ASF)

Disease Profile

ASF is a serious infectious disease of domestic and wild pigs of all breeds and ages. Its importance is due to the **high lethality** in domestic pigs and wild boar, the great diffusion capacity and the lack of treatment and vaccine. The ASF virus is endemic in sub-Saharan Africa, where the virus infects wild and domestic suids as well as ticks of the genus Ornithodoros. Nevertheless, there have been several incursions of the disease out of Africa (Europe, South America and the Caribbean) between the 1960s and 1970s, which had a high cost of eradication. In 2007 the disease was introduced into Georgia, from where it spread to other eastern European countries. Currently, the disease affects **18 European countries**, 10 of them belonging to the European Union. In 2018, the virus first reached the Asian continent, from where it has spread rapidly to 12 countries.

Risk

The current situation of African swine fever has acquired a pandemic dimension and suggests an **imminent risk for world swine production.** The disease has spread to 47 countries on three continents and 77% of the total swine population is already living in an infected area. China, the main pig producer, with about half the head of pigs from around the world, has lost more than 37% of its porcine population. Globalization has increased the risk of ASF being introduced into free areas. The main risks of ASF spread are the continuous movement of infected wild boar populations in Europe, the poor levels of biosecurity in farms and the movement of live pigs and risk products coming from infected areas.

What do we have?

Diagnostics: A number of **good and fast diagnostic tools** for different types of samples are available for both virus and antibody detection. Most of the existing tools allow early detection of the disease and a confident diagnosis in any epidemiological situation of affected countries. There are also good diagnostics tools for on-site first-line diagnosis.

Vaccines: Vaccination is considered to be the most efficient strategy and solution for emerging infectious diseases. Regrettably, attempts over many years to develop a vaccine for ASF have **failed.** Last year several vaccines prototypes for domestic pig and wild boar have been described with very promising results. A EU project, "VACDIVA", has been financed with 10 million euros by the European Union with the objective of developing and effective vaccine against ASF over the next four years (VACDIVA H2020 Grant ID: 862874).

Pharmaceuticals: The use of antivirals has been proposed as a control alternative until a commercial vaccine is obtained. Several prototypes have been determined so far and their efficacy has been tested under in vitro conditions, however, in vivo studies have still to be conducted.

What do we need?

- Elucidation of the immune response to infection for the identification of target proteins and genes for vaccination.
- Characterisation at genome level of ASF virus infection with different isolates.
- Characterisation of the different epidemiological scenarios worldwide for ASF and design ASF control and eradication strategies for each of them.
- Diagnostics: i) expansion of field validation for all tests and appropriate specimens; ii) established cell lines that make virus isolation a cost-effective test for its implementation at the National Reference Laboratories; iii) improvements in molecular characterization tests to determine the source of the outbreaks; and iv) develop DIVA test to allow and accurate monitoring of the effectiveness of the potential vaccine.
- Major efforts to provide an effective and sufficiently effective, safe and DIVA vaccine for wild boar and domestic pigs.

Read the full chapter here.

Bluetongue

Disease Profile

Bluetongue viruses (BTVs) are present in a broad band of countries extending approximately between 40°N and 35°S although in some regions it may extend to 55°N. Classical BTVs have been shown to be limited to regions where vector species of *Culicoides* are present and within these regions **vector transmission** is limited to those periods of the year when adult *Culicoides* are active. Recently, a horizontally transmitted small ruminant adapted BTV has been identified. BTV infects domesticated and wild ruminants. The vast majority of infections are clinically unapparent. Clinical disease is most often seen in sheep and occasionally in goats and cattle. Severe disease can also occur in some wild ruminants. The severity of clinical signs depends on BTV strains, breed and immune status of the host.

Risk

The whole of Europe must be considered at risk from further incursions of BTV and other *Culicoides* transmitted orbiviruses. Local climate change could lead to increasing local temperatures, exacerbating these risks. BTV has recently **expanded its geographic range** and is able to cross borders due to the wide distributions of vector species of *Culicoides.* Reassortment is a frequent process that plays an important and on-going role in evolution of BTV. The continuous evolution of the BTV situation in the southern part of the Mediterranean basin poses to Southern European countries a permanent threat of new BTV strain incursions for which no immunological tools are available.

What do we have?

Diagnostics: Many different antibody detection ELISA kits are commercially available including competitive and double antigen ELISAs. These methods enable the detection of serogroup-specific antibodies in the serum and milk of infected or vaccinated animals. Real-time PCR detection assays are also available commercially. They provide a versatile system able to give information on virus serogroup and serotype within a few hours. **Neither serological DIVA nor pen side tests are currently available.**

Vaccines: Live attenuated and inactivated vaccines remain the only vaccines commercially produced to prevent Bluetongue. They can successfully control and, in some circumstances, eradicate the infection. All of the current monovalent live or inactivated vaccines are however type specific. Cross-protection can only be generated by serial vaccination with multiple serotype vaccines.

Pharmaceuticals: No specific treatment is available, other than supportive care.

What do we need?

- Research to fill the gaps in relation to immunity, strains and isolates, transmission and spread, reservoirs, carriers and geographical distribution. These are closely linked to the research requirements to develop effective control tools.
- Further development of existing real-time PCR assays to detect new BTV isolates/variants. In this context, harmonization of procedures to amplify the full-length of each genome segment of BTV isolates by NGS is required.
- More effective diagnostic protocols by multiplexing existing or novel diagnostic assay systems to better detect mixed infections.
- More effective and cross-serotype subunit-vaccines that are DIVA assay compatible and generate a stronger immune response from a single inoculation are essential.
- Incentives for producers to develop, test and produce in anticipation of crisis. The “next generation” strategies, many with DIVA capability, did not have the chance to be launched on the market or tested on a large scale.
- A continuous dialogue among researchers, laboratories, and policy-makers to gain a deeper understanding of new developments, increase mutual knowledge, and share a unique and integrated strategic approach to address the continual evolution of BTV.

Read the full chapter here.

Contagious Bovine Pleuropneumonia (CBPP)

Disease Profile

CBPP is widespread in Africa and it is also present in other regions of the world, including the Middle East and parts of Asia although the situation in Asia is unclear. There have been no reported outbreaks in Europe since 1999. In Africa it is mostly a problem of nomadic areas and large ranches where there is close contact between large groups of animals. High levels of disease can occur where unrestricted movements occur which is a particular problem in times of drought, war or civil unrest. CBPP is currently **one of the most serious diseases of cattle in Africa**, causing estimated losses of over US$ 2 billion per annum. Directly there is the loss of animals with reduced production of meat and milk. The disruption to the development of cattle industry in African countries especially where animals need to be moved from production areas for further fattening is a major constraint on the industry.

Risk

The disease was successfully eradicated from Europe and other parts of the world but there has been less success in Africa with the spread of disease over the past 20 years. There are difficulties in identifying carrier and sub-clinically CBPP infected cattle. In Africa the inability to enforce movement controls for a variety of reasons, inadequate vaccines, reduced vaccination in some areas, poor diagnosis, financial constraints and lack of slaughter of whole infected herds all contribute to the maintenance of the problem. Also the role played by chronic carriers (lungers) is still an unclarified issue and remains a major scientific gap in the spread of the disease.

What do we have?

Diagnostics: Both the complement fixation test (CFT) and c-ELISA are highly specific and sensitive in detecting CBPP infection in acutely infected cattle. Detection of chronically infected cattle is weak especially with CFT.

Vaccines: Control of the disease is based on vaccination campaigns using **attenuated vaccine** strains such as T1/44 and T1/SR. Current vaccines are live and freeze-dried. The consistent application of CBPP vaccines in Namibia has seen the gradual reduction of CBPP outbreaks in the northern parts of the country.

Pharmaceuticals: Cattle owners often resort to **antimicrobial treatment** in an attempt to reduce disease damage and mortality rates. Antibiotic treatment may greatly reduce the transmission to healthy contacts but this requires treatment of all affected cattle in a group.

What do we need?

- Research on the establishment of infection (pathogenicity factors, immunopathology, virulence factors, genomics) and the persistence of infection in chronically affected animals (e.g. reservoirs).
- A pen side test capable of detecting both acute and chronic infections.
- A safer, more effective and better characterised vaccine to allow more effective disease control strategies to be implemented. DIVA technology is a critical gap in CBPP prevention and control tools. There is a debate regarding either the development of a new generation of potent CBPP vaccines/subunits or to rely on improvements in the current vaccines with regards to the biology of the vaccine strains and /or adjuvants and pH adjustments.
- An experimental animal model for CBPP disease.

Read the full chapter here.

Classical Swine Fever (CSF)

Disease Profile

CSF is endemic in parts of Asia, Africa, Southern America, and parts of Eastern Europe where there are recurrent relapses in areas where the virus is endemic in the wild boar population. It was eradicated in Australia (1962), Canada (1962), New Zealand (1953), USA (1978) and most countries in the EU. Occasionally outbreaks recur in highly industrialised countries. The introduction of CSF into a disease-free country has a disastrous effect on the pig industry and the economy. There is a **high economic impact** especially in areas with high pig density and with the loss of export markets for pigs and pork products associated with the consequent movement and trade restrictions. CSF can also impact on poor communities in countries with back yard pig production where pigs are used to supplement income.

Risk

Due to increased world-wide traffic, intensified trade contacts and tourism **the risk of (re-) introduction of the disease has increased.** Spread of disease might also be facilitated by intensified contacts and the factors mentioned above.

What do we have?

Diagnostics: Commercial ELISA kits with varying quality are available by different manufacturers, both for antigen and antibody detection. In addition, commercially available monoclonal antibodies and conjugates can be used for different staining techniques. Easy-to-perform pen side tests for the detection of CSF virus-specific antibodies are available but have deficiencies in terms of sensitivity. For detection of viral RNA commercial real-time RT-PCR kits targeting different regions of the viral genome are available. RT-PCR is the most sensitive method for detection of CSF virus. **Marker ELISAs** to distinguish infected from vaccinated animals are available but are not suited for individual animal testing.

Vaccines: Vaccination with modified live virus strains is effective and safe in preventing losses and eradication of the disease provided that accompanying control measures are implemented. In countries which are free of disease, or where eradication is in progress, **vaccination is usually prohibited.** Live vaccines are widely used for domestic pigs as injection vaccines and for wild boars as oral vaccines. Local vaccines of undefined quality are available in some countries. Due to financial and political restraints availability of vaccines is limited in some countries resulting in insufficient vaccine coverage.

Pharmaceuticals: There is no therapy for CSF and in Europe any treatment is forbidden by EC legislation.

What do we need?

- Research towards CSF pathogenesis, immunity, transmission and spread, reservoirs, and geographical distribution as well as cross-reactivity between CSF virus and other pestiviruses.
- High standard of education and maintenance of awareness towards CSF including disease monitoring.
- Incentives for industry to develop and produce new generation (marker) vaccines and robust accompanying DIVA assays.

Read the full chapter here.

Foot and Mouth Disease (FMD)

Disease Profile

FMD is widely distributed with only Northern Europe, North America and Australia/New Zealand being completely free while many developing countries in Asia, the Middle East and in Africa, in particular, have significant problems with endemic FMD. Positive progress with eradication has continued in South America, the last known focus of infection having been in Venezuela with limited spread to neighboring Colombia. OIE and FAO have launched a global initiative to support regional and national control.

FMD is an important animal disease with a considerable impact on livelihoods and trade for many developing countries with endemic infection as well as major trade implications when outbreaks occur in a previously free region. The economic impact is significant and prolonged for countries or regions with endemic FMD while **epidemics are extremely costly** in terms of disease control, proving freedom from infection and trade implications.

Risk

FMD is **closely associated with poverty** and is widespread in many developing countries. The pressures for movements of people and products brought about by political instability and continuing globalisation enhance risks for international spread of the disease. Therefore, it is of utmost importance to bring FMD under control in these settings, taking into account the wildlife situation, as the reduction of infectious virus in these areas will provide a significant reduction in the risk of introduction of FMD virus to FMD free areas

What do we have?

Diagnostics for FMD are available from a small number of commercial suppliers. Some reagents can be obtained from OIE/FAO Reference Laboratories or are produced for local use in National or Regional Laboratories. The main commercial tests include serology ELISA kits for non-structural proteïn testing and for structural antibodies of some serotypes. New commercialised tests for detection and serotyping of virus have become available from the National and OIE Reference Laboratory for FMD in Brescia, Italy.

Vaccines: Current, killed vaccines are quite efficient, provided that they are applied before exposure to live virus, that the vaccine strain has been carefully selected to match the outbreak strain, that sufficient amount of intact antigen is included in the vaccine and that the vaccine is of good quality. Disadvantages of the current vaccines include the dangers inherent in their large-scale production from virulent virus, the necessary provision of a cold chain and the short duration of protection elicited. Not all strains of FMD virus are covered fully by the limited number of vaccine strains commercially available and new variants emerge periodically. In the USA, adenovirus vectored vaccines have become commercially available for some serotypes with a reduced risk for FMD virus escape during production or from incomplete inactivation. Another promising line of research is the development of recombinant empty capsids which may have enhanced stability and could be produced without the need to handle live FMD virus.

Pharmaceuticals: There may be some potential for the use of antivirals in FMD control but there would be considerable challenges in both developing and licensing such products.

What do we need?

- Faster diagnostics and sensitive pen side tests along with the development of more effective and specific tests for differentiating between antibodies due to infection and vaccination.
- Sufficient panels for test validation across all serotypes and species.
- Knowledge about virus transmission and persistence in vaccinated populations and reliability of tests to differentiate vaccinated from infected animals.
- Support for fundamental immunology and for animal studies.
- Knowledge on circulating isolates in endemic regions for selecting the vaccine antigens in endemic settings.
- Better serological predictors of protection afforded by vaccination.

Read the full chapter here.

Lumpy Skin Disease (LSD)

Disease Profile

LSD virus (LSDV) is a member of the genus *Capripoxvirinae.* All breeds of cattle and Asian water buffalo are susceptible to disease. The impact on production can be considerable. Mortality can reach above 10%. In addition, losses incurred due to export bans can be significant. Transmission is mediated primarily **by biting and blood feeding arthropods.** Transmission may occur indirectly via, for example, infected saliva and nasal discharges but is considered to be inefficient. Spread of the disease can be related to movement of cattle.

Risk

LSD occurs in most African countries with sporadic outbreaks in the Middle East. In 2012, the disease **re-appeared** in the northern part of Israel and then spread swiftly within the Middle East region. In 2015 the disease spread into Saudi Arabia, Bahrain, Greece and into the Caucasus region. In 2016, LSD continued to spread into Bulgaria, Serbia, Montenegro, North Macedonia, Kosovo and Albania and further. LSD currently represents an immediate threat to central parts of Russia, Ukraine, Afghanistan and Pakistan. LSDV is a potential agriterrorist agent.

What do we have?

Diagnostics: Many PCR-based tests are available commercially. Some of these differentiate wildtype and vaccine strains of LSDV. Formal validation of most of these tests has not been undertaken.

Vaccines: Live attenuated "Neethling" LSDV strain vaccines are able to prevent LSDV. They are used under emergency legislation in Europe. Annual booster vaccinations are recommended. The use of live-attenuated vaccines against LSDV is problematic in epidemic areas where their use can result in trade restrictions.

Pharmaceuticals: Antibiotics to control secondary infections.

What do we need?

- Improved reliable high-throughput serological tests to support disease surveillance and eradication activities. DIVA capability.
- Characterisation of the vector-borne transmission to enable focused vector-control strategies.
- Understanding of the fundamental immunology and pathology of LSDV in order to underpin development of future novel disease control tools such as a non-live vaccine.

Read the full chapter here.

Peste Des Petits Ruminants (PPR)

Disease Profile

PPR affects sheep, goats, and a large number of cloven-hoofed animals, both wild and captive, with a mortality rate of 50-80% in a susceptible population. The disease spreads mainly by direct contact with discharges from infected animals. Extensive systems with communal resources and seasonal migration facilitate disease transmission. No carrier or reservoir has yet been identified.

PPR has expanded to cover large regions of Africa, the Middle East and Asia. Southern Africa is still free of the disease, but it appears to be spreading in that direction. PPRV is circulating endemically in Turkey. There have been outbreaks in Georgia and Mongolia in 2016/2017, areas where the disease had never been reported before. PPR is one of the most economically important diseases in developing countries and a **global effort is now going on to eradicate PPR**, coordinated by FAO and OIE.

Risk

The increase of animal movement for commercial and trade purposes (e.g. the massive imports of small ruminants to the Middle East), transhumance and nomadic customs along with extensive farming practices have all contributed to the maintenance and global spread of PPR. Emergence in the EU may occur via the illegal importation of animals, notably from North Africa or Turkey. Movement of wildlife (e.g. wild deer) throughout Europe may also play a role in disease emergence and spread.

PPR virus infection has for many years been **one of the most important constraints** to the increase in production of small ruminants in sub-Saharan Africa and parts of Asia. The presence of disease can limit trade, export, import of new breeds and the development of intensive livestock production. PPR represents a significant threat to food security.

What do we have?

Diagnostics: Syndromic diagnosis can be difficult in areas where multiple diseases circulate. Immunocapture-ELISA, and nucleic acid amplification are the most currently used diagnostic tests for PPRV identification. Serological tests including the competitive ELISA and virus neutralisation are also routinely used to assess herd exposure where mild disease may circulate and/or vaccination status. Commercial serological and virological diagnostic kits are available, but for the routine use in developing countries where PPR is endemic (Asia, Middle East and Africa) these kits are too expensive.

Vaccines: Current live attenuated vaccines for PPR provide a good immunity which may last for at least 3 years, but vaccinated animals cannot be distinguished serologically from naturally infected animals. Commercially available live attenuated PPR virus vaccines are available from more than 20 vaccine production companies and government laboratories in Africa, the Middle East, Asia and Turkey. There are no commercial vaccines authorised for use in Europe. **New generations of vaccines are under development:** recombinant Capripox-based PPR vaccine able to protect against both Capripox and PPR, DIVA vaccines, conventional live attenuated vaccine with high stability in lyophilized form.

What do we need?

- Identification of factors involved in the variation of host susceptibility, determinants of PPR virus pathogenicity, the importance of animal species other than sheep and goats in the epidemiology, the potential importance of indirect transmission of virus, and the transboundary transmission dynamics of PPR virus, notably in complex multispecies systems.
- Better farmer and veterinary awareness, improvement of the vaccination process and involvement of stakeholders, and early detection of (re)occurrence for rapid response and the effective management of possible outbreaks of PPR.
- DIVA tests to provide meaningful assessment of vaccine coverage and epidemiological surveillance where the virus is circulating. Pen side tests for genome detection and non-invasive tests adapted to wildlife are also needed.
- Highly stable lyophilized vaccines that do not require a cold chain during transport.

Read the full chapter here.

Rift Valley Fever (RVF)

Disease Profile

RVF virus (RVFV) is able to infect many species of animals causing severe disease in domesticated animals including **cattle, sheep, camels and goats.** Sheep are most susceptible to disease. Humans are very susceptible with flu-like symptoms prevailing, although serious complications including retinal lesions, encephalitis and hemorrhagic fever may develop in 1-2% of patients. RVF virus is usually transmitted among ruminants through bites from infected **mosquitoes** which are the biological vectors. After first incursions, the virus is generally maintained by low-level circulation among ruminants and mosquitoes and possibly by transovarial transmission of the virus to mosquito eggs. Transmission of RVF virus by mechanical means via biting flies is also possible. **Human infections** are generally attributed to contact with raw meat, blood and other body fluids during the slaughtering of viremic animals.

RVF has been recognised exclusively in African countries with some incursions into the Middle East and Indian Ocean islands. RVF usually occurs in epizootics, which may involve several countries in a region. Epizootics follow the periodic cycles of exceptionally heavy rain, which may occur very rarely in semi-arid zones (25–35-year cycles), or more frequently (5–15-year cycles) in higher rainfall savannah grasslands.

Risk

A number of reviews have concluded that the risk of the introduction and spread of RVFV in Europe is low. Recent evidence following the reappearance of RVFV in East Africa, and, more recently, in West Africa suggests that the virus remains active and that spread of the virus is sensitive to **climate changes.** Other changes due to socio-economic effects, increasing human populations, demand for meat and uncontrolled movements of livestock all indicate that the risk of an introduction into the Mediterranean basin and central Europe will continue to increase.

There remains a concern that RVF virus could spread in Europe and Asia after a first introduction.

What do we have?

Diagnostics: A range of diagnostic tests including the virus neutralisation test (VNT) and ELISA. The VNT remains the gold standard but ELISAs are progressively replacing VNT. A competition ELISA which allows diagnosis of ruminant sera is commercially available.

Vaccines: Both live-attenuated and inactivated vaccines are available for veterinary use and have been applied in the field for many years. Each type has disadvantages and there is an urgent need for a vaccine with equal, or greater, efficacy to the live-attenuated Smithburn vaccine but which is as safe as the inactivated vaccine. The novel live-attenuated Clone-13 vaccine has improved safety and is considered a major advance in the battle against RVF. Emergency vaccination seems to be the only effective way to control the disease. There are no vaccines licensed for use in Europe.

What do we need?

- A substantial effort to better understand the ecology of RVFV vectors and epidemiological processes in Africa: develop predictive and quantitative risk models and maps, identify key environmental drivers, and implement risk-based surveillance and control methods.
- Vaccines that can be applied in RVF-free areas as emergency vaccines.
- Anticipation of an incursion of RVF in RVF-free areas by developing contingency plans, registering vaccines and development of novel diagnostic tools.

Read the full chapter here.

Sheep and Goat Pox (S&GP)

Disease Profile

Sheep pox virus (SPPV) and Goat pox virus (GTPV) belong to the genus Capripoxvirus and both are antigenically and genetically closely related to each other and to Lumpy skin disease virus. Only sheep and goats are the natural hosts of SPPV and GTPV. Strains of SPPV do pass between sheep and goats, and vice versa. Typically, however, distinct host preferences exist such that most strains of SPPV or GTPV exhibit greater virulence in the homologous host, while some are equally virulent in both species. Recombination may occur which results in a range of host susceptibility and virulence. No carrier status has been recognized following infection with either virus. The mortality rate in endemic areas may be between 5 and 10% but can reach 100% in imported, fully susceptible sheep.

Risk

Most of Europe and the Americas are now free from endemic sheep pox although, recently, it has made frequent incursions into Greece. There is a **need to identify high risk countries** where there is potential spread of disease, e.g. from Turkey into Greece and from China into Vietnam and Mongolia. Both SPPV and GTPV have a long incubation period and are easily spread by direct and indirect contact. Animals accidentally or intentionally infected could travel a considerable distance before showing disease, and could then disperse and spread disease. Capripoxviruses are a potential animal bioterrorist agent.

What do we have?

Diagnostics: Primary diagnosis using tests such as virus isolation, electron microscopy and PCR are considered relatively straightforward. Neutralization tests which are considered the "gold standard" for antibody detection are not suited to high-throughput screening of sera. Reliable high-throughput serological testing remains problematic due to insufficient sensitivity of currently available tests.

Vaccines: Several live attenuated vaccines made from different strains of capripox virus are currently available. They will provide protection against all strains of capripoxvirus as all strains so far examined share a major neutralisation site. Immunity generated following vaccination with live attenuated strains is expected to last more than 1 year.

What do we need?

- A highly sensitive and specific ELISA, based on recombinant antigens, with no requirement for infectious reagents to detect antibodies against capripoxviruses in vaccinated animals as well as in infected animals.
- A simple, validated conventional PCR method for the differentiation of SPPV from GTPV and for the differentiation of SPPV and GTPV from LSDV. Unfortunately, recombination between SPPV and GTPV can complicate identification of the viruses.
- A new vaccination programme rather than a new vaccine (including education, implementation).
- Identification and characterisation of proteins with putative virulence and host range functions, as well as those involved in modification/evasion of the host immune response, to facilitate the development of an improved, "universal" live attenuated vaccine.

Read the full chapter here.

Swine Vesicular Disease (SVD)

Disease Profile

SVD virus is a member of the genus *Enterovirus* within the family *Picornaviridae*. Swine (domestic and wild pigs) are the only susceptible species. SVD has become a milder condition than previously and can be easily missed. It is possible that outbreaks are not reported unless severe clinical signs resembling foot-and-mouth disease (FMD) are seen. SVD does not cause serious production losses but surveillance, control and eradication measures are costly. Nowadays, the **impact of SVD is low,** morbidity is low and mortality nil. Excretion of the virus in faeces rarely exceeds 3-4 weeks but the virus may persist in the environment for much longer periods.

Risk

The risks of transmission are associated with the movement of pigs or contaminated materials and transport vehicles from countries where the disease is not diagnosed due either to inadequate surveillance systems or to sub clinical occurrence.

What do we have?

Diagnostics: Currently available diagnostic tests are **well validated.** The 5B7-competitive ELISA for antibody detection reported in the OIE manual underwent extensive validation in several EU National Reference laboratories, before being considered as the reference screening test. There are commercial ELISA kits for detection of antibodies, which are based on the same principle and perform very similarly to the 5B7-competitive ELISA. Reagents for antigen detection based on ELISA and for antibody detection by 5B7-competitive ELISA (as described in the OIE manual) are available from the two OIE reference laboratories. Virus Neutralisation Test, remains the reference test to confirm singleton reactors identified by ELISA. RT-PCR reported in the OIE manual proved to be more sensitive and reliable than virus isolation.

Vaccines: There is currently no commercial vaccine available against SVD and vaccination is not permitted in the EU. **Stamping out** infected herds has been the main strategy in Europe and was effective. There has never been a need for the use of SVD vaccine although experimental studies show they work.

What do we need?

The main importance of SVD has been that it is clinically **indistinguishable from FMD,** and any outbreaks of vesicular disease in pigs must be assumed to be FMD until investigated by laboratory tests and proven otherwise. Because good diagnostic tests are available for this purpose and because the worldwide incidence of clinical SVD has diminished, the importance of SVD has decreased. It remains to be seen, whether or not, delisting of SVD by OIE and consequent reduction in surveillance and control efforts will result in the viral agent becoming more prevalent, and if so, if this will be associated with any changes in disease expression.

Read the full chapter here.

West Nile Fever

Disease Profile

West Nile virus (WNV) is an enveloped single-stranded RNA flavivirus. There are 8 distinct lineages dominated by lineages 1 and 2. WNV is maintained in nature by cycling between birds as amplifying hosts and mosquitoes which are competent biological vectors. In mosquitoes, the virus must multiply and reach the salivary glands before it can be transmitted to a vertebrate host. **Mosquitoes** disperse WNV by transmission to many susceptible species of birds, mammals, amphibians and reptiles. **Equids and humans** are the most sensitive mammals to WNV infection but are dead end hosts. In horses, 10–20% of infected animals may develop neurological signs and the case fatality rate ranges from 23% to 57%. When human infection results in clinical disease, it is usually a flu-like illness with fever. Less than 1% of human cases develop meningoencephalitis. WNV is now endemic in Africa, USA, Central Europe and the Mediterranean region, West and Central Asia. The apparent increase in WNV infections in some parts of the EU could be attributed to improved surveillance, diagnosis and reporting.

Risk

Outbreaks in North America and Europe are difficult to predict and the long-term epidemiology of WNV infection in Europe remains uncertain. In central and southern Europe, WNV may be evolving towards an endemic state, punctuated by occasional large outbreaks.

Introduction and spread of WNV is usually attributed to movement of infected wild birds or importation of infected vectors. Climate change may lead to changes in the distribution of vectors, and more rapid development of WNV in vectors.

What do we have?

Diagnostics: Domestic livestock are dead-end hosts and have a transient viraemia not detectable using currently available RT-PCR techniques. Several test kits are available in Europe but are generally for use in laboratories. Most are based on competitive ELISA. A major problem for WNV serological assays is the high degree of cross-reactivity between WNV and antibodies against other flaviviruses and, in humans, the longevity of IgM.

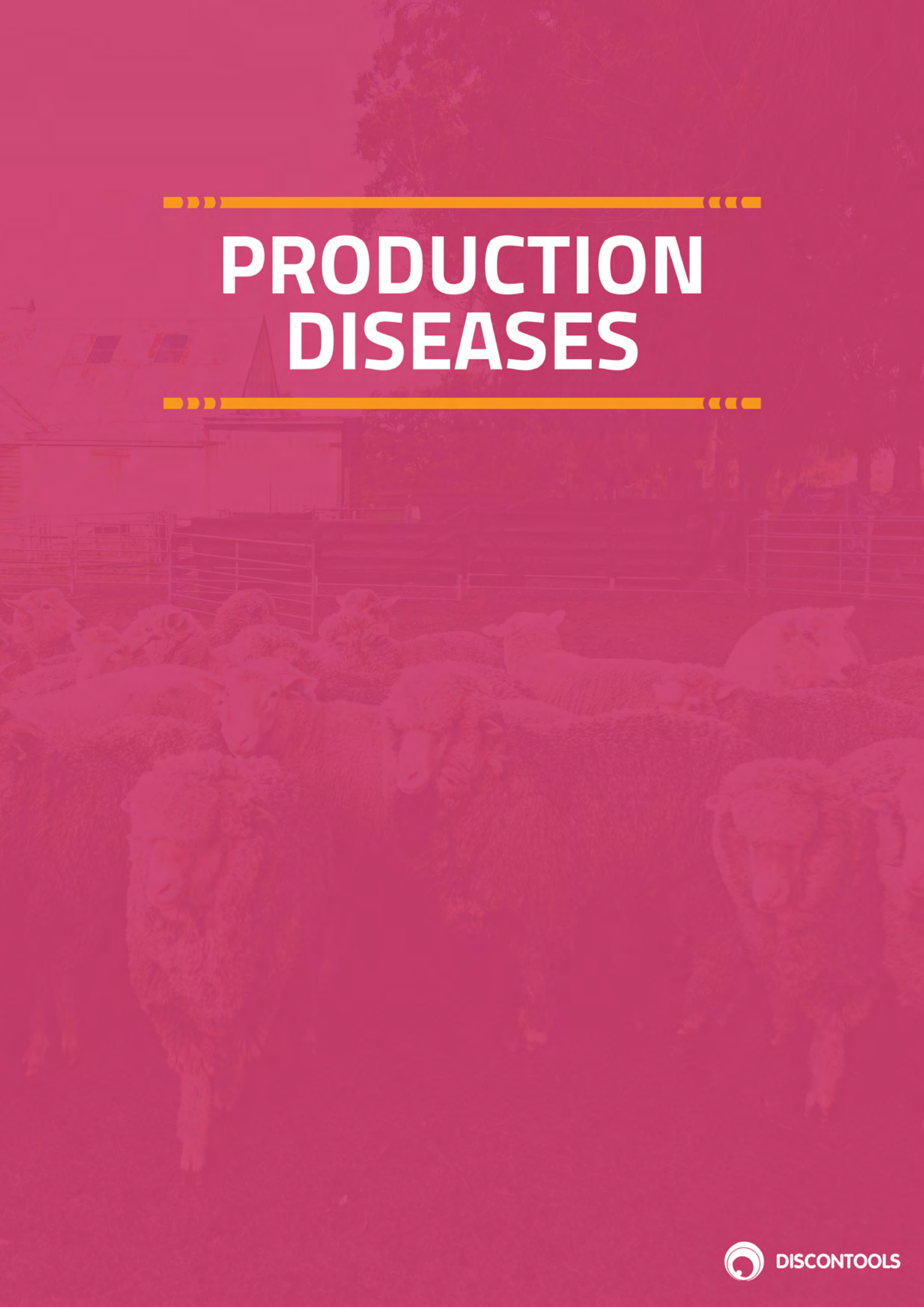
Vaccines: WNV vaccines currently sold in the EU have good safety and efficacy profiles.

What do we need?

- Knowledge on the impact of climate change on vector distribution and patterns of virus transmission.
- Strengthening and integrating animal and human surveillance and development of preparedness plans and capacity for detection and response to outbreaks.
- DIVA serological tests based on non structural proteins of WNV to discriminate antibodies arising from natural infection from those arising from vaccination both in the clinical setting and during surveillance.
- Highly sensitive PCR methods for species such as horses that do not develop a high concentration of virus in tissues.
- Establishment of the maximum duration of immunity and protective efficacy for currently available vaccines, and protective status following natural infection should be assessed so that horse owners can decide if annual vaccination is necessary to protect their horses against re infection.
- A single dose vaccine with early onset of immunity and long duration of immunity.

Read the full chapter here.

PRODUCTION DISEASES



DISCONTOOLS

Bovine Respiratory Syncytial Virus (BRSV)

Disease Profile

Infection with BRSV is a major contributor to the **multi-pathogen bovine respiratory disease complex** which results in a substantial economic loss for the cattle industry worldwide. BRSV infections associated with respiratory disease occur predominantly in young beef and dairy cattle. It is the single most important respiratory viral pathogen of calves. Mortality is usually less than 5% in young calves with deaths resulting from BRSV infection alone or as a result of secondary bacterial pneumonia. The transmissibility of BRSV is high with rapid spread of the virus between immunologically naive animals within herds and between herds. BRSV gains entry to susceptible cattle through the respiratory tract where it replicates and causes disease.

Risk

Worldwide the **ubiquitous** and endemic character of infection in dairy and especially beef cattle causes major losses to the industry. Large volumes of antibiotics are used in the veal production sector to try and control respiratory disease.

What do we have?

Diagnostics: Antigen detection enzyme immunoassays have been developed, but sensitivity is low. Other antigen detection assays are fluorescent antibody and immunoperoxidase staining. Conventional or real time PCR-based tests, which have high sensitivity and specificity, are used for routine diagnosis as well as for research purposes. Antibody detection kits for BRSV antibodies are available. Currently, there are no DIVA tests available but an SH protein-based ELISA might be a good option.

Vaccines: Two monovalent and many multicomponent vaccines containing modified-live or inactivated BRSV are currently on the market for intramuscular or intranasal administration in cattle. The immunity conferred by BRSV infections or vaccination is probably short lived so that frequent vaccination may be necessary. Intranasal vaccination with live attenuated BRSV vaccine induces rapid protective immunity, which is useful when disease occurs in very young calves.

Pharmaceuticals: As with other viruses, antibiotics have no effect on the BRSV infection. However, antibiotic treatment is indicated in attempts to control the secondary bacterial infections. An antiviral may have a place in future as well as other agents that have a disease mitigating effect at low cost, in combination with antibiotics or anti-inflammatories.

What do we need?

- Comparative studies of the **immunobiology** of human and bovine RSV. BRSV is structurally and antigenically related to human (H)RSV. BRSV in calves is an excellent model for development of HRSV vaccines and pharmaceutical products.
- Better fundamental understanding of the pathogenesis and epidemiology of BRSV. The role of genetic variation in calves on disease severity and those aspects of the virus which determine virulence, the survival of BRSV in the environment and the existence of carriers and reservoirs of infection are poorly understood.
- **More effective vaccines,** especially of the DIVA type, combined with biosecurity measures based on identified routes of virus introduction in herds to combat the disease successfully in a well-controlled manner in endemic areas.
- Efficient **new therapeutics** to limit excessive inflammation associated with BRSV infection to avoid the use of antibiotics to limit bacterial super-infections and to ensure animal welfare.

Read the full chapter here.

Bovine Viral Diarrheoa (BVD)

Disease Profile

Bovine viral diarrhoea (BVD) is caused by genetically and antigenically distinct viruses belonging to three different species of the Pestivirus genus within the Flavivirus family, bovine viral diarrhea virus 1 (BVDV1), BVDV2 and HoBi-like viruses (alternatively BVDV3). Cattle of all ages are susceptible to infection with these viruses. Clinical signs range f**rom sub-clinical to fatal** (mucosal disease and haemorrhagic syndrome). Acute infections may result in transient clinical disease with variable symptoms (respiratory disease, diarrhea, fever, leukopenia). The virus spreads mainly by contact between infected cattle or via indirect contact, **but vertical transmission** plays the major role in its epidemiology and pathogenesis. Infections of the bovine foetus may result in abortions, stillbirths, teratogenic effects or immunotolerance leading to lifelong persistent infections.

Risk

The disease results in major economic losses for the cattle industry worldwide. **Reproductive effects** are the most prominent [abortions, deformed offspring, **persistently infected animals (PI)**] but significant financial losses also occur through a general impairment of health in endemically infected herds including immunosuppressive effect of the virus, leading to increased secondary infections and death of affected animals. The presence of PIs, which continually shed virus, is a serious risk for any herd. PIs are efficient vectors and their presence is associated with decreased general health and productivity within the herd. Their role in the epidemiology of the disease cannot be overestimated.

What do we have?

Diagnostics: Diagnostic kits are commercially available for testing of blood, ear notch or milk samples. The majority of testing is performed to identify and remove PIs. Direct detection of PIs is done by antigen capture ELISA or genome detection. Blocking or indirect ELISAs are used for the detection of antibodies in serum, plasma and milk and are commercially available.

Vaccines: Modified-live and inactivated vaccines are available globally although efficacy and safety are still an issue. BVDV control programmes based on elimination of PIs and improved biosecurity are underway in a number of countries and regions. Most, but not all, of these control programs include systematic vaccination. There are no vaccines licensed for the prevention of infection with HoBi-like viruses.

Pharmaceuticals: No pharmaceutical therapy is available commercially. Prophylactic treatments and antibiotics may be used to treat secondary infections.

What do we need?

- BVDV eradication programmes are ongoing in many countries and have been successful in eliminating or effectively reducing the prevalence of infection. While suitable tools for BVD control are available, obstacles to worldwide eradication of BVD includes insufficient regional information on level of exposure, prevalence of PI animals and BVD causative agents present and insufficient support by influential individuals/groups within the industry, academia and authorities.
- Research in BVD pathogenesis and immunity should target the role of innate and cellular immunity; the action of neutralising antibodies versus cell-mediated immunity in foetal protection; the mechanism(s) of immune suppression and mechanism(s) associated with pathogen synergy that result in increased virulence of other pathogens.
- Opportunities for diagnostic developments are linked to differentiating vaccinated from exposed cattle and for the differentiation of the three viral species for the purposes of control program design and international trade. One-site and multiplex test systems could contribute to control programmes and reduced testing costs.
- A vaccine with close to 100% efficacy in foetal protection, that is safe for use in pregnant animals, would be necessary for BVD control using vaccination alone.

Read the full chapter here.

Contagious Agalactia (CA)

Disease Profile

CA is a **highly infectious disease of sheep and goats.** The main pathogen is *Mycoplasma agalactiae.* CA presents itself differently in sheep and goats. In sheep the disease is a less severe and is caused almost always by *M. agalactiae*, while in the goats it is a serious illness that can be caused by *M. agalactiae* and other Mycoplasmas. Clinical disease can be manifested in an acute, sub-acute or chronic form. Mastitis, arthritis, keratoconjunctivitis and blindness can occur in both male and female sheep and goats. Horizontal transmission occurs by contact between infected animals and/or the environment shared with infected animals. Vertical transmission can occur by means of suckling milk from infected mothers. Animals become infected by ingestion or occasionally by inhalation. Aerosol transmission is possible over short distances. Transmission via fomites is possible.

Risk

The disease occurs in southern Europe, Western Asia, the USA and North Africa. The current geographical location of the disease suggests it is prevalent in sub-tropical regions and therefore climate change may enhance spread to currently clear areas.

What do we have?

Diagnostics: Commercial ELISA kits for serological monitoring are available. Agar medium plates for the detection of *M. agalactiae* are available. Conventional serological tests for identification of mycoplasmas are slow and laborious and are being replaced by molecular methods.

Vaccines: Globally live attenuated vaccines and inactivated vaccines are available but the use of live vaccines, whilst being the most antigenic, is banned in Europe despite good results in Turkey. Live attenuated vaccines are considered more effective than inactivated vaccines. Formalin inactivated, adjuvanted vaccines are available for use in Europe but there is little data on the efficacy of these inactivated vaccines. A multivalent formalin inactivated vaccine incorporating all four causative mycoplasmas and adjuvanted with saponin and aluminium hydroxide appears to show some promise.

Pharmaceuticals: Antibiotics (tetracycline, macrolide, florfenicol, tiamulin and fluoroquinolones) may clear the clinical signs but often the organism is not cleared and the sub-clinically infected animal goes on shedding the organism for potentially years afterwards.

What do we need?

- Knowledge on the factors associated with r**eactivation of *Mycoplasma***, pathogenicity mechanisms and the contribution of the host immune response to lesion development in mammary gland and lung and disease.
- Further work on the **transmission mechanisms:** the role of pneumonia as part of the transmission process, role of insects, significance of aerosol transmission.
- A **marker vaccine** together with a suitable diagnostic means of distinguishing between vaccinated and infected animals. P48 is a prospective marker vaccine, but to-date has only been tested experimentally.
- **Antibiotics** with increased efficacy/distribution that could prevent the continued excretion of mycoplasma. Screening of novel chemicals and plant extracts against CA mycoplasmas is also possible. Future therapy is likely to remain with the use of antibiotics but new antibiotics may be restricted for human use.

Read the full chapter here.

Poultry coccidiosis

Disease Profile

Coccidiosis of chickens, turkeys and other poultry hosts is caused by species of the genus *Eimeria*. Seven species infect chickens and at least seven species are described in turkeys. Disease severity is variable and depends on many factors including the *Eimeria* species involved, virulence of the strains, infection load, age and immune status of the host. The main effects of coccidia are due to **destruction of gut epithelia**, villous atrophy and for some species, disruption of sub-epithelial tissues. Sub-epithelial disruption by *E. tenella* and *E. necatrix* causes severe haemorrhage in chickens directly causing death. Gut epithelial damage by coccidia and the resulting protein leakage also renders hosts more susceptible to infection by a wide range of bacteria and may increase carriage of zoonotic agents.

Risk

It is very rare to find commercial flocks not infected with coccidia. Once a flock is infected, accumulation of oocysts in the litter is more or less continuous, as infective oocysts are ingested and shed asynchronously. All poultry are at risk by contact with faeces. The threat of disease **increases with greater intensity of rearing** in countries with high poultry commercialization, and also in poorer countries with less sophisticated husbandry and control methods. Coccidiosis is a **particular risk to organically grown poultry** where the use of anticoccidial drugs is prohibited. Monitoring of such flocks has demonstrated that mortality rates may reach as high as 30%.

What do we have?

Diagnostics: **No commercial kits** are available and there are no rapid tests to differentiate drug sensitive from drug resistant parasites. PCR assays are available and the seven chicken *Eimeria* species can be simultaneously detected and discriminated in a single-tube multiplex PCR assay. Quantitative PCR assays have also been developed for the seven species. PCR diagnostic assays have recently been reported for four turkey *Eimeria* species.

Vaccines: **Attenuated live vaccines** comprising sporulated oocysts of different species/strain combinations depending upon the target market (i.e. broilers, breeders, layers) are available for use in chickens. Production capacity in chickens limits the availability of these live vaccines.

Pharmaceuticals: Different classes of **anticoccidial drugs** (ionophores and synthetic compounds) are available and widely used as additives in feed for the prevention of coccidiosis. These drugs vary in their efficacy depending upon several factors of which acquired resistance by the parasites is the most problematic. A few anticoccidial drugs are available to treat birds that are suffering from coccidiosis usually by including a soluble compound in the drinking water.

What do we need?

- Increased knowledge on (i) *Eimeria* population structure and diversity with relevance to control (ii) *Eimeria* infections in the turkey, (iii) the control of parasite replication, gene expression and stage differentiation, (iv) the effects of coccidiosis on the spread and behaviour of other avian gut pathogens, including several zoonotic agents.
- **Rapid diagnostic tests** for strain differentiation, including distinguishing drug resistance/sensitivity and vaccine strains from field strains. Rapid methods to determine the immunological cross-reactivity of *Eimeria* strains (especially newly emerging genotypes and antigenic variants).
- Vaccines: (i) **vaccines that do not require cycling** via oocysts in the litter to achieve solid protective immunity; (ii) attenuated vaccines for use in turkeys. The development of next generation recombinant or subunit anti-coccidial vaccines will depend on the identification of effective vaccinal antigens.
- **Novel anticoccidial drugs** with modes of action that differ from those of existing compounds.

Read the full chapter here.

Environmental Mastitis

Disease Profile

Environmental mastitis is defined based on epidemiological criteria (environment as main source of the pathogen with transmission from the environment to individual cows) and contrasted to contagious mastitis (infected cow as main source of the pathogen with transmission from cow to cow). Many mastitis pathogens can originate from or be spread via the environment. They include **a large number of bacterial species.** Species affected by environmental mastitis include cattle, sheep, goats, buffalo and camels. Environmental mastitis can manifest as subclinical mastitis (no visible abnormalities) or clinical mastitis which can be mild (abnormalities in milk only), moderate (abnormalities in milk and udder) or severe (systemic signs). Severe environmental mastitis may result in sepsis and may be fatal.

Risk

Morbidity and mortality are highly variable between herds, groups within herds, seasons, farm types, etc. Outbreaks, by definition, are short periods of unusually high incidence or mortality, whereby more than 10% of a herd may be affected or killed in a few weeks to months. With the exception of toxin-producing *Staph. aureus*, there is very little evidence that environmental mastitis pathogens in dairy cattle pose a risk to human health. The use of antimicrobials in mastitis treatment and control could contribute to selection for antimicrobial resistance in causative pathogens, which may also be infectious to humans.

What do we have?

Diagnostics: Intramammary infection is the most common cause of mastitis and can be diagnosed by demonstrating presence of a pathogen (in non-contaminated samples). This can be done through culture or through molecular methods (PCR). Culture has traditionally been performed on various agar plates in diagnostic laboratories, but a growing array of on-farm diagnostics has recently become available, including plates with selective or indicator media, petrifilms and semi-automated on-farm culture systems.

Vaccines: A **growing range of vaccines** has become available on the European market in recent years, including vaccines with label claims for protection against mastitis caused by *E. coli, Staph. aureus* or *Strep. uberis* in dairy cattle and against *Staph.* aureus in sheep and goats. Evidence for their efficacy from independent field studies is mixed with generally stronger evidence for prevention of losses due to *E. coli* than for other pathogens.

Pharmaceuticals: There are numerous **antimicrobials** on the market for treatment of mastitis. Non-steroidal **anti-inflammatory drugs** are available for supportive treatment. Societal concern about antimicrobial use and antimicrobial resistance is currently driving a shift in thinking about treatment, and restrictions on antimicrobial use are in place in a growing number of areas. Prevention of environmental mastitis during the dry period can be achieved with teat sealants, and with improved hygiene and dry cow management.

What do we need?

- A standardised **typing system** to establish a likely environmental origin, mode of transmission or prognosis for mastitis cases.
- Tools for monitoring pathogen load in the environment.
- Improved knowledge of the **innate immune system** in the host response, including but not limited to the role of macrophages, lymphocytes and cytokines. This is needed to develop improved vaccines.
- Continued efforts to **bridge the gap in uptake of recent insights** into environmental mastitis in veterinary practice and herd health management programmes. The impact of climate change, labour shortages and reduced use of antimicrobials on mastitis incidence and animal welfare is unknown.

Read the full chapter here.

Bovine Herpes Virus 1

Disease Profile

Infectious bovine rhinotracheitis / infectious pustular vulvovaginitis (IBR/IPV), is an infectious disease of cattle due to infection with bovine herpesvirus-1 (BoHV-1). The virus can infect mainly the **upper respiratory tract** or **the reproductive tract.** The virus is endemic and nearly worldwide in the cattle population although it has been **eradicated in some countries** like Switzerland, Austria, Denmark, Sweden and Germany. The natural host of BoHV-1 is bovines with no proof of another domestic or wild ruminant reservoir. IBR is usually a herd infection with most animals in a contact group involved. Mortality is low but the economic loss can be important due to trade restrictions or exclusion from breeding programmes (bulls). Infected animals (so-called "reagents") are lifelong latent carriers which can reactivate the virus and infect naïve animals. Free regions have to be therefore antibody free (or free from BoHV-1-antibodies in marker-vaccinated regions).

Risk

The major risk for introduction into a farm or region is direct or indirect contact to infected animals. A major risk are **latently infected cattle** which reactivate the virus. Those animals are therefore a major target of all eradication programmes. Marker vaccination can reduce the risk and can be used on a population level to enhance eradication efforts in an early phase of a programme. There is no reported incidence in humans.

What do we have?

Diagnostics: Both conventional and real-time **PCRs** can be used to detect the virus. Retrospective diagnosis of BoHV-1 infection and analysis of the carrier status can be made by measuring antibody titres in paired sera samples. Antibody detection can be done via serum-neutralisation (SN) tests and various indirect or blocking BoHV-1 ELISAs which are currently available. The **gB-ELISA** is the gold-standard for BoHV-1 antibody detection. The use of marker vaccines is important in the differentiation of infected and vaccinated animals that can be made by the simultaneous use of ELISAs detecting whole virus or glycoprotein B (gB) antibodies and ELISAs detecting glycoprotein E (gE) antibodies. Diagnostics of BoHV-1 is high standardized and numerous nationally licensed assays are available.

Vaccines: Live-attenuated and inactivated vaccines are commercially available which can be administered intramuscularly or intranasally. Various sub-unit and vectored vaccines have also been tested experimentally. Marker vaccines are commercially available and are licensed by a number of companies with or without DIVA capacity. The use of **gE-deleted marker vaccines** is state-of-the-art for eradication prorammes in regions with a high BoHV-1 prevalence.

Pharmaceuticals: As with other viral diseases, there is no direct treatment for the infection.

BoHV-1 infections still have an important economic impact in the cattle industry and this is not only as a unique infection of cattle but also as part of the bovine respiratory disease complex. Furthermore, in many countries bull stations have to be free of BoHV-1. Currently eradication programmes for BoHV-1 are running in several countries, where gE negative DIVA vaccines are used in combination with the companion diagnostic gE ELISA test. The DIVA vaccines as well as the accompanying diagnostic tests are well established and on a very high quality level.

What do we need?

- Improved knowledge about the latent infection in vaccinated animals.
- Vaccines which could block latent infection and reactivation of BoHV-1.
- Marker vaccines with an improved duration of immunity (>1 year).
- Improved ELISAs for the sensitive and specific detection of BoHV-1-gE-specific antibodies in milk samples.
- Improved harmonization of test protocols and eradication programmes.

Read the full chapter here.

Liver Fluke

Disease Profile

Liver fluke is caused by mainly *Fasciola hepatica* (*F. hepatica*) in temperate areas and *F. gigantica* in the tropics. It affects a wide range of mammal species, with most problems occurring in **ruminants.** The disease is found on every continent but is particularly prevalent in areas of high rainfall and temperatures above 10^{0}C where the intermediate **freshwater snail host** is abundant. The life cycle is seasonal, occurring in the winter in Mediterranean countries when conditions are suitable for development and in the summer in northern climes where the winter is too cold. Both **temperature and rainfall** and other environmental and physical factors have a profound effect on the incidence. The disease occurs in three forms – acute, sub-acute and chronic. Acute disease may lead to sudden death which is common in sheep, but rarely occurs in cattle. During sub-acute and chronic disease, clinical signs usually occur as a result of the migration of immature fluke and their feeding on liver tissue causing damage to the parenchyma, anaemia and fibrosis. The adult flukes in the bile ducts feed on blood causing anaemia, cholangitis and weight loss.

Risk

Human liver fluke disease is included in the WHO classification of Neglected Tropical Diseases. It is very rare in Europe but in some parts of the world the disease is a major public health issue. The incidence of human infection with *F. hepatica* is estimated at 2.4 million with 180 million people at risk.

Currently the most urgent risk is the **development of resistance** to current pharmaceutical products. The predicted effects of climate change may also significantly increase the risk of the disease and there is the potential for an increase in the incidence of the disease among herbivores which could lead to increased risk to the human population in some areas.

What do we have?

Diagnostics: There are commercial antibody detection tests for cattle but not for sheep. These detect exposure but not necessarily current infection. Also commercially available are copro-antigen detection ELISAs that can be used in sheep and cattle. Faecal egg counts remain the gold standard to confirm live infection but fail to diagnose infection in the high-risk pre-patent period thereby delaying appropriate management responses.

Vaccines: There are no vaccines currently available but a number are under development.

Pharmaceuticals: The prophylactic use of **anthelmintics** is currently the main method for prevention and control. There are a number of anthelmintics available, triclabendazole being the anthelmintic of choice because of its proven efficacy against young immature stages of *Fasciola* spp. Other than triclabendazole (TCBZ) there are no fully effective drugs against young juvenile stages of the parasite which are highly pathogenic.

What do we need?

- More information about how the predicted effects of **climate and environmental change** are influencing the survival and development of the environmental stages of the parasite.
- An understanding of the **immune responses** to fluke (innate and adaptive; protective and suppressive) in naturally exposed ruminants.
- **Genome mapping** to: aid in identification of drug resistant isolates, improving our understanding of drug resistance to different flukicides; develop tools for diagnosis; and differentiating between species and identifying hybrid species.
- Pen-side tests, herd level tests to identify heavily infected beef herds, tests for diagnosis for acute infection or pre-patent infections.
- **Drugs** that are effective against the young immature stages of the parasite.
- **Vaccines** targeting all stages and suitable for any host species.
- Good control programmes no longer reliant on the exclusive use of anthelmintic prophylaxis to address the problems with drug resistance.

Read the full chapter here.

Mycoplasma bovis

Disease Profile

M. bovis is an important pathogen of **cattle.** The clinical disease can be very variable and include mastitis, pneumonia, arthritis and genital disorders and can occur in cattle of all ages. Infected cattle can become asymptomatic carriers and may shed the organism through nasal discharges or in milk for months to years without showing clinical signs. **Other species** may become infected, or be carriers with cases having been reported in sheep, goats, buffaloes, bison, swine, deer and chickens.

Risk

There is no evidence for human disease caused by *M. bovis* but a few cases have been reported in immuno-compromised patients. *M. bovis* can spread very rapidly once introduced into a herd. Spread to new herds is usually due to the **movement of asymptomatic carriers** being purchased and introduced into a clean herd. The primary routes of infection are usually by close contact through direct nose to nose transmission via aerosols and/or by the ingestion of infected milk.

What do we have?

Diagnostics: Diagnosis is by the isolation and identification of *M. bovis* from bulk milk tank or from cows with clinical mastitis by culture or use of molecular methods such as PCR, R-T PCR, micro-array or by using PCR with denaturing gradient gel electrophoresis (DGGE) to differentiate the species of mycoplasma. The main antibody test in use is the indirect ELISA. Some commercial ELISA kits are available for antigen and antibody detection. The sensitivity and specificity of these kits has been revised and still being reviewed. Methods for diagnosis should include antibiotic sensitivity testing and determining antibiotic resistance in real time.

Vaccines: Commercially available vaccines are licensed in the USA. These are Bacterin type vaccines with a number licensed for prevention of respiratory disease and others for the prevention of mastitis. No commercial vaccines are licensed for *M. bovis* in Europe. Autogenous vaccines are produced by several companies for use solely in the USA but data about their effectiveness is sparse.

Pharmaceuticals: *M. bovis* as with other organisms in the group lacks a cell wall, which means the organism is **resistant to some commonly used antibiotic therapies** which can also be expensive and ineffective. There is a poor response to treatments especially in cases of chronic respiratory disease or mastitis. The US Food and Drug administration have approved the only antibiotic (tulathromycin) for the treatment of bovine respiratory disease linked to *M. bovis.*

M. bovis is a major constraint on intensive production affecting intensive beef production particularly in feed lots and milk production in high yielding herds. The following factors summarises the problems: i) No effective vaccines available, ii) Insidious infection not always easily diagnosed, iii) Difficult to eliminate from a herd, iv) Difficult to assess the cause of the bovine respiratory disease complex when a number of other pathogens are also involved and finally v) Development of antibiotic resistance to many of the antibiotics currently in use.

What do we need?

- Increased knowledge on host-pathogen interactions to develop safe and effective vaccines: mechanisms of host invasion, transmission within the host, predilection for specific sites, intermittent shedding, differences in resulting clinical signs, the role of variable surface proteins.
- The identification of protective antigens through genomic, bioinformatics, proteomic, immunological and biological approaches.
- The design of molecular typing schemes for *M. bovis* disease surveillance to support the development of more specific and sensitive tests.
- Effective antibiotic treatment regimens to address antibiotic resistance.

Read the full chapter here.

Nematodes

Disease Profile

There are a **large number of genera and species** but here only nematodes of the gastrointestinal tract (GI) of **ruminants and pigs** are considered. Livestock welfare and production (both meat and dairy) are negatively affected by gastrointestinal nematode infections, which are one of the main constraints to efficient livestock production worldwide. The effect of ruminant nematodes is mainly in growing animals where subclinical infections can lead to reduced weight gains. In adult animals infections can result in milk yield losses, lower conception rates, poor carcass quality and reduced wool yields. The impact of pig nematodes is largely unknown although liver condemnations may be up to 20 % in certain countries.

Risk

In ruminants, parasitic gastroenteritis mainly occurs during the **grazing** period and will vary according to latitude. Infection levels are determined by management as well as environmental (temperature, humidity) factors. Changing climate can exacerbate parasitoses by increasing the level and duration of pasture infectivity. Nematode infections in general do not transfer between animals and humans. However, the issue of drug resistance is growing both in animal and human populations.

What do we have?

Diagnostics: **Coprological (microscopical) methods** are used for all gastrointestinal nematodes and all hosts to identify and quantify eggs and with coproculture to identify L3 stage larvae. **Serological methods** involve measuring serum pepsinogen levels to assess the degree of damage due to abomasal nematode infections. A bulk-tank milk *Ostertagia ostertagi* ELISA is used to assess nematode exposure in adult cows. Morbidity markers have been described in sheep. Pig nematodes are mainly diagnosed by faecal examination for eggs and occasional reports from abattoir of milk spots in the liver as well as a recently developed antibody ELISA. DNA-based methods for species differentiation are increasingly described but not used for routine diagnosis.

Vaccines: A vaccine against Haemonchus contortus reduces worm numbers and worm egg output by > 90% and is available in Australia. Prototype vaccines against *Ostertagia ostertagi* and *Cooperia oncophora* reduce worm egg output by 60% and 90%, respectively during a two month challenge period.

Pharmaceuticals: Control of relies largely on **anthelmintics.** All anthelmintics are very effective at reducing susceptible worm burdens. However, anthelmintic resistance of GI nematodes in ruminants is increasing worldwide as a consequence of the intensive usage of the currently available products.

What do we need?

- Development and implementation of holistic control strategies using improved diagnostics, host genetics, nutrition and pasture management to reduce the reliance upon anthelmintics and the threat of anthelmintic resistance.
- Easy-to-use diagnostics to identify those animals requiring treatment and tests for early detection of anthelmintic resistance.
- Anthelmintics with new mode of action than currently available.
- Development of complementary control measures: vaccines, bio-active forages, nutraceuticals.

Read the full chapter here.

Paratuberculosis (ParaTB)

Disease Profile

Paratuberculosis (or **Johne's disease**) is caused by *Mycobacterium avium* subsp paratuberculosis (MAP). Paratuberculosis is an untreatable, intestinal disease of ruminants characterised by a **slow progressive wasting** of the animal with increasingly severe diarrhoea. MAP can affect camelids and wildlife, including deer and rabbits. In cattle there are 3 stages of disease. Calves are particularly susceptible and often ingest MAP during the first month of life. This is followed by a long latent period during which the animals are neither clinically affected nor infectious. During the latent period, animals remain clinically normal but then become infectious by intermittently excreting MAP in low numbers in their faeces. Finally, clinical disease may occur.

Risk

Meta-analyses have demonstrated that the association of MAP with **Crohn's disease** in humans is specific and cannot be denied, although a causal role has not yet been demonstrated. Furthermore, transmission from cattle to humans has never been proven. However, addressing JD worldwide should be considered a proactive step in ensuring consumer confidence if a link was to be established between JD and Crohn's disease.

With the long latent period the speed of spread is difficult to assess but high numbers of calves can be infected at any one point in time if hygiene and husbandry are unsatisfactory. Generally infection is introduced into a herd by the purchase of infected animals.

What do we have?

Diagnostics: There are commercial kits available for ELISAs to detect antibody, interferon-gamma kits to detect cellular immune response and culture and PCR kits to detect the organism and bacterial DNA. Tests can be divided in **early-stage diagnostics** (detecting pro-inflammatory immune responses, e.g. interferon-gamma assays), **late-stage diagnostics** (detecting anti-inflammatory immune responses, e.g. IgG1 ELISA) and **herd-level diagnostics** (based on environmental sampling or bulk-tank milk analysis). None of the existing tests are apt to reliably detect latent infections, and all tests may result in low rates of false-positive reactions under field conditions. The chronic nature of infection makes test interpretation a challenge.

Vaccines: A **killed vaccine** has been widely applied in Australian sheep herds, where it has become the dominant JD control practice. Using this killed vaccine reduced the prevalence of MAP infection and faecal shedding, and mortality in Australian sheep herds considerably. This vaccine does not prevent MAP infection and can therefore not be used on its own to eradicate MAP infection. In cattle no effective vaccine is available, and the lack of an efficacious vaccine that protects against infection with MAP is hampering control programmes.

What do we need?

- Research towards the **protective immune responses.** Detailed studies with relevant antigens in relevant host tissues besides blood are needed.
- Work on **genetic resistance and disease susceptibility** may aid the understanding of pathogenesis and host response.
- New and improved tools to control MAP infections are required and should be a priority. There is a need to **increase the sensitivity of the diagnostic and screening tools**, especially when applied to early infected animals. An important requirement is for cost-effective and specific immuno-diagnostics that can discriminate between "non-infected", "exposed", "MAP infected" and "infectious" animals.
- **Improved vaccines** which prevent excretion of the organism and ideally protect young animals from infection, do not result in interference with diagnostic tests and do not cause cross reactions with the bTB test are required.

Read the full chapter here.

Porcine circovirus 2 (PCV2)

Disease Profile

PCV2 is the necessary but not usually self-sufficient cause of a variety of manifestations that are known as porcine circovirus diseases (PVCD). All species of pigs appear to be affected including wild boar and feral pigs. Many pigs are infected without displaying clinical symptoms of disease and some of these animals act as carriers. The **variety of clinical syndromes** includes the Post Weaning Multi-Systemic Wasting Syndrome (PMWS), the Porcine Dermatitis and Nephropathy Syndrome and reproductive failure which is manifested as mid-late term abortions or farrowings with increased numbers of stillborn and mummies. PCV2 has been shown to contribute to a variety of disease complexes including enteric and respiratory diseases and gastric ulcers.

Risk

The history and circumstances for PCV2 emergence are largely unknown and it is not possible to predict the appearance of new, more pathogenic versions of the virus. There was some evidence that the severe diseases seen globally in the beginning of the century was linked to the emergence of specific genotypes, but the variability of disease may also be related to many other factors such as immune status to PCV2, time of infection, pig genetics, standards of management in the widest sense, and in particular to the health of the herd and the other concurrent diseases. The virus transmits easily because of its ubiquitous nature in the environment. As yet not understood effects on the host make it very difficult to control. There is no evidence of human infection, no evidence of vectors and probably most pigs are infected.

What do we have?

Diagnostics: Clinical signs, post-mortem demonstration of PCV2 material by immunohistochemical or in-situ hybridisation which is available in most laboratories worldwide. Quantification of virus load in serum by real time qPCR is possible, but the results are doubtful as a diagnostic tool to predict clinical impact. Diagnosis is still complex and is best made at the herd level with the necessary help of local laboratories.

Vaccines: Both recombinant and inactivated full-virus vaccines are available in sows and piglets. Also combination vaccines where PCV2 are combined with vaccines against *Mycoplama hyopneumoniae* have been launched in Europe. All the vaccines appear to be successful in reducing losses due to PMWS and are capable of producing protective levels of colostral antibodies and to protect young piglets prior to acquisition of infection in the growing phase.

What do we need?

- Unravelling of the **mechanisms of pathogenicity**: why this virus existed in the pig population for a long time and then in the mid to late 1980s suddenly started to cause disease.
- Continuing research on the **fundamental immunology** of the pig and its relation to PCV2 infection: the role of cell-mediated immunity and immune modulatory role of PCV2.
- A repeatable, reproducible **model of experimental disease.**
  Pen-side tests that assess need and/or impact of vaccination would be beneficial.
- **Improved vaccines** that require reduced number of injections, can be applied by easier routes and/or can include more antigen combinations in vaccines against common pig pathogens.
- A new generation of T-cell stimulants or intermediary **metabolism modulators** which could help to control the infection.

Read the full chapter here.

Poultry Red Mite

Disease Profile

Infestation of laying hen houses with poultry red mites (*Dermanyssus gallinae*) causes major animal welfare and economic problems for the egg-producing industry worldwide, costing in excess of €231 million per year in the European Union alone in control and production losses. *D. gallinae* is a strictly hematophagous **(blood-feeding) mite** and is a reservoir and/or vector of important avian and zoonotic diseases, including *Salmonella* Enteritidis and avian influenza virus. The mites spend most of their lives off of the host, returning during the hours of darkness to feed on hens for short periods of time (<1h), and can form large populations in the accommodation of birds in commercial egg laying operations. Once introduced into farm buildings, the mites are extremely difficult to manage successfully. Even in empty animal accommodation, the mites can survive for prolonged periods without a bloodmeal and under cold conditions.

Risk

Infestation of commercial egg-producing flocks with *D. gallinae* is both endemic and epizootic; in Europe **83% of egg production units report infestation.** Distribution is worldwide resulting from long distance spread via trade activity. Inert objects such as cages and any object involved in poultry transportation are implicated in spreading the mites.

What do we have?

Diagnostics: Most diagnosis is by visual inspection of shed furniture (undersides of feeding troughs, perches etc) and simple visual scoring methods can be used as a rough guide to the scale of the problem. There are also various types of **mite-traps** which can be used to monitor populations. Manual traps rely on regular checking for presence of live mites and some companies offer a counting service.

Vaccines: Multiple recombinant antigens have been trialled in both laboratory and field conditions but none, as yet, has demonstrated suitable efficacy for exploitation.

Pharmaceuticals: There are sprayed **pesticides** for application to the premises (organophosphates and the spinosyn spinosad) and an **orally-applied acaricide**, supplied through the drinking water and licensed as a veterinary medicine (the isoxazoline fluralaner). A number of other treatments and preventative interventions are available including predatory mites; plant-based feed or drink additives; sprayed silica dust; standard hygiene measures; use of detergent and water to clean hen houses and equipment; physical barrier systems; use of heat treatments in empty hen houses etc.

What do we need?

- **Host-pathogen interactions knowledge:** chemical interactions with the host, between mites and with the environment; interactions with natural enemies; parameters of the temporal and spatial dynamics of populations and how these are affected by environmental conditions; zoonotic aspects of infestation and disease transmission; the true vector capacity of the mites for bacterial and viral pathogens; effect of numbers of mites per hen on production and mortality.
- **Vaccine research:** identification of optimum antigen constituents; optimisation of routes of vaccine administration; modelling of different vaccine efficacies/modes of action on population; cost-benefit analysis of vaccines.
- Standardisation of sanitation/treatment methodologies and adoption of **integrated pest management strategies**; knowledge of off-target ecosystem effects; analysis of the potential for resistance against the newer actives; development of new classes of actives.
- Low cost technologies with high sensitivity and specificity for either the parasite or the pathogens that they carry.

Read the full chapter here.

Porcine reproductive and respiratory syndrome (PRRS)

Disease Profile

This disease is the most **important endemic pig disease** having a negative impact on the health and welfare of piglets and sows and is continuously causing production losses. Until 2018 PRRS virus (PRRSV) was divided into two genotypes, PRRSV-1 (former European type) and PRRSV-2 (former American type), sharing only 55-70% of similarity at the genome level. According to the newest classification of International Committee on Taxonomy of Viruses, previous genotypes are now considered to form two distinct species with proposed names Betaarterivirus suid 1 and Betaarterivirus suid 2, classified within two separate subgenuses in the Genus *Betaarterivirus* of the *Arteriviridae* Family. The clinical outcome of PRRS virus infections is very different between strains. In general, strains of PRRSV-1 tend to be less aggressive than the ones of PRRSV-2. A **variety of clinical syndromes** have been described from subclinical to high morbidity/mortality (up to 30-50% for highly virulent strains). Clinical signs may last 3 months or longer, especially when naïve animals are introduced. Once infected, herds tend to remain so.

Risk

The virus is genetically on the move and the **high mutation rate** is problematic for diagnosis and future control of PRRS. There is a major concern over the possibility that **highly virulent strains may emerge** and that these PRRSV mutants may be difficult to control by using the currently registered vaccines, as by now, none of the available vaccines induces universal and total protection. Import restrictions only concern countries free from PRRSV infections (Sweden, Finland, Norway, Switzerland, Brazil, Australia, New Zealand) or countries with implemented eradication program (Chile, Hungary). In most of the other countries, PRRS remains endemic.

What do we have?

Diagnostics: Diagnostic kits (PCRs, ELISAs) are available worldwide and are very effective to determine the presence of the PRRS virus in a population. Nevertheless, it is questionable if they can pick up all circulating isolates.

Vaccines: Both live attenuated and inactivated vaccines are available containing either PRRSV-1 or PRRSV-2. Inactivated vaccines are safe but not efficacious, as it has been demonstrated that they cannot control viremia post-challenge by themselves. They can only boost the existing immune response in sows. Attenuated vaccines are more effective, but they **do not confer complete protection** and some level of shedding as well as horizontal and vertical transmission have been reported. There is no possibility to differentiate vaccinated from infected animals, except sequencing or in some cases differential RT-PCR.

Pharmaceuticals: No antivirals are available against PRRSV, however, coinfections with bacterial diseases are very common and are controlled with antibiotics.

What do we need?

- **Whole genome analysis** to obtain correct genetic trees as a basis for epidemiological studies (evolution) and to identify the parts of the genome that are linked to the ability to spread, pathogenicity, virulence, immune evasion and immunogenicity.
- **Continuous validation of diagnostics** with the appearance of new PRRSV isolates. It is important to monitor the genetic sequences of new viruses to ensure that they are detected in the existing PCR/ELISAs. To achieve this, a pan-European PRRS database should be created that would allow simultaneous comparison of PRRS isolates representing most countries in Europe.
- **New generation vaccines** that provide universal protection and that allow differentiating vaccinated animals from infected ones (DIVA). To achieve this, new approaches to vaccine production should be considered, such as multivalent vaccines or subunit vaccines.

Read the full chapter here.

Actinobacillus pleuropneumoniae (APP)

Disease Profile

APP infects domestic and feral pigs and wild boar and usually causes **respiratory disease.** Clinical signs are most common in the finishing phase after 12 weeks of age. Maternal immunity may protect pigs from disease outbreaks until that age. The disease can be present as hyper-acute infection where pigs are found dead, pigs showing only fever and no further clinical signs, acute outbreaks usually occurring in non-immune animals with a lethality of 15-20%, and sub-acute infection with lesser and variable mortality. Chronic disease in endemically infected herds can result in pigs with reduced growth performance or pigs with chronic lung alterations (lung abscesses or sequesters) found at slaughter. Pigs can carry the pathogen on their tonsils without a serological response. Overall the disease can have a considerable effect on production, especially if there is no adequate herd immunity against the strain causing problem or if stressors or coinfecting agents are present.

Risk

APP is not recorded as causing human disease. Apart from economic losses to farmers, the treatment of APP infection increases the quantitative use of antibiotics and thereby the risk of development of antimicrobial resistance transferrable to humans. There is an economic impact at the abattoir, because pigs affected have to be handled separately as they often require pleural stripping and entry into a separate market. All of this negatively affects packer margins.

What do we have?

Diagnostics: A final diagnosis is based on clinical signs, gross post-mortem examination, histopathology with immunohistochemistry confirmation, culture, and a range of further molecular biological diagnostic tests. The biggest challenge for serological tests is, that nearly all herds are endemically infected, so that most animals are positive for antibodies depending on age. Results of serotype-specfic ELISA are difficult to interpret, because often antibodies against several APP serotypes are detectable. Cross-reactions with antibodies against other bacteria cannot be excluded.

Vaccines: Commercial vaccines are available worldwide. Bacterins are often used in North America, while sub-unit vaccines and combined vaccines, both containing toxins are widely used in Europe.

Pharmaceuticals: Swine pleuropneumonia is traditionally controlled by **antibiotic treatment to prevent death cases.** The carrier status of pigs and the development of lesions cannot be prevented by antibiotic treatment. A wide variety of antibiotics can be used following good practice guidelines which are different in the different countries. In most cases, tetracyclines, ampicillin, penicillins, trimethoprim and sulphonamides, tiamulin, fluorchinolones and others are effective.

What do we need?

- Knowledge about specific factors of the innate **immune defence mechanisms** and their stimulation by specific vaccine components and adjuvants.
- Diagnostic techniques based on serotype or sero-group specific antigens to **avoid cross-reactions** and facilitate the interpretation.
- **Improved PCR diagnostics** for isolates of all serotypes. Easy and poor invasive methods should be established, to collect small amounts of relevant specimen (tonsil-biopsy) for PCR diagnostic. Diagnostic methods should allow to make the distinction between APP as the cause of disease or as a benign coloniser.
- **More efficient commercially available vaccines** that do not only reduce signs of acute disease but also prevent colonisation and transmission of the agent. The use of live attenuated vaccine is an interesting approach; autogenous vaccines are used in practice, but warrant further investigation.
- Investigations towards the mechanisms of antibiotic resistance induction and the extent of antimicrobial resistance in APP should be monitored.
- Feasible and economic eradication strategies.

Read the full chapter here.

Staphylococcus aureus mastitis

Disease Profile

Staphylococcus aureus causes a variety of diseases in man and animals. Mastitis is the main disease caused in ruminants, including cows, sheep, goats, camels and water buffalo. Many other animal species can be affected. In dairy cows, ewes and goats the most economically important condition caused by *S. aureus* is a contagious mastitis. The pathogen is primarily **transmitted during the milking process** as the bacteria are spread to uninfected quarters by teat cup liners, milkers' hands, wash cloths, and flies (fomites). Most infections in dairy cattle are subclinical and chronic, persisting frequently over the ongoing lactation and possibly the following lactations, with more or less clinical flare-up. Severe forms are more frequent in goats and ewes than in cows.

Risk

Direct mortality in bovine dairy herds is low but the indirect loss resulting in **premature culling due to *S. aureus* incurable mastitis** can be high in problem herds. Direct mortality can be high in heifers, ewes and goats.

Human infection caused by bovine-specialized clones is rare. Yet, a few isolates from bovine mastitis are related to methicillin-resistant *S. aureus* (MRSA) human strains, and exchange of genetic mobile elements between human and bovine strains is likely. The fact that coagulase negative staphylococci (the most common bacteria isolated from milk) frequently carry antimicrobial resistance genes, that can potentially transmit to *S. aureus* is also of concern and surveillance of mastitis pathogens for antimicrobial resistance genes seems prudent.

What do we have?

Diagnostics: Etiological diagnosis is currently by bacteriological analysis of aseptically taken milk samples from individual mammary glands. The risk of contamination during sampling, phases of low shedding and time to get result are impediments to bacteriological diagnosis. Specific PCR can be used to identify bacterial DNA in aseptically taken milk samples. Quantitative PCR-based commercial reagent kits for detection of mastitis-causing pathogen are available but a rapid, specific cow-side screening test is not currently available.

Vaccines based on killed bacterins are currently approved in both the EU and US. Their efficacy is either limited or variable **or in need of large scale field evaluation.** Numerous attempts to induce protection with subunit vaccines have been carried out or are on-going, so far without convincing results. Current vaccines primarily stimulate humoral immunity but the level of opsonising antibody in milk is poor.

Pharmaceuticals: Numerous products are marketed and both lactating and dry cow therapies are widely available. **Antibiotic therapy** during lactation may improve the clinical condition but usually does not eliminate infection. Dry-cow therapy is considered the most effective, but may also be unsuccessful, especially for long lasting infections.

What do we need?

- A rapid, cow side or in-line pathogen **specific diagnostic kit** to timely implement pathogen-oriented treatment.
- **A vaccine that prevents intramammary infection** or accelerates cure after infection, or which contributes to increasing treatment efficiency. None of the vaccines studied to date have achieved these goals. Identification of protective immune mechanisms and correlates of protection is necessary. Apart from effective vaccines, we also need a good definition of effectiveness for mastitis vaccines.
- **Improved therapies** that utilize flexible treatments that are pathogen dependent. The use of peptide antimicrobials may offer the option of no withdrawal times, blanket fresh cow therapy and heifer treatments. Novel antimicrobial compounds that act intracellularly are under development. Narrow spectrum antibacterials that are not considered critical for human use are needed.

Read the full chapter here.

Swine Mycoplasmosis

Disease Profile

Mycoplasmosis is a term frequently used to denote **enzootic pneumonia of pigs**, but could in fact refer to disease caused by three species of *Mycoplasma*, i.e. *M. hyopneumoniae*, *M. hyorhinis* and *M. hyosynoviae. M. hyopneumoniae* is the primary causative agent of enzootic pneumonia, which is historically one of the most common chronic respiratory diseases of swine. *M. hyorhinis* can cause polyserositis, arthritis, pneumonia and otitis media in piglets, while *M. hyosynoviae* can cause arthritis in fattening pigs. Among the three species *M. hyopneumoniae* is economically the most important and the most studied. Infections are found primarily in domestic pigs. The mycoplasmas are found worldwide and are endemic with no evidence of epizootic strains. Transmission occurs most commonly via direct contact with carrier animals.

Risk

The majority of antimicrobials are used against respiratory disease, in which *M hyopneumoniae* is often involved. **Antimicrobial medication** could be significantly reduced if *M. hyopneumoniae* infections were eliminated and absent.

What do we have?

Diagnostics: The diagnosis is made from the clinical history, post-mortem appearance, histopathology and confirmatory laboratory tests. These include culture of fresh tissue using immunohistochemistry, immunofluorescence on smears and frozen sections, and conventional and quantitative real-time PCR on nasal and tracheobronchial swabs and bronchoalveolar lavage fluid. Antigen and antibody ELISAs have also been described. Many commercial diagnostic kits are available worldwide but there are no kits for *M. hyorhinis* and *M. hyosynoviae.*

Vaccines: Vaccines are available for *M. hyopneumoniae* and recently also one against *M. hyorhinis.* These include killed organisms or extracts, with adjuvants. In a few countries, attenuated vaccines are available. Vaccination alone is not sufficient to eliminate the organism from a herd. There are no licensed vaccines for *M. hyosynoviae.*

Pharmaceuticals: Many different antimicrobials have shown to be effective including tetracyclines, macrolides, lincosamides, florfenicol, pleuromutilins, fluoroquinolones. Acquired antimicrobial resistance, mainly against fluoroquinolones and macrolides-lincosamides has been described.

M. hyopneumoniae eradication has been achieved by different strategies. There is always a risk for re-infection, especially in pig dense areas, after having obtained *M. hyopneumoniae*-free status. The main obstacle is the failure of farmers to adopt a **strict all in /all out policy by age with proper cleaning and disinfection**, drying and repopulation with disease free stock. Also, more emphasis should be placed on proper housing, management and biosecurity and/or vaccines.

What do we need?

- More knowledge on i) the virulence factors and mechanisms in all three mycoplasmas and ii) the protective immune responses against *M. hyopneumoniae.*
- Further determination of **mycoplasma genome** to understand the way in which the pathogen regulates the immune response.
- Elucidation of the relationships between the bacterial, viral and mycoplasma infections.
- Knowledge on the **economic impact** of *M. hyorhinis* and *M. hyosynoviae* infection.
- Improved vaccines for *M. hyopneumoniae* and **effective vaccines** for *M. hyorhinis* and *M. hyosynoviae.*
- **Improved use of antibiotics and treatment strategies** to minimize potential for the development of resistance and for minimizing clinical disease due to *M. hyorhinis* and *M. hyosynoviae.*

Read the full chapter here.

Tropical theileriosis

Disease Profile

Theileria spp. are obligate intracellular **tick-borne protozoan parasites** infecting mammalian hosts. Several *Theileria* spp. species infect **cattle**; the two most important species are *T. parva* and *T. annulata. Theileria parva* causing **East Coast fever** (ECF) is restricted to sub-Saharan Africa. **Tropical theileriosis**, by *T. annulata* is present from North Africa (from Mauritania to Sudan and in Ethiopia) and Southern Europe through the Middle East and into Southern Asia. Sporadic cases of *T. annulata* are reported in northern Spain (Atlantic climate zone) *Theileria* sporozoites are transmitted to animals through the saliva of the feeding ticks of the genus *Hyalomma*. *T. annulata* occurs in cattle, yaks, water buffalo and camels. Tropical theileriosis is more severe in European breeds, with a mortality rate, in non-treated animals of 40 – 90% while the mortality rate in indigenous cattle breeds from endemic areas can be as low as 3%.

Risk

One of the potential risks is the spread of the disease to other previously uninfected areas due to expansion of tick habitat as a result of **climate change**. Global warming may influence the geographical distribution of the tick, the tick abundance and the vectorial capacity of the tick which in turn will affect the distribution and incidence of the disease. The second important impact relates to the severe **constraint on the ability to develop or increase production capacity of indigenous stock** in the currently affected areas in order to avoid food shortages resulting from human population growth.

What do we have?

Diagnostics: Serological tests as immunofluorescence assay, ELISA, PCR assays and lateral flow devices (LFD), together with identification of schizonts in Giemsa-stained smears from blood or lymph node biopsies are used for diagnosis. There are however **no commercial ELISA kits.** The detection of carrier animals remains a challenge as they harbour low parasitaemias that are difficult to detect using parasitological and even molecular methods.

Vaccines: Live vaccines produced by attenuating parasite-infected leukocytes have been used to immunise cattle against *T. annulata.* They are commercialised in Turkey and India. Live vaccines present **difficulties in storage and delivery** which are the main constraints although quality control and production are also issues.

Pharmaceuticals: Chemotherapeutic compounds such as buparvaquone (and in some countries parvaquone) with theilericidal properties have been used but tend not to completely eradicate the infection thus leading to the development of carrier states persisting during several months and even years.

What do we need?

- Epidemiology research on the effect of **climate change** the current epidemiological situation in Europe and the risk of introduction of the parasite in new European regions (mainly South Europe).
- **Host-pathogen interactions**: the impact of host cell type on disease pathology; host genetic differences in cellular activation and response to infection; immunomodulation
- Validation of the **parasite antigens** that have been identified to confer protective immunity and development of optimal delivery routes.
- The molecular mechanisms that control sporozoite production and parasite stage differentiation and of tick-transmission to identify **methods to block transmission.**
- **New vaccines** with improved storage capacity or based on completely new type such as DNA vaccines (recombinant or sub-unit vaccines).
- Development of **new drugs** to address the observed reducing efficacy of buparvaquone.

Read the full chapter here.

Varroosis

Disease Profile

Varroa destructor is an external **parasitic mite of honeybees** and is found worldwide except Australia and some parts of Oceania and Europe and the centre of Africa. It is now endemic in Europe where it was first reported in the 70s It is an established obligate parasite which cannot survive without its host, the honeybee, for more than 2 weeks. The *Varroa* mite is also a known disease vector and can transmit and activate certain viruses. Clinical signs are detectable in the case of severe infestation with almost 100% mortality if not treated. The symptoms are often due to the associated bee viruses. *Varroa* can be easily transmitted between colonies in the same apiary and transmitted over the bees' flight range (2-3 km) through robbing, swarming or drifting.

Risk

Colony losses are directly related to *Varroa* infestation if the parasite is not properly controlled. This leads to a decrease in the number of honeybee colonies for pollination (pollination ecosystems for both wild flora and crops) and decreasing income for beekeepers.

What do we have?

Diagnostics: No commercial kits are available but qualitative and quantitative standardised methods are available from the OIE (2018). Almost all honeybee colonies in the EU are infested with *Varroa* mites and therefore, quantitative diagnostic tools are required for appropriate control strategies. No serological tests are available for routine laboratory diagnosis.

Vaccines: No vaccines are available.

Pharmaceuticals: Several types of treatments are used. These include i) synthetic pyrethroids (tau-fluvalinate and flumethrin, mostly used as strips), ii) coumaphos (trickling and strip), iii) amitraz which is widely used in the commercial "beekeeping world" (strips and fumigation), iv) organic acids: formic acid (evaporating), oxalic acid (trickling and sublimation), lactic acid (spraying) and v) essential oils: mainly thymol-based products (evaporating), some other substances with potential. The list of regulatory approved products varies from country to country with limited or no availability of veterinary medicines in many countries. However, the cascade system can be used in this case in agreement with the competent national authority.

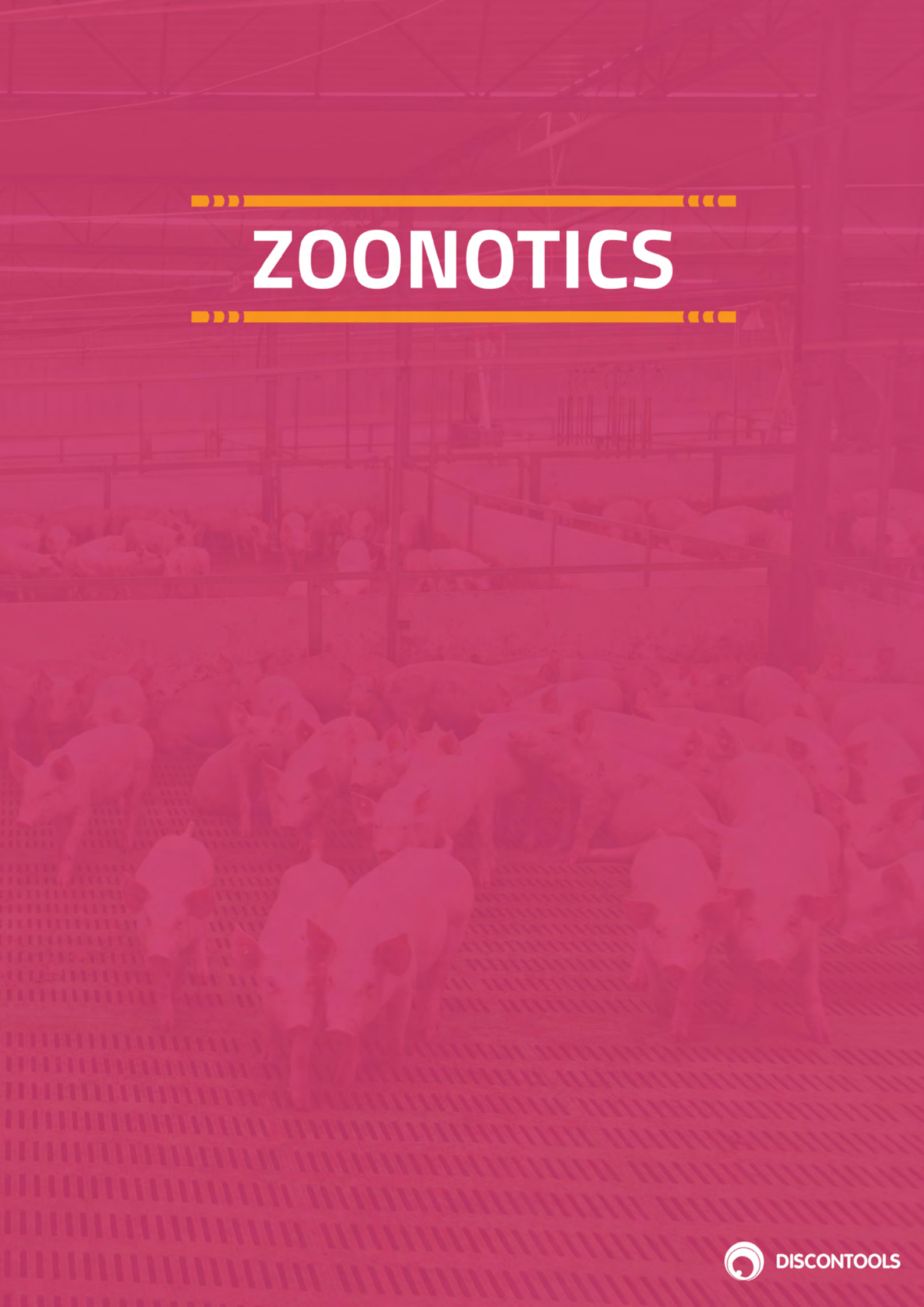
Varroa represents a dangerous pest with **limited availability of effective and easy-to-apply control methods**. The available diagnostic methods are not satisfactory. The active ingredients used for the control of *Varroa* mite infestation have been identified already 25-30 years ago. Despite the increased availability of veterinary medicinal products, treatment strategies overall are poor and need to be integrated with improved beekeeping management strategies. In addition, common recommendations for diagnosis and control by veterinary/extension services is often lacking, are poorly followed by beekeepers or has insufficient coverage of the territory.

What do we need?

- **New veterinary medicinal products** and encouragement of chemical testing for *Varroa* control.
- **Integrated protocols** based on veterinary medicines treatments and beekeeping practices.
- **Diagnostics** for an early and easy detection of the disease along with a tool to assess the colony health in relation to immunity, virus loads and stress status.
- A method to test the efficacy and detect possible resistance to treatments.
- Research on possibilities and feasibility of **biological control.**
- Development of selection criteria for the **breeding** of honeybees naturally tolerant/resistant to *Varroa.*
- Knowledge on **honeybee immunity** and assessment of the possible application of vaccines within the beehive.

Read the full chapter here.

ZOONOTICS



DISCONTOOLS

Anthrax

Disease Profile

Anthrax caused by *Bacillus anthracis*, can be found **worldwide**. Bacilli sporulate when released by the dying or dead animal into the environment. The spores are more resistant than the vegetative form to extremes of heat, cold, pH, desiccation, ultraviolet light, gamma radiation and chemicals and can lie dormant for years in soils. **All mammals, including humans**, appear to be susceptible to anthrax. Wild and domestic herbivores such as cattle, sheep, and goats are the most susceptible. Spores found in the soil are the main reservoir for anthrax. Herbivores are usually infected by exposure to spores from soil-contaminated food or water. Wild carnivores can become infected through the consumption of infected animals. Disease in animals can be per-acute or acute or sub-acute to chronic.

Risk

Risks of infection in humans are mainly associated with the **handling of infected carcasses and contaminated animal products,** including hides and skins from infected animals. There is the potential for anthrax to be used in bioterrorism. Failure to vaccinate in endemic areas, or to follow effective disposal procedures of infected carcasses will lead to continued environmental contamination with spores. Cultural practices could put certain groups at high risk of contracting anthrax. Risks are reduced by improving the effectiveness of veterinary services, diagnostic capabilities and education of the public.

What do we have?

Diagnostics: Commercial diagnostic kits are not available. Methods for the demonstration of encapsulated *B. anthracis* in blood or tissues from fresh anthrax-infected carcasses and growth of the organism on blood agar plates have been described (see OIE Manual for Terrestrial Animals).

Vaccines: The most widely used vaccine for the prevention of anthrax in animals is the Sterne-strain vaccine. This vaccine is a non-encapsulated live variant strain of *B. anthracis* developed by Sterne in 1937.

Pharmaceuticals: Many antibiotics are effective against *B. anthracis.* In animals, treatment is rarely possible though due to the rapid course of the disease.

Anthrax can be controlled if **vaccination programmes** are adhered to and if **effective disposal of carcasses** and contaminated materials is practised. Effective veterinary services and diagnostic capability are necessary to prevent and control anthrax. It is important to have a public communication strategy, which provides accurate and authoritative information.

What do we need?

- More information from areas where the disease is endemic and better reporting systems.
- Better understanding of the **ecology of anthrax** in the environment and the routes of infection; the possible existence of carrier states, potential reservoir animals and sub-clinical infections; sporulation the fate of *B. anthracis* in carcasses.
- Environmentally friendly decontamination products and methods.
- **Specific, rapid and inexpensive diagnostic** tests that can be operated with minimal training in the field. A better understanding is needed of the disease in animals to identify early markers of infection.
- Simple and reproducible methods to isolate spores from environmental samples are required.
- **Vaccines** with longer-lasting immunity, higher stability and decreased cost of production.

Read the full chapter here.

Brucellosis

Disease Profile

The brucellae bacteria comprise **several species and infect a wide range of animals**. Cattle, yaks, water buffaloes, sheep, goats, reindeer, camelids, swine, horses, hares, seals (pinnipeds), dolphins and porpoises (and other toothed whales), and dogs are known to be susceptible. Whereas *B. melitensis*, *B. abortus*, *B. canis* and *B. ovis* have well defined characteristics, *B. suis* shows a great internal diversity in terms of both taxonomy and pathogenicity. In animals, abortion, birth of weak offspring, infertility and genital lesions in males are the most common manifestations of brucellosis. The rate of abortions varies between 0 to 40% in cattle, sheep, goats and swine.

Risk

Human infection comes from direct or indirect contact with animals and animal products. A figure of 500,000 new human cases/year worldwide is often quoted but there is no reliable data for most countries. The human populations at greatest risk are those that regularly come into contact with infected animals and those that consume unpasteurised dairy products.

Less than 20 countries are free of brucellosis in livestock. The **movement of infected animals** is the main mechanism for the spread of disease between herds. The lack of outward clinical signs of disease in animals other than abortion and fertility reduction means that detection is difficult without a sustained and expensive surveillance programme.

What do we have?

Diagnostics: Many commercial diagnostic kits are available worldwide but, although costs of tests are generally competitive, they are out of reach for many areas in Africa or Asia. Almost all kits **require cold storage** and this may be a problem in some resource poorer regions.

Several methods such as the CFT, iELISA, cELISA, a fluorescence polarisation assay, Rose Bengal test and brucellin skin tests are available for the detection of *B. abortus*, *B. melitensis* or *B. suis*. Penside serological assays, such as lateral flow assays, are in development but are not yet in validation trials. There are no commercially available PCR kits that claim to detect *Brucella* DNA.

Vaccines: Vaccines are **only available against *B. abortus* (cattle) and *B. melitensis* or *B. ovis* (small ruminants)** infections. The effective vaccines are currently live attenuated strains.

Pharmaceuticals: Therapy is seldom used in animals.

Although some argue that the tools required to control the disease are available and are effective if properly applied, **improved and cheaper tools are needed** as current costs of control are unsustainable for most economies where brucellosis is prevalent.

What do we need?

- A better understanding of the epidemiology, diagnosis and immunoprophylaxis of brucellosis in less common livestock species (camelids, yaks, water buffaloes, ...).
- **Improved vaccines** (more protective, stable and affordable and less pathogenic), including immunologically tagged vaccines and complementary DIVA tests.
- A better understanding of latent infection in animals.
- **Socio-economic studies** under different situations to prioritize interventions in developing countries.
- **Molecular methods for typing** of Brucella strains.

Read the full chapter here.

Bovine Spongiform Encephalopathy (BSE)

Disease Profile

BSE is a **degenerative disease of the central nervous system.** Cattle are the main species affected, although people have been infected as have captive wild ungulates, goats and felids. The BSE agent is a **prion**, which is comprised largely of a self-replicating, protease-resistant protein known as PrPSc, a misfolded conformer of a normal host-encoded protein (PrPC). In addition to 'classical BSE' (C-BSE), unusual or atypical forms of BSE have been identified in a number of countries. Two different molecular PrPSc patterns have been described, the L-type with a lower molecular mass than C-BSE, and the H-type with a higher molecular mass of the protease-resistant prion protein. These two atypical forms of disease do not have the same pathology, i.e. the pattern of lesion distribution and PrPSc accumulation in the brain. In addition, animals do not display the same clinical signs as C-BSE.

Risk

Variant Creutzfeldt-Jakob disease (vCJD), first reported in March 1996, affects younger human patients and is linked to exposure to BSE. C-BSE, as well as L-type BSE, are experimentally transmissible to a range of species, including humanised transgenic mice and non-human primates. Most cases of vCJD are believed to be of dietary origin, following ingestion of food containing the infective agent, particularly before the statutory removal of specified bovine risk materials from food- and feed chains.

The case numbers of C-BSE **have declined rapidly**, which is undoubtedly related to the strict controls on ruminant protein and its use in animal feed. Occasional cases still occur, including cases in younger animals, 5-8 year old (both in the EU and North America), that were born many years after the feed bans were put in place. It is unclear whether these can be attributed to poor implementation of the feed bans, or whether they support the hypothesis that, in line with the hypotheses about the atypical types of disease, C-BSE was originally a rare, potentially spontaneous disease of cattle, in which case occasional cases will continue to occur.

What do we have?

Diagnostics: Commercial kits are available to confirm disease on examination of the brain material removed from an animal. These include high-throughput Western blot, lateral flow immunoassays and ELISA tests to screen large numbers of samples.

Vaccines: The development of vaccines so far seems an insurmountable challenge.

Pharmaceuticals: None available, nor required for animal health applications.

What do we need?

- A diagnostic test to identify BSE **in live animals.**
- A test for the detection of **environmental and/or feed contamination** with the BSE agent.
- Research towards the **early pathogenesis** at both the animal and cellular level.
- A good experimental model to study pathogenesis.
- More information on the **zoonotic potential of atypical forms** of BSE and more epidemiological data with which to undertake effective risk assessments.

Read the full chapter here.

Bovine Tuberculosis (BTB)

Disease Profile

BTB caused by mainly by *Mycobacterium bovis* but also increasingly by *M. tuberculosis*, affects cattle, other domesticated animals and certain wildlife species. Other species of the *M. tuberculosis* complex previously considered to be *M. bovis* include *Mycobacterium caprae* and *Mycobacterium pinnipedii.* These species are also known to be zoonotic. While *M. bovis* causes zoonotic TB in humans, the majority of TB cases in **humans** are caused by *M. tuberculosis*. **Cattle** are considered the primary target for BTB, species such as goats are also highly susceptible and can maintain infection in the absence of cattle. **Wildlife** can act as maintenance hosts or reservoirs and represent a serious problem in several countries. In cattle, BTB is usually a **slowly progressive condition** with no obvious signs of disease in the early stages. In the later stages, symptoms include emaciation, fever, weakness, lack of appetite and respiratory distress. Infections can remain persistent for years.

Risk

Human disease caused by *M. bovis* is rare in countries with successful BTB control and eradication programmes, established meat inspection procedures and milk pasteurisation. Where BTB is poorly controlled in livestock and consumption of raw milk or unpasteurised dairy products is frequent, BTB may represent a human health risk. In countries without disease control, cattle-to-cattle transmission rate can be high, particularly when animals are kept intensively. There is a high risk of farm to farm and transboundary spread of infection through the movement of infected cattle. Pre-movement testing reduces this risk but testing may not detect all infected animals.

What do we have?

Diagnostics: The predominant method for diagnosis of BTB in live cattle is the **tuberculin skin test. IFN-γ release assays** (IGRAs) have also been developed and are being increasingly applied. When used in combination with skin tests, overall sensitivity is increased.

Vaccines: At present the only potentially available vaccine is BCG, which is a live attenuated strain of *M. bovis* used for humans since the 1920s. The use of BCG will however compromise specificities of tuberculin-based tests and the development of DIVA tests for cattle is essential. **Improved vaccines** for cattle are under active development based on genetically modified BCG or *M. bovis*, DNA, protein or virally vectored subunits, used stand-alone or in conjunction with BCG. BCG vaccines may reduce *M. bovis* in wildlife reservoirs and an injectable vaccine has been licensed for use in badgers in UK.

Pharmaceuticals: Antimicrobial treatment is not applicable for BTB control in livestock.

What do we need?

- The development of defined **skin test reagents** based on specific *M. bovis* antigens to overcome the limitations of largely undefined and difficult to produce and standardize tuberculins.
- Rapid, specific and simple **diagnostic tests for live animals**, particularly for cattle in developing countries, and for wildlife species.
- Improved delivery systems for the application of **vaccines in wildlife.**
- Further investigations into the **host pathogen interactions** and the immune response to support the development of new vaccines and better diagnostic tools.
- A better understanding of the **epidemiology of *M. bovis*** infections in cattle and cattle herds to enable strategies for the use of new vaccines when available.
- Information on infection by and pathogenesis of *M. bovis*, *M. caprae*, *M. pinnipedii* and even *M. tuberculosis* in other animal species.

Read the full chapter here.

Campylobacteriosis

Disease Profile

Campylobacteriosis represents an important and worldwide public health problem and is considered to be the **most important infectious food-borne disease.** *Campylobacter* organisms are ubiquitous in animals and the environment worldwide. *C. jejuni* and *C. coli* can colonise the intestinal tract of most, if not all, mammals and birds, where they rarely cause disease. In humans, infections with *C. jejuni* and *C. coli* cause diarrhoea, abdominal pain, fever, headache, nausea and vomiting. Most cases of campylobacteriosis are self-limiting within a week, but some cases may require medical treatment including hospitalization. The vast majority of human cases (about 99%) are sporadic rather than outbreaks.

Risk

Campylobacter remains the main food poisoning agent in high income countries and has a major impact in low income countries. There is a significant underreporting of cases, hampering the possibility to calculate the total burden of the disease. The WHO estimates that **1% of the population contract campylobacteriosis each year.** Reports on risk factors for human infection indicate that the consumption of food (poultry meat, cross contaminated food products, raw milk and contaminated water) is the main source of infection, followed by direct contact with colonized animals. Fifty to eighty % of campylobacteriosis cases may be attributable to campylobacters from the poultry reservoir.

What do we have?

Diagnostics: There are diagnostic methods described by International, European or National standards. There are no serological assays in routine use for the detection of colonisation of *C. jejuni* and *C. coli* in livestock although ELISAs have been described in the literature for all host species. A range of tests are available for testing food samples. Real time PCRs are available as kits but need to be used within an equipped laboratory.

Vaccines: AThere are **no effective vaccines** available for the prevention of enteric *Campylobacter* colonization in birds or mammals.

Pharmaceuticals: The main control of *Campylobacter* in livestock is based on **biosecurity measures.**

What do we need?

- **Effective vaccines** to prevent or control infection in poultry and other animals.
- **Rapid tests** for the detection of live *Campylobacter* including on-farm kits which could detect high levels of colonization in poultry flocks.
- A better understanding of pathogenicity in humans through the development of a suitable animal model that mimics human disease.
- Information on the effect of **biosecurity measures** under different conditions.
- More research on **sources of infection and routes of transmission** particularly in livestock other than poultry.
- More information and monitoring on the development of antimicrobial resistance in *Campylobacter.*

Read the full chapter here.

Crimean Congo Haemorrhagic Fever (CCHF)

Disease Profile

The virus which causes CCHF is a zoonotic arbovirus which is a member of the *Nairovirus* genus. It is transmitted by **ticks**. Ticks of the genus *Hyalomma* are particularly important to the ecology as they appear to be the most competent vector for the virus. CCHF virus (CCHFV) has been isolated from a number of animal species including cattle, sheep, goats, hares, hedgehogs, dogs and mice. The virus infection has been commonly demonstrated among smaller vertebrate wildlife, such as hares and hedgehogs. They are believed to act as amplifying hosts and maintain the virus in nature and act as a source of the virus for the immature *Hyalomma* ticks which feed on them. Although CCHFV may infect a wide range of domestic and wild animals there is no evidence that the virus causes disease in animals. The viremia in animals lasts about 2 weeks.

Risk

CCHF poses a serious threat to **public health** due to its high mortality rate, its modes of transmission, and its extensive geographical distribution. Ticks are a major route for the transmission of the virus to humans. Secondary cases are frequently seen due to **human to human** transmission via percutaneous or per mucosal exposure to blood and body fluids containing the virus. Others may acquire the virus from direct contact with blood or other infected tissues from viraemic livestock. Over the last years, **CCHF outbreaks have become more frequent in several European countries and neighbouring areas**, and an increase in the number of large outbreaks caused by CCHFV has been observed. Climate changes and the recent emergence of CCHF in Spain (the first human cases in Western Europe) are a cause for concern in Europe. At present, there are very limited measures available to break the cycle.

What do we have?

Diagnostics: CCHF can be diagnosed by isolating the virus from blood, plasma or tissues. CCHFV is identified by indirect immunofluorescence or reverse transcription-polymerase chain reaction (RT-PCR) assays. Serology can identify animals that have been infected or exposed to CCHFV. An IgG ELISA can detect antibodies for the remainder of the animal's life. A commercial diagnostic kit is available for detecting CCHF in animals.

Vaccines: There are no CCHFV vaccines for animals. An animal vaccine would help to interrupt the CCHFV cycle, thus helping to reduce disease prevalence.

Pharmaceuticals: None in animals as there is no evidence of clinical disease.

CCHF is a human disease. Animals and ticks are involved in the virus cycle in nature. The control of ticks and biosecurity to prevent contact between humans and potential sources of infection are the main ways of disease control at present.

What do we need?

- Sensitive and bio-safe **diagnostic tools** for CCHFV.
- Better collection of specimens and serum panels from patients, animals and ticks.
- **Animal vaccines** that could help to prevent the establishment of the enzootic cycle.
- More information on the pathogenesis and immune response, especially in humans
- Effective methods of **vector control.**
- Evaluation studies on intervention and control strategies.
- Tools to monitor and **predict virus migration** caused by altered tick distribution as a result of climate change or animal movements.
- Knowledge about potential re-assortment and recombination events between virus genomes and on the phylogeny and evolution of the virus.

Read the full chapter here.

Chlamydiosis *(C. abortus)*

Disease Profile

Chlamydia abortus (C. abortus; formerly Chlamydophila abortus) is a major cause of **abortion and foetal loss in sheep, goats, cattle and pigs.** *C. abortus* occurs worldwide and is endemic in many countries. Infection poses problems worldwide in the main sheep rearing areas and can also impact on goats, cattle and pigs. Asymptomatic carrier animals infected with *C. abortus* are the main reservoir. Ewes can remain persistently infected after the initial abortion and can excrete the organism. Abortion storms can occur in sheep flocks following the introduction of infected ewes and abortion may occur in up to 30% of the ewes and as many as 60-90% of pregnant goats. *C. abortus* is mainly excreted on dead lambs, placentas and uterine discharges.

Risk

C. abortus is a **zoonosis** but reports of human cases are rare. Abortion and severe illness can occur in pregnant women. The risk to humans is mainly limited to pregnant women who have contact with the organism through pregnant sheep or goats, especially during the lambing or kidding season.

What do we have?

Diagnostics: There are a number of tests for the detection of antibodies, including the complement fixation test and ELISAs. Tests are also available for the detection of antigen, including ELISA and fluorescent antibody tests. PCR and microarray assays have been developed more recently. Identification of the agent can be made by examination of smears from placental cotyledons or foetal stomach contents. Detecting the presence of subclinical *C. abortus* infection in non-pregnant sheep is difficult, as current serological tests **do not detect latent carriers.** PCR-RFLP tests exist for DIVA analysis.

Vaccines: Inactivated and attenuated live vaccines are available for use in sheep but not cattle. The incidence and severity of abortions in ruminants can be reduced by the use of vaccines but at present these **do not confer complete protective immunity** and do not prevent shedding at parturition. Vaccination will not eradicate infection from a flock. The live vaccines have been shown to cause disease in some animals.

Pharmaceuticals: Long acting tetracyclines given at the correct period will reduce the severity of infections and abortions, although abortions may still occur depending on the extent of pathological damage to the placenta and infectious organisms may still be shed at birth. **Antibiotic treatment** has been considered as the most practical measure for control of disease in cattle where the abortions are more sporadic.

What do we need?

- **Vaccines** which are cheaper to produce, prevent shedding, give 100% immunity and do not cause disease. This will likely be based on recombinant protein technology, as multi-component vaccines.
- **Diagnostic tools** to identify the latent carrier and serological tests to differentiate naturally infected from vaccinated animals.
- More knowledge concerning the **transmission of infection**: the role of wild-life species in the spread of infection, the infective dose and how long the organisms are viable in fluids and placenta, the stability of the organism in the environment and the effect of weather and temperature.
- A greater knowledge of the **pathogenesis** in goats, cattle and pigs is required.
- A better understanding of the **immune response** of sheep and other ruminant species and pigs to infection and to vaccines.

Read the full chapter here.

Cryptosporidiosis

Disease Profile

Cryptosporidiosis is caused by **protozoan parasites** belonging to the genus *Cryptosporidium*. The most common species causing disease in mammalian livestock animals is *C. parvum* whereas both *C. parvum* and *C. hominis* are important human pathogens. *C. parvum* has a wide host range, is predominantly a parasite of young hosts, and is responsible for a substantial proportion of both sporadic and outbreak-related cases of **human** cryptosporidiosis, particularly in high-income countries. The oocysts are protected by an outer shell which allows them to survive outside the host for long periods (>6 months) in a moist, cool environment. The oocysts are also very resistant to chlorine-based disinfectants, and there are limited options for effective chemical disinfestation.

Risk

Cryptosporidiosis remains a significant public health threat. In immunocompetent hosts, it usually causes self-limiting **diarrhoea, affecting any age group**. However, cryptosporidiosis is the second cause of diarrhoea-associated mortality among young children living in low-income countries, and ranked as the fourth most commonly reported cause of infectious gastrointestinal disease. Infection is initiated through ingestion of infective oocysts by direct contact with infected hosts or indirectly by consumption of contaminated food or water. **Animal husbandry practices** in relation to housing, feeding, cleaning and disinfection, and birthing patterns and facilities can all have an impact on the spread of disease.

What do we have?

Diagnostics: A variety of **antibody-based commercial detection kits** are available, all of which rely on the capture of oocyst wall antigens from concentrated or un-concentrated faecal samples. These include immunofluorescent microscopy tests, ELISA and immunochromatography based kits. **Quantitative real time PCR kits** are also available. Acid-fast or fluorescent (such as auramine phenol) staining methods, with or without faecal concentration, are most frequently used in clinical laboratories. The Heine "negative stain" method on concentrated stool is cheap and reliable but requires phase contrast microscopy.

Vaccines: No vaccines are currently available.

Pharmaceuticals: **Halofuginone lactate** is approved for use in new-born calves in Europe, and prevents or reduces diarrhoea caused by *Cryptosporidium parvum*. Paromomycin is known to be effective in high doses for the treatment of cryptosporidiosis in animal models. This drug is normally indicated for the treatment of intestinal amoebiasis, and is approved at lower doses than required for the treatment of cryptosporidiosis.

Cryptosporidiosis is a widespread zoonosis of **major clinical importance in the developing world**, and is of concern in the developed world. The parasite has a ubiquitous distribution and it is almost impossible to eliminate. Future control strategies could result from passive immunity derived from vaccinated dams and strategic application of therapeutic compounds.

What do we need?

- The discovery of genes, biochemical pathways and protective antigens through mining of the ***Cryptosporidium*** **genomes** to develop novel therapies and/or vaccines
- A **vaccine** to provide passive immunity to neonatal livestock.
- Effective **biocides** to reduce environmental contamination with oocysts.
- Cheap, reliable, on-site **diagnostic tools** and a high throughput PCR assay able to differentiate species or genotypes of interest.
- Sensitive, standardized assays for the early detection of infection, and of asymptomatic carriers, and the development of ISO standards.

Read the full chapter here.

Porcine Cysticercosis

Disease Profile

Porcine cysticercosis is an infection of pigs with the larval stages of the parasitic **tapeworm *Taenia solium.*** Humans are the definitive host of the adult tapeworm. Segments containing eggs are shed in the faeces. If eggs from infected humans are ingested by pigs, oncospheres are released that penetrate the intestine and migrate to muscle tissue and develop into cysticerci. The parasite life cycle is completed when humans ingest undercooked pork containing cysticerci. **Humans** can also acquire cysticercosis upon accidental ingestion of tapeworm eggs. The most serious form is neurocysticercosis (NCC) when cysticerci establish in the central nervous system (CNS). Epileptic seizures and headaches are the most common symptoms of NCC. Death can occur suddenly with heavy infections or, in low infections, when hydrocephalus is created.

Cysticercosis in pigs causes economic loss through condemnation of infected meat and offal.

Risk

Cysticercosis is classified as a **neglected zoonosis.** *T. solium* is found principally in Mexico, Central and South America, sub-Saharan Africa, non-Islamic countries of Asia, including India and China where there are free-ranging, scavenging pigs and where sanitation is lacking. Taeniasis and cysticercosis are rare in the US and most parts of Europe, but cysticercosis is increasing in non-endemic regions as a result of international travel and migration. NCC requires imaging for diagnosis which leads to an underestimation of incidence in areas where such facilities are lacking. *T. solium* eggs can spread from human to human through contaminated food and drinking water or by direct contact.

What do we have?

Diagnostics: Diagnosis in animals is usually based on the detection of the cysticerci at **meat inspection** or necropsy. Tests for antibodies or antigens in serum are not used currently for the diagnosis of cysticercosis in animals except for epidemiological purposes.

Vaccines: The first commercial vaccine for porcine cysticercosis has been launched in 2016 in India.

Pharmaceuticals: Human cysticercosis is currently treated using albendazole, praziquantel or a combination of drugs. Human taeniasis is treated by praziquantel or niclosamide. In pigs, oxfendazole kills muscle cysts but dead cysts leave lesions that potentially make the carcase inedible for as long as 6 months.

The most sustainable and cost-effective method may be good sanitation and preventing contact between pigs and tapeworm eggs excreted by people. Strategies including mass drug administration (MDA) in humans and MDA and vaccination in pigs may accelerate control/elimination.

What do we need?

- Better knowledge of the **distribution of infection and delineation** of areas of high prevalence, particularly of neurocysticercosis.
- Further information on the effectiveness and **cost-benefit** of (alternative) control/elimination strategies of the infection in humans and pigs in different epidemiological settings.
- Studies on *T. solium* **egg survival.**
- Availability of **simple tests** to detect *T. solium* infections in humans, of pen-side diagnostic tests for individual pigs and for detection of infected carcasses in the abattoir.
- A serological test which is able to **detect living cysts** in the brain.
- A **serum bank** with well documented serum and cerebrospinal fluid samples to study sensitivity, specificity, reproducibility of serological tests.

Read the full chapter here.

Echinococcosis

Disease Profile

Cystic echinococcosis (CE), also known as hydatidosis or **hydatid disease**, is caused by the larval stages of various species of the *Echinococcus granulosus (sensu lato)* complex. *E. granulosus s.l.* occurs worldwide and affects mostly the liver and the lungs forming expansive growing cysts in a variety of intermediate hosts, mainly ungulates, and in humans. Domestic dogs and wild canids are the definitive hosts, harbouring the worm in the intestine.

Alveolar echinococcosis (AE) is caused by *Echinococcus multilocularis* occurring across the northern hemisphere. AE predominantly affects the liver as a slow growing, invasive and **destructive tumour-like lesion.** The adult tapeworm resides in the small intestine of the definitive hosts (dogs and wild canids). In the intermediate rodent host (mainly voles) the larval alveolar form occurs in the liver.

Risk

Definitive hosts of *Echinococcus spp.* pass worms, segments and eggs in the faeces and contaminate the environment. Humans acquire the infection via ingestion of *Echinococcus* eggs by direct contact with the **egg-contaminated environment** (hand mouth contact) or by consumption of contaminated water or food (vegetables, fruits). The latest estimate of the global public health impact of CE is 188,079 new cases per year, with a disease burden of 183,573 DALYs. For AE, it was estimated that 18,451 true AE cases occurred in 2010 worldwide, resulting in a global disease burden of 687,823 DALYs. Both, CE and AE in humans may remain silent for years before the enlarging metacestodes in the affected organs cause symptoms. CE is a major neglected zoonosis in southern Europe.

What do we have?

Diagnostics: Highly sensitive and specific molecular tests are available for the detection and genotyping of *Echinococcus spp.* in clinical material. Molecular tools applying commercial DNA-isolation kits are state of the art for the specific diagnosis in definitive host faeces.

Vaccines: An **effective recombinant vaccine** "EG95" for livestock animals has been developed and is available as a commercial product in China and in South America. It is effective against *E. granulosus* sensu stricto in sheep, goats and cattle. It is not known if it is effective against other species in the *E. granulosus s.l.* group.

Pharmaceuticals: Intestinal infection in dogs can be treated with high efficacy with **praziquantel**. *E. granulosus s.l.* control programmes including several praziquantel treatments a year have been implemented in the past in several European programs without convincing success. In the case of *E. multilocularis*, reduction in transmission has been achieved by use of praziquantel baits for foxes in rural and urban environments.

What do we need?

- Harmonized **reporting systems** for AE and CE in humans and animals.
- Standardization of validated **molecular tools** for the detection of *Echinococcus spp.* eggs for assessing the degree of contamination of matrices, water and food
- Well-designed, integrated, long lasting **CE control programmes** based on deworming of dogs, vaccination of lambs and culling of old intermediate hosts
- Improved specific and sensitive **fast tests** for the diagnosis and monitoring of control programmes of CE in livestock and intestinal infections in dogs
- European manufacture and registration of the **EG95 vaccine** for livestock and political will and funding to undertake control programmes.

Read the full chapter here.

Hepatitis E Virus (HEV)

Disease Profile

HEV is the only member of the *Hepeviridae* family in the Orthohepevirus genus. It is a highly variable virus and there are at least 4 known major mammalian genotypes.

Primary transmission of the virus is through water and food particularly when faecally contaminated. In animals, infection is asymptomatic. Infection in humans can vary from asymptomatic or mild disease with fever and nausea to acute hepatitis with symptoms indistinguishable from other types of acute viral hepatitis. It is mostly a self-limiting disease with mortality rates of 0.5% - 4% in infected individuals and (in the case of genotype 1) up to 20% in pregnant women;

Risk

HEV is a very stable virus. There are an increasing number of notified cases in humans. HEV is the most important cause of clinical hepatitis in adults throughout Asia and in some European countries. The number of symptomatic infections is estimated to be 1 per 300,000 per year in developed countries. **An increase of HEV prevalence in domestic pigs in developed countries is reported, resulting in an increasing public health threat.**

High risk populations include veterinarians, slaughterhouse personnel, travellers to hyperendemic area and people who consume raw and undercooked meats. People with underlying liver disease, immunosuppression and pregnant women are at risk of severe disease.

There is a **high potential for transboundary spread** of the disease through the transport of pigs and pig products and byproducts.

What do we have?

Diagnostics: Commercial kits (EIA, ELISA or rapid tests) are available for use in humans. However, there is no HEV kit approved by the US FDA yet for distribution in the United States. Several real-time RT-PCR kits are available but there is a need for validation of commercially licensed kits. Commercial diagnostic kits for use in pigs are available but may be needed in other animal species also.

Vaccines: At least two good vaccine candidates have been developed for humans. No vaccine is available for use in animals but a vaccine for pigs could reduce concerns over food safety and zoonotic infection.

Pharmaceuticals: Antiviral therapy is cost-prohibitive for use in animals.

What do we need?

- Improved, harmonized and standardized HEV **diagnostics.**
- An efficient ***in vitro*** **cell culture** system for HEV to study infectivity, viability, survival and immunity and for development of vaccines and antivirals.
- Commercially available **HEV vaccines** in all HEV endemic regions for the control of infection in human or animal populations.
- Until now a licensed vaccine is available in China only.
- Further development of HEV vaccines and vaccine efficacy studies are required.
- Improved **surveillance** for HEV in humans, animals and animal produce.
- **Knowledge about transmission** in humans and animals and about spread from pigs to humans.
- Knowledge on the role of animals other than pigs in zoonotic transmission to humans and the extent of foodborne transmission.
- Knowledge whether HEV infection in swine populations causes **economic losses** especially during co-infections with other swine agents (PCV-2, PRRSV) and whether there would be other benefits (beside reducing the risk of pork safety) in vaccinating commercially reared pigs.

Read the full chapter here.

Leishmaniasis

Disease Profile

Leishmaniasis represents a complex spectrum of diseases caused by intracellular protozoan parasites and transmitted by blood-sucking female phlebotomine sand flies. The leishmaniases are usually grouped into 2 main entities: zoonotic leishmaniases, where domestic or wild animal reservoirs are involved in the transmission cycle and humans play a role of an accidental host, and anthroponotic leishmaniases, where man is the sole reservoir and source of vector infection. Most of leishmaniasis entities are zoonotic by nature and reservoir hosts are usually wild mammals. Clinically, leishmaniases are broadly divided into **visceral leishmaniasis (VL)** and the **cutaneous/mucocutaneous forms (CL)**. VL in humans is usually lethal in the absence of therapy. CL is a chronic skin disease in humans and non-human hosts which tends to resolve spontaneously over time. Humans are also susceptible to several other *Leishmania* species leading to a **spectrum of clinical diseases.**

Risk

About **2 million new cases of human VL occur every year** in the endemic zones of Latin America, Africa, the Indian subcontinent, the Middle East, Central Asia, China and the Mediterranean region.

In humans, risk factors include famine, malnutrition, mass migration, civil disturbance, poor economic conditions and crowding. Proximity to infected dogs is a risk factor for both human and canine zoonotic VL infection. Cooler temperatures and a reduced vector activity season have limited the spread of infection northwards in Europe, but global warming is likely to affect the distribution of zoonotic VL.

What do we have?

Diagnostics: Demonstration of parasites in smears, imprints or culture of infected tissues still represents the golden standard for leishmaniasis diagnosis worldwide, but is of low sensitivity. Commercial diagnostic kits are available for serological diagnosis with good performance to assess clinical disease.

Vaccines: Currently, **no vaccine** for human leishmaniasis is available anywhere in the world. Two canine vaccines are available in EU based on either purified excreted-secreted proteins of *L. infantum* or recombinant Protein Q from *L. infantum.*

Pharmaceuticals: **Several therapeutic agents** exist for both humans and dogs including pentavalent antimonials, liposomal amphotericin B deoxycholate and paromomycin. Miltefosine is available for human and dog treatment too. In general, human cases of VL or CL are successfully treated with cure rates exceeding 95%. None of the currently available drugs leads to a definitive cure in dogs and relapses can occur after treatment.

What do we need?

- An effective, safe and affordable **vaccine** for controlling the disease in dogs and in humans.
- Further research towards the **pathogenesis** of the various *Leishmania* and vector species.
- Research towards the environmental and climatic features that affect the **geographical spread** of sand flies and canine transmission.
- Elucidation of the **role of dogs** in *Leishmania* parasite cycles other than those of *L. infantum* as well as the **role of cats** in the epidemiology of zoonotic VL needs to be elucidated.
- Better, easy to use, **diagnostic tools** that are sensitive and specific.
- New canine and human **pharmaceutical options**, and clinical trials of combined therapies.

Read the full chapter here.

Leptospirosis

Disease Profile

Leptospirosis is a common **disease of livestock, pet animals and wildlife.** Animals can become chronically infected and remain carriers for life and reservoirs of infection for animals and humans. Animals can be divided into maintenance hosts and incidental hosts. The disease is maintained in nature by chronic infection of maintenance hosts.

In **humans**, the most common clinical presentation is acute **undifferentiated fever**. Further symptoms include headache, chills, muscle aches, vomiting, jaundice and anaemia. If not treated, kidney damage, meningitis, liver failure, and respiratory distress can develop. In animals, presenting signs for acute leptospirosis can include agalactia, jaundice, haemoglobinuria, meningitis and acute renal failure. Stillbirth, birth of weak offspring and infertility can all be associated with chronic leptospirosis. Leptospires can survive in moist conditions outside the host for many days or even weeks especially in fresh water, soil, and mud. Disease is often seasonal, being most common during the rainy season in the tropics and in the summer and autumn in temperate regions.

Risk

Leptospirosis in humans occurs worldwide with the **total number of cases estimated to exceed one million each year** but it is a neglected zoonosis that is poorly diagnosed in many parts of the world. The incidence probably ranges from 0.1 to 1 per 100,000 per year in temperate climates to 10 or more per 100,000 per year in the humid tropics. Infection in man is mainly from direct contact with the urine of infected animals or indirectly from ingesting contaminated food or water. Rodents are implicated frequently in human cases. People who work outdoors or with animals, such as farmers, sewer workers, veterinarians and dairy workers face leptospirosis as an occupational hazard.

What do we have?

Diagnostics: Commercial kits, comprising lateral flow and latex agglutination methodologies, are available for diagnosis of human disease. There are species and serovar specific commercial ELISA kits for serovar Hardjo infection in cattle and serovar Bratislava infection in pigs. Commercial ELISA kits and Rapid Diagnostic Tests (RDTs) are available for dogs. A milk ELISA can detect antibodies in samples from individual cows or in bulk milk.

Vaccines: The majority of commercial vaccines used in animals are inactivated whole cell cultures of one or more serovars of *Leptospira spp.* Live attenuated vaccines have been developed. Effective Leptospirosis vaccines are available for use in pigs, cattle and dogs. Vaccines are serovar-specific and may not provide coverage against other serovars.

Pharmaceuticals: Antibiotics may be used in beef herds if there is an abortion storm but in dairy herds antibiotics may be restricted to non-milking animals due to withdrawal periods for milk. Antibiotics are also used as feed additives for the control of leptospirosis in pigs. Antibiotics used to treat leptospirosis include the tetracyclines, penicillin/ampicillin, dihydrostreptomycin, streptomycin and the fluoroquinolones.

What do we need?

- **Improved vaccines and tests** which discriminate between vaccinates and natural infection. There is a requirement for *Leptospira* serovar *hardjo* vaccine for sheep.
- **Identification of all animal reservoirs** responsible for the maintenance of the many different *Leptospira* strains and serovars. Improved understanding **of risk factors for transmission.**
- **Assessment of the true disease burden**, including the productivity losses and socio-economic impact of disease and the costs and benefits of prevention and control measures.

Read the full chapter here.

Nipah Virus

Disease Profile

Two members of the genus *Henipavirus* in the family Paramyxoviridae, Nipah virus (NiV) and Hendra virus (HeV) can infect and cause disease in number of mammalian species including humans, monkeys, pigs, horses, cats, dogs, ferrets, hamsters and guinea pigs. NiV infections of human and domestic animals have now been documented in Malaysia, Bangladesh and northern India with case fatality rates reaching almost 90% in some outbreaks. To date (2017) close to 600 human cases of NiV disease in humans have been reported. **Person-to-person** transmission has been documented. **Fruit bats** (flying foxes) in the genus Pteropus are the natural hosts for NiV and HeV. NiV infection of pigs is characterised by fever with respiratory involvement and nervous signs have been frequently reported. Low mortality rates are generally reported and asymptomatic infections appear to be common. **Pigs** are known to shed virus in respiratory secretions and saliva. Natural infection of dogs with NiV causes a distemper-like syndrome with high mortality rates. Field infections have also been reported in cats and horses, with fatalities observed in both species.

Risk

This is a **re-emerging zoonosis with a high case fatality rate in humans.** The zoonosis appears to be limited to certain countries in Asia with fruit bat populations. The direct impact on farms and the pig industry may be significant as the first intervention will very likely be culling. In Malaysia, over one million pigs were culled to stop spread of the disease in the original outbreak. Mass culling and carcass disposal can represent a major logistical problem due to the dangerous zoonotic nature of the agent. There is a high disruption to pig meat production and trade in affected areas. The ease with which NiV can be grown, its highly pathogenic nature and its broad host range making it a potential agent for bioterrorism.

What do we have?

Diagnostics: Diagnosis of NiV infection is by virus isolation, detection of viral RNA or demonstration of viral antigen in tissue collected at necropsy. The complete genome of NiV has been sequenced and PCR-based methods have been used to detect the virus and are being validated in a number of laboratories. The availability of safe laboratory diagnostic tests is limited and is non–existent in low biosafety conditions.

Vaccines: There are **no vaccines** currently available for NiV although promising results were reported from experiments in swine, cats, and hamsters.

Pharmaceuticals: No specific treatment is available for veterinary purposes and, if available, the use of therapeutics would be problematic given biosecurity concerns regarding exposed animals.

What do we need?

- **In-depth knowledge** concerning many aspects of the distribution, epidemiology, pathogenesis and control of NiV.
  - Research towards the immunology, ecology, maintenance and transmission of NiV in bat populations.
  - Knowledge about routes of infection, susceptibility, infectious doses and intra- and inter-species transmission of NiV in all known susceptible species (pigs, dogs, cats, goats, cattle, horses).
- **Diagnostic tests suitable for low containment laboratories.**

Read the full chapter here.

Orthopox viruses

Disease Profile

There are multiple zoonotic pathogens within the genus Orthopoxvirus (OPXV) which includes three virus species of significant consequence to human and animal health. These are vaccinia virus/buffalopox virus (VV/BPXV), cowpox virus (CPXV), and monkeypox virus (MPXV). VV/BPXVs causes **scabby lesions and ulcers** affecting bovids, sylvan and peridomestic rodents and humans. CPXV occurs naturally in sylvan rodents and causes pustular rash and fever in cattle, humans, domestic felines, zoo animals and rodents. MPXV is a smallpox-like illness with disseminated **pustular rash** and fever in primates and rodents.

Risk

Risks for outbreaks of VV/BPXV are greatest where traditional, non-mechanised dairy production occurs. The spread of VV/BPXV may have a devastating impact on rural, artisanal dairies where production depends on a small number of cows or buffaloes. The experience in the United States with zoonotic transmission of MPXV, which entered the country via imported exotic animals, underscores the importance of being prepared to manage a potentially catastrophic situation.

Recent human Orthopoxvirus infections in Europe have occurred in pet owners, zoo workers and veterinarians. Infections with VV/BPXVs or CPXV can be life-threatening in immune-compromised subjects. Human infection with Congo Basin variants of MPXV are fatal up to 15% some of the time.

What do we have?

Diagnostics: At present there are no robust or commercial antibody tests in use for poxviruses and this can lead to misdiagnosis with other pathogens causing vesicular disease in ruminants. Several laboratories in the EU including national public health (and defence) laboratories in the UK, Germany, Spain, France and Italy have the capacity to perform nucleic acid based testing for the presence of orthopoxvirus signatures in clinical specimens.

Vaccines: Vaccines for prevention of OPXV infection in animals are currently **unavailable** and none are currently thought to be under development.

Pharmaceuticals: There are no approved veterinary treatments for poxvirus-related infections but anti-virals have been tested successfully in the laboratory.

What do we need?

- A better understanding of the **identity and distribution of reservoirs** for OPXV associated zoonotic agents. This needs to include identification of i) virus reservoirs (particularly rodent), ii) range of permissive hosts/transmitting hosts, iii) sylvatic transmission cycles and principal opportunities/risks for spill over.
- **Burden assessments** of OPXV diseases in Europe and worldwide.
- **Vaccines** against OPXV-associated zoonoses that provide durable cross-protection against infection with multiple species and that pose little to no risk of transmission between humans.
- Antigen or nucleic acid-based rapid detection assays.
- **Leveraging bio-terror preparedness activities to combat OPXV:**
    - Training clinicians who can identify suspected cases of OPXVs-associated illnesses in humans and animals;
    - Build diagnostic testing capacity to rapidly identify a poxvirus-associated aetiology and to identify the species of virus involved;
    - Build capacity for appropriate sanitary measures, which may include quarantine and vaccination;
    - Make therapeutic treatments available for persons experiencing severe illness due to infection with any one of these agents.

Read the full chapter here.

Parapox viruses

Disease Profile

The genus *Parapoxvirus* (PPV) includes three members for which zoonotic transmission has been reported: bovine papular stomatitis virus (BPSV), which infects cattle/camels, pseudocowpox virus (PCPV) affecting cattle/reindeer/dromedarius/humans and orf virus (OV) which can infect sheep/goats/reindeer/muskox/humans. All cause contagious skin infection. PPV associated infectious diseases are found throughout the world. PPV diseases are normally self-limiting with low impact on individual animals. Severe outbreaks of OV can occur where lesions are extensive and proliferative and do not spontaneously regress. Scabs contain millions of virus particles which, when they dry up and drop off the animal, will contaminate the environment for years. PPVs are highly transmissible (almost 100% morbidity on affected farms). The majority of PPVs are transmissible to man with disease considered an occupational hazard to people in close contact with ruminants.

Risk

PPV infections and in particular orf have a great economic impact to those **rural communities that are reliant on livestock farming for their livelihood.** OV is in the top twenty most important viral diseases of sheep and goats globally in terms of impact on the poor. There is likely to be underreporting of the occurrence of zoonotic poxvirus infections worldwide as appropriate diagnostic assays are not readily available, and the stigma attached to producers and hunters due to contact with these agents is considerable. These are classic neglected zoonoses with considerable potential to cause significant disease in humans and animals.

What do we have?

Diagnostics: ELISAs and PCRs are available but are performed at academic institutions or in public health reference laboratories. There are **no routine diagnostic tests** in use for poxviruses which can lead to misdiagnosis with other pathogens causing vesicular disease in ruminants.

Vaccines: Limited licenced vaccines are available only for OVs but efficient and safe vaccines providing long lasting immunity are not available. All current vaccines are fully virulent live viruses that can themselves cause outbreaks of disease. No vaccines are under development for specific use in animals.

Pharmaceuticals: There are no approved veterinary treatments for poxvirus related Infections with none available commercially. Antivirals have been tested successfully in vitro, ex vivo and in vivo experiments.

What do we need?

- An **assessment of worldwide PPV strain variability** to develop accurate diagnostics test that can differentiate between endemic and imported isolates.
- Knowledge on the **stability of live virus** under ambient conditions. Several aspects of virus genotype associated pathology remain undefined.
- A **standard diagnostic test** needs to be established to assess PPV associated disease across Europe.

  Deeper understanding of the burden, distribution and risk factors of zoonotic poxviruses globally.
- **Vaccines** capable of providing sterile immunity.
- Rapid and reliable **diagnostic tests** capable of distinguishing between the PPVs and other agents causing vesicular disease in ruminants especially the notifiable diseases.

Read the full chapter here.

Q Fever

Disease Profile

Q fever is a zoonotic disease caused by the bacteria *Coxiella burnetii.* Outside the animal host, the bacterium becomes a spore-like resistant form enabling it to survive for variable periods in the environment and be a source of infection. Cattle, sheep, and goats are the primary reservoirs of *C. burnetii*, but other animals may play a role as secondary reservoirs.

C. burnetii infection in animals can persist for several years. There is consensus among public health and veterinary professionals that **most of the human Q fever outbreaks are linked to small ruminants, abortion waves on large farms representing the major risk.** In humans, clinical symptoms of Q Fever may only be seen in around half of all people infected with *C. burnetii.* Infection is often self-limiting but some patients develop a flu-like illness and severe disease, which is very difficult to cure, develops in a few patients. Mortality rates in humans can be 1-2%.

Risk

Q Fever is **under-diagnosed and under-reported** and there is no reliable assessment of the number of cases worldwide. Q fever was a major public health problem in the Netherlands with over 4,000 human cases notified over the years 2007-2010. Control measures in goats (culling) were implemented to control Q fever in humans. Veterinarians, laboratory workers, farmers, abattoir workers and people living in proximity to herds or abattoirs are most at risk of exposure. Transmission to humans mainly occurs through the inhalation of contaminated aerosols. Other risks include direct contact with infected animals especially during parturition.

C. burnetii is a potential biological warfare agent being very infectious (low infectious dose) and very durable in the environment as well as capable of windborne spread.

What do we have?

Diagnostics: Diagnosis of infection can be made by direct isolation of the organism from tissues or by immunohistochemical staining for the antigens but PCR techniques are now recognised as the most sensitive method to detect *C. burnetii.* A number of serological tests are available, including indirect immunofluorescence, ELISA and complement fixation. Bulk tank milk testing by PCR and antibody ELISA can be used for monitoring *C. burnetii* infection in dairy herds.

Vaccines: Animal vaccines have been developed and several are commercially available. Vaccination with an inactivated vaccine has been effective in cattle, goats and sheep and has reduced clinical problems as well as reducing shedding of the organism but is not eradicating the disease.

Pharmaceuticals: Several antibiotics have been used in the treatment of infection in humans. In animals, antibiotics may suppress rather than eliminate infections and their efficacy is under study and debate.

What do we need?

- **Improved diagnostic techniques:** standardisation of current tests; serological tools capable of distinguishing between previous infection and new infection as well as tests between infected and vaccinated animals (DIVA); a molecular method for the assessment of bacterial viability, especially in environmental samples and milk samples.
- Safer to produce, less expensive, more effective, **new-generation vaccines.**
- More insights into the **epidemiology, transmission and pathogenesis of infection:** (i) elucidation of the role of wildlife, pet animals and ticks in the transmission and maintenance of *C. burnetii*; transmission routes within and between herds; the kinetics of bacterial shedding in goats, sheep and cattle, especially in the absence of clinical signs; the environmental conditions which facilitate the sporulation and survival of the organism outside the host assessments of the efficacy of different control schemes.
- More knowledge on the **efficacy of control approaches** including the use of vaccines in livestock.

Read the full chapter here.

Rabies

Disease Profile

Rabies virus (RABV) is a Lyssavirus transmissible to all mammals. The animal hosts that maintain RABV in nature are **carnivores and bats.** Other animals do not play a role in the maintenance of the disease, but are victims of the disease itself. Infection is usually spread **by the bite of an infected animal.** Typical signs include sudden behavioural changes and progressive paralysis leading to death. It is estimated that more than 59,000 people die of rabies each year globally. About 95% of human deaths occur in Asia and Africa, where dogs continue to be the main carriers of the disease. Vampire-transmitted rabies is endemic in Latin America.

Risk

Failure to control rabies in dogs in developing countries will result in continued high mortality each year and will create possibilities for spill-over events into wildlife. In general, better surveillance and field diagnostic tools are required. Decreasing the exposure rate between wildlife species and rabies vectors is essential and understanding the efficacy of rabies vaccines in wildlife species is critical, including whether the vaccine is safe to be used in endangered species.

What do we have?

Diagnostics: Rabies diagnosis is **only possible post-mortem** and the target sample is the central nervous system of a symptomatic animal. Agent identification using the fluorescent antibody test (FAT) provides a reliable diagnosis in 98–100% of cases. Direct immunohistochemical tests (dRIT) as well as molecular based methods are nowadays accepted as alternatives to FAT. Rapid immunochromatographic kits are commercially available as Lateral Flow Devices (LFD), but their accuracy is still debated. Virus neutralisation (VN) assays in cell cultures are the prescribed tests for post-vaccinal antibodies for international trade. Alternatively, an ELISA using antibody to the G protein that is known to correlate with VN assays may be used.

Vaccines: Cheap and safe RABV vaccines are available, which are effective and induce solid immunity. A **wide range of vaccines are authorised** globally for use in humans, cats, ferrets, horses, sheep, cattle, and dogs. The development of oral vaccines has enabled the eradication of rabies from the red fox population throughout most of Europe. In addition, programmes for oral vaccination of wildlife such as raccoons, coyotes, foxes, and skunks are being undertaken in North America.

Pharmaceuticals: Antiviral agents, interferon and massive doses of rabies immunoglobulin have been used to treat human cases, but they only seem to prolong the clinical course without affecting fatality.

What do we need?

- **Longer lasting (perhaps lifelong) rabies vaccines.** Additionally, a combination of rabies and contraceptive vaccines would provide a valuable tool in the fight against rabies in dogs. New vaccines for lyssaviruses not covered by current vaccines are also needed.
- Replacement of the current *in vivo* assay for **vaccine potency testing** by a combination of *in-vitro* testing and consistency monitoring.
- Validation of **field tests** to allow a rapid follow-up of biting and suspect animal cases, particularly in the developing world.
- **Disease mechanisms:** why do some animals survive RABV infections and shed virus for longer periods? Why does the virus sometimes stay in an 'eclipse' phase for weeks, months or even years?
- **Cost benefit analyses** to assess the effectiveness and economies of strategic control plans.
- More epidemiological data on **newly described lyssaviruses:** bat species involved; species barriers, spill-over infections.

Read the full chapter here.

Salmonellosis

Disease Profile

Salmonellae are found **worldwide in both warm and cold blooded animals and in the environment.** The two most commonly encountered serovars in cases of food poisoning of humans are *S. Enteritidis* and *S. Typhimurium*. The usual sign of salmonellosis in animals is diarrhoea, even though in the great majority of the cases *Salmonella* infection is asymptomatic. In humans the disease causes diarrhoea, abdominal pain, fever, headache, nausea and vomiting. In severe cases septicaemia and further complications may develop. The most serious cases are generally among infants, small children, the elderly and those with suppressed immunity.

Risk

There has been a reduction in the number of reported cases of salmonellosis in humans in the EU in recent years, largely as a result of improved control of *S. Enteritidis* in poultry. There has, however, been an increase in *S. Typhimurium*, thought to be associated with increased pig-meat related cases. Human infection is greatest in the summer and this is thought to be associated with difficulties in maintaining food at lower temperatures and use of undercooked meat.

What do we have?

Diagnostics: Whole blood tests and serum agglutination tests have been used for a long time and ELISAs are now in routine use. Serological cross-reactions between different serovars and even with some non-*Salmonella* organisms can occur, so bacterial isolation must be used for confirmation. PCR and micro-array based antigen tests have been described. A molecular serotyping test targeting the main *Salmonella* serovars has been developed and OIE validated. Several commercial immunodiagnostic kits for *S. Enteritidis* and *S. Typhimurium* are available.

Vaccines: There are many inactivated vaccines that are used against salmonellosis. Live vaccines have been used in some countries although EU legislation dictates that they are not used unless an appropriate method is provided to distinguish wild type strains of *Salmonella* from vaccine strains. Genetically modified vaccines are available in certain countries. **The current vaccines reduce the infection and mortality in poultry** and other species and are not guaranteed to prevent infection.

Pharmaceuticals: The use of antibiotics for the treatment of salmonellosis in many countries is very limited and is normally **restricted to cases where the disease is serious and life threatening.** Antimicrobials shall not be used as a specific method to control Salmonella in poultry according to current European legislation. Prevention of infection may be aided by the use of prebiotics, probiotics and competitive exclusion agents.

What do we need?

- **New vaccine developments:** multi-serovar/serogroup protection, use of attenuated and safe strains during egg production, use of attenuated live *S. Thyphimurium* in pigs and cattle, marker vaccines.
- **Improved diagnostic methods** and techniques for strain identification and typing, including test for on-farm use.
- **More epidemiological knowledge:** serovar variability in different countries; relative risk of different sources of infection; longitudinal and quantitative data on herd infection and environmental contamination dynamics
- **More knowledge concerning virulence factors and host/pathogen interactions** in the main target species.
- **Validated procedures** for minimising *Salmonella* populations on large farms, especially pig farms.
- **Cost benefit analyses** of control measures to provide convincing evidence of the value of investment in *Salmonella* prophylaxis.

Read the full chapter here.

Toxoplasmosis

Disease Profile

Toxoplasmosis is caused by the protozoan *Toxoplasma gondii* and is a relevant zoonotic disease of humans and homeothermic vertebrates. Felids, including domestic cats, are definitive hosts that can shed oocysts with their faeces, thus causing environmental contamination. In addition to infections that occur by accidental oral uptake of food or water contaminated with oocysts, it is assumed that a large proportion of affected humans may have become infected by consuming meat or other animal products that contained infective parasitic stages of *T. gondii*. Human toxoplasmosis includes congenital and postnatally acquired toxoplasmosis. Congenital toxoplasmosis may cause abortion, the birth of severely affected children (e.g. hydrocephalus, seizures, retardation) or children developing symptoms of toxoplasmosis in later life (e.g. ocular toxoplasmosis). In most cases, postnatally acquired *T. gondii* infections have no severe consequences for infected humans. *T. gondii* may also be pathogenic to livestock, as it is an important abortifacient for small ruminants.

Risk

Risk factors for livestock are **cat-related**, but there are also others associated with a potential contamination of fodder or water, with access to a potentially contaminated environment or with the possibility to prey on infected intermediate hosts like rodents.

In humans, risk factor studies suggest that the **consumption of raw or undercooked meat** is a major source of *T. gondii* infections in Europe. The environmentally resistant *T. gondii* oocysts, shed by domestic cats, also contribute to an unknown extent to human infections.

What do we have?

Diagnostics: Commercial serological tests, based on both, native or recombinant proteins, are available for humans and many animal species. For some animal species, the existing serological tests seem to not be reliable in identifying animals that could transmit the infection to consumers if this meat is consumed under-cooked. DNA detection methods are readily available.

Vaccines: For humans no vaccination has been developed yet. There is only **one vaccine available in the veterinary sector for use in sheep.** It is a live vaccine, commercially and seasonally available in a few regions of the world (including France, Ireland, New Zealand, Norway, Spain and UK). It has a short shelf life of a few days and needs refrigerated delivery. Furthermore, it is not suitable for use in pregnant sheep or sheep close to mating. It is potentially infective for users and should not to be handled by pregnant women.

Pharmaceuticals: In the veterinary livestock sector, only symptomatic treatment is available, aiming at reducing clinical signs during acute infection (e.g. fever).

What do we need?

- **More cell-biological knowledge on the extra-cellular stages** of *T. gondii*, e.g. the oocysts excreted by definitive hosts or the parasitic stages developing in the gut of felids. These stages are of utmost importance if blocking vaccines for young cats are going to be developed
- **Reliable and sensitive detection of viable parasites in meat.**
- **Multiplex assays** to improve and accelerate slaughterhouse surveys and examinations.
- **Tests to differentiate** the acute from a chronic infection or differentiating between infections caused by different stages of the parasite (e.g. tissue cysts vs. oocysts driven infections).
- More **user-friendly and safer vaccines**, predominantly to reduce abortions in livestock. Optimally, such vaccines are subunit or DNA vaccines. Vaccines to increase food safety by preventing food animals to establish tissue cysts following vaccination seems to be an additional application.
- A **transmission blocking vaccine for young cats** to reduce the oocyst contamination in the environment.

Read the full chapter here.

African Trypanosomiasis

Disease Profile

Trypanosomiasis is caused by trypanosome protozoans that inhabit the blood plasma, the lymph and various tissues of their hosts. Human African Trypanosomiasis (HAT), or sleeping sickness, only occurs in Sub-Saharan Africa. Untreated, the disease is always fatal in humans and devastating epidemics have occurred over the last century.

African Animal Trypanosomiasis (AAT) is caused by a number of trypanosome species and subspecies. The most important species have a wide host range among domesticated and wild animals. Both HAT and AAT are mainly transmitted through the bite of tsetse flies, which occur in Sub-Saharan Africa. A wide range of wild and domestic animals can act as reservoirs of the parasites. Tsetse-transmitted animal trypanosomiases cause acute to chronic disease with signs including intermittent fever, anaemia, loss of appetite and weight in acute forms, and emaciation and eventually death in chronic forms; morbidity and mortality rates can be high.

Risk

HAT affects mostly poor populations living in **remote rural areas of Africa.** In 2007, the number of new cases reported was 10,769. Recently, country level, WHO, bilateral and NGO HAT control programmes claim to have brought the resurgence of the disease under control, although HAT continues to be under-reported in most affected communities.

AAT occurs in 37 sub-Saharan countries covering about 9 million km2 and threatens an estimated 50 million head of cattle. It acts as a **constant drain on livestock productivity and livestock keepers' time and money.** Those affecting cattle are the most important economically since they are a major cause of reduced meat and milk production and limit the use of draught power for agricultural production.

What do we have?

Diagnostics: There are **no commercially available kits** for the diagnosis of AAT. Several parasite detection techniques can be used, including the microscopic examination of wet and stained thick or thin blood films or examination of the buffy coat following blood centrifugation. PCR techniques can identify parasites at the genus, species or subspecies level. Indirect fluorescent antibody tests and ELISAs are routinely used for the detection of antibodies in cattle.

Vaccines: **No vaccines** are available at the present time.

Pharmaceuticals: **Trypanocidal drugs** for use in cattle and other animals are limited to three compounds, diminazene aceturate, homidium and isometamidium chloride. Drugs are used both therapeutically and prophylactically. Prophylactic use of trypanocidal drugs to prevent the disease in animals can also protect people. Trypanocidal drugs are becoming more expensive and their efficacy is reduced by the appearance of chemoresistance.

Tsetse control by applying insecticide to cattle has been shown to be effective by reducing the numbers of tsetse in an area which in turn means fewer cattle will be bitten.

What do we need?

Due to its biological nature and its links with agro-ecological settings, the disease constitutes a complex and vast sub-Saharan problem to be solved. Investments have to spread over five main areas:

- human resource development;
- improved technology for diagnosis and disease treatment;
- improved vector control;
- increased exchange of information;
- regional, national and local institutional support.

Read the full chapter here.

Verocytotoxigenic *Escherichia coli* (VTEC)

Disease Profile

Most *Escherichia coli* bacteria are harmless commensals inhabiting the gastrointestinal tracts of animals and humans. However, certain strains produce potent toxins and are known as verocytotoxin-producing *E. coli* (VTEC) or STEC (Shiga toxin producing *E. coli*). VTEC are zoonotic pathogens, occurring worldwide, which can cause severe human illnesses and have ruminants, particularly **cattle**, as their natural reservoir. More than 100 different serotypes have been identified as VTEC, with **O157:H7** as the serotype most commonly associated with severe human disease. VTEC can cause a wide spectrum of **disease in humans**, ranging from mild uncomplicated diarrhoea to severe bloody diarrhoea and the haemolytic uremic syndrome (HUS), a potentially life-threatening kidney condition which is mainly observed in children. Interestingly, most VTEC infections in animals are asymptomatic. VTEC can survive in the environment for extended periods of time. VTEC can spread within the farm environment by direct contact, contamination of water, feed and environment, and by other animals such as flies, rodents and birds.

Risk

Surveillance systems are in place in industrialized areas such as Europe, North America, Japan, and Australia. In the USA, the incidence is estimated to be around 100,000 cases per year. The prevalence and epidemiology of VTEC infection is poorly known in developing countries. Food sources identified as providing a risk of infection include undercooked ground beef, unpasteurised milk and dairy products and contaminated fresh produce. Good food hygiene is essential to prevent zoonotic transmission.

What do we have?

Diagnostics: In general, the laboratory tools for VTEC O157 detection are adequate, while those for VTEC non-O157 detection are in some cases poor.

Vaccines: A number of commercial vaccines have been produced and are used in some countries. However, generally uptake has been poor.

Pharmaceuticals: In cattle, neomycin administration is effective at eliminating most O157, but not commonly used.

In the abattoir: Cleaning of animals before slaughter and tying off the rectum post slaughter.

What do we need?

- A better knowledge of the **general ecology of VTEC**: survival of VTEC in soil and farm environments and the role of wildlife in the epidemiology; relative importance of the different routes of transmission and sources of infection; animal husbandry procedures which could mitigate the risk of contamination of the environment.
- Better understanding of the **mechanisms of the pathogenesis** of infection in humans and of **colonisation** in livestock to identify targets for diagnostics and vaccines.
- More research on the dynamics of infection in animals including the **factors involved in super shedding** and determining whether tools and markers can be developed to identify super shedders.
- Evaluation of **bacteriophages and probiotics** as possible approaches to control.
- Better rapid diagnostics for surveillance and the management of clinical human cases.

Read the full chapter here.

Table of abbreviations

AAT	African Animal Trypanosomiasis
AE	Alveolar echinococcosis
AHS	African Horse Sickness
AI	Avian Influenza
APP	Actinobacillus pleuropneumoniae
ASF	African Swine Fever
BCG	Bacille Calmette Guérin
BoHV1	Bovine Herpes Virus 1
BPSV	Bovine Papular Stomatitis Virus
BPXV	Buffalo Pox Virus
BRSV	Bovine Respiratory Syncytial Virus
BSE	Bovine spongiform encephalopathy
BTB	Bovine tuberculosis
BTV	Bluetongue Virus
BVD	Bovine Viral Diarrhoea
CA	Contagious Agalactia
CBPP	Contagious bovine pleuropneumonia
C-BSE	Classical bovine spongiform encephalopathy
CCHF	Crimean Congo Haemorrhagic Fever
CE	Cystic echinococcosis
c-ELISA	Competitive enzyme-linked immunosorbent assay
CFT	Complement fixation test
CL	Cutaneous/mucocutaneous Leishmaniasis
CNS	Central nervous system
CPXV	Cow Pox Virus
CSF	Classical Swine Fever
DGGE	Denaturing gradient gel electrophoresis
DIVA	Differentiating infected from vaccinated animals
DNA	Deoxyribonucleic acid

dRIT	Direct rapid immunohistochemical test
EC	European Commission
ECF	East Coast Fever
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
FAO	Food and agricultural organization of the United Nations
FAT	Fluorescent antibody test
FDA	Food and Drug Administration
FMD	Foot and Mouth Disease
GI	Gastrointestinal
GTPV	Goat Pox Virus
HAT	Human African Trypanosomiasis
HEV	Hepatitis E Virus
HeV	Hendra Virus
HRSV	Human Respiratory Syncytial Virus
IBR	Infectious Bovine Rhinotracheitis
i-ELISA	Indirect enzyme-linked immunosorbent assay
IFA	Immunofluorescence assay
Ig	Immunoglobulin
IGRA	Interferon gamma release assay
IPV	Infectious Pustular Vulvovaginitis
ISO	International Standards Organisation
JD	Johne's Disease
LFD	Lateral flow device
LSD	Lumpy Skin Disease
MAP	Mycobacterium avium subspecies paratuberculosis
MDA	Mass drug administration
MPXV	Monkey Pox Virus
MRSA	Methicillin-resistant Staphylococcus aureus
NCC	Neurocysticercosis

NGS	Next generation sequencing
NiV	Nipah Virus
OIE	World Organisation for Animal Health
OPXV	Orthopoxvirus
OV	Orf virus
ParaTB	Paratuberculosis
PCPV	Pseudocowpox Virus
PCR	Polymerase chain reaction
PCV2	Porcine Circovirus 2
pH	Potential hydrogen
PI	Persistently infected animal
PMWS	Post Weaning Multi-systemic Wasting Syndrome
PPR	Peste des Petits Ruminants
PPV	Parapox Virus
PRRS	Porcine Reproductive and Respiratory Syndrome
RABV	Rabies Virus
RDT	Rapid diagnostic test
RFLP	Restriction fragment length polymorphism
RNA	Ribonucleic acid
RT-PCR	Real time polymerase chain reaction
RVF	Rift Valley Fever
S&GP	Sheep and Goat Pox
SPPV	Sheep Pox Virus
STEC	Shiga toxin producing Escherichia coli
SVD	Swine Vesicular Disease
TB	Tuberculosis
TCBZ	Triclabendazole
US(A)	United States of America
vCJD	Variant Creutzfeldt-Jacob Disease
VL	Visceral Leishmaniasis
VNT	Virus neutralisation test
VTEC	Verocytotoxigenic Escherichia coli
VV	Vaccinia Virus
WHO	World Health Organization
WNV	West Nile Virus

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This booklet was produced with support of **AnimalhealthEurope**

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