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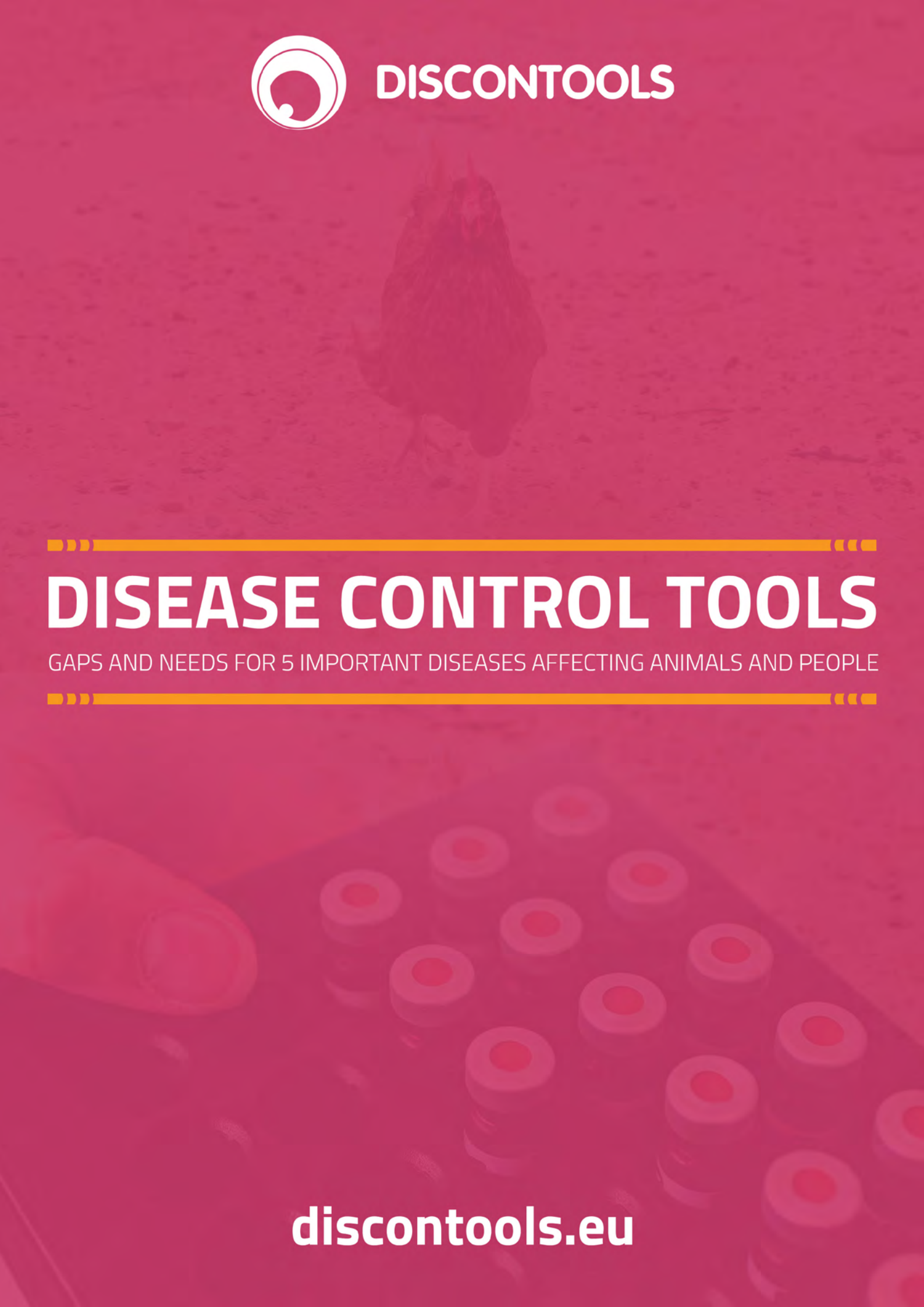

DISEASE CONTROL TOOLS

GAPS AND NEEDS FOR 5 IMPORTANT DISEASES AFFECTING ANIMALS AND PEOPLE

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Editorial

They are finally here! The DISCONTOOLS Disease Sheets: 53 infectious diseases summarised in one page each, with the DISease CONtrol TOOLS available, and those we need to improve or secure animal health and welfare.

The original plan was to distribute the Disease Sheets during the DISCONTOOLS symposium 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 (29 April 2021, Brussels). Confinement, shifted priorities in lab testing and the subsequent economic crisis has deeply affected the work of farmers, veterinarians and animal health researchers. This will undoubtedly have an impact on many animal diseases, for instance through reduced monitoring and surveillance activities, interrupted lab work and increased wildlife-livestock contacts. Veterinary sciences have an important role to play to prevent and control human and animal pandemics. Therefore, we selected 5 emerging or impactful human diseases in which animals play an important role and distribute them on the occasion of the CWG AHW & STAR-IDAZ web interactive workshop "Pandemic! A one health view of emerging infectious diseases – What veterinary sciences can contribute" (30 June 2020).

However, with the distribution of the DISCONTOOLS Disease Sheets we hope to highlight not only the zoonotic and potentially pandemic diseases, but to re-point the focus on any animal disease (zoonotic, epidemic, endemic) where new knowledge and control tools are needed.

Over the coming months, AnimalhealthEurope will disseminate one to two Disease Sheets on a weekly basis. At the end of the campaign, we will make all 53 Disease Sheets available in an e-booklet. They have been carefully prepared with the resounding support of over 400 experts from academia, government and industry. They may be a useful resource to the benefit of animal health funders, researchers and students to focus research in needed areas.

Over the past 4 years, 23 new medicines were marketed in Europe on DISCONTOOLS listed diseases. Despite this progress, important gaps remain. We hope the Disease Sheets will make a useful contribution to the continued support for research, the delivery of new scientific insights and control tools and thus the improvement of animal and public health.

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These sheets have been prepared for the occasion of the CWG AHW & STAR-IDAZ web interactive workshop "Pandemic! A one health view of emerging infectious diseases – What veterinary sciences can contribute", 30 June 2020.

Like what you see? Register here to receive more Disease Sheets in the future.

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.

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. 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.

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 USD 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.

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 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.

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