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Annual Review of Animal Biosciences

African Swine Fever Epidemiology and Control

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Keywords

African swine fever, transmission, pathogenesis, epidemiology, control strategy, vaccine

Abstract

African swine fever is a devastating disease that can result in death in almost all infected pigs. The continuing spread of African swine fever from Africa to Europe and recently to the high–pig production countries of China and others in Southeast Asia threatens global pork production and food security. The African swine fever virus is an unusual complex DNA virus and is not related to other viruses. This has presented challenges for vaccine development, and currently none is available. The virus is extremely well adapted to replicate in its hosts in the sylvatic cycle in East and South Africa. Its spread to other regions, with different wildlife hosts, climatic conditions, and pig production systems, has revealed unexpected epidemiological scenarios and different challenges for control. Here we review the epidemiology of African swine fever in these different scenarios and methods used for control. We also discuss progress toward vaccine development and research priorities to better understand this complex disease and improve control.

1. INTRODUCTION

1.1. History of African Swine Fever

ASF: African swine fever

ASFV: African swine fever virus

In the early 1900s, African swine fever (ASF) was reported in East Africa as an acute hemorrhagic fever causing the death of almost all infected domestic pigs. The source of infection was identified as a virus that spread from an ancient sylvatic cycle (1, 2). Since then, African swine fever virus (ASFV) has spread to most sub-Saharan African countries (3). Transcontinental spread of ASFV occurred first to Portugal in 1957 and 1960 and from there to other countries in Europe, the Caribbean, and Brazil (4). Eradication was achieved by the mid-1990s, except in Sardinia, where the disease remains endemic. The 2007 introduction to Georgia in the Caucasus heralded a new transmission era, as ASFV subsequently spread to the Russian Federation, Ukraine, and Belarus and in 2014 to the EU Baltic States and Poland. By 2018, the infection had also spread to Belgium, Hungary, the Czech Republic, Romania, Bulgaria, Slovakia, and Serbia (5–9). In 2018, the situation worsened considerably when ASFV was detected in China, which contains half the world's swine population. Widespread dissemination in China has been followed by spread to Mongolia, Vietnam, Cambodia, North Korea, Myanmar, Laos, and the Philippines (**Figure 1** and **Supplemental Videos 1–3**). Further spread in Asia and other territories is likely (9, 10). The high socioeconomic impact of ASF results from loss of business in the pig production chain, costs of disease control, and loss of trade. Large epidemics can result in dramatic reductions in the size of national pig herds and inflation of prices of pig and pork products. They can also have a devastating psychological impact on farmers and cause mortality in wild boar populations.

Supplemental Material >

1.2. Virus Etiology

ASFV is a large double-stranded DNA virus and is the only member of the Asfarviridae family (11) (see **Supplemental Figure 1**, **Supplemental Table 1**). The genome varies in length between approximately 170 and 193 kbp, mainly owing to gain or loss of multigene family members. Essential genes include those required for the cytoplasmic replication and transcription of the virus genome (12) and most of the 68 virus proteins detected in virus particles (13, 14). Many ASFV genes inhibit

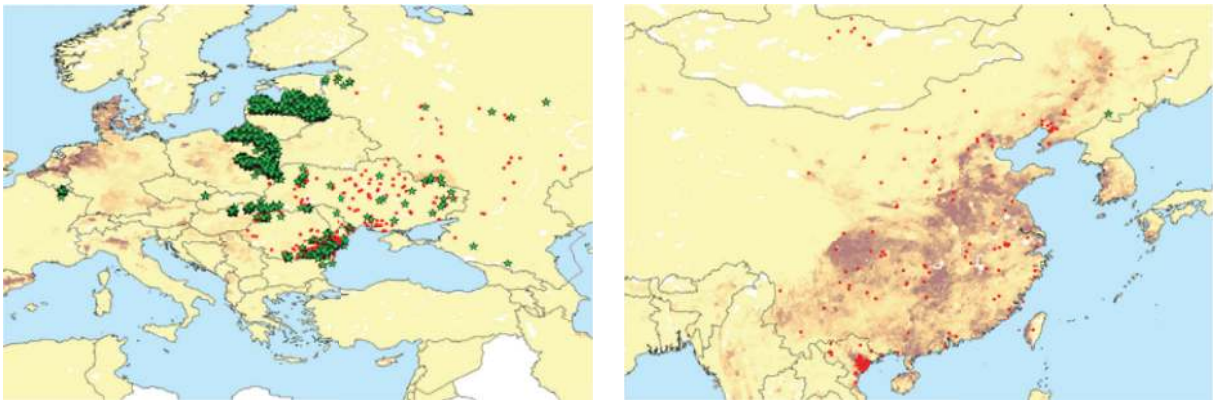

Figure 1

Spatial distribution of reported African swine fever (ASF) outbreaks in domestic pigs and cases in wild boar in 2018 and 2019 in Europe and East Asia, over a raster map of pig density. Both maps are shown at the same spatial resolution (darker brown means higher density; red dots are domestic pigs, and green stars are wild boar) (spatial data on pig density taken from 143; ASF outbreak data are from FAO Empres-I) (see also **Supplemental Videos 1–3**).

TYPE I INTERFERON ANTIVIRAL RESPONSES

Type I interferon activates the main host early innate antiviral response. This response is induced when host pattern recognition receptors recognize specific pathogen-associated molecular patterns and activate downstream signaling pathways, which result in activation of transcription factors such as IRF3 to increase transcription of type I interferon genes. Following translation, these are secreted from infected cells and bind to receptors on the infected cell or neighboring cells. This results in activation of JAK/STAT signaling pathways and leads to transcription of several hundred interferon stimulated genes. These include genes for proteins that induce an antiviral state in cells to limit virus replication and others, including cytokines and chemokines, that activate host innate and adaptive immune responses.

host defenses, including type I interferon, the main host antiviral pathway, and programmed cell death, or apoptosis (see sidebar titled Type I Interferon Antiviral Responses). Deletion of these genes from the virus genome provides an attractive route to produce rationally attenuated vaccine candidates. Half or more of the genes are of unknown function (15, 16). The accurate proofreading of DNA polymerase and virus-encoded base excision DNA repair system result in a low mutation rate in ASFV DNA. The lack of related viruses means recombination with other viruses is very unlikely. Thus, the risk of ASFV jumping a species barrier is considered to be negligible.

1.3. Pathogenesis in Domestic and Wild Suids

The host range of ASFV is restricted to suids and soft ticks of the *Ornithodoros* species. In its wild suid hosts in Africa, ASFV infection causes mild clinical signs and can result in longer-term persistent infections (17, 18). In contrast, most ASFV isolates cause an acute hemorrhagic fever, with a case fatality rate approaching 100%, in domestic pigs and wild boar (19, 20). Diseases observed in domestic pigs and wild boar include acute and peracute forms (21–23), which are caused by highly virulent isolates and result in death within 4 to 15 days postinfection. Moderately virulent isolates cause lower case fatality (30–70%). Low-virulence isolates result in low or no case fatalities and absence of vascular lesions. However, signs of chronic disease can be observed. The clinical signs of acute ASF include high fever, loss of appetite, and increasing lethargy and morbidity. Bloody diarrhea, vomiting, and abortion may also be observed (see **Supplemental Figure 2**). Infection is associated with very high levels of virus in blood (up to 10^9 $TCID_{50}$/mL) and tissues. Wild boars (*Sus scrofa*) show the same acute signs of disease as domestic pigs (19, 21, 23). Most isolates circulating in Europe, the Russian Federation, and Asia cause the acute form of disease, although some reduced-virulence isolates have been obtained from infected wild boar in the Baltic States (24, 25). Animals that recover from disease may remain infected for several months (26).

Supplemental Material >

1.4. Transmission

ASFV can be transmitted by direct contact between infected animals and by ingestion of infected pork or other contaminated materials (7, 27–29). Fomites such as clothing, transport trucks, or feed supplies may act as a source of infection. Soft tick vectors of *Ornithodoros* spp. play an important role in transmission in warthog burrows. They can also play a role in transmission on pig farms in regions where they are present. Transmission from persistently infected to uninfected animals has been demonstrated (26, 30, 31). However, evidence is lacking for a role of long-term carrier status in ASF transmission in the field (32). There is increasing speculation around the potential role of

mechanical arthropod vectors, such as stable flies (*Stomoxys calcitrans*) or tabanids (33, 34), owing to the peaks of outbreaks in domestic pig herds observed during summer months in the current epidemic in Europe. But there is so far no conclusive evidence that these play a significant role in the spread of the disease. Transmission mechanisms have been reviewed recently (23, 35, 36).

2. EPIDEMIOLOGY OF AFRICAN SWINE FEVER

2.1. The Domestic Pig Sector

Effective prevention and control policies for ASF must take into account the features of pig production systems and associated value chains. Basic principles of infectious disease transmission indicate that the higher the density of susceptible animals and of pig farms, and the higher the rate of indirect or direct contacts between pigs and farms, the faster an infectious disease will spread through a population. ASF is no exception in this respect. In the absence of effective vaccines, understanding the importance of different transmission mechanisms of ASFV within and between farms is critical. In most ASF outbreak investigations, the source of introduction cannot be reliably identified, which farmers and other epidemiologically relevant actors may perceive as a justification for avoiding changes in biosecurity behavior (see sidebar titled Biosecurity Measures). The amount of virus introduced by any mechanism will vary substantially depending on factors such as stage of clinical disease of pigs and treatment of feed or materials to inactivate the virus. The survival of ASFV for extended periods in the environment and in different biological matrices means that contaminated materials have a more important role in transmission than for many other infectious diseases (37–39). These mechanisms are underestimated by farmers and other stakeholders. The survival of virus in processed pork meat for several weeks is counterintuitive to consumers and other actors involved in the pork food system.

The connectedness of pork food systems and their links with wild boar populations play key roles in maintenance of the virus both within local, national, and regional systems and for making long-distance jumps. Analysis of pig trade networks in several European countries emphasized the need to recognize this structure in the design of pig health surveillance systems and during disease outbreaks (40, 41). The potential for live pig trade networks between EU member countries to spread ASF has also been recognized, especially when there is a long period between infection and reporting of disease (40). During outbreaks on the border between Kenya and Uganda, producers tended to sell sick pigs through markets in communities farther away from their usual outlets, potentially driving the long-distance spread of the virus (42). Despite a complex epidemiology involving four potentially connected transmission cycles [(*a*) between warthogs and soft ticks, (*b*) between the wild boar carcass environment and potentially susceptible suids, (*c*) between soft ticks and domestic pigs, and (*d*) within domestic pigs (27)], ASFV transmission dynamics are with few exceptions driven by the domestic pig cycle within the pork food system. This is the case in most parts of Africa today (3, 43), in large parts of the affected countries in Europe and the

BIOSECURITY MEASURES

Biosecurity is a term used to describe measures that reduce the risk of pathogen spread. Typically, these measures prevent introduction of infection, for example, by quarantining new pigs delivered to farms, changing clothes and disinfecting boots, not feeding kitchen waste (swill) to pigs, using heat treatment to destroy virus, and disinfecting transport trucks.

Caucasus (34, 44, 45), and in the recently affected countries in East and Southeast Asia (10). The only exceptions are the countries in the European Union where the disease is maintained and perpetuated within the wild boar population independently of domestic pigs (27, 46). Therefore, spread dynamics of ASFV vary mainly depending on the characteristics of local or regional pork food systems, in combination with the ability of national animal health authorities and other relevant stakeholders to prevent and control the disease. In Africa, the pork sector is dominated by small-scale farms, typically with fewer than 10 pigs, and characterized by low input–low output production and poor biosecurity (43, 47–49). Although the pig population on the African continent accounts for less than 4% of the global pig population, it has more than doubled during the last 30 years (**http://www.fao.org/faostat/en/#home**), as a consequence of increased demand for pork by a rapidly expanding urban middle class (3, 47, 48). ASFV has expanded far beyond its traditional boundaries in East and Southern Africa during the last few decades, and it is currently present in the majority of countries with any significant pig population (43). Moreover, with a growing pig population and increased pig husbandry and trade, the number and frequency of outbreaks have increased, including in the historically affected areas. In most parts of Africa today, ASFV spread dynamics are thus driven within a domestic pig cycle by socioeconomic factors in the pork food system. On the European continent, EU countries are characterized by a pork food system that covers most Member States, facilitated by the ability to move pigs at different stages of the production process to optimize cost-effectiveness. The European Commission (EC) together with each Member State's veterinary authority provides a strong institutional context in which policies can be delivered fairly effectively. Most of the affected countries within the European Union have therefore managed to prevent extensive ASFV spread within the domestic pig sector during the current epidemic. However, in Romania, where almost half of the total pig population is kept by noncommercial keepers on 630,000 holdings, more than 1,000 outbreaks were reported during the second half of 2018, and the situation is still not under control (50). Eastern Europe, outside the European Union, has a pork food system consisting of a mix of small and large pig farms. The veterinary institutions are not as well-resourced as in the European Union, and therefore ASFV is likely to be endemic in several of these countries, such as the Russian Federation.

EC: European Commission

On the Asian continent, the situation is still emerging, and the Islamic countries are likely to have slowed down the spread of ASFV to East and Southeast Asia. The importance of pork consumption varies enormously between countries in East and Southeast Asia. China and Vietnam have gone through much more rapid economic development than other low- to middle-income countries in that region, and in 2017, together with EU countries, it had the highest per-capita pork consumption in the world (**https://data.oecd.org/**). This has led to rapid increases in pork consumption over relatively short time spans, particularly when compared with western countries, where the current pork food systems have evolved relatively slowly over much larger time periods and therefore appropriate husbandry methods could be adopted, partly owing to government policy pressure (10). Thailand has experienced gradual economic development over the last 15 years, and the structure of its pork food system has adapted to the geographical variation in pork demand. This means that large-scale commercial pig farms are now concentrated in urban and peri-urban areas, where transport costs for feed and to markets are lowest and demand is fairly stable (51). In contrast, small-scale pig producers are more common in rural and remote parts of the country and supply rural markets, where demand can fluctuate. In comparison, the more recent and more rapid economic growth in Vietnam and China has resulted in their national pork food systems responding by increasing the number of small farms (fewer than 500 pigs) primarily, rather than increasing the individual herd sizes (52–54). But farm management and hygiene behavior along the value chain have not been improved and therefore cannot compensate for the increased risk of infectious pathogen spread resulting from the larger number of farms and increased trade. Instead,

FAO: UN Food and Agriculture Organization

preventive use of antimicrobials has been scaled up, in addition to farmers widely accepting higher pig mortality than they would in high-income countries. In China, the small-scale farmers are not able to carry the economic burden of feed rations that are optimized for pig weight gain and include soy or corn. Instead, they have used locally produced feed, which often included, and potentially still includes, food waste as a cost-effective source of protein. This practice improves the resilience of small-scale pig farming to the price fluctuation of the so-called pork price cycle (55).

The role that feeding kitchen waste to pigs plays in ASF virus transmission led to this practice being prohibited in China in late 2018 (56). Another important feature of pork food systems in China and Vietnam is a fairly large number of consumers who insist on access to warm or fresh meat, which is typically sold through wet markets (53, 57). These wet markets provide a much greater biosecurity challenge than supermarkets in terms of risk management of ASFV spread.

The business opportunities resulting from economic growth have resulted in complex trade networks and value chains within the pork food system, involving many different stakeholders (54, 58, 59). The political influence of these stakeholders varies significantly. This often means that farmers have little influence, whereas other actors further up the value chain (traders, processors, and retailers) have major influence, which in turn has implications for the type and effectiveness of animal disease control and prevention policy measures that can be implemented. The complexity and the sheer size of the pork food system in China suggest that any control or prevention measure for ASF will be very difficult to implement. The patterns of the outbreaks reported so far in both China and Vietnam (between August 2018 and April 2019 for China and February 2019 and April 2019 for Vietnam) support this hypothesis. From an epidemiological and eco-social perspective, the pork food systems in Europe and currently in Africa represent a much simpler challenge than that of China, with its extremely high density of pigs over a large contiguous geographical space (see **Figure 1**). To put it into perspective, in 2017 Mainland China reported a total population of 435 million pigs, which was 45% of the total global population of 976 million pigs according to the UN Food and Agriculture Organization (FAO) (**http://www.fao.org/faostat/en/#home**). This compares with 147 million pigs in the EU countries in the same year on a total land area approximately half as large as China's, and approximately 38 million pigs in Africa, recognizing that in the European Union and Africa, regions of high pig density are highly spatially clustered, whereas the high–pig density areas in China cover large parts of the country's territory.

The proportion of small-scale pig farms varies among European countries (60). In Eastern European countries, a high proportion of farms still have fewer than 400 pigs, with those in Romania, Croatia, Slovenia, Lithuania, and Bulgaria having even fewer than 10 pigs. The situation in the Russian Federation, Ukraine, and Belarus is very similar. At the other end of the spectrum are western and northern EU countries, where more than 80% of farms have more than 400 pigs. Most outbreaks of ASF in Europe have occurred in countries with high proportions of small-scale pig farms, suggesting that these farms have an important role in the spread of the virus. The recent spread in 2018 and 2019 in Romania supports this hypothesis. Countries in Eastern Europe that have fairly high percentages of large farms, such as Estonia, were able to control and prevent onward spread of infection among domestic pigs. The mechanisms responsible for the spread are anthropogenic and have been reviewed recently (27, 61). These mechanisms also apply to countries in Africa and East and Southeast Asia, although the relative importance of the different transmission mechanisms varies even more than it does between European countries. The main reason for this in China and Southeast Asia is the much higher density of pigs, together with the highly complex pork food systems that have evolved rather rapidly with very limited regulatory input from governments during the last 10 to 20 years.

2.2. Wildlife Reservoirs

Infected wildlife can become a reservoir for transmission of virus to domestic pigs. It is therefore important to establish the extent of infection and mechanisms of virus persistence in these hosts, as well as their role in ASFV transmission.

2.2.1. African wild suids and soft ticks. The warthog–tick sylvatic cycle of ASFV was first described in the 1970s in East Africa and was further investigated for different geographical areas (17, 18, 62, 63). This cycle exists exclusively in the distribution area of the *Ornithodoros moubata* complex of species, which is limited to East and Southern Africa (43). To date, only the *O. moubata* complex has been shown to be fully competent for ASFV in Africa, and the frequency of its transmission to the domestic pig value chain through tick bites remains unclear (see sidebar titled Vectors for African Swine Fever Virus). Other pathways of pig infection, such as the ingestion of carcass remains from wild African suids, have been rarely studied (17, 63).

Evidence is lacking for a sylvatic cycle involving wild suids and soft ticks in West and Central Africa (18, 64) for several ecological reasons. For example, xerophilic *Ornithodoros* soft ticks cannot survive in humid tropical and equatorial forest habitats (65). In these forests, wild suids other than warthogs are predominant but do not use underground habitat suitable for those endophilic soft ticks (18). Even in the drier zones of West and Central Africa, warthog burrows do not necessarily harbor the same deep structure as in East and Southern Africa, and this may have prevented the establishment of soft ticks (3).

Importantly, isolates from the sylvatic cycle have greater genetic diversity, owing to the long-term evolution of virus in these hosts (43, 66). Based on partial sequencing of the gene for the major capsid protein, 24 virus genotypes have been identified, with few exceptions, within warthog burrows in East and Southern Africa (67–69). Some virus genes may have evolved to facilitate replication and transmission in this cycle; for example, the virus protein CD2v/EP402R is responsible for virus particle attachment to red blood cells and enhances virus uptake and replication in ticks (70). In general, countries where this sylvatic cycle occurs have a higher diversity of genotypes circulating within the domestic pig value chain (43), probably owing to occasional spillover from the sylvatic cycle. In contrast, virus incursions to other areas in West Africa and to other continents have involved only genotypes I and II. In these areas, the genetic diversity among isolates collected over long time periods and from different geographical regions is very limited (68, 71).

VECTORS FOR AFRICAN SWINE FEVER VIRUS

Vector competence is defined as the physiological ability of a vector organism to acquire, maintain, and transmit an infectious agent. Soft ticks of the *Ornithodoros* complex are the only species that act as competent vectors for African swine fever virus (ASFV). ASFV replicates in the *Ornithodoros moubata* species and can be transmitted between males and females of this species transstadially, transovarially, and between males and females transsexually. Ticks can be infected by feeding on infected suids and transmit to those hosts during feeding. *Ornithodoros erraticus* ticks acted as vectors for ASFV in southern Spain and Portugal, but in this tick species transovarial transmission has not been demonstrated. ASFV has been shown to replicate in other *Ornithodoros* species, and it is assumed that these could act as vectors if they come into contact with susceptible suids. Soft tick species attach for feeding on hosts for a limited period and thus infest only those hosts, such as warthogs, which return to a suitable permanent home. In contrast, mechanical vectors do not support pathogen replication but may ingest the pathogen during feeding and spread this to other animals on which they feed.

Table 1 Epidemiological characteristics of different wild suid species with respect to African swine fever transmission (17, 18)

Epidemiological characteristics	Wild boar (*Sus scrofa*)	Bushpig (*Potamochoerus larvatus*)	Red river hog (*Potamochoerus porcus*)	Warthog (*Phacochoerus africanus*)	Giant forest hog (*Hylochoerus meinertzhageni*)
Geographical distribution	Europe and Asia	East and Southern Africa, Madagascar	Central Africa	African savannahs	East and Central Africa
Detected in natural populations	Yes	Yes	No	Yes	Yes
Natural resistance	No	Yes	Suspected	Yes	Yes
Natural mortality if infected	Yes	No	Unreported	No	No
Virus maintenance in natural populations	Yes	Unknown	Unknown	Only in presence of argasid ticks	Unknown
Horizontal transmission	Yes	Unknown	Unknown	No	Unknown

Several other African wild suid species are susceptible to ASFV infection but naturally resistant to the disease, including the giant forest hog (*Hylochoerus meinertzhageni*) and two species of *Potamochoerus*, the red river hog (*Potamochoerus porcus*) and bushpig (*Potamochoerus larvatus*) (17). However, their role in ASFV transmission has been insufficiently studied (see **Table 1**).

2.2.2. Eurasian wild boar. After the first introduction of ASFV Genotype I to Europe during the 1960s, the seroprevalence reported in wild boar in Mediterranean habitats ranged between 0.5% and 10.5% (72, 73). At the time, it was thought that wild boar were unable to maintain the virus within their populations in the absence of reinfections through contacts with infected domestic pigs. However, several important lessons have been learned since the incursion of ASFV into Georgia in 2007, some of which contradict these initial conclusions. Firstly, because 95% of the cases reported in the European Union since 2014 have occurred in wild boar populations, it is now clear that the virus, depending on ecological context, may be able to persist in wild boar populations without reintroduction from infected domestic pigs. Secondly, the transmission between individuals results in a slow rate of spread, ranging between 1.5 and 5 km/month, depending on the local wild boar densities (27, 74, 75). Thirdly, ASFV can persist in wild boar carcasses and the surrounding environment for months, retaining the ability to infect other susceptible suids (76). ASFV can remain infectious in stagnant water from 50 to 176 days (27). The behavioral response of wild boar to exposure to carcasses of their own species varies: Carcass consumption has been reported in Spain (77) but not in Germany (76). The role that carcass consumption between sympatric species can play in Africa is unknown, although tropical temperatures and scavengers will shorten carcass and virus persistence.

The cold and moist climate found in Eastern and Central Europe during winter favors environmental persistence of the virus (78). Finally, the probability of contacts between wild boar and potential soft tick vectors of ASFV is considered negligible, as wild boar do not have permanent resting places that would be suitable for those endophilic ticks. In Portugal, *Ornithodoros erraticus* was found in farms using traditional pig housing (*malhadas antigas*) and very rarely in rabbit burrows surrounding those farms (79). In the Ukraine, *Ornithodoros verrucosus* was found only in burrows of snakes and small mammals and in limestone cliffs on riverbanks, with limited access to wild boar. Moreover, the distribution range of both tick species has greatly declined over the

last decades, probably owing to changes in pig production systems, the destruction of natural wild habitats, and the reduced spread of ticks to new areas (80, 81).

2.3. The Domestic Pig–Wildlife Interface

Interactions between domestic and wild or feral pigs can facilitate the transmission of ASFV in either direction. Transmission of the virus from domestic pigs to African wild suids has limited impact in terms of morbidity and mortality because the wild suids are naturally resistant to disease. However, these introductions may affect virus maintenance in naïve but resistant populations of wild suids. In any case, the introduction of the virus into new territories and species can have devastating effects, as has been observed in free-ranging populations of wild boar in Europe. It could have similar effects in local, and potentially endangered, wild suid populations in Asia (82), such as the babyrusa (*Babyrousa babyrussa*), the Visayan warty pig (*Sus cebifrons*), or the Malaysian bearded pig (*Sus barbatus*).

Interactions between wild and domestic pigs can occur as a result of natural interactions or in response to human practices. Natural interactions involve contacts between live individuals, as a consequence of vector-borne transmission, or contacts with infected carcasses from wild or domestic individuals. Domestic pigs and wild suids tend to interact when both populations share the same habitat and when pig farms have low levels of biosecurity. Worldwide, wildlife habitat encroachment caused by human demographic growth, combined with the expansion of small-scale pig production and the fact that pigs are major crop raiders (83), facilitates interactions between domestic pigs and wild suids. In Eurasia, reported interactions between wild boar or feral pigs and domestic pigs are much higher because they belong to the same species, but also because for decades *S. scrofa* populations have been increasing. In Europe, the main drivers of interest of wild boar in domestic pig habitats are sexual attraction of males toward domestic sows, which occurs mainly in autumn, and food availability in periods of resource scarcity (84). *S. scrofa* is well distributed in Asia, and those interactions occur but are seldom reported in the literature (85). The level of contamination in the environment from infected wild boar carcasses increases the risk of spillover to domestic pigs.

Domestic pigs can become infected when soft ticks colonize pig pens and bite susceptible individuals. In Portugal, naturally infected *O. erraticus* were shown to maintain the virus for up to five years (86). Transmission to naïve pigs was observed at least one year after the initial disease outbreak. In Africa, there is limited evidence on the role of soft ticks in ASFV persistence and transmission in domestic pig areas (87). Interface zones in East and Southern Africa, where domestic pigs may share their habitat with warthogs and ticks, would allow for exchange of ASFV and ticks between sylvatic and domestic cycles (88). In Mozambique, tick populations in domestic and wild pig areas were found to be genetically distinct, suggesting tick exchanges between these cycles were infrequent. However, virus exchange was supported because a higher proportion of domestic pigs was positive for antitick antibodies in interface areas close to national parks, and high nucleotide identity was detected between viruses from the sylvatic cycle and those that caused outbreaks in domestic pigs (66). Some authors succeeded in collecting soft ticks from warthogs (25, 89–91), indicating warthog movements could be a pathway by which ticks can be moved from the sylvatic to the domestic cycle (2). In Europe, the potential role of mechanical vectors such as *Stomoxys* or *Tabanidae* in spreading ASFV is supported by the observation of seasonal peaks of ASF cases in pig farms during summer months (92).

Human practices can facilitate interactions between wild and domestic animals. The mismanagement of carcass offal by hunters or farmers in rural areas can act as an effective pathway for

ASFV transmission between wild and domestic populations in rural areas of Africa (63), Europe (85), and Asia.

3. CONTROL OF AFRICAN SWINE FEVER

The potential for spread within wildlife reservoirs and the domestic pig production cycle and across the interface between wildlife and domestic pigs must be understood and taken into account to develop effective integrated control strategies.

3.1. Control Strategies in Domestic Pigs

The strategies for controlling disease in domestic pigs varies depending on several factors, although some general principles apply, as described below.

3.1.1. General principles. Effective prevention and control of ASFV infection require input from a wide range of stakeholders involved in the pork food system. In this context, national animal health authorities have a key role in developing and implementing appropriate policy instruments, i.e., biosecurity regulations, surveillance strategies, and outbreak response policies (93). They are typically based on current understanding of the epidemiology of the disease but very often do not explicitly take socioeconomic or cultural factors into account. If this results in limited stakeholder acceptance, the policy instruments will be of poor effectiveness, which has been one of the reasons for the continuing spread of ASFV in many countries. The likely behavioral responses of stakeholders to policy instruments, as well as the possibility of feedback loops between different instruments, must be taken into account. As an example, if feeding of food waste is prohibited, farmers need to look for alternative sources of protein for their pigs. If these are too costly, they will be tempted to access illegal sources of food waste. In fact, as a result of increased demand for these alternative protein feeds, such as soy meal, their cost will increase and further add to the temptation to use illegal sources or discontinue pig farming temporarily or permanently. Furthermore, many pig-producing countries, including Vietnam and China, would have to import larger quantities of soy meal, which impacts their national balance of trade. Well-resourced veterinary services, specifically from high-income countries, are typically in a better position to coerce actors involved in the pork food system to comply with the various instruments included in the control and prevention policies. In contrast, low- to middle-income countries need to tailor their policy instruments by explicitly taking account of socioeconomic and cultural factors so that farmers and other actors along the pork value chain are incentivized to accept the policies and change their behaviors accordingly. Doing so requires, first, a sufficient understanding of the relevant socioeconomic factors and, second, knowledge about what incentives would work (94, 95). In most cases, neither is available, because the required social-science research has not been conducted, and the veterinary services do not have the technical capacity to take such factors into account when developing their policies.

Effective control and prevention require up-to-date information about the spatial distribution of different farm types, including the number of pigs each of these represent, and about the flows of pigs between farms, slaughterhouses, and markets. In reality, this information is available only for high-income countries, which means developing effective control and prevention policies is very difficult. The FAO has published several booklets that describe in detail contingency plans as well as strategies for detection and diagnosis of ASFV (96–98).

3.1.2. Role of vaccination in African swine fever control and prevention policies. Once vaccines become available for ASFV, their use must be embedded in an ASF control and prevention policy that is based on a sound understanding of ASF epidemiology within the local eco-social context, including human behavior–associated risk pathways and human behavioral responses to the different policy instruments. Vaccines will not replace the need to achieve behavior change among key actors along the pork value chain to effectively control the spread of ASFV. The reason is that, as with most animal diseases, achieving a sufficiently high vaccination coverage at the population level is impossible; with ASFV, that effect is even more severe owing to the extended survival period of the virus in pork products and the risk of reintroduction from other unvaccinated populations, indicating the virus will remain endemic. A significant danger is that due to the enormous socioeconomic impact of ASF in affected countries, policy makers will be tempted to allow the use of apparently promising vaccine candidates before their effectiveness has been evaluated thoroughly.

3.1.3. Financial compensation after culling. Levels and timeliness of financial compensation and connected socioeconomic factors will influence actors' willingness to report (95). This is one of the most important policy instruments available to regulatory veterinary authorities, and it is important for effective prevention, as well as to achieve early reporting of ASF cases. Such compensation must be based on a thorough socioeconomic analysis to prevent it from failing its objectives, because otherwise it may either economically incentivize farmers to tolerate outbreaks or prevent them from reporting suspect ASF cases for fear of economic losses. In most outbreaks, both types of behavior occur because the financial compensation policies are too broad and therefore do not consider the diversity of socioeconomic contexts within which farmers and other actors along the pork value chain operate.

3.1.4. Prevention. Given the widely demonstrated difficulties in controlling and eradicating ASF in affected countries, a major focus of veterinary authorities and the pork industry must be on preventing the introduction of ASFV into countries, regions within countries, and farms or local wild boar populations. Overviews of farm-level biosecurity measures in different countries and farm types have been published (99, 100). At a national level, border inspection activities should aim to prevent legal and illegal importation of infected live pigs, pork products, or food waste. Moreover, awareness campaigns targeting categories of people traveling between affected and non-affected countries or regions should aim to reduce risky anthropogenic behaviors. The likelihood that farmers and other important actors in the pork food system will implement effective biosecurity measures will depend on the specifics of the local socioeconomic context and on how well policy instruments are tailored to it (101). Experimental gaming methods involving local actors could be used to determine how behavior change can be achieved (102).

3.1.5. Surveillance for early detection. Control of ASF requires a surveillance system that detects ASF outbreaks as early as possible, as well as the ability to respond to outbreaks quickly and efficiently so that ASFV spread can be prevented and, ideally, eradicated. A key element of ASF control strategies is the early detection of infected domestic and wild pigs. This is important for any infectious disease, but even more so for ASFV, because the virus survives for extended periods in the environment and in pork products. Therefore, any onward spread prior to detection will have a major adverse impact on the ability to contain or stop spread.

The design of a sufficiently sensitive ASF surveillance system requires a sound understanding of the epidemiology within the local eco-social context, which then allows it to be risk based and therefore result in optimum use of usually limited financial and staff resources (103). Several

scientific reviews (23, 27, 35, 61, 99) demonstrate the vast knowledge about the different risk factors for ASFV spread. But their relative importance must be investigated locally, as it will vary between different local eco-social contexts. In comparison, it is actually easier to ensure that suitable diagnostic laboratory infrastructure is available, assuming access to qualified staff and adequate financial resources.

Both passive (observer-initiated) and active (investigator-initiated) surveillance system components may be used, but the passive component is of major importance for early detection in domestic and wild pigs (104). Passive surveillance is based on farmers, other actors involved in the pork food system, and anyone encountering potentially diseased wild pigs notifying the veterinary authorities of their suspicion. Active surveillance implies actively looking for infected or clinically diseased domestic and wild pigs and sampling legal and illegal live pig and pork imports at border inspection posts.

The effectiveness of passive surveillance for early detection of ASF depends on the willingness of different types of actors involved in the pork food system, particularly those who are able to observe pigs alive prior to slaughter, to report suspect cases. Among these, farmers are most important. They must, first, be able to recognize any suspected cases of clinical ASF as early as possible following introduction of infection to their pig herd and, second, be willing to report them immediately. Realistically, clinical symptoms in a single pig may not be sufficiently recognizable to catch a farmer's attention. They will more likely respond to several pigs presenting with the relevant symptoms. This is where the epidemiological transmission dynamics of ASFV within affected pig herds become important (35). The number of pigs that show symptoms will depend on the mechanism of introduction of the virus, i.e., whether multiple pigs became exposed simultaneously, such as through contaminated feed, or smaller groups of pigs became exposed through introduction of a single source, such as an infected pig. Experience from outbreaks in Europe and Asia indicates that farmers are likely to detect disease only two weeks or more after the first case (depending on the size of the herd, among other factors), once they notice unusually large numbers of pigs with clinical signs and an increase in mortality (105). This scenario applies in particular to single introductions, whereas simultaneous exposure to ASFV of multiple groups of pigs across a herd, such as through contaminated food waste, should result in farmers recognizing the disease earlier. Another factor is that farmers of herds in which moderate to high levels of mortality are normal will take longer to recognize the introduction of ASFV, and this may be more frequent in low- to middle-income countries. In countries with a well-resourced government veterinary service, in which the government collects carcasses of dead pigs, the government can incentivize farmers to report any suspicions by implementing routine random sample testing of carcasses for ASFV (106). The role of hunters in early detection has been described in detail (27, 61) and is not further discussed here.

Active surveillance in the domestic pig sector involves diagnostic testing of live or dead pigs for presence of virus primarily and antibodies secondarily, given the delay in the appearance of the latter post-infection (29, 96). In situations with endemic infection, antibody testing can be useful for elucidating disease dynamics and detecting emergence of new genetic variants of reduced virulence, but not for early detection purposes. Routine virus testing can become part of an active surveillance system for ASF, such as has been implemented in China for slaughterhouses, where a selection of pigs from every slaughter batch must be sampled. No data are available yet to demonstrate the utility of the approach. In addition, China has approved the use of ASF diagnostic testing by large pig farms, which some large commercial pig companies now use routinely. No data are available publicly that would allow assessment of the impact of this method on the ASF situation in China. It is also unclear how these policies are linked to the national policy and how

the consequences of detection of positive pigs will be managed. But clearly, these methods have potential to increase the probability of ASFV detection at the population level.

3.1.6. Response to an outbreak. Many publications recommend response strategies in the event of an ASF outbreak (97, 98). As with any disease control response, forward and backward tracing of potentially infected contacts is essential to identify the source and potential onward spread of infection. Unfortunately, these very important activities are very difficult to conduct in highly complex pork food systems, such as in Vietnam and China, but also in less intensive systems, such as in Africa, particularly when some contacts with transmission risk potential have an illegal or informal background. Establishing protection and surveillance zones with pig movement restrictions and associated ASFV search activities around an outbreak are other important parts of the response strategy. The decision making in relation to possible preventive culling of pigs at risk of infection is not straightforward, in terms of whether only pigs on the affected farm, only part (if any) thereof, or those on neighboring farms or within a given radius should be culled (107). These decisions must take account of epidemiological and eco-social considerations. If that has not been done, extensive culling can spread infection owing to farmers moving pigs before they can be culled. Furthermore, farmers and field staff conducting culling operations are likely to experience severe mental distress (108, 109). Given the multitude of epidemiological and eco-social factors that need to be considered, it is a major challenge for national and local disease control authorities, particularly in low- to middle-income countries, to develop an integrated, locally adapted perspective that can inform the design of an effective outbreak response policy.

3.2. Control Strategies in Wild Boar

In ASF-affected countries in the European Union, most ASFV incursions have occurred via introduction into wild boar populations, from an anthropogenic source or through infected wild boar movement. These infected wild boar populations provide a reservoir of infection for domestic pigs and will result in trade restrictions. In Belgium and the Czech Republic, where virus introductions were affecting exclusively wild boar populations at a single point, the following strategy was applied (8, 28): Initially, a zonation determining the infected zone, and surrounding buffer and control zones, was established as soon as possible. In the Czech Republic, the infected zone was physically isolated with fences to reduce the risk for natural spread of the disease in free-ranging wild boars and to delineate the restricted areas. Although there is no universal agreement with respect to the epidemiological suitability and cost-effectiveness of fences for ASF control in wild boar populations, it seems plausible that fencing could limit their movements and therefore present a barrier for spread of the virus. In the infected and buffer zones, feeding and hunting bans were established to cause minimal disturbance to the affected and at-risk populations. Effective wild boar carcass surveillance systems aimed at efficiently detecting and removing infected carcasses were promoted. In this process, all animals found dead were collected and rendered under strict biosecurity measures. In the control zone, strict wild boar depopulation strategies were recommended to reduce wild boar densities as much as possible with minimal disturbance. Collaborations with hunting communities and relevant authorities were instrumental throughout the process for achieving satisfactory results. These measures were implemented successfully in the Czech Republic, which was the first country to regain official freedom from disease, 19 months after the first incursion in June 2017. The EC is currently recommending these same measures for other EU countries. However, they cannot be transferred to any given country without major adjustments based on the ecological, epidemiological, and social context (**Figure 2**).

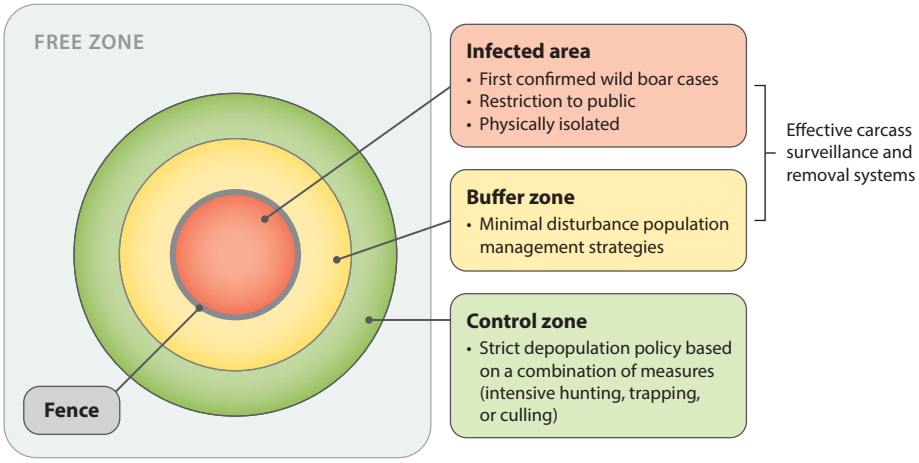

Figure 2

Schematic representation of wild boar management areas suggested at the beginning of an outbreak in a new territory. The size of the areas and the combination of measures to be implemented in each area require regular monitoring and updates, based on the progress of the epidemiological context. The fence indicated is a control strategy that could be used to both prevent movement of wild boars and delineate the restricted area.

3.3. Vaccine Development

The lack of a vaccine limits options for ASF control because vaccination is widely accepted as the most effective way to control infectious diseases (110). Outstanding successes have included the global eradication of smallpox and rinderpest (111–113). However, failures include attempts to control ASF via vaccination in Spain and Portugal, because the live attenuated strains used caused unacceptable chronic disease post-immunization.

3.3.1. Desirable criteria for African swine fever virus vaccines. An EC report and recent reviews summarize progress toward a vaccine and necessary steps still to be completed (114, 115). They concluded that good progress had been made but that a vaccine that could be used in the field would take several years. The desired characteristics for an ASFV vaccine, elicited by expert opinion (see **Supplemental Table 2**), include, most importantly, high efficacy in pigs of all ages and prevention of transmission of challenge virus, as well as safety in all age groups of pigs. A first-generation vaccine may not meet all of the other desired criteria but must meet the requirements of relevant regulatory authorities.

Supplemental Material >

3.3.2. Impact of vaccination on trade and diagnostic tests to distinguish infected from vaccinated animals. Reporting of ASF outbreaks, in disease-free regions, results in trade restrictions. Confirmation of freedom from disease is required to regain permission to export. Thus, a critical factor in the decision to vaccinate is the disease status of the region and whether a diagnostic test is available to confirm freedom from disease. In regions where freedom from disease is not an issue, vaccination may also be used to reduce the burden of disease and prevent further spread.

DIVA: differentiation of infected from vaccinated animals

So-called differentiation of infected from vaccinated animal, or DIVA, tests can be used to monitor vaccine effectiveness, as well as to confirm freedom from disease. The best DIVA tests detect an antibody response to infection but not to the vaccine strain, such as those used in vaccines for Aujeszky's disease (116). A DIVA diagnostic test may be used during the later stages of a vaccination

campaign, when eradication becomes the goal. Thus, an efficacious ASFV vaccine that prevents challenge virus replication and does not cause unacceptable clinical signs post-immunization is likely to be effective in many of the current epidemiological scenarios. Accompanying DIVA diagnostic tests may be developed and used later in the campaign.

3.3.3. Vaccination of wild boar populations. Use of vaccines aimed at wild boar populations results in additional requirements. First, the vaccines must be immunogenic after oral administration and sufficiently stable in the external environment to maintain potency when exposed to extreme environmental factors (115). Second, for an oral immunization scheme to be feasible, a suitable delivery device in the form of bait is needed (117). These baits must be stable; effective in reaching individuals of different sexes and ages; and traceable and safe for wild boar, as well as for non-target species and the environment. Meeting all these requirements in a marketable product will be challenging in terms of experimental studies and field trials, as well as costly and time consuming. However, vaccination has been used successfully to control classical swine fever disease in wild boar via delivery of live attenuated vaccine in baits. For this reason, the prospect for oral ASFV vaccination of wild boar using baits is considered good.

3.3.4. Vaccines for African swine fever virus: state of play. The complexity of the ASFV genome and virus particles has been a major factor in delaying vaccine development. Inactivated virus particles fail to protect against ASFV challenge (118, 119). Observations that pigs that recover from infection with less virulent isolates were protected against challenge with related virulent virus (120) showed that vaccination was possible and that live attenuated vaccines were most likely to be successful within a shorter time frame. Correlates for protection are poorly characterized, and depletion of $CD8^+$ cells showed that these are required for live attenuated virus–induced protection (121). Antibodies also have a role in protection (see sidebar titled Protective Immune Mechanisms) (122). The key virus antigens involved in protection have not been fully characterized.

3.3.5. Live attenuated vaccines. Several live attenuated ASFV vaccine candidates, either produced by passage in cell culture or naturally occurring (123, 124), induce good protection but

PROTECTIVE IMMUNE MECHANISMS

Immune responses correlating with protection against ASFV challenge are poorly understood. One study established that cellular immunity is likely to be essential for protection because antibody-mediated depletion of $CD8^+$ T cells abrogated the protection induced by a live attenuated strain. The types of cellular responses required for induction of protection have not been characterized. However, evidence suggests that antibodies also play a role because passive transfer of serum from protected to naïve pigs induced a delay in onset of clinical signs. Induction of high levels of natural killer cells also correlated with protection induced by a live attenuated strain. The antigens required to induce protection are poorly characterized. Protein targets for neutralizing antibodies have been identified, including p54/E183L, p30/CP204L, and p72/B646L. Recombinant proteins p54 and p30 induced protection in one study but not another. Neutralizing antibodies do not appear to be fully effective in protection, but it is unknown if other antibody-mediated mechanisms have a role. DNA vaccination with libraries of plasmids containing short DNA fragments induced protection from death in the absence of antibodies, although clinical signs and higher levels of virus replication after challenge were observed. Screening of pools of antigens expressed in viral vectors or delivered by DNA vaccination has been used to identify other potentially protective antigens.

cause unacceptable adverse clinical reactions, including a chronic form of disease in some vaccinated pigs. Increasing knowledge of the functions of ASFV-encoded genes has opened a route for targeted gene deletions to produce rationally attenuated ASFV vaccines.

Deletion of genes for inhibitors of the type I interferon response (125–129) results in attenuation of virulent virus and induction of protection against challenge, with little or no apparent replication of challenge virus. Importantly for the eventual commercial development of vaccines, deletion of these genes does not reduce virus replication in cells, so high titers can be obtained in culture.

Deletion of the ASFV gene for the adhesion protein CD2v has also been successful, at least in the BA71 genotype I genetic background. This resulted in attenuation and induction of protection against genotype I and genotype II strains (130). However, deletion of this gene from the virulent genotype VIII Malawi strain did not reduce fatality, although onset of clinical signs and virus dissemination were delayed (131). Deletion of the B119L (9GL) gene, a component of a redox pathway involved in virus assembly, reduced virus replication in macrophages but also resulted in virus attenuation and induction of protection in several virulent isolates. However, a genotype II virulent isolate was less attenuated (132, 133). In the latter case, deletion of a second gene, *DP96R*, was required to attenuate the virus sufficiently and induce protection (134).

Among the lessons learned is that the genetic background of the virus can affect the phenotype of virus gene deletion mutants. This probably reflects the varying redundancy of genes for inhibitory proteins in different virus genetic backgrounds. Thus, deletion of different gene combinations may be required to obtain attenuated vaccine candidates in varying genetic backgrounds. Vaccines that are cross-protective between ASFV genotypes will be required in countries where more than one genotype is circulating. The extent and correlates of cross-protection are poorly understood, although antibodies induced against the virus surface membrane protein EP402R/CD2v have been described as one correlate (135, 136).

3.3.6. Subunit vaccines. The development of subunit vaccines, defined as those that deliver a proportion of the virus, has lagged behind that of live attenuated vaccines owing to the need to identify potentially protective antigens. Recombinant proteins of p30/CP204L, p54/E183L, and CD2v/EP402R have been shown to confer partial protection in some studies. DNA vaccination with a library expressing multiple small-virus DNA fragments or pools of host-restricted or defective virus vectors (for example, Modified Vaccinia Ankara or human adenovirus) expressing ASFV antigens induced partial protection (115).

4. RESEARCH PRIORITIES

4.1. Control Strategies

The complexity and interconnectedness of eco-social systems around the world mean that it is very difficult to stop the global spread of ASFV, and the disease is likely to remain endemic in many of the currently affected countries and spread to new ones. Because China and Vietnam together keep approximately half of the world's pig population, the large epidemic in these countries has had an impact on the global pork food system in terms of supply and prices of feed, pigs, and pork products. Reliance on culling of all pigs on infected farms and potentially in-contact farms as a main control measure may be effective from a theoretical epidemiological perspective, but the practical impact of such a policy instrument will likely be compromised by the behavioral responses of those actors in the pork food system, particularly if their livelihood will be adversely affected.

Further, the processes associated with culling have a negative impact on pig welfare, the environment, and public opinion, in addition to resulting in loss of quality protein. It is therefore essential to develop ASF outbreak response policies that avoid small- or large-scale mass slaughter of domestic pigs or wild boar. Options include (*a*) containing the virus within quarantined areas of a farm and avoiding slaughter of uninfected animals; (*b*) slaughtering and processing products from pigs potentially exposed to AFSV at infected premises under conditions of adequate biosecurity; and (*c*) implementing measures to inactivate any potential virus, for example, by heat treatment of pork products. This protocol, if implemented reliably, would reduce risk of spread while still getting some value from the meat in areas where compensation is not possible. This was practiced during the ASF outbreaks in Cuba in 1980 (137). It is important to minimize the adverse impact of any outbreak response measures on actors in the pork food system to achieve the necessary level of risk reduction rather than adopting an unnecessarily precautionary approach. For example, the longer movement restrictions are in place on farms, the higher the density of pigs on the farm will become, causing animal welfare issues and costs to the farmer. The longer a slaughterhouse is closed, the longer pig traders and retailers will lose income, and pork prices will increase. If actors in the pork food system accept the proportionality of the outbreak response measures, they will be more likely to implement prevention measures and report suspected ASF cases.

The control and eradication measures for ASFV among wild boar populations in the Czech Republic, following presumed introduction at a single site, have apparently been successful and are also being used elsewhere. Strategies involving reduction of the wild boar population ahead of the epidemic are being applied in Poland, Germany, and France. A major outstanding challenge will be to monitor the distribution, density, and infection of wild suids in affected Asian countries and to limit their contact with domestic pigs. The scientific evidence base for the effectiveness of different types of ASFV control and eradication strategies in wild boar populations must be improved, while keeping in mind that the public is unlikely to accept the use of wild boar culling as a routine control and prevention measure. Epidemiological and economic analyses of the suitability of different approaches for establishing ASFV-free epidemiological entities, such as compartments or geographical zones, must be conducted. The dynamics and evolution of pork food systems in different eco-social contexts must be better understood. Further, policy options are needed for influencing the system's evolution such that the risk of infectious disease spread can be mitigated more effectively, instead of resulting in uncontrolled and unpredictable risk of disease emergence, as has been the case so far, particularly in low- to medium-income countries around the world.

4.2. Epidemiology

As discussed above, it is not understood how ASFV is being spread in complex pork food systems such as those in China and Vietnam. The transmission pathways and their interdependence and relative importance must be determined so that tailored control strategies can be developed. As part of this, social science research must be used to understand the role of the behavior of different actors involved in the pork food system, and if and how it can be changed. Further knowledge of the mechanisms by which ASFV persists and is transmitted in domestic pigs, wild suids, and vectors will help to ensure effective control during the predicted increased pork demand in Africa fueled by increased population growth, urbanization, and economic demand. Priorities are to define the boundaries of the warthog–tick sylvatic cycle, the drivers affecting the soft tick vectors' presence and distribution, the mechanisms of virus transfer from the sylvatic to the domestic cycle, and the exchanges and evolution of strains from the sylvatic cycle within the domestic pig cycle. In addition, the burden of ASFV infection and the role of other African suids in the epidemiology of the disease remain to be elucidated (85). In newly infected areas of Asia and Southern Europe,

further research is required to determine the distribution and susceptibility of wild suids and potential vectors. Knowledge is required on the competence of the different soft tick species and the mechanisms of ASFV persistence in and transmission by soft ticks. Identification of ASFV or tick markers to predict their competence in maintaining and transmitting virus is needed.

4.3. Vaccination and Other Tools for Control

More basic understanding in relation to topics such as virology, immunology, and pathogenesis is required to facilitate the development of vaccines and other tools for control. Pathogenic mechanisms associated with different ASF disease outcomes are also poorly understood and are particularly relevant in avoiding unacceptable clinical signs, such as the chronic form of disease, which can be induced by some live attenuated viruses.

4.3.1. Next steps in vaccine development. To progress promising live attenuated vaccine candidates to commercial development, fine tuning of genes deleted is required to achieve optimal safety and efficacy. Immune correlates for protection should be identified to facilitate evaluation of candidates. Genes coding for immunogenic proteins that can be modified or deleted to create targets for DIVA diagnosis must be identified. Scale up in a commercial environment must be established, as well as larger-scale safety and efficacy testing carried out prior to vaccine registration and licensing. This is likely to take several years. To develop subunit vaccines, further research is needed to identify key antigens involved in inducing protective cellular and antibody responses. This would help to improve efficacy and identify a gene format that could be commercially developed. In the longer term, this approach could lead to safer vaccines, particularly for use in the domestic pig sector in countries where disease is endemic.

4.3.2. Alternative control tools. Additional tools to enhance the effectiveness of current control strategies must be considered. These include treatment of clinical disease by small-molecule antivirals. Several antivirals are effective in reducing ASFV replication in cell culture (138–140), but none have been tested in pigs. The proposed use of antivirals for transboundary animal diseases is to reduce virus replication and thus the virus load in the event of disease outbreaks.

Gene editing could produce ASFV-resistant pigs. This approach has been used to produce pigs that are resistant to porcine reproductive and respiratory syndrome virus infection by inactivating the CD163 gene coding for the virus receptor (141). Classical swine fever virus–resistant pigs were produced by inserting small hairpin interfering RNAs targeting parts of the virus genome (142). Understanding the mechanisms of natural resistance to the virus may help to identify genetic determinants that could be transferred to domestic pigs to make them resistant to ASFV. This approach has potential to aid control in farming sectors with a structured pig breeding system but is not appropriate for disease control in wildlife.

SUMMARY POINTS

- African swine fever virus can cause death in a large proportion of infected pigs and wild boar.
- The continuing and currently unstoppable spread through the global pork food system represents a major threat to global food security.

- The African swine fever virus is a complex DNA virus in its own virus family, and neither a vaccine nor a treatment against the disease is available.
- A permanent reservoir of African swine fever virus is present in a wildlife cycle in South and East Africa.
- The main drivers of global African swine fever virus spread include the characteristics of pork food systems, including pig density; farm size distribution and biosecurity; socioeconomic drivers; behavior of actors in the pork food system; and the effectiveness of, and stakeholder trust in, veterinary services.
- In some countries in Northern Europe, ASFV is maintained almost entirely in wild boar populations, where it spreads via contact between infected animals, as well as through infected carcasses and environmental contamination.
- Current ASF control and prevention policies are tailored mainly to high-income countries' eco-social conditions and are of only limited effectiveness in low- to middle-income countries, where the level of residual accepted risk after policy implementation can often be higher, given the importance of other socioeconomic factors.

FUTURE ISSUES

- Better understanding of virus–host interactions, including mechanisms of immune evasion, is required at the molecular, cellular, and whole-animal level to facilitate vaccine development and other control tools.
- Correlates for protection and pathogenesis should be identified to evaluate candidate vaccines and predict pathogenesis of circulating strains.
- The role of vectors and wild suids in transmission of African swine fever virus should be further studied.
- The relationship between the evolution of pork food systems and infectious disease risk (including African swine fever) must be better understood based on interdisciplinary research, so that preventive measures can be taken.
- The epidemiological and eco-social impact of different outbreak response policies must be evaluated within relevant local contexts, so that policy makers can make an informed policy choice that achieves the necessary level of risk reduction (proportionate response), rather than opting for a precautionary policy instrument that will affect, or may be perceived as unfairly adversely affecting, only selected actors in the pork food system.
- Control policies that avoid mass culling of domestic pigs and wild boar should be evaluated.

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2. Provides the first description of African swine fever disease in pigs.

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RELATED RESOURCES

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