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Review

African swine fever: how can global spread be prevented?

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African swine fever (ASF) is a devastating haemorrhagic fever of pigs with mortality rates approaching 100 per cent. It causes major economic losses, threatens food security and limits pig production in affected countries. ASF is caused by a large DNA virus, African swine fever virus (ASFV). There is no vaccine against ASFV and this limits the options for disease control. ASF has been confined mainly to sub-Saharan Africa, where it is maintained in a sylvatic cycle and/or among domestic pigs. Wildlife hosts include wild suids and arthropod vectors. The relatively small numbers of incursions to other continents have proven to be very difficult to eradicate. Thus, ASF remained endemic in the Iberian peninsula until the mid-1990s following its introductions in 1957 and 1960 and the disease has remained endemic in Sardinia since its introduction in 1982. ASF has continued to spread within Africa to previously uninfected countries, including recently the Indian Ocean islands of Madagascar and Mauritius. Given the continued occurrence of ASF in sub-Saharan Africa and increasing global movements of people and products, it is not surprising that further transcontinental transmission has occurred. The introduction of ASF to Georgia in the Caucasus in 2007 and dissemination to neighbouring countries emphasizes the global threat posed by ASF and further increases the risks to other countries.

We review the mechanisms by which ASFV is maintained within wildlife and domestic pig populations and how it can be transmitted. We then consider the risks for global spread of ASFV and discuss possibilities of how disease can be prevented.

Keywords: African swine fever; molecular epidemiology; transmission; arthropod vectors; pigs

1. AETIOLOGY

African swine fever (ASF) is caused by a large, double-stranded DNA virus, African swine fever virus (ASFV), which replicates predominantly in the cytoplasm and is the only member of the Asfarviridae family, genus *Asfivirus* (Dixon *et al.* 2005).

2. HISTORY AND DISTRIBUTION

ASF was first described in Kenya in the 1920s as an acute haemorrhagic fever which caused mortality approaching 100 per cent in domestic pigs. It was noted that disease outbreaks occurred when domestic pigs came into close contact with wildlife species, particularly warthogs (*Phacochoerus aethiopicus* and *Phacochoerus africanus*). The source of the infection was identified as a virus carried by warthogs which did not show clinical disease (Montgomery 1921). Following these early descriptions, ASF has been reported in most sub-Saharan African countries. Initial reports were from countries in East and southern Africa where the virus is recognized to have been present in its wildlife hosts for a very long time (reviewed in Penrith *et al.* 2004). However, the disease has spread through central and West Africa and was introduced to Indian Ocean islands including Madagascar in 1998 (Roger *et al.* 2001) and Mauritius in 2007 (OIE WAHID 2009).

The first spread of ASF outside Africa was to Portugal in 1957 as a result of waste from airline flights being fed to pigs near Lisbon airport. Although this incursion of disease was eradicated, a further outbreak occurred in 1960 in Lisbon and ASF then remained endemic in the Iberian peninsula until the mid 1990s. In Spain, a species of soft tick, *Ornithodoros erraticus*, was identified as a vector and reservoir for the virus (Sanchez-Botija 1963) and, following this discovery in Europe, ticks of the *Ornithodoros* spp. which include *O. moubata*, *O. porcinus domesticus* and *O. porcinus*

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porcinus, were identified as vectors and reservoirs for the virus in Africa (Plowright *et al.* 1969).

Outbreaks of ASF were reported subsequently in a number of other European countries, including Malta (1978), Italy (1967, 1980), France (1964, 1967, 1977), Belgium (1985) and The Netherlands in 1986. The disease was eradicated from each of these countries but in Sardinia it has remained endemic since its introduction in 1982 (Plowright *et al.* 1994).

Cuba, in 1971, was the first country in the Caribbean region to report infection with ASF (Seifert 1996), and the virus was believed to have been introduced from Spain. ASF was further reported in the late 1970s in several Caribbean island countries—Cuba (1978, date of last occurrence 1980), Dominican Republic (1978, date of last occurrence 1981), Haiti (1979, date of last occurrence 1984; Wilkinson 1989). ASF was reported in Brazil in 1978 and was probably introduced from Spain or Portugal through food waste carried by transcontinental flights and/or animal products imported by tourists (Lyra 2006). The date of the last reported occurrence was 1981.

In 2007, further transcontinental spread of ASF occurred with the introduction of ASF to Georgia in the Caucasus region. Delays in recognizing ASF resulted in its widespread distribution to neighbouring countries, including Armenia, Azerbaijan and several territories in Russia. The Russian epidemic has since been reported from the territories of Chechnya, North Ossetia-Alania, Ingushetia, Orenburg, the Stavropolskiy Kray (Stavropol), the Krasnodarskiy Kray (Krasnodar) and now further westwards into the Rostovskaya Oblast, which has common borders with the Ukraine. The reports of infection in wild boar on several occasions will complicate eradication (Beltran-Alcrudo *et al.* 2008; OIE WAHID 2009).

3. IMPACT OF AFRICAN SWINE FEVER

ASF has a severe socio-economic impact, both in areas where it is newly introduced and where it is endemic. The high impact is most apparent in countries with a significant commercial pig industry. In Africa, ASF has potentially devastating effects on the commercial and subsistence pig production sectors, but the greatest losses are usually inflicted on the poorer pig producers who are less likely to implement effective prevention and control strategies (Edelsten & Chinombo 1995) or basic biosecurity. The farmers also often lack financial resources to restart production in the absence of compensation schemes. In countries such as Cote d'Ivoire and Madagascar, the introduction of ASF resulted in the loss of between 30 and 50 per cent of the pig population (El Hicheri *et al.* 1998; Roger *et al.* 2001).

ASF also has serious implications for food security, as pig production is an important source of human dietary protein in many countries, particularly in areas where beef production is difficult. Pigs very efficiently convert food waste and agricultural by-products into high quality protein and they have a relatively short production cycle.

The introduction of ASF into countries outside Africa has had similarly dramatic impacts. In addition to high mortality rates, ASF infection results in the loss of status for international trade and the implementation of drastic and costly control strategies to eradicate the disease. In Cuba, the introduction of the disease in 1980 led to a total cost, including the eradication programme, of US $9.4 million (Simeon-Negrin & Frias-Lepoureau 2002). In Spain, the final 5 years of the eradication programme alone were estimated to have cost US $92 million (Arias & Sanchez-Vizcaino 2002). Given the effect on pork production and trade as well as the costs of eradication, it has been estimated that the net benefit of preventing ASF introduction in the USA amounts to almost US $4500 million: nearly 5 per cent of the value of total sales of pork products (Rendleman & Spinelli 1994).

4. EPIDEMIOLOGY OF AFRICAN SWINE FEVER

Transmission and maintenance of ASFV can occur in a sylvatic cycle and/or in a domestic pig cycle. A range of wild and domestic pig species are susceptible and different tick vector species can be involved. Depending on the presence or absence of wild suids and arthropod vectors and the type of pig production system, the epidemiology varies substantially between countries, regions and continents.

(a) *Sylvatic cycle*

The role of wild pigs in the epidemiology of the disease is well described for warthogs in East and southern Africa (Thomson 1985; Wilkinson 1989; Plowright *et al.* 1994), but information is scarce for other African regions and for other wild pig species (Jori *et al.* 2007). Horizontal or vertical transmission is not thought to occur between warthogs and maintenance of the virus is dependent on a sylvatic cycle involving soft ticks of the *Ornithodoros* spp. (Plowright *et al.* 1994). Young warthogs become infected when bitten by resident infected *O. moubata* ticks while still in the burrow and develop a transient viraemia lasting two to three weeks. This is sufficient to infect ticks feeding on viraemic individuals (Thomson *et al.* 1980). Studies in eastern and southern Africa showed that infection rates of free-living warthogs were rarely below 80 per cent in areas where the tick vector was present (Plowright *et al.* 1994).

In West Africa, the existence of a sylvatic cycle has never been demonstrated, except for a single record of *Ornithodoros* spp. in a warthog burrow in Sierra Leone (Penrith *et al.* 2004). Studies in Senegal and the surrounding countries did not find argasid ticks in warthog burrows (Vial *et al.* 2007) and there is no evidence for ASFV circulation in warthog populations in West Africa (Taylor *et al.* 1977).

Bushpigs (*Potamochoerus larvatus*) occur in most of sub-Saharan Africa and Madagascar, but their role in the epidemiology of ASF remains largely unexplained. Their involvement as free-living hosts of ASFV has been demonstrated under experimental (Anderson *et al.* 1998; Oura *et al.* 1998) and natural conditions in eastern (De Tray 1963), southern (Mansveld 1963) and West Africa (Luther *et al.* 2007*b*). When challenged with ASFV, bushpigs develop sufficient levels of viraemia to infect *Ornithodoros* spp. ticks and susceptible domestic pigs. However, they do not show clinical signs and seem to require higher levels of virus than domestic pigs to become infected

(Anderson *et al.* 1998). Bushpigs have been suspected to be reservoirs of ASFV in areas where domestic pigs became infected in the absence of warthogs in Malawi (Haresnape *et al.* 1985). Evidence of infection has been identified repeatedly by virus isolation in East and southern Africa (De Tray 1963) and by polymerase chain reaction (PCR) in the Democratic Republic of Congo (DRC; L. K. Mulumba-Mfumu, personal communication) and Nigeria (Luther *et al.* 2007*b*). In Africa, other infected wildlife reservoirs, such as the giant forest hog (*Hylochoerus meinertzhageni*), have been reported occasionally (Thomson 1985) but their role is currently considered negligible (Penrith *et al.* 2004).

Wild boar (*Sus scrofa*) and feral pigs are susceptible to ASFV and show similar clinical signs and mortality to domestic pigs. Evidence of ASFV infection in wild boar was reported from the Iberian Peninsula (Wilkinson 1984; Arias & Sanchez-Vizcaino 2002), Sardinia (McVicar *et al.* 1981; Laddomada *et al.* 1994; Mannelli *et al.* 1997) and most recently in Russia (OIE WAHID 2009). In areas where domestic pigs were free of the disease, very low prevalence or absence of seropositive wild boars was reported (Perez *et al.* 1998) suggesting limited persistence of the virus in wild boar populations without contact with infected domestic pigs (Laddomada *et al.* 1994; Perez *et al.* 1998; Ruiz-Fons *et al.* 2008). Given the recent development in the Caucasus region and the current situation in Sardinia further research is needed to elucidate the competence of wild boar to act as infection reservoir, and needs to consider potential differences in virulence of ASFV strains.

Infected *Ornithodoros* ticks are able to retain the virus for long periods and transmit it to susceptible hosts. Their role is therefore mainly to maintain ASFV in an area. In most eastern and southern African countries, and in some countries of central Africa, ASFV is transmitted by ticks of *Ornithodoros* spp. (Plowright *et al.* 1994). In addition, members of *Ornithodoros* spp. can transmit ASFV from tick to tick through transstadial (Hess *et al.* 1989), sexual and transovarial transmission (Plowright *et al.* 1970) allowing the virus to persist even in the absence of viraemic hosts.

Argasid ticks are common in pig pens in Africa and the Mediterranean (Wilkinson *et al.* 1988; Haresnape & Wilkinson 1989). In some parts of Spain a significant association was found between the presence of *O. erraticus* and the occurrence of outbreaks (Perez-Sanchez *et al.* 1994). *Ornithodoros erraticus* ticks can maintain the infection for four months after their last blood meal (Sanchez-Botija 1963). In addition, adults and large nymphs can survive for periods of up to 5 years or longer when they are able to occasionally feed on pigs, leading to a possible long-term maintenance of the virus (Oleaga-Perez *et al.* 1990). The presence of ASF was seen to decrease only as the tick populations became extinct because of absence of hosts over an extended period of time (Oleaga-Perez *et al.* 1990). The role of the tick as a long-term reservoir was suggested in Portugal when, in 1999, ASF re-emerged on a farm that had been affected previously and infected ticks were found on the premises.

Five other *Ornithodoros* species have been experimentally infected with ASFV. Four of these are in North America and the Caribbean Basin: *O. coriaceus*; *O. turicata*; *O. parkeri* and *O. puertoricensis* (Hess *et al.* 1987) and *O. savignyi* (Mellor & Wilkinson 1985) which occurs in desert areas of North Africa. Moreover, *O. sonrai*, which is present in West Africa, and *O. tholozani*, which is present in parts of North Africa, the Caucasus region and parts of Asia are also potential vectors for ASFV (Vial *et al.* 2007). Transmission by other blood-sucking invertebrates such as lice, mites, flies and ixodid ticks has not been demonstrated (Mellor *et al.* 1987).

(b) *Domestic pigs*

Most isolates of ASFV cause an acute haemorrhagic fever in domestic pigs which results in mortality approaching 100 per cent within 8–12 days post-infection. The onset of viraemia is observed from 3 days post-infection and can rise to a peak of over 10^8 HAD (haemadsorption units)$_{50}$ ml^{-1}. Moderately virulent isolates and low virulent isolates have also been described and recovered pigs can remain persistently infected for periods of 6 months or more (Wilkinson 1984; Oura *et al.* 2005). Recovered pigs may transmit virus to uninfected pigs either directly or through ingestion of infected pork products.

Transmission through direct contact between domestic pigs can occur for up to 30 days after infection, or for eight weeks in the case of contact with blood products, e.g. during fighting or mating (Wilkinson 1989). Moreover, ASFV can persist in tissues for several months and the exposure of domestic pigs to poorly disposed-of carcasses or the feeding of frozen or insufficiently cooked or cured pork products can result in infection (Wilkinson 1989). ASFV has been shown to survive for 30 days in pepperoni and salami sausages, and for more than 100 days in Iberian-cured pork products and Parma hams (Farez & Morley 1997). ASFV can persist in the environment for several days. For example, contaminated pig pens in the tropics were shown to remain infectious to domestic pigs for 3 days, but not for 5 days (Montgomery 1921). The resistance of virus to inactivation (Wilkinson 1989) means transmission by fomites, such as clothing, equipment and vehicles, is a risk.

(c) *Transmission between the sylvatic cycle and domestic pigs*

Infection through direct contact between domestic pigs and warthogs has not been observed and transmission from warthogs to domestic pigs is largely dependent on ticks of the *Ornithodoros* spp. Adult warthogs may transport infected *Ornithodoros* ticks from the burrow to areas used by domestic pigs, exposing them to ASFV (Horak *et al.* 1983; Thomson *et al.* 1983). Alternatively, domestic pigs that feed on, or are fed ASFV-contaminated warthog carcasses or come in contact with warthog faeces could become infected (Thomson *et al.* 1980). This transmission route is perhaps more important for wild suids such as bushpigs

or giant forest hogs, which do not live in burrows (Roger *et al.* 2001) and their contact with *Ornithodoros* ticks is likely to be accidental. In addition, bushpigs have experimentally been shown to transmit ASFV to domestic pigs by direct contact (Anderson *et al.* 1998) and, as these animals can be common in areas of cultivation (Vercammen *et al.* 1993), this route may also be of epidemiological significance. Wild boar are clinically affected by ASFV in a similar manner to domestic pigs, hence where free-ranging domestic pig and wild boar populations overlap, both should be considered in epidemiological investigations.

Where ASFV-infected *Ornithodoros* ticks and wild suids occur, they present a potential risk to domestic pigs. However, in several ASF-endemic areas of Africa, the available evidence suggests that transmission of ASF from wildlife reservoirs and/or between pigs by *Ornithodoros* ticks is relatively unimportant in the maintenance of the disease in domestic pig populations. In these areas it is expected that factors enabling pig-to-pig transmission are important in allowing the disease to persist. The evidence for the relative importance of transmission from wild suids or argasid ticks is presented in tables 1 and 2.

5. MOLECULAR EPIDEMIOLOGY OF AFRICAN SWINE FEVER VIRUS

Advances made in molecular typing methods have contributed considerably to improved understanding of the epidemiology of ASF. The ASFV genome varies in size between 170 and 190 kb, depending on the isolate, and encodes between 160 and 175 genes. Most genome length variation results from insertions and deletions of members of different multigene families that are located close to the genome termini (Chapman *et al.* 2008). Differentiation between ASFV isolates relies on genetic methodologies. Early comparative studies used restriction fragment length polymorphisms (RFLPs; Wesley & Tuthill 1984; Vinuela 1985) but these methods have now been replaced by PCR amplification and nucleotide sequencing.

RFLP analyses demonstrated that outbreaks in domestic pigs in Europe, the Caribbean and Cameroon in West Africa between 1957 and 1986 were closely related, indicating that the disease had spread over several continents, probably because of a single introduction from a wildlife source in Africa into domestic animals (Wesley & Tuthill 1984; Vinuela 1985). Viruses isolated from pigs in Malawi between 1982 and 1989 were also closely related (Sumption *et al.* 1990). In contrast, ASFV isolates from soft ticks collected from warthog burrows over a 2-year period in four areas in Zambia showed considerable variation over the full genome (Dixon & Wilkinson 1988).

Phylogenetic analysis using different gene regions has made it possible to compare many more isolates (figure 1). The first such comparison, including a large number of viruses from many geographical origins, demonstrated that analyses of the *B646L* gene (encoding one of the major structural proteins, VP72), could successfully distinguish 10 major ASFV genotypes on the African continent—of which five corresponded to the geographical groupings distinguished by RFLP analysis (Bastos *et al.* 2003). The largest group comprised isolates from 24 countries in Europe, South America, the Caribbean and West Africa, the so-called ESAC-WA genotype or genotype I with a highly conserved *B646L* gene (Bastos *et al.* 2003). Nine other genotypes occurred in East and southern Africa where the sylvatic cycle occurs and provided evidence of spill-over from the sylvatic cycle to domestic animals. More detailed studies using the *B646L* gene region identified 13 genotypes in eight countries in East Africa. Significantly, genotype I, thought to be present only in the domestic pig cycle, was found in a sylvatic cycle in East Africa (Lubisi *et al.* 2005). In addition, a homogeneous pig-associated lineage linked outbreaks that had occurred in Mozambique, Zambia and Malawi over a 23-year period. In southern Africa, a further six novel genotypes were identified based on sequencing of the *B646L* gene, bringing the total number to 22 (Boshoff *et al.* 2007). As in East Africa (Lubisi *et al.* 2005), some genotypes in southern Africa were country-specific, while others had transboundary distributions (Boshoff *et al.* 2007). These data have clearly demonstrated that greater genetic variation occurs where the sylvatic cycle is present and that occasional transmission occurs between the sylvatic and domestic cycle in addition to long-term circulation of conserved viruses within domestic pigs.

Analysis of other gene regions was carried out to assist with outbreak tracing. Analyses of the central variable region (CVR) within the *B602L* open reading frame identified 12 differently sized products within the ESAC-WA genotype (Phologane *et al.* 2005). Sequencing from a larger set of isolates from this genotype (Nix *et al.* 2006) revealed 19 subgroups. The large conserved B646L genotype VIII, which defines virus causing outbreaks between 1961 and 2001 in four East African countries, was further characterized into seven discrete amino-acid lineages while a combined B646L–CVR analysis identified eight lineages (Lubisi *et al.* 2007).

The current approach for molecular discrimination is therefore to use the *B646L* gene for genotyping, and either sequencing the CVR of closely related isolates, or combined PCR of several other gene regions to distinguish sub-groups. This approach was used recently to reveal that the ASFV isolates introduced into the Caucasus and Mauritius were both genotype II (Rowlands *et al.* 2008; OIE WAHID 2009). Genotype II has been found circulating in domestic pigs in Mozambique, Zambia and Madagascar (Bastos *et al.* 2003, 2004; Penrith *et al.* 2007) and it is suggested that this virus may have been introduced to Georgia from infected meat taken from ships in the Black Sea port of Poti and being fed to domestic pigs (Beltran-Alcrudo *et al.* 2008).

6. REGIONAL PATTERNS, RISK FACTORS FOR SPREAD AND OPTIONS FOR CONTROL

(a) *Africa*

In endemic areas, spread at local level is often associated with free-ranging pig production, local pig

Table 1. The relative importance of the different transmission cycles in the maintenance of ASF in the domestic pig population in different countries of eastern and southern Africa.

country	Malawi	Zambia	Mozambique	Madagascar
endemic areas	Central region (Haresnape & Wilkinson 1989).	Eastern province (bordering endemic regions in Malawi). Outbreaks reported from other regions (Samui *et al.* 1996).	Regions close to Malawi and Zambia (Haresnape *et al.* 1988; Penrith *et al.* 2007). Outbreaks have been reported throughout the country (Penrith *et al.* 2007).	Throughout. First reported 1997.
presence of ticks	*Ornithodoros* spp. are widespread in the endemic area (Haresnape & Mamu 1986) and have been shown to be infected with ASFV (Haresnape *et al.* 1988).	*Ornithodoros* spp. were absent from pig pens in eastern provinces (Wilkinson *et al.* 1988).	*Ornithodoros* spp. present.	*Ornithodoros* spp. present.
maintenance of disease	Tick-to-pig and pig-to-pig transmission. Wild suids do not appear to be involved in the maintenance of the disease (Haresnape *et al.* 1985, 1988), although these were found to be infected with ASFV in eastern and southern Malawi (De Tray 1963; Mansveld 1963).	Pig-to-pig transmission. A Sylvatic cycle involving warthogs has been identified in national parks and surrounding areas (Wilkinson *et al.* 1988). Transmission from warthogs to pigs via ticks is unlikely, although roadside culverts might constitute a potential area of interface (Geigy & Boreham 1976; Wilkinson *et al.* 1988).	Pig-to-pig transmission cycles are probably more important than sylvatic cycles (Penrith *et al.* 2007). An association between disease and *Ornithodoros* spp. has not been identified in the endemic area (Penrith *et al.* 2004). A sylvatic cycle is suspected to be present in at least one wildlife zone (C. Quembo 2008, unpublished data).	Pig-to-pig transmission. Despite the potential for sylvatic and tick-to-pig transmission (Roger *et al.* 2001; Rousset *et al.* 2001), there is no evidence for involvement of ticks and/or bushpigs in epidemiology of the disease (Jori *et al.* 2007).
other information	In affected regions, high levels of seropositivity have been observed in apparently healthy animals (Haresnape & Wilkinson 1989).		Warthogs are typically limited to national parks and game reserves, and losses due to ASF are reportedly high in the buffer zones around such areas (Penrith *et al.* 2007).	The lack of biosecurity measures (Costard *et al.* 2008), trade patterns and behaviour of pig owners in case of suspicion of disease are likely to be very important for the transmission and dissemination of the virus.

Table 2. The relative importance of the different transmission cycles in the maintenance of African swine fever in the domestic pig population in various countries of western and central Africa.

country	Senegal	Nigeria	Cameroon
endemic areas	Casamance (Southwest region). First reported 1957.	18 affected states out of 26 (Luther *et al.* 2006). First reported 1997 (Odemuyiwa *et al.* 2000).	Southern provinces only (Awa *et al.* 1999). First reported 1982.
presence of ticks	Argasid ticks are not present in the southwest of Senegal. *O. sonrai* ticks were collected in 2006 from pig farms North of Gambia, and some were found to be infected with ASFV (Vial *et al.* 2007).	Occurrence of *Ornithodoros* spp. in animal burrows is unknown, although ticks were absent from domestic settings in northern and southern Nigeria (Hoogstraal 1956).	*Ornithodoros* spp. may be present in Cameroon (Hoogstraal 1956), but were found to be absent in an extensive survey of the main pig producing areas (Ekue & Wilkinson 1990).
maintenance of disease	Mainly pig-to-pig transmission, the role of ticks in epidemiology of the disease is considered limited (Vial *et al.* 2007). Warthogs are present in some areas but there is no evidence of their infection with ASFV (Jori *et al.* 2007).	Role of sylvatic reservoir unknown. Attempts to isolate virus from bushpigs and warthogs have been unsuccessful (Taylor *et al.* 1977), although ASFV genomic DNA detected in a warthog (Luther *et al.* 2007*a*), and a red river hog (Luther *et al.* 2007*b*).	Pig-to-pig transmission is most likely. Bushpigs (red river hogs) are present in endemic areas (Vercammen *et al.* 1993) but warthogs are absent (Ekue & Wilkinson 1990).
other information		Due to lack of implementation of a slaughter and compensation policy in the country, and given the widespread occurrence of the disease with potential involvement of sylvatic reservoirs, ASF is likely to become established as an endemic disease (Otesile *et al.* 2005).	Although the mortality rate in the initial 1982 epizootic was more than 80 per cent (Ekue & Tanya 1986), a variety of genetic isolates are now known to circulate. These have levels of virulence, and associated mortality, ranging from low (Ekue *et al.* 1989) to high (Ekue & Wilkinson 1999).

movements and lack of basic biosecurity measures. Many opportunities occur for contact within the marketing chain. Distances travelled can be considerable, often along watercourses as, for example, in the Democratic Republic of Congo. In other areas, such as in Madagascar and Senegal, traders travel between villages and collect pigs to bring to live animal markets or places of slaughter. Mixing of live animals at markets and during transport is frequent. In most rural areas, small local slaughtering facilities are poorly equipped and sewage, as a source of food, is directly accessible to other animals. Smallholder farmers often lack awareness in relation to ASF and its mechanisms of transmission. In Madagascar, many pig owners sell all their animals as soon as they suspect the presence of ASF (Randriamparany *et al.* 2005), thereby contributing to the maintenance and spread of the disease in some pig production areas.

Control measures in these epidemiological scenarios need to focus initially on the most important risk factors for spread of the disease, such as live animal markets, free-ranging domestic pigs, and farm visits by stakeholders in the production chain. In Madagascar, the government prohibited free-ranging pig production and live animal markets in the early 2000s in an attempt to reduce the risk of disease transmission but veterinary services lacked resources to achieve compliance with the regulations. Since such measures require changes in traditional farming and marketing habits, pig farmers are more likely to comply if they receive a meaningful benefit from these regulations and are involved in their development.

The presence of a sylvatic cycle in some endemic areas of Africa makes the control of ASF more difficult. South Africa has a declared ASF control zone where potentially infected warthogs and *O. porcinus* ticks occur (South African Department of Agriculture 2008). South of this boundary, which runs approximately east to west across the 24°52′ S line, the country is deemed free of ASF. Movement of pigs, warthogs and their products from the north of the country is controlled by permits. In the north, pig farming is only allowed where contact between domestic pigs and the sylvatic cycle is prevented by double-fence barriers and other biosecurity measures. A number of commercial farms exist in this infected zone and they are able to trade if they are recognized as compartmentalized production units according to OIE standards, and have never suffered any outbreaks of ASF. Limited outbreaks of ASF occur infrequently in this zone when pigs are not kept in confinement, and farmers are discouraged from keeping free-ranging pigs.

For transboundary spread, movements of infected pigs and pork products are considered very important (Haresnape 1984; Wilkinson 1984). Formal or informal cross-border trade of live pigs or pork products

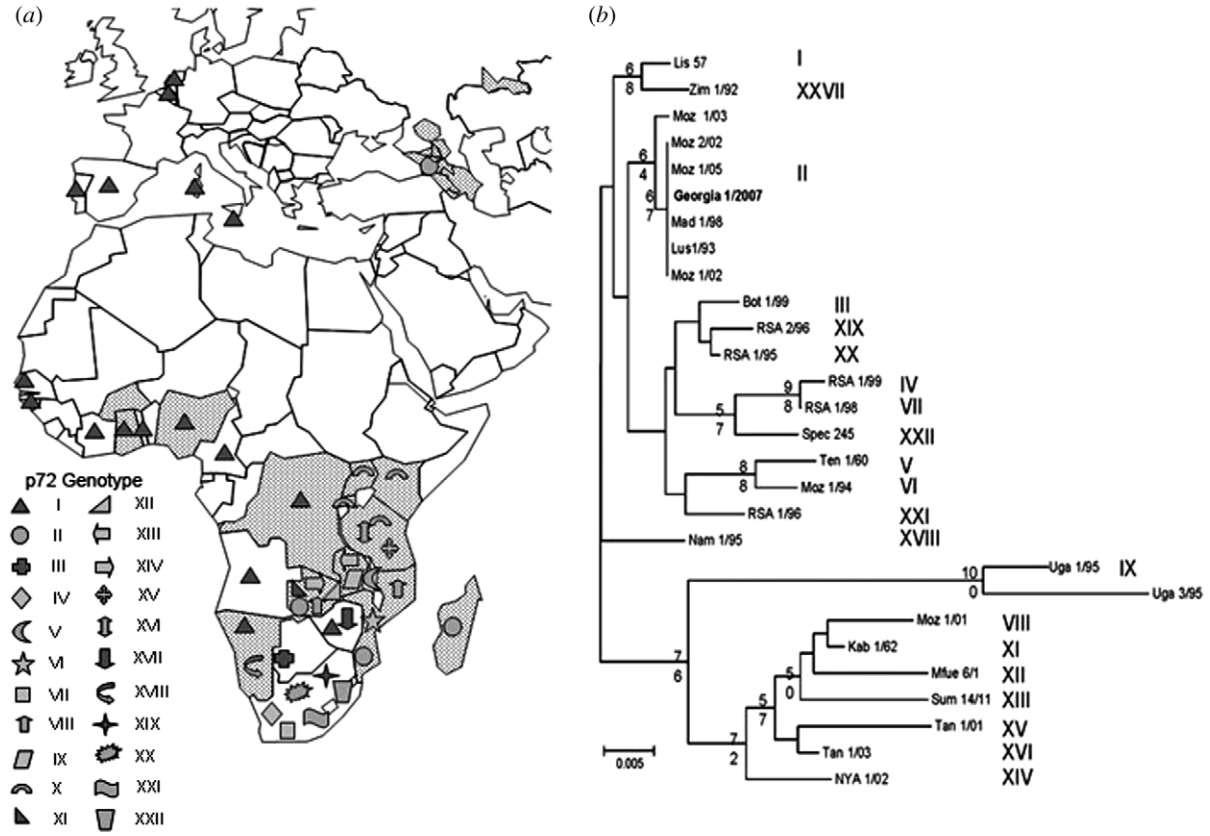

Figure 1. Distribution of African swine fever virus (AFSV) genotypes. (*a*) Map showing African swine fever (ASF) outbreaks between 2003 and 2008. Shading indicates a country within which an outbreak has occurred. Symbols represent ASF genotypes (determined by B646L (p72) sequencing) known to be in circulation within that country (Basto *et al.* 2003; Lubisi *et al.* 2005; Boshoff *et al.* 2007; Rowlands *et al.* 2008). (*b*) Phylogram depicting the *B646L* gene relationships of selected isolates representative of the 22 AFSV genotypes. Because all the Georgian isolates had identical nucleotide sequences, only one isolate is presented in the tree (in boldface). The consensus tree was generated from 1000 replicates; only bootstraps more than 50 per cent are shown. Genotypes are indicated in roman numerals. Moz, Mozambique; Lis, Lisbon; Zim, Zimbabwe; Mad, Madagascar; Bot, Botswana; RSA, Republic of South Africa; Spec, Spencer; Ten, Tengani; Nam, Namibia; Uga, Uganda; Tan, Tanzania; Kab, Kabu. Scale bar indicates number of nucleotide substitutions per site (Rowlands *et al.* 2008).

is likely to have resulted in the dissemination of disease from infected to neighbouring areas in Africa, either via direct contact with infected animals, or contact with contaminated fomites or pork waste. It needs to be recognized that in the absence of officially regulated trade, informal or illegal trade will be of particular significance (Zepeda *et al.* 2001). Transboundary spread also occurs through movements of infected wildlife such as warthogs and bushpigs, together with the soft tick vector. The distribution of the latter may be affected by climate change or by spread to new habitats via the movement of warthogs. The recent creation of transnational protected areas across Africa is thought to expand the available habitats for wildlife and facilitate movements of wildlife disease reservoir species across borders (Bengis 2005). Meat products from wildlife also pose a risk for ASFV dissemination (Bengis 1997).

(**b**) *Europe and the Caucasus*

Within the European Union (EU), strict import controls for animals, animal products and animal by-products have been put in place to mitigate the risk of highly contagious animal diseases. However, illegal or uncontrolled imports of pig meat products, either accidentally by tourists returning from endemic countries or, more importantly, intentionally by smuggling meat products for personal or commercial use, presents a continuous threat (Wooldridge *et al.* 2006). To mitigate the risk of infection for domestic pigs through exposure by swill feeding, EU countries have to comply with the Animal By-Product Regulation that was developed following the foot-and-mouth disease (FMD) outbreak in Europe in 2001 (European Union 2002). The absence of such regulations may have led to the introduction of ASF into the Caucasus region.

The history of ASF outbreaks in Europe highlights the factors affecting spread and the challenges for eradication. In regions with mainly housed commercial pig production, spread was successfully prevented in the past through strict animal movement control and implementation of culling policies. In contrast, extensive pig production systems with poor biosecurity facilitate the establishment of the disease in the first place, as was seen in Portugal and southwest Spain in 1960 (Bech-Nielsen *et al.* 1993*a*,*b*). The presence of soft ticks of the genus *O. erraticus* and the close contact of wild boar with domestic pigs further hindered efficient disease control in these areas (Sanchez-Vizcaino 1992; Perez *et al.* 1998). In the northeast of Spain, where intensive pig husbandry is

predominant, the disease spread quickly with devastating consequences for the whole production sector. However, in this part of the country control measures have proven to be more successful and with the introduction of a comprehensive national eradication programme in 1985, 96 per cent of the country was considered free of ASF within 2 years (Anon. 1990) and disease persisted only in the southwest of the country. Besides extensive monitoring activities, the eradication programme focused on improving biosecurity on farms, strict animal movement controls and increased disease awareness of pig farmers. In Sardinia, where the disease first occurred in 1978, endemicity is the result of extensive pig farming that has been practised for centuries (Firinu *et al.* 1988) and of the presence of endemically infected wild boar. Following an increase in reported outbreaks in 2004, the European Commission approved an eradication plan for Sardinia that includes targeted surveillance and control in high-risk areas for wild boar and domestic pigs, stricter enforcement of biosecurity and increased control of export of pig meat products (European Union 2005).

The importance of wildlife reservoirs for disease maintenance has been clearly demonstrated in the past and therefore the recent outbreaks in Georgia and the subsequent spread of the disease to Armenia, Azerbaijan and Russia (OIE WAHID 2009) are of great concern to the growing pig industry in many eastern European countries. The situation has been further complicated and control options made more difficult by the spread of the disease into the local wild boar populations (OIE WAHID 2009). Further west- or eastward spread could adversely affect the pig sector in many countries. For instance, the pig industry in the Ukraine is an important growing agricultural sector with massive foreign investments into large-scale pig farming. Backyard farms and free-ranging pigs seem to be limited; however, the presence of wild boar could lead to spread of ASF to Moldova, Romania, Hungary, Slovakia, Poland or Belarus.

(c) *East, Southeast Asia and Australasia*

Countries of eastern and austral Asia have never been affected by ASF. Because of the dependence of the national economies on livestock production-related export industries, New Zealand, Australia, Japan and South Korea have very effective sanitary regulations for pork and live animal imports and waste food disposal. Recent animal health emergencies (e.g. bovine spongiform encephalopathy—BSE, classical swine fever—CSF and avian influenza) convinced the Japanese and Korean governments of the need to further strengthen their veterinary services' capacity to deal with such outbreaks (Ozawa *et al.* 2006). As in other parts of the world, feeding of pigs with illegally imported animal products is a highly important pathway for entry of diseases such as FMD, CSF and ASF. This was acknowledged in an external evaluation of surveillance plans in New Zealand (Pearson 2002).

Although ASF has never occurred in Southeast Asia, introduction could result in massive losses, considering the importance of pig production and pork consumption in this part of the world. China holds nearly 50 per cent of the world pig population (den Hartog 2004), and its pork production is likely to keep increasing. Other Southeast Asian countries also keep significant pig populations, mainly for household consumption and local marketing. The risk of introduction of ASF into this region has increased recently through China's intensified trade and development aid links with African countries (Beuret *et al.* 2008), since some of these countries are endemic for ASF or have recently declared outbreaks (e.g. Nigeria, Zambia and Tanzania). Increases in demand for pork during Asian cultural events and festivals are likely to be accompanied by an increased risk of introduction and spread of infectious diseases such as ASF. Illegal import of animal products through Taipei International airport was also considered to be more likely during the period between Christmas and Chinese Lunar New Year (Shih *et al.* 2005).

In China, the high pig density and large proportion of small-scale pig producers create suitable conditions for the spread of infectious diseases. Large numbers of live animal movements and related products at the regional level have been reported to occur specifically along the southern Chinese borders (Rweyemamu *et al.* 2008), and these could lead to the spread of ASF within the region. The extensive free-ranging pig husbandry systems in large parts of Asia would complicate the implementation of control measures.

In addition, potential wild pig reservoirs of ASF exist in these regions. Southeast Asia is considered the origin of the *Sus* genus, with seven of the eight species being present and six considered to be endemic (Mona *et al.* 2007). This region, particularly the insular part, has the highest wild pig species diversity in the world (Lucchini *et al.* 2005). If susceptible to ASFV, these wild suid populations could become a reservoir of infection and, for the rare species, even accelerate their extinction. *S. scrofa*, with many subspecies in South and Southeast Asian ecosystems (Nowak 1991), could also become a reservoir. In Australia, large feral pig populations (*S. scrofa*) that are principally derived from introduced domestic pigs (Gibbs 1997) could potentially be involved in the spread and maintenance of ASF. Knowledge of Asian ticks, including soft ticks from *Ornithodoros* (*Alectorobius*) spp. (Brown *et al.* 2005) is scarce and studies are needed on their distribution, ecology and potential for disease transmission (Ahmed *et al.* 2007).

(d) *America*

In the USA and Canada, pork production has increased during the last decade (den Hartog 2004). USA is one of the top world pork import and export countries (FAS USDA 2006). The main threat to pig herds in these countries is the introduction of ASFV-infected pork products in waste food from planes and ships arriving from endemic countries. Similar to Europe, strict rules governing waste disposal (USDA 2009) reduce the risk of ASF introduction. In addition, efficient surveillance, tracing along supply and commodity chains, and strict control and prevention policies should allow early detection of

ASF outbreaks and slaughter of all animals from infected premises combined with compensation for affected stakeholders.

In some countries of South America, especially Brazil, animal production is developing rapidly and is supported by a well-organized breeding industry. In 2005, Mexico, Brazil and Chile were among the top world pork-exporting countries and Mexico was also among the top world pork-importing countries (FAS USDA 2006). Central and South America had ASF outbreaks in the 1970s and 1980s. In the Caribbean, ASF resulted in swine depopulation programmes that, in some cases, involved culling of the only livestock owned by low-income rural families. The less developed countries in this area are still exposed to the consequences of an introduction of AFSV through delayed detection owing to poorly effective surveillance systems and likely ineffective control in the absence of adequate funds. The occurrence of extreme climatic events and political instability or conflicts in countries such as Haiti (Chatterjee 2008; Nel & Righarts 2008) further weakens the veterinary infrastructure and capacity, and therefore facilitates the introduction and spread of exotic viruses such as ASFV.

Wild Tayasuidae (*Tayassu* spp.) indigenous in the Americas are not susceptible to ASFV (Fowler 1996). However, feral pigs are widespread in North and South America and the Caribbean Islands. This fact, together with the presence of argasid ticks in the Caribbean, has been a concern for the US (McVicar *et al.* 1981; Gibbs & Butler 1984). Nevertheless, ASF was controlled and eradicated from Hispaniola and Cuba despite the involvement of feral pigs (Simeon-Negrin & Frias-Lepoureau 2002).

7. VACCINE DEVELOPMENT

There is currently no vaccine available for ASFV, although there is no doubt that this is feasible. Protection can be achieved by inoculation of pigs with low-virulence isolates obtained by passage in tissue culture or by deletion of genes involved in virulence, as well as low-virulence isolates from the field (Lewis *et al.* 2000; Leitao *et al.* 2001; Boinas *et al.* 2004). The mechanism of protection involves cell-mediated immunity, since depletion of CD8+ T cells abrogates protection (Oura *et al.* 2005; Denyer *et al.* 2006). A role for antibodies in protection is also suggested since passive transfer of antibodies from immune pigs conferred partial protection to lethal challenge (Onisk *et al.* 1994). In experiments using recombinant proteins, partial protection was achieved using a combination of two proteins, p54 and p30, as well as with recombinant CD2-like protein (Ruiz-Gonzalvo *et al.* 1996; Gomez-Puertas *et al.* 1998). The failure to achieve complete protection in these experiments may be because of the delivery method of the antigens and/or because more or different antigens are required to confer protection.

Further research is required to develop effective vaccines. Identification of ASFV genes involved in virulence and in evasion of the host's immune response (for review see Dixon *et al.* 2008) makes the development of rationally attenuated vaccines through sequential deletion of these genes realistic. However, extensive testing of the safety of such vaccines is required before their use in the field. An alternative safer approach would involve the development of defective non-replicating ASFV vaccines. These approaches have the advantage that many antigens are expressed and no prior knowledge of which are protective is required; however, high containment facilities are required for vaccine production.

Alternative approaches based on expression of protective antigens are feasible but first require identification of those antigens. The development of high-throughput methods for constructing recombinant viral vectors opens a route for global analysis of the protective potential of all ASFV-expressed genes.

One concern about the use of ASFV vaccines is the genetic diversity of strains circulating in some countries. Recent experiments have demonstrated cross-protection between different genotypes and therefore it may be possible to develop vaccines which can cross-protect against infection with several genotypes. Moreover, in some regions isolates of just one genotype are circulating. These include countries in West and central Africa (genotype I), the large endemic region including Malawi and Zambia (genotype VIII) and the Caucasus and Russia (genotype II).

8. PREVENTING GLOBAL SPREAD

The review of the current situation in endemic regions, including insights gained through molecular epidemiology and lessons learnt from past outbreaks in non-endemic areas, highlight the complexity of ASF epidemiology. To combat ASF globally, surveillance and control need to be managed at three levels: (i) locally at points of occurrence; (ii) at regional level in endemic and adjoining areas; and (iii) globally by preventing transboundary and transcontinental spread through animal movement and products.

In the absence of an effective vaccine, direct and indirect pig-to-pig transmission and contact with wildlife reservoirs need to be limited in endemic areas to reduce disease burden. Increasing early detection would also improve the chances of disease control measures making them more effective. International agencies and donors should promote local capacity development, research activities including risk assessment, and regional coordination of emerging swine disease surveillance including ASF. For the implementation of control programmes in endemic or epidemic areas, tools for rapid detection would allow a timely diagnosis and ensure involvement at the local level in control. Lateral flow devices for detecting virus antigens have been used successfully in the global rinderpest eradication programme and have the potential for use in ASFV control. Other technologies including pen-side PCR tests could be used, although the equipment required may be more expensive.

Capacity building is also required to improve the ability of regional and national laboratories to confirm suspicious cases and to assist surveillance activities. For local control in countries with a large small-scale pig-holder population, educational programmes to

increase disease awareness and improved access to animal health services are required. In countries where the disease is endemic, where most pig owners are poor smallholders and where veterinary services lack resources to achieve compliance with regulations, the involvement of farmers is essential in the development of control strategies that will be applied effectively. In order to eradicate the disease in endemic areas, the role of wildlife reservoirs needs to be further investigated, including wild suids in Africa and wild boar in Sardinia and in the Caucasus. The distribution of *Ornithodoros* species in the Caucasus region and their capacity to act as vectors for ASFV also needs to be investigated.

The feasibility of creating ASF-free zones within an endemic area was shown in South Africa and should serve as an example for localized disease eradication and prevention that will benefit trade, and thereby generate incentives for producers to support large-scale eradication programmes. Achieving ASF freedom is only realistic when all stakeholders perceive clear benefits from such a status and therefore are likely to comply with the necessary prevention and control measures. Effective communication and involvement of all stakeholders at each stage of the process together with the support of national and international veterinary authorities is pivotal to the success of such programmes.

To prevent the spread of ASF at global level through movement of livestock, countries are advised to follow international standards as outlined by the World Organization for Animal Health OIE (OIE 2008). Strict regulations regarding animal by-products have proven effective in many developed countries and are critical given the high tenacity of the virus in meat products and in the environment. This has also been recognized by many developing countries. For example, following FMD outbreaks, the Philippines implemented an effective policy incorporating quarantine and control of waste food from ships and planes (Gleeson 2002). Comprehensive risk assessments are needed for all currently free countries with pig production relevant to farmers' livelihoods in order to identify which introduction pathways are most important and inform targeted or risk-based surveillance strategies.

Risk assessments are also needed in endemic countries to identify the main mechanisms for spread in the pig production chain and thus target control measures effectively. Data required for such risk assessments include density and geographical distribution of susceptible animal species—including feral and wild pigs—and any relevant arthropod vectors, as well as the structure of the pig production and marketing sector at national and regional level. The effectiveness of surveillance systems, early warning and early response capacity, existing policies for test-and-slaughter and other preventive measures need to be assessed. The level of international cooperation, political, commercial and tourism-related links are also important, as are the level of economic development and other issues such as cultural and religious events that may influence trade patterns (Shih *et al.* 2005). Data indicating potential sources of infection (e.g. ASF prevalence in export countries) should take into account the under-reporting of ASF outbreaks in endemic countries, in some cases associated with the economic development level of a country or political factors.

Lessons learnt from previous outbreaks and from outbreaks of similar diseases such as CSF in many countries worldwide should be considered when designing control programmes. Improved effectiveness of control also includes the need for continued research aimed at the development of an effective vaccine, since this may well have to be used together with other prevention and control measures in endemically affected countries.

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