

Combining livestock trade patterns with phylogenetics to help understand the spread of foot and mouth disease in sub-Saharan Africa, the Middle East and Southeast Asia

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Summary

International trade in animals and their products is recognised as a primary determinant of the global epidemiology of transboundary diseases such as foot and mouth disease (FMD). As well as causing serious production losses, FMD is highly contagious, being transmitted through multiple routes and hosts, which makes it one of the most important diseases affecting trade in livestock. Its occurrence has dramatic consequences for the agricultural economy of a normally disease-free country, as well as for the livelihoods and income generation of developing countries where the disease continues to be endemic. In the dynamic of FMD virus (FMDV) dispersal across the globe, phylogenetic inference from molecular sequences of isolated viruses makes a significant contribution to investigating the evolutionary and spatial pathways underlying the source of FMD epidemics. Matching data on livestock movement with molecular epidemiology can enhance our fundamental understanding when reconstructing the spread of the virus between geographical regions, which is essential for the development of FMD control strategies worldwide. This paper reviews the global situation of FMD in the last ten years, combining phylogenetic insights with information on livestock production systems and international trade to analyse the epidemiological dynamics of FMD and the sources of FMDV introductions at a regional level in sub-Saharan Africa, the Middle East and Southeast Asia.

Keywords

Foot and mouth disease – Livestock production system – Livestock trade – Middle East – Phylogeography – Southeast Asia – Sub-Saharan Africa.

Introduction

Foot and mouth disease (FMD) is the most contagious disease of domesticated and wild cloven-hoofed animals, caused by a virus of the *Aphthovirus* genus in the *Picornaviridae* family. Foot and mouth disease virus (FMDV) exists as seven different serotypes (O, A, C, Southern African Territories [SAT] 1, SAT 2, SAT 3 and Asia 1), which are not uniformly distributed across the

globe. The FMDV infection is maintained within three continental epidemiological clusters in Africa, Asia and South America that can be further subdivided into seven major virus pools (Fig. 1) (52). Multiple serotypes co-circulate and distinct patterns of virus evolution occur within each of the defined pools. Six out of the seven serotypes have been recorded in Africa (O, A, C, SAT 1, SAT 2, SAT 3), while in the Middle East and Asia only four serotypes (O, A, C, Asia 1) are normally present, although there have been periodic incursions of exotic serotypes

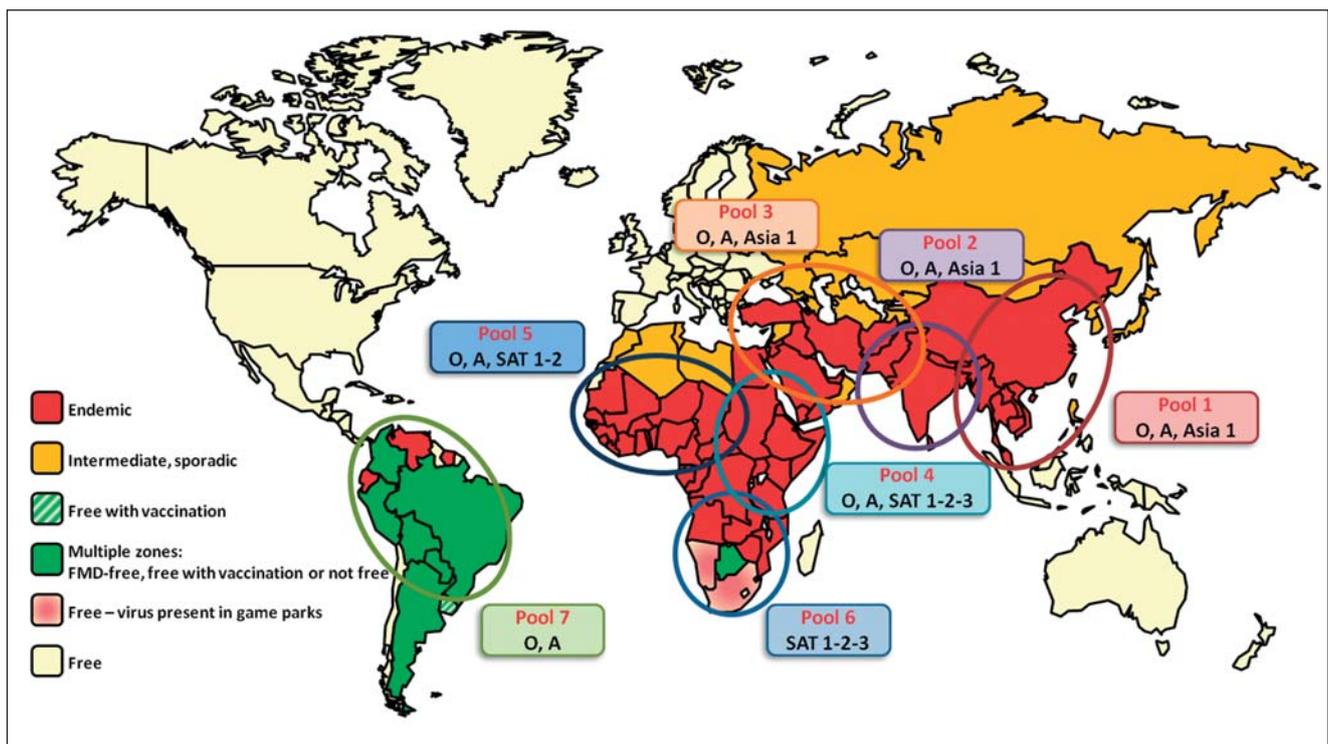


Fig. 1
Conjectured foot and mouth disease status in 2010 with regional foot and mouth disease virus pools and predominant virus serotypes

Modified from Paton *et al.*, 2009 (52)

from Africa into the Middle East. The FMDV serotypes have been subdivided into groups based on genetic distances in the virus protein 1- (VP1-) coding region (36, 56). These groups have been named 'topotypes' since they usually occur in defined geographic regions (56). The arbitrary cut-off for the division of these topotypes has been set at ~15% or ~20% nucleotide difference for the Eurasian and Southern African serotypes, respectively (56).

In some cases, within the topotypes, further subdivisions have been made, with named sub-lineages and even sub-sub-lineages, e.g. O/ME-SA/PanAsia-2^{ANT-10}. Eleven topotypes have been defined for serotype O (Fig. 2), namely:

- Cathay
- East Africa (EA) 1
- EA-2
- EA-3
- EA-4
- Europe-South America (EURO-SA)
- Indonesia (ISA) 1
- ISA-2
- Middle East-South Asia (ME-SA)
- Southeast Asia (SEA)
- West Africa (WA).

Only three topotypes each have been defined for serotypes A and C: namely, Africa, Asia and EURO-SA, while all Asia 1 viruses fall into a single unnamed topotype (Fig. 3). In Africa, the situation is more complex with 9, 14 and 5 topotypes being defined for SAT 1, SAT 2 and SAT 3, respectively; these are currently simply numbered, but more descriptive names have recently been proposed (40).

Although FMD does not usually cause high mortality in susceptible animals, it decreases productivity, which in turn significantly affects farmers' livelihoods. Since livestock are highly important in the agriculture-based economy and social structure of many countries, FMD has a serious impact on food security, rural income generation, and the national economy by impairing livestock trade (27). Transmission of FMDV most readily occurs during direct contact between acutely infected and susceptible animals, often following movement of infected animals. Indirect transmission is less common but can be effected through contaminated people or objects, especially through the consumption of contaminated animal products, such as meat, offal or milk, which may be fed to pigs or calves. Primary infection of ruminants is usually by the respiratory route, whereas pigs are more often infected by the oral route (15). Consequently, if the index case cannot be attributed to the movement of infected animals, then in pigs the most probable source is an infected animal

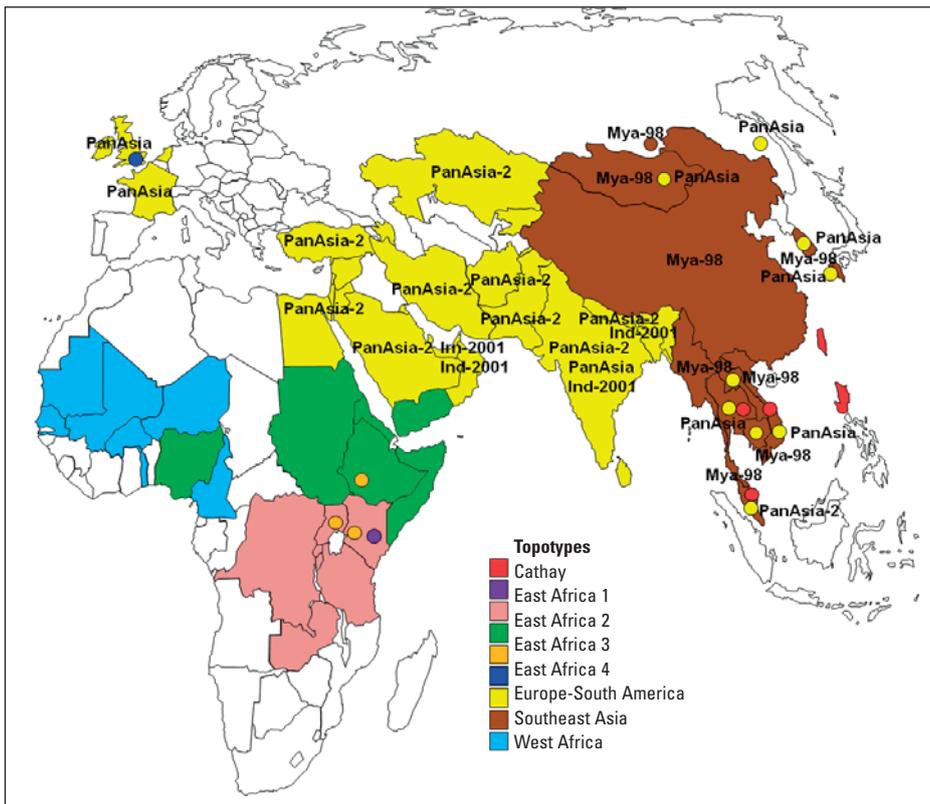


Fig. 2
Serotype O foot and mouth disease virus topotypes: distribution in sub-Saharan Africa, the Middle East and Southeast Asia

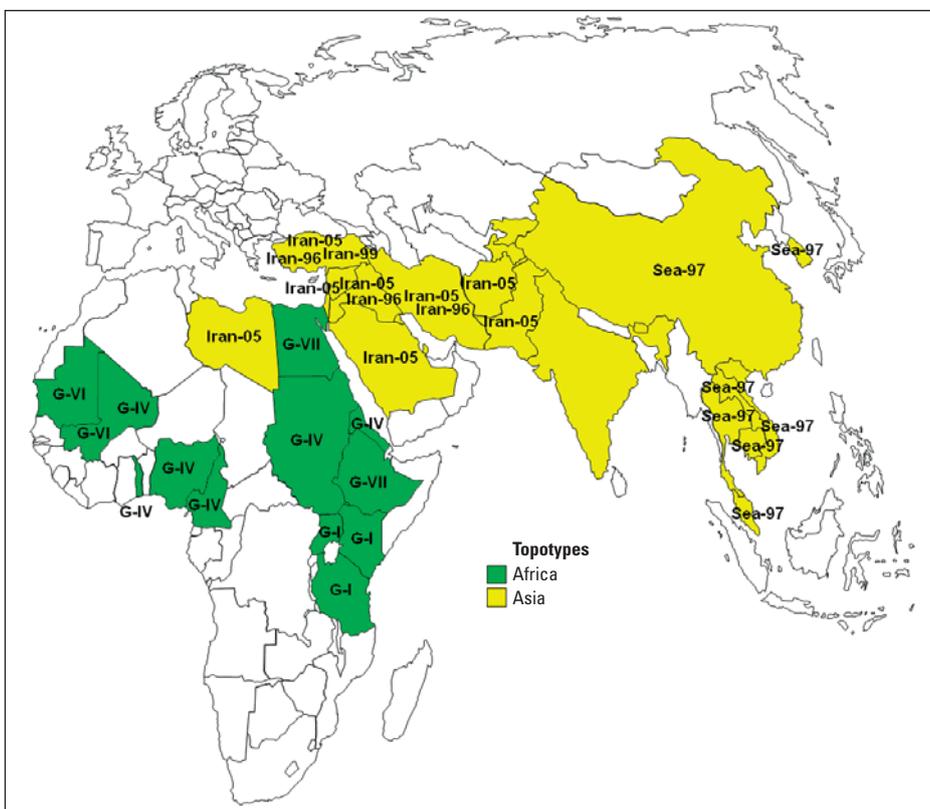


Fig. 3
Serotype A foot and mouth disease virus topotypes: distribution in sub-Saharan Africa, the Middle East and Southeast Asia

product which has found its way into their feed. In contrast, if the index case is in ruminants, then fomite transfer is more likely, e.g. via people or plant-based fodder (61). Within endemic regions, movements of both animals and their products can be important causes of the spread of FMDV, whereas for introductions of FMD into previously infection-free countries the source of virus has frequently been attributed to feeding waste food to pigs, as in the 2001 outbreak in the United Kingdom (UK) (59), or to other, less common causes of spread, such as virus escape from vaccines or laboratories or long-distance airborne dispersal of the virus (69).

Therefore, movements of animals and animal products are the main risk factors involved in the cross-border spread of transboundary diseases such as FMD, especially in countries where such movements are poorly regulated. Several factors could be considered to determine the probability of entry of FMD viruses into countries through trade in livestock and animal products, such as the:

- prevalence of infection in the source country
- volume of seasonal and trade-related movements (legal or otherwise) in animals and their products, which is highly influenced by price differentials
- potential for transmission to susceptible animals in the importing country and probability of spread, detection and control within the country after virus introduction
- survival capacity of the virus in animal products and in the environment and factors influencing this
- role of wild animals as potential vectors for spread.

Considering the origin of a virus responsible for a new outbreak usually requires piecing together whatever evidence can be found and trying to trace the causative event involved. Knowledge of the livestock systems, animal movements, marketing structures and trade routes is essential in understanding the epidemiological patterns of FMD viruses spreading within and between regions. However, it is often not possible to determine the exact source of a particular introduction because of incomplete information, especially where undisclosed illegal practices are concerned. Although we are often dealing with insufficient information on outbreak sources, matching information on livestock movement and classical epidemiological data with phylogenetic analysis and molecular epidemiological data can provide crucial insights for assessing the trends of FMDV dispersal at regional and global levels. This review describes the information of this type that is available for three important regions of FMDV endemicity: sub-Saharan Africa, the Middle East and Southeast Asia.

Livestock systems and foot and mouth disease distribution in sub-Saharan Africa

Marketing and livestock production in sub-Saharan Africa

The livestock sector is the mainstay of the socio-economic life for much of sub-Saharan Africa. Nomadic pastoralism, agro-pastoralism, settled mixed farming and urban stall feeding are the most practised forms of livestock farming. The evolution of an intra- and extra-regional trade in sub-Saharan Africa is mainly linked to the pastoral and agro-pastoral systems and is characterised by well-defined, extensive, seasonal, internal and cross-border livestock movements (4). The cross-border trade is the most significant form of 'clean' trade in East Africa. It is generally concentrated along the boundaries of Kenya, Ethiopia, Somalia and Sudan, and is characterised by several main routes (Fig. 4):

- eastern Ethiopia/Somaliland
- south-eastern Ethiopia/north-eastern Kenya/south-western Somalia
- eastern Ethiopia/Central Somalia
- Ethiopia/Djibouti border
- eastern Sudan/eastern Ethiopia
- south-western Sudan/north-eastern Kenya.

About 10% of cross-border trade passes through official channels. Consequently, most of the intra-regional trade in livestock is unrecorded, but it is estimated that its value exceeds US\$60 million (€45 million) per annum (47). There are at least two ways in which the informal economy can be considered: the first is in terms of internal or domestic economic practices and the other is in regard to external trade. The latter, as reflected in unofficial cross-border trade, assumes considerable importance in the Horn of Africa, predominantly in Somalia (45). The Horn of Africa region is the major livestock export market for the Arabian Peninsula and the Gulf States, driven by domestic demand in Yemen, Oman, the United Arab Emirates and Saudi Arabia, which account for approximately three million imported animals annually (Figs 5 and 6). Cattle, sheep and goats, either trekked or trucked from pastoralist areas in Sudan, Ethiopia, Kenya and Somalia to final markets, are shipped through the ports of Berbera, Bossaso, Port Djibouti and Port Sudan. In the first semester of 2010, the ports of Berbera and Bossaso alone exported 1,500,000 head of sheep and goats, and 128,000 head of cattle, which accounted for about 90% of all animal exports from the region (25). This trade in live animals makes a considerable contribution to the regional economy in terms of export earnings. A large number of ruminants

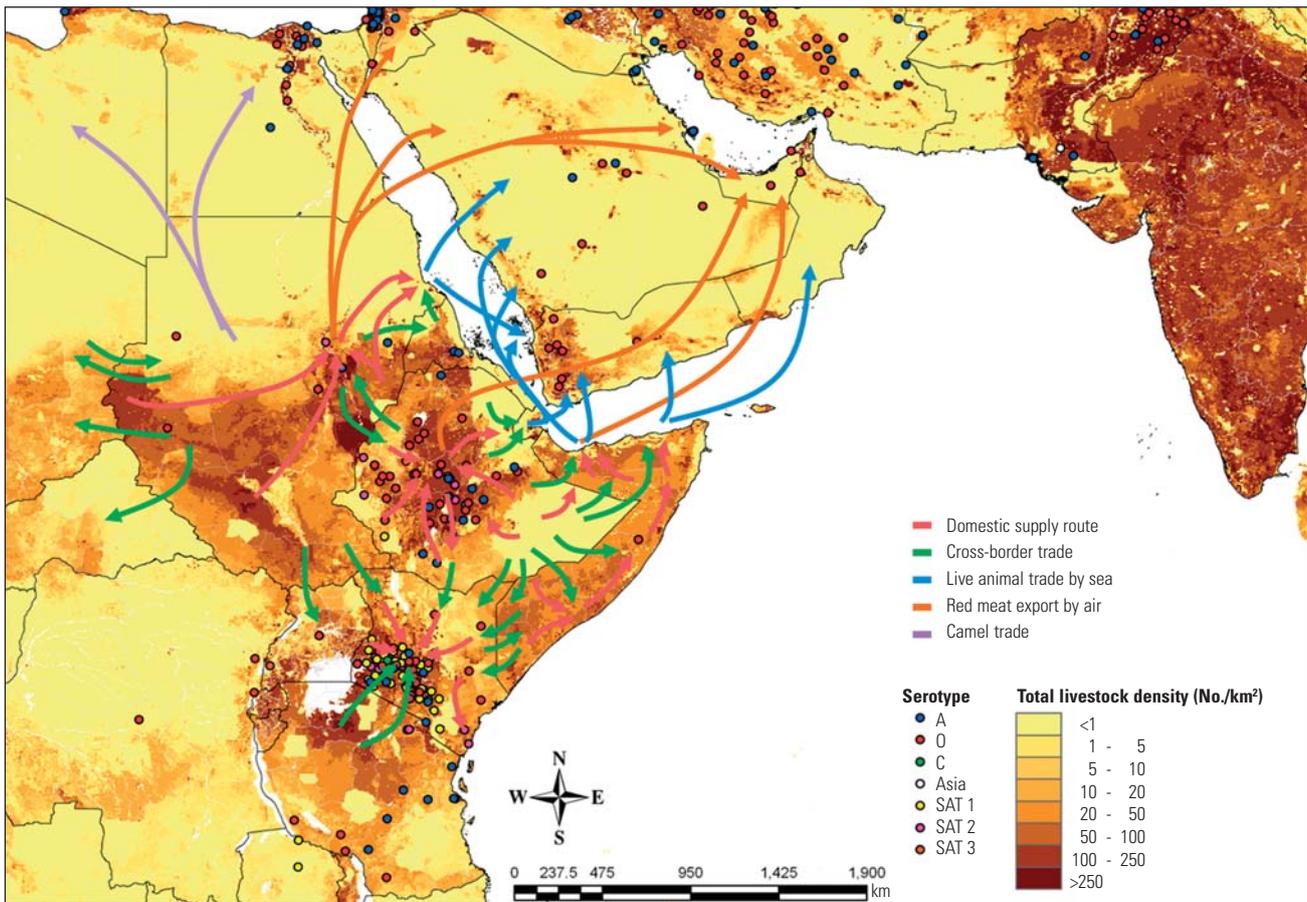


Fig. 4
Mapping cattle density, foot and mouth disease isolates, livestock movements and intra-/extra-regional trade routes in East Africa

Total livestock density layer data sourced and adapted from *Gridded livestock of the world*, Food and Agriculture Organization of the United Nations (76)

have been traditionally smuggled within the region. For instance, the bans on imports from Africa by the Gulf countries, following the Rift Valley fever (RVF) outbreaks in 1997 to 1998, 2000 and 2006 to 2007 (65), have led to increased illegal livestock sales from Ethiopia through Somalia and Kenya and, to a lesser extent, through Sudan and Djibouti (64).

Foot and mouth disease epidemiological patterns and history of infections in sub-Saharan Africa

Recently, Rweyemamu *et al.* (55) and Knowles (35) defined the epidemiological clusters of FMD in Africa based on prevalence data, serotype and toptype distribution, and expert opinions on animal movement, farming system and impact of wildlife. Two main clusters were identified for the sub-Saharan African region:

– the Horn of Africa, also called the Intergovernmental Authority on Development or IGAD cluster, comprising Djibouti, Eritrea, Ethiopia, Kenya, Somalia, Sudan and Uganda

– the Great Lakes cluster, also known as the East African Community (EAC) or Southern-East Africa cluster, comprising Tanzania, Uganda, Kenya, Rwanda and Burundi.

Each of the above proposed clusters is characterised by a substantial diversity of circulating FMDV strains and topotypes. This diversity is directly linked to the complexity of the livestock system and the marketing structure, reflecting their significant influence on the dynamic epidemiology of FMD events in the region. All but the Asia 1 FMDV serotypes have been found circulating in sub-Saharan Africa during the 2000 to 2010 decade, while the last reported case of serotype C dates from 2004 in Kenya (Table I), where a close genetic identity was found between the isolated virus and a local vaccine strain (39). However, serological evidence of this serotype has been reported more recently in samples collected from cattle during a 2009 surveillance study in Eritrea (60), aimed at investigating whether infections could have derived from resident or imported animals. Moreover, further evidence of antibodies against serotype C FMDV comes from analysis of sera collected

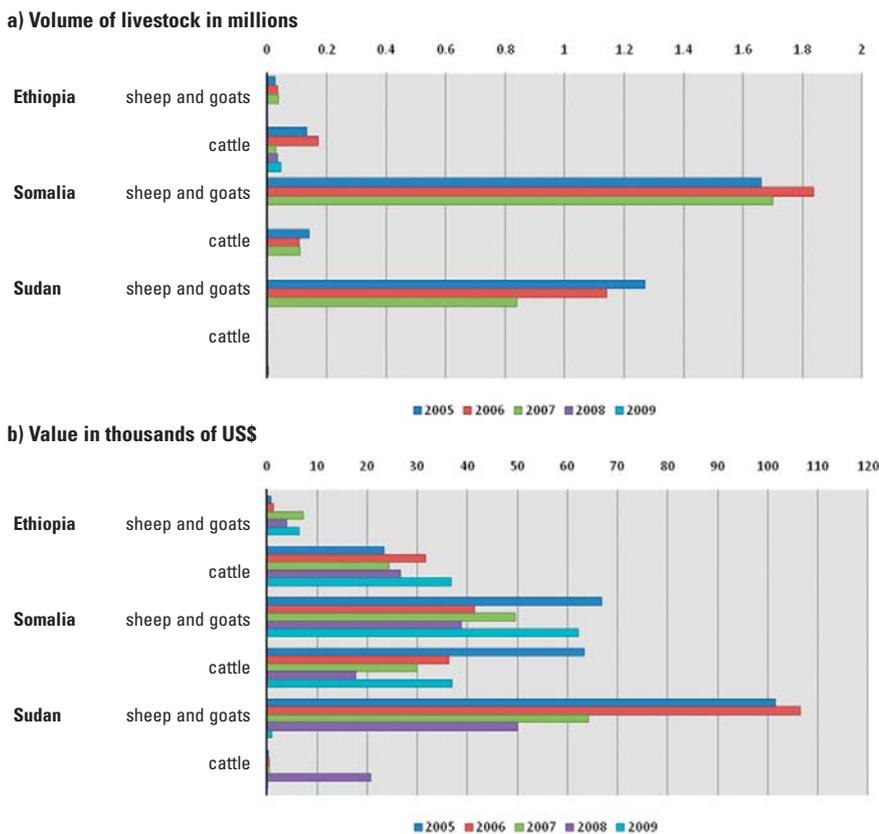


Fig. 5
Livestock exports from the East Africa region for 2005 to 2009

Source: International Trade Centre (33) and UN COMTRADE (67)

from the region during 2006 and 2008 (A. Di Nardo *et al.*, unpublished data). Although the recent evidence for serotype C might be explained by serological cross-reactions between different serotypes, further investigations are warranted to determine whether or not serotype C is actually still present. This is especially so considering the lack of data on FMD prevalence and serotype circulation from large areas of Central and East Africa that could constitute a reservoir of this virus infection, as described for the historical persistence of rinderpest virus of African lineage 2 in East Africa (49). Foot and mouth disease virus type O is the most prevalent and dominant serotype causing most of the outbreaks in the region, and the distribution of different strains and topotypes shows a clustering effect: the EA-3 topotype has been recorded in Ethiopia (2005, 2007 to 2010), Sudan (2005, 2008) and Somalia (2007), while the EA-2 topotype circulates in Kenya (2006, 2008 to 2010), Uganda (2002, 2007), and Tanzania (2004, 2008 to 2009). Viruses belonging to an older EA-1 topotype, once widespread in East Africa, appear to be restricted to eastern Kenya. The EA-4 topotype has occurred mainly in Uganda (1998 to 2003), only occasionally being found in Ethiopia (2005) and Kenya (2010). A similar epidemiological pattern can be observed for the distribution of type A virus genotypes: the genotype I (G-I) has been recorded in

Kenya (2003, 2005 to 2006, 2008 to 2009) and Tanzania (2008 to 2009); the G-IV genotype in Sudan (2006) and Eritrea (2010); while the G-VII genotype has been reported in Ethiopia (2000, 2002, 2007 to 2009) and Kenya (2005). Ecosystem diversity and pastoralists' adaptability in coping with seasonal variation in grazing availability and climatic changes, as well as the characteristic three-tier, livestock-marketing system, may be considered the main determinants of FMDV distribution across sub-Saharan Africa. Three main risk areas for FMDV circulation may, therefore, be considered:

- the border areas between Kenya, Tanzania and Uganda
- the Somali ecosystem (including the Somali region of Ethiopia, Somalia and the north-eastern region of Kenya)
- the bordering areas between East Sudan, North Ethiopia and Eritrea.

Each of these areas exemplifies the marketing and farming system of the entire region in closed settings, which are mutually linked since the rangelands represent essentially similar ecological, ethnic and socio-economic contexts. Nevertheless, the cross-border livestock trade takes place not only as a result of better price offers than the home markets, but also because of proximity to cross-border

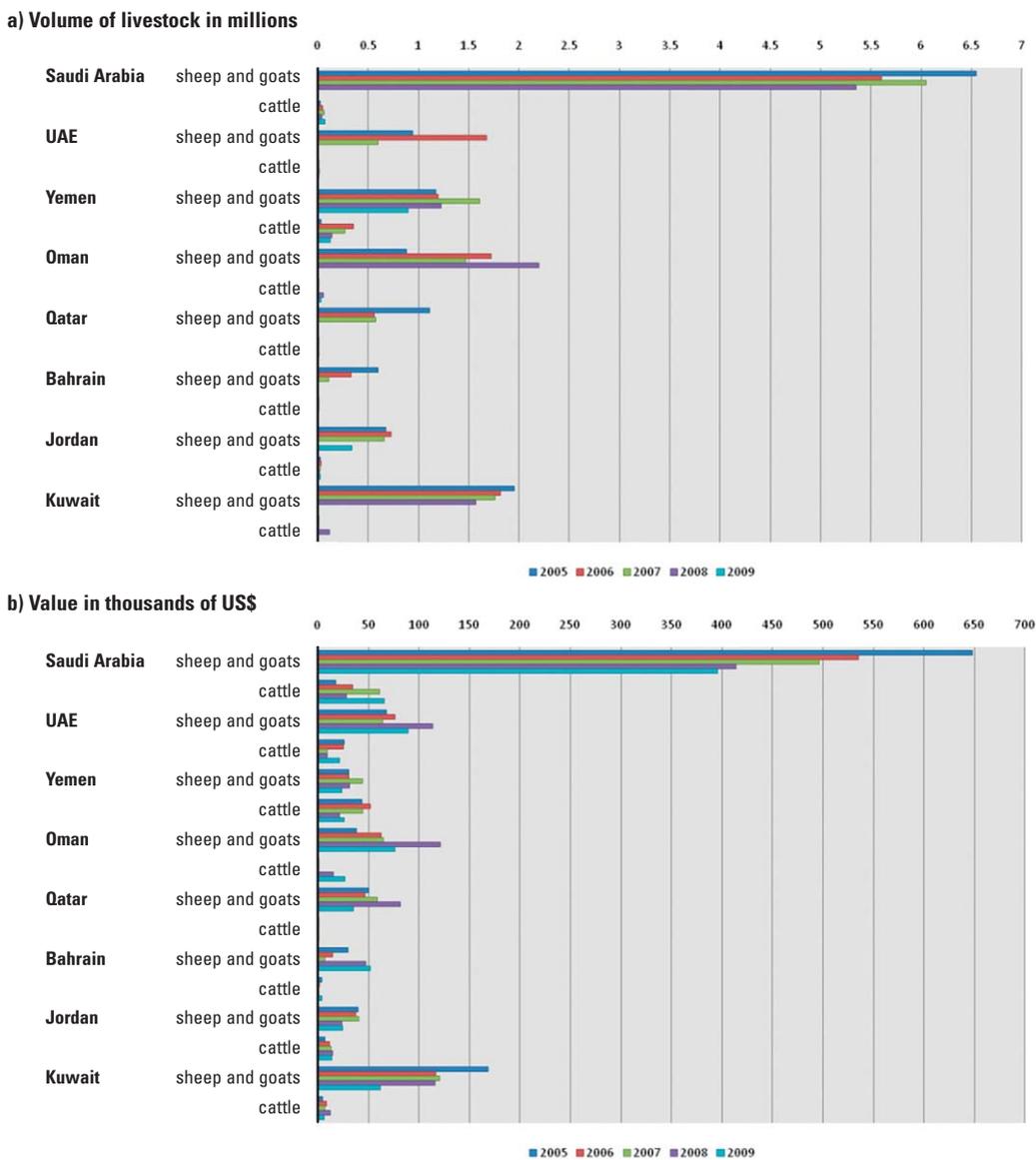


Fig. 6
Livestock imports to the Middle East region for 2005 to 2009

UAE: United Arab Emirates

Source: International Trade Centre (33) and UN COMTRADE (67)

rather than to domestic markets. For example, two-thirds of the animals offered on the markets in the Narok District of the Rift Valley Province in Kenya are sourced from neighbouring regions of Tanzania, as well as trekked from areas further west, and then moved north towards Nairobi (3). Animals sold in the Nairobi terminal markets are also sourced from southern Ethiopia for the markets in Marsabit District of the Eastern Province in Kenya (44). Similar patterns, although much less predictable, can be defined for the Uganda-Kenya trade route (85). Notably, the Kenya and Tanzania rangelands boast one of the greatest areas of wildlife biodiversity in Africa, shared with pastoralist groups which are, in turn, forced by the impact of climatic changes in the timing of rains and frequency of

droughts to move up to 30 km daily to get water and pastures and to encroach on protected wildlife zones (i.e. the Tarangire wildlife dispersal area), resulting in human-wildlife conflict, with increasing rates of contact between domestic and wildlife species and risk of disease transmission. The role of wildlife species such as African buffalo (*Syncerus caffer*) and impala (*Aepyceros melampus*) in the epidemiology and maintenance of FMD SAT serotypes has been well documented in wildlife conservancy areas of Zimbabwe and South Africa (7, 32, 66, 73), and their potential role in East Africa has also been assessed (10). Experience has shown that, although Cape buffalo do not normally exhibit clinical signs of FMD, they act as long-term carriers of SAT-type viruses, providing

Table I
Total number of foot and mouth disease outbreaks and serotypes recorded in the East African, Middle Eastern and Southeast Asian regions during the 2000 to 2010 decade

East Africa	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010*
Djibouti	–	–	–	–	–	–	–	–	–	–	–
Egypt	+ [O]	–	–	–	–	–	31 [A, O]	1 [O]	2 [O]	8 [O, A]	–
Eritrea	–	+	+	+	+ [O]	–	+ [A]	+ [A]	+ [A]	+ [A]	–
Ethiopia	+ [A]	+ [A]	+ [A]	+ [O]	+ [O]	+ [O, A]	+ [O]	+ [O, A, SAT 1, SAT 2]	+ [O, A]	+ [O, A, SAT 2]	+ [O, SAT 2]
Kenya	+	+	+ [O, SAT 2]	+ [A]	+ [O, C, SAT 1, SAT 2]	+ [O, A, SAT 1, SAT 2]	+ [A, SAT 1]	+ [O, SAT 2]	+ [O, A, SAT 1, SAT 2]	+ [O, A, SAT 1, SAT 2]	+ [O, SAT 1]
Somalia	–	–	–	–	–	–	–	+ [O]	–	–	–
Sudan	–	–	–	+	+	+ [O]	+ [A]	+ [SAT 2]	7 [O, SAT 2]	–	–
Tanzania	113 [SAT 1]	75 [–]	62 [–]	160 [–]	410 [O, SAT 2]	59 [–]	135 [–]	+	+ [O, A]	+ [O, A, SAT 2]	–
Middle East	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010*
Afghanistan	–	–	+	+	+ [Asia 1]	–	–	+ [O, A]	–	+ [O, A]	+ [O, A]
Bahrain	+	+ [O]	+	+	+	–	+ [O]	+ [O]	1 [O, A]	1 [A, Asia 1]	–
Iran	+ [O, A]	+ [O, A, Asia 1]	+ [O, A]	+ [O, A]	+ [O, A, Asia 1]	+ [O, A]	15 [O, A]	578 [O, A]	258 [A]	+ [O, A]	+ [O, A]
Iraq	+ [O, A]	+ [O]	+ [A]	–	+	–	+ [A, O]	+ [O, A]	148 [–]	1 [A]	–
Israel	–	–	–	–	+ [O]	1 [O]	1 [O]	30 [O]	7 [O]	14 [A]	–
Jordan	–	–	–	–	–	–	3 [O, A]	+ [O, A]	–	1 [–]	–
Kuwait	+ [SAT 2]	–	+ [O]	–	–	–	+ [O]	2 [O]	6 [O]	1 [A]	–
Lebanon	+	+	+ [O]	+ [O]	–	–	+ [O]	2 [–]	1 [–]	11 [A]	–
Oman	+	+ [O]	+	–	+	–	+ [O]	+ [O]	85 [–]	–	–
Pakistan	+	–	+ [O, A, Asia 1]	+ [O, A, Asia 1]	+ [Asia 1]	+ [O, Asia 1]	+ [O, A]	+ [O, A]	+ [O, A, Asia 1]	+ [A, Asia 1]	+ [O, A]
Palestinian Autonomous Territories	–	–	+ [O]	+	+	–	5 [–]	26 [O]	–	+ [A]	–
Qatar	+	+ [O]	–	–	–	–	+ [O]	+ [O]	–	–	–
Saudi Arabia	+ [SAT 2]	+ [O]	+ [O]	+	+ [O]	+ [O, A]	+ [O, A]	+ [O]	+ [O]	+ [O]	–
Syria	–	–	+ [O, A]	–	–	1 [–]	–	1 [–]	–	–	–
Turkey	+ [Asia 1]	–	–	–	–	+ [O, A]	13 [A]	4 [O, A]	251 [O, A]	+ [O, A]	+ [O, A]
United Arab Emirates	+ [O]	+ [O]	–	+ [O]	–	–	+ [O]	+ [O]	1 [O]	1 [O]	+ [O]
Yemen	–	+	+	+ [O]	+ [O]	–	+ [O]	+ [O]	+ [O]	+ [O]	–
Southeast Asia	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010*
Cambodia	32 [O]	25 [–]	45 [O]	21 [–]	34 [O]	52 [–]	52 [O, A]	4 [O, A]	39 [O, A]	41 [–]	7 [–]
Laos	140 [O]	136 [O, Asia 1]	29 [O]	122 [O, A]	88 [O]	2 [O]	41 [O, A]	60 [O, A]	55 [O, A]	18 [O]	0 [–]
Malaysia	3 [O]	33 [O]	32 [O, A]	27 [O, A]	34 [O, A]	41 [O, A]	58 [O, A]	70 [O, A]	137 [O, A]	98 [O, A]	17 [O]
Myanmar	11 [O, Asia 1]	28 [O, Asia 1]	29 [O]	7 [O]	35 [O]	16 [O, Asia 1]	29 [O, A]	14 [O]	11 [O]	21 [O]	7 [O]
Philippines	328 [O]	221 [O]	241 [O]	132 [O]	27 [O]	19 [O]	0	0	0	0	0
Thailand	103 [O, A]	180 [O, A, Asia 1]	170 [O, A]	421 [O, A]	240 [O, A]	152 [O, A]	17 [O, A]	34 [O, A]	52 [O, A]	50 [O, A]	2 [O]
Vietnam	26 [O]	17 [O]	40 [O]	29 [O]	49 [O, A]	53 [O, A, Asia 1]	34 [O, A, Asia 1]	19 [O, Asia 1]	61 [O, A, Asia 1]	214 [O, A, Asia 1]	70 [O]

* Data available for January to October

–: no information available

+: cases reported

SAT: South African Territories

Source: Data compiled based on country reports to the World Organisation for Animal Health (OIE) (Handistatus II and World Animal Health Information Database or WAHID); Food and Agriculture Organization of the United Nations (Emergency Prevention Systems Global Animal Disease Information System database or EMPRES-i); OIE Regional Coordination Unit, Bangkok, Southeast Asia Foot and Mouth Disease Campaign and the World Reference Laboratory for Foot-and-Mouth Disease, Pirbright, United Kingdom

sources of infection for other cloven-hoofed species, both domestic and wild (71, 72). A recent evolutionary study on SAT 1 viruses isolated in Kenya and Tanzania between 1977 and 2007 highlights the potential for cross-border exchange of FMDV through transboundary livestock and wildlife movements (57), ascribing southern Africa as a likely source of virus introduction into eastern Africa. Therefore, such an ecosystem provides the potential for FMD to create an endemic stability by viral circulation, not only through the congregation of multiple domestic flocks and herds in livestock markets sourced from different areas of the region, but also through contacts between domestic and wild ruminants.

Route of foot and mouth disease virus spread from sub-Saharan Africa

The ability of FMD viruses to move outside their sub-Saharan African endemic areas of occurrence has been confirmed by outbreaks of African FMDV strains reported in previously unaffected areas of the Middle East and North Africa. Southern African Territory 2-type viruses were isolated in a dairy herd in Saudi Arabia and, near the Saudi border, in a nomadic herd in Kuwait during April and June 2000. Phylogenetic analysis revealed a high level of sequence identity (>90%) between the Saudi Arabian virus and a virus isolated in Eritrea in 1998, demonstrating that the north-eastern African region was the most likely source of the viruses introduced into the Middle East (8). Furthermore, Libya reported a SAT 2 outbreak in 2003, with the causative virus sharing a common origin with the Saudi Arabian isolate and a virus collected from Cameroon in 2000 (11), demonstrating a link to virus strains from south of the Sahara.

While the trade in live animals from the Horn of Africa may represent the most likely risk for SAT 2 virus introduction into the Middle East, sources of the Libyan outbreak may be linked to the extensive movement of nomadic flocks across the Sudano-Sahelian region. For centuries, the most successful adaptive strategy of pastoral production systems in sub-Saharan Africa has been the high mobility of herds along well-defined migratory routes, dictated by the availability of natural resources, social conflict and animals' dietary needs (23). Dairy production occupies a central place in the management of this system and, although the sale of live animals is not the main aim, it is the primary source of cash income. Therefore, pastoralism has always played an important role in the sub-Saharan Africa trade in livestock and, as a general observation, most of the West and Central African countries are affected by cross-border transhumance, either as departure countries or as reception or transit countries. For instance, a main import basin for livestock trade comprises Benin, Cameroon,

Chad, Niger and Nigeria. Some trade flows come from Burkina Faso and Mali, while other, even less frequent flows occur from Chad and Niger towards the countries of North Africa (34). In addition, the Darfur region in Sudan is a key area for inbound and outbound livestock movements to and from Chad and the Democratic Republic of Congo, dictated by transhumance of flocks in search of better pastures.

Further evidence for a link between livestock movements from West African countries to North Africa and FMD spread is provided by the SAT 2-type outbreaks recorded in 2005 in Niger, caused by viruses closely related to the Libyan isolate. Nonetheless, the majority of the livestock trade goes to Nigeria, driven by the protein demand of a growing population (one-fifth of the total African population). Recent viruses submitted in 2008 and 2010 from Nigeria to the Food and Agriculture Organization (FAO) World Reference Laboratory for FMD, Pirbright, UK, have further highlighted the close relationship between viruses isolated in West and East Africa, ascribing a possible origin of the Nigerian type O and SAT 2 viruses to the Horn of Africa countries, perhaps in Sudan (80, 83). Therefore, there are clear overlaps between viruses of African pool 4 and pool 5, and human activities involving the seasonal movement of nomadic tribes are the most likely primary causes of virus movement in both directions.

Routes of introduction of FMDV from West Africa to the northern countries have been further illustrated by the FMD type O outbreaks recorded in 1999 in the Mediterranean Maghreb region (20). Viruses causing infections in Algeria, Morocco and Tunisia were found to be closely related to each other and very similar to strains isolated from countries on the west coast of Africa (Ghana, Côte d'Ivoire and Guinea). Although the introduction into Morocco has been ascribed to butchers' bullocks illegally imported from Algeria (due to the location of the outbreaks detected and the species affected), the spread of WA O topotype originated from a movement of zebu cattle into Algeria that took place in 1999 (56). Moreover, a conspicuous livestock flow, mainly involving small ruminant species, has been historically routed from Mauritania and Mali to Algeria and Morocco through Western Sahara, where transboundary diseases, such as peste des petits ruminants, are most likely spread by transhumance and the live animal trade (A. Di Nardo *et al.*, unpublished data); a possible further source of virus introduction from West Africa into the Mediterranean Maghreb region.

Another example of the northward spread of FMD within East Africa has been the introduction of an African type A FMDV strain into Egypt. During January and February 2006, clinical cases of FMD were recorded in eight governorates of north-eastern Egypt. Phylogenetic analysis

confirmed the close relationship of the Egyptian virus with those occurring in East Africa, specifically the Africa topotype, G-VII genotype, already reported in Kenya and Ethiopia (42). The same strain was again recorded in February 2009 in Egypt, suggesting that the virus had become endemic in the country. Although no categorical information concerning the origin of the virus has been published, unofficial reports suggest that importation by a sea route from Ethiopia, of infected animals for slaughtering, was the most likely route of introduction. Consistent with this hypothesis was the contemporary report of cases of lumpy skin disease detected at quarantine posts in animals from Ethiopia (24).

The risk of exporting African lineages of FMDV by livestock trade from the Horn of Africa was again confirmed by the presence of the type O EA-3 topotype of FMDV in Yemen in 1989 to 1990, 1995, 2003 to 2004, 2006 and 2008 to 2009. Once again, phylogenetic analyses revealed a close relationship between the Yemen isolates and those characterised for Somalia and Ethiopia (79, 81, 82). The majority of the livestock imported into Yemen are sourced from eastern Kenya and Ethiopia, through the local markets in Somalia, and end up concentrated around the ports of Berbera and Bossaso for shipment. The history of the spread of transboundary diseases from East Africa into the Arabian Peninsula recalls the RVF outbreaks that affected Saudi Arabia and Yemen in 2000 to 2001, the first reported outside Africa (12). Although the mechanism of the introduction of the RVF virus (RVFV) remains unknown, genetic analysis of viruses collected in Saudi Arabia and Yemen reveals a close relationship to viruses isolated during the large outbreaks that occurred in Kenya, Somalia and Tanzania in 1997 to 1998 (62), highlighting how the RVFV may have been spread through trade in infected livestock. Even after the ban on livestock imports imposed by Saudi Arabia and Yemen, unofficial sources reported that the Mukulla facility and the port of Aden in Yemen continued to import livestock (22), clearly emphasising how the uncontrolled movement of live animals may perpetuate the risk of introducing transboundary diseases into new regions.

Livestock systems and foot and mouth disease distribution in the Middle East

Marketing and livestock production in the Middle East

Livestock products contribute significantly to the diets of both rural and urban populations in the Middle East. Owing to the arid and semi-arid ecosystems, a wide range

of traditional management systems has evolved to optimise the use of resources. Many rely on movement, either nomadic pastoralism or seasonal transhumance, to winter and summer pastures. However, significant changes in livestock production have taken place in the last decade, mainly as a result of oil wealth, resulting in new systems of mechanised nomadism employing vehicles for supplying animal feed and water, and modern communication systems for identifying grazing areas (9). Therefore, more extensive, opportunistic and erratic livestock movements are now the norm, especially in countries such as Jordan, Saudi Arabia, Syria and Iraq. In addition, the increasing demand for animal protein has shifted the livestock production system towards modern feedlots near urban centres, operating at a high productivity level but retaining their links to the pastoralist system. In the vast area of the Arabian Peninsula, the extensive pastoral and nomadic livestock populations are connected through a livestock trade system driven by demand from the Gulf States (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates) (Fig. 7), which collectively accounts for about 80% of the sheep, goat and cattle imports into the region (Fig. 5). Saudi Arabia is the largest importer of live animals, receiving approximately three to five million sheep and one million goats annually. Trade in live animals in the Middle East is much greater than trade in meat. This preference has various explanations, such as local traditions for the slaughter of live animals for consumption, and religious festivals that require the sacrifice of small ruminants. For example, much of the import figure is accounted for by the substantial inflow of small ruminants for the major Muslim festivals (Hajj, Ramadan, Eid ul-Fitr and Eid ul-Adha), which account for 10 to 15 million live animals, primarily supplied by the Horn of Africa (16).

Foot and mouth disease epidemiological patterns and history of infections in the Middle East

Foot and mouth disease is endemic and widespread among ruminants in the Middle East (Table I), but periodic and devastating epidemics do occur, spreading rapidly across national and regional borders. Broadly speaking, the Middle East could be considered a 'mixing vessel' for introducing FMD viruses from either the Far East or African countries and, therefore, the region is characterised by a constantly evolving FMD epidemiological status. The emergence of FMDV strains from Central Asia, through the Middle East and to West Eurasia has been referred to as 'waves of infections' since the appearance of the A₂₂ strain in 1964 to 1972 (5), with a clear pathway of spread along defined routes. Links between virus isolates from Afghanistan, Pakistan, Saudi Arabia, Iran and Turkey suggest that FMD probably spreads from South-Central

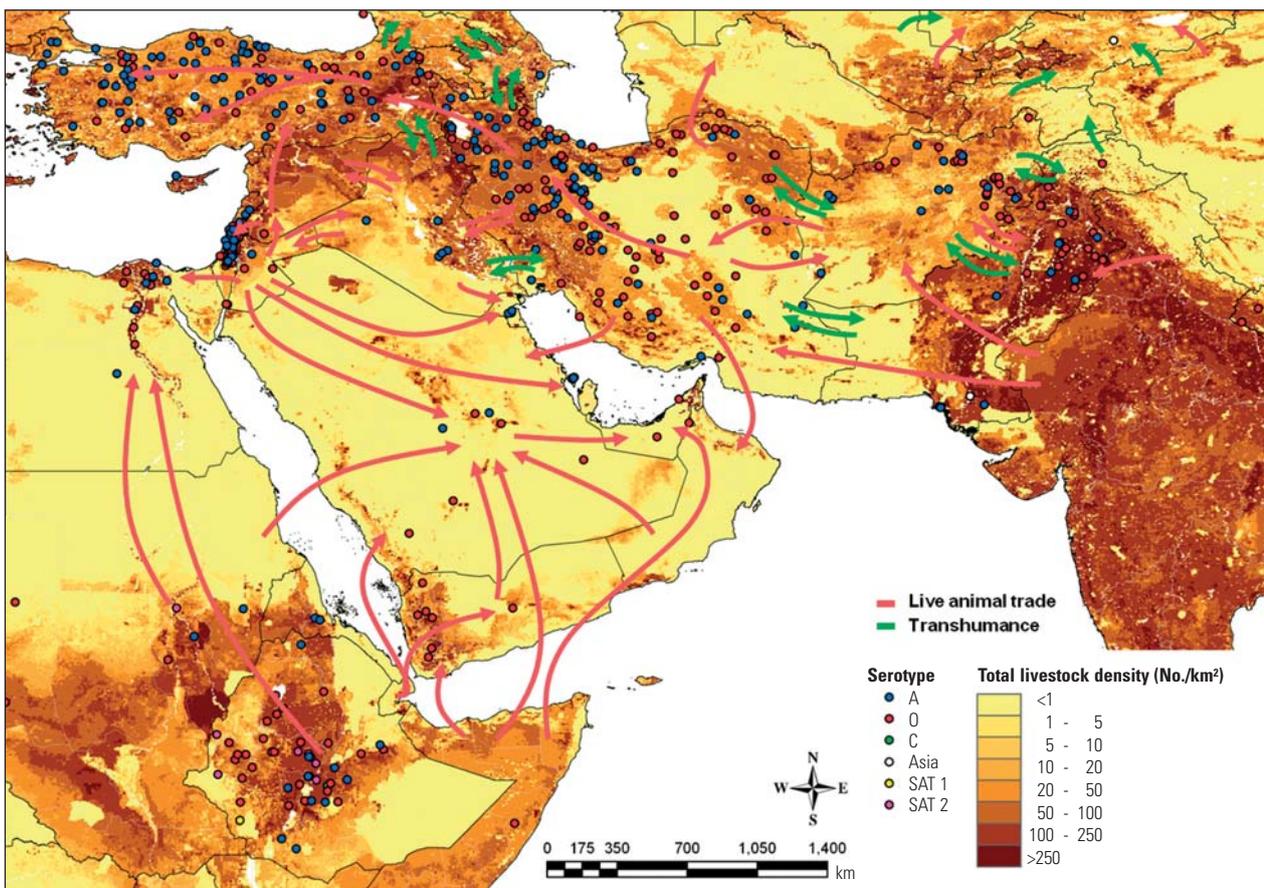


Fig. 7
Mapping cattle density, foot and mouth disease isolates, livestock movement and intra-/extra-regional trade routes in the Middle East

Total livestock density layer data sourced and adapted from *Gridded livestock of the world*, Food and Agriculture Organization of the United Nations (76)

Asia westwards along what has been termed the 'Ruminant Street' (63). Studies on the geographical distribution and density of livestock populations in South Asia and the Middle East have defined areas of continuous livestock density between the Mediterranean Basin and southern Asia, involving Pakistan, Afghanistan, Iran and Turkey, and in which Iran takes up a central position (75), creating a narrow east-west connection just south of the Caspian Sea and acting as a corridor for the spread of pathogens. Historically similar epidemiological patterns of virus infections have also been recorded during the rinderpest era (54).

In recent years, these epidemiological dynamics of FMDV movement have been exemplified by the emergence of the A-Iran-05 and O-PanAsia-2 FMDV lineages. The A-Iran-05 lineage was first detected in Iran in 2003, before it was recognised to the east in Afghanistan (2004) and Pakistan (2006). Westward spread to Saudi Arabia and Turkey occurred in 2005, and to Jordan in late 2006 (37), with generalisation throughout the Middle East region by 2009. Unlike the A-Iran-05 strain, the O-PanAsia-2 lineage seems to have originated in India in 2001 but, like the type A strain, moved westwards to Pakistan and Iran in 2005 and then became widespread within the entire Middle East

region by 2007, reaching Egypt in late 2007. Since 2005, the A-Iran-05 and O-PanAsia-2 strains have become the dominant virus strains in the Middle East. However, different genetic sub-lineages have recently been reported to have evolved in different parts of the region, defining a cluster effect in the genetic diversity of those FMD viruses within the region. This epidemiological finding indicates that, although these viruses share a common ancestor, they have been evolving and had different epidemiological histories prior to their detection. First recorded in Afghanistan in 2007, the A-Iran-05^{AFG-07} sub-lineage has been reported predominantly in Pakistan, Afghanistan and in Iran, with some additional cases in Bahrain and Turkey, while the A-Iran-05^{BAR-08} sub-lineage, first isolated in Bahrain in 2008, is widespread within the western part of the Middle East (Israel, Palestinian Autonomous Territories, Lebanon, Kuwait, Iraq and Iran), and was reported in Libya in 2009. Although no information is available about the source of the outbreak, the close relationship (>99%) between the Libyan isolates and those collected in the same year in Iraq and Kuwait suggest that the virus may have been introduced by trade in live animals or meat from the Gulf States. Furthermore, the first notified outbreak was located near Benghazi, where large meat and livestock import companies operate.

More evidence of the evolutionary clustering of FMDV comes from the recent evolution of the O-PanAsia-2 strain in different sub-lineages (41). While the reported O-PanAsia-2^{FAR-09} and O-PanAsia-2^{ANT-10} sub-lineages are clustered mainly in Iran, the O-PanAsia-2^{BAL-09} and O-PanAsia-2^{PUN-10} are only reported in the areas bordering Afghanistan, Pakistan and the north-east of Iran. In terms of FMD ecology, the eastern regions of Afghanistan can be considered an extension of the western Pakistan ecosystem, since the two regions are linked by contiguous livestock populations, transhumance routes, and two-way trade and fattening enterprises. Moreover, extensive transhumance and cross-border movement routes exist along the Iran/Pakistan borders, with seasonal contraction and expansion in response to grazing availability. A few years earlier, a similar pattern of ecological distribution of FMDV in the area comprising Afghanistan, Pakistan and eastern Iran was described for viruses collected between Afghanistan during 2003 and 2005 and belonging to the O and A serotypes (58). Type A isolates collected between 2004 and 2005 from the Herat and Nangarhar provinces of Afghanistan were grouped together, along with viruses collected in Sistan and Baluchestan Province in Iran during the same year. Interestingly, while a type O FMDV sequenced within the O-PanAsia lineage was grouped with a virus previously reported in Iran in 1999 (38), two other O-PanAsia isolates from Zabol and Ghazni provinces were found to be more closely related to viruses collected from 2003 to 2004 in Nepal, Bhutan and Malaysia. During the same period, similar phylogenetic relationships were found among viruses collected from the Punjab and Sindh provinces in Pakistan, demonstrating common ancestry with the Nepal and Bhutan viruses, although showing adaptation to the Pakistan ecosystem (74). Therefore, the evolution and emergence of the A and O serotypes of FMDV in different sub-lineages may be a reflection of the different ecosystems and characteristics of the livestock systems present in Afghanistan and Pakistan, and the western countries. This may be further complicated by the potential for the introduction of novel virus variants from India and Central Asia, coupled with the ability to move across countries in a relatively short time frame.

Foot and mouth disease transmission routes in the Middle East: the case of Turkey

In the dynamic epidemiology of FMD in the Middle East, Turkey, with its large indigenous ruminant population, constitutes a particular epidemiological cluster for the evolution of A-Iran-05 and O-PanAsia-2. Starting in August 2007, the A-Iran-05^{ARD-07} sub-lineage was recorded in Ardahan Province near the border with Georgia and then spread almost to the entire Turkish territory. Additionally, a new sub-lineage (named A-Iran-05^{EZM-07}) was isolated in June 2008 in Eskisehir Province but, until now, has been reported only in the Aegean region. More

recently, a new O-PanAsia-2 sub-lineage (named SAN-09) was isolated in May 2010 in Tokat Province. Neither Turkish A-Iran-05 nor O-PanAsia-2 sub-lineage viruses were recorded in other parts of the Middle Eastern region, indicating that, to some extent, Turkey constitutes a one-way inflow route of virus introduction from the east via livestock trade. Cattle entering Pakistan and Afghanistan from India are mainly directed to local markets for slaughter or move on to Iran through the Herat market. From there, they may continue to move to the central regions of Iran or onwards to Iraq and Turkey. In the latter case, they enter at the eastern border for trucking towards the western half of the country, where most consumption centres are located. It is noteworthy that the disease persists in provinces such as Ankara, which has a deficit of small ruminants, and Erzurum, which has a surplus (28).

Examples of the consequences of these connections for the spread of FMD are seen from molecular characterisation and comparison of A-Iran-05^{BAR-08} and A-Iran-05^{AFG-07} isolates. Those from Eastern Anatolia in 2009 and 2010 showed close phylogenetic relationships with viruses from Iran in 2009. In addition, the O-PanAsia-2^{FAR-09} and O-PanAsia-2^{ANT-10} sub-lineages reported in mid-2009 were also closely related to Iranian viruses isolated in 2009 and 2010. One more example is provided by the Asia 1 virus responsible for the FMD outbreaks in Turkey in 1999. Molecular epidemiological studies suggest that these virus strains were earlier isolated in India and Nepal and moved from there into Pakistan and Iran in 1999, then spread westwards from 1999 through 2001 into the South Caucasian region, causing outbreaks in Armenia, Georgia and on the Greek-Turkish border, without any traceable origin (69). Previously, similar epidemiological patterns of Asia 1 virus spread were recorded in 1973 and between 1983 and 1985 (68). More recently, outbreaks of the Asia 1 serotype have been reported in Bahrain in April 2009. The isolated virus has shown a close genetic relationship (>94%) with those circulating during 2008 and 2009 in India, sharing a common origin with earlier isolates from Bangladesh (1996) and India (1999), and meaning that, although Asia 1 outbreaks are sporadically recorded in Middle East countries, virus sources may be attributed to introductions from the Indian subcontinent through the live animal trade.

One more piece of evidence about the probable introduction of exotic FMDV into the Middle East region from India is the report of the outbreaks caused by the type O Ind-2001 FMDV strain during 2008 and 2009, in an unvaccinated collection of dorcas gazelles (*Gazella dorcas*) and sika deer (*Cervus nippon*), and in a second, vaccinated collection of blackbuck (*Antelope cervicapra*), sand gazelles (*G. subgutturosa marica*) and other wild ruminants held in Dubai, the United Arab Emirates (6). Viruses collected from the two outbreaks were found to be closely related

(>94%) to FMDV Ind-2001 strains previously isolated in India (2000 to 2001). Although the source of infection was not confirmed, the introduction may have originated from imported livestock, since local veterinarians diagnosed FMD on a sheep farm adjacent to the wildlife collection before the reported outbreak. Official reports from veterinary authorities in Kuwait, about their refusal to unload a shipment laden with 950 sheep and goats from India with evident clinical signs of FMD and bluetongue (26), may support this hypothesis.

Livestock systems and foot and mouth disease distribution in Southeast Asia

Marketing systems and livestock production in Southeast Asia

Domestic livestock production of all species in Southeast Asia has been growing steadily over the last ten years and

now provides 25% of the agricultural output value. In this sector, production is largely in the hands of smallholders, so that animals are located in village production systems and may be housed in simple pens or run free in the village. Therefore, livestock enterprises are very small, dealing with a range of animal species, including pigs, cattle, water buffalo (*Bubalus bubalis*) and chickens, and most of the livestock farming system forms an integral part of the agri-ecological sector. Mahadevan and Devendra (48) classified ruminant production systems in Southeast Asia and the Pacific into three categories:

- the extensive system
- systems combining arable cropping
- systems integrated with tree cropping.

In this regard, buffalo and cattle serve a variety of purposes: they may be used for draught power, manure production and meat production or provide income if sold. Moreover, a semi-industrialised commercial sector exists, which is totally market-oriented and has grown very rapidly, along with the rest of the regional economy. As a result of recent improvements in political stability and growing liberalisation of economic policies, there has been an

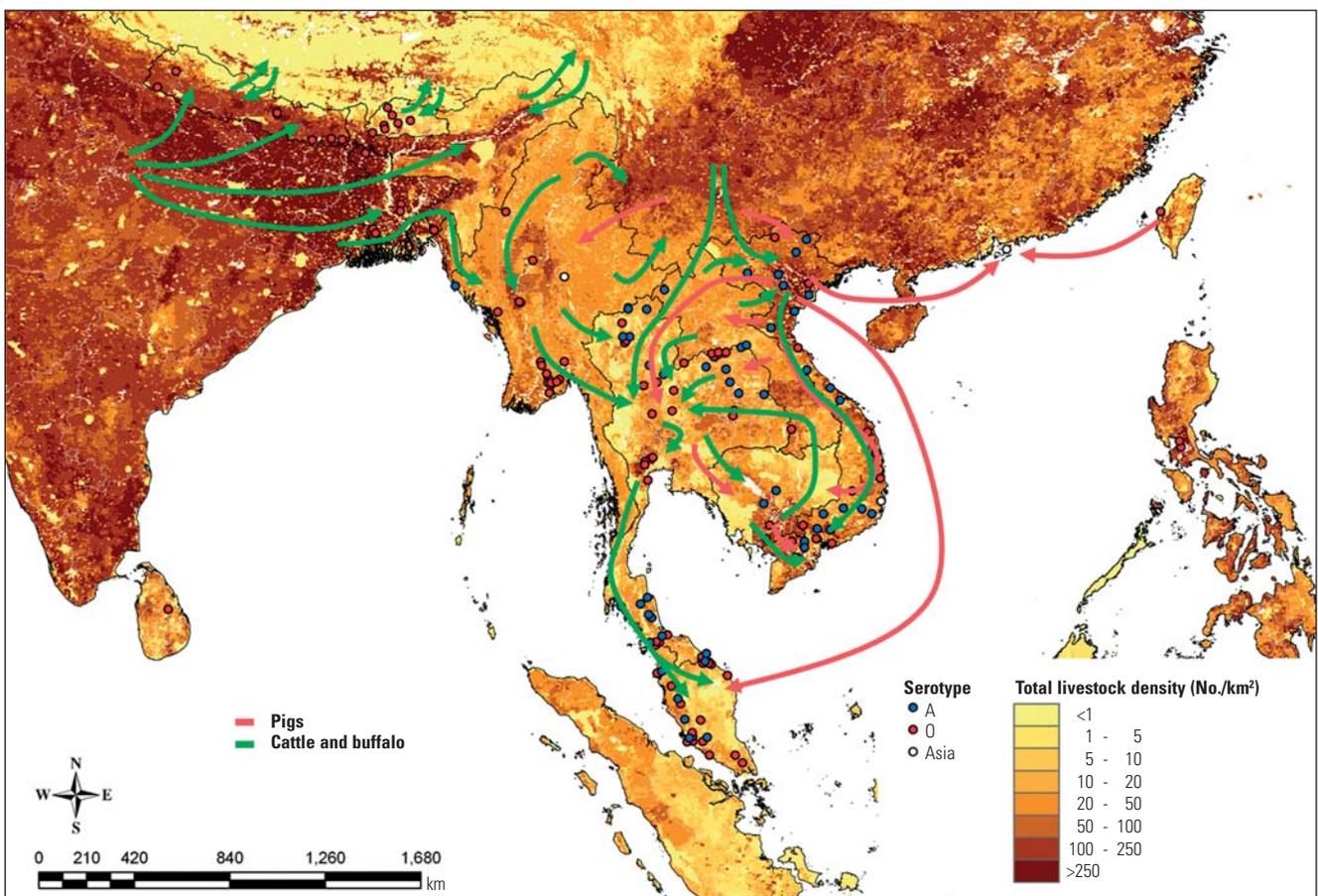


Fig. 8
Mapping cattle density, foot and mouth disease isolates, livestock movement and intra-/extra-regional trade routes in Southeast Asia

Total livestock density layer data sourced and adapted from *Gridded livestock of the world*, Food and Agriculture Organization of the United Nations (76)

increased movement of livestock across international borders. All the countries comprising the Southeast Asian region have open borders and thus the regional trade routes in large ruminants and pigs are complex (Fig. 8) (50). The direction of animal movements is dictated by the supply and demand of the marketplace and so can vary considerably, especially within countries (Table II). Vietnam acts as the principal centre for pig exports through Laos to Thailand, Malaysia, Cambodia, and out of the region to Singapore and Hong Kong, while there are large movements of cattle from the northern provinces to the southern markets (especially to Ho Chi Minh City) (13). Equally, Myanmar represents a major source of livestock to the Malaysia-Thailand zone, mainly supplied from its central region. Animal movement pathways show Myanmar livestock as widely distributed throughout the Southeast Asian mainland. Moreover, large numbers of cattle are imported into Myanmar from Bangladesh, which in turn receives up to two million head of cattle per year from Nepal and India as a result of insufficient domestic beef production, differences in market prices and religious practices.

Conversely, Thailand is the largest importing country of cattle and buffalo from Myanmar, Laos and Cambodia. The main trading route involves cattle moving within the country to the Bangkok market and towards the south to supply markets in Malaysia. Since the local supply of fresh meat cannot meet the demand for local consumption, Malaysia takes up a central position for the importation of livestock into the Myanmar-Thailand-Malaysia (MTM) peninsula, with around 80% of its imports of beef and buffalo meat originating from India (30). Laos is

considered a pathway for the movement of suckling pigs from Vietnam to Thailand, for large ruminants from Cambodia to Thailand (through the southern regions), and from the People's Republic of China (hereafter referred to as China) to Thailand (through the north-western regions). On the other hand, and depending on the time of the year and other market factors, pigs may enter into Cambodia from Vietnam and Thailand and move to the southern Vietnamese regions, while cattle reared in the north-east move on the hoof to markets either in Phnom Penh or towards Thailand.

In recent years, due to an increase in demand, uncharacteristic livestock movements have been taking place from China to the Southeast Asian countries, mainly involving the movement of pigs through Vietnam and large ruminants through Laos. Within the Southeast Asia market chain, livestock traders act at different levels: whereas small traders are involved in livestock trade within districts and provinces, large traders and livestock companies engage in cross-border trading. However, since many of the transboundary movements are unregulated, much of this trade is not officially acknowledged and therefore informal cross-border routes tend to prevail (77). It is worth mentioning that livestock transporters travel rapidly across countries delivering 'transit' cattle, i.e. from Thailand to the Vietnamese border depots and vice versa. Transport operators have a poor understanding of how livestock diseases spread. Therefore, trucks are washed infrequently and disinfection is not attempted (13), further increasing the dispersal of FMDV infection between and within countries of the Southeast Asia region.

Table II
Southeast Asian trade in large ruminants and pigs at country level: imports/exports and price ranking

Large ruminants	Cattle (millions)	Buffalo (millions)	Imports	Exports	Price ranking
Cambodia	3.34	0.72	–	+++	Moderate low
Laos	1.35	1.16	–	+++	Moderate low
Malaysia	0.8	0.14	+++	–	High
Myanmar	12.63	2.84	–	++++	Low
Thailand	9.34	1.58	++	++	Moderate
Vietnam	6.88	3.00	++	–	Moderate high

Pigs	Cattle (millions)	Pigs (millions)	Imports	Exports	Price ranking
Cambodia		2.74	+++	–	Moderate high
Laos		1.97	++	–	Moderate
Malaysia		2.08	+	+	Moderate low
Myanmar		6.95	+	–	Moderate low
Thailand		9.31	+/-	++	Moderate low
Vietnam		26.56	–	++++	Low

Source: adapted from Abila, 2009 (2)

Foot and mouth disease epidemiological patterns and the history of infections in Southeast Asia

Foot and mouth disease is not widely distributed within the region and, although epidemics occur at relatively frequent intervals, the occurrence of events varies spatially and temporally. Indonesia, Singapore, Brunei, East Malaysia and much of the Philippines are recognised as free from the disease, while Cambodia, Laos, peninsular Malaysia, Myanmar, Thailand and Vietnam have endemic infection. Types O, A and Asia 1 are the only three serotypes endemic in the region (Table I). Type O is the most common circulating serotype with three distinct topotypes, consisting of the SEA topotype, the ME-SA topotype, and the Cathay, pig-adapted topotype. First recorded in Myanmar, in 1998, the Mya-98 strain of the SEA topotype causes outbreaks throughout the region. Phylogenetic analysis reveals how different introductions may be sourced from different countries and similar viruses can consequently be found in various countries. For example, isolates from Thailand in 2007 can be divided into a number of different sub-lineages. Viruses collected from the north-east provinces (Udon Thani, Khon Kaen) were found to be closely related to isolates reported in Laos, whilst those submitted from the southern provinces (Songkhla, Surat Thani) were reported as matching with viruses from Malaysia. Moreover, a molecular epidemiological study of Malaysian type O Mya-98 viruses collected between 2000 and 2009 has demonstrated how those viruses were interleaved with sequences of other samples collected in the region and grouped with contemporaneous isolates from neighbouring countries (1).

Malaysia is dependent on imports of live cattle and frozen beef to meet domestic demand and the principal livestock route moves southward through Thailand via Bangkok, where a large auction market exists, sourcing animals from different parts of the Southeast Asian region – principally, suckling pigs from Vietnam and buffalo and cattle from Myanmar. Within Myanmar, animals move from the north to the south, and large numbers of cattle cross the border to Thailand and travel on to Malaysia. Malaysian authorities recently reported that a shipment of 353 head of cattle imported from Thailand were sent back after they were detected as having clinical signs of FMD at the quarantine posts (53). Serological surveys of animals imported into Thailand from Myanmar demonstrated that up to 70% had been previously exposed to the disease (78). Therefore, Myanmar could be considered a key country in terms of regional epidemiology and spread of FMDV, due to the very large ruminant population and their significant export flow into the MTM peninsula.

Furthermore, Myanmar is a recipient country for livestock imports from Bangladesh which, in turn, is dependent on cattle trade from Nepal and India. The linkage with India and Bangladesh is clearly demonstrated by the introduction of the O-PanAsia-2 strain in Southeast Asia. Although this type O lineage is widespread in the Middle East and on the Indian subcontinent, within Southeast Asia it has only been reported in Malaysia in 2003 and again during 2005 and 2009. The close relationship (>97%) of the Malaysian viruses with those previously collected in India (2001), Nepal (2003) and Bhutan (2003) supports the hypothesis of introduction by importation of infected buffalo meat from India (55).

In addition, a recent study on viruses collected from Bangladesh in 2009 provides further evidence on the dispersal of FMDV strains from India to the East (46). Owing to differences in religious practices and competitive market prices, cattle and buffalo move from India and Nepal to Bangladesh, where neither border control nor animal quarantine facilities exist. Therefore, FMDV spread in the MTM peninsula might be associated with both legal and illegal livestock movements between countries, driven by the significant animal inflow from the Indian subcontinent.

In contrast to the type O strains of FMDV, the Asia topotype, the only topotype of serotype A identified in Southeast Asia, is represented by a strain that is indigenous to the region, and introductions from India seem less common. This virus had not been reported in Myanmar, although widely isolated from the other Southeast Asian countries. However, specific FMDV type A antibodies were detected in buffalo samples collected during 2008 and 2009 from the Yangon, Ayeyarwady and Magway regions (70). Although virus was not isolated, this may provide evidence of the presence of type A FMDV in Myanmar and, therefore, outbreaks caused by this strain may circulate undetected or the virus may originate from further west (i.e. the Indian subcontinent) (29). In confirming the above hypothesis, a type A Asia topotype FMDV was isolated in November 2010 from cattle resident in the Mungdaw district (Rahkine State), north-west Myanmar, close to the border with Bangladesh and India. This first reported case of type A Asia topotype FMDV in Myanmar was found to be closely related (>90%) with viruses previously circulating in 2000 in India (84).

The genetic diversity of the type A FMDV encountered in Southeast Asia within a short space of time suggests multiple introductions. In fact, the Asia topotype spread within Southeast Asia can be clarified by the phylogenetic relationship among viruses collected from different Southeast Asian countries. While isolates collected in Thailand from 2005 to 2007 were grouped together with viruses from Malaysia and Laos, Cambodian isolates from 2006 and 2008 were only matched with contemporary

viruses from Laos. In addition, viruses collected between 2008 and 2010 from Thailand, and in 2009 in Malaysia, fell into another group which included contemporary viruses from Vietnam. Interestingly, type A Asia topotype viruses isolated during outbreaks in 2009 in China and 2010 in the Republic of Korea were also included in the same group as the Thai, Malaysian and Vietnamese viruses.

This is not the only report of the relationship between viruses from Southeast Asia and China. In fact, type Asia 1 FMD viruses responsible for outbreaks in China in the Yunnan province and in Vietnam during 2005 and 2006 were also related to viruses originating from Thailand (1998) and Myanmar (2005) (68). Again, the emergence of the pig-adapted strain or Cathay O topotype, which represents a fourth FMD epidemiological cycle in Southeast Asia (19), may be attributed to the movement of pigs across the Chinese border into the Northern Vietnamese Province. Cathay isolates appeared on mainland Southeast Asia in Vietnam in 1997 and were recorded again in 1999, 2004, 2006 and 2008, with limited independent spread into Thailand and Malaysia in 2005.

Since these viruses do not appear to be closely related to contemporary viruses of the same strain from the Philippines or Hong Kong, it seems more likely that they were introduced from elsewhere, most likely mainland China, via introductions of live pigs or pork (21). Additionally, in 2010, FMD viruses belonging to the O/SEA/Mya-98 lineage were detected in Hong Kong (Special Administrative Region), China, the Republic of Korea, Japan, Mongolia and eastern Russia (51) (Knowles *et al.*, unpublished data). Phylogenetic studies indicate a close relationship between this virus and those present in Malaysia, Myanmar and Thailand in 2009 and point to at least two independent virus introductions into the region from Southeast Asia (Knowles *et al.*, unpublished data).

Discussion

The globalisation of livestock trade offers many benefits and economic opportunities, but also represents a constant and increasing threat for the persistence and spread of devastating transboundary disease outbreaks (17). Enhanced global livestock production has been driven by the increased demand for animal protein by a growing world population and by access of more countries to lucrative livestock markets. Economic development itself facilitates FMD control and consequent improved access to export markets. At global and regional levels, the movements of livestock and their products, on many different scales, are immensely complex. This increases the risks for the spread of infections, and the probability that all countries may eventually be exposed to the

introduction and spread of exotic epidemic diseases. Theoretically, real-time evaluation of changing trade practices should be a useful tool to predict disease emergence, but it is not often achieved and requires further development.

Changes in livestock keeping also impact upon the risk of viral spread and diversification; for example, in developing countries, where industries are being transformed by the implementation of more intensive farming units overlaid on top of the traditional small-scale system (i.e. pastoralist and smallholder production present in sub-Saharan Africa and Southeast Asia). Furthermore, such changes often outpace improvements in the animal health institutions required for effective disease control within complex ecosystems.

Genetic characterisation of FMDV has revealed that particular serotypes and strains of the virus occur and evolve in specific ecosystems, with periodic extensions of range of either short or long duration (55). This implies the existence of relative barriers to the spread of the virus; most likely trade-related barriers, although other factors may affect the establishment of endemicity. Molecular epidemiology, with its power to resolve transmission pathways, has contributed enormously to our understanding of spatial and evolutionary traits underlying FMD outbreaks. However, phylogenetic analyses on their own do not directly reveal the mechanisms of local and regional spread and taxonomic relationships do not entirely explain the dynamics of FMD. Additionally, the resolving power of the sequence data is affected by the length of the determined genome sequence, e.g. full genome sequences offer greater resolution for outbreak tracing than VP1 alone. The possibility of genetic recombination within and among FMDV serotypes also needs to be taken into account, since this may be a mechanism for generating novel virus strains with altered phenotypic characteristics. Certainly, FMD epidemics involving large host populations would be expected to provide ideal conditions for the occurrence and amplification of evolutionary shift and for recombination between virus strains (18).

This paper is intended to be an initial and largely descriptive attempt at matching the available information on livestock movement and trade patterns with molecular genotyping data, to provide a synopsis of the risk factors and mechanisms involved in the epidemiological dynamics of FMDV dispersal across regions.

In the last ten years, much research has focused on understanding epidemic pathways in normally disease-free countries (for example, the outbreaks that occurred in the UK in 2001 and 2007) and using a combination of conventional and molecular epidemiological approaches (14). Less effort has been directed towards assessing the

interplay between ecosystem conditions and the more complicated FMD dynamics within endemic settings. This review has therefore targeted three important regions of FMDV endemicity, namely sub-Saharan Africa, the Middle East and Southeast Asia. The principal aim has been to review the availability of complementary phylogenetic and trade data and to draw out obvious inferences, but no quantitative analysis has been attempted.

The association between trade and the introduction and spread of FMDV is perhaps best appreciated for the Middle East, where it has long been recognised that epidemics involving new strains are repeatedly associated with the importation of animals from Asia and Africa. This pattern has been amply reconfirmed by a series of incidents in the last ten years, including the introduction of East African strains of type A FMDV into Egypt and type O into Yemen, and the introduction and long-term circulation of type O strains; first O-PanAsia, later replaced by O-PanAsia-2. The ultimate origin of the widely dispersed A-Iran-05 strain has not been determined. These events highlight increasingly close trade links between the 'Ruminant Street', the Horn of Africa and the Indian subcontinent, as well as increased cross-border livestock movements. In Southeast Asia, there have also been clear examples of the endemic regional cycle of virus circulation being periodically reinforced by novel introductions from outside; recent examples being the appearance of the O-PanAsia and O-Cathay strains. In sub-Saharan Africa, the complex interplay between local and distant animal movements and the persistence and spread of FMDV is least well studied and understood. Additional uncertainty surrounds the role of wildlife as a reservoir for infection of domestic species.

Despite efforts to link and reinforce laboratory activities through the formation of FMD reference laboratory networks, only incomplete data are available for phylogenetic studies in many endemic areas, due to insufficient sampling and poor spatial and demographic meta-data. In addition, there are extremely limited data on livestock networks to explain the established phylogenetic patterns. This knowledge gap represents a significant constraint in understanding the dynamics of FMDV spread. An important requirement is to establish how epidemic and metapopulation disease dynamics modulate selective forces to drive long-term phylogenetic patterns. Bayesian phylogeography offers a promising approach to incorporate the spatial and temporal dynamics of gene

flow and provide a biogeographical perspective (43). It could contribute significantly to evolutionary hypothesis testing, focusing not only on viral phylodynamics but also on molecular evolution (31).

To achieve this objective, a comprehensive approach is needed to monitor and predict the impact of livestock movements and trade patterns on the dispersal of FMDV. This requires both field and genetic data collection at the levels of both individual hosts and populations. The systematic collection of this information should be a priority for research, as elucidating the phylodynamics of FMD epidemics has important implications for public health management and disease control. Additional studies employing whole genome sequencing are also warranted, not only to improve the resolution of tracing, but also to reveal the occurrence and impact of recombination between FMD viruses in relation to the emergence of new strains.

Sustained and coordinated responses across political boundaries are necessary to control inter- and intra-regional FMD dispersal. The FAO is predicting the need for a 50% increase in global food production by 2030 to sustain the expected growth in human population. Since most of this production will have to be met by developing countries, the control of FMD is a key issue for global food security. The identification of critical control points for livestock movements and risk pathways of FMDV spread is a key prerequisite for intervention strategies contributing to progressive pathways for the worldwide control of FMD.

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Prise en compte concomitante de la phylogénétique et de la structure des échanges d'animaux d'élevage pour expliquer la propagation de la fièvre aphteuse en Afrique subsaharienne, au Moyen-Orient et en Asie du Sud-Est

A. Di Nardo, N.J. Knowles & D.J. Paton

Résumé

Le commerce international d'animaux et de leurs produits est l'un des principaux facteurs déterminant l'épidémiologie des maladies transfrontalières telles que la fièvre aphteuse à l'échelle mondiale. Outre les pertes de productivité qu'elle induit, la fièvre aphteuse est extrêmement contagieuse, ayant plusieurs hôtes et diverses voies de transmission, ce qui en fait l'une des maladies les plus importantes affectant le commerce du bétail. L'apparition de la fièvre aphteuse dans un pays précédemment indemne a des conséquences catastrophiques sur l'économie agricole nationale ; dans les pays en développement où elle sévit à l'état endémique, la fièvre aphteuse représente une menace pour la subsistance et les revenus des éleveurs. Les inférences phylogénétiques à partir des séquences moléculaires des virus isolés s'avèrent très utiles pour déterminer la dynamique de la propagation du virus de la fièvre aphteuse dans le globe et contribuent à élucider les voies évolutives et spatiales intervenant dans les épidémies de fièvre aphteuse. La recherche de correspondances entre les déplacements du bétail et l'épidémiologie moléculaire fournit des éléments de compréhension qui permettent de retracer le chemin de propagation du virus sur plusieurs régions géographiques, condition fondamentale pour mettre en place des stratégies efficaces de lutte contre la fièvre aphteuse dans le monde. Les auteurs font le point sur l'évolution de la fièvre aphteuse dans le monde depuis dix ans, et examinent les découvertes phylogénétiques ainsi que l'information disponible sur les systèmes de production animale et sur les échanges internationaux pour analyser la dynamique épidémiologique de la fièvre aphteuse et les sources d'introduction du virus au niveau régional, en Afrique subsaharienne, au Moyen-Orient et en Asie du Sud-Est.

Mots-clés

Afrique subsaharienne – Asie du Sud-Est – Commerce international de bétail – Fièvre aphteuse – Moyen-Orient – Phylogéographie – Système de production animale.



Uso combinado de la filogenética y la distribución del comercio ganadero para entender mejor la propagación de la fiebre aftosa en el África subsahariana, Oriente Medio y el Sudeste asiático

A. Di Nardo, N.J. Knowles & D.J. Paton

Resumen

Es bien sabido que el comercio internacional de animales y productos de origen animal es uno de los principales factores que determinan la epidemiología

mundial de las enfermedades transfronterizas, tales como la fiebre aftosa. Además de las graves pérdidas que causa en la producción, la fiebre aftosa es muy contagiosa, ya que se transmite a través de muy diversos huéspedes y vías de transmisión, lo que hace que sea una de las más importantes enfermedades que afectan al comercio de ganado. Su aparición en un país hasta entonces libre de ella entraña consecuencias dramáticas para la economía agrícola. No menos graves son sus efectos sobre los medios de subsistencia y los ingresos de los países en desarrollo donde la enfermedad aún es endémica. En la dinámica de la propagación planetaria del virus de la fiebre aftosa, las inferencias filogenéticas a partir de las secuencias moleculares de cepas aisladas resultan de gran ayuda para investigar las rutas evolutivas y espaciales que subyacen a los focos epidémicos de la enfermedad. Al cotejar la epidemiología molecular con datos sobre el movimiento de los ganados se abren pistas esclarecedoras para reconstruir la propagación del virus entre regiones geográficas, lo cual es requisito previo para definir estrategias de lucha contra la fiebre aftosa a escala mundial. Los autores pasan revista a la situación de la fiebre aftosa en el mundo durante el último decenio, combinando información filogenética con datos sobre los sistemas de producción ganadera y el comercio internacional para analizar así la dinámica epidemiológica de la enfermedad y los focos de introducción del virus en las regiones del África subsahariana, Oriente Medio y el Sudeste asiático.

Palabras clave

África subsahariana – Comercio de ganado – Fiebre aftosa – Filogeografía – Oriente Medio – Sistema de producción ganadera – Sudeste asiático.



References

1. Abdul-Hamid N.F., Hussein N.M., Wadsworth J., Radford A.D., Knowles N.J. & King D.P. (2010). – Phylogeography of foot-and-mouth disease virus types O and A in Malaysia and surrounding countries. Doi: 10.1016/j.meegid.2010.11.003. *Infect. Genet. Evol.*, **11** (2), 320-328.
2. Abila R. (2009). – World Organisation for Animal Health (OIE) Southeast Asia Foot and Mouth Disease (SEAFMD) campaign and its link to animal movement projects. In Proc. 8th Meeting of the Lower Mekong Working Group for Foot and Mouth Disease Zoning Animal Movement Management, 23-25 November, Ho Chi Minh City, Vietnam. OIE, Paris.
3. Agriconsortium (2003). – Livestock and livestock products production and marketing system in Kenya, final report. Kenya/European Commission/Agrisystem Limited, Aylesbury, United Kingdom.
4. Aklilu Y., Irungu P. & Reda A. (2002). – An audit of the livestock marketing status in Kenya, Ethiopia and Sudan (Vol. I). Community-based Animal Health and Participatory Epidemiology Unit, Pan African Programme for the Control of Epizootics, Organization of African Unity/Interafrican Bureau for Animal Resources, Nairobi, Kenya. Available at: www.igad-data.org/index.php?option=com_docman&task=doc_details&gid=1259&Itemid=42 (accessed on 14 October 2010).
5. Arrowsmith A.E.M. (1975). – Variation among strains of type A foot-and-mouth disease virus in the Eastern Mediterranean region 1964-1972. *J. Hyg. (London)*, **75** (3), 387-397.
6. Bailey T., O'Donovan D., Kinne J. & Wernery U. (2009). – Observation of foot-and-mouth disease in vaccinated and unvaccinated wildlife in the United Arab Emirates. *Wildlife Middle East Newsletter*, **4** (1), 4. Available at: www.wmenews.com/newsletters/File/Volume-4/Issue-1/WME_V4_I1_en.pdf (accessed on 14 October 2010).

7. Bastos A.D., Boshoff C.I., Keet D.F., Bengis R.G. & Thomson G.R. (2000). – Natural transmission of foot-and-mouth disease virus between African buffalo (*Syncerus caffer*) and impala (*Aepyceros melampus*) in the Kruger National Park, South Africa. *Epidemiol. Infect.*, **124** (3), 591-598.
8. Bastos A.D., Haydon D.T., Sangare O., Boshoff C.I., Edrigh J.L. & Thomson G.R. (2003). – The implications of virus diversity within the SAT 2 serotype for control of foot-and-mouth disease in sub-Saharan Africa. *J. gen. Virol.*, **84** (6), 1595-1606.
9. Bourn D. (2003). – Livestock dynamics in the Arabian Peninsula: a regional review of national livestock resources and international livestock trade. Consultancy report by the Environmental Research Group Oxford Ltd for the Food and Agriculture Organization of the United Nations, Rome. Available at: ergodd.zoo.ox.ac.uk/download/reports/Livestock%20Dynamics%20in%20the%20Arabian%20Peninsula.pdf (accessed on 14 October 2010).
10. Bronsvoort B.M.C., Parida S., Handel I., McFarland S., Fleming I., Hamblin P. & Kock R. (2008). – Serological survey for foot-and-mouth disease virus in wildlife in East Africa and estimation of test parameters of a nonstructural protein enzyme-linked immunosorbent assay for buffalo. *Clin. vaccine Immunol.*, **15** (6), 1003-1011.
11. Bronsvoort B.M.C., Radford A.D., Tanya V.N., Nfon C., Kitching R.P. & Morgan K.L. (2004). – Molecular epidemiology of foot-and-mouth disease viruses in the Adamawa province of Cameroon. *J. clin. Microbiol.*, **42** (5), 2186-2196.
12. Centers for Disease Control and Prevention (CDC) (2000). – Outbreak of Rift Valley fever – Yemen, August – October 2000. *Morb. Mort. weekly Rep.*, **49** (47), 1065-1066.
13. Cocks P., Abila R., Bouchot A., Benigno C., Morzaria S., Inthavong P., Van Long N., Bourgeois-Luthi N., Scoizet A. & Sieng S. (2009). – Study on cross-border movement and market chains of large ruminants and pigs in the Greater Mekong Sub-Region. In Project report for the Food and Agriculture Organization (FAO), Asian Development Bank (ADB) and the OIE Sub-Regional Coordination Unit for Southeast Asia (OIE-SEAFMD), Bangkok. Available at: ulm.animalhealthresearch.asia/newsletters/FAO_ADB_OIE_Cross-Border%20movement%20study_Final%20Report.pdf (accessed on 14 October 2010).
14. Cottam E.M., Thebaud G., Wadsworth J., Gloster J., Mansley L., Paton D.J., King D.P. & Haydon D.T. (2008). – Integrating genetic and epidemiological data to determine transmission pathways of foot-and-mouth disease virus. *Proc. Biol. Soc.*, **275** (1637), 887-895.
15. Cottral G.E. (1969). – Persistence of foot-and-mouth disease virus in animals, their products and the environment. *Bull. Off. int. Epiz.*, **71** (3-4), 549-568.
16. Davis F.G. (2006). – Risk of Rift Valley fever epidemic at the haj in Mecca, Saudi Arabia. In Biological disasters of animal origin. The role and preparedness of veterinary and public health services (M. Hugh-Jones, ed.). *Rev. sci. tech. Off. int. Epiz.*, **25** (1), 137-147.
17. Domenech J., Lubroth J., Eddi C., Martin V. & Roger F. (2006). – Regional and international approaches on prevention and control of animal transboundary and emerging diseases. *Ann. N.Y. Acad. Sci.*, **1081**, 90-107.
18. Domingo E., Ruiz-Jarbo C.M., Arias A., Garcia-Arriaza J. & Escarmis C. (2004). – Quasispecies dynamics and evolution of foot-and-mouth disease virus. In Foot and mouth disease: current perspectives (F. Sobrino & E. Domingo, eds). Horizon Bioscience, Norfolk, United Kingdom, 457 pp.
19. Dunn C.S. & Donaldson A.I. (1997). – Natural adaptation to pigs of a Taiwanese isolate of foot-and-mouth disease virus. *Vet. Rec.*, **141** (7), 174-175.
20. European Commission for the Control of Foot-and-Mouth Disease (EuFMD) (1999). – FMD situation in Europe and in other regions: summary of the type O foot-and-mouth disease situation in North Africa as of 29th March, Appendix 3. In Report of the 33rd Session of EuFMD, 9 April, Rome. Available at: www.fao.org/ag/againfo/commissions/docs/genses33/app03.html (accessed on 14 October 2010).
21. European Food Safety Authority (EFSA) (2006). – Opinion of the Scientific Panel on Animal Health and Welfare on request from the European Commission related to: assessing the risk of foot and mouth disease introduction into the EU from developing countries, assessing the reduction of this risk through interventions in developing countries/regions aiming at controlling/eradicating the disease, and tools for the control of a foot and mouth disease outbreak: update on diagnostics and vaccines. *EFSA J.*, **313**, 1-34. Available at: www.efsa.europa.eu/en/efsajournal/doc/ahaw_op_ej313_fmd_en1.pdf (accessed on 14 October 2010).
22. Fleming D.E., Hammadi N., Alqadasi M.M.A. & Saed K. (2008). – Livestock movement and trade study for the Yemen agricultural support program. Report prepared by ARD Inc. for the United States Agency for International Development. ARD, Burlington, Vermont. Available at: pdf.usaid.gov/pdf_docs/PNADP686.pdf (accessed on 14 October 2010).
23. Food and Agriculture Organization of the United Nations (FAO) (2001). – Pastoralism in the new millennium. FAO Animal Production and Health Paper 150. FAO, Rome. Available at: www.fao.org/DOCREP/005/Y2647E/y2647e00.htm (accessed on 14 October 2010).
24. Food and Agriculture Organization of the United Nations (FAO) (2007). – Foot-and-mouth disease: situation worldwide and major epidemiological events in 2005-2006 (K. Sumption, J. Pinto, J. Lubroth, S. Morzaria, T. Murray, S. de La Roque & F. Nejeumi, contributors). *EMPRES Focus On Bull.*, **1**. Available at: www.fao.org/docs/eims/upload/225050/Focus_ON_1_07_en.pdf (accessed on 14 October 2010).
25. Food Security and Nutrition Analysis Unit (FSNAU) (2010). – Integrated database system. Available at: www.fsnau.org/ (accessed on 14 October 2010).
26. Foot-and-Mouth Disease Newsletter (FMD-News) (2010). – United Arab Emirates. UAE bans import of livestock with epidemic disease (01 March 2010). Available at: fmd.ucdavis.edu/news.php (accessed on 14 October 2010).

27. Forman S., Le Gall F., Belton D., Evans B., Francois J.L., Murray G., Sheesley D., Vandersmissen A. & Yoshimura S. (2009). – Moving towards the global control of foot and mouth disease: an opportunity for donors. *Rev. sci. tech. Off. int. Epiz.*, **28** (3), 883-896.
28. Gilbert M., Aktas S., Mohammed H., Roeder P., Sumption K., Tufan M. & Slingenbergh J. (2005). – Patterns of spread and persistence of foot-and-mouth disease types A, O and Asia-1 in Turkey: a meta-population approach. *Epidemiol. Infect.*, **133** (3), 537-545.
29. Gleeson L.J. (2002). – A review of the status of foot-and-mouth disease in South-East Asia and approaches to control and eradication. In *Foot and mouth disease: facing the new dilemmas* (G.R. Thomson, ed.). *Rev. sci. tech. Off. int. Epiz.*, **21** (3), 465-475.
30. Gleeson L.J., Samuel A.R. & Knowles N.J. (2003). – Epidemiology of foot-and-mouth disease in Southeast Asia. In *Foot and mouth disease: control strategies* (B. Dodet & M. Vicari, eds). Elsevier, Paris, 85-102.
31. Grenfell B.T., Pybus O.G., Gog J.R., Wood J.L.N., Daly J.M., Mumford J.A. & Holmes E.C. (2004). – Unifying the epidemiological and evolutionary dynamics of pathogens. *Science*, **303** (5656), 327-332.
32. Hargreaves S.K., Foggini C.M., Anderson E.C., Bastos A.D.S., Thomson G.R., Ferris N.P. & Knowles N.J. (2004). – An investigation into the source and spread of foot and mouth disease virus from a wildlife conservancy in Zimbabwe. *Rev. sci. tech. Off. int. Epiz.*, **23** (3), 783-790.
33. International Trade Centre (ITC) (2010). – Trade competitiveness map. ITC, United Nations Conference on Trade and Development/World Trade Organization, Geneva. Available at: www.intracen.org/ (accessed on 14 October 2010).
34. Kamuanga M.J.B., Somda J., Sanon Y. & Kagone H. (2008). – Livestock and regional market in the Sahel and West Africa: potential and challenges. Report of a Joint Initiative of the Economic Community of West African States and the Sahel and West Africa Club/Organisation for Economic Co-operation and Development. Available at: www.donorplatform.org/component/option,com_docman/task,doc_view/gid,1357/Itemid,98/ (accessed on 14 October 2010).
35. Knowles N.J. (2009). – FMD distribution in Africa: types, topotypes and virus pools and their relevance for ecosystem based surveillance and control programs. In *Proc. Workshop on the Development of a Long Term Action Plan (Roadmap) for Improved Surveillance and Control of FMD in Africa*, 26-30 January, Nairobi, Kenya. Available at: www.fao.org/ag/againfo/commissions/en/eufmd/report_workshops.html (accessed on 14 October 2010).
36. Knowles N.J. & Samuel A.R. (2003). – Molecular epidemiology of foot-and-mouth disease virus. *Virus Res.*, **91** (1), 65-80.
37. Knowles N.J., Nazem Shirazi M.H., Wadsworth J., Swabey K.G., Stirling J.M., Statham R.J., Li Y., Hutchings G.H., Ferris N.P., Parlak U., Ozyoruk F., Sumption K.J., King D.P. & Paton D.J. (2009). – Recent spread of a new strain (A-Iran-05) of foot-and-mouth disease virus type A in the Middle East. *Transbound. emerg. Dis.*, **56** (5), 157-169.
38. Knowles N.J., Samuel A.R., Davies P.R., Midgley R.J. & Valarcher J.-F. (2005). – Pandemic strain of foot-and-mouth disease virus serotype O. *Emerg. infect. Dis.*, **11** (12), 1887-1893.
39. Knowles N.J., Swabey K.G., Midgley R.J., Davies P.R. & Wadsworth J. (2006). – Global molecular epidemiology of foot-and-mouth disease virus type C. In *Proc. 14th Meeting of the European Study Group on the Molecular Biology of Picornavirus*, 26 November – 1 December, Saariselkä, Inari, Finland.
40. Knowles N.J., Wadsworth J., Hammond J.M. & King D.P. (2010). – Foot-and-mouth disease virus genotype definitions and nomenclature. In *Proc. Open Session of the European Commission for the Control of Foot-and-Mouth Disease Standing Technical Committee*, 28 September – 1 October, Vienna.
41. Knowles N.J., Wadsworth J., Parlak U., Ozyoruk F., Nazem Shirazi M.H., Ferris N.P., Hutchings G.H., Stirling J.M., Hammond J.M. & King D.P. (2010). – Recent events in the evolution of foot-and-mouth disease in the Middle East. In *Proc. Open Session of the European Commission for the Control of Foot-and-Mouth Disease Standing Technical Committee*, 28 September – 1 October, Vienna.
42. Knowles N.J., Wadsworth J., Reid S.M., Swabey K.G., El-Kholy A.A., Abd El-Rahman A.O., Soliman H.M., Ebert K., Ferris N.P., Hutchings G.H., Statham R.J., King D.P. & Paton D.J. (2007). – Foot-and-mouth disease virus serotype A in Egypt. *Emerg. infect. Dis.*, **13** (10), 1593-1596.
43. Lemey P., Rambaut A., Drummond A.J. & Suchard M.A. (2009). – Bayesian phylogeography finds its roots. *PLoS comput. Biol.*, **5** (9), e1000520. Doi:10.1371/journal.pcbi.1000520.
44. Little P.D. (1996). – Livestock trade and food security in the Kenya/Somalia borderlands. Institute for Development Anthropology, Binghamton, New York.
45. Little P.D. (2003). – Somalia: economy without state. Indiana University Press, Bloomington & Indianapolis, Indiana.
46. Loth L., Osmani M.G., Kalam M.A., Chakraborty R.K., Wadsworth N.J., Knowles N., Hammond J.M. & Benigno C. (2011). – Molecular characterization of foot-and-mouth disease virus: implications for disease control in Bangladesh. *Transbound. emerg. Dis.* (in press).
47. McPeak J. & Little P.D. (2005). – Pastoral livestock marketing in East Africa: research and policy challenges. ITDG Publishing, Rugby, United Kingdom.

48. Mahadevan P. & Devendra C. (1986). – Present and projected ruminant production system of Southeast Asia and the South Pacific. *In Forages in Southeast Asian and South Pacific agriculture* (G.J. Blair, D.A. Ivory & T.R. Evans, eds). Proc. international workshop, 19-23 August 1985, Cisarua, Indonesia. ACIAR Proceedings No. 12. Australian Centre for International Agricultural Research (ACIAR), Canberra, 7-11.
49. Mariner J.C. & Roeder P.L. (2003). – The use of participatory epidemiology in studies of the persistence of rinderpest in East Africa. *Vet. Rec.*, **152** (21), 641-647.
50. Ozawa Y. (1993). – Strategy options for the control of foot-and-mouth disease in Southeast Asia. *In Proc. International Workshop on Diagnosis and Epidemiology of Foot-and-Mouth Disease in Southeast Asia*, 6 September, Lampang, Thailand, 79-84.
51. Paton D.J., King D.P., Knowles N.J. & Hammond J. (2010). – Recent spread of foot-and-mouth disease in the Far East. *Vet. Rec.*, **166** (18), 569-570.
52. Paton D.J., Sumption K.J. & Charleston B. (2009). – Options for control of foot-and-mouth disease: knowledge, capability and policy. *Philos. Trans. roy. Soc. Lond., B, biol. Sci.*, **364** (1530), 2657-2667.
53. ProMED-mail (2010). – Foot and mouth disease, bovine – Malaysia ex Thailand. PRO/MDBS-mail 16 November 2010, archive no. 20101116.4152. Available at: www.promedmail.org/pls/apex/f?p=2400:1202:3133487045703150::NO::F2400_P1202_CHECK_DISPLAY,F2400_P1202_PUB_MAIL_ID:X,85854 (accessed on 14 October 2010).
54. Roeder P.L., Taylor W.P. & Rweyemamu M.M. (2006). – Rinderpest in the twentieth and twenty-first centuries. *In Rinderpest and peste des petits ruminants: virus plagues of large and small ruminants* (T. Barrett, P.-P. Pastoret & W.P. Taylor, eds). Academic Press, Elsevier Ltd, London, 105-142.
55. Rweyemamu M., Roeder P., Mackay D., Sumption K., Brownlie J., Leforban Y., Valarcher J.-F., Knowles N.J. & Saraiva V. (2008). – Epidemiological patterns of foot-and-mouth disease worldwide. *Transbound. emerg. Dis.*, **55** (1), 57-72.
56. Samuel A.R. & Knowles N.J. (2001). – Foot-and-mouth disease type O viruses exhibit genetically and geographically distinct evolutionary lineages (topotypes). *J. gen. Virol.*, **82** (3), 609-621.
57. Sangula A.K., Belsham G.J., Muwanika V.B., Heller R., Balinda S.N., Mesembe C. & Siegismund H.R. (2010). – Evolutionary analysis of foot-and-mouth disease virus serotype SAT 1 isolates from East Africa suggests two independent introductions from southern Africa. *BMC evol. Biol.*, **10**, 371.
58. Schumann K.R., Knowles N.J., Davies P.R., Midgley R.J., Valarcher J.-F., Raoufi A.Q., McKenna T.S., Hurtle W., Burans J.P., Martin B.M., Rodriguez L.L. & Beckham T.R. (2008). – Genetic characterization and molecular epidemiology of foot-and-mouth disease virus isolated from Afghanistan in 2003-2005. *Virus Genes*, **36** (2), 401-413.
59. Scudamore J.M. (2002). – Origin of the UK foot-and-mouth disease epidemic in 2001. Department of Environment, Food and Rural Affairs (Defra), London. Available at: www.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/fmdorigins1.pdf (accessed on 14 October 2010).
60. Sebhatu T.T., Dekker A. & Moorman R.J.M. (2010). – Serological evidence of foot-and-mouth disease virus serotype C & SAT-1 infections in Eritrea. *In Proc. Open Session of the European Commission for the Control of Foot-and-Mouth Disease Standing Technical Committee*, 28 September – 1 October, Vienna.
61. Sellers R.F. (1971). – Quantitative aspects of the spread of foot and mouth disease. *Vet. Bull.*, **41** (6), 431-439.
62. Shoemaker T., Boulianne C., Vincent M.J., Pezzanite L., Al-Qahtani M.M., Al-Mazrou Y., Khan A.S., Rollin P.F., Swanepoel R., Ksiazek T.G. & Nichol S.T. (2002). – Genetic analysis of virus associated with emergence of Rift Valley fever in Saudi Arabia and Yemen, 2000-2001. *Emerg. infect. Dis.*, **8** (12), 1415-1420.
63. Slingenbergh J. (2003). – Clarifying disease spread in the Eurasian ruminant street. *In Report of the 35th Session of the European Commission for the Control of Foot-and-Mouth Disease*, 9-11 April, Rome, 111-115.
64. Solomon A., Workalemahu A., Jabbar M.A., Ahmed M.M. & Hurissa B. (2003). – Livestock marketing in Ethiopia: a review of structure, performance and development initiatives. ILRI Socio-economics and Policy Research Working Paper 52. International Livestock Research Institute (ILRI), Addis Ababa.
65. Soumare B., Thys E., Berkvens D., Hashi A. & Van Huylenbroeck G. (2006). – Effects of livestock import bans imposed by Saudi Arabia on Somaliland for sanitary reasons related to Rift Valley fever. *Outlook Agric.*, **35** (1), 19-24.
66. Thomson G.R., Vosloo W. & Bastos A.D.S. (2003). – Foot and mouth disease in wildlife. *Virus Res.*, **91** (1), 145-161.
67. United Nations Statistics Division (UNSD) (2010). – Commodity trade statistics database (COMTRADE). UNSD, New York. Available at: comtrade.un.org/db/default.aspx (accessed on 14 October 2010).
68. Valarcher J.-F., Knowles N.J., Zakharov V., Scherbakov A., Zhang Z., Shang Y.-J., Liu Z.-X., Liu X.-T., Sanyal A., Hemadri D., Tosh C., Rasool T.J., Pattnaik B., Schumann K.R., Beckham T.R., Linchongsubongkoch W., Ferris N.P., Roeder P.L. & Paton D.J. (2009). – Multiple origin of foot-and-mouth virus serotype Asia 1 outbreaks, 2003-2007. *Emerg. infect. Dis.*, **15** (7), 1046-1051.

69. Valarcher J.-F., Leforban Y., Rweyemamu M., Roeder P.L., Gerbier G., Mackay D.K., Sumption K.J., Paton D.J. & Knowles N.J. (2008). – Incurion of foot-and-mouth disease virus into Europe between 1985 and 2006. *Transbound. emerg. Dis.*, **55** (1), 14-34.
70. Verin B., Edwards J., Babu A., Di Nardo A., Grazioli S., Brocchi E., Paton D., Benigno C., Sumption K. & Parida S. (2010). – Detection of FMDV in carrier buffalo in South East Asia. *In Proc. Open Session of the European Commission for the Control of Foot-and-Mouth Disease Standing Technical Committee*, 28 September – 1 October, Vienna.
71. Vosloo W., Bastos A.D., Kirkbride E., Esterhuysen J.J., van Rensburg D.J., Bengis R.G., Keet D.W. & Thomson G.R. (1996). – Persistent infection of African buffalo (*Syncerus caffer*) with SAT-type foot-and-mouth disease viruses: rate of fixation of mutations, antigenic change and interspecies transmission. *J. gen. Virol.*, **77** (7), 1457-1467.
72. Vosloo W., Boshoff K., Dwarka R. & Bastos A. (2002). – The possible role that buffalo played in the recent outbreaks of foot-and-mouth disease in South Africa. *Ann. N.Y. Acad. Sci.*, **969**, 187-190.
73. Vosloo W., Thompson P.N., Botha B., Bengis R.G. & Thomson G.R. (2009). – Longitudinal study to investigate the role of impala (*Aepyceros melampus*) in foot-and-mouth disease maintenance in the Kruger National Park, South Africa. *Transbound. emerg. Dis.*, **56** (1-2), 18-30.
74. Waheed U., Parida S., Khan Q., Hussain M., Ebert K., Wadsworth J., Reid S., Hutchings G., Mahapatra M., King D., Paton D. & Knowles N. (2010). – Molecular characterisation of foot-and-mouth disease viruses from Pakistan, 2005-2008. *Transbound. emerg. Dis.*, **58** (2), 166-172.
75. Wint W. (2003). – Ruminants, seasons, and grazing in the Middle East. Consultancy report by the Environmental Research Group Oxford Ltd for the Food and Agriculture Organization of the United Nations, Rome. Available at: ergodd.zoo.ox.ac.uk/download/index.htm (accessed on 14 October 2010).
76. Wint G.R.W. & Robinson T.P. (2007). – Gridded livestock of the world. Food and Agriculture Organization of the United Nations, Rome. Available at: www.fao.org/ag/AGInfo/resources/en/glw/home.html (accessed on 14 October 2010).
77. Wongsathapornchai K., Salman M.D., Edwards J.R., Morley P.S., Keefe T.J., Van Campen H. & Weber S. (2008). – Assessment of the likelihood of the introduction of foot-and-mouth disease through importation of live animals into the Malaysia-Thailand-Myanmar peninsula. *Am. J. vet. Res.*, **69** (2), 252-260.
78. World Organisation for Animal Health (OIE) (2001). – Report of the 7th meeting of the OIE Sub-Commission for Foot-and-Mouth Disease in South-East Asia, 26 February – 3 March, Yangon, Myanmar. OIE, Paris.
79. World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) (2007). – Quarterly OIE/FAO FMD Reference Laboratory Report (July – September 2007). Available at: www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm (accessed on 14 October 2010).
80. World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) (2008). – Quarterly OIE/FAO FMD Reference Laboratory Report (April – June 2008). Available at: www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm (accessed on 14 October 2010).
81. World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) (2009). – Quarterly OIE/FAO FMD Reference Laboratory Report (January – March 2009). Available at: www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm (accessed on 14 October 2010).
82. World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) (2009). – Quarterly OIE/FAO FMD Reference Laboratory Report (July – September 2009). Available at: www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm (accessed on 14 October 2010).
83. World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) (2010). – Quarterly OIE/FAO FMD Reference Laboratory Report (April – June 2010). Available at: www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm (accessed on 14 October 2010).
84. World Reference Laboratory for Foot-and-Mouth Disease (WRLFMD) (2010). – Quarterly OIE/FAO FMD Reference Laboratory Report (October – December 2010). Available at: www.wrlfmd.org/ref_labs/fmd_ref_lab_reports.htm (accessed on 21 December 2010).
85. Zaal E, Siloma M.O., Andiema R. & Kotomei A. (2006). – The geography of integration: cross-border livestock trade in East Africa. *In Pastoral livestock marketing in East Africa: research and policy challenges* (J. McPeak & P.D. Little, eds). ITDG Publishing, Rugby, United Kingdom, 145-168.

