ORIGINAL ARTICLE

Incursions of Foot-and-Mouth Disease Virus into Europe between 1985 and 2006

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Summary

Foot-and-mouth disease (FMD) is one of the biggest threats to animal health in European countries. In the last 22 years (1985–2006), FMD has occurred 37 times in 14 European countries. Serotype O was most frequently involved in these outbreaks followed by A, C and Asia 1. Sometimes, epidemics were very limited and at other times, they were the cause of devastating economic losses. In most cases (22/37), the origin of the outbreaks could not be determined. For some of these outbreaks, however, routes of introduction and spread were identified through epidemiological inquiries. Moreover, in some cases, the origin of the virus was also traced by phylogenetic analysis of the partial or complete sequences of VP1 genes. Lessons learned from the outbreaks are still useful as most of the same risk factors persist. However, efforts made by FMD-free countries to help those where the disease is endemic are a valuable strategy for the reduction of the global risk. The present and the future potential sources of FMD infection need to be identified to best focus European efforts.

Introduction

In different parts of the world, foot-and-mouth disease (FMD), as one of the most contagious animal diseases, remains one of the biggest economic threats to agriculture and other sectors, such as the tourist industry. Most European countries currently have the status of being free from FMD without vaccination. However, FMD remains close to the borders of Europe and regularly makes incursions into the European Union (EU).

Foot-and-mouth disease virus (FMDV) is still present in large parts of Africa and Asia and to some extent, South America. It can be introduced into Europe by live-infected animals or by meat and other products derived from infected animals; in either case by legal or illegal importation. Other routes of introduction may also be possible, such as both short and long range airborne spread (long range possible only under certain specific circumstances), spread on fomites (for example animal transportation vehicles), via an escape of virus from a laboratory or vaccine plant, the use of improperly inactivated vaccines, the movement of people from an infected area (tourists and immigrants) or a malicious, intentional introduction as an agro-terrorism weapon. All these modes of spread are documented as having occurred, except, as yet, agro-terrorism.

The serotypes of FMD are not uniformly distributed in the regions of the world where the disease still occurs. In Africa, six of the seven serotypes of FMD (O, A, C, SAT 1, SAT 2, SAT 3) occur, while Asia contends with four serotypes (O, A, C, Asia 1) and South America only three (O, A, C). Occasionally, there have been incursions of types Asia 1 from Southern Asia in Iran and of SAT 1 and SAT 2 from Africa into

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the Middle East at the crossroad between Africa, Europe and Asia. Type C outbreaks have been reported with greatly decreasing frequency worldwide in recent years.

It is very often difficult to get a full explanation of the circumstances leading to the introduction of FMDV because of the illegal nature of some animal and animal product movements, but also because of the stochastic events necessary for the success of a viral introduction. In addition, the lack of surveillance and epidemiological data, linked with the lack of veterinary infrastructure in many developing countries make the tracing more difficult. However, progress with molecular sequencing techniques has enabled the genetic comparison of virus isolates allowing the source of outbreaks to be traced with far greater precision than was possible hitherto using serological techniques (Knowles and Samuel, 2003). Additionally, phylogenetic analysis of complete or partial sequences of the VP1 gene of FMD viruses allows them to be classified into sub-serotypic groups termed topotypes and, within a topotype, into strains.

In this paper, we will review the various outbreaks of FMD that have occurred in EU countries between 1985 and 2006, period for which data are reasonably accessible, and simultaneously their possible origins based on phylogenetic data. Then, we try to identify other potential sources of entry of FMDV into Europe that might have been responsible for past outbreaks or that could cause them in the future.

Outbreaks of FMDV in Europe from 1985 to 2006 and Their Origins

Laws and regulations on imports and animal movements in Europe and in other FMD-free countries around the world are based on the Office International des Epizooties (OIE) Code for Terrestrial Animals (OIE, 2005). When FMD virus is introduced into a free country, it is often attributed to some illegal action. Nevertheless, it is not always possible to trace their origin. Causes of an introduction into a country can be classified into the following proven or attributed categories:

1 Illegal introduction of live animals from infected neighbouring countries by smuggling or with forged certificates: e.g. Italy 1993, Greece 1994.
2 Legal or illegal importation of meat and animal products: e.g. Russia 1995, Balkans 1996, UK 2001.
3 Escape from laboratories: e.g. Germany 1987, Russia 1993.
4 Use of improperly inactivated vaccines: e.g. Italy 1985–1986.
5 Indirect contacts: e.g. immigrants in Greece in 1996.
6 Unknown origins: e.g. Bulgaria 1993, 1996, Greece 2000.

Foot-and-mouth disease virus has occurred 37 times in Europe (in both member and non-member EU countries) during this period. Table 1 indicates the likely origins for the primary outbreaks and the total number of secondary outbreaks for each introduction, where known. FMD has been officially reported by Albania ($n = 1$), Bulgaria ($n = 3$), Federal Republic of Germany ($n = 2$), France ($n = 1$), Greece ($n = 3$), Italy ($n = 10$), Former Yugoslav Republic (FYR) of Macedonia ($n = 1$), Spain ($n = 1$), former USSR or Russia (western part of) ($n = 8$), the Netherlands ($n = 1$), Turkish Thrace ($n = 3$), the UK (including UK Northern Ireland) ($n = 1$), Republic of Ireland ($n = 1$), and Former Yugoslav Republic Serbia-Montenegro ($n = 1$). Serotypes O, A, C and Asia 1 were involved in 20, 11, 4 and 1 cases respectively. FMD viruses responsible for those outbreaks originated in the Middle East or southern Asia and none were from Africa or South America. Serotype C has not been reported in Europe since it last occurred in Italy in 1989.

The total ban of preventive vaccination of cattle, as was practised in many European countries until the early 1990s, did not result in an increase in the total number of primary outbreaks in Europe over the subsequent decade; however, it may explain the change in the origin of the viruses involved. Despite some missing phylogenetic data characterizing outbreaks in Europe anterior to the 1990s, the genetic and antigenic characteristics available suggest a change in the pattern of FMD outbreak origins. These were mainly from within Europe and from South America up until 1990 and from the Middle East and Asia after 1990. The relaxation of FMD control measures in Caucasian countries following the fall of the iron curtain in 1989, as well as the ban of vaccination in EU (and thereby the use of vaccines that might not have been properly inactivated), could be components of the explanations. Indeed, a change in the source of virus and in the route of entry has been observed: many outbreaks were caused by laboratory escape and badly inactivated vaccines up until 1990 versus introductions via infected animals and products after this date.

Review of the spread of FMDV after introduction in Europe

Historical features characterizing outbreaks that have occurred in the past in Europe (e.g. route of introduction, species involved, spread, etc.) may provide useful information on what might occur again in the future. In this section, available information will be reviewed and analysed on how the virus spread after its introduction in the different outbreaks in Europe during the past 20 years

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Table 1. Likely origin of the primary FMD outbreaks in Europe (1985–2006)

Year	Serotype	Topotype	Place and country	No. outbreaks	Origin
1985	A	Euro-SA	Italy	110	
	C	Euro-SA	Italy	20	
1986	A	Euro-SA	Toledo, Spain	1	
	C	Euro-SA	Italy	48	
	O	nk	Italy	1	
	A	nk	Italy	101	
1987	O	Euro-SA	Federal Republic of Germany	2	Laboratory escape?
	A	nk	Italy	167	
	O	ME-SA	Riga, Latvia, USSR	1	
	O	ME-SA	Moscow butchery, Russia		
	O	ME-SA	Yaroslavl', Russia		
1988	O	Euro-SA	Federal Republic of Germany	4	Laboratory escape?
	C	Euro-SA	Italy	7	
	O	ME-SA	Belgorod, Russia		
	O	ME-SA	Yaroslavl', Russia		
1989	C	Euro-SA	Italy	73	
	A	Euro-SA	Italy		
1990	A	ASIA	Khanty-Mansi Autonomous area, Russian Federation		
1991	O	ME-SA	Bulgaria	1	Unknown
1993	O	ME-SA	Italy	57	Cattle imported with forged certificate
	O	ME-SA	Bulgaria	1	Unknown
	A	ASIA	Spasskoe, Vladimir, Russia	1	Laboratory escape
1994	O	ME-SA	Greece	95	Illegal import of Sheep
1995	O	ME-SA	Kirkloreli, Turkish Thrace	1	Illegal movment of cattle
	O	Cathay	Moscow, Russia	1	Import of pork meat
1996	A	ASIA	Albania	130	Import of meat on bone
	A	ASIA	FYR of Macedonia		
	A	nk	Federal Republic of Yugoslavia (Serbia-Montenegro)		
	O	ME-SA	Turkish Thrace	2	Illegal movement of cattle
	O	ME-SA	Greece	39	Illegal immigrants
	O	ME-SA	Bulgaria	1	Unknown
2000	Asia 1		Greece	14	Unknown
2001	O	ME-SA	UK*	2060	Illegal introduction of animal product and swill feeding
	O	ME-SA	UK (Northern Ireland)*	?	Spread from UK mainland
	O	ME-SA	Eire	1	Spread from Northern Ireland?
	O	ME-SA	France	2	Spread from UK
	O	ME-SA	The Netherlands	26	Spread from France?
2006	A	ASIA	Turkish Thrace	?	From Anatolia

nk, not known.
*In the text these two outbreaks were considered as the same since Northern Ireland belong to the UK.

(Leforban and Gerbier, 2002; European Commission for the Control of Foot-and-Mouth Disease, 1989, 1991, 1993, 1995, 1997, 1999, 2000, 2001).

FMD outbreaks in Italy and Spain

Prior to 1990, outbreaks of FMDV types A and C in Italy and Spain were either closely related to European vaccine strains or most closely related to South American outbreak strains (Figs 1 and 2).

Ten FMD epidemics occurred in Italy and Spain between 1985 and 1993. In Italy, serotypes O ($n = 2$), A ($n = 4$) and C ($n = 4$) were recorded, whereas in Spain only a single type A outbreak occurred in 1986.

In Italy, an epidemic of FMDV A, which had started in December 1984, continued until August 1985 and resulted in 110 outbreaks. The VP1 sequence of one virus isolate collected on 3 December 1984 (ITL/1/85) was identical to the Italian vaccine strain A_5/Parma/ITL/62 (Fig. 1). On 25

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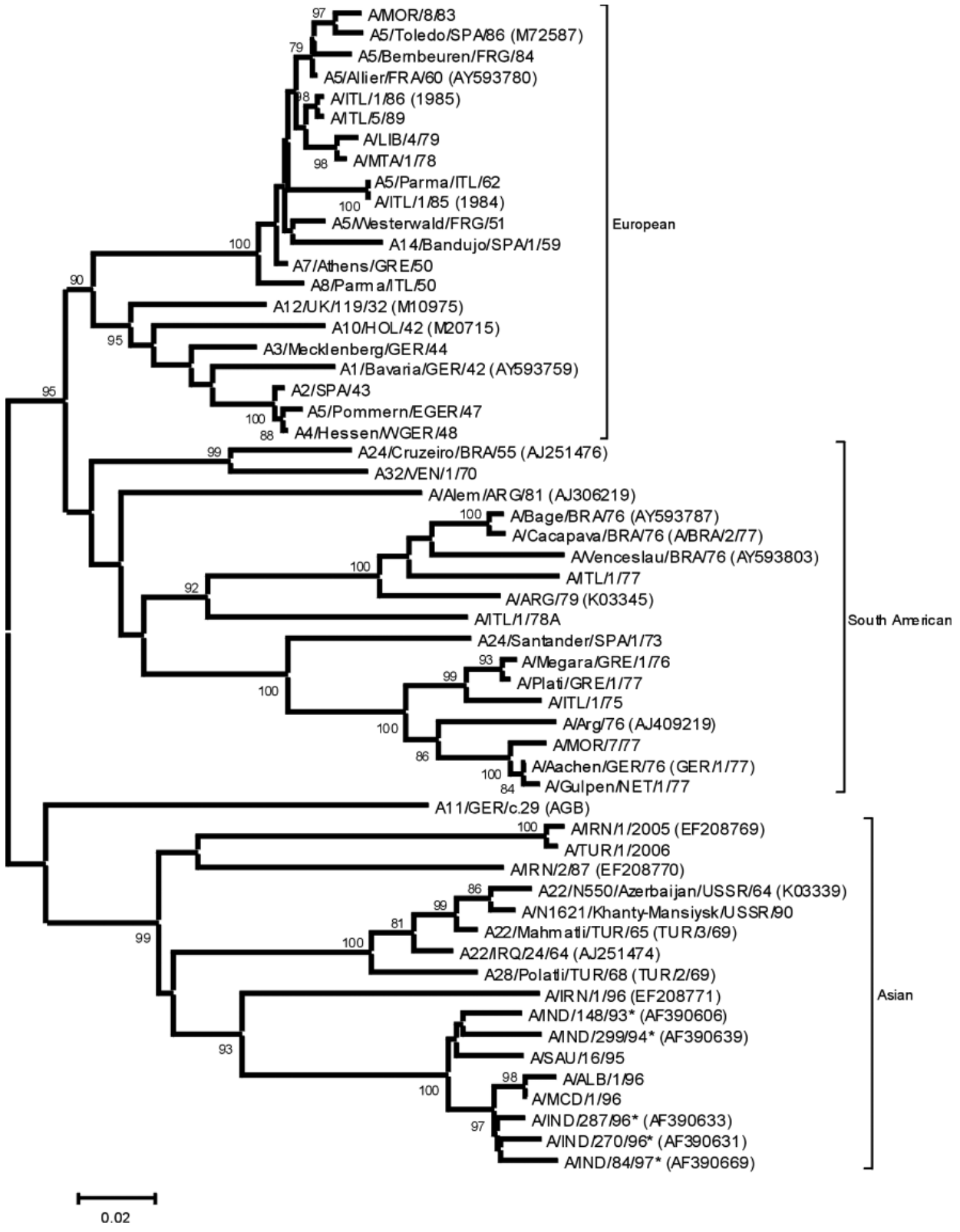

Fig. 1. Mid-pointed routed neighbour-joining phylogenetic tree showing the relationships between foot-and-mouth disease type A viruses.

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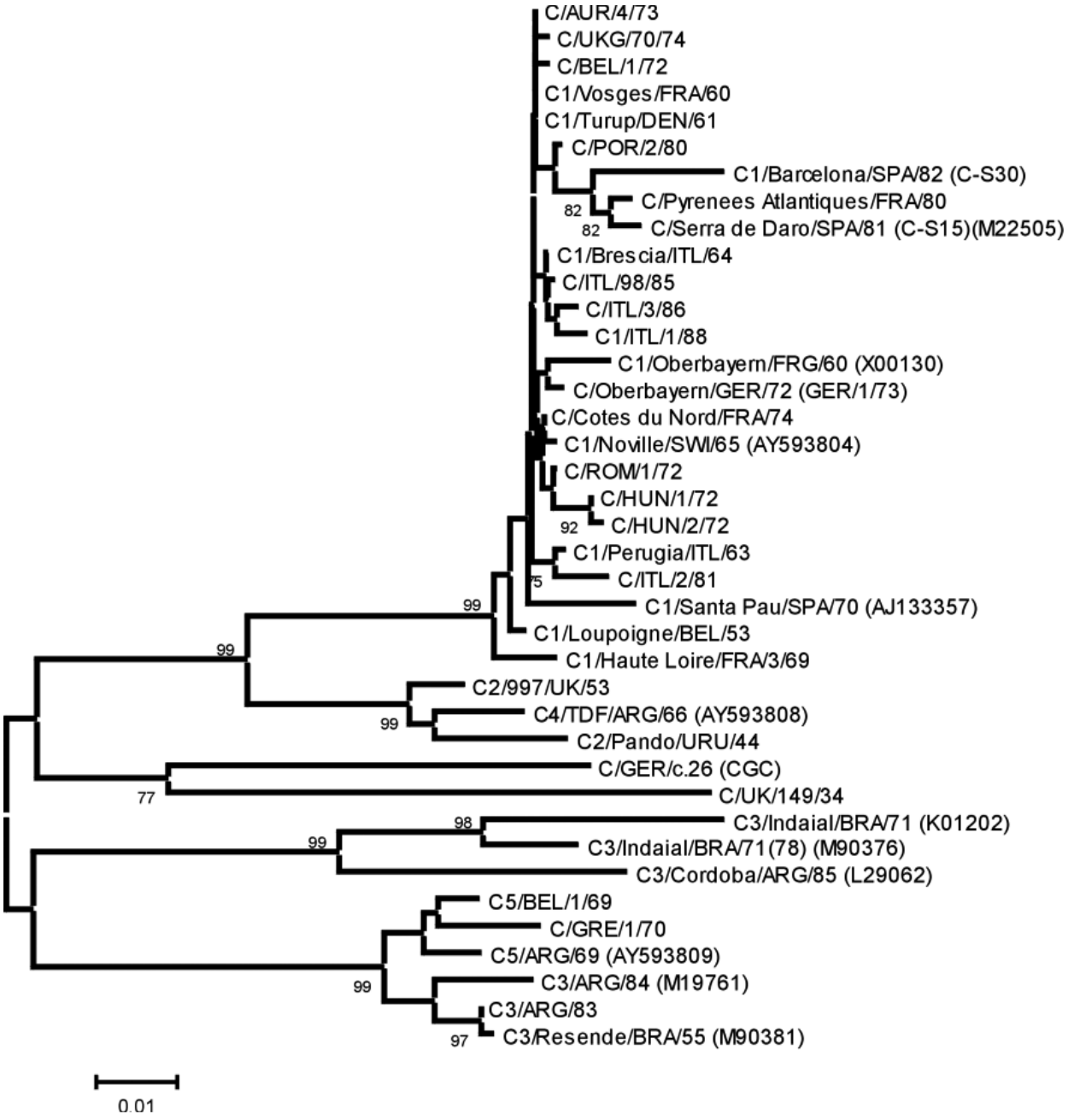

Fig. 2. Mid-pointed routed neighbour-joining phylogenetic tree showing the relationships between foot-and-mouth disease type C viruses.

December 1985, a primary outbreak of FMD was confirmed in the Region of Veneto, Province of Verona. The virus isolated was identified as a member of the A_5 subgroup, however, serological tests (both at the IZS Brescia, Italy and Pirbright laboratories, UK) suggested a lack of identity with the A_5/Parma/Italy/62 vaccine virus. At the time, Rnase T_1 oligonucleotide mapping of this virus also showed that A_5/Verona/Italy/85 (A/ITL/1/86) was different from both the A_5/Parma/Italy/62 and A_5/Modena/Italy/84 viruses (A/ITL/1/85) (N. J. Knowles, unpublished data). More recent analysis of the complete VP1 gene sequence has shown a closer relationship to A_5/Allier/FRA/60 (Fig. 1), a vaccine strain commonly used in some other European countries.

From November 1985 to April 1986, an epidemic of FMDV C occurred in Italy with 20 and 48 cases recorded in each year respectively (European Commission for the Control of Foot-and-Mouth Disease, 1989).

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The complete VP1 sequences of two isolates (C/ITL/98/85 and C/ITL/3/86) from this epidemic were very closely related to the Italian vaccine strain C_1/Brescia/ITL/64 (Fig. 2).

Additionally in 1986, in Italy, FMD outbreaks of serotypes O ($n = 1$) and A ($n = 101$) occurred (European Commission for the Control of Foot-and-Mouth Disease, 1989). Virus isolates from these outbreaks have not yet been sequenced and it is, therefore, not possible to ascertain their precise origin. Again in 1986, a single outbreak of FMDV A occurred in Toledo, Spain. Analysis of the complete VP1 sequence showed a close relationship to A_5/Allier/FRA/60, a vaccine strain in use in Spain at the time (Saiz et al., 1991; Fig. 1).

In 1987, FMD outbreaks of serotype A ($n = 167$) occurred in Italy, and in 1988 and 1989, of serotype C. No sample from the serotype A outbreak is currently available for sequence analysis. On 26 June 1988, an outbreak of FMD of serotype C was detected in the Montepulciano Commune, Siena Province, Tuscany, Italy. The herd consisted of 1992 pigs and 70 sheep, of which 105 pigs were affected. Seventy-five of these died. All animals were slaughtered and buried. Protection and control areas were set up. Ring vaccination was implemented but only in sheep. On 7 July a further outbreak was detected in cattle at Castiglione del Lago, Perugia Province, Umbria, approximately 22 km from the first outbreak. In July and August 1988, outbreaks occurred in pigs at Bagnolo Mella, Brescia Province, Lombardy (approximately 300 km from the two earlier outbreaks). Finally, FMD outbreaks of the same strain occurred in pigs and cattle at Brescia in April 1989 and from Modena in April/May 1989 (European Commission for the Control of Foot-and-Mouth Disease, 1991). Sequence analysis of C/ITL/1/88 (Montepulciano) showed a close relationship to both the vaccine strain C_1/Brescia/ITL/64 and the field outbreak viruses from 1985 to 1986 (Fig. 2). Further analysis of viruses from the 1989 episode revealed the same relationships (Knowles, 1990; Martinez et al., 1992; Meyer et al., 1994).

In May 1989, FMDV A was isolated from an outbreak in pigs in Naples. Serological tests at Brescia suggested that, although the isolate belonged to the A_5 subgroup, again it was serologically distinct from the virus involved in 1987. Comparison of the complete VP1 sequence (A/ITL/5/89) revealed a close relationship with A/ITL/1/86 (actually from 1985) and A_5/Allier/FRA/60 (Fig. 1). These viruses were also related to viruses isolated from outbreaks of FMD in Malta in 1978 and Libya and Tunisia in 1979 (Fig. 1).

As isolates of FMDV-serotype A responsible for outbreaks in Italy in 1985 and 1989 were genetically very closely related to A_5/Allier/FRA/60, it appears that these outbreaks might have a laboratory escape origin or have been caused by an improperly inactivated vaccine. Isolates of FMDV-serotype A collected in Spain in 1986 were also genetically related to A_5/Allier/FRA/60 and isolates collected in Spain, Portugal and Morocco in 1983 and West Germany in 1984 (Beck and Strohmaier, 1987; Marquardt and Adam, 1989; Fig. 1).

In 1993, outbreaks of serotype O occurred in Italy. This was the first occurrence of FMDV in the EU after the European ban on vaccination and was a cause of great concern. In this epidemic, 53 cases followed the introduction of cattle via Prosecco, near Trieste, from a neighbouring country through the port of Bari. They were destined for slaughterhouses in the Basilica and Campania Regions but some of them were sold to farmers, mainly in the south, except for one shipment, which after a short time in the south, went to the Roverchiara district of Verona Province in the northeast. When they entered Italy, the cattle were accompanied by animal health certificates that were later shown to be false (European Commission for the Control of Foot-and-Mouth Disease, 1995). Analysis of the complete VP1 sequence of O/ITL/1/93 (Fig. 3) and partial VP1 sequences from other isolates (Nunez et al., 2006), showed close relationships to viruses present in Middle Eastern countries in 1991 (Oman) and 1992 (Israel).

FMD outbreaks in Central Europe and Balkans region

In the Federal Republic of Germany, FMD outbreaks of serotype O occurred in 1987 ($n = 2$) and 1988 ($n = 4$). In October 1987, the outbreaks occurred in Grossburgwedel (Hannover, Lower Saxony). The cattle in both herds were situated in pastures approximately 60 m apart and at 1 km from a vaccine plant. Control measures were implemented and no new cases were detected; the restrictions were lifted 1 month later. However, on 1 January 1988, two outbreaks of FMD were detected in the Burdorf Commune approximately 15 km from the outbreaks reported in October 1987. On 5 and 10 January 1988, further outbreaks were diagnosed in the Burgwedel Commune at 100 m from each other. It was considered that a virus from a laboratory might have escaped and was the origin of this outbreak (Knowles et al., 1988; Fig. 3).

Based on sequences of the VP1 gene, FMDV isolates of serotype O responsible for the outbreak in the Federal Republic of Germany in 1987 and 1988 were very closely related to O_1/Kaufbeuren/FRG/66 but slightly different from each other, supporting the view that these two epidemics were independent (Fig. 3; Knowles et al., 1988).

In 1991 and 1993, FMD outbreaks of serotype O occurred in Bulgaria; both with very limited viral spread. The first outbreak occurred in July 1991 near the village of Stefan Karadjovo in Boliarovo close to the border with Turkey. It was brought under control by stamping out of all animals on the infected premises and by ring

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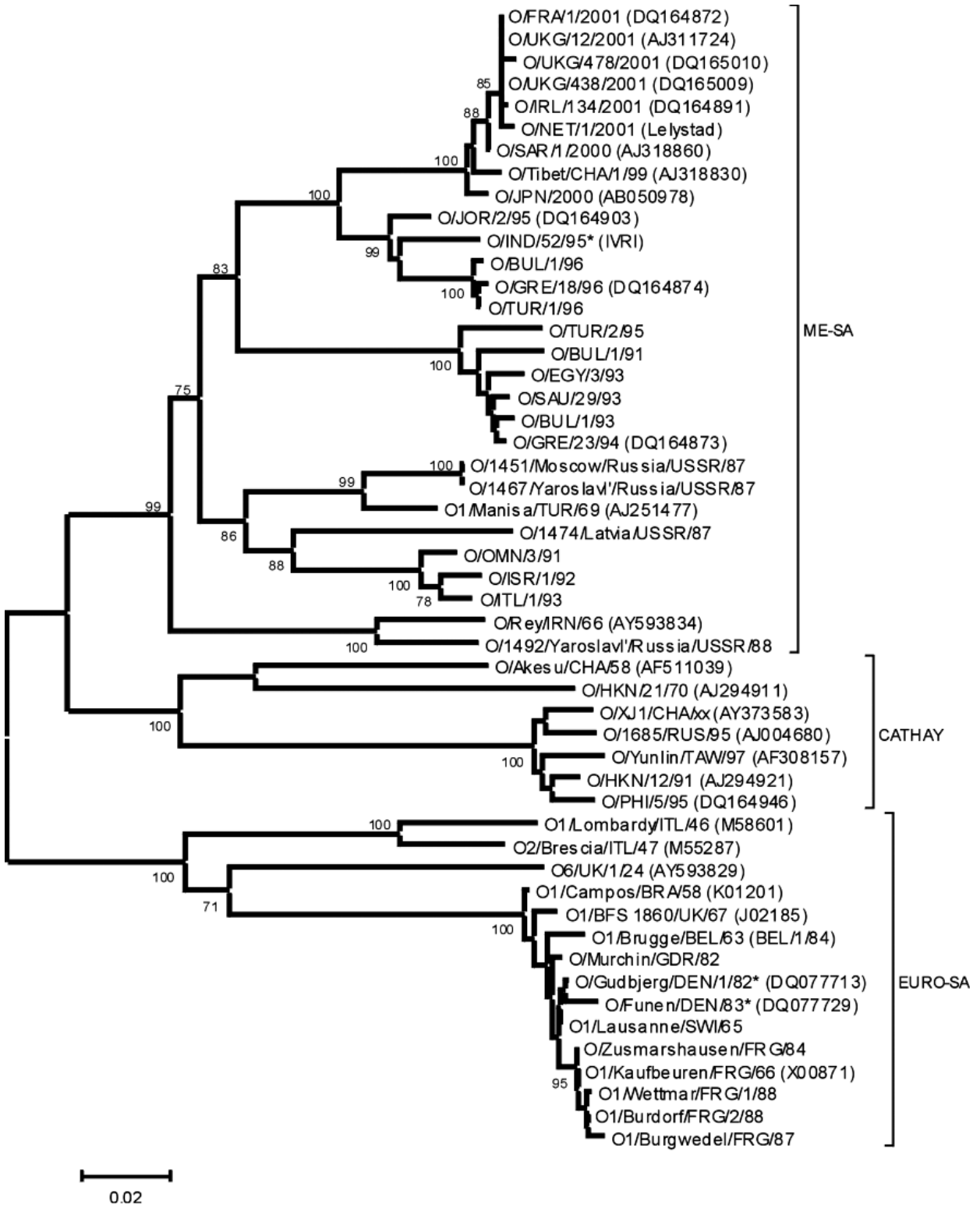

Fig. 3. Mid-pointed routed neighbour-joining phylogenetic tree showing the relationships between foot-and-mouth disease type O viruses.

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vaccination. The virus did not spread and no secondary outbreak was reported. Phylogenetic analysis of partial VP1 gene sequences showed that the virus was closely related to a group of viruses circulating in the Middle East since 1987 (Samuel et al., 1993). The second outbreak occurred in 1993 in cattle near the village of Simeonovgrad, Haskovo Region about 60 km from the border with Turkey. The disease was brought under control by stamping out with no vaccination. The virus did not spread and no secondary outbreak was reported. More recent analysis of the complete VP1 sequences of O/BUL/1/91 and O/BUL/1/93 showed that these viruses are in the same genetic group as the viruses from Saudi Arabia and Egypt in 1993, Greece in 1994 and Turkish Thrace in 1995 (Fig. 3).

In August 1994, an FMD outbreak of serotype O occurred in Greece and spread through the movement of sheep. The disease was introduced into the sheep population of Lesbos Island in July and remained unnoticed until August when a consignment of infected sheep was transported to the mainland where it infected cattle which developed clinical signs of the disease (Fig. 4). In a third phase, according to retrospective serological evidence, the virus spread to several prefectures in the sheep population with or without the development of symptoms. Ninety-five cases were recorded in Lesbos Island and on the mainland (Mackay et al., 1995). The disease was most probably introduced to Lesbos through illegal sheep trade from Turkey. The origin of this virus was probably the Middle East as discussed above (Fig. 3).

An FMD outbreak of serotype O occurred in Bulgaria and Greece in 1996. Between July and September 1996, 39 outbreaks of type O were reported in the Prefecture of Evros in eastern Greece, bordering Turkish Thrace. It was considered likely that the disease had spread across the border. In situations of close geographical proximity, several different potential routes of introduction may be considered, including movement of live animals, movement of people and commodities across the border and short range, airborne spread. A stamping out policy was applied. In October 1996, a single outbreak of type O was reported in the village of Malko Sharkovo in the Jambol District of Bulgaria, very close to the border with Turkish Thrace. Infected and in-contact animals were destroyed. Rigorous protection measures were applied including stamping out, movement control and disinfection. No vaccination was applied. There was no secondary spread. Complete VP1 sequence analysis showed that viruses from all three outbreaks (O/BUL/1/96, O/GRE/18/96 and O/TUR/1/96) were closely related to each other and also related to viruses isolated in 1995 from India and the Middle East (Fig. 3).

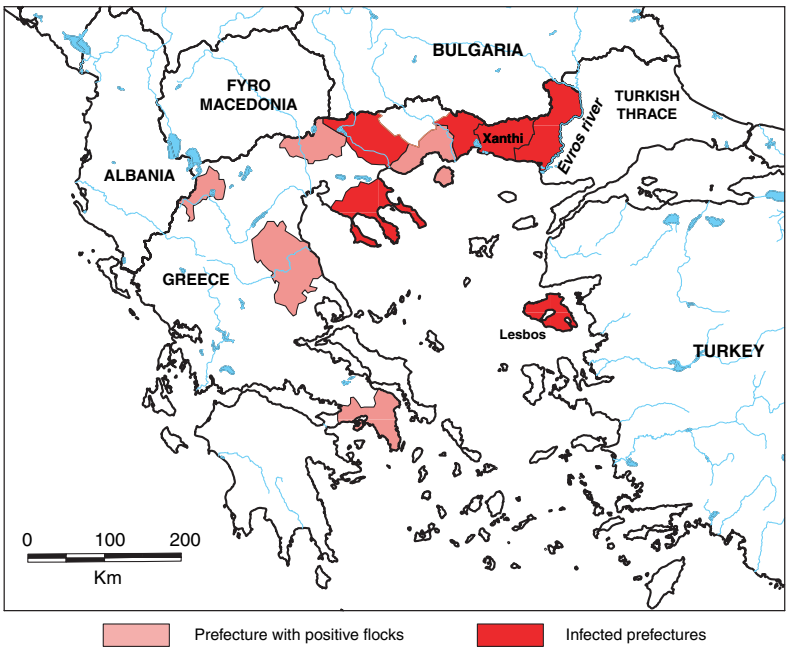

Fig. 4. Foot-and-mouth disease in Greece in 1994. Prefectures where clinical cases were observed are shown in dark red. Prefectures where positive sheep flock have been detected in a serological retrospective survey are shown in pink. Although the number of outbreaks (clinical cases) was limited to 95 (mainly cattle) in four prefectures, the serological survey carried out in sheep in other prefectures by the Greek National Veterinary Services with the support of the FAO FMD WRL (IAH Pirbright) revealed that seropositive sheep were also present in five other prefectures. It is likely that those sheep had been subclinically infected and therefore FMD cases were not reported.

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In 1996, a large epidemic of FMDV of serotype A began in the Western Balkans. This epidemic was characterized by the spread of FMDV by animal movements and indirect contacts. After introduction, through the import of infected buffalo meat into Albania in the period preceding the outbreak, the virus circulated in pigs and in the sheep population near a meat-processing unit of Korce district in the South East of the country. The disease remained unnoticed until it infected cattle in May that showed typical signs of the disease. The meat originated from an infected country and was destined for the meat factory in Korce. The virus infected pigs that were fed scraps from the factory where the infected meat was processed. Ten villages were subsequently infected in Albania. Clinically affected animals were destroyed and the remaining susceptible animals in the infected households/villages were slaughtered. A double-round, ring vaccination with the A_{22} Iraq vaccine strain was carried out in a zone of approximately 50 km radius around Korce under the co-ordination of EUFMD. Some 266 048 animals (including all susceptible species) were vaccinated twice at intervals of 3–4 weeks. The spread of the disease rapidly stopped following this vaccination and no further outbreak was observed after the second round of vaccination. The disease was reported in June 1996 in the FYR of Macedonia. Seventeen outbreaks occurred in the Skopje District and one in the Titov-Veles District. In the FYR of Macedonia only cattle showed clinical disease. In the 18 infected villages, the cattle population (total 4360) was stamped out. Two rounds of vaccination of cattle were carried out around the affected villages and approximately 120 000 head were vaccinated. In July 1996, the Veterinary Service of the Federal Republic of Yugoslavia (Serbia-Montenegro) reported FMD in Kosovo close to the border with Macedonia but this was not confirmed by an expert mission or by serology (European Commission for the Control of Foot-and-Mouth Disease, 1997). The complete VP1 sequences of A/MCD/1/96 and A/ALB/1/96 were obtained and showed a close relationship with viruses from India and Saudi Arabia, both countries suspected as being the origin of the infected meat (Fig. 1).

In 2000, FMDV-serotype Asia 1 occurred for the second time in Europe (an outbreak had previously occurred in Greece in 1984). The route of introduction is unknown; however, infection had been present in Anatolian Turkey since 1999. FMD was confirmed in the Evros Delta on the Greek-Turkish border on July 2000 and FMDV Asia 1 type was isolated. In total, 14 outbreaks were reported and approximately 5400 bovines, 2300 sheep/goats and 300 pigs were killed and destroyed either in the outbreaks or in contact holdings. Eradication of FMD was achieved by applying a stamping out policy and verified by a serological investigation. According to the Greek Authorities, there were three primary incursions of FMD along a 60-km front of the Evros River. The propagation to a distant prefecture (Xanthi) was due to 'human factors'. As for the 1996 outbreak, the introduction and spread of the virus was related to geographical proximity with Turkey. Under this geographical proximity different routes of introduction were considered including movement of live animals, movement of people (illegal immigrants) and commodities across the border but the exact routes of introduction and propagation were not clarified. Phylogenetic analysis of the complete VP1 gene demonstrated that the field isolate Asia1/GRE/2/2000 responsible for the outbreak in Greece was closely related to isolates collected in Iran and Turkey in 1999 (Fig. 5). These viruses were also closely related to viruses collected in Armenia and Georgia in 2000 (Valarcher et al., 2005; Knowles et al., 2006). Earlier isolates belonging to the same lineage were found in India, Nepal and Pakistan (Fig. 5).

In February 2006, outbreaks of FMD-serotype A were detected in Turkish Thrace. The origin of this virus was probably from Anatolia through animal movements. Due to the control measures implemented by the Turkish authorities, including emergency vaccination with an EU-supplied vaccine, the disease was contained and did not spread to neighbouring countries. Phylogenetic analysis of the complete VP1 gene showed a close relationship of the Turkish virus (A/TUR/1/2006) to a virus isolate from Iran (A/IRN/2005) (Fig. 1). This lineage was first detected in Iran in 2003 and has become widespread in that country. Spread to other countries in the Middle East [Saudi Arabia, Jordan, Pakistan and Turkey (Anatolia)] occurred in 2005 and 2006 (Wadsworth et al., 2006).

FMD outbreaks in the former USSR and Western Russia

FMD outbreaks of serotypes O ($n = 6$) and A ($n = 2$) that occurred in the western region of the former USSR or Russia were reported in 1987, 1988, 1990, 1993 and 1995. Baltic and eastern regions of the USSR had been FMD-free since 1987. However, a number of outbreaks of both O and Asia 1 have recently occurred in Russia close to the border with the People's Republic of China (Valarcher et al., 2005; Knowles et al., 2006). FMD reappeared in Transcaucasia where situation is apparently difficult (Asia 1 in July 2000 in Georgia, coming from Aremenia, for instance).

An outbreak of FMD-serotype type A was reported on 28 January 1990 on two small neighbouring farms (a pig farm and a cattle farm) in the Sovetsky District, Khanty-Mansi Autonomous Okrug, part of the Tyumen Oblast. An emergency vaccination program of all FMD-susceptible animals, including 50 000 pigs, was carried out in the risk zone. Analysis of the complete VP1 sequence

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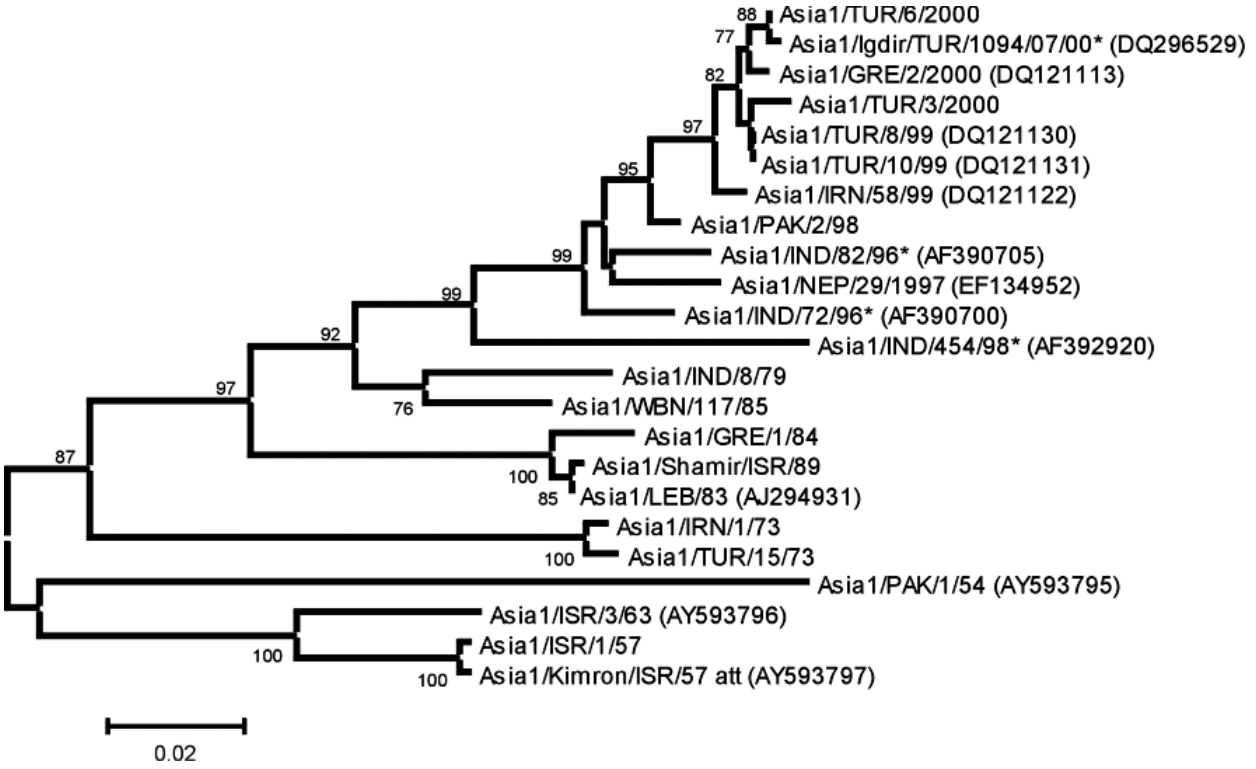

Fig. 5. Mid-pointed routed Neighbour-joining phylogenetic tree showing the relationships between foot-and-mouth disease type Asia 1 viruses.

showed a close relationship to the Russian vaccine strain A_{22}/N550/Azerbaijan/64 (A. Scherbakov and V. V. Drygin, personal communication, 1997; Fig. 1).

Six sporadic FMD outbreaks were reported in 1991, five of type O_1 and one of type A_{22}, all in the southern area. In 1992, only one outbreak of FMD-serotype O was reported but the exact location of the outbreak is unknown.

During 1993, an FMD-type A_{22} outbreak occurred in cattle at Spasskoe in the Vladimir Region. All FMD-susceptible animals including 1500 pigs were vaccinated directly on the farm and in the area under threat. The disease occurred due to the escape of virus from the nearby FMD vaccine plant. A partial sequence of the VP1 gene confirmed a close relationship to A_{22}/N550/Azerbaijan/64 vaccine strain (A. Scherbakov and V. V. Drygin, personal communication, 1997).

An FMD-type O outbreak occurred on a pig-farm in the Moscow Region in June 1995. Five thousand and eight hundred pigs of different ages were housed in 15 buildings. The pig-farm was located very close to the meat-processing plant where meat from China and south-eastern Asia was processed. Phylogenetic analysis of the VP1 gene (A. Scherbakov and V. V. Drygin, personal communication, 1997) showed that the virus belonged to the CATHAY topotype which is normally only found in the Far East (Fig. 3; Samuel and Knowles, 2001a).

FMD outbreaks in Western Europe

In 2001, a large outbreak caused by FMDV-serotype O occurred in the UK (England, Wales, Scotland and Northern Ireland) with subsequent spread to the Republic of Ireland, France and the Netherlands. The first outbreak in the UK was diagnosed on 20 February 2001 in pigs at an abattoir in the Southeast England near Brentwood in Essex. This outbreak was linked to a pig farm feeding swill in the Northeast England at Heddon-on-the-Wall, Northumberland, which supplied pigs to the abattoir and which was probably infected in early February. This farm was identified as the primary source of the epidemic and investigations revealed that the waste food was not being heat treated, as required by law, prior to its being fed to the pigs. Airborne virus from there infected a nearby cattle and sheep holding in mid-February, i.e. before the first outbreak was confirmed in Essex. Movements of infected sheep from Northumberland through a series of markets resulted in extensive spread in the Northwest and Southwest England. Additional movements of sheep resulted in the dissemination of the virus to Scotland, Wales, Northern Ireland, the Republic of Ireland and France (Fig. 6).

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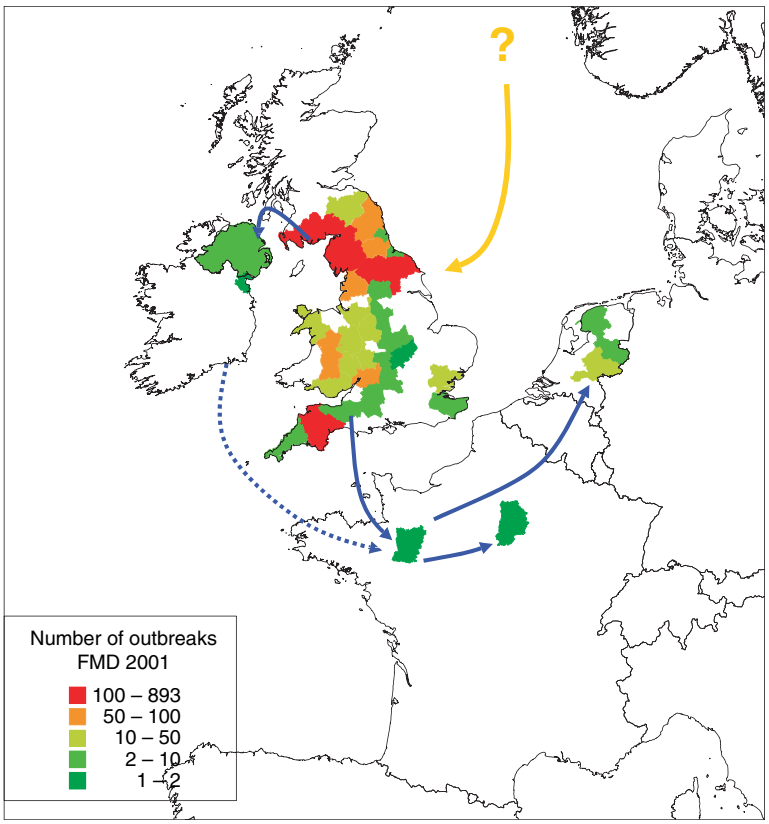

Fig. 6. The routes of dissemination of FMDV from the UK in the 2001 epidemic.

Irish calves that had been in contact in France with sheep imported from the UK probably spread the virus to the Netherlands. Early warning and prompt action, including stamping out and emergency vaccination (in the Netherlands), controlled the disease in all the countries infected via the UK.

The reason for the extensive spread of the disease in the UK was the long delay of about 3 weeks before the detection/notification of the first case, coupled with widespread trading in sheep that did not show obvious signs of disease. At the time of notification, there were already approximately 70 active outbreaks located in different areas. In this context, the tracing of the large number of movements of live animals which took place during the long period at risk was very laborious (Sutmoller et al., 2003). The causal virus was quickly identified as the PanAsia strain, a member of the ME-SA topotype (Knowles et al., 2001; Samuel and Knowles, 2001b; Fig. 1). Subsequently, complete genome analysis was undertaken and confirmed the close relationship with the UK/2001, France/2001, South Africa/2000, Japan/2000 and China/1999 isolates (Mason et al., 2003; Nobiron et al., 2005). VP1 sequencing also confirmed the relationship of the Dutch outbreaks to those in the UK (A. Dekker, personal communication, 2001). A detailed phylogenetic study of the UK 2001 outbreak, involving the determination of 23 complete genome sequences, was recently published and demonstrated the power of this analysis for farm-to-farm tracing (Cottam et al., 2006).

The UK outbreak lasted for some 8 months and was controlled by stamping out without vaccination. There were 2030 infected farms involved and susceptible species on these and on a further 8000 premises in contact were slaughtered to a total of 4 million animals plus a further 2.5 million killed on welfare grounds (Scudamore and Harris, 2002).

Genetic characteristics of FMDV European isolates in the past 22 years

In respect of the last 22 years, the genetic analysis of many virus strains that have been responsible for major FMD epidemics in Europe and its neighbours, combined with epidemiological assessments of disease and livestock population dynamics, have shown that the origin of such outbreaks has been the Middle East and Asia, including the type A introduced in Albania in 1996 and the Asia 1 type introduced into Greece in 2000. In contrast, there is no evidence of introduction of FMDV from South America or Africa to Europe in the last 20 years. Sub-Saharan

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Africa (Eastern Africa or the Soudan-Sahel region) constitutes a reservoir of infection for EU's neighbouring regions and therefore pose an indirect risk to Europe. Based on the available data it is possible to trace the origin of some outbreaks as described above.

New FMD epidemics continue to arise frequently as evidenced during the last decade by the Cathay O topotype pandemic of the 1990s in the Far and Middle East, the type O Pan-Asia topotype pandemic of the late 1990s and the FMDV-type Asia 1 pandemic in Asia which started in 2003 and is gaining pace in Central Asia and China, together with waves of type A topotypes flowing westwards from southern Asia. Most recently, there have been new epidemics of type A (A Iran 05 type) and type O (new O Pan-Asia lineage) affecting southern Asia and the Middle East.

Lessons to be Learnt from the Recent History of Virus Spread in Europe

Several lessons have been learned from the foregoing section on the introduction and the spread of FMD. Due to incomplete reporting, it can be difficult to identify the exact origin for the introduction of the virus into a free country or region, but the spread of the virus after its introduction is easier to trace.

Routes of introduction and dissemination

The spread of FMD

An appreciation of the multiple underlying factors involved in the pathogenesis and spread of FMD is important for the understanding of the several routes and their differing importance in the dissemination of the disease. These aspects have recently been extensively reviewed in quantitative terms for the major susceptible species (Alexandersen et al., 2003).

The analysis of the field history of several outbreaks reported above reveals that the movement of infected live animals is one of the most important routes for the dissemination of the virus after its introduction and that, for example, sheep played a major role in this in Greece in 1994 and in the UK in 2001.

However, other routes of diffusion, such as infected animal products, fomites and indirect contacts, can be involved in the introduction and the spread of FMD, especially if the environmental conditions are favourable for virus survival.

Airborne transmission over long distances requires the combination of particular circumstances, including temperature, humidity, wind speed and direction. It played a prominent part in the large 1967/68 epidemic in the UK, but did not play a major role in long distance spread of the virus in the 2001 UK outbreak. This route may, however, have contributed to 'local spread' together with other routes like movement of people, indirect contacts, fomites, etc. Indeed, it was airborne spread from the index case on the pig farm to the sheep farm in Northumberland that is believed to have initiated the large scale spread of disease by live sheep in the UK in 2001.

The role of pigs

Infected swill distributed to pigs has often been the origin of outbreaks of disease, including not only FMD but also swine vesicular disease, classical swine fever and African swine fever.

For animal products contaminated with FMDV, the likelihood of the virus causing infection is dependant upon susceptible animals ingesting the infected product in sufficient quantity to initiate disease. Specifically, and apart from the import and movement of infected live animals, feeding contaminated swill or catering waste to pigs is by far the most common means of establishing FMD. Pigs are the most likely susceptible animal to have access to swill or waste and once infected, pigs generate very large quantities of airborne virus. Moreover pigs are kept under both backyard systems, often without careful surveillance and also in large numbers under intensive management with the potential to create massive amounts of airborne virus. If the rules on prohibition of swill feeding to pigs are not strictly followed, there is a high risk of spread of FMDV introduced through imported meat. For example, the introduction of the disease in Albania in 1996 and in the UK in 2001 – both resulting in major epidemics – were most probably due to feeding pigs with improperly treated swill or catering waste. Consequently, the EC legislation for swill feeding prohibition has been reinforced in 2002 to try to eliminate the risk of introduction of the FMD by this route (EC, 2002).

The pig is well known for its potential role as an amplifier and disseminator of virus through airborne transmission. However, this mechanism of transmission has not played a major role in the later spread of the disease in recent outbreaks in Europe. Indeed, during the 2001 outbreak, no further clinical cases of disease in pigs were reported and confirmed by laboratory investigation in the UK after the index and primary cases, or in Ireland, France and the Netherlands. Although the possible tropism of viral strains for certain species might have played a role, it is worthwhile to highlight that FMD did not reach the densely populated pig production areas in the East of the UK. The same observations apply to Bulgaria and Greece where in the six outbreaks which hit this region during this period no disease reported in pig farms. This is partly related to the low density of the pig population in the areas concerned. Finally, the lack of

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pig involvement in the later spread of outbreaks could also be explained by the compartmentalized systems of production, which exclude or limit the contact between ruminant and porcine. Such contacts are important for the spread of disease under the traditional systems of production where different species are raised together on the same farm or share common grazing. In 1989 in Italy, cow milk products fed to pigs were a route of transmission between the two species around Modena.

The role of sheep

As symptoms of FMD in sheep are frequently mild or inapparent, the virus may have circulated unnoticed for a prolonged period in a sheep population by the time the disease is diagnosed. Sheep are also considered a minor species in Europe, often receiving less attention than cattle and pigs. In addition, the sheep trade has recently increased greatly inside EU countries and throughout Europe, frequently because of special EU subsidies for this species.

The outbreak in 1994 in Greece started in sheep on the island of Lesbos, but it remained undiagnosed for several weeks until infected sheep transported to the mainland passed the infection to cattle. Similarly, the 2001 epidemic in the UK confirmed that sheep can play a major role in the spread of the disease: the disease was widely disseminated by the marketing and movement of infected sheep exhibiting few obvious signs of clinical disease and most of the 2060 infected premises in the UK were sheep farms. Similarly the presence of the disease was only recognized when classical clinical lesions was first noticed in pigs.

The important role of sheep to propagate the virus silently has also been demonstrated in North Africa, Turkey and in the Middle East (Donaldson, 2001).

Laboratory escapes and insufficiently inactivated vaccines

Examples of outbreaks caused by laboratory escapes include those that occurred in Germany in 1987 and 1988 and in Russia in 1993. One of the most risky processes of laboratory manipulation is the growth of virus in bulk for vaccine antigen production, but stricter biosecurity regulations have made it possible to produce FMD vaccines in a safer manner. Guidelines for biosecurity measures in FMD laboratories were formulated by the EUFMD Commission in 1993 (European Commission for the Control of Foot-and-Mouth Disease, 1993) and a list of the laboratories and vaccine manufacturers authorized to manipulate FMD virus in the EU is annexed to Directive No. 2003/85EC. In addition, the 2004 Edition of the OIE 'Manual of Diagnostic Tests and Vaccines for Terrestrial Animals' indicates that FMDV (for diagnostic and vaccine production purposes) should be handled only in P3 bio-containment facilities (OIE, 2004). The risk of escape of FMDV from a laboratory is low, as long as those biosafety measures are followed. Only the laboratories that fulfil these measures are authorized to manipulate FMDV and virulent material in Europe. However, despite the new biosecurity requirements the risk of escape of virus from laboratories and vaccine plants cannot be excluded and certain countries discourage or prohibit institutes from manipulating FMDV on their territory.

Improperly inactivated vaccines were the source of disease on a few occasions, as suggested by phylogenetic data as presented above. This occurred until the inactivation with formalin was abandoned and replaced by inactivation with binary ethyleneimine (BEI). This risk was one of the reasons which led to the recommendation to stop mass prophylactic vaccination of cattle in the EU and since it has been banned on this was introduced in 1992, vaccines has not been implicated as the source of disease in Western Europe.

No intentional introduction of FMDV has been reported so far in Europe or elsewhere. This does not mean that that criminal introduction of virus has never been attempted, but if it occurred, it was unsuccessful. This route must be considered as a serious threat under the current unstable political situation in many parts of the world and appropriate measures to reduce this risk should be implemented, especially in laboratories which keep stocks of viral strains for diagnosis and research purposes.

Risk factors

Socioeconomic and ethnic factors in the spread of FMD

The difficult economic situation in Albania in 1996 led to cheap buffalo meat from an infected country being allowed (or at least not rigorously prohibited) to be imported. Subsequently, the spread of the disease between Albania and the FYR of Macedonia was clearly facilitated by the close relationship between the populations of the same ethnic group on both sides of the border.

This ethnic factor also plays a major role in the spread of the disease in border areas between Turkish Thrace, Bulgaria and Greece despite the apparent existence of adequate control measures at the border. Thrace must be considered as a unique epidemiological entity (Garland, 2001). In the last 10 years, six introductions of the disease have taken place from Turkish Thrace to border areas of both Greece and Bulgaria. When FMD occurs in Turkish Thrace, the risk of introduction to neighbouring countries increases dramatically and despite the reinforcement of the control measures in the border areas the virus is likely to 'spread by proximity' and to reach the neighbouring countries. This risk is further increased when the

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differential between these neighbouring countries in the price of animals and animal products is high. That was the case for many years in this region but since 2002 prices seems higher in Turkish Thrace than in Bulgaria and this may help to reduce the risk. Recent outbreaks in Thrace in early 2006 and 2007 have not resulted in spread to Greece or Bulgaria. Trade differentials have also accounted for the spread of FMD westwards across the Middle East and also between countries in the Southern Cone of South America.

The role of religious festivals

Religious festivals increase the risk of dissemination of FMD in Europe. This is well known in Muslim countries including Turkish Thrace, but the 2001 episode of FMD in Europe revealed for the first time the extensive movements of animals – particularly sheep – from different origins, which take place during the week preceding the Aid el Kebir feast in Western Europe. This trade was responsible for the introduction of the virus to France through infected sheep from the UK.

Markets have also played a major role in spreading the disease. The practise of purchasing sheep from different origins prior to the feast for fattening also contributes to increasing the risk of dissemination of FMD and other diseases.

The dissemination of the virus in sheep populations in certain prefectures of Greece in 1994 is also partly related to the movement of sheep in relation to religious practices (e.g. gifts to monasteries). The Chinese New Year is also a period of important exchange of commodities of animal origin and the 1997 outbreak in Taiwan could have been related to this feast.

Livestock management factors

During the last decades, changes in livestock management practices have modified the type of risk factors for the introduction and the spread of FMD. Indeed swill feeding, considered as a most important route of introduction or spread in the past, is now banned in the EU, and common grazing or mixed ruminant and pig herds are rare in many European countries. Nowadays, animals can travel a very long distances and potentially spread FMD while weaker animal diseases surveillance in extensive herds might delayed the detection of the disease. On the other hand, application of biosecurity measures in intensive herds might limit the introduction and the spread of disease.

The importance of early recognition

The delay between the first occurrence of the disease and its recognition is a major determinant of the subsequent spread of the disease and the gravity of the outbreak.

In the outbreaks in Greece 1994 (in Lesbos Island), Albania 1996 and UK 2001, this delay was estimated to have been long i.e. between 2 and 4 weeks and probably more. In those three outbreaks, the spread of the disease was extensive and in the case of the UK it became temporarily uncontrollable.

In contrast, it is likely that the detection of the disease was rapid in Bulgaria in 1991, 1993 and 1996 and the three primary outbreaks were rapidly brought under control before they had contaminated other farms. This was also demonstrated by the rapid detection and control of the disease in Ireland, France and the Netherlands in 2001 (Leforban, 2003). In these latter instances the authorities had the advantage of forewarning and of practising extra vigilance following the report of the outbreak in the UK.

Control options

The role of buffer zones in preventing the introduction of the disease to Europe

Vaccination in Turkish Thrace was progressively abandoned in the late 1980s by the Turkish authorities, with the objective of gaining the OIE status of an FMD-free zone without vaccination. However, this objective was unrealistic in the local context where the movements of animals between Anatolia and Thrace are difficult to strictly control. It has been shown that the Istanbul markets, as a place of contact between animals of different origins, has played a major role in the introduction of the virus into Turkish Thrace. Most of the outbreaks in the region during this period were attributed to cattle returning from the Istanbul market where they came in contact with infected animals and this pattern has continued up to the present time. Therefore, after 1995, Turkey was encouraged by the European Commission (EC) to resume official vaccination with a quality controlled vaccine in Thrace and to reinforce surveillance. Very close cooperation is now established between the EC and Turkish authorities and huge progress has been made regarding vaccination coverage and surveillance which contributes to reducing the risk of introduction of the virus to neighbouring countries.

Based on the same objective of reducing the risk to Europe, a buffer zone has also been established by EUFMD with the EC support in the Caucasus region since 1999 (Garland, 2001; Leforban and Gerbier, 2002).

Experience with vaccination as a tool for control

Although not strictly prohibited by EC legislation, vaccination was discouraged as a tool for control at least until 2001. With the exception of the Netherlands in 2001, none of the EU countries infected during 1990s (Italy in

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1993, Greece in 1994, 1996, 2000, the UK, France and Ireland in 2001) used vaccination for controlling the disease (Leforban, 2002, 2003).

Ring vaccination and stamping out were used in Bulgaria in 1991 but in 1993 and 1996 stamping out was used without vaccination. In all instances the disease was rapidly brought under control without spread from the primary focus (European Commission for the Control of Foot-and-Mouth Disease, 1995).

Apart from Bulgaria in 1991, the only other occasion from 1991 to 2001 where vaccination was used as a tool for control was in 1996 in Albania and Macedonia. Vaccine was supplied by the EC (partly from the EU vaccine bank) and a double round of ring vaccination with a 50-km radius was carried out around infected premises/villages. A total of 266 000 animals of all species were vaccinated in Albania and 120 000 cattle were vaccinated in Macedonia. The disease stopped spreading and although retrospective serological testing demonstrated that a few infected animals had not been stamped out in the infected zone, those animals did not play a role in the perpetuation and spread of the disease. This could be interpreted as a practical demonstration that ring vaccination with a safe, potent vaccine incorporating the appropriate virus strain can stop the spread of and eliminate the clinical disease (Leforban, 1999). Ring vaccination was also used in the Netherlands in 2001 and the disease stopped spreading. In this instance all the vaccinated animals were eventually slaughtered (employing so-called 'suppressive vaccination') to minimize the time and testing which would have been necessary under the then prevailing OIE recommendations so as to regain the premier trading conditions for livestock and livestock products. At the end of 2005 and in 2006, following the outbreak of FMD serotype A in Turkish Thrace an emergency vaccination with an appropriate vaccine strain was implemented to control these outbreaks which were rapidly brought under control.

Assessing the Possible Sources of FMDV to Europe which did not Result in FMD Introduction

While FMDV has been introduced only 37 times in European countries between 1985 and 2006 (see Table 1) the virus is permanently or occasionally present in countries bordering Europe as well as in distant regions linked to Europe by transport and trade. In this section, the FMD outbreaks that threatened Europe during this period are analysed, which, by chance and/or due to risk management measures did not result in FMD being introduced into Europe. We do not intend to cover all countries where FMD occurred during this period but only those that we consider as the most relevant and for which data are available.

Turkey and Caucasus

FMD continues to be endemic in Anatolia (Turkey). This area location has always been considered as the major potential source of new viruses for Europe (Parlak et al., 2007). As demonstrated in several occasions in the past and recently in 2005–2006, Iran, Iraq, India and Pakistan are the sources of new strains of FMDV spreading to Turkey. Turkey plans to adopt a package of measures from 2007 to reduce the incidence of FMD and to improve surveillance and control. The objective over 5 years is to achieve the reduction in the distribution of hotspot areas of infection in the east and south-east Anatolia.

Trans-Caucasus countries have been mainly disease free but are bordered by endemic areas (Turkey and Iran). Trans-Caucasus countries could be effectively maintained free of FMD through improved regional control of the disease in north-east Turkey and western Iran, and with improved measures in their border regions.

Therefore, most of the efforts to protect Europe have been concentrated on establishing buffer zones between those infected countries/areas (Turkey, Caucasus) and Europe. Programmes for vaccination zones were organized and coordinated by the FAO EUFMD and funded by EC.

Russia, the Commonwealth of Independent States (CIS), Romania and neighbouring countries

Russia may act as a natural buffer zone between Central Asia and Europe. FMDV circulates actively in East Asia, which is a permanent source of virus for neighbouring regions. Because of the poor economic situation and the absence of real surveillance, FMD tends to become endemic also in central Asian countries and the ongoing risk for Central European countries, such as Romania, Bulgaria, Ukraine, Moldova, and Belarus, is not negligible. These countries are currently free of FMD but due to their geographical location, they are at risk of infection from their neighbours by proximity or through the illegal trade of infected animals or products.

For example, commercial exports of pork and beef by China and India, respectively, to countries, such as Albania and Moldova, represent a potential risk for the EU. Indeed, in addition to the risk that they take for themselves, they put also their neighbours at risk (e.g. Romania and Serbia-Montenegro) and that may subsequently represent further danger by exporting meat to EU countries. There is also evidence of attempts to introduce

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commercial quantities of pork and beef illegally into the EU directly from India and China.

North Africa and the Near East

In general, the higher FMD risk for Europe has been perceived as coming from the countries with endemic disease in the Southeast of Europe, in the Middle East and in North Africa – as indicated through arrows in the map shown in Fig. 7.

This perception has been confirmed for the Middle East which has been the traditional source of new FMDV strains and serotypes regularly introduced, mainly through the Balkans, towards Europe. In contrast, for more than 50 years there has been no report of FMDV having been introduced into Europe from North Africa. The last report of such an introduction was in 1937–1938 when the disease was introduced into France although the port of Marseille (and Bordeaux) and from there it spread to all of Western Europe.

This has not been for lack of disease in North Africa. FMDV has been introduced into the Maghreb (Algeria, Morocco and Tunisia) on several occasions. Between 1967 and 1983, FMD was reported eight times: three times in Algeria (1967, 1977 and 1982), twice in Morocco (1977 and 1983) and three times in Tunisia (1975, 1979 and 1982).

In 1983, the virus was FMDV-type A_5 and was introduced into Morocco with imported sheep from the Iberian Peninsula (Beck and Strohmaier, 1987; Fig. 1).

Between 1989 and 1992, severe outbreaks caused by type O (O/Tunisia/1989) moved from east to west appearing successively in Tunisia (end of 1989), Algeria (May 1990) and Morocco (February 1991) causing severe disease with high mortality, particularly in small ruminants. The viruses involved in these outbreaks probably all originated from the Middle East (Samuel et al., 1999).

In 1999, a FMD outbreak caused by type O that occurred in Algeria had a West African origin based on a molecular epidemiological study (Samuel and Knowles, 2001a). The virus spread to several willayas in western and eastern parts of Algeria causing 165 outbreaks and eventually it reached Tunisia (three outbreaks) and Morocco (11 outbreaks). This was a particularly significant development, as it indicated that the virus could

Fig. 7. Perceived risk of FMD introduction in Europe in early 1990s. When EU decided to ban preventive vaccination in cattle to adopt a unique system of FMD prevention based on early detection and stamping out together with reinforcement of the control measures on the borders, the main risk of introduction was the Middle East through Mediterranean sea, Turkey and Caucasus. North Africa and especially the Maghreb was also regarded as an additional potential source of virus to Europe. The recent history of FMDV introductions to Europe confirmed that the Middle East has been the main source of virus while North Africa has never been at the origin of FMDV introduction to Europe although the virus has been occasionally introduced in the region as it happened in 1999.

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have travelled across the Sahara (previously generally considered as an impassable natural barrier) perhaps with infected cattle transported in trucks across the desert.

An outbreak of FMDV SAT 2 was reported in Libya in 2003. This serotype had not been detected in North Africa since an outbreak occurred in Egypt in 1950. Isolates collected during this outbreak showed the closest match to viruses from Cameroon in 2002, Saudi Arabia in 2000 and Eritrea in 1998 (Valarcher et al., 2004).

At the time of the last episode in North Africa in 1999, important measures were taken in European countries (EC decision 1999/292/EC) to prevent the introduction of the virus. Those measures consisted mainly in disinfection of trucks returning from infected countries. It is uncertain whether those risk mitigation measures were sufficient to prevent the introduction of the virus to Europe or whether this was just good fortune.

The absence of introduction of FMDV from Africa to Europe is surprising, considering the geographical proximity of the coasts and the movement of livestock, animal products and people across the Mediterranean Sea. Although, it must be emphasized that, in contrast to the Middle East where FMD is endemic, FMD is introduced sporadically into North Africa, and consequently represents a lower risk to Europe for the introduction of the disease (Donaldson, 1999). However, it is surely cost effective for the EC to support a coordinated programme to help maintain the favourable FMD status of the Maghreb countries, and thereby to create an efficient buffer to protect Europe from the risk of FMD coming from Africa.

Eastern and Southern Africa

Ethiopia and other countries of the Horn of Africa that are currently infected by FMD, export sometime huge quantities of meat and live animals to the Middle East and recently to Egypt. Despite the efforts by the authorities in the countries of origin and of importing countries to mitigate this risk through quarantine measures, FMDV is regularly introduced through the exports of animals and products. A recent example is the introduction to Egypt of a new type A virus (A/Egypt/2006) closely related to an east African strain (Knowles et al., 2007). However, recent outbreaks in Saudi Arabia are all of Asian origin (Knowles et al., 2005).

The unstable political situation in certain countries of Southern Africa exporting beef to Europe may be an additional risk factor to Europe. In this case, the risk would probably be associated with legal beef imports from a country, which might not yet recognise infection in its territory.

South America

In 1967 in the UK there was a large-scale epidemic due to type O FMDV and although the origin could not be precisely identified the most likely cause was thought to have been infected meat imported from South America. In 1977, a type A virus originating from South America was introduced with the import of frozen beef (Fig. 1). This virus also appeared in Germany (1976) and the Netherlands (1977) and was most closely related to A/Arg/76 (Fig. 1). Distinct, but related viruses were also found in Italy (1975) and Greece (1976 and 1977) indicating possible multiple introductions of South American viruses into Europe (Fig. 1). Other viruses with a probable South American origin were also found in Spain in 1973 and Italy in 1977 and 1978 (Fig. 1). In fact, A/ITL/1/78A was a virus isolated from bone marrow of swine meat imported from Brazil into Italy (Fig. 1).

Following past FMDV introductions into Europe via imports from South America (meat) and south-eastern Europe (live animals), a strategy for risk reduction has been implemented for imports from these areas. This have included measures for reduction of the FMD prevalence in these areas and also for the importation by the EU of de-boned and maturated meat or heat-treated meat from countries practicing vaccination in South America.

It is important to emphasize that the FMD situation in South America, traditionally an exporter of meat to Europe, has considerably improved during the last three decades despite the re-occurrence of FMD in Argentina, Uruguay and Brazil in 2000 and in 2005/2006.

Future Risks for Europe

The available data indicates that several areas of the world are associated with considerable movement of bi-ungulates and among them, there are the Middle East, South and South East Asia and China, the Sahel, and East Africa, all of which have been identified as having a high burden of endemic FMD.

Illegal imports of live animals originating from the Middle East continue to represent a threat to Europe, primarily but not exclusively to south-eastern Europe. Illegal importation of infected meat and meat products and possibly legal importation of other animal products such as sausage casings (derived from intestines) from South-East Asia, China and Southern Asia are a threat that is more evenly spread throughout the EU.

Meat and animal products originating from infected animals and imported illegally probably poses a greater risk to Europe than disease in countries with an

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established and regulated meat trade with Europe. Specifically, there is an increasing trade-driven movement of livestock commodities in Asia. The supply-demand gradient for livestock commodities in these regions seems to gravitate towards either Europe or countries in EU neighbouring regions (North Africa, Middle East and CIS). Thus, there is clear indication that of the FMD-free, non-vaccinating regions of the world, Europe are particularly vulnerable to FMD incursions.

The discrepancy between the potential high risk of introduction through infected meat and animal products and the fact that during the past 20 years no case of introduction by importing meat product has been proven may be explained as follows. First, the products originating from infected countries are not systematically infected with FMD virus and secondly, they are usually consumed in urban areas. Under such situations, the probability of FMDV-infected products being given to pigs is low. As for meat imports the prohibition of feeding untreated swill to pigs since 1992 in the EU, and the outright ban on feeding swill to pigs in force from November 2002 has contributed significantly to reducing the risk of transmission through this route.

Within Europe much progress has been made by country to gain the OIE status of 'Free from FMD without vaccination'. Two categories of European countries can be distinguished: those that are recognized by the OIE as free of FMD without vaccination and those that are not. Almost all European countries west of the Russian federation fall into the first category. In the second category, we can distinguish those that are effectively free countries and those in which some outbreaks might occur. Belarus, Serbia and Montenegro, and Moldova are countries free of disease for considerable periods (more than 5 years) but which have not yet applied for official recognition of freedom. The Russian Federation, where outbreaks reported are very few, probably because of preventive measures along the borders with countries in the south, centre and east which are not free of FMD and in which true prevalence is difficult to establish. The Russian Federation may gain the status of FMD freedom without vaccination for its western European region and enclaves (e.g. Kaliningrad enclave within EU).

The major risk of FMD remains outside of Europe. Most of the factors and circumstances, which affected the introduction, and spread of the disease in Europe from 1991 to 2005 have not changed, and most of them are unlikely to change. Therefore, many of the historical observations reported above on the routes of introduction and on the spread of FMDV are still relevant for the future. These include geographical proximity with infected areas and commercial as well as ethnic, sociological, economic and religious factors. As Europe experiences greater immigration to reinvigorate its ageing and shrinking population, it is likely that these factors will become more important in disease transmission in future. In addition, whereas live animals represent more of a regional threat, large-scale importation of infected meat, meat products and other animal products, such as casings, or small-scale importation, such as in hand baggage, including bush meat, are a direct threat to Europe. Consequently, the various sources of FMD around the world that might be responsible for introductions have been reviewed by Rweyemamu et al. (2008).

Conclusions

Over these past 20 years, the number of FMD outbreaks within Europe has been regularly decreasing. Nevertheless, the danger of incursions remains constant as proven with the recent epidemics in Western Europe in 2001 and in Turkish Thrace in 2005/2006. Sources of viruses involved in outbreaks during these 20 years have been very diverse but Asia remains a frequent origin. FMD virus has been introduced into Europe by different routes with illegal animal movements as a major pathway. In contrast and even if all risk cannot be excluded, escapes from laboratories and outbreaks following utilization of insufficiently inactivated vaccines have significantly decreased because of improvements made in biosecurity in FMD laboratories and in inactivation process of the viral antigen in FMD vaccines.

Actually, most of Europe is free of FMD without vaccination except for Turkish Thrace and some Russian regions. These regions remain an obvious door for the introduction of FMD as they neighbour FMD endemic zones. However, globalization of trading activities and human population movements make all reservoirs of FMD a potential danger.

FMD introductions into Europe are increasingly expensive in their impacts and consequences. Europe has developed protective mechanisms to counteract vulnerability, such as import restrictions, border controls and inspections in exporting countries. These control measures reduce the risk of infection importation but they do not reduce the risk to zero. Based on these facts, the EU is helping countries in many areas to eradicate FMD. Global progressive control of FMD is anticipated to require at least 20–30 years. Therefore, FMD control in endemic areas supplements rather than replaces the current EU strategy.

The introduction of FMDV into the UK in 2001 showed that it is always difficult to predict from where

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and to which country FMD can be introduced either in the near future or in the long term. As proof of this, an expert opinion exercise carried out in 2001 considered the UK as unlikely to become infected, although it correctly predicted contaminated waste food as a highly likely source (Report of the EUFMD Research Group, Borovets, 2000). A better understanding of the movements of animals and their products in relation to the risk of infection would be highly desirable. In this respect, it is expected that the EFSA risk analysis, published in 2006 which collated information on the FMD situation in different regions of the world and on animal product movements (legal and illegal) and cross-referenced these data, will help reduce the level of uncertainty (Anonymous, 2006).

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