# CURRENT GLOBAL SITUATION OF EMERGING INFECTIOUS DISEASES OF LIVESTOCK

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## ABSTRACT

*The past decade has seen the rise of new diseases and the reemergence of many economically important livestock diseases worldwide. Expansion of global trade, rapid transport facilities, increase in population of both humans and animals, free movement of animals and animal products, environmental changes, and greater exposure to wildlife have all contributed to the emergence and reemergence of animal diseases. This Bulletin discusses the global distribution and outbreaks of the more important emerging livestock diseases, particularly the OIE (World Organisation for Animal Health) List A viral diseases, that have reemerged as a major threat during the last few years, such as foot-and-mouth disease (FMD), bluetongue, lumpy skin disease, avian influenza, Newcastle disease, and hog cholera.*

## INTRODUCTION

The unexpected reappearance of foot-and-mouth disease (FMD) in northern Europe has been a reminder of the vulnerability of the intensive integrated livestock industry to incursions of highly transmissible virus diseases. The production and welfare consequences were a small part of the total economic impact of the FMD outbreak that affected the United Kingdom (UK), Eire, France, and the Netherlands during 2001. The interference with trade of live animals and animal products, and the cost of reestablishing freedom from FMD to satisfy trading partners, far exceeded the direct cost of the control program. But possibly the most significant effect in the UK was the public's perception of the disease. Tourists from within UK and from abroad were discouraged from visiting affected areas by official policy, by the prospect of seeing mounds of decaying carcasses or funeral pyres, and by the fear that they might inadvertently carry the FMD virus back to their own uninfected regions or countries. The Ministry of Agriculture, Fisheries and Food of the UK was dissolved and its functions were taken over by the new Ministry of Environment, Food and Rural Affairs. Public confidence in the ability of the government to provide leadership during a national disaster was eroded.

Outbreaks of exotic diseases can no longer be seen as a problem for the agricultural sector, but have taken on a political perspective that does not bode well for the future. If politicians are to be reassured that control of these diseases can be left in the hands of those best qualified to deal with them, then it is essential that veterinarians maintain their expertise in the diagnosis and epidemiology of exotic diseases. It is also necessary to ensure that veterinarians have the necessary resources available should they be required in an emergency situation. Only in this way can a repetition of the disaster that occurred in the UK be avoided.

This Bulletin concentrates on the OIE List A viral diseases that have reemerged as a major threat during the last few years.

Keywords: emerging livestock diseases, OIE List A viral diseases, distribution, transmission, outbreaks, foot-and-mouth disease (FMD), lumpy skin disease, avian influenza, newcastle disease, classical swine fever

## FOOT-AND-MOUTH DISEASE

Foot-and-mouth disease (FMD) in the highly productive beef and dairy breeds found in Europe, North America, and Australasia is characterized by severe clinical signs. Index cases on farms exposed to low-level aerosol virus may develop only mild or even subclinical infection, but as the virus replicates in the first infected animal and is produced in large quantities, so the remaining animals in the herd develop multiple vesicles in the mouth and on the feet and udder. The disease is considerably less obvious in the breeds of cattle indigenous to Africa and Asia, where FMD is mostly endemic. However, FMD is also economically important in these regions. It further reduces an already low milk yield, causes the death of young calves, and interferes with the ability of the adult cattle to pull a plough or cart.

FMD is caused by strains of seven immunologically distinct serotypes of virus (O, A, C, SAT 1, SAT 2, SAT 3, and ASIA 1). Recovery from infection with a strain of one serotype does not provide protection against strains of the other six serotypes. In many of the FMD endemic regions, more than one serotype may be circulating. This creates waves of infection as different serotypes enter and infect the susceptible animals and then move on, to reappear a few years later as a new susceptible population becomes established. Alternatively, one serotype may persist in a region and rarely appear clinically, producing only mild infection in the young stock as they lose their maternal antibodies. Clinical disease may then only be seen when a new serotype is introduced.

**Distribution**

FMD is endemic in Africa, except in Morocco, Algeria and Tunisia. Its distribution is restricted to game parks in South Africa, Namibia and Botswana, but the current situation in Zimbabwe is unclear. Most countries in Asia also have endemic FMD. Russia is free of FMD, although it is now threatened by the reestablishment of FMD in the southern republics of the former Soviet Union. In 1997, FMD entered Taiwan where it has remained, but incursions into South Korea and Japan during 2001 were eradicated. In the Philippines, FMD is restricted to Luzon Island in the north of the country. Indonesia is free of FMD, and Malaysia is periodically affected close to its border with Thailand. In South America, considerable progress had been made in eliminating the disease from Uruguay, Argentina, Paraguay, and southern Brazil. However, in the last two years FMD returned to these areas, and control by vaccination has been reintroduced. Chile, Guyana, Surinam, and French Guiana have remained free of FMD. Central and North America are also free of FMD, while USA has been FMD-free since 1929 and Canada since 1952, as is Australasia.

Europe stopped routine vaccination against FMD at the end of 1991, but since then there have been outbreaks in Italy in 1993 (type O); Greece in 1994 (type O), 1996 (type O), and 2000 (type ASIA 1); Bulgaria in 1993 (type O) and 1996 (type O); and Albania and Macedonia in 1996 (type A) (Kitching, 1998). During 2001, there was an outbreak of type O in the UK, which spread to Eire, the Netherlands, and France (Gibbens *et al.*, 2001). All these outbreaks were successfully eliminated by slaughtering all affected and in-contact animals, movement controls, and disinfection, with or without vaccination.

During the 2001 outbreak in mainland Great Britain, 4 million FMD susceptible animals in 10,157 premises were slaughtered, made up of 2026 premises reported as infected, 4762 premises which were considered dangerous contacts to infected premises, and 3369 premises contiguous to infected premises. An additional 2.5 million animals were slaughtered for reasons relating to welfare. The origin of the outbreak was untreated waste food fed to pigs, but the disease was not reported by the farmer, and it remained unrecognized for almost a month, by which time it had spread extensively in the sheep population. In the Netherlands, to where the FMD spread from UK through France, 60,000 predominantly cattle were slaughtered, together with an additional 200,000 cattle sheep, goats and pigs that had been vaccinated against FMD to help prevent further spread. The vaccinated animals were slaughtered to allow the Netherlands to quickly reestablish its international trading status.

**Transmission**

FMD is usually spread by the movement of infected animals. Susceptible cattle that come into contact with an infected animal, whether sheep, goat, pig or wildlife species, may be infected by the respiratory route or through an abrasion on the skin or mucous membranes. Cattle are very susceptible by the respiratory route, requiring as little as 20 TCID50 of virus to establish infection, but may require 10,000 times more to become infected by the oral route. Calves drinking infected milk can be infected by insufflation of milk droplets as they drink. Virus may also enter the host through abrasions on the skin or the mucous membranes. Of the domesticated susceptible species, cattle are the most likely to be infected by aerosol virus generated by other infected animals, particularly pigs, because of their larger respiratory volume when compared with small ruminants, as well as their higher susceptibility by this route of infection compared with pigs.

In 1981, cattle on the Isle of Wight in the UK were infected by wind-borne aerosol virus produced by infected pigs in Brittany, France, and carried over 250 km across the English Channel. Infected cattle also produce up to Log10 5.1 TCID50 of aerosol virus per day, and a large dairy herd could infect neighboring herds with their combined output of virus (Sorenson *et al.*, 2000). The transmission of FMD virus within an unvaccinated herd is usually rapid, as was seen during the recent UK outbreak, in which over 90% of a group could be showing clinical signs by the time disease was first identified (Alexanderson *et al.*, 2002). Even within a vaccinated herd, the aerosol production of virus from a single infected animal can overcome the immunity of others in the herd resulting in a further increase in the level of challenge and the appearance of clinical disease. Milk and semen from infected cattle may contain virus up to 4 days before the onset of observable signs, but peaks at Log10 6.7 TCID50 per ml of milk and Log10 6.2 TCID50 per ml of semen as vesicles first appear. Urine may contain Log10 4.9 TCID50 per ml and faeces Log10 5.0 TCID50 per gram.

Ruminant animals that have recovered from infection with FMD virus, and vaccinated ruminants that have had contact with live virus may retain infection in their pharyngeal region for a variable period of time. The carrier is defined as an animal from which live virus can be recovered after 28 days following infection. This is not an exceptional situation, and over 50% of ruminants exposed to live FMD virus become carriers; pigs, however, do not become carriers. The duration of the carrier state depends on the species and individual; the African buffalo may carry virus for over 5 years, cattle for over 3 years, sheep for up to 9 months, and goats and wild ruminants for shorter periods of time; for South American camelids, no carrier state exists. Eventually, the carrier does eliminate the virus.

The virus persists in the basal layer cells of the pharyngeal epithelium, particularly of the dorsal soft palate (Zhang and Kitching, 2001). It is not detectable by existing methods in the more superficial layers of cells. Also, it is not clear how the virus is excreted into the pharynx, nor is it clear how the virus changes from a lytic agent which destroys the host cell, into one that can establish a persistent infection. It is possible that a mutation reduces the ability of the persistent virus to shut down host cell metabolism, and it may be further speculated that eventually a further back mutation restores its lytic action and the virus is ultimately eliminated, but this remains to be proven.

The establishment of the carrier state and its duration depends on the host species, but it probably also depends on the strain and serotype of FMD virus and even on the breed of host species. All three serotypes of the SAT viruses are found in the wild African buffalo populations of Botswana and Zimbabwe, but rarely are the commercially farmed Brahman cattle of the region found to be carrying either SAT 1 or SAT 3. During the last 20 years there have been a series of outbreaks of SAT 2 in the FMD-free areas of Zimbabwe, and one Brahman bull in particular, remained a carrier of SAT 2 virus for over 3 years. Also during the 1991 outbreak of SAT 2 in Zimbabwe, it was notable that the European cattle, although affected, carried the virus for a shorter period than the Brahman. The SAT viruses occasionally spread out of Africa into the Middle East, most recently into Saudi Arabia during 2000. But while the O, A and ASIA 1 serotypes persist in this region, in spite of limited attempts at control, the SAT

viruses eventually die out. This implies that the cattle, sheep, and goats are unable to maintain the SAT serotypes, or conversely, these serotypes require particular host species, either the Brahman for SAT 2 or the African buffalo. Similarly, the distribution of ASIA 1 serotype would suggest that it is constrained from establishing itself outside of Asia.

Whether the geographical restriction of serotypes and even strains of FMD virus is related to their ability to establish the carrier state in particular susceptible species or breeds is not known, but should that be the case, it presents a powerful argument for the importance of the carrier in the epidemiology of FMD.

**Carriers causing outbreaks**

It has not been possible, under experimental conditions, to show transmission of FMD virus from a carrier bovine to a susceptible in-contact bovine, in spite of a considerable number of attempts. In one series of experiments, carriers were inoculated with dexamethasone in order to depress their immune systems, and kept in contact with susceptible cattle, but this had the reverse effect of causing the virus to disappear from the pharynx, only to reappear once the treatment was stopped (Ilott *et al.*, 1997). Even dosing the in-contact animals with dexamethasone failed to result in transmission. A further experiment in which carriers were infected with rinderpest virus, which destroys host T cells, also failed to increase the level of pharyngeal FMD virus.

An experiment with carrier African buffalo, kept in contact with susceptible cattle and additional susceptible buffalo, did succeed, but the results were difficult to explain (Dawe *et al.*, 1994). A group of three FMD-free buffalo was infected with SAT 2 virus and kept in an enclosure with four susceptible cattle on an island in Lake Kariba. The buffalo developed clinical FMD, and recovered, without transmitting disease to the cattle. The buffalo all became carriers, and four months later, two further FMD-free buffalo were introduced. Seven weeks after the introduction of the two additional buffalo, the cattle developed clinical FMD, which then spread to the two new buffalo. What triggered the transmission event was not clear, but the cattle were confirmed to be infected with the same virus as was carried by the originally infected buffalo. All the animals were monitored throughout the experiment, and regular samples were collected from the pharynx to confirm the continuing persistence of the virus. The transmission of SAT 2 virus from the carrier buffalo to the cattle under controlled conditions was also shown by Vosloo *et al.* (1996).

There have been a number of anecdotal accounts of carriers starting new outbreaks of FMD in the field (Salt, 1993). The strongest evidence of the involvement of carriers comes from Zimbabwe in 1989 and 1991. Following an outbreak of SAT 2 FMD in 1987, cattle on affected and neighboring farms were vaccinated and kept in quarantine for 18 months. Following this, off-farm movement was allowed, but there soon were further outbreaks, shown by nucleotide sequencing as being due to the same virus as the 1987 outbreaks, associated with cattle from the quarantined farms. The same control program was implemented in this new series of outbreaks, and again, vaccinated farms were quarantined for 18 months. After this period, the cattle were moved from one of the vaccinated farms which had been close, to a known infected farm near Bulawayo, but which itself had not been identified as being infected. Cattle were moved to a feedlot north of Harare, where a new outbreak occurred. This was shown by nucleotide sequencing to be due to the same strain of SAT 2 virus that had caused the 1989 outbreaks. Although the cattle which had been moved were not individually identified and sampled, samples taken from their farm of origin showed the presence of carriers. What was particularly interesting was that no vaccine had been used on the farm since 1989, and a new population of susceptible young stock was now present on the farm, together with the carrier animals, but no transmission of virus had taken place. However, when the carriers were moved and mixed with cattle from other farms, transmission had occurred. It is not possible to prove this scenario, but the hypothesis is that the stress of moving and mixing the carrier cattle was sufficient to cause these animals to start excreting sufficient virus to precipitate a new outbreak.

**Identifying the carrier and subclinically infected animal**

The definitive identification of carrier or subclinically infected animals is the recovery of live FMD virus from these animals. The preference of the virus for the epithelium of the pharynx makes this tissue the most suitable to sample, a procedure which can be carried out using the 'probang' sampling cup (Kitching and Donaldson, 1987). This is a hollow metal cup with a slightly sharpened edge, attached from the center of its bowl by a long wire, approximately half a meter long, to a handle at its free end, which can be pushed into the mouth of the animal being tested, over the base of the tongue into the pharynx. The cup is then withdrawn, collecting as it is pulled out, mucous and superficial cellular material from the pharynx. The contents of the cup are usually mixed with a neutral buffer solution, and if not examined immediately, kept frozen over liquid nitrogen or on dry ice (solid carbon dioxide). Live virus can be cultured on sensitive tissue culture such as primary bovine thyroid cells or lamb kidney cells. Carrier animals, which have either recovered from clinical disease or have been vaccinated and subsequently acquired infection following contact with live virus, will also have high levels of specific anti-FMD virus antibody present in their pharyngeal mucous. Treatment of the probang sample with Freon or Arcton can help dissociate the virus/antibody complexes, and increase the possibility of recovering virus on tissue culture. Subclinically infected animals, other than those with partial vaccinal immunity, will not usually have detectable antibody levels at this stage of infection.

The quantity of virus present in the pharynx of carrier animals can vary considerably over time, and the successful recovery of virus will depend on this and other factors, such as the subsequent handling of the sample and the skill of the operator. Possibly only 50% of carrier animals will be identified from the examination of a single probang sample, but this percentage can be increased by repeating the sampling procedure at two weekly intervals. Regular sampling of a group of vaccinated cattle on a farm in Saudi Arabia soon after an outbreak of FMD showed that some animals failed to yield positive sample on every occasion, but the identification of live virus in later samples indicated that they would have been falsely declared negative. The sensitivity of the test can be improved by using polymerase chain reaction (PCR), which identifies small quantities of viral genome present in the sample (Zhang and Alexandersen, 2003). There is also the unresolved question as to the significance of a positive PCR result. The PCR identifies only part of the viral genome, and would be positive even if the genome was itself fragmented and unassociated with any live virus. Therefore, while a positive PCR is highly suggestive of previous infection, the animal from which the sample was collected could no longer be carrying live virus, and no longer represent any risk of causing a further outbreak.

Testing of animals suspected of having subclinical infection may also include animals that have only recently been infected and have not yet developed clinical disease. Mucous samples from the nose and mouth can be collected to detect the low levels of virus present, but because tissue culture techniques for virus isolation may take up to 96 hours to complete, by which time these animals would be clinically obvious, the more rapid PCR test can be used. Methods have been designed to carry out large numbers of PCR tests on 96 well microtitre plates, which would allow rapid screening of at-risk animals at the start of an outbreak, or to determine the extent of a rapidly spreading outbreak. In addition, blood samples can be collected from suspect animals for identification of viraemia, either by PCR or inoculation of tissue culture.

During the 2001 outbreak of FMD in the UK, the spread of disease in subclinically infected sheep was responsible for its widespread dissemination and persistence. Advantage could have been taken of the use of blood samples to help identify infected animals, for although the isolation of virus from blood is restricted to a 3-day viremic period, the samples could have been simultaneously tested for the presence of specific anti-FMD virus antibody, as a sheep, like any other susceptible species that is or has been recently infected, will either be virus or antibody positive – or sometimes both.

Carrier animals will also have specific antibodies to FMD virus. This will be true

whether they have recovered from infection or been vaccinated. In countries that identify vaccinated animals by a brand or an ear tag, there should not be a problem in distinguishing animals that are antibody positive as a result of vaccination from those that are positive following recovery from infection. However, the difficulty is in identifying those vaccinated animals that have had contact with live virus, and become carriers.

**Non-structural proteins (NSPs)**

FMD virus has a positive sense, single-stranded RNA genome of 8400 nucleotides that codes for 12 proteins, 4 of which are structural and make up the capsid of the virus, and 8 of which are non-structural, which together allow the virus to replicate in an infected cell. The structural genes are identified as 1A, 1B, 1C and 1D, while the non-structural as L, 2A, 2B, 2C, 3A, 3B, 3C and 3D. The functions of the proteins for which the non-structural genes code have not all been fully identified, and it is beyond the scope of this paper to describe the current opinions (Rueckert, 1996). The vaccine used to help control outbreaks of FMD is a dead preparation of whole virus particles in an oil or aluminium hydroxide/ saponin adjuvant. There will be no replication of the virus following vaccination, and the vaccinated animal will develop antibodies to the structural proteins of the virus present in the viral capsid, some of which will be neutralizing, and protect it from subsequent infection. Because there is no viral replication, there is no expression of the non-structural proteins (NSPs), and the animal will not develop antibodies to these proteins – although some vaccine do contain low levels of these NSPs depending on the manufacturing process, in particular 3D, and there can be a low antibody response to the NSPs, more obvious in multiply vaccinated animals.

Animals that have recently recovered from infection will have antibodies to the NSPs, because as the virus reproduces in its tissues, these proteins will be expressed and stimulate the production by the host of specific antibodies. The detection of these antibodies can, therefore, be used to identify those animals that have had FMD, and which may, therefore be still carrying live virus. A variety of tests have been developed to detect these antibodies, including ELISA and EITB (OIE, 2000), using pure NSP antigens expressed in viral (baculovirus) or plasmid (*E. coli*) expression systems (Fig. 1). These tests have been predominantly designed to detect NSP antibodies in cattle, and are less useful in sheep and pigs. Sheep, in particular, probably because of the frequently subclinical nature of FMD, may fail to develop detectable levels of these antibodies. Even in cattle, there is considerable individual variation in the amount of antibody produced to each of the NSPs, and consequently the period of time after

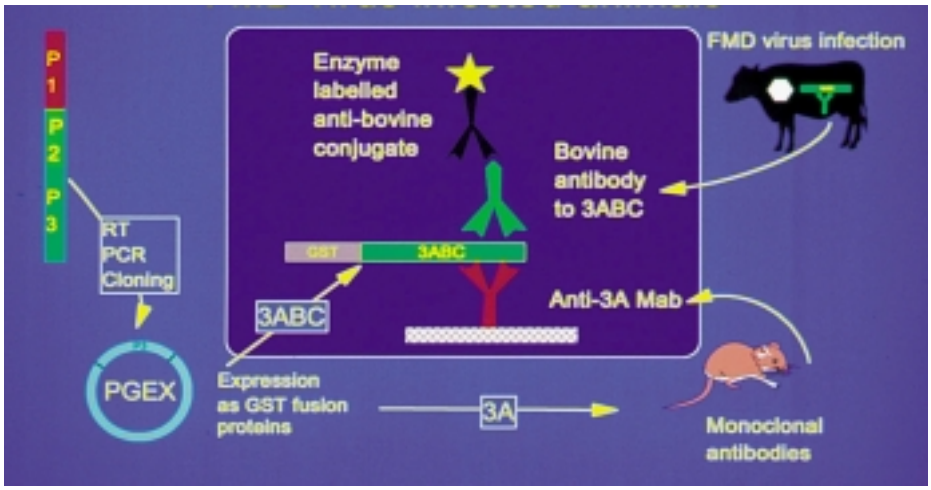


Fig. 1. Molecular techniques in the identification of FMD virus infected animals.

infection each can be detected. The 2C antibodies may be detectable for 12 months, while the 3ABC antibodies persist longer; it is likely that the severity of the infection is the major influence on the levels and the subsequent duration of detection of the NSP antibodies.

In South America the EITB, which uses a Western blotting technique to detect the antibodies to five of the NSPs, 3A, 3B, 2C, 3D and 3ABC, was successfully used to support the local FMD control programs, and the ultimate recognition by OIE of freedom from FMD, particularly for regions of Brazil (Bergmann *et al.*, 1998). A 3ABC ELISA was used to define the limits of the 1996 outbreak of FMD in the Balkans, and antibody to the 3ABC polyprotein is considered the single most reliable indicator of infection (Mackay, 1998).

There is, however, a problem with the NSP tests on an individual animal level. Some cattle that have been vaccinated, particularly with a high potency vaccine as might be used in an outbreak in a previously FMD-free country, will fail to develop antibodies to the NSPs should they have contact with live virus. This is because their level of immunity prevents any significant viral replication, and therefore, expression of the NSPs. However, they could become carriers of live virus. On a herd basis, even potent FMD vaccine will not protect 100% of the cattle, and should the herd become exposed to live virus, some will support replicating virus even though they do not show clinical disease, and sero-convert to some of the NSPs, in particular to 3ABC. Thus, by testing the whole herd, it would be possible to diagnose the previous encounter with live virus and the potential for the presence of carriers, assuming, of course, that the whole herd was exposed to the same challenge. The test may fail if only a few animals contacted live virus, perhaps as an aerosol from a neighboring infected farm, and these could all have been sufficiently immune to prevent the expression of the NSPs.

The test for the antibodies to the NSPs is a significant advance in the detection of the carrier animal. However, it has its limitations, and cannot be used reliably on an individual animal to exclude its potential to be carrying live virus, and even when used on a whole herd, it would be unable to provide a guarantee. The possibility of carrier animals creating fresh outbreaks is probably extremely small, and this can be further reduced by using probang and serological tests. But, however small the risk, if importing countries have a choice, they are likely to choose to import their live animals and animal products from areas where there is no FMD vaccination or possibility of the presence of carrier animals. Until the identification of the carrier is 100% certain, FMD will remain the most significant constraint to trade in susceptible animals and their products.

## BLUETONGUE

Bluetongue (BT) is an infectious, noncontagious disease of ruminants characterized by congestion, oedema, and haemorrhage. The disease is caused by strains of orbivirus, within the family Reoviridae. The genus orbivirus, Reoviridae also contains Ibaraki disease virus of cattle, epizootic haemorrhagic disease virus of deer (EHD), African horse sickness virus, and Colorado tick fever virus. There are 24 immunologically distinct BTV serotypes that have so far been identified by virus neutralization tests. However, it is probable that more types will be identified in the future. Bluetongue virus is sensitive to low pH, and storage at -20$^{o}$C; it is partially resistant to lipid solvents.

### Distribution

The distribution of BTV is approximately defined by the latitudes 40$^{o}$N and 35$^{o}$S, which includes most of Africa, the Middle and Far East, northern Australia, USA, Central America, and South America north from southern Brazil, Paraguay and Bolivia. Not all the BTV types are found throughout this enzootic region, and the distribution of the different types can vary between years. The closely related EHD group of viruses have been isolated in North America, Canada, Nigeria, and Australia, whereas, Ibaraki disease virus is restricted to South Korea, Japan, Philippines, and Indonesia.

Bluetongue was first diagnosed in South Africa in sheep at the beginning of the 20$^{th}$ century. It was seen outside Africa in 1943 in Cyprus, although it had possibly been present in Cyprus as early as 1924. Subsequently, BT was diagnosed in Israel in 1951, in Pakistan in

1959, and in India in 1963. A disease which was first identified as sore muzzle of sheep in Texas in 1948 and in California in 1952 was diagnosed the following year as BT. Between 1956 and 1960, BTV caused a major epizootic in sheep in Portugal and southern Spain, which reportedly resulted in the loss of 180,000 animals, but the virus then disappeared from the region.

In 1977, outbreaks of bluetongue due to serotype 4 were reported in sheep in Cyprus, which spread into western Turkey, and then in 1979 and 1980, onto the Greek islands of Lesbos and Rhodes, respectively. During 1998, serotype 9 was reported present in Bulgaria and central Greece, and then also in Turkey in 1999. In 1999 serotypes 4 and 16 were found in Greece, and the following year serotype 16 appeared in Turkey. Meanwhile, in the western Mediterranean, serotype 2 was found in Tunisia in 1999, and the following year in Tunisia, Algeria, Italy, and the islands of Sicily, Sardinia, Corsica, Majorca, Menorca (Baylis *et al.*, 2001). Serotype 4 appeared in Sardinia in 2003.

**Transmission**

The distribution of BTV between 40°N and 35°S reflects the distribution of its main biological vectors, certain tropical and subtropical species of *Culicoides* midges, in particular *Culicoides imicola* in Africa and the Middle East, *C. variipennis* in North America and *C. brevitarsis, C. fulvus* and *C. wadai* in North Australia.

The adult female *Culicoides* lays her eggs in damp muddy areas containing decaying vegetable material or in cattle dung, two to six days after a blood meal. Depending on the temperature these eggs may hatch in two to three days into larva. The larval stage lasts 12-16 days, followed by pupation and, two to three days later, the emergence of the adult *Culicoides*. In the subsequent 24 hours the adults take a blood meal and mate, and they will continue to take a blood meal every three to four days until the end of their life, which may last for 70 days but probably rarely exceeds 10. Optimum conditions are between 13 and 35°C. Larvae of temperate species can remain dormant over winter and pupate the following spring. Seven to ten days after taking a BTV-infected meal, vector species of *Culicoides* midge are able to transmit virus.

*Culicoides* usually feed at dusk, during the night or at dawn, and are subject to being transported, sometimes over considerable distances, by strong wind currents. The passive movement of infected *Culicoides* is considered responsible for the introduction of BT into areas usually outside the enzootic region, such as western Turkey and Cyprus. This introduction of BTV into an area may be associated with abnormal wind currents or may be a regular occurrence. The winds of the Intertropical Convergence Zone annually reintroduce BTV-infected *Culicoides* to South Africa from Central Africa. The movement of BTV into Sudan from Central Africa is also associated with a prevailing wind from the South. However, BT may also become enzootic in new regions as climatic changes allow the main vectors to extend their breeding sites or, alternatively, virulent strains of new serotypes of BTV may be introduced into an area already infected with mild or avirulent strains.

Within BT enzootic regions the prevalence of seropositive animals may be very localized around areas particularly suitable for the breeding and survival of *Culicoides*; so-called 'hot spots'. The possibility also exists for new species of *Culicoides* to take on the role of BTV vectors; it has recently been shown that some British species of *Culicoides* can biologically transmit BTV under experimental conditions.

Bulls may shed BTV in their semen intermittently during the viraemia following infection. Bowen *et al.* (1985) classified bulls into three categories: those from which virus could not be isolated form the semen (the majority), those form which only low titers of virus were isolated on less than three occasions, and those which shed virus over a two to three week period. Bluetongue virus could only be isolated from the semen when there was a concurrent viraemia. Six out of nine susceptible heifers inseminated with the BTV-contaminated semen became pregnant, and three of the nine became viraemic. None of the calves born at term showed any clinical abnormality. Considerable importance has been attached to reports of a bull that was persistently infected but seronegative from

birth, and intermittently shed virus in semen over an 11-year period (Luedke *et al*., 1982). Attempts to duplicate the conditions that produce persistently BTV-infected, seronegative calves have been unsuccessful.

The recent incursions of BTV into southern Europe have been correlated with an increased northern distribution of the vector *C. imicola* (Baylis *et al.*, 2001), and this group have been able to predict the abundance of *C. imicola,* and thus the potential for outbreaks of BT, by using remote sensing techniques to collect data on 41 parameters. Of these variables, those related to vegetation were the most significant in predicting *C. imicola* prevalence. It is not clear why this BTV vector should be extending its distribution further into southern Europe, although it may be a consequence of climatic warming. It is also possible that *C. obsoletus*, a more temperate species of *Culicoides* implicated in the spread of African horse sickness during the outbreaks in Spain over 10 years ago, may be involved in some of the recent spread of BTV (Mellor and Boorman, 1995).

## LUMPY SKIN DISEASE

Lumpy skin disease (LSD) is a pox disease of cattle characterized by fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, oedema of the skin, and sometimes death (Fig. 2). The disease is of economic importance because it causes reduced production, particularly in dairy herds. It also causes damage to the hide.

**Distribution**

Lumpy skin disease is caused by strains of capripoxvirus that are antigenically indistinguishable from strains causing sheep pox and goat pox. However, LSD has a different geographical distribution to sheep and goat pox, suggesting that cattle strains of capripoxvirus do not infect and transmit between sheep and goats. Until 1988 LSD was confined to sub-Saharan Africa, but then spread into Egypt. There has been only one laboratory-confirmed outbreak of LSD outside Africa, in Israel in 1989, which was eliminated by slaughter of all infected and in-contact cattle, and vaccination. Outbreaks reported in Bahrain and Reunion in 1993 were not confirmed by virus isolation.

Lumpy skin disease was first seen in Zambia in 1929, and was originally thought to be an allergic reaction or the consequence of multiple insect bites. It spread from Zambia into Botswana and South Africa, where it affected over eight million cattle causing major economic loss. In 1957 it entered Kenya, associated with an outbreak of sheep pox (Weiss, 1968). In 1970 LSD spread north into

Fig. 2. Lumpy skin disease (LSD) on cattle.

the Sudan, by 1974 it had spread west as far as Nigeria, and in 1977 was reported from Mauritania, Mali, Ghana and Liberia. Another epidemic of LSD between 1981 and 1986 affected Tanzania, Kenya, Zimbabwe, Somalia and the Cameroon, with reported mortality rates in affected cattle of 20%. However, the true extent of this epidemic was not clear, and it probably affected a considerable area of central Africa. In 1988 LSD became established in Egypt, and in 1989 a single outbreak was reported in Israel. LSD must be considered to have the potential to become established outside Africa. The principle method of transmission is mechanical by arthropod vector (Carn and Kitching, 1995a; Chihota *et al.*, 2001).

**Transmission**

Transmission of LSD virus is thought to be predominantly by insects, natural contact transmission in the absence of insect vectors being inefficient. Transmission by insects is mechanical, with no replication of virus occurring in the vector, and it is probable that a large number of biting and blood feeding insects are capable of spreading the virus. This is sometimes reflected in the distribution of the lesions, with more papules being seen on the legs if the insect vector is predominantly feeding on those sites. It is probable that mosquitoes are responsible for transmission in the more severe outbreaks because they are likely to inoculate virus directly into the bloodstream, and this method of infection is more likely to produce generalized clinical signs (Carn and Kitching, 1995b).

## AVIAN INFLUENZA

Avian influenza (AI) is an orthomyxovirus infection of wild and domestic birds characterized by oedema of the head, diarrhoea, reduced egg production, respiratory signs and death within 48 hours. However, there are many strains of AI virus, all of which belong to type A influenza, but which may be identified by different combinations of the haemagglutin and neuraminidase surface antigens. Traditionally strains containing H7 were considered virulent, causing fowl plague, but virulence has also been associated with other H antigens, in particular H5, and some strains containing H7 are of low pathogenicity. Strains of AI virus may be pathogenic in one species of bird, but not in others. 20 % of wild migratory ducks in North America are asymptomatically infected with strains of AI virus, but some of these are highly pathogenic when transmitted to domestic poultry. Pathogenicity of AI virus strains is defined by testing in laboratory chickens or by nucleotide sequencing. Strains of AI virus may also infect other domestic animals such as pigs and horses and also humans.

**Distribution**

Because of their association with migratory birds, AI virus strains are distributed worldwide, but may only occasionally appear in domestic poultry. In 1997, an H5N1 strain appeared in Hong Kong and spread to humans, infecting 18 and killing 6, and resulted in the almost total depopulation of poultry in the Territory. Since then, genomic variants with the H5N1 antigens have reappeared on regular occasions, resulting in further slaughter of affected poultry and the introduction of vaccination, and two further human cases and one death. During 2003, the presence of a low pathogenic H7N2 strain was detected in Connecticut, USA, similar to a strain previously detected in the live poultry markets in New York. Almost 3 million poultry were quarantined and vaccinated.

An outbreak of highly pathogenic AI due to a H7N7 strain affected poultry flocks in the Netherlands, Belgium and Germany during 2003, and also spread to humans. In the Netherlands almost 30 million chickens on 255 premises were slaughtered, in Belgium 3 million poultry on 8 premises were culled, and in Germany there was a single outbreak. The origin was thought to be a Dutch farm with free ranging poultry, close to water where wild ducks were common. Although the birds on the farm were seropositive for a low pathogenic strain of AI, high pathogenic H7N7 had previously been isolated from the migratory ducks and waterfowl. H7N1 and H7N3 strains had also been found in chicken and turkey flocks in Italy during the previous four years.

**Transmission**

Transmission of AI virus between wild and domestic birds is often through shared and contaminated drinking water. There are large quantities of virus in the faeces and respiratory exudates and in eggs produced during early infection - although the embryos will usually die. Spread between poultry premises is commonly by contaminated fomites, litter and vehicles, and on the clothing and hands of people, although with the Dutch strain, probably also by infected individuals. Pigs have been infected with some strains, and may provide an environment for a more human specific mutation. Experiments to infect pigs with the Dutch strain were successful, although the virus failed to transmit between pigs, or maintain itself in pigs without frequent reintroductions from poultry. The ability of one strain of virus to recombine with another within a single host, as could have occurred during the Hong Kong and Dutch outbreaks if one of the infected people had already been infected with a human influenza strain, raised the possibility on each occasion of a new strain with the virulence of the poultry strain and the ability to easily transmit between humans, leading to a world wide pandemic.

What particularly characterized the Dutch outbreak strain was the apparent ease with which it spread directly to humans. Although the Hong Kong outbreak of 1997 had shown that avian strains could directly affect humans, there had been no human to human transmission, and opinion was that the virus would first have to adapt to transmission between humans by passage in pigs, whose cells shared receptor characteristics with both humans and birds. However, in the Netherlands there were 83 confirmed cases of human H7N7. 79 of these showed conjunctivitis, and 13 mild influenza like illness, and there was one death. Three family members of two poultry workers developed respiratory disease, suggesting that with this strain, human to human transmission was in fact possible. Extreme precautions were taken to reduce the infection of people involved in the depopulation, including vaccination, administration of viricidal drugs, face masks and goggles.

## NEWCASTLE DISEASE

Velogenic Newcastle disease (ND) is a Type 1 avian paramyxovirus infection of poultry characterized by neurologic signs, oedema of the head, respiratory distress, loss of egg production, diarrhoea and high mortality in affected flocks (Fig. 3). Wild species of birds are also infected but many fail to show clinical signs, and psittacine species and some other wild species can develop persistent infection. Severe disease has been seen in cormorants and fancy pigeons.

**Distribution**

The presence of velogenic strains of ND in wild and pet birds potentially allows the virus a worldwide distribution, although only when the virus becomes established in the domestic poultry population is it considered a problem. On the 1st October 2002, an exotic strain of ND virus was confirmed in the state of California, USA. It was originally identified in the "back yard" flocks from which were derived fighting cocks, but because the practice of cock fighting was illegal in California, it became very difficult to trace infection between flocks. The disease spread to Arizona and Nevada, and during the eradication program, which took approximately eight months, almost 19000 premises were quarantined, 931, including 17 commercial flocks were confirmed positive, and 3.5 million birds were slaughtered. Sequence

Fig. 3. Newcastle disease.

analysis of the strain indicated it was identical to a strain present in Mexico. A single outbreak also occurred in a "back yard" flock in Texas, but the sequence of the virus causing the outbreak was different from the California strain, indicating a second introduction.

**Transmission**

Introduction of ND virus into a commercial premise is usually by contaminated fomites such as egg trays, vehicles or people, although inadvertent contact with wild birds can be responsible. The legal or illegal movement of persistently and subclinically infected psittacine birds from South America has been a frequent cause of its introduction into Europe and North America, although the movement of fighting cocks into USA from Mexico was probably the cause of the California and Texas outbreaks.

## CLASSICAL SWINE FEVER (HOG CHOLERA)

Classical swine fever (CSF) is a highly contagious virus disease of pigs caused by a strain of pestivirus, closely related to bovine virus diarrhoea virus and border disease virus of sheep. Some strains can spread between species and cause disease. CSF can be acute, characterized by high fever, depression, multiple internal and superficial haemorrhages and death, subacute or chronic, characterized by general poor health, susceptibility to other infections and low mortality. The virus can cross the placenta and cause persistent infection without an antibody response.

**Distribution**

CSF has been eradicated in Australia, USA and Canada, but is present in European wild pig populations, particularly in Germany, Italy and Sardinia, from where it occasionally spreads into the domestic pigs. In 1997/98 it caused an outbreak in the Netherlands in which over 10 million pigs were slaughtered to bring it under control and eradicate the virus. In 2000 it spread into the UK for the first time since 1986. 16 herds became infected, on which 41,500 were slaughtered, and a further 31,900 pigs were slaughtered on 40 contiguous farms (Fig. 4). The initial outbreak was missed because the disease was not acute, and clinically resembled porcine dermatitis and nephropathy syndrome which was also known to be on the farm (Paton, 2002).

Strains of CSF virus can be divided into three groups and several subgroups by comparing an approximately 190 nucleotide sequence from the E2 region of the genome. The UK outbreak was caused by a strain

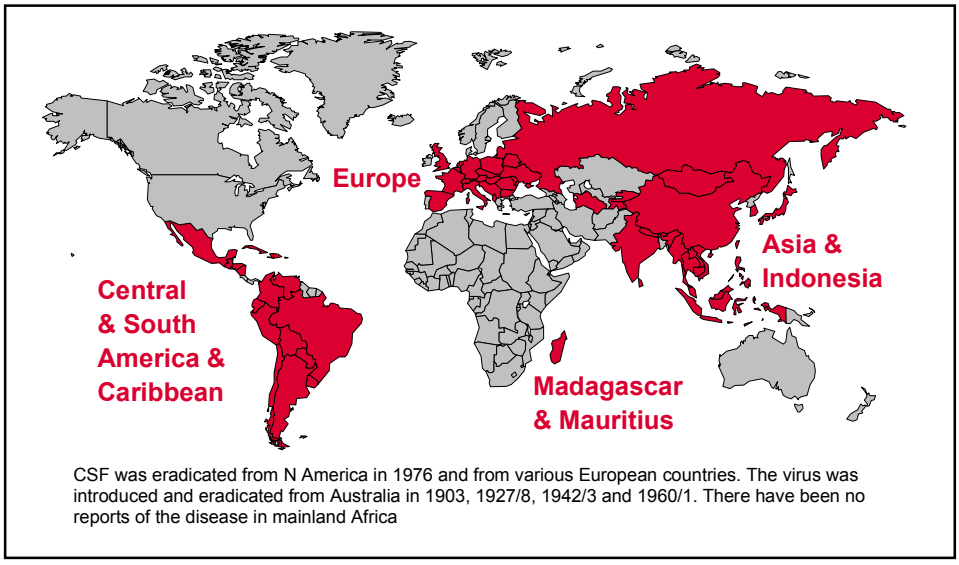


Fig. 4. Reports of classical swine fever since 1990.

within the 2.1 subgroup, which is not present in Europe, but found in south east Asia.

**Transmission**

CSF is transmitted between infected and susceptible pigs, particularly by persistently infected animals. However, meat and other products from infected animals can contain large amounts of virus, and excretions can contaminate fomites and food material which might later be fed to pigs. The two outbreaks of CSF in the UK prior to 2000, in 1971 and 1986 had been caused by feeding untreated waste food to pigs - similar to the cause of the 2001 FMD outbreak - but it was not clear how the 2000 outbreak had started. The first pigs affected were being kept outdoors, a practice becoming more common in the UK as animal welfare lobbies become more influential, and it was speculated that a passerby had thrown infected meat, perhaps present in a sandwich, into the field in which the pigs were kept. A second possibility was the spraying of virus contaminated water onto nearby fields from a neighboring abattoir. Although the disease had been present within the UK from mid June, it was not detected until early August. The strain caused only mild disease in the adult sows which were first infected, and it did not appear clinically obvious until it had spread to weaned pigs on a grow out operation linked to the same company. In all the pig company controlled about 140 farms, and the outbreak was predominantly confined to within this organization, although there was some spread to neighboring farms. In view of the highly infectious nature of CSF virus, and that it had remained undetected for almost 3 months, it was fortunate that the structure of pig farming within the UK had kept it restricted in its distribution.

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