1 Overview

(a) Introduction

1.1 This report looks forward to how the country should prepare itself against any further invasions of highly infectious exotic diseases and how it should respond if an outbreak occurs. Our Inquiry has been much influenced by two issues. The first is the livestock industry itself, which is essential to the nation, has a farm-gate turnover of £7.5 billion and a standing population of 11 million cattle and calves, 7 million pigs, 42 million sheep and lambs, and 170 million poultry (Chapter 2). The recent Curry Commission[1] outlines the major difficulties it faces, which centre on a lack of profitability and a structure that is production driven rather than consumer led. Animal health is critical to its viability and Curry states his views that (page 50) *'in view of England's abysmal animal health record in recent years, DEFRA in consultation with the industry need to devise and implement a comprehensive animal health strategy'*. The second issue has been the public reaction to the foot-and-mouth outbreak of 2001. It has eroded trust in, and increased suspicion of, Government actions while raising questions in the public mind about strategies for disease control that only cull animals. The public wishes to see alternative strategies examined and we have responded by exploring in detail the use of emergency vaccination during an outbreak (Chapter 8 and 9). Separately, we have considered what would be required for routine (prophylactic) vaccination to become the preferred long-term strategy (Chapter 8). Our report is accordingly strategic and wide-ranging. Our remit did not, however, cover, nor were we funded to undertake the follow-on research required by many of our recommendations, and that is needed to implement them. This will have to be undertaken by DEFRA over the coming months, and the extent of this work should not be underestimated.

1.2 All the evidence shows that speed is vital in handling outbreaks of infectious diseases, and this necessitates planning of a high order and an executive empowered by wide acceptance of the strategies being adopted. During the course of our Inquiry, we have become convinced that the public should be involved, through its elected representatives, in approving both the broad principles underlying disease control strategies and the associated contingency plans. No longer is it sufficient for plans to be issued by the executive alone, largely because some policies are viewed as controversial by one stakeholder or another and this weakens the ability to combat the disease invasion. Our first major recommendation is therefore designed to address this issue. **We recommend that the UK Government bring before Parliament for debate a framework for the Contingency Plans covering the principles involved in handling outbreaks of infectious exotic diseases and the resources required for their implementation. (R1.1)** The more detailed plans for each disease should be made publicly available for scrutiny and comment.

1.3 The prevention and control of infectious diseases require coordinated actions from a range of Government departments, although DEFRA takes the lead at an operational level and the equivalent for the devolved administrations. The extent of central Government involvement in last year's foot-and-mouth outbreak, including the Prime Minister's own role and that of the Cabinet Office emergency management system and the Army, showed the breadth of interests involved. If future outbreaks are to be avoided, or at least minimised in their effects, a similar coordinated approach will be needed to respond to the Recommendations in this Report (and those of the Anderson Inquiry).

1.4 It is hoped that incursions of exotic diseases will remain rare events. The gaps between the previous three outbreaks of foot-and-mouth disease were 13 and 30 years respectively. Because public and political memories are short, the country should institutionalise procedures that regularly review disease threats to the nation, changes in farming, our preparedness for attack and whether scientific advances allow for major changes in strategy. Accordingly, **we recommend that the Prime Minister establish a formal procedure to review at three-yearly intervals:**

- **the level of threat from imported diseases of livestock;**
- **changes in livestock farming practices that could affect our vulnerability to disease;**
- **scientific and therapeutic advances that could affect policy options;**
- **the UK's, and Europe's, state of preparedness. (R1.2)**

1.5 For at least 300 years, European agriculture was threatened by the 'great plagues' of rinderpest, foot-and-mouth disease and contagious bovine

pleuropneumonia, which caused major health and welfare problems and badly affected livestock productivity. Some of these were eradicated in parts of Europe but their international nature led in 1924 to the establishment of the Office International des Epizooties (OIE), which put in place worldwide regulations to constrain the most infectious diseases. Later, these regulations became enshrined in trade law, so that it is the economic consequences that have come to dominate a nation's response to these diseases. In this Inquiry we have focused upon a subset of the most infectious diseases which pose particular risks to the UK (Chapter 3). Inevitably, our work has been dominated by foot-and-mouth disease (98% of the submissions relate to this one disease) but virtually all of our conclusions apply equally to the other highly infectious exotic diseases, and the report needs to be read with that in mind.

1.6 A number of endemic infectious diseases also affect the health of UK livestock, and we offer an overview on some of these in Chapter 3. Most concern has been expressed about cattle tuberculosis, but because Professor John Bourne is leading an independent scientific group on cattle tuberculosis for DEFRA we have eschewed specific consideration of this disease. Like Curry, we believe there must be a complete overhaul of the arrangements governing animal health. This should cover both exotic and endemic infectious diseases and include potential food-borne zoonoses such as *Salmonella, Escherichia coli* and *Campylobacter*. The overhaul should develop national strategies for research and development, and establish linkage between production subsidy and animal health; it should also develop improved linkages between livestock farmers and their veterinarians.

1.7 The most serious diseases (classified by the OIE as 'List A') constitute major health hazards to livestock whether in extensive or intensive systems. Foot-and-mouth is one of the most infectious diseases known (see Chapter 3). Unchecked, it would infect the great majority of livestock. It seriously affects animals' productivity and results in mortality of up to 90% in lambs and young pigs. The result is economically serious and Harvey[2] noted that, after the 1967 outbreak, farm prices rose by some 10%, about £1 billion p.a. in today's prices. Other List A diseases (e.g. classical swine fever, Newcastle disease) affect the welfare and productivity of animals to at least as serious an extent. With the exception of highly infectious avian influenza (see Chapter 3 and also *Getting ahead of the curve*[3]), OIE List A diseases are not significant human health hazards.

(b) Origins of this Inquiry

1.8 After the outbreak of foot-and-mouth disease in 2001 the Government commissioned three Inquiries. It asked the Royal Society (as the UK's national academy of sciences) '*to review scientific questions relating to the transmission, prevention and control of epidemic outbreaks of infectious diseases in livestock in Great Britain, and to make recommendations by Summer 2002*' (Terms of Reference in Annex A). The other Inquiries were the policy commission on 'The future of farming and food' led by Sir Don Curry[1], and the 'Lessons learned Inquiry' under Dr Iain Anderson. Our Inquiry makes no direct observations upon the handling of the foot-and-mouth outbreak of 2001 but, inevitably, it has been shaped by many of the issues that emerged during the outbreak, as were the vast majority of submissions.

1.9 That outbreak was the worst experienced by Britain since proper records began and involved 2030 cases spread across the country.[4] Some 6 million animals were culled (4.9 million sheep, 0.7 million cattle and 0.4 million pigs), which resulted in losses of some £3.1 billion to agriculture and the food chain. Some £2.5 billion was paid by the Government in compensation for slaughtered animals and payments for disposal and clean up costs.[5] About 4 million of the animals were culled as part of disease control (1.3 million on infected premises, 1.5 million on farms defined as dangerous contacts not contiguous with the infected premises, and 1.2 million on contiguous premises, many of which were also defined as dangerous contacts). The others died under various types of 'welfare cull'. At one stage, it was suggested that in addition to the six million animals mentioned above there could have been up to 4 million further young animals killed 'at foot' (i.e. slaughtered but not counted). DEFRA believe that these estimates of additional 'at foot' animals are, however, likely to be high, because at least some of these young animals were included in their original figures. The foot-and-mouth outbreak had serious consequences upon tourism—in both city and country—and other rural industries.

1.10 The UK has not been alone in facing major viral epidemics of List A animal diseases in recent years. Perhaps the most relevant are the foot-and-mouth outbreaks of the same type O pan-Asia strain in Taiwan and Korea and an A-strain outbreak in Uruguay. In the Republic of Korea an outbreak was detected in March 2000, the first for 66 years. Fifteen separate outbreaks occurred, all in cattle. The control strategy involved culling all infected and neighbouring

farms within a radius of 500 m along with the emergency vaccination of regions around the infected farms. A total of 800 000 cattle and pigs were vaccinated. The outbreak ended within weeks and subsequently most of the vaccinated animals entered the Korean food chain. There have also been major swine fever outbreaks in Europe, most notably in Germany (1993) and in The Netherlands and other EU countries (1997/98). The last of these outbreaks lasted for 13 months and involved the culling of 900 000 pigs for disease control (78% in The Netherlands) along with 8.8 million for reasons of 'welfare' (90% in The Netherlands) at a total compensation cost of just under €2 billion. This outbreak greatly affected views on disease control in The Netherlands and was instrumental in altering the ways in which such diseases were to be handled in the future. Britain suffered a classical swine fever outbreak in 2000 but it was contained with the loss of a few thousand pigs. Classical swine fever outbreaks occur regularly, underlining the risks that exist. Finally, swine vesicular disease and avian influenza have appeared in Italy, African swine fever in the Iberian peninsula, and bluetongue, previously rare in Western Europe, has been reported in Spain, France and Italy.

1.11 After each of the major outbreaks of foot-and-mouth disease in Britain in the 20th century, Inquiries were established by the Government to comment upon the origins of the outbreak, how it was stamped out and what changes should be introduced.[6–9] In all cases the policy of remaining 'disease-free' and stamping out any disease has been confirmed, although Northumberland[9] did demand changes to the rules governing the importation of animal products (the UK had not yet entered the EU).

Other inquiries

1.12 A number of investigations are being undertaken after the 2001 outbreak. Interest is considerable and this is exemplified by the nearly 2 500 submissions made to the three Government-commissioned Inquiries in the UK. A report was carried out on behalf of the Economic Affairs and Planning Committee of the French Senate[10]. The Environment, Food and Rural Affairs Committee of the UK Parliament (the Select Committee for DEFRA) published a report[11] in January 2002, along with its proceedings and minutes of evidence. Issues raised by them and dealt with in this report include the following: the international surveillance mechanisms covering infectious diseases (paragraph 43c in ref. 11), livestock movement bans and standstill restrictions (43f, g), farm databases (43h), culling policies (43k) and vaccination issues (43n). The Devon County Council published their own investigation[12]. The Royal Netherlands Academy of Arts and Sciences published a short document[13] in January 2002. The EU Parliament has established their own Temporary Committee on Foot-and-Mouth Disease with a remit to produce a report by November 2002. The National Audit Office are publishing their report on 'The 2001 Outbreak of Foot and Mouth Disease' this summer.

Our Inquiry

1.13 As an academy of sciences we have focused particularly upon areas where science may be able to help in combating these diseases by minimising the spread of infection and providing new tools to aid in its elimination. In particular we concentrate on the following: the roles of modelling and epidemiology in understanding, quantifying and predicting disease spread (Chapter 6), improving livestock management practices (Chapter 5), the opportunities afforded by modern diagnostics (Chapter 7) and vaccination (Chapter 8). Throughout, however, we accept that it is the application of this knowledge which is most important and we have focused upon the practicalities, perhaps at the expense of overly complicated scientific background (Chapter 9).

1.14 As an Inquiry we took a scientific and practical approach. Committee members (Annex B) included two with consumer and food interests, a livestock farmer, four veterinarians (two in livestock practice) and eight scientists. We operated in plenary session, through subcommittees and by meetings with interested parties. Semi-formal discussions were held with a number of key players from the UK and Europe. Some 80 meetings were held and 6 visits were made to farming areas and to scientific laboratories. An initial call for views and a public call for evidence resulted in about 400 submissions (Annex C). Many of these were substantial and reflected considerable investment of effort: we are indebted to everyone for their views. The evidence along with agreed reports of the most important meetings are available on the Society's website (www.royalsoc.ac.uk/inquiry/index.html) and on the enclosed CD-ROM.

1.15 Although our Inquiry is written for the UK Government, it has been drafted in the knowledge that it is the EU that collectively sets the regulatory framework and legislation for the control of highly infectious diseases (Chapter 4). In December 2001 a conference was convened by the Belgian Presidency of the EU in Brussels to discuss the control of foot-and-mouth disease (www.cmlag.be/eng/conference.html). This was

noteworthy because some countries signalled their clear wish to move towards using emergency vaccination as a prime element in any future control strategy, and to seek the necessary regulatory changes that would allow the recovery of full trading status within six months (see Chapter 4). The German memorandum submitted to this EU conference stated:

> *Germany favours the following approach: if emergency vaccinations in the form of ring vaccinations around an FMD outbreak or in neighbouring regions densely populated with cloven-hoofed animals become necessary, all cloven animals are vaccinated with a specific vaccine and identified. After a waiting period of at least thirty days, all vaccinated herds are officially examined using a validated test to distinguish vaccinated and infected animals. If no antibodies against non-structural proteins of the FMD virus are detected in this examination, products derived from vaccinated animals become marketable without reservation.*

This has now been reflected in a change to the OIE Code—as explained in Chapter 4.

(c) The public background and the possibilities

1.16 In paragraph 1.1 we mentioned the strong view, expressed in public opinion across the EU, that in the event of a major outbreak it was not appropriate to employ culling alone to eradicate an infection. That view was articulated not only in Britain but as vociferously in Holland, where emergency vaccination as permitted by the EU was used to control the outbreak but subsequently the vaccinated animals were culled and did not enter the food chain.

1.17 Contrasts have been drawn with the procedures used to treat human infectious diseases and the public cannot understand why young livestock (which are already vaccinated against many diseases) could not be vaccinated against diseases such as foot-and-mouth disease or classical swine fever (Chapter 3). Our Inquiry attempts to explain the issues and how an international commitment to producing vaccines capable of inducing lifelong immunity to a broad range of viral strains could transform the situation (Chapter 8).

1.18 A long-term possible alternative to vaccination might be to treat infected livestock with anti-viral drugs. Although they would be expensive to develop, such drugs could one day help to contain an outbreak. Currently about two dozen are available. Twenty years ago there were only three, and it has been the HIV and hepatitis epidemics that have stimulated the discovery of new drugs. The same approaches could be applied to the development of drugs that target infectious diseases of livestock but such drugs are expensive to discover and manufacture. Although most existing drugs are targeted at specific viruses, particularly HIV, some are active against a variety of DNA and RNA viruses; Ribavarin is the first 'broad spectrum' synthetic chemical agent of this type. It is difficult to conceive of using such anti-virals against an outbreak in general livestock except for rare animals and thoroughbred horses. They might prove useful in lowering the risk of carrier animals during emergency vaccination but again it is difficult to imagine how such an approach could be cost effective. Although not appropriate now, this area of clinical medicine is moving fast and this conclusion should be periodically reviewed.

1.19 A third long-term alternative would be a genetic approach to produce disease-resistant breeds. The issues are summarised well by Bishop & Glass[14]. Usually animals do exhibit some resistance to disease and it should be possible to identify regions of the genome (quantitative trait loci) that affect susceptibility. Loci have been uncovered that confer a measure of resistance against scrapie, *Salmonella* in chickens, and nematode infections. In two viral diseases of chickens – avian leucosis and Marek's disease – disease-specific resistance genes have been identified by the Institute for Animal Health, and the development of genetic maps of the chicken offers new possibilities for the identification of further resistance genes.[15] In other large animal species the situation with genetic resistance to viral diseases is less advanced and, because pursuing the research would be very costly, it is essential to define the aims precisely. Epidemiology and modelling can generate estimates of the likely success of programmes to breed for resistance and hence the strategic directions in which research in this area should be directed. The Roslin Institute has chosen porcine reproductive and respiratory syndrome as a suitable target disease, but worldwide other important candidates must exist. So far any breeding programmes for disease resistance have usually focused upon serious endemic diseases rather than exotic diseases that occur rarely in the developed world. An exception to this might be the swine fevers, not least because classical swine fever is now endemic in many European wild boar populations.

1.20 A separate issue has been raised on several occasions: is the UK somehow peculiarly vulnerable to animal health problems? This is not something upon which science can pass a verdict but a number of changes might lead to that perception. These include food safety concerns that a generation ago did not command public attention; demand for cheaper food; changes in livestock farming methods; poor profitability, which has lowered health expenditure on animals (see Chapter 2 and also ref. 1); a reduction in the size of the state veterinary service (described in more detail by the Lessons Learned Inquiry); a decrease in farm disease surveillance (currently only some 15% of veterinary effort within the UK is spent on farm animals, much less than a generation ago); a decrease in the research base; and a perception that infectious diseases are no longer a problem. These issues are addressed in various parts of this report. In parallel, global threats are increasing, as discussed in Chapter 5. The scale and intensity of people and trade movements into the UK must be among the largest on the planet and perhaps this makes us especially prone to importing exotic diseases. The issue of policing our national frontiers is considered in Chapter 5, and DEFRA issued a draft action plan[16] on illegal imports of animal and plant products in April 2002.

1.21 Our Inquiry has attempted to reflect the changed nature of public concerns in the new century. Issues such as human health, food safety, animal welfare, and a suspicion about 'authority' all figure more strongly than in previous generations. These issues go well beyond the control of infectious disease but we would recommend the Farm Animal Welfare Council's report[17] (see also Chapter 9 below). Equally important is consumer confidence in the food itself. This led to the Government establishing the Food Standards Agency. The foot-and-mouth outbreak is perceived as having damaged confidence, partly because of the aura surrounding such a problem and partly because of difficulties in offering unambiguous advice on issues during the outbreak. One area of especial relevance to our recommendation on emergency vaccination is information from the Food Standards Agency[18], which emphasises that animals are vaccinated against 33 diseases already, that none of these are known to pose any threat to human health and that food products from vaccinated animals therefore do not constitute any known hazard.

1.22 We hope that our most useful contribution is our attempt to offer an alternative framework for handling outbreaks. This framework would combine speed of response in culling infected premises (IPs) and dangerous contacts (DCs), aided by rapid diagnostics and coupled with early implementation of emergency vaccination. The vaccinated (and non-infected) animals later enter the food chain. This is considered in Chapter 9. We recognise that the operational detail needs developing further by the Government.

(d) The issues of 'disease-free' status

1.23 A central issue in developing policy on highly infectious exotic diseases is whether a country should strive to remain 'disease-free' or accept that a disease such as foot-and-mouth disease should be allowed to become endemic. Virtually without exception, expert evidence and witnesses argued for remaining 'disease-free'. We concur with the ideal of trying to remain disease-free and point to the considerable hazards to animal health and welfare, let alone the economics, of moving away from 'disease-free'. Accordingly we conclude that Britain should not abandon its policy of being a country free of highly infectious exotic diseases, and our third main recommendation is therefore: **that the UK should continue to strive for 'disease-free' status against highly infectious diseases (such as those listed in the OIE's List A). (R1.3)**

1.24 The European experience has been instructive. Even as recently as the 1970s and 1980s, outbreaks of List A diseases such as classical swine fever and foot-and-mouth disease occurred regularly. The European aim of being 'disease-free' was approached by using two different strategies. In most countries routine vaccination largely prevented the emergence of serious outbreaks; pig farmers, for instance, were able to live with classical swine fever and stay in business. The diseases were under control *but the viruses had not been eliminated from the countries in question*. The alternative strategy, adopted in the UK, Ireland and Denmark, was based on eradicating the disease without recourse to vaccination: this eliminated both the disease and the virus from the countries in question. European Commission studies showed a clear economic advantage in adopting the second strategy, although the proviso was added that the same level of disease protection could be achieved by other measures. The implication was clear that if such other measures were found wanting, routine vaccination might have to be reintroduced. On this basis vaccination against classical swine fever and foot-and-mouth disease ceased across the EU in 1990 and 1991 respectively.

1.25 The next question concerns the nature of the 'disease-free' status. The OIE recognise two categories:

- 'Disease-free without (routine) vaccination – the highest level of status
- 'Disease-free with (routine) vaccination, which incurs some trade restrictions (explained in Chapter 4)

We have addressed the question of what status the UK should aim for, and we looked both at the European experience and the scientific, technical, and economic issues involved.

1.26 Intra-Community trade and imports from non-member countries were little affected but it had the advantage of allowing trade with all non-member countries. Many laboratories producing vaccines within Europe closed as vaccine production was greatly reduced. In addition, more effort was expected to strengthen measures against the risk of invasion from countries outside the EU where the disease remained endemic, and to eliminate outbreaks expeditiously should they occur. This last point is critical because the economic model (which incidentally did not consider other costs in animal health or to the economy more generally) rested upon relatively few animals being culled in the event of a disease outbreak. The model has been entirely upset by the classical swine fever outbreak in The Netherlands during 1997 and the foot-and-mouth outbreak in Britain during 2001.

1.27 All Member States are considered 'disease-free' unless outbreaks occur. In the event of an outbreak, stamping-out is applied, together with movement restrictions and other measures. Member States agreed to make full use of the provision for 'Regionalisation'. This means that when an outbreak or outbreaks occur the relevant Member State has to apply strict controls to a defined area, and control and eradicate the disease *within* that area, but free movement of animals/products can take place *outside* the defined area. This use of regionalisation has proved useful and the principles are accepted by the OIE. Trading partners of the EU apply control measures that are similar or very similar to those adopted by the EU. Until recently the EU policy of disease-free status without vaccination has thus served the Community well.

1.28 The steps that can be used to determine whether these conditions are being met include improvements in the following: much improved early warning systems with proper risk management (Chapter 5), improved surveillance on and off farms (Chapter 5), proper systems to minimise the risk of importing diseases (Chapter 5), stricter movement controls during normal farming, along with heightened biosecurity (Chapter 9) and improved research and development to devise new control strategies. Finally we need strengthened contingency plans for handling an outbreak that have been exposed to public scrutiny, are tested regularly and are properly resourced (Chapters 9 and 10).

1.29 We have looked at the balance of cost-effectiveness for using and not using routine vaccination. While it would be possible to vaccinate all susceptible livestock, there are a number of significant scientific and technical problems (such as the range and variablity of viral strains, like human flu, and the length of immunity conferred by present vaccines) associated with routine vaccination. These are explained in Chapter 8. Economically the cost-effectiveness balance depends on the predicted incidence of major outbreaks. If one assumes that the severity and numbers of future outbreaks continues at historic levels, (i.e. a major outbreak every 20–30 years), then there is no strong economic case in favour of routine vaccination. Assuming that those conditions continue to be met, then we judge that the balance remains against the use of routine vaccination, and in favour of the UK retaining the present status of 'disease-free without vaccination'.

1.30 But, we must stress that those assumptions may well not continue to hold. The international level of threat to the UK of infectious diseases may well increase.The country's level of defences and preparedness must be improved, as must our ability to control an outbreak. At the same time vaccine science should develop vaccines with longer effectiveness and wider viral strain coverage, and we argue for enhanced international research to that end. All these developments must therefore be kept under review as we have argued above. Our fourth main recommendation accordingly contains a major proviso. **Providing that the level of international threat does not increase; there are improved import controls; and there is a demonstrable improvement in the arrangements for handling disease outbreaks, then we recommend that the UK should not adopt a policy of routine vaccination, and should retain the internationally recognised status of 'disease-free without vaccination'. (R1.4)**

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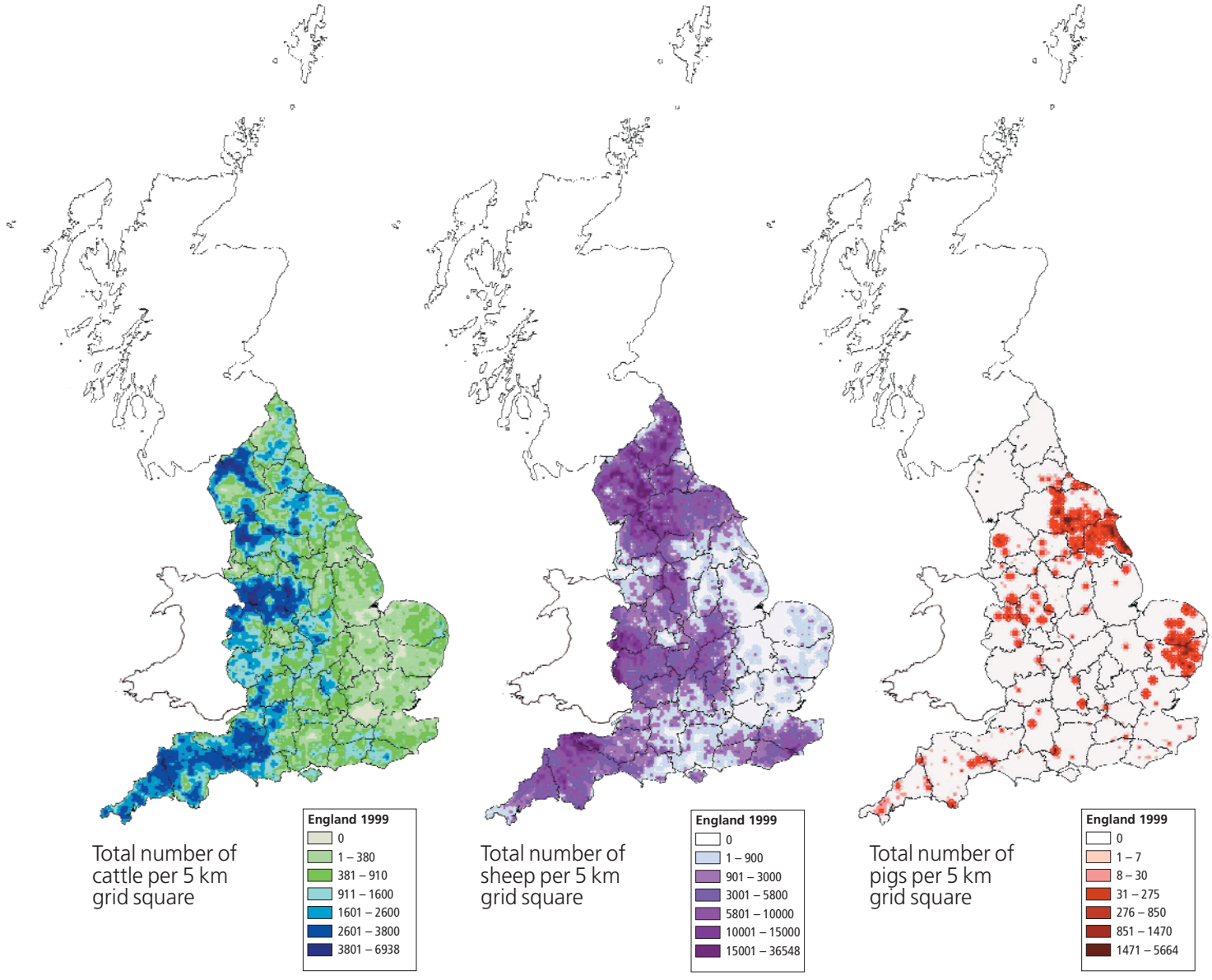
2 The modern livestock industry

(a) General situation

2.1 The UK livestock industry remains highly significant within Europe. For example, the UK is third behind France and Germany in terms of dairy cow numbers, and third behind The Netherlands and Denmark in terms of yield per cow. It has the most concentrated sheep industry in the Northern Hemisphere. Overall, livestock production has been shaped by decades of direct and indirect government support which aimed at improving production, reducing the nation's reliance upon imported food and generally keeping prices relatively low for the consumer. These policies eventually led to an oversupply of some commodities, at least within Europe as a whole, and restrictions on production began to be imposed in the 1980s. From the mid-1990s, much of the profitability has drained from the industry, leading, in the view of Curry[1], to a situation that requires many of the reforms that have been introduced into modern industry,

Figure 2.1. Maps of livestock distribution in England, showing livestock numbers per 5 km grid square. Data for Scotland and Wales do not exist in comparable format.



commerce and the enlightened parts of the 'public' (not-for-profit) sector. The following sections give a very brief overview of the main features, the statistics being drawn from the DEFRA Census of June 1999 [error in printed copy]

2.2 Although meat demand worldwide continues to increase (Chapter 5), the National Food Survey[2] for the year 2000 shows that household consumption of meat and meat products in the UK reached a peak in about 1979/80. After stabilising in the mid-1980s, it has declined slowly, with larger falls in 1990 and 1999. In 1999 individual consumption was 20% lower than in 1979 and 11% lower than in 1989. Within this overall picture, trends show an increase in poultry consumption and meat sold in meat products and ready-prepared meals. Consumption of beef and veal, despite the general downward trend, showed a 13% increase from 1999 to 2000. Household consumption of milk has declined for most of the past 25 years, although there has been some levelling off recently. Sales of semi-skimmed milk rose consistently throughout this period and have exceeded that of whole milk from 1995 onwards. Consumption of yoghurts, dairy desserts and 'other milks' (including soya and goat's milk) has risen sixfold over the past 25 years. The consumption of cream and cheese fluctuates but remains fairly constant.

2.3 Across the UK about one-half of all agricultural land – itself about 80% of the land surface – is used for cattle (including dairying) and sheep (figures 2.1 and 2.2). The distribution within the four countries is 35% in England, 64% in Scotland, 87% in Wales and 90% in Northern Ireland. Arable land takes 33% of total agricultural land; the vast majority of this lies in England. A proportion of arable crops goes into animal feed. The pig and poultry industries are highly intensive and directly take only small amounts of land (114 000 ha out of about 17 000 000 ha total agricultural land) although their food requirments also take up land. Pigs are located mainly in England (84% of the total) and largely in the east as shown in figure 2.1, which also shows for England the predominance of sheep and cattle in the west and north. Poultry are more widely dispersed, with a particularly high concentration, relative to the human population, in Northern Ireland.

Figure 2.3. Value of UK livestock production (£ millions) in 1996 and 2000.

	1996	2000	Decrease (%)
Milk	3 495	2 393	32
Beef and veal	2 546	2 000	21
Sheep meat	1 295	960	26
Pig meat	1 374	794	42
Poultry meat	1 526	1 303	15
Total	10 236	7 450	27

2.4 The value of UK livestock production (farm-gate prices) in both 1996 and 2000 is shown in figure 2.3. A comparison underlines the 27% decrease that has occurred over a period of only five years and reflects the depressed state of the industry.

2.5 Another longer-term trend has been an increase in farm size and a reduction in the number of individual farm holdings. This trend may well accelerate as farmers endeavour to improve efficiency and recover lost profitability. While just under half of farm holdings (arable, mixed and livestock) are still 20 ha or less (figure 2.4), two-thirds of agricultural land is represented by 17% of the holdings. All of these are in excess of 100 ha. In 1967, farms of this size represented 38% of all agricultural land.

Figure 2.2. Land use in the UK

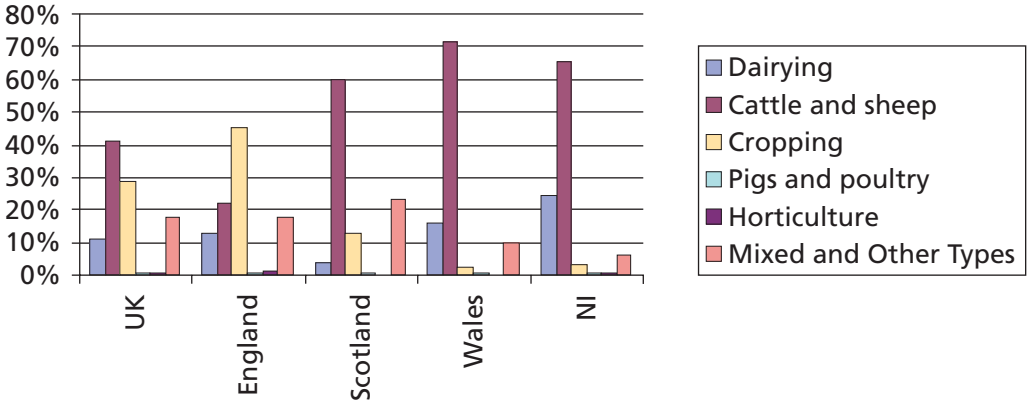


Figure 2.4. Analysis of UK livestock holdings by size and total area.

Holding size	Holdings	As % of total	Total area (ha)	Average holding size (ha)	As % of total area
<20 ha (<100 acres)	104 592	44	819 889	8	5
20–100 ha	94 360	39	4 627 861	49	27
100–300 ha	32 464	14	5 234 710	161	31
>300 ha	8 167	3	6 223 287	762	37
Total	239 583	100	16 905 750	71	100

Figure 2.5. Numbers of livestock holdings, animals and average herd or flock size in the UK.

		No. of holdings	No. of animals	Average no. of animals per holding
Cattle and calves	Total	123 663	11 350 322	92
	Dairy herd	33 892	2 438 128	72
	Beef breeding herd	69 568	1 903 004	27
Pigs	Total	12 416	7 264 356	585
	Breeding herd	8 475	796 640	94
Sheep and lambs	Total	86 293	44 011 055	510
	Breeding flock	82 131	20 237 157	246
Poultry	Total	31 099	168 354 000	5 413
	Laying flock	26 530	37 221 014	1 403
	Broilers	2 000	101 577 207	50 789

Figure 2.6. UK livestock numbers in 1967 and 2000.

		1967	2000	Change (%)
Cattle and calves	Total	12 342 000	11 339 000	–8%
	Dairy herd	3 901 000	2 353 000	–40%
	Beef herd	1 273 000	1 879 000	+48%
Pigs	Total	7 107 000	6 523 000	-8%
	Breeding herd	824 000	738 000	–10%
Sheep and lambs	Total	28 885 000	42 261 000	+46%
	Breeding flock	14 223 000	21 406 000	+34%
Poultry	Total	125 624 000	168 354 000	+34%
	Laying flock	75 556 000	29 330 000	–61%
	Broilers	37 774 000	106 534 000	+182%

2.6 The total numbers of livestock, the numbers of holdings with the various classes of livestock, and the average herd or flock sizes are shown in figure 2.5. The trends for large livestock since the 1967 foot-and-mouth outbreak are shown in figure 2.6.

(b) Cattle

2.7 Since 1967 the number of cattle has fallen by 8% to 11.3 million in 2000. The most significant decline has been the 40% decrease in the number of dairy cattle. The average dairy herd has increased from 28 to 81 cows. Annual milk yields have increased from 3 700 to 6 000 litres per cow in 2000. It is possible that the number of active dairy farms could halve in the coming years. Over the same period the beef-breeding herd has increased by nearly 50%. In 1974 there was an EU subsidy to encourage dairy farmers to cease milk production and convert to beef production, and changes began at that time (figure 2.6).

2.8 There are large concentrations of dairy farms in the lowland areas on the west side of England, in southwest Wales and in areas of Scotland where grass is plentiful and rainfall is high. The UK imports 33% of its butter and 38% of cheese but this is counterbalanced by exports of milk powder, cream and condensed milk.

2.9 There are essentially two systems of beef production in the UK. First, there are the specialist beef-breeding cattle, which are extensively grazed and whose calves are suckled on the dams for 5–7 months before weaning and then often transferred to specialist rearers or finishers. They are slaughtered between the ages of 15 and 30 months. Beef-breeding herds tend to be found on the more extensive grazing on the uplands, particularly in Wales and Scotland. The second system is to rear calves from dairy cows that have been sired by beef bulls or that are male dairy calves not required for breeding. These calves are weaned at 2–7 days old and reared by specialist calf rearers and finishers. Again, they are slaughtered between the ages of 15 and 30 months. Cattle over 30 months old are not, at the moment, slaughtered for human consumption, as a food safety measure to reduce exposure to bovine spongiform encephalopathy (BSE).

2.10 The UK is slowly losing its self-sufficiency for beef and veal. It supported 79% of the home market in 2000 compared with 89% in 1996, and 95% in 1989–91. This decrease has happened in spite of a slight decrease in consumption and the ban on exports of beef, which were about £1 billion per year before 1996. In 2002 imports may rise to their highest level as a proportion of consumption since the early 1960s.

2.11 The relative health and condition of cattle reared under conventional or organic systems is a matter of general contention[3] and is clearly in need of high quality research (addressed in Chapter 5).

(c) Sheep

2.12 The number of sheep rose as a result of the UK joining the EU, a consequent reduction in lamb imports from New Zealand and the creation of new markets for sheep meat within the EU itself. Technical developments such as improved vaccines for clostridial and other infectious diseases, effective anthelminthics and improved sheep management systems also aided productivity. The number of breeding sheep has increased from 14.2 million to 21.4 million although the total number of sheep (including lambs) recorded at the June 1999 census has been declining slowly since the early 1990s (figure 2.6).

2.13 The UK has the most concentrated sheep population in the Northern Hemisphere but flocks are still largely kept under more extensive conditions than any other farm livestock. They also receive the least amount of feeding stuffs, living mostly on grass and home-grown conserved fodder. The husbandry of sheep follows a regular cycle, with the key events occurring at the same time each year (tupping, lambing and shearing). The industry is loosely integrated; animals reared on the hills and uplands tend to move to the lowlands for breeding or for finishing for slaughter. This stratification of the sheep industry is the explanation for the major movements of sheep in the autumn and late winter and, hence, for large market structures.

2.14 After England with about 9 million breeding sheep, Wales is the next most important region with about 5 million, Scotland with 3.5 million and Northern Ireland with 1.5 million (1999 figures). Large numbers of lambs born in Wales and Scotland are moved for finishing to the lowlands, and particularly to England. The profitability of sheep production is heavily dependent on production subsidies. In 2000, subsidies accounted for 50% of total output in hill flocks, 42% in upland flocks and 27% in lowland flocks[4]. In 2001, subsidies (the ewe premium) were reduced but changes in the regime have increased payments again in 2002. The ewe premium is paid on sheep retained on farms between 4 February and 15 May.

2.15 Overall, the UK is close to 100% self-sufficient in sheep meat, with the value of imports equalling exports. The value of exports before 2001 was about £200 million a year for carcass meat and £20 million a year for live sheep, most of which (one million live animals) are intended for slaughter. Ninety-eight per cent of the sheep exports are destined for the EU.

(d) Pigs

2.16 The pig industry is not subsidised and operates in a competitive market on a world-wide basis. Breeding herd pig numbers in the UK peaked in 1998 at 780 000 breeding sows after the swine fever outbreak in The Netherlands. Since then, numbers have fallen to 610 000 in 2000, the lowest for several decades. During the same period, however, imports of pig meat rose sharply so that the UK was only 92% self-sufficient in pork and 45% in bacon in 2000,

compared with 112% and 52% respectively in 1998. Pigs are very prolific animals, producing 20 or more young pigs per sow each year, and produce their first litters before one year of age. The size of the industry changes rapidly and there have always been cycles of high profitability encouraging increased production followed by periods of poor prices and a significant number of producers going out of business. The current period of depression, since 1998, has lasted longer than previous cycles in the pig industry.

2.17 The pig industry is concentrated into certain regions, with 44% of breeding pigs in eastern England. Outdoor pig production has become more popular recently, and currently 30% of breeding pigs and 4% of pigs being fattened are kept outdoors. (By contrast, in The Netherlands most pig production is intensive and indoors, offering better biosecurity and disease control.)

2.18 Pigs are fed on concentrated feed that consists mainly of cereal and protein supplements such as soya bean and fishmeal. Feed represents a high proportion of the cost of rearing pigs and ranges from 55% to 70% depending on the market price received for pigs. Waste material from plants producing food for human consumption is widely used, either as an ingredient in purchased concentrate feed (e.g. biscuit, chocolate) or purchased direct and mixed with purchased cereals on the farm (e.g. whey, skimmed milk, cheese waste, bakery waste, ice cream).

2.19 Waste food from catering establishments such as hotels, restaurants and schools has traditionally been collected and fed to pigs as swill. Because of the real risk of transmission of foot-and-mouth disease, swine fever and swine vesicular disease viruses, all pig keepers who fed swill had to be licensed and the swill boiled for one hour before it was fed. Swill feeding accounted for about 1% of food supplied to pig production before it was finally banned in the UK in May 2001.

2.20 Mainly for disease prevention, there is a tendency for pig production to operate on separate units for different stages of production, albeit the units may or may not be on the farm of birth. Breeding units keep piglets until weaning at 3 weeks, when the piglets are moved to specialised nursery units. They stay there until 10–14 weeks of age, when they are transferred to units specialising in finishing. The rationale for this arrangement is that for most infections passive immunity from the colostrum wanes at 3–4 weeks and if the pigs are moved at this point to a disease-free environment they are likely to remain relatively free of many endemic diseases.

2.21 The majority of commercial breeding sows are high-performance hybrid animals bred by a specialist company. They are replaced regularly and it is normal practice for replacement gilts (females under 10 months) to be delivered monthly on many pig farms. This does pose a risk of importing infectious disease, but on-farm isolation and quarantine are practised and a period of integration is allowed before the newly purchased animals are bred. Every effort is normally made to match the disease status of the breeding herd with that of the receiving herd, to avoid importing new infectious diseases and to ensure that the immune status of the newly purchased animals is similar to that in the established herd.

2.22 At the end of their productive life, boars and sows are slaughtered for human consumption: the meat is used for sausages and other products, the majority being exported to the continent, as there is a limited market for sow meat in the UK. The abattoir in Essex where the first case of foot-and-mouth disease was diagnosed in 2001 slaughters most of the cull boars and sows in the UK.

2.23 In recent years Vietnamese pot-bellied pigs have become popular as household pets. These are just as susceptible to swine fever and foot-and-mouth disease as farmed pigs and pose a risk to the livestock industry if they are fed waste food containing imported meat products. Hence, the feeding of household scraps to pigs was made illegal in the 1970s when swill was identified as the main transmission mechanism for swine vesicular disease. However, it remains difficult to enforce.

(e) Poultry (excluding eggs)

2.24 Poultry production is also without subsidy and competes in a world market. The value of poultry meat production is about £1 300 million. Chicken accounts for about two-thirds of this, with turkey accounting for a large part of the remainder. The structure of the industry has changed substantially over the past 20 years with a trend towards large integrated companies. It is estimated that over half of all birds now produced are grown on farms owned by the large integrated companies.

2.25 Domestic production as a proportion of total consumption was 89% in 2000. This has decreased from 93% in 1996 and 96% in 1989–91. Imports have risen over the past decade, partly to offset the increase in consumption. Most of the imports are from the

EU although there is evidence that imports from other countries are increasing.

2.26 The poultry industry has achieved major advances in productivity in the past 50 years and is now the prime source of cheap protein. It accounts for about half of domestic meat consumption. Over the past 25 years the body weights of broilers have increased by 30% and feed conversion efficiency by 10%. As regards disease control, the industry pays great attention to health schemes, biosecurity, genetic improvement of stock and the widespread use of vaccination against various diseases.

2.27 The main types of production fall within three categories:

- *The conventional intensive indoor system* with layers in cages, and broilers and turkeys on floors at high density. To prevent the introduction of infectious diseases, priority is given to biosecurity and birds are vaccinated against several infectious diseases. This system has come under pressure to improve welfare, to diminish the transfer of zoonoses (e.g. *Salmonella*, *Campylobacter*) through eggs and meat (but see Chapter 3) and to reduce emissions that cause environmental pollution.
- *'Barn' production* is a lower-density indoor system in which the birds are reared on deep litter but with some access to the outside.
- *Free-range and/or organic production systems.* In recent years there has been a demand for eggs and meat from poultry with improved welfare and health environments. Strict rules have been adopted with regard to 'free-range', the use of organic feed, the time required for growth, stocking density and restrictions on the use of antibiotics and other medicinal products. There are some indications that these changes might increase the risk to the flock of infectious diseases, for example by being more likely to be exposed to infections in wild birds. In some countries (Sweden, Canada) outdoor systems have been banned.

(f) Horses

2.28 The non-racing equine industry has a total annual turnover of £2.8 billion. It is heterogeneous and the many different components of the horse population do not mix directly. Other than for horses in northern England and Scotland[5] there is little information available on the horse population, but the most recent estimate was 975 000.[6] Of these, about 20% are registered with breed societies, 8% for formal sporting activities, including racing, and a further 30% are thought to be used in other organised activities such as hunting, pony clubs and riding clubs. Information should improve in 2004 when recently announced legislation makes holding a passport compulsory.

2.29 There are about 10 000 semi-feral horses (for example Exmoor and New Forest ponies), 35 000 registered for Olympic disciplines and about 40 000 registered Thoroughbreds, of which about 10 000 race in any year. Thoroughbreds and those horses undertaking Olympic-type sports already have passports, and it is these animals that may travel extensively with minimal quarantine restrictions.

2.30 About 35 000 horses are disposed of annually[6] and about 11 000 of these[7] enter the human food chain in the EU.

(g) Fish farming

2.31 We are aware that fish farming is a growing area of importance and regret that were unable to give the issue adequate attention. Further study is warranted, not least because of the industry's highly intensive nature and the associated disease problems (see Chapter 3).

2.32 Whereas capture fisheries production increased only slightly during the 1990s, output from aquaculture (farmed fish, shellfish and algae) rose by more than 10% p.a. (from 13 million tonnes in 1990 to 28.3 million tonnes in 1997).[8] This outstripped increases in land-based farm animal production, which even for poultry as the fastest-growing sector averaged only 5% p.a. About 70 million salmon and trout are farmed in the UK each year, making farmed fish the second largest livestock sector after poultry. Salmon is the most economically important farmed fish in Europe, with the UK second only to Norway as the region's biggest producer, generating over 129 000 tonnes in 2000. Trout farming, although significant, is on a smaller scale and Scotland produced 5 800 tonnes in 1999. The economic value is about £300 million p.a. at farm-gate prices.

2.33 As elsewhere in the farming industry, the trend is for fewer, larger farms to develop. In 2000, 15 salmon-farming companies controlled 74% of total production. The vast majority of farmed fish are reared intensively, characterised by very large numbers of fish at high stocking density. In recent years UK salmon stocking densities have

Figure 2.7. Exports of livestock and livestock products from the UK (£ millions).

	1995			2000		
	EU	Non-EU	Total	EU	Non-EU	Total
Beef and veal	540.1	60.1	600.1	20.4	0.6	21.0
Pig meat (excl. bacon & ham, etc.)	200.3	45.3	245.7	127.7	38.4	166.0
Ham, etc.	15.1	1.2	16.3	20.2	1.1	21.4
Live pigs	29.7	5.8	35.5	12.4	0.7	13.1
Sheep meat	307.5	6.4	313.8	198.0	3.8	201.8
Live sheep	106.0	0.0	106.0	72.0	0.0	72.0
Milk/milk products	611.7	184.5	796.1	466.1	167.9	634.0
Poultry	191.6	38.2	229.9	156.6	28.8	185.4
Total	**2002.0**	**341.5**	**2343.4**	**1073.4**	**241.3**	**1314.7**

Source: Statistics (Commodities and Food) DEFRA June 2002.

decreased from 25–30 kg/m^3 (which is common in Norway) to 15–20 kg/m^3. Farmed fish usually take 18 months to reach market size (3–4 kg). Wild salmon vary considerably in growth rate but can take two to four years to reach the same weight.

(h) Exports

2.34 This section provides very brief information on the exports of livestock and livestock products before the epidemic in 2001. Figure 2.7 indicates the scale of exports and how they have been affected by the ban on beef exports resulting from BSE.

2.35 The UK also exports liquid milk and butter and it has been estimated that in 2000 approximately £52 million worth of butter and £36 million worth of liquid milk were exported.[9] Between 1997 and 2000 the UK exported about 200 000 tonnes of pork per year (valued at £151 million and £143 million respectively), most of which was to EU countries. The largest importer by volume and total value was Germany, but in terms of value for the product the most important importers were Japan, Denmark, the Irish Republic and France. Small volumes of bacon were also exported, mainly to the EU. According to the MLU[9], about one-quarter of the national pig production in 2000 was exported, making this sector vulnerable to changes in exports. The value of pig exports is almost equal to that of imports but the UK imports pork cuts such as loin, and exports pork bellies and shoulder.

2.36 Between 1997 and 2000 the UK exported about 100 000 tonnes of sheep meat per year, of which nearly all went to the EU countries. The total value of sheep meat exports from the UK in 1999 and 2000 was £202 million each year. The EU countries are the most significant importers of this product and, within the EU, France imports approximately 70% of the meat exported from the UK to the EU. The NFU[9] estimated that sheep exports were about one-third of national production, making this sector vulnerable to changes in exports. The NFU also states that the value of imports of sheep product is equal to that of the exports. However, the UK imports heavy lamb cuts and exports light lamb carcasses, which are not equivalent products.

2.37 Live sheep intended for slaughter are also exported: 1 130 000 in 1999 and 764 000 in 2000.[10] The values of exports of livestock and livestock products for the years before 1996 and for 2000 are summarised in figure 2.7. The export of beef was banned in 1996 because of concerns about BSE and at the same time the consumption of home-produced beef was confined to animals under 30 months old.

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3 Infectious diseases of livestock

(a) List A and List B diseases and definitions

3.1 This chapter describes the major infectious diseases classified by the Office International des Epizooties (OIE) as being of greatest economic significance, and gives a short overview of the other main diseases affecting each of the livestock sectors. In the specific case of foot-and-mouth disease (FMD) we have given much fuller references to the statements made.

3.2 The OIE classify the 95 currently most infectious diseases into List A (15 diseases) and List B (80). Our Inquiry focused upon a subset of the List A diseases. While recognising the major significance of the transmissible spongiform encephalopathies (TSEs) to the livestock industry in the UK, we have not covered them in this report because substantial independent scientific advisory machinery exists in this area.

3.3 List A contains those transmissible diseases '*that have the potential for very serious and rapid spread, irrespective of national borders, that are of serious socio-economic or public health consequence and that are of major importance in the trade of animals and animal products*'. This list is headed by FMD, reflecting just how infectious the virus is. The situation with regard to the incidence of List A diseases in the UK is shown in figure 3.1.

3.4 List B contains 80 diseases '*that are considered to be of socio-economic and/or public health importance within countries and that are significant in the international trade of animals and animal products*'. Most of these affect farm livestock, poultry and horses. Many do not occur in the UK but some are endemic and are therefore subject to continuing control at farm level by various means, including vaccination and/or biosecurity means. Notifiable diseases are those where suspicion of disease must be reported to DEFRA and where legislation exists with the aim of controlling or eradicating the infection. The notifiable diseases of particular importance to farm livestock in the UK are given in figure 3.2. Views were expressed that at least three of the non-notifiable List B diseases might actually be of greater significance: bovine viral diarrhoea, Johne's disease (*Mycobacterium avium paratuberculosis*) and infectious bronchitis. The other List B diseases affect fish, rabbits, molluscs, crustaceans and bees.

3.5 As in human health, dangerous infectious diseases emerge anew at regular intervals. This comes about because the disease either moves from one species to another, emerges from a part of the world where it has lain relatively safely within wild animals, or appears in a new guise after changes in livestock husbandry practices. In the past two decades at least nine new animal

Figure 3.1. The 15 List A diseases and their incidences in the UK.

OIE List A disease	Last reported in UK	Species at risk
Foot-and-mouth disease (FMD)	2001	All cloven-hoofed livestock
Rinderpest	1877	Cattle
Contagious bovine pleuropneumonia (CBPP)	1898	Cattle
Vesicular stomatitis	Never	Horses, cattle, pigs, wildlife species
Lumpy skin disease	Never	Cattle
Rift Valley fever	Never	Cattle
Peste des petits ruminants	Never	Sheep, goats
Bluetongue	Never	Sheep, goats, wild ruminants
Sheep and goat pox	Never	Sheep, goats
Classical swine fever (CSF)	2000	Pigs
African swine fever (ASF)	Never	Pigs
Swine vesicular disease (SVD)	1982	Pigs
Newcastle disease (ND)	1997	Poultry, pigeons, wild birds
Avian influenza (fowl plague)	1992	Poultry, wild birds
African horse sickness	Never	Horses

Figure 3.2. Other notifiable diseases in the UK (excluding those of fish).

Notifiable disease	Last reported in Great Britain	Species at risk
Anthrax	1997	Bovine, other mammals
Aujesky's disease	1989*	Pigs, other mammals
Bovine spongiform encephalopathy (BSE)	2002	Cattle, sheep, humans
Brucella abortus	1993*	Cattle, humans
Brucella melitensis	1956	Sheep, goats
Brucella ovis	Never	Sheep, goats
Contagious agalactia	Never	Sheep, goats
Contagious equine metritis (CEM)	1997	Horses
Dourine	Never	Horses
Enzootic bovine leucosis (EBL)	1996	Cattle
Epizootic haemorrhagic virus disease	Never	Deer
Epizootic lymphangitis	1906	Horses
Equine viral arteritis	1998	Horses
Equine viral encephalomyelitis	Never	Horses
Equine infectious anaemia	1976	Horses
Glanders and farcy	1928	Horses
Paramyxovirus of pigeons	2001	Pigeons, wild birds, poultry
Rabies	1970	Dogs, most mammals, humans
Scrapie	2002	Sheep, goats
Teschen disease	Never	Pigs
Tuberculosis (bovine TB)	2002	Cattle, deer, badgers, wildlife, humans
Warble fly	1990	Cattle, deer, horses

*Present in Northern Ireland.

diseases have emerged, including bovine spongiform encephalopathy (BSE), feline AIDS, bovine immunodeficiency virus, seal 'distemper' (morbillivirus), equine arteritis, Hendra virus and, very seriously for the pig industry, post-weaning multi-systemic wasting syndrome (PMWS), porcine dermatitis and nephropathy syndrome (PDNS), and caseous lymphadenitis.

3.6 Our Inquiry took advice as to how we should limit the study to the major causes of concern and that led us to concentrate on seven List A diseases: FMD, classical swine fever (CSF), African swine fever (ASF), avian influenza (AI; also a zoonosis), Newcastle disease (ND), bluetongue (BT) and African horse sickness (AHS) (both transmitted by insect vectors). It is hardly surprising that FMD dominated our proceedings virtually to the exclusion of even the other six diseases. We concluded that the Government should commission a small group to look in depth at each of the other diseases, as well as emerging threats from new diseases, and this information should guide the development of the over-arching national strategy for animal disease research proposed in Chapter 10 and the updating of contingency plans in Chapter 9.

(i) Foot-and-mouth disease (FMD)

The disease and its effects

3.7 FMD is probably the most contagious virus known in mammals and affects more than 33 species. Cattle, sheep, goats, pigs and buffalo are the most important susceptible species among farmed animals. The disease is characterised by a short fever, loss of appetite, dullness, vesicular lesions and lameness. The lesions of the mouth, tongue and feet are especially severe in cattle, as are foot lesions and lameness in pigs. In smaller ruminants, such as sheep or goats, the disease often takes a milder form in adult animals. In young animals, especially lambs and piglets, the virus can cause an acute myocarditis resulting in sudden death. Survivors are left in a weakened state and can succumb at a later stage.[1] During the outbreak of 2001 lamb death was sometimes the presenting sign that FMD virus (FMDV) was present on a farm.

3.8 All the professionals associated with the livestock industry that we consulted believed that a major outbreak of FMD would be disastrous for animal productivity within the highly developed livestock production systems of Europe,

Australasia and North America. The evidence to support this opinion is necessarily limited because FMD has always been eradicated in these areas before it has reached an endemic state. As a result, quantitative information is sparse but overall direct losses in livestock productivity have been estimated at 25% due to reduced growth rate and decreased milk yield. It must never be forgotten that endemic FMD was so disruptive of farming in continental Europe that a 30-year campaign was mounted against it, bringing the disease to the point of ceasing vaccination in 1990/91.

3.9 Data from over a century ago in Britain suggested mortality rates in adult animals within infected herds at 0.8% in cattle, 1.2% in sheep and 6.8% in pigs.[2] In other parts of the world mortality in young animals has on occasions attained 90% in lambs, 50% in piglets and 25% in calves. Serious effects upon milk yields are well established in dairy cows, and there are a number of secondary consequences including mastitis and endometritis, as well as chronic lameness. The analogy drawn by some observers between FMDV and 'the effects of the common cold' is incorrect and ignores the welfare aspects of pain in the acute disease state, the mortality in young animals, and the long-term deleterious effects on the animal (Brooksby 1982, cited in ref. 3).

3.10 More information is available where FMD is still endemic. Ellis & Putt[4] estimated the effects in those areas of Kenya where commercial cattle rearing was important. Mortality rates varied from 2% in unimproved Zebu cows to 5% in improved dairy cattle. Abortions occurred at a level of 8%, and there were delays in conception of some 8 weeks. If a lactating cow became infected there was a 50% decrease in milk yield that was not recovered during that lactation. Growth of young animals was badly affected, delays of 6 months on reaching maturity not being uncommon. In oral evidence to our Inquiry, Dr Peter Roeder from the FAO gave further examples, quoting effects in India and Bangladesh, where FMD is endemic. The capacity of buffalo herds to work during rice planting is halved, and milk yields decrease by 80%. When endemic, infections often occur serially with some herds falling ill three times a year. The livelihoods of families that depend on animals for food and power can be severely affected.

3.11 There is much information available about FMD. Summaries are available in textbooks on exotic animal diseases and there are general reviews[5–10], subject-specific reviews[11–20], web sites (e.g. AVIS (http://www.iah.bbsrc.ac.uk/AVIS/), OIE (http://www.oie.int/eng/en_index.htm) and DEFRA (http://www.defra.gov.uk/)) and a CD produced by the Wildlife International Network[21]. The main OIE/FAO Reference Laboratory for FMD is located within IAH, Pirbright, and it maintains a database with over 17 000 scientific publications on the disease. However, as with all studies on long-established infectious diseases, the available methodology has developed and improved over time. Research priorities have also changed with the result that funding for FMD has not allowed the subject to advance as rapidly as other areas. The extreme communicability of FMD dictates that research must be performed in high-security laboratories, and for certain studies must involve farm animals. These practicalities, together with the wide host range, limit the number of experiments that can be done and the number of serotypes and strains that can be studied. Unsurprisingly, the information accrued over the years has been obtained through many unrelated studies conducted over at least the past 50 years with different strains of virus, widely different laboratory methodology and assay systems of variable sensitivity.

3.12 No summaries were available during the 2001 outbreak in Britain that satisfied the needs of those responsible for important aspects of controlling the epidemic, such as undertaking risk analysis, although access to the primary literature itself was always available through the index at Pirbright. Hence several literature surveys were undertaken to collate relevant information from published papers, and we commissioned a rapid one ourselves[22]. We conclude that there is a lack of consistent information arising from studies with standard procedures or 'protocols'. Furthermore, there was insufficient work linking small-scale experimental work to field studies during FMD outbreaks. There is an urgent need for a comprehensive review of the available information and for the development of a consistent and coherent database of the basic information that would be required during an outbreak. Inevitably, this will require additional research to complete the study, not least to ensure that differences between FMD strains currently active across the globe are properly characterised and that standard procedures are adopted to define new strains when they are identified. With regard to other infective agents in the OIE's List A, it seems that the situation with consistent biological information is generally worse.

3.13 Despite this relative lack of consistent quantitative information, especially with regard to differences between the various strains, their

Figure 3.3. Maximum virus excretion/secretion routes in cattle.

Secretion/excretion route	Proportion of maximum daily output
Vesicle fluid/epithelium	700 000
Saliva	100 000–400 000
Milk	20 000
Urine	5 000
Faeces	13 000–40 000 (very wide variation)*
Breath	1

*The variation for faeces reflects the method of collection, i.e. direct from the rectum or from the contaminated floor of the pen.

effects upon different species and breeds of animals, and the doses of virus challenge, it is possible to give a general outline of the virus and its characteristics.

Viral infectivity

3.14 FMDV is a single-stranded RNA virus and a member of the family Picornaviridae, genus *Aphthovirus*. Like other viruses, it multiplies by using the cellular machinery of the organisms it infects. As copies of the original infecting FMDV are made in enormous numbers, they are excreted by a variety of routes including the disease lesions, saliva, exhaled air, milk, urine, faeces and semen. FMDV consists of seven serotypes. Each serotype can contain a number of different strains. The serotypes are clinically indistinguishable but antigenically and serologically distinct. The UK outbreak virus in 2001 was identified as a serotype O, strain pan-Asia.[23]

3.15 In theory, only one infectious particle can initiate infection in a susceptible animal, although in reality larger doses are required, depending on the route of infection. Whether or not infection becomes established probably depends to an extent on the status of the animal's immune system. Between 10 and 20 infectious particles can cause infection by the respiratory route in sheep and cattle.[24,25] Pigs are more resistant to infection by aerosol (Denny & Donaldson, unpublished observations, cited in ref. 26).[27,28] Cattle are relatively sensitive to lower doses of virus and this might well be a function of respiratory tidal volume. For example, at a virus concentration of one particle per litre of air, a cow would inhale 10 infectious doses in 2 minutes, whereas sheep and pigs would take 30 minutes.[7,29] In the 1967–68 epidemic it was found that the attack rate for dairy herds increased with herd size: only 1% of herds with less than 10 cows were infected, in contrast with 29% for herds with over 80 cows.[30] In the 2001 outbreak a similar pattern was found, with smaller farms being substantially less susceptible than larger ones.[31] The nature of pig diets and their ability to become infected through food makes them especially vulnerable.

3.16 The scale of infection is attributed to the large amounts of virus excreted by the infected animals in the pre-clinical period.[32] The incubation period of FMD is generally 2–14 days,[33] with the incubation period being inversely proportional to the dose.[25,34] This variability of incubation period complicates consideration of infectiveness before clinical signs appear but the general picture in cattle shows that saliva can contain virus up to 10 days before lesions appear; milk and semen 4 days before; and exhaled breath, faeces and urine 1–2 days before (summarised by Sanson[7]). A more recent study[35], under conditions in which the incubation period was much shorter, shows the development of virus levels in the blood and breath. The amount of virus excreted by different routes varies widely, as shown in figure 3.3, which brings together data from a number of studies on cattle cited in two reviews[6,11]. However, a consideration of the papers cited indicates significant discrepancies in the figures, probably due to differences in the viral strains studied and in the sensitivity of the systems of detection employed. It is clearly important to obtain comprehensive and consistent information for each main animal species on the excretion of and susceptibility to the main strains of FMDV.

3.17 Species differ in how much virus they excrete. At the height of infection, pigs can excrete up to 400 million infectious particles per day, whereas cows and sheep excrete up to about a million infectious particles per day.[5] Virus production can be prolonged in the throat region and can continue intermittently for six months or more.[14,15,20,36–38] Pigs do not appear to exhibit a carrier state. (The issue of the carrier state is considered in detail in Chapter 8.)

Survival

3.18 Virus particles retain their capacity to infect for much longer periods when the temperature is low[39] and humidity is high[32]. Infectivity is not readily destroyed by ultraviolet radiation but is particularly vulnerable to acid conditions below pH 6 and alkaline conditions above pH 10. Whereas infectivity might be stable for weeks under neutral conditions (pH 7), it survives for only 2 minutes in a slightly acidic (pH 6) environment[40].

*Figure 3.4. Most likely method of spread of FMD in each geographic area (*n = *1849).*

	Most likely method of spread										
Group*	Airborne	Milk Tanker	Infected animals	Other fomite	Person	Vehicle	Suspect swill	Local†	Under investigation	Total	Local percentage
Anglesey			1					12		13	92%
Durham	3		5	1	4	1		82	7	103	80%
Cumbria	2	6	38	3	23	9		839	45	964	87%
Devon	1	1	8	1	9	2		146	19	184	79%
Essex and Kent			4		1	1		5	5	16	31%
Hereford			11	3	12			118	24	168	70%
East Lancashire	2	2	1		1	3		31	5	45	69%
North Yorkshire	3	2		1	1	4		66	21	98	67%
Northumberland	4		1		5		1	53	6	70	76%
Staffordshire			7		4	4		53	17	85	62%
Wales	3		2	1	8	1		35	14	64	55%
Yorkshire and Lancshire			4					11	4	19	58%
Sporadic cases			5	1	2	3		3	5	19	16%
Grand total	18	11	87	11	67	28	1	1454	172	1849	79%
Total percentage	1%	1%	5%	1%	4%	2%	0%	79%	9%	100%	

From information available on 1 August 2001

*Names of groups represent the area where many cases in the group occurred; not all cases in a group were necessarily located in the named county.

†'Local': new Infected Premises (IP) within 3 km of a previously confirmed IP and more than one possible conveyor indentified.

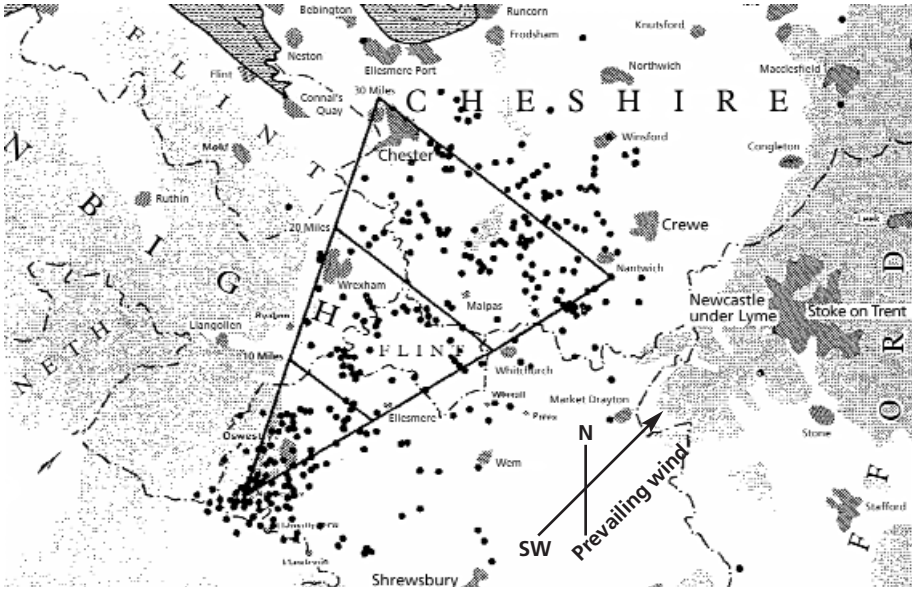
3.19 In milk and its products the virus is relatively resistant to heat (reviewed by Donaldson[18]). Pasteurisation at 72 °C does not fully inactivate all the virus[41] and in the cream component of milk it can survive for 15 seconds at 93 °C, although 3 seconds at 'UHT' temperatures (148 °C) will inactivate the virus[42]. Walker et al[43] found that heating naturally infected milk at 100 °C for more than 20 minutes inactivated the virus.

3.20 Survival times of virus in other animal products vary, and are important for international trade considerations. Of major concern is survival in muscle and meat products. Beef muscle becomes acidic as it matures at temperatures above 4 °C and at such temperatures the virus is inactivated within 24–72 hours. However, the virus can survive for weeks or months in refrigerated internal organs, bone marrow and residual blood. For example, it has been found to survive for over 200 days in bone marrow at 4 °C (reviewed by Arambulo[44]) and for up to 400 days at 4 °C on meat packaging materials contaminated with blood, serum, lymphoid tissue and fat.[45] Smoking and other non-thermal preservation methods do not seem to inactivate the virus rapidly.

3.21 On bovine hides, the virus survived for up to 352 days at 4 °C,[46] and for between 11 and 72 days on wool, depending on temperature and the virus strain.[15] Survival times on other materials vary from 11–14 weeks on contaminated footwear to more than 200 days on hay (Kindyakov 1940, cited in ref. 47). The virus can survive for 2–5 days on pasture during the summer (Kindyakov 1960, cited in ref. 48; Voinov 1956, cited in ref. 49) or for up to 30 days at 1.3 °C (Kindyakov 1960, cited in ref. 48; Shilnikov 1959, cited in ref. 49). Survival is longer when the virus is located beneath the soil surface and under leaves than on the surface (Podrezova 1969, cited in ref. 47). But South American workers only managed in 2 out of 11 experiments to infect susceptible animals on pastures artificially infected 22–96 hours previously (Campion & Gatto 1961, cited in ref. 49). The variability found between studies is likely to depend greatly on factors such as the strain of virus, level of contamination, temperature, humidity and pH.

3.22 The inactivation of FMDV by physico-chemical methods is typically biphasic: there is an initial sharp decrease, followed by a slow, prolonged decline. The virus population in the second phase

Figure 3.5. Airborne spread of FMD virus during the 1967–68 epidemic.



is often very resistant, especially in the presence of organic matter but whether it is infective remains to be established.

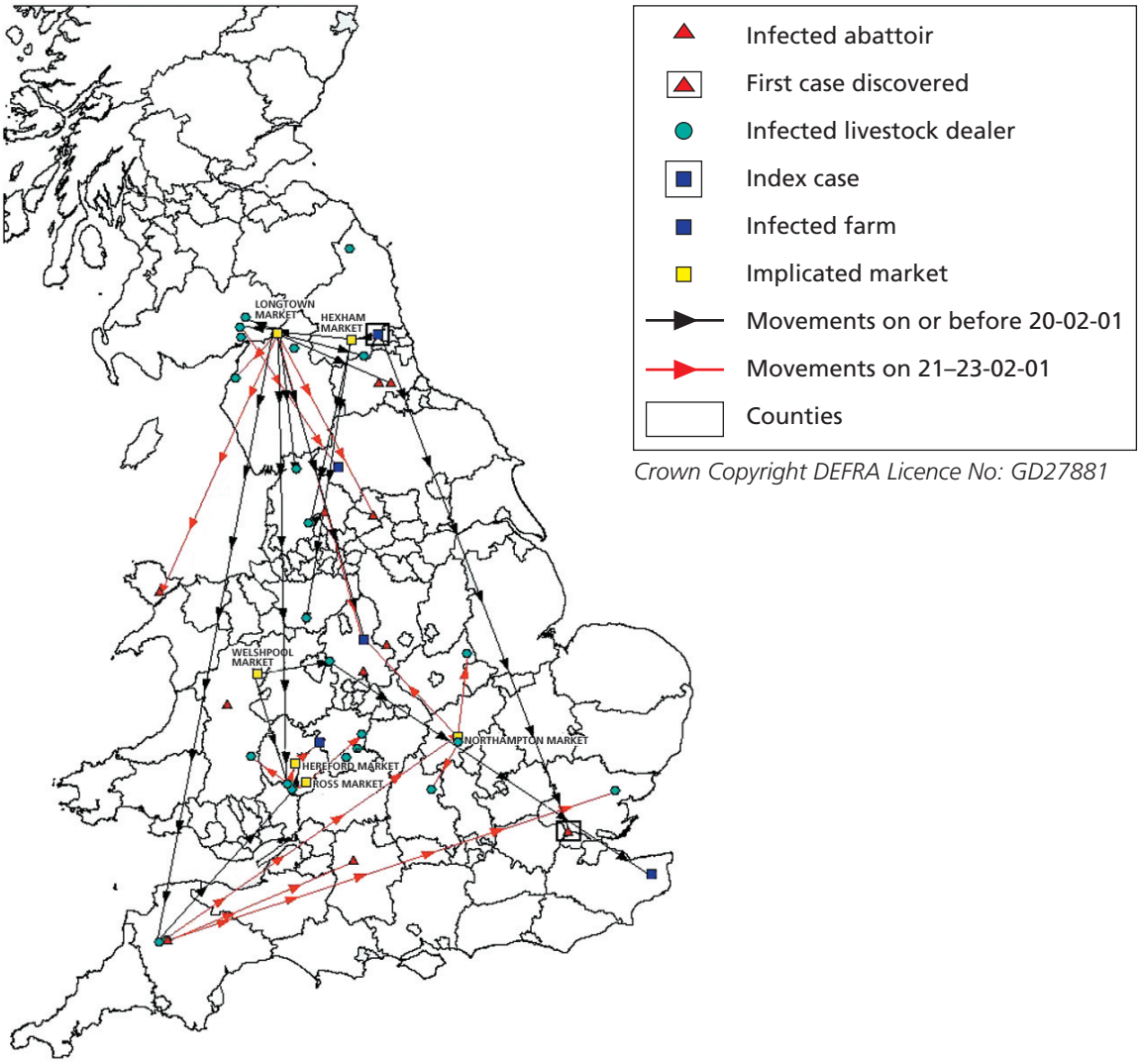
Modes of transmission

3.23 Given their critical importance to both understanding and controlling FMD, and with so much at stake in the event of another outbreak, we were disappointed that quantitative studies of the different routes of transmission were so difficult to find. Such information is needed both for improved biosecurity and for developments of disease models and has implications for risk analysis associated with the holding of rural sports events and general access to the countryside beyond restricted areas, all matters of economic significance and great public concern. Field studies are, of course, impossible to conduct in countries with disease-free status, and we recognise the difficulty of producing reliable quantitative data in this area. The information given below is therefore inevitably incomplete. Earlier inquiries[50,51] have devoted substantial parts of their reports to discussing the modes of transmission. Yet we remain in the situation shown in figure 3.4. A plan for applied research is needed and we recommend accordingly.

3.24 We do nevertheless present below what is known about the various mechanisms for the transmission of the virus:

- *Airborne* FMDV can be exhaled as an aerosol, or aerosols can be produced by splashing of virus-contaminated secretions and excretions such as urine, or by the washing of milk parlours or livestock sheds. The pathogen can then travel a considerable distance, several kilometres, in the air on a gently moving wind with low turbulence.[26,52–54] Because turbulence is generally less marked over water than over land, airborne spreading up to 250 km over water can occur (Murphy et al 1999, cited in ref. 10), leading to suggestions that the 1981 outbreak of FMD on the Channel Islands and the Isle of Wight in 1981 could have been caused by windborne virus from France.[55] The fact that the viruses involved in the contemporaneous French and British outbreaks were virtually identical reinforced this possibility. Airborne spread was also implicated in the 1967 epidemic as shown in figure 3.5, which is taken from the Northumberland report[51]. However, in 2001 and in the 1951/52 outbreak[50] airborne spread seems not to have been a common cause of secondary outbreaks, with only 1% of cases being attributed to this route (see figure 3.4).[26,56] Anecdotal evidence is always rife about FMD transmission and in Cumbria spread along valley floors in the direction of the prevailing wind has led to comments that windborne spread was more significant than the published figures suggest. Windborne spread might also have played an important role in the spread of the disease from pigs, very early in the 2001 epidemic.
- *Direct animal-to-animal contact at the farm boundary.* This need not necessarily be through nose-to-nose contact because many pathogens can become airborne from the respiratory tract of infected animals as aerosol and then travel some distance in suitable

Figure 3.6. Movement of FMD-infected animals before 23 February 2001, and locations of implicated markets, abattoirs and dealers.



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climatic conditions. Similarly, infection can be transmitted passively by wildlife vectors moving between separate groups of animals and watercourses. Nevertheless, proximity of animals belonging to different herds or flocks or to different holdings must be a major risk factor and underlies many of the decisions to cull neighbouring farms in an epidemic.

- *Livestock animal movement.* This was amply demonstrated in 2001 as being the significant method of spreading disease in long-distance jumps. Early- to mid-February is a time of significant seasonal movement of sheep, and figure 3.6 shows the scale of the distribution of the virus before the first case was diagnosed on 20 February 2001 (black lines) and the further distribution of virus between then and 23 February (red lines), when a movement ban was instituted throughout the UK. Animals in the later stages of incubation or in the acute pre-clinical stage can infect naïve animals directly, or indirectly through the contamination of instruments, implements, pens, roads, lairage facilities and transport vehicles. At livestock sales it is usual for potential purchasers, as well as auction staff, to handle the animals—often quite closely, to inspect mouths, check ear tags, and so on—and cross-contamination is likely to be high. It is also highly likely, early in the 2001 FMD outbreak, that some of the sheep would have been incubating the disease and would have been highly infectious. However, given the difficulties in diagnosing FMD in sheep, and the relative lack of awareness at that time, it is not surprising that these were missed. It is the enormous dangers inherent in moving animals that leads to proposals for standstill periods becoming obligatory at all times
- *Humans.* With the decreasing numbers of permanent staff employed on farms, it is

inevitable that there is more sharing of stockmen, equipment and contractors. Many farms employ a 'relief' milkman, stockman or tractorman who is not permanently employed on that farm and who might have several part-time farm jobs. Similarly, families might run two or three farms together, with regular movements of people between them. In many areas of the country farms are not single 'ring-fenced' units because, over the years, areas of land might have been bought and sold, resulting in a patchwork of intermingled holdings (frequently referred to as fragmentation). Professional assistance on farms is required in which direct contact with stock is unavoidable, including veterinary visits and artificial insemination technician visits. Other potential vectors are animal dealers, hoof trimmers, sheep shearers, bulk milk collectors, feed deliverers, milking parlour engineers, dairy hygiene inspectors, DEFRA and trading standards officials, and nutrition advisors. A study in Holland[57] looked at risk factors for the introduction of bovine herpes virus 1 to dairy farms previously free of the virus, and showed that farms should prevent cattle from mingling with other cattle and that professional visitors to the farm should always wear protective clothing on the farm. Veterinarians involved with large animal practice are potentially a high-risk group because they are likely to deal frequently with sick individuals, often very closely. There is a theoretical risk that tourists on country roads and footpaths close to infected areas can spread disease, particularly if their route brings them into intimate contact with animals, but the actual risks from this source are poorly understood and require proper investigation.

- *Vehicles.* It is unlikely that routine cleansing and disinfection of livestock vehicles are adequate to destroy some infectious pathogens (the virus responsible for swine vesicular disease (SVD) is particularly resistant to disinfectants), and there is a strong suspicion that at the start of the 2001 epidemic transport vehicles might have been a factor in transmitting the disease. A range of other vehicles are also necessary for normal farm operation. Milk is collected daily or every second day for which the milk tanker must come close to the farm dairy, which might be close to stock. A hose is then run from the tanker to the bulk milk tank. During an outbreak there is potential for cross-contamination via this hose, as well as the possibility of spillage of contaminated milk and the transport of pathogens on the tanker itself. During the process of developing a vacuum within the bulk tanker, there is a release of air through a valve, which has the potential of causing an aerosol; viral filters can be fitted to prevent this, but these are used routinely only when an outbreak has been reported. A large part of dairy cow rations is purchased feed, with most farms being able to store enough to last for 2–4 weeks; so again feed lorries are essential for dairy cattle but less so for beef and sheep units. At certain times of the year there are also other deliveries, including fertiliser and bedding, and with less on-farm labour, many farmers now use external contractors to plough, sow, harvest, and spread slurry and manure. All these machines potentially can transport disease.
- *Wild animals as susceptible species.* Many wild animals live and feed around farms and some are naturally susceptible to FMD. Others may act as mechanical vectors. Hedgehogs are particularly susceptible to FMD. McLauchlan & Henderson[58] reported on the occurrence of a natural infection in hedgehogs in connection with outbreaks on farms near a Norfolk village during 1946. From July to September of that year, 56 hedgehogs were trapped on infected farms. Nine had lesions, and five of these animals yielded virus of the same type, which was found concurrently in cattle. It seemed probable that hedgehogs were responsible for some secondary outbreaks.[59] Deer in the UK are known to be susceptible to FMDV,[60,61] but there is apparently no evidence to implicate them as carriers during 2001. Home ranges for deer are usually small, but the considerable distances travelled by red deer stags before and after the rut might mean that they were more likely to transmit the disease after an outbreak in the autumn. About 200 blood samples from wild boar shot in The Netherlands during the hunting season 2001/02 were examined for antibodies against the virus but were all found to be negative.[62] Other species, rats and most notably birds, have been considered as vectors for the disease, but although some have been shown to be susceptible after inoculation with virus there are no reports of natural infection in these species and any role would have to be as mechanical carriers of infection (reviewed by Capel-Edwards[59]). The role, if any, of such animals in the epidemiology of FMD in Britain is generally considered to be minor.
- *Wild animals as mechanical vectors.* The species that might act as mechanical

vectors—such as badgers, foxes, feral cats, sparrows, starlings, pigeons and geese—can routinely be seen scavenging in animal feed, both indoors and outdoors; and carrion feeders such as crows, ravens and even birds of prey will feed on carcasses. Birds can carry virus on their feathers or in their gastro-intestinal tract for short periods; it has been shown that starling droppings remain infective for 26 hours, and their feathering remains infective for up to 91 hours.[51] These birds routinely feed on livestock rations and invade sheds where animals are kept. It has also been postulated that the disturbance caused by the culling and subsequent cleaning and disinfection of infected premises will drive these wild animals away. They will then seek food and shelter elsewhere – potentially a nearby farm – and this could lead to the spread of disease.

3.25 Examination of figure 3.4 (taken, with permission, from ref. 56) indicates that only 14% of 1849 disease outbreaks in 2001 could be attributed with any degree of certainty to a specific transmission mechanism; 79% were classified as 'local spread', which was defined as spread between infected premises within 3 km of each other, where more than one possible conveyor of infection was identified. The exact mechanisms of local spread are unknown but Gibbens et al[56] surmise: *'it is believed that the majority will be from either local aerosol spread between animals or contamination in the area near an infected premise, resulting in infected material on roads or other common facilities'*. During the 1967–68 outbreak in the UK, 91% of cases were 'local spread'.[63]

3.26 Overall, the commonest transmission may well be probably by close contact when an infected animal inhales the aerosols exhaled by an infected animal. Animal movements are therefore crucial in spreading the disease. People have been shown to carry virus in their nose for up to 2 days after examining infected animals and to be capable of subsequently transmitting the disease to susceptible animals.[64,65] We have not found good experimental studies that demonstrate viral transmission by vehicles but because the virus survives on footwear and other inanimate objects, the possibility exists that movements of people and vehicles, such as equipment, implements, instruments, tractors, feed lorries and milk tankers can spread the virus.[66] Greater fragmentation of farms seemed to have increased the transmission of the virus in the 2001 outbreak, possibly because of the higher frequency of personnel and vehicle movement between land parcels.[31] The risk of infection spreading from properly constructed pyres appears low. Concentrations of viral particles away from the immediate source were estimated as being between one hundredth and one ten-thousandth times lower than the minimal infectious dose estimated for airborne infection of cattle.[68]

Phylogenetic tracing of the source of an outbreak

3.27 A further area of concern relates to our ability to tie down unequivocally the precise source of the virus that has been imported and begins an outbreak. Again this concerned Gowers[50] and Northumberland[51]. Sometimes legal issues intrude, but modern molecular tracing can provide a much superior way forward in the future and we recommend that DEFRA should develop the science and technology required for this.

3.28 On the basis of data for the most variable region of the virus, the virus strain most closely related to the virus responsible for the 2001 FMD outbreak in the UK was first isolated during an outbreak in South Africa that began in September 2000. This strain differs by only a single nucleotide difference in region VP1 of the genotype, while the next most closely related strain from Japan (JAP/2000) differs by an additional three nucleotides. VP1 is the most variable region of the virus because it is under strong immune selection. FMDV sequences evolve at an average rate of approximately 1% per year. The error rate during virus replication is very high, such that in theory every replicated genome can have at least one mutation. Although many such mutants will be non-viable, synonymous mutations (i.e. those that do not cause a change in the viral protein sequence) will usually be passed on. With the advent of efficient long-range PCR (polymerase chain reaction) and high-throughput sequencing capabilities, there is little justification for limiting phylogenetic analyses to the VP1 region of a relatively small number of isolates. Analysis of the entire genomes of multiple virus isolates from the relevant period could increase the confidence in the conclusion that the origin of the virus was South Africa by increasing the temporal resolution of the analysis and possibly narrowing the evolutionary time window between isolates from the two countries. However, there are only so many isolates available for testing, and there is a limit to how sensitive this type of analysis can be. Phylogenetic analysis is probabilistic rather than deterministic, so it is still not possible to use it to prove beyond doubt that the virus came directly from South Africa rather than through an intermediate or from a common upstream location.[23]

(ii) Classical swine fever (CSF)

3.29 CSF is a viral haemorrhagic disease affecting pigs and wild boar that causes severe production losses and can occur in hyperacute, acute or chronic forms. The acute form of the disease is typical of that seen when a virulent strain of the virus is introduced into a susceptible population. The associated illness has a sudden onset with high fever, anorexia, dullness and huddling, diarrhoea and an unsteady gait, with spread to all age groups. After several days there may be a purple discoloration of the skin of the ears, abdomen and legs. Death is usual within a week of the onset of signs and the mortality rate can approach 90%. Infection of pig foetuses *in utero* with a virus of low to moderate virulence may result in nervous signs, shaking, prenatal or early postnatal death, the birth of diseased piglets or the birth of apparently healthy but virus-excreting piglets.

3.30 The disease was eradicated from the UK in the 1960s after a period of mass routine vaccination that reduced the prevalence to a level at which 'stamping out' finally eliminated the infection. Since then the UK has been maintained 'disease-free without vaccination' and this remains the preferred future by the pig industry, which overall is much more integrated and intensive than other large livestock. There have been a small number of outbreaks attributed to the feeding of untreated waste food. The CSF outbreak in 2000 was more serious, being the first in the UK for 14 years and causing disease on 16 farms. It proved very difficult to stamp out, not least because the index case was in a herd of outdoor sows and the disease might have been present for up to 2 months.

3.31 CSF is caused by a virus of the Flaviviridae family, which can survive in some forms of meat processing such as curing and smoking. There is only one serotype, and since it is clinically indistinguishable from ASF, diagnosis depends upon laboratory methods: virus isolation, antigen detection, genome details and antibody detection. Unlike FMDV, it is stable in a protein-rich environment and is destroyed only by being heated to about 60 °C for about 10 minutes.

3.32 CSF is highly contagious and capable of rapid spread in susceptible pig populations. Accordingly, an outbreak of CSF will severely disrupt the pig industry and the speed of control of the outbreak will relate directly to the rapidity of diagnosis.

3.33 Transmission occurs by direct contact with infected pigs, the ingestion of products from infected pigs or pig meat products, and contact with infected material, which may have been physically transported by birds, flies or humans. Long-distance aerosol transport is not considered a factor. CSF is endemic in the wild boar population in Germany, which overspills into the local domestic pigs from time to time and causes outbreaks of varying sizes. It should be noted that there is now a wild boar population in the south of England—whose infection status is unknown.

3.34 Post-mortem lesions arise from damage to large and small blood vessels and the lymphoid system. Lymph nodes are marbled red and pinpoint haemorrhages are found on the epicardium, in the kidneys, urinary bladder and skin, and haemorrhages in the small intestines that lead to the production of button ulcers in the gut wall.

3.35 Diagnosis is also complicated by the similarity to two other viral diseases that are being recognised with increasing frequency, PMWS and PDNS. These two new diseases are poorly understood but are similar clinically and pathologically to CSF, and laboratory testing is frequently required to differentiate them from CSF. They cause significant losses, and posed considerable problems with differential diagnosis in the 2000 UK outbreak.

3.36 Modern laboratory diagnostics for CSF have now been developed (Chapter 7), including a reverse transcriptase – polymerase chain reaction method for viral RNA. Interestingly, CSF virus exerts an immunosuppressive effect that delays the appearance of antibodies until the third or fourth week of illness so that serological techniques are really only useful for detecting strains with low virulence and for any post-disease surveillance monitoring.

3.37 Attenuated live vaccines are available but are generally prohibited in countries where the disease is not endemic because economic assessment favours the disease-free status, there is a risk of vaccine reversion and their use would complicate serological surveillance, which is an ongoing process in the pig industry. A new EU directive on the control of CSF, however, provides for emergency vaccination under certain conditions. Although marker vaccines have been developed on the expression of a single CSF virus protein (E2), the accompanying serological tests that would differentiate between antibodies derived from infection and those from the vaccine cannot be configured to provide both high specificity and high sensitivity. This reduces the value of using the subunit E2 vaccine in Europe.

3.38 Control of disease outbreaks is currently through

the slaughter of all pigs on infected premises, close contacts, movement bans and disinfection of infected and suspected premises. This is the policy throughout the EU and routine vaccination has not been used since 1990.

(iii) African swine fever (ASF)

3.39 ASF is a highly contagious haemorrhagic disease caused by a large DNA virus and is clinically and pathologically indistinguishable from CSF. It is of economic importance because of serious production losses and is endemic in wild and domestic pigs in a number of countries in southern and east Africa. In the field the main transmission is via direct contact with infected pigs up to one month after infection, or the ingestion of waste food containing infected pig meat or pig products. Blood is infectious for up to six weeks. Infection can also be spread through infected ticks or mechanically through flies.

3.40 It was first identified in Portugal in 1957, was eradicated, but reappeared again in 1960 and became established in most of the Iberian peninsula. It has occurred and been eradicated in Malta in 1978, Italy in 1983, Belgium in 1985 and The Netherlands in 1986 but is still endemic in Sardinia. Eradication was declared successful in Portugal in 1993 and in Spain in 1995. There was a recurrence in Portugal in 1999. Factors related to persistence of infection in the population include movement of pigs, extensive pig husbandry systems, (i.e. outdoor pig keeping) and soft tick (*Ornithodorus moubata*) vectors.

3.41 Subacute and chronic forms have been described but occur in endemic areas where local breeds of pigs have self-selected for resistance. Thus in Sardinia, where the virus is endemic, not all pigs die after infection with ASF. Otherwise, a high susceptibility rate can be expected in European breeds; European wild pigs are also fully susceptible. In Africa the virus is maintained in a cycle involving a soft tick vector. Recovered pigs are persistently infected for up to one year and possibly for life.

3.42 Because ASF is clinically and pathologically indistinguishable from CSF, diagnosis requires laboratory tests: virus isolation, antigen detection, genome details and antibody detection (Chapter 7).

3.43 No vaccine is available against ASF and so control is currently through the slaughter of all pigs on infected premises, disposal of the carcasses and disinfection. It is necessary to undertake serological testing of all pig farms in the defined control zone.

(iv) Avian influenza (AI)

3.44 AI is a bird disease that is capable of causing very high mortality (up to 100%) in poultry, and until 1981 the highly pathogenic form was known as fowl plague. Because some strains have the potential to infect humans, robust contingency plans are required.

3.45 Influenza viruses (family Orthomyxoviridae) are grouped into three antigenic types, A, B and C, each type representing a genus. Only type A affects birds. Of the 15 haemagglutinin subtypes, only two strains, H5 and H7, cause highly pathogenic avian influenza (HPAI) but these cause mortalities of up to 100%. Some strains within H5 and H7, and all within the other subtypes, may potentially cause low pathogenic avian influenza (LPAI). There is also some evidence that LPAI viruses within subtypes H5 and H7 can mutate to HPAI virus after introduction into domestic poultry. Of the 18 reported outbreaks of HPAI worldwide over the past 40 years, about half have been confined to the first infected farm, but in five outbreaks (most recently in Italy in 1999/2000) there was significant spread to numerous other farms.

3.46 It seems likely that most types of the virus are maintained in wild birds, particularly migratory water fowl but also shore birds and gulls. HPAI viruses have only rarely been isolated from free-living birds, and usually these have been in the vicinity of outbreaks of HPAI in poultry. Because wild birds are a possible source of infection, if only of LPAI, it is normal practice for poultry farms to limit the contact of farmed birds with wild ones because of the risk of infection with LPAI, which might mutate to virulence.

3.47 There is particular concern about HPAI since it is potentially zoonotic (capable of infecting humans). In 1997 a lethal AI virus was transmitted directly from chickens to humans in Hong Kong who had been in close contact with the birds. Six of the 18 clinically diagnosed cases were fatal. A perspective by Webster[68] points out that this 1997 virus seems to be relatively close to that which caused Spanish influenza in 1918. The response of the authorities in Hong Kong was drastic but wise: they slaughtered all chickens immediately.

3.48 Once there has been an outbreak of HPAI in poultry, spread seems to be primarily by the transfer of infected faeces but also occurs by contaminated feed, water, equipment and clothing. The prevention of secondary spread of infection therefore depends on the maintenance of good biosecurity, including minimum contact

with the poultry; movement controls on and off farms; ensuring that all equipment and vehicles are disinfected before access to the farm is permitted; and ensuring that any pick-up or drop-off points for essential items such as eggs and feed are kept well away from the poultry flocks.

3.49 Clinical signs can vary from sudden death or respiratory symptoms, excessive lachrymation, sinusitis, oedema of the head, cyanosis of unfeathered skin, and diarrhoea. However, these signs do not provide a conclusive diagnosis, which must be made by isolation of the virus and demonstration of its virulence.

3.50 Diagnostic tests are inevitably complicated by the variety of subtypes and the need to distinguish between HPAI and LPAI. Confirmation usually requires access to an OIE reference laboratory, which in the UK is the VLA (Chapter 7).

3.51 The EU Scientific Committee on Animal Health and Welfare recommended the elimination of H5 and H7 viruses in poultry (so that these do not mutate to virulence in domestic birds) and wished as a preliminary step to establish their incidence in wild birds and domestic poultry. So far no monitoring scheme has been adopted. Prophylactic vaccination has been banned in most countries because it interferes with stamping-out policies and, although it reduces the amount of virus shed from birds subsequently challenged, it does not eliminate it, and may well encourage the development of antigenic variation. Emergency vaccination may be carried out to control an outbreak. Present control consists of the slaughter of all birds on farm, the disposal of carcasses and all animal products, cleansing and disinfection and a wait of a further 21 days before restocking.

(v) Newcastle disease (ND)

3.52 ND is a viral disease of birds caused by infection with avian paramyxovirus type 1 (APMV-1), of which there are nine serotypes. Strains of APMV-1 differ greatly in the severity of the disease that they cause, so ND is a definition of the disease, not of the infection. Migratory wild birds might be responsible for the primary introduction of infection, but ND isolates from wild birds have usually been of low virulence.

3.53 Strains vary greatly in their pathogenicity for chickens and have been allocated to five 'pathotypes' ranging from highly pathogenic to those producing asymptomatic enteric infections.

3.54 APMV-1 is endemic in many countries and prophylactic vaccination is widely practised in commercial poultry. Proper diagnosis is essential since vaccine strains can be recovered in such situations from birds dying of an otherwise unrelated cause. It is also possible for vaccinated birds to acquire and excrete virulent virus while remaining healthy (i.e. carrier state). Within the EU such birds would be slaughtered under ND legislation. Accordingly, the diagnostic routines for AMPV-1 are governed by the need to determine the pathogenicity of the recovered strain. Laboratory diagnosis is considered in Chapter 7. The last outbreak in the UK was in 1997 and was probably introduced by wild birds.

3.55 The virus can survive in the dead host and excretions for some weeks, and faeces can remain infective for over a month at 37 °C. Disease transmission is largely via infected faeces, and biosecurity is required between wild and domestic birds, including racing pigeons. The potential for racing pigeons to introduce ND into a country or area has been highlighted by the introduction, probably from mainland Europe, of the disease in racing pigeons in Cornwall in 1983; within a year, 869 pigeon lofts were infected. Spread to poultry occurred in 1984, when there were 23 outbreaks of ND. Compulsory vaccination of racing birds was introduced in April 1984, yet there were still 16 confirmed outbreaks in pigeons in 1999.

3.56 ND virus is a human pathogen but does not cause severe or long-lasting symptoms. As no known human-to-human infection has been reported, those at risk are farm and laboratory workers and veterinarians.

3.57 The highly pathogenic form of the disease appears suddenly and spreads rapidly. In laying birds there is a sharp decrease in egg yield, increased respiration and progressive prostration associated with profuse bright green diarrhoea, and death occurs within a few days. With other forms, nervous signs such as head tremors and torticollis, and respiratory symptoms such as coughing and gasping, are seen. In the milder form, coughing accompanies weight loss, depression and a decrease in egg production.

3.58 Pathological lesions include haemorrhage and necrosis in the proventriculus, gizzard and small intestines, laryngitis and catarrhal tracheitis.

3.59 A large majority of the countries rearing poultry commercially rely on vaccination to keep ND in check, although in Norway, Sweden and Finland vaccination is prohibited and control is by 'stamping out'. Prophylactic vaccination is voluntary in the UK, where both live attenuated

and dead vaccines are used. In contrast in The Netherlands and some other EU countries vaccination is compulsory. Outbreaks of disease or infections with virulent virus are, however, dealt with by slaughter and disposal of all birds on infected premises and by movement restrictions in the area. The on-farm slaughter of large numbers of birds poses particular problems that need to be addressed with the provision of suitable equipment for culling humanely. The Inquiry did note views from the British Poultry Veterinary Association that vaccination will provide effective control in commercial flocks and that although there is a risk of introduction of disease into 'backyard flocks', it would pose little risk to vaccinated flocks.

(iv) Bluetongue (BT) and African horse sickness (AHS)

3.60 These two diseases are caused by very similar viruses, which exist in relatively large numbers of serotypes (24 in BT and 9 in AHS). Both viruses are transmitted by certain species of *Culicoides* biting midge, and the abundance of these midges determines when disease is most likely to occur: in late summer and autumn. There is some tentative evidence that one or more of the common British species of *Culicoides* might be able to transmit these viruses. This requires resolution, not least because although BT virus has previously been found mainly between latitudes 35° S and 40° N, it has been found as far north as 50° in North America and China, is now present in Spain, France, Italy and the Balkans and so might move into Britain. AHS is mainly confined to sub-Saharan Africa but has previously been present in Spain and Portugal and several other countries to the east of Africa.

3.61 BT virus usually causes severe disease only in certain breeds of sheep but can occur in subclinical form in other ruminants. AHS virus usually occurs only in horses and related species, although occasionally dogs have also been infected.

3.62 The main mechanism for transmission for both is via biting midges, the females of which suck blood about every four days during their 2–3-week lives. The midges become infected via the blood of a viraemic animal and then incubate the virus for 7–10 days before infecting a susceptible animal through a subsequent bite. The bite of a single infected midge is enough to infect an animal and cause an outbreak. BT virus can be transmitted from mother to foetus.

3.63 The BT virus's northward migration has almost certainly required some means of maintaining the virus over the winter in carrier animals, because in many areas the climate is too cold for the vectors to survive throughout that season. Further research is required, probably on a European basis because of the significant threat to all EU states with significant sheep populations. The UK has no formal surveillance for BT virus; initial detection of the disease relies on clinical recognition by farmer or veterinarian.

3.64 Clinical appearance. Acute cases of BT are usually observed only in sheep, in which the diagnosis can be based on fever accompanied by oedema of the head region and swelling of the tongue—sometimes to the extent that it cannot be contained in the mouth—accompanied by cyanosis (hence 'bluetongue'). Towards the end of a week-long febrile period, coronitis (inflammation of the coronary band above the hoof) develops on the feet, causing pain and lameness. Torticollis is another late-appearing sign. Mortality rates can reach 70% but, even in European breeds, the vast majority of cases will probably be either mild or subacute, consisting of various combinations of the above signs in a less acute form. Clinical diagnosis is an unreliable guide to the presence of BT virus and diagnosis is dependent on laboratory-based methods (Chapter 7).

3.65 AHS virus, which is a typical orbivirus with nine serotypes, can cause epidemics with an 80–90% fatality rate in (non-zebra) equids and solipeds. The virus generally tends to stop circulating or die out during periods when no insect vectors are 'on the wing' but it can be reintroduced to non-endemic areas by acutely infected hosts or by the movement of infected vectors, which can occur over long distances when wind assisted. Imported zebras have acted as important sources of infection; viraemia in this species tends to last considerably longer than in the horse and because these animals are resistant to clinical disease, infectious individuals are almost impossible to detect by clinical examination. The disease is endemic in regions of southern Africa.

3.66 Antibody responses are accepted by the EU as adequate diagnosis of disease. Clinically, the following three syndromes are described after infection.

- The pulmonary form, which is generally fatal, is associated with an acute pulmonary oedema in which, after a sudden onset, the presenting signs are pyrexia, dyspnoea, abdominal breathing, paroxysms of coughing, and a copious discharge of frothy fluid from the nostrils. Animals try to gain relief by standing with their forelimbs apart and their head extended. They evince anxiety

and sweat profusely. Death is within 4–24 hours of the onset of signs.

- The cardiac form is characterised by signs of circulatory failure. There is a pronounced and characteristic swelling of the supraorbital fossae, at times extending to the neck, brisket, ventral thorax and abdomen. The mortality rate is about 50% and the course of the disease is relatively long (four to eight days).
- Horsesickness fever: in this form little more than pyrexia is noted. It can be expected in previously recovered horses when infected with an additional serotype.

3.67 Concerns exist about the safety and efficacy of the only available vaccines for AHS virus and BT virus, which are live attenuated preparations manufactured in South Africa. No vaccines are currently available in the EU because the killed virus vaccine containing Type 4 strain is no longer available. What is required in the short term is safety and efficacy testing of the existing live vaccines and, in the longer term, the development of safe, effective, inactivated or subunit vaccines. More research is needed upon aspects of these two viruses and of their vector species.

(b) Diseases affecting the main livestock sectors

3.68 The rest of this chapter describes briefly the main infectious diseases affecting the different sectors of the livestock industry. More detail on some of the most serious diseases is given in a series of specialist reports commissioned specially for this Inquiry (available on our CD-ROM and website www.royalsoc.ac.uk/inquiry).

(i) Cattle

3.69 There are a wide range of infectious diseases of cattle, ranging from those on the OIE's List A to those endured or controlled on a routine basis on many farms but which have implications for production welfare (most of these are on the OIE's Lists B and C and other lists). As noted above, we are not covering the TSEs in this report. Those cattle diseases on the OIE's List A are described in the following paragraphs.

3.70 FMD is described above.

3.71 Rinderpest, or cattle plague, is a viral, pyrexic disease associated with inflammation progressing to sloughing and necrosis of the mucosa of the mouth, nose, eyes and vagina and later severe gastrointestinal signs (profuse haemorrhagic diarrhoea). It is potentially infective for all members of the order Artiodactyla but in particular infects bovines, swine and deer. The State Veterinary Service was established in the UK specifically to deal with rinderpest, which in the 18th and 19th centuries was responsible for the deaths of millions of cattle in Europe. Morbidity is usually close to 100% and mortality can be in excess of 90%. There is only one serotype of the virus, a member of the morbillivirus group of viruses, as are canine distemper, measles and phocine distemper. An effective live attenuated vaccine is available and a FAO-sponsored world eradication campaign based on the use of the vaccine has been largely successful, with only two pockets of disease remaining in Africa and the Indian subcontinent.

3.72 Contagious bovine pleuropneumonia (eradicated from the UK in 1898) is a mycoplasmal, pyrexic condition that rapidly progresses to a painful thoracic condition followed by death from anoxia due to thrombosis in the pulmonary vessels. It has been reported in southern Europe and is still one of the significant animal plagues in certain parts of the world, particularly in nomadic herds. Morbidity in susceptible herds is about 90% and mortality is about 50%. Of the surviving animals some 25% make a complete recovery. Treatment with specific antibiotics can be undertaken in countries where a 'stamping-out' policy is not applied, but within the EU eradication is the goal. Live attenuated vaccines are available and are used in many African countries.

3.73 Vesicular stomatitis is a vesicular disease of pigs, cattle, sheep and horses, in which vesicles are found in and around the mouth and lips, feet and teats. Many species of wildlife are susceptible. It can also cause an influenza-like disease in humans, particularly farm workers in endemic areas. The disease is clinically indistinguishable from FMD or SVD and is endemic in the Americas. It has never been identified in the UK. Differential diagnosis from FMD is essential except when it occurs in horses. The virus is transmitted directly by the transcutaneous or transmucosal route and has been isolated from sandflies and mosquitoes, which suggests that it might be insect borne.

3.74 Lumpy skin disease is a viral, pyrexic condition that can progress to generalised painful nodules in the skin, subcutaneous tissues and even musculature. These lesions can then become necrotic and form deep scabs. The causal virus is the Neethling pox virus and the disease occurs in parts of Africa. Morbidity is about 50% and mortality 10%. The mode of transmission is not completely understood but the role of insects is suspected to be important. No treatment is

available but protection can be provided with a modified Neethling virus vaccine. The disease has never been recorded in the UK.

3.75 Rift Valley fever, also known as enzootic hepatitis, is a zoonotic disease that affects mainly sheep and cattle and to a lesser extent goats and camels. It is caused by an insect-borne RNA virus of one main antigenic strain. The condition is found only in Africa, and transmission is by mosquitoes. Symptoms include anorexia and weakness, salivation, diarrhoea, abortion and potentially high mortality in calves. See the section below on sheep.

3.76 Within the OIE's List B there are 26 diseases that can affect cattle, including the following.

(i) Diseases eradicated from Britain, such as enzootic bovine leucosis (1996) and bovine brucellosis (1993, but still reported in Northern Ireland and in the Republic of Ireland), which are still notifiable in the UK and subject to routine surveillance via bulk milk and blood sampling. Anthrax is a notifiable disease last recorded in the UK in 1997, but given the ability of anthrax spores to lie dormant for many years, the disease cannot truly be said to have been eradicated, and all sudden unexplained deaths in bovines are subjected to testing for anthrax. Rabies (1970 in an imported dog) is notifiable and although it is not primarily considered a bovine disease, cattle can be very susceptible.

(ii) Diseases that are notifiable, and subject to eradication schemes, include bovine tuberculosis and BSE.

(iii) Diseases that are frequently recorded and endemic in the UK, such as infectious bovine rhinotracheitis/infectious pustular vulvovaginitis, echinococcosis/hydatidosis, malignant catarrhal fever, leptospirosis, and paratuberculosis (Johne's disease).

(iv) Diseases that are less likely to occur in the UK owing to the absence of suitable vectors or to other climatic or management factors; these would include trypanosomiasis and screw-worm infections.

3.77 There are several other common UK bovine infectious diseases listed by the OIE, including listeriosis, clostridial infections, mucosal disease/bovine viral diarrhoea, coccidiosis, *Salmonella* infections and warble infestation (a notifiable disease).

3.78 Finally there are infections that are not listed, such as those caused by respiratory syncytial virus, *Pasteurella* spp., *Haemophilus somnus*, parainfluenza virus (PI3), rotavirus, coronavirus, *Escherichia coli*, *Trichophyton* spp. (ringworm), *Neospora*, infectious mastitis organisms, tick-borne fever and babesiosis. An emerging disease that has been introduced recently into the UK is *Mycoplasma bovis*.

3.79 Some of these diseases are relatively easy to control by vaccination and closed-herd policies, but others have complex disease profiles and can be harder to control. For example, paratuberculosis (Johne's disease) is regarded in many parts of the world as a highly significant pathogen that severely affects production, but eradication from a herd can be very difficult and costly. There is also a suggestion that paratuberculosis might be zoonotic. The aetiology of others, such as digital dermatitis, has not yet been clearly defined.

3.80 Zoonotic conditions are also significant, and there are several bovine infectious diseases in this category, including anthrax, brucellosis, tuberculosis, leptospirosis, listeriosis, Q fever, salmonellosis and ringworm.

(ii) Sheep

3.81 The stratification of the sheep industry presents major problems for disease control and biosecurity because there are massive movements of sheep at certain times of the year, culminating in the autumn sales. The potential for disease spread is great, especially for endemic diseases such as enzootic abortion of ewes and maedi visna but also for the epizootic diseases as happened with the 2001 outbreak of FMD. Because sheep are susceptible to a number of the diseases classified by the OIE in List A, the potential for their spreading rapidly through the UK sheep population is great if any of them are inadvertently introduced. The long-distance travel and mixing of sheep in markets is surely a significant risk factor in disease spread.

3.82 FMD is obviously the greatest threat. Sheep are, however, unlikely to be the primary source of the infection in the country and are likely to become infected from another species, but their potential to disseminate the infection is considerable. The situation is compounded by the fact that the disease in sheep is less easily recognised than in most other susceptible species.

3.83 BT is described above.

3.84 Sheep pox and the closely related goat pox are found in Africa (north of the Equator), Turkey, the Middle East, India, Nepal and parts of China. There have been frequent incursions into Europe

from Turkey (e.g. into Italy (1983), Greece (1988 and 1995–97) and Bulgaria (1995–96)). The disease manifests as a malignant pox disease characterised by fever, multiple non-vesicular swellings on the skin and mucous membranes, rhinitis, conjunctivitis, respiratory distress and death. The risk of introducing this severe condition into Europe depends on how well the borders with Turkey can be policed. If sheep pox did get into the UK the effects would probably be severe owing to the concentration of the sheep population and the high susceptibility of some of the British breeds of sheep.

3.85 *Peste des petits ruminants* (PPR) – a List A disease – is caused by a morbillivirus that is antigenically very similar to, but serologically indistinguishable from, rinderpest virus. It is an economically important disease of sheep and goats in sub-Saharan Africa. It also occurs in a belt from Turkey through the Middle East and the Indian subcontinent to Bangladesh. Clinical signs include high fever, anorexia, depression, shivering and reluctance to move. Also prominent can be nasal catarrh, oral erosions with salivation, and projectile diarrhoea. Rinderpest (cattle plague) is caused by another morbillivirus that can also occasionally infect sheep, causing signs ranging from being inapparent to a syndrome identical to PPR.

3.86 Rift Valley fever is a mosquito-transmitted viral disease of sheep as well as cattle. Goats are occasionally affected. In sheep the disease is characterised by high mortalities in newborn lambs and abortion storms in pregnant ewes. The disease can assume epidemic proportions under conditions that favour the vector, especially high rainfall. It has been identified in most sub-Saharan countries and as far north as Senegal and Egypt. Humans can become infected by close contact with affected animals or laboratory specimens. The chances of introduction into the UK would seem to be remote.

3.87 There are 22 diseases of sheep that are included in the OIE's List B classification, some of which are present in the UK, e.g. maedi visna, pulmonary adenomatosis, scrapie, and enzootic abortion of ewes. They cause significant welfare problems (e.g. foot rot) and are major sources of economic loss to sheep flocks in this country. Several others on this list could be equally significant if introduced, e.g. contagious agalactia and ovine epididymitis (*Brucella ovis*).

(iii) Pigs

3.88 Because the pig industry is without direct production subsidies there is a greater incentive to ensure rapid eradication of infectious diseases and/or protection through vaccination and improved biosecurity. Pigs are fed concentrated feed, most of which is purchased. Because the feeding of swill lies behind many outbreaks of infectious viral diseases, this practice was finally banned in Britain in 2001. The significant recent move to rearing pigs outdoors alters the risk pattern of infectious diseases. The following paragraphs describe List A diseases of pigs.

3.89 FMD (see above) is the greatest threat to the pig population. This risk is compounded by the fact that although pigs are less susceptible to aerosol infection than other species they are susceptible to oral infection, and diseased pigs produce large quantities of virus which cause spreading to neighbouring farms. There is huge potential for spread if the disease breaks out in areas with a dense populations of pigs such as those in the east of England. The disease should be readily identifiable in pigs if the farmer is alert to the risk. The clinical signs include lethargy resulting from a high body temperature, and also lameness and vesicles on the snout, lips, teats and on the coronary band of the feet.

3.90 CSF and ASF are described above.

3.91 Swine vesicular disease (SVD) is a contagious disease of pigs, caused by an enterovirus and characterised by vesicles on the coronary band and heels. Strains vary in virulence but disease is not severe or of any economic importance other than it is clinically indistinguishable from FMD, and any outbreaks of SVD must be assumed to be FMD until diagnosed in the laboratory. Waste food, i.e. swill, was implicated in many of the outbreaks in the UK in 1972 onwards. The last outbreak in the UK was in 1982. It is thought to be endemic in Italy, and sporadic outbreaks have occurred in other EU countries. More recently a number of outbreaks occurred in Belgium, The Netherlands, Spain and Portugal that were linked to the movement of infected pigs or contaminated livestock lorries from Italy.

3.92 Vesicular stomatitis is vesicular disease of pigs, cattle, sheep and horses in which vesicles are found in and around the mouth and lips, feet and teats.

3.93 Aujeszky's disease (pseudorabies) is caused by a herpes virus and is included in the OIE's List B. It is important to pig producers and was successfully eradicated from Britain by a policy of test and slaughter. This was possible because the prevalence was already low and is of particular interest since eradication was financed by a levy.

The last recorded case was in 1989. It is still present in Northern Ireland, where it is controlled by vaccination, as it is in other EU countries. It is notifiable and the current policy is to stamp it out if it reappears.

3.94 Other diseases in the OIE's List B such as porcine reproductive and respiratory syndrome (PRRS) and atrophic rhinitis are endemic in UK pigs, and transmissible gastro-enteritis occurs sporadically. All of these cause serious production losses. Other viral diseases that have appeared in recent years include swine influenza, PRRS, PDNS and PMWS. Swine influenza and PRRS were imported but the origin of PDNS and PMWS is as yet unknown, although they have been reported in a number of other countries. Enzootic pneumonia caused by mycoplasma is widespread in pigs and causes reductions in productivity; it has been controlled on some farms by the development of specific pathogen-free breeding herds. The economic effects of the disease have been significantly reduced more generally by the use of vaccine.

(iv) Poultry

3.95 The control of poultry diseases has to accommodate the diversity in poultry production systems and the fact that the wild bird population is a potential reservoir for certain important infectious diseases. For the purpose of trade within the EU poultry means fowl, turkeys, guinea fowl, ducks, geese, quail, pigeons, pheasants, partridges and ratites that have been reared in captivity for breeding, the production of meat or eggs for consumption, or the restocking of game.

3.96 The conventional intensive indoor system is one in which laying birds are in cages, and broilers and turkeys are kept at a high density. With the aim of preventing the introduction of infectious microorganisms, high priority is given to biosecurity; birds are usually vaccinated against a number of infectious diseases such as coccidiosis (caused by a gut parasite) and *Salmonella*. Intensive production units have come under pressure in recent years to improve welfare, to apply health programmes in which priority is given to the control of zoonotic diseases (*Salmonella* and *Campylobacter* infections), and to decrease residues from veterinary medicinal products that are used routinely.

3.97 AI and ND are described above.

3.98 In List B of the OIE there are 13 poultry diseases that can cause serious health problems and economic losses. The viral diseases listed are infectious bursal disease (Gumboro disease), Marek's disease, avian infectious bronchitis, avian infectious laryngotracheitis, duck virus hepatitis and duck virus enteritis. These are regarded as endemic in all or parts of Britain and, with the exception of duck virus enteritis, are controlled by routine prophylactic vaccination. Of the listed bacterial diseases, the pathogen causing avian tuberculosis is capable of giving rise to a progressive disease in humans that is difficult to treat, especially in immunocompromised individuals. Humans can also become infected with *Chlamydophila psittaci*, the causative agent of avian chlamydiosis, resulting in serious, sometimes fatal, illness.

(v) Horses

3.99 AHS (see above) is the only equine disease on the OIE's List A.

3.100 There are 15 diseases specific to horses on the OIE's List B. The most significant of these are the following.

(i) Encephalitides include Japanese B encephalitis (JE), Venezuelan equine encephalitis (VEE), Eastern equine encephalitis (EEE), Western equine encephalitis (WEE) and West Nile fever (WNF). All are potentially infectious to humans and notifiable and are transmitted by mosquitoes. VEE, EEE and WEE are alphaviruses in the family Togaviridae. JE is a flavivirus.[69]

(ii) Japanese B encephalitis is endemic throughout South East Asia, China and Japan. Its main reservoir is avian, chiefly herons and egrets. Horses and humans are generally considered to be incidental hosts, although pigs can also amplify the virus during outbreaks. The rate of clinical disease during outbreaks appears directly proportional to vector density and it is unlikely transmission would occur in the UK. Clinical cases could occur in animals returning from competition or breeding in endemic areas, and these could pose some risk to the health of personnel dealing with them. Vaccination with whole-virus killed vaccines has been successful in preventing disease in both humans and horses in Japan for many years. Clinical cases are thought to occur frequently in China, where vaccination is not practised. Vaccine efficacy is generally considered to be good, although a single case was confirmed in a vaccinated horse in Hong Kong in 2001. It is not feasible to prevent circulation of the virus in wildlife.

(iii) West Nile Fever (WNF) presents concern because migratory birds form the major disease reservoir; horses and humans, in whom fatalities occur, are incidental hosts.

The disease received publicity during recent outbreaks in the Camargue and in New York (2001). Since its first ever appearance in North America in 2000, the virus seems to have become endemic there, particularly in states such as Florida that have a high population density of birds and mosquitoes. Deaths of horses caused by this infection were diagnosed in both France and the USA, and human fatalities occurred in the USA. The main infection cycle occurs between mosquitoes and susceptible bird species and the virus is promiscuous. High-level viraemias are uncommon in horses but there is some evidence that viraemias in horses might be sufficient to infect some insects. Egrets were thought to have introduced the infection to France when migrating from the endemically infected areas of Sudan. It seems unlikely that the horse has a major role in the transmission of infection, but reports from several outbreaks suggest that the horse is a valuable sentinel species for the disease in humans, with cases occurring earlier in horses than in humans. A whole-virus killed vaccine has recently been approved for use in North America, although this can be expected to prevent only the disease rather than its transmission. Migrating wild birds (egrets) and mosquitoes co-exist in the UK. Climate changes, through alterations to insect vector densities, might increase the likelihood of cases occurring in the UK, particularly in the south of England, where egrets now nest in most summers. Equine sero-surveillance and surveillance of the causes of equine neurological disease would probably be the most efficient way of providing early warning of outbreaks or spread.

(iv) Western equine encephalitis is distributed throughout the Western Hemisphere. Again, the major transmission cycle is between passerine birds and mosquitoes. Horses and humans are thought to be incidental hosts, although some viral amplification can occur in domestic birds and mammals. As with JE, the horse is considered a dead-end host because viral levels during viraemia remain below those required to infect mosquitoes. Vaccination is effective for the prevention of clinical disease in horses but the disease remains an economically important pathogen of working horses in several South American states.

(v) Eastern equine encephalitis is distributed throughout the eastern seaboard of the USA. Like WEE, the natural vertebrate hosts are passerine birds, although in contrast the mosquito vectors tend to pass the virus preferentially to birds. The infection tends not to occur in epidemics, but more typically causes sporadic disease in humans, horses and other animals. Epidemics in horses do occasionally occur, particularly in late autumn in Caribbean countries during the migration of birds from the USA. This virus has also caused fatalities in veterinarians dealing with cases, as well as in cases thought to have been transmitted by normal insect vectors. Like WEE, vaccination with whole-virus killed vaccine is effective at preventing clinical disease in horses and might be useful at reducing transmission during epidemics in horses.

(vi) Venezuelan equine encephalitis is caused by a large number of closely related viruses. Six subtypes are now recognised, with the first having six variants. At least two of these are highly pathogenic for horses and have the ability to cause major epidemics. The horse is the major reservoir species of epidemic strains, which are promiscuous in terms of insect vectors and vertebrate hosts. Recent and severe human and equine epidemics have occurred in Texas and Mexico. Other less pathogenic strains have sylvatic cycles, being more host-restricted, and they tend not to cause epidemics. Very-high-level viraemias (virus particles in the blood) occur in horses (10^{10} virus particles/ml) and transmission by aerosol occurs readily. Infection of laboratory workers is common. As with the other encephalitides, whole-virus killed vaccines are effective at preventing disease in horses and also seem effective at preventing the spread of epidemic strains in horses.

3.101 Introduction of any of these viruses to the UK would most probably be via a live horse coming from an epidemic area. Although this is unlikely and would potentially be controllable through imposed movement restrictions during epidemics, the effects of an outbreak on both the equine and human populations could be significant. No work has been done to determine whether or not the densities of vectors and hosts in the UK would be high enough to propagate an epidemic.

3.102 Other diseases. Hendra virus can cause fatal pneumonia and encephalitis in both humans and the horse. (Hendra virus is very closely related to Nipah virus, which has caused problems in Malaysia.) It was first reported in Australia, where the fruit bat is the natural reservoir host. All human cases thus far reported have been derived via horses. Of particular concern with this disease is the large movement of 'shuttle' thoroughbred

stallions, which move between the UK and Australia on a six-monthly rotation. There are no specific Hendra-related import controls in place for horses returning to the EC from Australia. Hendra has been categorised by the Advisory Committee on Dangerous Pathogens as a category 4 pathogen; no vaccine currently exists, and control is by movement restrictions and slaughter.

3.103 Equine influenza. Although there is no evidence for the transfer of equine influenza to humans, it is theoretically possible that a major antigenic shift in equine influenza could lead to an outbreak in both humans and horses, as has occurred previously from other species. Disease surveillance could alert authorities to any major antigenic shift occurring in equine influenza.

(v) Fish farming

3.104 Farmed fish are susceptible to a wide range of diseases that are potentially very serious owing to the highly intensive nature of growing within cages.

3.105 Seven of these are listed by the OIE:

- infectious salmon anaemia (ISA),
- viral haemorrhagic septicaemia (VHS),
- infectious haematopoietic necrosis (IHN),
- infectious pancreatic necrosis (IPN),
- spring viraemia of carp, which infects carp and a number of other species including goldfish, pike, roach, rudd, tench and Wels catfish,
- bacterial kidney disease, and
- gyrodactylosis (*Gyrodactylus salaris*).

3.106 An outbreak of ISA in May 1998 caused three-quarters of British salmon farmers to be quarantined, and 4 400 tonnes of fish were slaughtered without compensation. Monitoring after the outbreak continues; the last confirmed case was in May 1999. The UK is currently an approved zone for VHS and IHN, the last confirmed case of VHS being on the isle of Gigha in 1994. As regards IPN, there are 231 current movement restrictions in place in Scotland (April 2002) out of approximately 600 active freshwater and marine salmon-rearing sites. Gyrodactylosis is not present in the UK. Clinical furunculosis (not an OIE-listed disease) is successfully controlled by vaccination and antibiotics.

(c) Conclusion and recommendations

3.107 The intention of this chapter has been to remind the reader of the large number of infectious diseases in livestock, of our relative ignorance in many cases and of the growing impact of globalisation and climate change. In particular, we are concerned at the lack of information on diseases such as FMD and HPAI, the danger of CSF entering the UK wild boar population, the northward migration of bluetongue and the potential for the encephalitides to enter the UK.

We recommend that DEFRA should:

- **undertake a systematic analysis of the information available on the relative threats to the UK from the range of diseases covered here (and other significant diseases such TSEs and tuberculosis), taking account of the impact of globalisation and climate change, in order to set priorities for the national strategy for animal disease and surveillance; (R3.1)**
- **undertake a comprehensive review of the available information on FMD, and develop a consistent and coherent database of the basic information that would be required during an outbreak; (R3.2)**
- **carry out urgent research into local transmission of FMD that will improve biosecurity in the field. (R3.3)**

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4 The trading dimension

(a) The world trading framework and the role of the OIE and its reference laboratories

4.1 The international rights or obligations of a country (such as the UK) in relation to trade derive mainly from the World Trade Organization (WTO) Agreement (1994) on the Application of Sanitary and Phytosanitary Measures ('the SPS agreement'). The WTO is the legal and institutional foundation of multilateral trade. Within the SPS agreement, WTO Member States have the right to adopt protective sanitary measures to the extent necessary to protect human and animal health, provided that the measures are based on *scientific* principles and are not maintained without sufficient continuing *scientific* evidence. Members are encouraged to base their national protective measures upon the relevant international standards, guidelines and recommendations that are issued by the OIE and the *Codex alimentarius* published by the joint FAO/WHO Food Standards Programme. Governments may introduce measures with a higher level of protection, but these must conform with the international obligations on risk assessments and offer a consistent approach to risk management. These restrictions are designed to inhibit countries from adopting practices which confer unreasonable trade advantages.

4.2 Those rules for risk assessments are laid down in the OIE Animal Health Code (tenth edition 2001), which regulates the 95 diseases in Lists A and B. The SPS Agreement recognises the OIE as the body responsible for the development and promotion of international standards, guidelines and recommendations for animal health and zoonoses. WTO Members must therefore respect OIE normative documents when establishing animal health conditions for the import and export of animals and their products. The recommendations in the Code are designed to prevent diseases from being introduced into the importing country, taking account both the nature of the commodity and the animal health status of the exporting country. Recommendations relating to a disease are based on the assumption that the importing country is free from that disease.

4.3 The OIE publishes a Manual of Standards for Diagnostic Tests and Vaccines, which describes internationally agreed laboratory methods for the diagnosis of List A and B diseases, along with requirements for the production and control of biological products (mainly vaccines). It also lists the OIE reference laboratories across the world. The UK has reference laboratories covering 11 List A and 16 List B diseases. Eight of these are at the Biotechnology and Biological Sciences Research Council's (BBSRC's) Institute for Animal Health (IAH) (List A: foot-and-mouth disease, swine vesicular disease, rinderpest, lumpy skin disease, sheep pox and goat pox, bluetongue, African horse sickness and African swine fever), and seventeen are at DEFRA's Veterinary Laboratory Agency (VLA) (List A: classical swine fever, highly pathogenic avian influenza, and Newcastle disease; plus 14 List B diseases). The Animal Health Trust at Newmarket is the OIE reference laboratory for equine influenza and equine rhinopneumonitis.

4.4 Currently the OIE relies on its reference laboratories and other experts to provide the technical input to its three technical commissions, which meet two or three times a year. It is reliant on the reference laboratories for the development of reagents and standards, and for the validation of standards and assays. But it does not have the resources to pay for these activities and therefore cannot set deadlines for completion. It does, however, use experts on an international front to handle the specific diseases. The OIE needs to evolve from a part-time reactive organisation reliant on goodwill, to a strong proactive international organisation by strengthening the Central Bureau and underpinning its Commissions and reference laboratories. With more full-time personnel it would be better able to use its international status. More frequent meetings of its commissions would speed up its response to disease crises and implement new science into regulations.

4.5 OIE reference laboratories within the EU receive some financial support from the EU, if they are also EU Reference Laboratories. It has been put to us that the financial support is inadequate and national sources have to be used to provide current services. Unfortunately, there are no significant financial allocations for developing new testing procedures and validating them for preparing sophisticated reagents, for collaborative studies on diagnosis and vaccines, or for work on List A diseases that might emerge in the EU. Yet it is these activities that are critical if new procedures are to evolve and become part of the OIE armoury.

(b) Trading and 'disease-free status'

4.6 To trade freely in animals or animal products, a country must be able to demonstrate that it is free from certain diseases. Any OIE Member State wishing to obtain recognition of freedom from a disease must demonstrate that it has:

- a reliable disease surveillance and reporting system,
- a reliable disease control and eradication programme, and
- a state veterinary service with independence and integrity.

4.7 In formal terms the OIE sets different levels of 'disease-free status' with the rules varying slightly between diseases. For foot-and-mouth diseases the levels are as listed in figure 4.1.

4.8 Until the end of May 2002, if a country or zone lost its disease-free status as the result of an outbreak of foot-and-mouth disease, disease-free status could only be regained under the conditions set out in figure 4.2. If a country or zone had used emergency vaccination it was faced with the choice of slaughtering all of the vaccinated animals, in which case it could re-apply for re-instatement three months after the last vaccinated animal was killed, or face a 12 month delay. Hence a 'vaccination-to-live' strategy would result in an additional 9 month delay over the use of a culling only policy.

4.9 In the light of advances in vaccines and diagnostics explained in Chapter 8, the OIE circulated proposals to include the additional conditions for regaining disease free status after emergency vaccination listed in figure 4.3. The proposals were supported by the General Assembly held in May 2002 and are now be part of the OIE International Code. These additional conditions reduce the delay following the use of emergency vaccination to 6 months.

(c) Trading within the EU

4.10 From the early days of the European Community, veterinary legislation sought to improve the health of the Community's livestock and to ensure that food of animal origin was safe. The first Community veterinary legislation on intra-Community trade in livestock was introduced in 1964, and rules governing the import of livestock into the Community were adopted in 1972. The Single European Act of 1987 restated the Community objective of a high status for animal and public health, and took the concept of removing obstacles to trade a step further, the major programme being to establish the internal market. For the veterinary sector this involved the development of new legislation to cover animal species and products not previously covered by legislation, and to provide the necessary mechanisms for the proper functioning of the internal market.

4.11 The creation of the single market in 1993 phased out veterinary frontier controls between Member States, and simultaneously a number of measures were adopted to prevent the spread of disease through trade in animals and products of animal origin. In principle, all new policies and legislation were based on the best available scientific knowledge. Key actions and measures to reduce trade barriers without lowering animal health safeguards included the following:

- guarantees as to the place of origin;
- stamping-out policy applied to all OIE List A disease;
- regionalisation policy applied in the event of epidemics;
- use of a computer system to provide advanced notification of animal movements (ANIMO, short for 'animal movement', which links all veterinary regions in the EU to ensure that the authorities at the destination are aware of the imminent arrival of animals);
- harmonising the use of vaccines;
- enhancing trust and confidence between Member States;
- improved external border inspection controls;
- a single crisis unit, with all the necessary powers, in charge of the eradication policy.

4.12 A number of these safeguards are particularly relevant to this Inquiry and it is worth stating more fully what the EU expects with regard to the following policies.

(i) Stamping out. '*…rapid elimination of the infectious agent (e.g. Foot-and-mouth disease). The policy calls for immediate action when a suspect case occurs and immediate depopulation when disease has been confirmed. The depopulation is applicable not only to the confirmed infected herd but also to all susceptible herds having an epidemiological link to the infected herd. The depopulation is accompanied by safe carcass disposal, cleansing and disinfection of infected premises and the implementation of certain other disease preventive measures'.* This policy applies to all 15 Member States of the EU, and Community financial support has been made available to enhance effective

Figure 4.1. Levels of 'disease-free status' for foot-and-mouth disease (FMD).

Status	Specific conditions to be met
FMD-free country without vaccination	• No outbreak for the past 12 months • No vaccination for at least 12 months • No importation of vaccinated animals since the cessation of vaccination
FMD-free country with vaccination	• No outbreak for the past two years • Routine vaccination with a vaccine complying with OIE standards • System of intensive surveillance for detection of viral activity
FMD-free zone without vaccination	• No outbreak for the past two years • No vaccination for at least 12 months • No importation of vaccinated animals since the cessation of vaccination • Surveillance zone, or physical or geographical barriers that separate the free zone from the infected territories
FMD-free zone with vaccination	• No outbreak for the past two years • Routine vaccination with a vaccine complying with OIE standards • System of intensive surveillance for detection of any viral activity • Buffer zone, or physical/geographical barriers separating the free zone from the infected territories

Figure 4.2. General conditions for regaining disease-free status after an outbreak of foot-and-mouth disease.

Status	Conditions for regaining status
Free country or zone without vaccination	• Three months after the last case where stamping out and serological surveillance are applied • *Or* three months after the slaughter of the last *vaccinated animal* where stamping out, serological surveillance and emergency vaccination are applied
Free country or zone with vaccination	• Twelve months after the last case where stamping out and serological surveillance are applied • *Or* two years after the last case where serological surveillance is applied without stamping out

Figure 4.3. Conditions for regaining disease-free status after an outbreak of foot-and-mouth disease. The use of emergency vaccination and non-structural protein testing—agreed on 28 May 2002.

Status	Conditions for regaining status
Free country or zone without vaccination	Six months after the last case or the last vaccination (according to the event that occurs latest), where the following are applied: • stamping out, • emergency vaccination, not followed by the slaughtering of all vaccinated animals, • serological surveillance; provided that a serological survey based on the detection of antibodies to non-structural proteins of foot-and-mouth disease virus demonstrates the absence of infection in the remaining vaccinated population
Free country or zone with vaccination	Six months after the last case where the following are applied: • stamping out, • serological surveillance, • emergency vaccination; provided that the a serological survey based on the detection of antibodies to non-structural proteins of foot-and-mouth disease virus demonstrates the absence of infection

implementation of the policy.

(ii) Regionalisation. The regionalisation policy is designed to restrict trade only from the designated region, while permitting trade (both national and international) to continue from the unaffected part of the Member State. It states, *'Regionalisation replaces the old policy applying measures at the borders of the affected country, a policy which is not compatible with the Single Market. In order to regionalise part of a Member State as distinct from a decision to block an entire Member State, a number of conditions must be met. These include:*

- *An in-depth epidemiological enquiry must have been carried out. The enquiry shall have provided sufficient information to enable the geographic limits of the affected region to be clearly defined.*
- *Active surveillance must be in place.*
- *Restrictions on movements out of and through the region must be well defined.*
- *The boundary of the region must be easily controlled.*
- *Eradication measures must allow the disease to be eradicated in a limited time.'*

(iii) Improved external border inspection controls. *'…that no Member State allows a consignment from a third country to be introduced on its territory without having been subjected to the veterinary checks required by the import legislation. Each Member State shall furthermore ensure that consignments are introduced only via an approved border inspection post. The requirements for the border inspection posts are harmonised by EU legislation and refer to requirements for facilities and staff and to the physical checks on consignments. The responsibility for the implementation of the import legislation and checks rests with the Member States.'*

4.13 Within the EU, the all-important recognition of disease-free status for a Member State or region after an outbreak takes account of the time factor referred to (by OIE) above, but greater importance is attached to the actual disease situation in the country in question and the results of post-disease surveillance. The European Commission, advised by the EU Standing Veterinary Committee (made up of the Chief Veterinary Officers of all member states), examines the cause of an outbreak or epidemic; the transmission of the infection, the effectiveness of the control measures applied, and the adequacy and scale of post-disease surveillance. In general the period required for regaining the status for trade *within the EU* is shorter than the period outlined by the OIE.

4.14 In the next chapter we consider further aspects of the EU's role in trade regulation.

5 Surveillance, biosecurity and livestock management

(a) Introduction

5.1 Global threats from exotic infectious diseases are not lessening, and nations that seek to remain disease-free must have, by definition, high-quality surveillance systems operating at international, national and local levels. This is self-evident and the question in the current context is whether the UK (and the EU) has world-class systems and, if not, how they can be improved. Science can have a role in providing answers, and our Inquiry considered how the existing precautionary structures – and there are many – could be strengthened to identify potential threats, to minimise the risks of disease introduction, and to ensure early recognition if the virus is imported. A number of bodies provided valuable opinions upon these matters, in particular the submissions and evidence from the IAH[1], VLA[2], Professor Pastoret[3], FAO[4] and the NFU[5]. We would also draw attention to *Getting ahead of the curve*[6], which considers the issues for human infectious diseases, and also a thoughtful review of surveillance systems for human diseases by MacLehose et al[7]. The authors of the latter argue for fundamental changes and most importantly for moving the system from an over-dependence upon the enthusiasm of individuals to a situation in which properly funded arrangements estimate risk and provide advice, using the most modern electronic communication technologies. These words apply as much to the surveillance of exotic infectious diseases in livestock as they do to human disease problems. There might also be a prospect of reducing the risk by improving livestock management practices, which we address later in this chapter.

(b) The global threat

5.2 Perceptive individuals and international bodies such as FAO and the WHO have observed for some years that trends were leading to a greater risk of importing exotic animal diseases. The Director General of FAO said (at the International Conference on Prevention and Control of Foot and Mouth Disease (FMD), Brussels, December 2001)[8], 'The last ten years have witnessed dramatic FMD epidemics resulting from the introduction of the disease into formerly free countries'. At the same conference, Ryan noted that 2000–01 had been the worst period for many years for FMD[8]. FAO believes that the EU is in a privileged position to promote international action against the disease, and urged the international community to establish an effective global information and early warning system on transboundary disease. The following factors contribute to the growing risk:

- A growing world demand for meat and meat products. Aggregate world meat consumption grows at 2–3% p.a. In developed countries meat consumption has not risen during the past 15 years but in the developing world it has doubled since 1980.[9]
- A growing international trade in meat and meat products. In 1999 the UK alone imported about 1.5 million tonnes of meat and 3.5 million tonnes of animal products (excluding butter).
- More livestock worldwide and increased movement of animals across national boundaries. The ease of transportation and new road systems, e.g. across the Sahara, increase the risk of invasion from infectious diseases. This includes FMD but also swine vesicular disease, classical swine fever, African swine fever, rinderpest, *peste des petits ruminants*, contagious bovine and caprine pleuropneumonias, and capripox (or goat pox).
- The growth in human travel. UK airlines doubled their available capacity in a decade; in 2000 there were 56 million visits by UK residents overseas, of which 5 million were to countries where many highly infectious animal diseases are endemic.
- Climate change. Bluetongue and West Nile viruses have spread as a result of global warming to the Mediterranean basin. Other diseases might also appear in the EU as a result of this trend, notably orbiviruses such as the Simbu serogroup (typified by Akabane virus), the epizootic haemorrhagic disease serogroup, African horse sickness and equine encephalitis.
- Exotic diseases entering a country, being eradicated from the livestock but becoming established in reservoirs of wild animals. Already this is creating outbreaks of classical swine fever because the virus is endemic in wild boar populations in Europe.
- Enlargement of international trading blocks. The EU, for instance, trades as a single entity and goods entering the Union at one point flow freely. The EU plans to enlarge further towards areas where many of the diseases are endemic.

- The intentional, malicious introduction of pathogens (bio-terrorism).

A risk analysis by FAO showed that 50% of the risk of introducing FMD to Europe was accounted for in three ways: illegal movements of livestock or animal products; foodstuffs carried by tourists or immigrants; and legal trade in animal products. The FAO commented: *'Strengthening of national border controls and of commodity inspections alone will not be enough to manage the risk of the international spread of FMD. …we need a global plan for the containment and progressive control of FMD at the source in the areas where it is still endemic'* (Africa, the Near East, Asia and South America) (EU Conference, December 2001).[8]

5.3 To illustrate the issues we consider two examples: FMD since 1990 and the northward spread of bluetongue (see also Chapter 3).

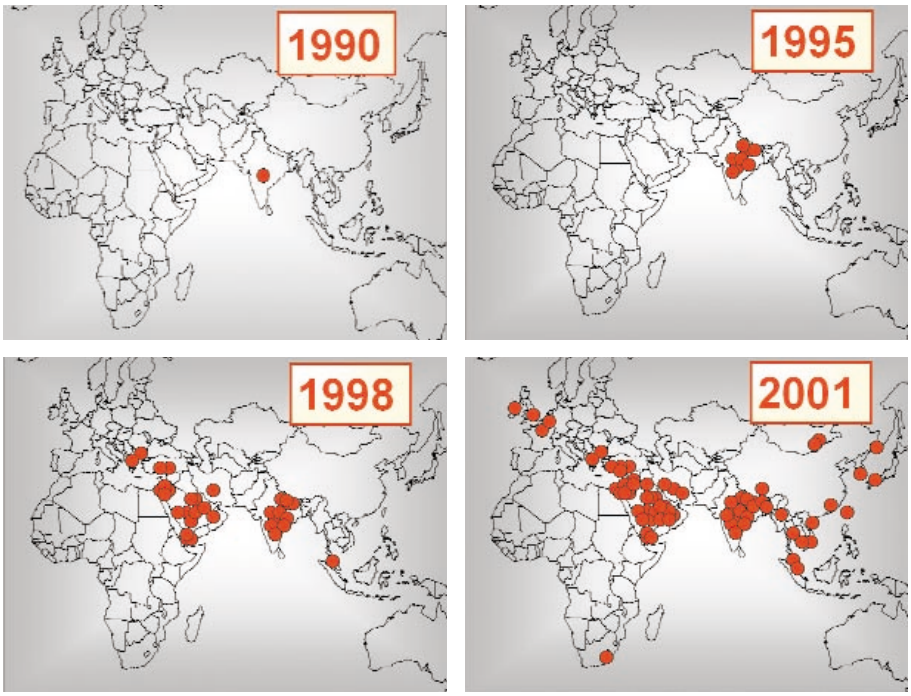
(i) FMD

5.4 The Type O pan-Asia strain of FMD virus, the strain in the 2001 UK outbreak, originated in Northern India in 1990 and has become pandemic, spreading across and becoming the dominant strain in the endemic regions of the Middle East, South Asia and South-East Asia. In 2000–01 it was successful in spreading great distances and affecting countries with a decades-long history of freedom from FMD, such as Japan, the Republic of Korea, Mongolia, South Africa, the UK, Ireland, France and The Netherlands. Figure 5.1 shows how this pandemic has developed and it could reasonably be claimed that the EU outbreak originating in the UK was only the latest in what is a worldwide outbreak of this particular viral strain (see also reference 10). Indeed, it raises the issue of the practical effectiveness of our early warning systems during 2000.

5.5 Another type O virus strain probably originated in West Africa and took advantage of the new trade routes between West Africa and North Africa resulting from the development of roads through the Sahara. Previously, the Sahara was thought to be an impenetrable barrier to the transmission of FMD because the transit times were too long for live animals to remain infectious. The end result was the outbreaks of this FMD viral strain in North Africa in 1999.

5.6 In 1998–2000 FMD outbreaks occurred in Iran, Turkey and Greece. It was of a type 1 Asian viral strain and is a good example of the significant role of economic forces in spreading disease. The price of a kilogram of meat in the markets of Istanbul was five times that on the Eastern border areas of Iran during that period; this demand gradient, coupled with improving political relations between Turkey and Iran as well as improved road infrastructure, led to an increase in trade, often illegal. FMD type Asia 1 spread inexorably across Iran and Turkey in farms located close to the main

Figure 5.1. The spread of Type O pan-Asia strain of FMD virus since 1990.



motorway network, until it finally infected Greece in 2000. It was the first outbreak of FMD type Asia 1 in Greece since 1961.

5.7 The FMD viral strain type SAT2 traditionally affects sub-Saharan Africa exclusively but it suddenly emerged in Saudi Arabia and Kuwait during 2000. The factors believed to be responsible for this spread were the increased trade in livestock from the horn of Africa to the Middle East.

5.8 As these examples illustrate, FMD is spread with increased trade. The pattern of spread has changed from the previous pattern of episodic 'natural spread' into adjacent countries and regions, to a pattern in which it jumps long distances to infect countries and regions distant from endemic areas. This further highlights the importance of effective early warning systems.

(ii) Bluetongue virus

5.9 Until the past three years or so, the occurrence of bluetongue in the eastern part of the Mediterranean basin was explained by sporadic introductions of infected *Culicoides* midge vectors into Turkey from the endemic areas of the Tigris and Euphrates rivers. Rarely did the virus move further into Greece and other countries; the virus did not over-winter to any significant extent and died out. However, a change was detected in 1998 when bluetongue virus was reported from several Greek islands, and in 1999 when an epidemic began of the same serotype in Bulgaria. Further west, separate epidemics have been associated with a different serotype of bluetongue in Tunisia and Algeria, spreading by infected vectors into Italy, France and Spain in 1999–2000. The pattern has continued in 2001, with further outbreaks being detected in Greece, Bulgaria, Kosovo and other surrounding countries.

5.10 In both foci the bluetongue virus seems to have over-wintered and reservoirs of infection might have been established. Studies on the vectors in Greece have also yielded some important new information indicating that some species of *Culicoides* not previously believed to transmit the infection might now be involved. The role of global warming not only in affecting the geographic range of vectors but also in the ability of the virus to multiply in different vectors requires attention.

5.11 Because of the well-documented threat of bluetongue continuing to progress northwards within Europe, governments should ensure that appropriate surveillance is put in place to track it and that contingency plans are formulated to limit the risks to Europe's extensive sheep population.

(c) International surveillance

5.12 As noted, FAO are calling for international action to meet the growing threat. But the challenges at the international level are twofold. The first is that two organisations are involved, each with a rather different focus: the OIE (effectively part of the World Trade Organization (WTO) system) and FAO (one of the UN family). Both perform some of the functions required, but neither has complete responsibility or the means to deliver the central function of international intelligence and early warning. The second is that both organisations are too dependent upon the altruism of nation states in supplying accurate information.

5.13 The OIE's 158 member countries undertake to report animal diseases detected on their territory; this information is disseminated either immediately or periodically, depending on the seriousness of the disease. Dissemination is via the OIE's web site, by email and in three publications: *Disease Information* (published weekly), *The OIE Bulletin* (published every two months) and the annual *World Animal Health* compilation.

5.14 The OIE has a distinct emphasis towards the protection of trade, and has developed rules that Member States can use to protect themselves from diseases without setting up unjustifiable barriers to trade.[11] Although these guidelines do not have the force of law they are recognised by the WTO as reference international sanitary rules, and member countries are unlikely to import animals or animal products that do not conform to the standards.

5.15 FAO's mission is to raise levels of nutrition and standards of living; to improve agricultural productivity; and to improve conditions of rural populations. It has 183 member countries. With its primary interest in agronomy, its interest in livestock disease is inevitably constrained. Nevertheless, in 1994 it established an Emergency Prevention System (EMPRES) for Transboundary Animal and Plant Pests and Diseases, to minimise the risk of animal disease emergencies. EMPRES has encouraged early warning systems to improve the awareness and knowledge of the distribution of disease or infection: GREP (the Global Rinderpest Eradication Programme) and RADISCON (the

regional animal surveillance and control network for North Africa, the East and the Arab peninsula). EMPRES publishes a quarterly surveillance bulletin, *The Transboundary Animal Disease Bulletin*. This contains few statistics but does contain useful background material based on field reports.

5.16 The European Commission for the Control of Foot-and-Mouth Disease (EUFMD; not to be confused with the Commission of the EU in Brussels) is a special body established under FAO in 1954, at a time when the disease was endemic in post-war Europe. It has 33 member countries covering most of Europe and acts as a forum to foster cooperation between Member States and to coordinate efforts to prevent and control FMD. EUFMD meetings are the main European fora for scientists working on FMD. The Commission has access to some funds for emergency vaccination programmes.

5.17 The overlap between FAO and the OIE was recognised in 1952 when the two organisations agreed a division of responsibilities:

- the OIE was to be responsible for collection and dissemination of information and statistics on the incidence and spread of livestock diseases throughout the world, promotion of meetings, dissemination of technical information, studying options for controlling the major diseases and tendering advice to FAO.
- FAO was to be responsible for assisting member governments in developing programmes for the control of important diseases, including the provision of technical assistance, collecting information on the incidence of livestock diseases from countries that are members of FAO but not the OIE, and providing such countries with OIE-type services.

5.18 We have concluded that in view of the heightened risks of infectious diseases spreading rapidly, this division of responsibility, as well as the underlying approaches, should be reviewed with the aim of strengthening its capability.

5.19 A problem in gathering the information to improve international awareness is that all bodies are largely dependent on Member States supplying accurate data. In practice, the quantity of such data varies widely. Given these problems, governments and international organisations look to other sources to fill the gaps and to provide immediate warning of disease threats. The main conduit for such information is the network of OIE reference laboratories (see Chapter 4). A good example is the OIE Reference Laboratory at Pirbright, focused on FMD. It undertakes a worldwide responsibility for the rapid identification of strain variations, allowing the development of appropriate serological techniques and vaccines (see also Chapter 8). It has built up considerable disease intelligence but is still over-dependent upon the goodwill of scientists and government institutes in those areas of the world where epidemics are occurring. This matter should also be considered in the review recommended above.

5.20 At present, early warnings reach governments by various routes, for example by publication in periodicals, and there can be delays in reporting disease because of potential adverse effects on a country's trade. More effective means need to be developed. We understand the US Department of Agriculture (USDA) has established a unit devoted to the collection and analysis of information related to foreign diseases. It scans databases, surveillance findings, media news, and academic and farming journals, identifying potential hazards to the USA. It contacts appropriate experts if necessary and performs rapid risk assessments. We recommend that the UK use its influence to persuade the EU to develop a similar centralised information system, incorporating all data, papers and other documents on livestock diseases, together with analysis and risk assessments.

(d) Imports: the rules for trade

5.21 Meat is the most significant livestock product for the movement of infectious disease agents around the world, whether traded legally or illegally. Increases in trade and personal travel heighten the risk of introducing diseases, and this is particularly true for FMD, CSF, African swine fever and swine vesicular disease. Many outbreaks are ascribed to the import of infected meat that somehow reaches livestock with live virus intact.

5.22 A regulatory system exists to control the trade in animals and animal products entering the EU from third countries.

- The European Commission is responsible for approving countries and facilities wishing to export to the EU, and this is performed by means of inspections. During the inspections attention is paid to the country's surveillance system, to the regularity and speed of reports to the OIE, and to passive and active surveillance in domesticated animals and in wildlife. When a country is approved, it must

report any confirmed occurrence of a List A disease to the European Commission within 24 hours.

- A country wanting to export cattle, small ruminants, pigs or untreated products of these species to the EU must have been free for the previous 12 months from rinderpest, FMD, contagious bovine pleuropneumonia, bluetongue, African swine fever, classical swine fever and Teschen diseases. It must have been free for the previous 6 months from contagious vesicular stomatitis, and vaccination must not have been carried out against these diseases during the preceding 12 months.
- A health certificate must accompany all animals and products of animal origin entering the EU. The principles of certification are those recommended by the OIE. The conditions for approved abattoirs and de-boning, cutting and processing plants are governed by legislation and on-the-spot inspections are conducted by the European Commission.
- Member States have to ensure that no consignment from a third country is introduced into its territory without having been subjected to the veterinary checks required by the import legislation, and must ensure that consignments are introduced only via an approved border inspection post. The harmonised EU legislation outlines the requirements for border inspection posts with regard to facilities and staff and the physical checks on consignments.
- Trade in live animals cannot be conducted without some element of risk, but the EU legislation governing the import of animals susceptible to FMD has been in place for about 25 years, and the European Commission believe that none of the consignments that have complied with the adopted import conditions have caused outbreaks in Member States of the EU.

5.23 Although we have no evidence that these systems are ineffective, there must be concerns about the number of infectious diseases entering the EU.

5.24 Intra-Community trade in animal products abides by the 'placing-on-the-market' provision. If a product is regarded as fit in one Member State, it is assumed to be fit for all. Responsibility for checks on fresh meat in the UK lies with the Food Standards Agency and the Meat Hygiene Service. Reliance is placed on commercial documentation and the oval health mark. Only random checks are permitted unless there is reasonable suspicion of illegal practice. Products not for human consumption (e.g. raw material for pet food) can be imported only from approved plants with the appropriate commercial documentation.

5.25 Controls on intra-Community trade in live animals are harmonised for cattle, sheep, pigs, poultry and horses. Additionally, a Directive known as the 'Balai Directive' imposes controls for Cervidae (the deer family) and zoo animals. Responsibility for control rests with the exporting Member State under directives. Health certificates indicate that the Member State or the exporting region of the Member State is free from OIE List A diseases. There are minimum residency requirements (apart from sheep that will not be used for breeding), and health requirements are graduated according to whether the exported animals are intended for breeding, fattening or slaughter. Clinical testing is normal for tuberculosis, brucellosis and enzootic bovine leucosis (EBL) in cattle, and Member States may require additional guarantees if they are free from a disease (e.g. Aujeszky's disease for pigs coming to the UK).

5.26 There is a legal obligation on the exporting Member State to notify the authority in the receiving Member State, via the ANIMO system (mentioned in Chapter 4), of consignments dispatched. Messages are exchanged between the regional veterinary staff (in the UK this is the Divisional Veterinary Manager). Animals must go straight to the notified destination but, for welfare reasons, may be rested at a staging point provided that they are kept separate from other animals. The competent authority in the receiving Member State is permitted to perform only random, non-discriminatory checks unless there is reason to suspect an illegal operation. Random checks in the UK are risk-based and targeted according to the disease situation in the exporting state.

5.27 Despite regulations designed to reduce the risk of importing infectious disease, during the past 30 years a number of infectious livestock diseases have been inported into the UK, mostly through imports of live animals. They include equine arteritis, contagious equine metritis, virulent infectious bovine rhinotracheitis, EBL (this has since been eradicated), *Leptospira hardjo, Haemophilus somnus, Mycoplasma bovis, Maedi visna*, caseous lymphadenitis, bovine immunodeficiency-like virus, porcine dermatitis and nephropathy syndrome / post-weaning multi-systemic wasting syndrome, blue ear disease in pigs (porcine reproductive and respiratory syndrome) and porcine influenza. With the exception of EBL these diseases are now

endemic. The demand for Canadian bulls in the 1970s resulted in the importation of five new infections. These are the penalties of trade.

5.28 A further source of risk brought to our attention is the risk of importing disease with exotic pets. This threat is not new but the scale can be alarming. In 1996 an estimated 7.3 million reptiles were kept as pets in the USA, and 93 000 cases of *Salmonella* infections are now attributable to reptile or amphibian contact. The Chief Medical Officer has also identified the potential health risks of *Salmonella* in the thousands of reptiles kept in the UK.

(e) Imports: policing the frontiers

5.29 Personal imports of meat from countries outside the EU are possible into the UK but are limited to 1 kg of fully heat-treated meat or meat products in a hermetically sealed container. EU rules do not require heat treatment. (Partly smoked products are the greatest hazard since certain viruses can exist in pig bones and meat for up to a year.) There is much anecdotal evidence, however, to suggest that the regulations are not enforced and are frequently ignored.

5.30 Many submissions to our Inquiry pleaded for a considerable strengthening in import controls. In particular the Association of Port Health Authorities in their evidence to us[12] said that '*it is relatively easy for illicit imports of products of animal origin to evade veterinary checks*', and that 'the current arrangements for preventing the illegal importation of products of animal origin are totally inadequate'. We were therefore pleased that in March 2002 DEFRA issued an Action Plan on Illegal Imports[13] committing the Government to a range of measures on illegal imports of animal and plant products. The aim is to 'reduce the risk of exotic animal and plant disease entering the country and then threatening our public health, and livestock, agriculture and horticulture industries'.

5.31 Key elements of the programme (lightly edited from the DEFRA Action Plan) are:

- *Risk assessment. To inform decisions about the nature of the risks from imports (personal and commercial), and the critical points at which action must be taken. As recommended by the Curry Commission on Farming and Food[14], a thorough risk assessment for meat imports led by the Veterinary Laboratories Agency (VLA) is underway. External stakeholder groups will be established to help inform and guide the risk assessment process. Targeted sample checks will be undertaken, in agreement with the enforcement agencies involved, where necessary to establish relevant risks.*
- *Cooperation between agencies. The government agencies involved in the importation of food and other goods are working closely together to achieve effective inter-agency coordination of checks. DEFRA will provide a published guide on the roles, responsibilities and powers of relevant agencies for preventing and detecting illegal consignments of products of animal origin.*
- *Effective intelligence to improve targeting of anti-smuggling measures. Action has already been taken to strengthen intelligence gathering and sharing between enforcement agencies. External stakeholder groups are being established to assist the Government in this work.*
- *Legal powers. Enforcement officers would be given new powers (already available to customs officers) in April to search baggage, etc., for illegal imports of meat.*
- *European action. Work with European authorities to clarify and potentially tighten enforcement of rules on third-country imports reaching the UK via other EU Member States, and to reform rules on personal imports.*
- *Publicity for the UK's rules on imports of animal and plant products, and the reasons for them. As results from the risk assessment and current market research on consumer impact come in, discussions will continue with representatives of airlines and others about how they can help.*
- *Deterrence. Work to ensure that passengers and shippers have a greater awareness of the consequences of bringing illegal food imports into the UK, and, taking account of the risk assessment, to establish the appropriate level and type of checks, and effective penalties.*
- *Other measures will include the pilot use of detector dogs to be underway by summer 2002; examination of the benefits of using X-ray equipment to scan containers and personal baggage to detect illegal imports, leading if successful to a trial; provision of 'amnesty' bins or equivalent measures to encourage the surrender of unintended illegal personal imports; to pursue amendment to the landing card to draw attention to import prohibitions; and research into available technologies that might help to detect illegal imports.*

5.32 We recommend the speedy implementation of DEFRA's Action Plan on Illegal Importing and we urge a much more coordinated approach by all

bodies – locally, nationally and internationally – concerned with import controls. In particular there must be much more effective awareness at airport arrivals. We draw attention to the import controls and awareness campaigns applied by major livestock-exporting countries such as Australia and New Zealand15; and offer the following points for DEFRA's consideration:

- EU rules on personal imports of meat or meat products from third countries should be harmonised and should allow the importation of such products only if they have been heat treated and are in sealed containers.
- Port health authorities need the same powers to control the import of products of plant origin as they have in controlling products of animal origin, because such consignments might be concealing animal products. Prior notification of consignments is required, and the cost of checks should be paid for by importers.
- There is a need for consistency in enforcing the law on importation. The responsibilities of enforcement authorities should be clarified and coordination between the various authorities should be improved. Costs should be met by central government(s).
- The development and application of biosensors—whether sentinel animals or mechanical devices—are needed to improve detection rates.
- Risk profiles for non-EU personal imports should be developed in the UK, but using this information might require considerable sensitivity and would have to be preceded by a sensible campaign of public awareness.
- More generally, quantative risk analysis of the range of different routes of entry is essential in order to target effort into priority areas.

(f) National surveillance

5.33 In this section we consider four separate but interconnected issues that we believe could significantly improve the nation's capacity to detect and contain an exotic disease invasion:
(i) responding to early warnings;
(ii) reducing animal movements;
(iii) surveillance on the farm: the farmer-veterinarian linkage; and
(iv) reducing risk on the farm: biosecurity and livestock management practices.

(i) Responding to early warnings

5.34 International disease surveillance must be constantly monitored by national machinery and, more importantly, it must lead to measured and considered decisions on what action is required.

5.35 Risk analysis should be applied more systematically, and at the highest levels of sophistication, to provide DEFRA with quantitative measures (including errors of probability) relating to risks of invasion from exotic diseases. We were pleased to learn that a risk analysis unit has been established within the VLA, and that unit provided valuable advice to our Inquiry. Risk analysis has also broadened in recent years to include predictive modelling and this offers the potential to identify crucial deficiencies and to provide insights into the chains of events necessary for a disease threat to become a reality. As explained in Chapter 6, models can be used to test 'what if' scenarios and thus to assess the relative benefits of different control measures; they mimic what happens in reality by describing mathematically the underlying biological processes.

5.36 During the past decade, risk analysis has also developed in relation to the international trade in livestock and livestock products. In this respect it is a tool intended to provide decision-makers with an objective and defensible assessment of the risks posed by a particular import proposal. Each disease is different and risk assessment must be related to the specific pathogen and exporting country or region. Import risk analysis must involve a detailed identification and evaluation of all the risks involved. It must therefore be continuous rather than an emergency activity that is undertaken only when the threat has already arrived.

5.37 Policy makers require not just risk assessments in absolute terms but relative assessments of all the various factors. This is a crucial point, especially in considering where and how to expend limited resources.

5.38 Consideration should be given to using elements of the control system (e.g. continuous diagnostic monitoring of milk and standstill arrangements; see Chapter 7 and 5.42) when formal risk assessments indicate a high or imminent risk of disease incursion.

(ii) Reducing animal movements

5.39 The most effective means of controlling widespread disease spreading during an outbreak is to reduce animal movements to a minimum and to institute standstill arrangements for animals brought onto a farm (Chapter 9). The history of exotic infectious disease spread shows many examples of long-distance jumps of the disease from the place where it was first detected (for example FMD in the UK in 1967 and 2001, and in The

Netherlands in 2001; and classical swine fever in The Netherlands and Italy in 1997.)

5.40 During an outbreak, few question whether such measures are necessary, although they do cause a range of genuine problems.[16] One of the most disturbing aspects of the 2001 FMD outbreak was the need to slaughter millions of animals that were trapped because of movement restrictions and/or other welfare problems (this included millions of lambs and calves 'at foot'). However, it is far more contentious whether movement controls and standstills should apply under normal farming conditions in the absence of disease outbreaks. From the standpoint of disease control, restricting the ability to move animals, particularly rapidly from holding to holding, will make it difficult for any outbreak to reach epidemic proportions.

5.41 Our Inquiry is well aware of the implications of standstill arrangements for local shows and tourism. Nevertheless any consideration should take account of the schemes introduced in the pig industry during the mid-1970s after swine vesicular disease. At the time these were strongly opposed but it was put to us by the Pig Veterinary Society[17] as follows:

> *The most frequent cause of spread of any infectious disease is by the movement of infected stock excreting virus, in the case of the List A diseases. This basic scientific fact was identified and acted upon in the pig sector by way of The Movement and Sale of Pigs Order 1975, amended and superseded more recently by PRIMO. This Order established the 21-day rule for pigs, which has been the basis upon which pig movements have been controlled in this country ever since. The principle is that no pig shall move off a premise for a period of at least 21 days after any pig has moved onto that premise except for licensed movements to slaughter-only market. The requirement for all pig movements to be licensed has meant that where it is suspected that infection may have been moved through a market, all other pigs in that market can be traced to their destination and from their origin where necessary. The 21-day rule is waived for pigs obtained from highly secure breeding stock supplying units being part of a recognised breeding pyramid which have been approved for the purpose by DEFRA (MAFF) veterinary staff. In addition, under the conditions of the Order, all pig movements are licensed and recorded by the producer, both records being kept for a period of at least 6 months. This order has served the pig industry well, and since 1975 no outbreak of notifiable disease has been confirmed in a source herd approved for this purpose. Another effect of this legislation is to render illegal the movement of pigs from market to market or through several holdings in a short space of time. Thus this one piece of legislation has slowed down the movements of pigs to the extent that any infectious disease has exceeded its incubation period long before pigs can move onto and infect another premise. A restriction on the speed of movement of other foot-and-mouth susceptible species should be a top priority. The industries concerned will resist this with strong and persuasive argument, as did the pig industry in 1975, but the pig industry has survived and benefited subsequently, interestingly with no major involvement in this foot-and-mouth outbreak after the index case. The sheep and cattle sectors will also adapt to and learn to appreciate this change.*

5.42 The precautionary principle would argue for such a permanent standstill period for all livestock species, as this would mean that an epidemic of the 2001 proportions would be unlikely to occur again, even if it were widely seeded at the outbreak. We realise, however, the complex issues involved in introducing such a standstill period in the sheep and cattle industries, in which vertical integration of the supply chains is much less developed, with breeding animals moving across the entire British Isles, and where animals move to more favourable conditions to be finished (for example from highland and hill country to the lowlands). Hence controls on animal movements for any significant period of time could be costly and difficult to implement, and could disrupt agricultural shows and other features of rural life. An analysis of tracing data at the start of the 2001 epidemic, before movement controls were in place, indicates that even a relatively short standstill period would have reduced significantly the size of the epidemic[18]. However, this effect is highly dependent on the particular circumstances, including the speed with which the first case is detected. To cover most eventualities, a period of 150–200% of the incubation period is required, hence the current 20 day period imposed at the start of the FMD epidemic. Quantitative risk assessments of the effect of shorter periods are difficult, but are urgently required to inform the

cost–benefit analyses for various standstill periods that DEFRA needs to undertake. If a permanent period of significantly less than 20 days is agreed, we believe that there should be arrangements for imposing a 20 day period at times when there is imminent risk of infections, such as when there is an outbreak elsewhere within the EU.

5.43 Traceability of animals is becoming more necessary as an adjunct to ensuring that there is knowledge about where animals move. The UK and the EU are likely to conclude that this is needed for sheep. From a scientific standpoint, traceability is viewed as primarily a policing function. Far more valuable in terms of disease control is an absolute reduction in animal movements.

5.44 For various reasons the number of abattoirs has decreased greatly in the UK from about 2 000 in 1970 to 411 in 2000.[19] Much has been written about how this might have caused increased animal movements to slaughterhouses and how this trend might be exacerbated by market competition between abattoirs. These issues need quantification and analysis before any conclusions can be drawn. As an editorial in the *Veterinary Record* points out[20], "it is now nearly seven years since EU Ministers agreed on international rules aimed at safeguarding the welfare of animals during transport, but improvements have been slow." The editorial urges veterinarians and the Government to improve the welfare of animals during transport. We recommend that DEFRA investigate all the issues connected with reducing animal movements and come forward with practicable solutions that strike the optimal balance between the legitimate interests of livestock owners, market systems and long-term disease control. In this investigation, DEFRA should bear in mind the following key points:

- finished/fattened animals from markets should be allowed to go only direct to slaughter or back to the holding from which they came that day;
- for both health (disease control) and welfare reasons, animals should be slaughtered as close as possible to the point of production;
- a period when animals may not move off a premises will significantly reduce the spread of infectious animal diseases.

5.45 This Inquiry did not consider the roles of markets in the cattle and sheep livestock industries but clearly, by bringing animals together in one place, markets can be a cause of disease spread. A variety of views were put to the Inquiry, ranging from encouraging the development of virtual markets, through to continuing with the large number of existing weekly markets (240 across Great Britain) and introducing a range of improvements that could reduce disease spread. These issues were addressed in detail by evidence from the auctioneers McCartneys[21]. We conclude that this is another area in which the Government, working with the relevent groups including—auctioneers and farmers, should develop more robust systems to balance freedom of movement against the need to reduce the spread of disease.

(iii) Surveillance on the farm: the farmer–veterinarian linkage

5.46 During an outbreak, once infection has been identified on a livestock unit (or in an area), biosecurity measures are critically important to contain the disease and to reduce the risks of onward transmission. This point is demonstrated by the fact that disease transmission was reduced once the strict and enforced 'Blue Box' restrictions were imposed in 2001. These controls included 'gate guards', movement logs, public road disinfection points and DEFRA officials travelling on milk tankers.

5.47 We reiterate the maxim that speed is essential in containing exotic diseases of the FMD or classical swine fever type. Virtually all outbreaks are examples in which surveillance was found wanting and the question for this Inquiry is whether the current system in Britain is as good as it can be, or needs to be. The centre of surveillance lies with the livestock farmer/owner aided by their veterinary practice. From all the evidence we received and the meetings and visits we held, we became convinced that the scale of interactions between farmer and veterinarian has diminished significantly and is affecting all aspects of animal health. This is compounded by changes in the charging regimes that make it more expensive to carry out laboratory studies of suspected disease conditions; this has happened at a time when profitability within the livestock industry – especially for cattle and sheep – is extremely low. We suggest that DEFRA, along with the industry, consumers and the veterinary profession, should revisit these issues, undertake a proper cost–benefit analysis and consider linkages between animal health arrangements on farms and any subsidy regime.

5.48 This could well begin by pursuing the Meah and Lewis consultation of 2000 on veterinary surveillance and revisiting the internal DEFRA (MAFF) report of Drummond[21].

5.49 Although the cornerstone of surveillance is the linkage between farmer and veterinarian, surveillance of the diseases in question is particularly difficult because the diseases are rare; they spread very rapidly in a susceptible population; and their clinical signs are not always evident. In such circumstances farmers and veterinarians tend not to think of a disease like FMD when animals are sick. Classical swine fever was absent from the country for 14 years before the outbreaks in 1999, and bluetongue in sheep has never been recorded in the UK. Maintaining 'disease awareness' for exotic diseases is a recognised problem in all countries from which the OIE's List A diseases are normally absent. The Australian authorities have commissioned a series of videos to raise national disease awareness. These describe the various exotic diseases that threaten Australia and are aimed at farmers and veterinarians. The USDA has prepared similar instructional videos. The IAH Pirbright has, over the years, produced videos, CD-ROMs and handbooks that describe FMD. DEFRA should clearly ensure that they have modern, well-produced videos and other materials available at all times for promoting disease awareness.

5.50 The VLA's evidence on surveillance in the context of exotic disease was particularly valuable[2]. They define *passive surveillance* as based on unsolicited information arising from activities that are not primarily intended to generate surveillance data. Its aims are to provide information on emerging diseases; to detect outbreaks of disease; and to uncover trends within endemic diseases. It does not provide sound information on the actual level of disease in a population of animals but is essential to detect outbreaks of new or emerging disease. *Targeted or active surveillance* is used to provide assurance of continuing freedom from disease, or to detect the emergence of an exotic disease as early as possible by targeting high-risk populations.

5.51 Both forms of surveillance are needed and yet they can fail. The recent epidemics of classical swine fever and FMD lead to two conclusions:

- passive surveillance will be effective only when there is dialogue between farmer, veterinarian, diagnostic laboratory and the relevant authority;
- passive surveillance can lose effectiveness if any one of the three components is missing. For example, the suspected index herd in the 2001 FMD outbreak was not detected early enough to prevent the spread of disease into neighbouring farms.

We have concluded that the current surveillance systems for exotic diseases are not as effective as they should be. Improving them is complex in view of the current financial plight of the livestock industries, but the core issues centre on the farmer–veterinarian linkage and the availability of diagnostics at cost-effective prices. We recommend that DEFRA take steps to ensure that all keepers of livestock (including that not kept for food production) are properly registered, and should submit to DEFRA each year the name of their nominated private veterinary surgeon and a health plan approved by the same veterinary surgeon.

(iv) Reducing risk on the farm: biosecurity and livestock management practices

5.52 As part of any national strategy to improve animal health[14] it is important to consider whether changes in livestock husbandry practices could reduce the risk of animals contracting exotic infectious diseases. This was argued by the pig and poultry veterinary associations, who are responsible for intensive livestock industries that are particularly at risk from disease spread[17,23], as well as by the Soil Association[24] and Norris[25]. The last two expressed the view that some current livestock practices (e.g. over-intensification, unnecessary movement of animals, feeding practices, animal welfare) can lead to a situation in which the risk of an animal catching and suffering from an exotic disease are increased. We concluded that the evidence is not sufficient to draw any firm conclusions except to observe that the issue warrants serious research, as does the problem of what to do with the very large quantities of waste food produced annually (estimated at around 50% of total production) whether or not it is fed to the animals. We discuss some of these points further below in the context of improving livestock management practices.

5.53 In part the issues fall under the general term 'biosecurity' and since last year this is something that all UK farmers are now familiar with. However, farmers tend to think of biosecurity in terms of 'sanitary barriers' – cleaning and disinfection at lane ends, shed entrances, and so on – whereas we believe the term should have a much wider application that includes:

- the prudent sourcing of stock,
- quarantine, and
- testing and vaccination.

5.54 Although farmers have practised some level of biosecurity in the past, it has usually been scant and informal in the sheep and cattle sectors. We have already noted that in the unsubsidised pig

and poultry industries, in contrast, the concept has been strongly embraced. The Danish pig rearers are quoted as having 'recognised the importance of animal health in market regulation and profit generation in due time'.[26] However, the current nature and practices of ruminant farming in the UK are not so easily addressed, partly because of the movement of animals (particularly breeding animals) between holdings, and partly because ruminant farming does not currently have the more rigid, pyramidal structure of the pig and poultry industries.

5.55 There have been advances, and papers by Wells[27], looking at biosecurity in US dairy herds, and Sanderson et al[28], investigating US beef suckler operations, conclude that management practices will have to be adjusted in the light of specific risk assessments of the likely introduction of infectious disease, and that producer education and veterinary involvement are important.

5.56 These papers addressed practices aimed at reducing the risks of introduction of infectious disease through imprudent sourcing of replacement stock, failure to quarantine, and failure to test or vaccinate, along with in-herd biosecurity such as management of the calving areas, manure management and sick cow management. Bates et al[29] looked at contact rates among livestock enterprises in California, especially with reference to potential FMD transmission, and concluded that direct and indirect contacts occur over a wide geographic area at a higher frequency on larger facilities. The authors suggest that a knowledge of contact rates would be useful for planning biosecurity as well as for modelling the transmission potential of FMDV.

5.57 The economic benefits of a more closed farming system have been modelled recently[30]. A simple static and deterministic mode was constructed of Dutch dairy farms by using known risk factors associated with bovine herpes virus 1 (BHV-1), onto which losses due to the introduction of bovine viral diarrhoea, *Leptospira hardjo* and *Salmonella dublin* were added. Although the most important risk factors were considered to be those involving direct animal-to-animal contact, management constraints did not always allow this risk to be eliminated completely, and other biosecurity measures such as vaccination, isolation and testing, and sanitary barriers are economically worthwhile. A further paper from the same group[31] looked at risk factors for the introduction of BHV-1 onto BHV-1-free dairy farms and showed that farms should prevent cattle, escaping or mingling with other cattle and that professional visitors to the farm (such as veterinarians, artificial insemination technicians and relief workers) should always wear protective farm clothing.

5.58 A paper by Leonard et al[32], which described a study of 249 dairy farms, concurred and suggested the principal factor giving rise to disease problems was the possibility of transferring disease through animal movements. The authors noted that the isolation of cattle after purchase or return from sales or markets was highly variable and quoted Pritchard[33], who argued that maintaining strict isolation for a four-week period after purchase is probably the most important single measure in preventing the introduction of disease when adding animals. A quarantine period gives the opportunity not only for new stock to display clinical signs of incubation, or latent disease, but also for the farmer or veterinarian to monitor the animals and for further testing or treatment to be undertaken. We addressed above the case for the wider application of the type of 'standstill' arrangements now in force in the pig industry.

5.59 Screening programmes are also needed to define the range of diseases that should be included before animals are introduced. This will be influenced by the economic or practical importance of the disease, the risk of introducing the disease, its epidemiology, the availability of low-cost and reliable tests, and whether or not the disease is already endemic in the population that is to be protected.[34]

5.60 Although on-farm quarantine screening with the use of appropriate tests might be useful, there are some diseases in which alternative strategies could be required in addition. These include examining the herd or flock of origin for evidence of disease and this is neatly demonstrated in figures 5.2 and 5.3. Figure 5.2 shows the probability of introducing Johne's disease onto a holding from different sources. Because of the recognised lack of sensitivity of currently available tests for Johne's disease (25% test sensitivity), it is safer to purchase animals from screened and monitored herds. Contrast this with figure 5.3, which demonstrates the effectiveness of testing individual cows for bovine viral diarrhoea before introduction (95% test sensitivity).[27]

5.61 Ford[35] looked at disinfection procedures for personnel and vehicles entering and leaving contaminated premises, and concluded that biosecurity measures were a small investment to keep a herd free of infectious disease although the cost–benefit balance of any biosecurity

Figure 5.2. Probability of purchasing one or more Mycobacterium paratuberculosis *infected cattle, by number and source of introduced cattle. (a) From Johne's infected herd. (b) From general population. (c) Testing from general population. (d) From level 1 herd. (e) From level 2 herd. (Modified from figures in Reference 27.)*

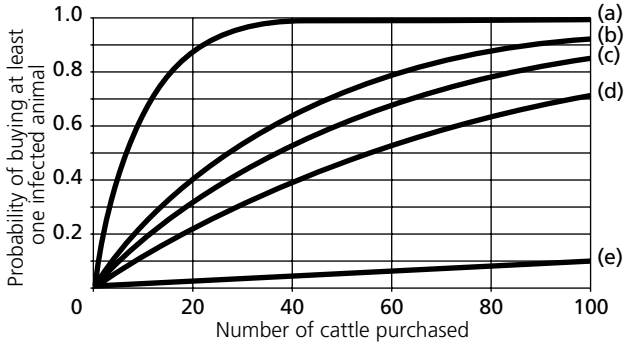
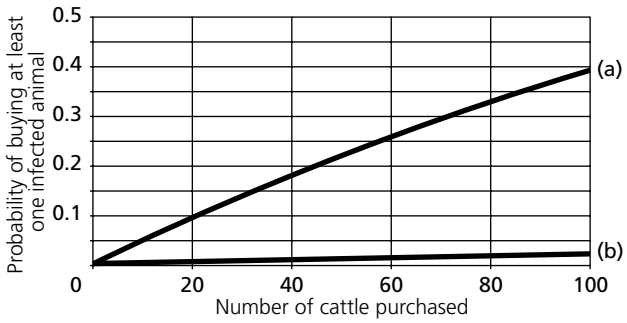


Figure 5.3. Probability of purchasing one or more cows persistently infected with bovine viral diarrhoea, by number and source of introduced cows. (a) From general population. (b) Testing from general population. (Also from Reference 27.)



system is between the economics associated with a particular type of production and the costs of implementation. Another aspect was emphasised by Vaillancourt[36], who concluded that the cost–benefit assessment of biosecurity measures is determined by people's perception of the level of risk to which they and their livestock are exposed. This is likely to influence their degree of compliance.

5.62 These relatively few studies demonstrate the potential value of improving biosecurity and 'disease minimisation on the farm'. We believe that this should receive specific encouragement through the establishment of an Applied Research Unit that would correlate and implement existing knowledge on the subjects of surveillance, biosecurity and livestock disease management. It would also coordinate and commission applied research specific to these fields and would also have an educational role. We envisage this Unit as a small multidisciplinary group, potentially attached to a research-rich university, based on the MRC model. It has become clear to us that there are parcels of information and knowledge in various places, but we feel that these must be integrated and consolidated into a legitimate recognised subject.

5.63 The remit for the new unit could include the following:

- research into the impact of different production systems, stress, and nutrition upon the animal's susceptibility to (and infectiousness with) defined infectious agents;
- the design of scientifically sound, comprehensive biosecurity systems at both national and local levels;
- the evaluation of management practices and possible improvements;
- research into the efficacy of various control methods in protecting farms from infections, and in preventing onward transmission from already infected units;
- research into the effects of various control options on the industry;
- informing and advising food and consumer agencies;
- educating and liaising with veterinarians, the livestock industries and the public.

(g) Recommendations

5.64 In the light of the points made in this chapter, we recommend that DEFRA should:

- **propose an EU-wide risk assessment unit and centralised database on surveillance and disease data, and a review of the bodies that provide early warning of animal disease threats; (R5.1)**
- **promote the speedy implementation of their Action Plan on illegal importing and of a much more coordinated approach at all levels by all bodies concerned with import control; (R5.2)**
- **investigate all the issues connected with reducing animal movements and come forward with practicable solutions that strike the optimal balance between the legitimate interests of livestock owners, market systems and long-term disease control; (R5.3)**

- **ensure that all keepers of livestock (including that not kept for food production) are properly registered and submit to DEFRA each year the name of their nominated private veterinary surgeon and a health plan approved by the same veterinary surgeon; (R5.4)**
- **establish an Applied Research Unit on Livestock Management Practices that will undertake or commission research leading to (i) the design of effective biosecurity measures against infectious animal diseases; and (ii) the design of livestock management structures and practices that improve animal health in terms of infectious diseases. (R5.5)**

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6 Epidemiology, data and modelling

(a) Introduction

6.1 To cope effectively with an outbreak of an infectious disease requires an understanding of its scale and spread, and this in turn requires access to high-quality data and analytical techniques for extracting the relevant information from those data. This chapter reviews what is needed in terms of data, statistical tools and mathematical models. It starts with a discussion of the factors that can combine to make outbreaks of infectious disease difficult to control, and enumerates the kinds of analyses needed to support decisions about controlling an outbreak of infection. It works through the different classes of input that feed into such analyses: real-time information about an ongoing epidemic; data about livestock, farms and geography; epidemiological understanding of the mechanisms of spread of infection; requirements and probable impact of possible control strategies; and finally logistical constraints on what can be achieved. There follows a discussion of the role of mathematical models in synthesising these disparate types of data into useful tools for comparing different control strategies. The chapter concludes with a discussion of what must be done in each of these areas to improve preparedness for future outbreaks.

6.2 Infectious disease outbreaks can be very variable in their characteristics and thus in the degree of effort needed to control them. Many submissions to this Inquiry pointed out that relatively light measures have controlled outbreaks of foot-and-mouth disease (FMD) before 2001. Indeed, an analysis of the 2001 UK FMD epidemic that looks separately at each regional outbreak shows a wide range of outcomes, with some local outbreaks dying out quite quickly and others rapidly escalating into large epidemics. Many factors combine to determine whether a particular outbreak is large or small. The stocking density and landscape setting of the farms are important, as are movements of potentially infected animals between sites. Meteorological conditions and the migrations of birds may be relevant in certain circumstances. With such a range of factors, coupled with random effects, even if regions seem identical the outcomes could well be different.

6.3 Epidemiology is the multidisciplinary study of the distribution and determinants of disease in populations, from the molecular level through field studies to modelling. The quality of the field data collected is critical to the quality of the policy decisions made and the value of analyses further down the line. Ultimately the role of epidemiology is to turn data into information which informs action and policy. Knowledge of the relevant details of a specific disease is essential, because the course of the infection within a host and the routes of transmission from one animal to another vary from one pathogen to the next. Much of this information can be gathered and held centrally, but it needs to be integrated rapidly with data on the current outbreak as they arrive. It is equally important to develop an understanding of how the various factors act in combination to affect the overall outcome.

6.4 Just as the natural course of any individual outbreak of infection is variable, so are the impact and resource requirements of different control strategies, and decisions about the most effective control procedures need to take account of such variability. To do so properly requires knowledge of the likely impact of a given intervention under different circumstances: local conditions, the particular character of the outbreak and the species that have been affected. Equally important is consideration of the constraints imposed by the availability of manpower and machinery. The disposition of those people who might be involved in diagnosis, culling and/or vaccination is closely involved with the control procedures to be used for the current outbreak. In a large outbreak the availability of equipment, disposal sites and overall command becomes a logistical operation of great complexity. The necessary preparedness and the integration depend on routine and recurring rehearsals of a range of alternative strategies at times when outbreaks of disease are not occurring.

6.5 The scientific technique employed in 2001 that had previously not been widely used in predicting and handling outbreaks of animal infectious disease was mathematical modelling. Those whose professional work (for example as farmers or veterinarians) is focused on individual animals can often—understandably—be mistrustful of complex and seemingly abstract mathematical models as guides to effective action on the ground, especially when this seems to contradict field experience. In other areas of science, the fruitful interplay between theory (often

expressed in sophisticated mathematical terms) and down-to-earth practicality is commonplace. Such an interplay puts, for instance, increasingly efficient aircraft in the sky, and increasingly advanced techniques in the surgical operating theatre. Modelling the dynamics of epidemics of infectious disease is a less developed discipline, but one that increasingly offers illuminating insights into the relative merits of alternative control strategies in outbreaks of infectious diseases in spatially and otherwise complex situations. All such models must, of course, base their fundamental structure and their relevant parameters firmly on observed facts and data. Ultimately they can only be trusted when we understand how the essentials of the conclusions relate to the initial assumptions.

(b) Why are some outbreaks of livestock infection difficult to control?

6.6 Epidemics of infectious diseases differ in both their underlying causes and their manifestation; in addition, epidemics caused by the agents considered here are rare. It thus becomes clear that experience and intuition alone are unlikely to be adequate guides to picking the best control strategies.

(i) How do epidemics grow and then decline?

6.7 Epidemics occur when new cases arise more quickly than they are removed. Conversely, epidemics go into decline when the rate of generating new cases is slower than the rate of removing cases. The rate of generating new cases depends upon the numbers or densities of susceptible and infectious individuals and the degree of contact between them. Eventually, epidemics decline for a variety of reasons:

- the number of susceptible individuals falls too low (either through the natural progression of the epidemic, as animals die or recover and are immune to further infection, or through interventions such as culling or vaccination);
- the contact rate between infected and susceptible individuals is lowered through improved biosecurity measures;
- the rate of removal of infected individuals is increased through faster detection and culling of infected farms or the pre-emptive culling of farms at high risk of having been infected.

6.8 The interplay of these factors is encapsulated in a single quantity called the effective reproduction ratio, often denoted by R. In essence this is the average number of individuals infected directly by a given infected individual during this individual's entire period of infectivity. If R is greater than one, the epidemic can grow, initially exponentially. If this happens, a quantity related to R, and in some ways more directly interpretable, is the doubling time of the epidemic in this initial phase (the time taken for the number of cases each day to double). For the recent FMD outbreak the initial doubling time was approximately 9 days. Eventually R decreases, either because of the effectiveness of control measures or because fewer individuals remain to be infected. The number of new cases per week reaches a peak and then declines until the end of the epidemic is reached. The aim of all control programmes is to reduce R. Only when R is below one (so that on average each case causes less than one new case) can an epidemic be claimed to be 'under control'.

6.9 The value of R at the time that the first infectious individual is introduced is known as the basic reproduction ratio, R_0; this can be used to determine whether or not a community can expect to withstand the introduction of new infections without experiencing a sustained epidemic. If the basic reproduction ratio can be kept below one by interventions such as vaccination, the community will be protected from major outbreaks of infection. This simple conceptual framework has been successfully applied in the design of many disease control programmes, such as mosquito control for malaria eradication, and vaccination rates for the control of infectious diseases of children and animal populations (see figure 6.6 below).

6.10 Because the progression of an epidemic is driven by so many different factors, the course of epidemics can be highly diverse. This is well illustrated by a comparison of the inferred mechanisms of spread of the most recent major epidemics of FMD in the UK (discussed in chapter 3.1). In the early stages of the 2001 epidemic, before the disease was identified, infected animals—particularly sheep—were transported around the country to markets and other farms (see figure 3.1). Before the first case was diagnosed, infection had already spread to 57 farms in 16 counties, and this spread had more than doubled by the time that a national movement ban was in place (J W Wilesmith, private communication, 2002). Furthermore, animal transport vehicles that had not been thoroughly cleaned and disinfected and had previously carried infected animals might have contributed to spreading disease. During this time R was high (figure 3.3). After this initial dispersal, most disease spread was local, from one farm to neighbouring premises by routes that have not

Figure 6.1. Local conditions determine the impact of a control policy. Because the rate of spread of infection varies locally, the same control policy does not have the same impact in all situations. As one example, areas with a low density of farms tend to have slower spread of infection (broken line in (a)) than areas where the landscape is more densely populated with farms (broken line in (b)). A control policy that acts to shorten the time from clinical signs to culling by 2 days might then be enough to end an epidemic in a low-density area (dotted line in (a)) but be insufficient to stop an epidemic of the same agent in the high-density area (dotted line in (b)).

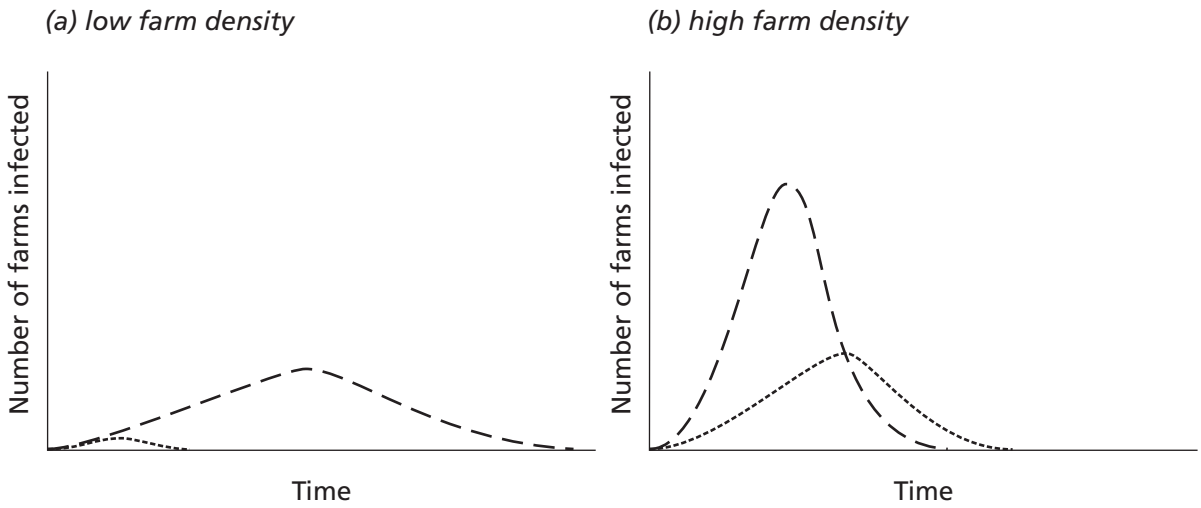
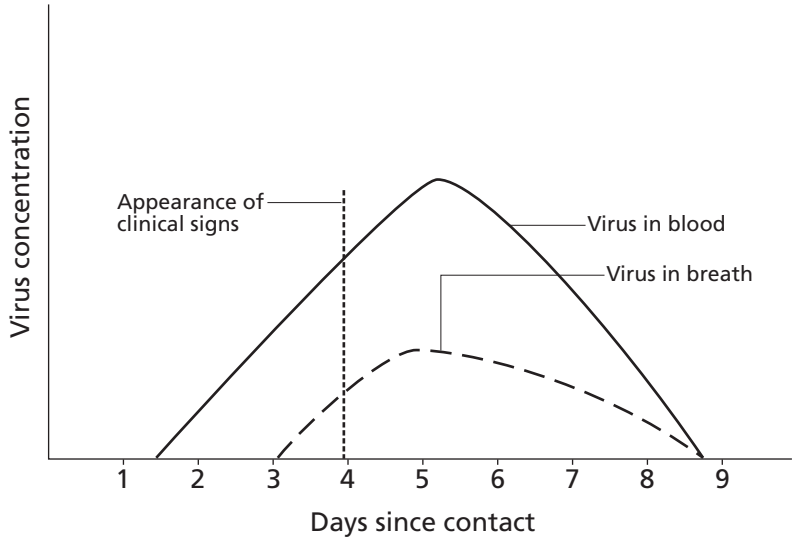


Figure 6.2. Development of virus in blood and breath relative to the appearance of clinical signs for a typical FMD infection in a single cow.



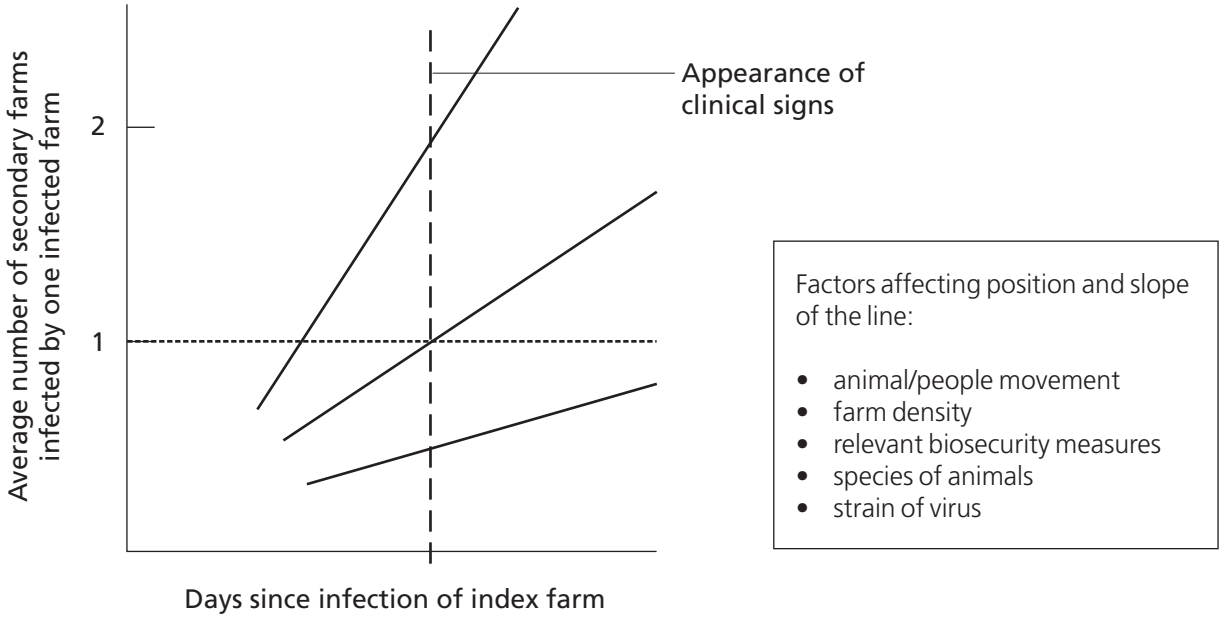
been adequately identified. *R* was significantly lower, but still greater than one.[1]

6.11 This inherent variability makes it very difficult to extrapolate experience from one epidemic to another. Thus, a control programme that is capable of rapidly terminating an epidemic in a region where infection spreads rather slowly can prove inadequate in an area where the natural rate of spread is faster (for example because farm densities are higher) (see figure 6.1).

(ii) The problem of early infectivity

6.12 An overriding difficulty in handling highly contagious animal diseases in unvaccinated populations is that infected animals may be infectious for several days before the appearance of clinical signs, and further days might pass before these signs are noticed. This is illustrated in figure 6.2, in which it can be seen that after infection there is a short period before the animal has any virus in its blood, and a further period before it becomes infectious by releasing virus in

Figure 6.3. The development through time of the number of secondary infections generated from one infected farm. The vertical line indicates the appearance of clinical signs. Three different degrees of infectiousness are illustrated. The lowest line represents the situation in which there is, for example, a low density of farms, and even several days after the appearance of clinical signs each infected farm has on average generated less than one secondary case. The highest line illustrates the situation in which there is a very high density of farms, and well before the appearance of clinical signs on average each infected farm has generated more than one secondary case. Factors other than density, including those shown in the box, can also determine the amount of infectivity and hence the position and slope of the line. For simplicity the degree of infectiousness is shown as being constant over the period some time before clinical signs appear until a few days afterwards. This was the picture obtained from preliminary analyses of the 2001 epidemic data, but requires further investigation. It is likely that the slope of each line increases until the farm is culled, at which point the slope decreases rapidly. Source: M Keeling, University of Warwick.



the breath and other excretions. This picture is complicated by variability in incubation periods (the time from infection to clinical signs) and by the secretion of virus by multiple routes. These subtleties are discussed, with reference to FMD virus, in Chapter 3.

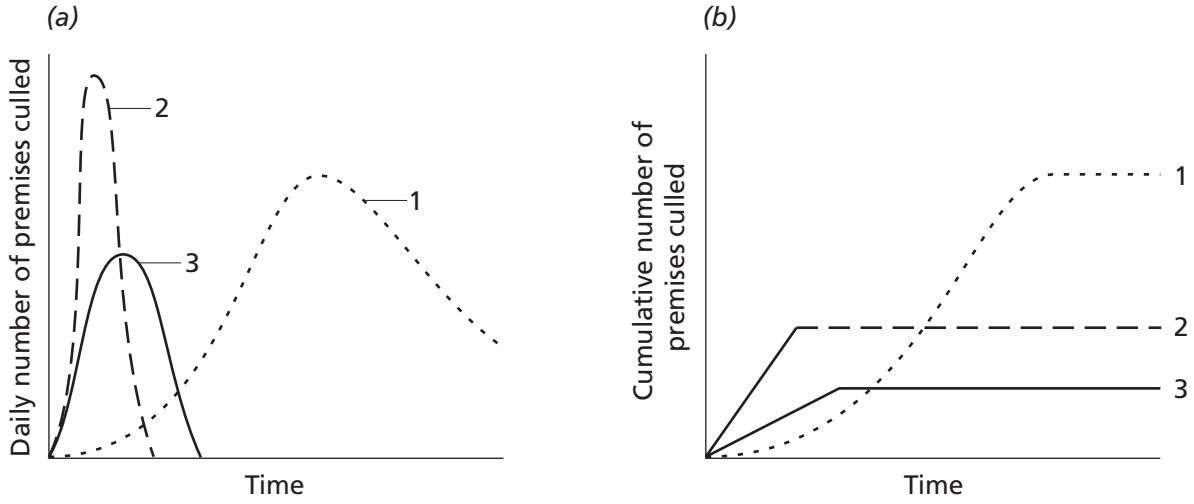
6.13 Hence, for many contagious viral diseases (including FMD), animals incubating the disease will have infected other animals on the same farm before disease is noticed. Consequently, all susceptible animals on a farm need to be treated as though they had been infected. A similar point applies to animals on neighbouring farms, which is why it has been usual to cull both the infected farm and any other farm suspected of having animals incubating the disease, because of either direct contact or indirect contact through wind, wild animals, and so on. An alternative would be to cull infected farms and to vaccinate around them so as to damp down viral spread; this is considered in Chapters 8 and 9.

6.14 The importance of rapid culling has been recognised for centuries* and was the subject of two papers[2,3] just before the 2001 epidemic. It is demonstrated in figure 6.3, which considers the development over time of the generation of secondary cases for three putative farm populations with different degrees of spread.

6.15 If farms are generating more than one secondary case before themselves showing clinical signs, it becomes necessary to introduce control

*A paper communicated to the Royal Society by Thomas Bates in 1714 ('A brief account of the contagious disease which raged among the milch cows near London in the year 1714.' *Phil. Trans. R. Soc. Lond.* **30**, 872–885 (1717–19)) reads in part as though it were only yesterday. In response to an outbreak of cattle plague (rinderpest) among the milk herds in Islington, a Mr Bates was charged with investigating and recommending immediate actions. The nation was forewarned because infections had occurred in continental Europe in the preceding years. He interviewed the farmers concerned, talked to veterinary experts and reported to the Lords Justices within one day. It was decided: (a) to purchase all cows in the herds affected, and to kill and burn them within 24 hours; (b) to fumigate all the cow sheds, which would be left unused, along with pastures, for three months; (c) to restrict the movements of persons looking after sick cattle; and (d) to report all future infections. Despite enacting these measures the cattle plague continued to spread, probably because many of the cowkeepers tried to keep the disease secret because it so badly affected their livelihood. So, towards the end of the epidemic, stronger measures were introduced to ensure compliance (though not as extreme as in one European country where farmers were ordered 'on pain of death' to kill their infected animals) and the animals were buried ten feet deep and covered in quicklime. In part, this last action was because in the absence of any scientific knowledge there were fears that the cattle plague might be connected to the Black Death, which had so devastated Britain 50 years previously.

Figure 6.4. Early and apparently harsh interventions can save animal lives in the long run. A control programme that stops an epidemic before it gets out of hand may seem harsh at the time, but by bringing an epidemic to a rapid close it can reduce the total number of animal lives lost. Where possible the strategy should be targeted to minimise the total number of premises culled. The figure shows two representations of the progress of an epidemic: the daily total number of farms culled (a) and the cumulative number of farms culled (b). Three possible interventions are compared in each as explained in paragraph 6.17. Under the first (some control: dotted line) where the effective reproduction number remains above one. The second (a harsh and quick control: dashed line) acts very rapidly to cull high risk premises and brings the epidemic under control very rapidly. The third (a more targeted approach: solid line) still brings the epidemic to a swift halt, but with fewer premises culled.



measures beyond the rapid culling of infected premises. If biosecurity measures are already at a maximum, these further measures must be either the rapid detection and culling of farms likely to have been infected by the index case, or vaccination.

6.16 Analysis of preliminary data supplied by DEFRA from the 2001 epidemic in the UK imply that early in the outbreak, on average, one infected premises had infected 1.2 other farms by 24 hours after its own infection was discovered. Thus, even a perfectly implemented cull of infected premises within 24 hours of discovery would not have controlled that epidemic until the disease itself had reduced the density of susceptible farms to such an extent that the epidemic ended naturally. In these circumstances additional control measures have to be rapidly chosen and implemented.

(iii) The benefits of decisive interventions

6.17 Figure 6.4 illustrates three control strategies for a rapidly evolving livestock infection, as follows:

- Strategy 1: this introduces some control measures such as rapid culling of infected farms, but these are insufficient to bring the epidemic under control and initially each infective premise infects more than one other premise before being culled. This strategy results in fewer premises being culled than if no control was exercised, but the epidemic could well progress for longer. The epidemic only comes to an end when the density of susceptible farms has fallen sufficiently. Only animals on infected farms are culled but the number is large.
- Strategy 2: this culls high risk premises associated with the infected premise quickly and harshly. This has two beneficial effects, first many infected premises are culled before disease is detected in them so the average duration of infection is greatly reduced, and secondly some uninfected farms are culled reducing the density of susceptible farms at highest risk of contracting infection in second and subsequent generations of infections, reducing the chance of onward spread. These harsh measures quickly bring the epidemic under control and because of this lead to a much smaller number of animals being culled overall. Although a substantial number of uninfected farms are culled, the total number of farms culled is greatly reduced.
- Strategy 3: this culls in a more targeted way and less harshly than strategy 2, but still brings the epidemic to a swift end, after a slightly longer period than strategy 2 and with more infected premises. However, the total number of premises culled is much smaller.

6.18 Provided sufficient logistical resources are available to carry it out strategy 3 appears superior to the others, but the challenge is to determine this optimum strategy for particular circumstances. Because of local differences in the rate of spread (fig 6.1) there will be no single optimal control strategy for the whole country. Furthermore, even with good data and quantitative modelling, it is difficult to determine the optimum strategy, and it will have to take account of, for example, possible air borne spread. Hence for safety's sake it is necessary to cull more farms than the theoretical optimum, if the epidemic is not to get out of control. Hence the importance of looking carefully at emergency vaccination.

6.19 A comparison of the three strategies in fig 6.4 illustrates a number of general points:

(i) An optimised strategy that rapidly terminates an epidemic can greatly reduce the number of farms infected and the number of farms culled—even if the epidemic is terminated by culling a large number of uninfected farms along with the infected farms. Farms culled that do not yet show symptoms are a mixture of premises incubating the disease and premises that were, at the time of culling, uninfected.

(ii) Strategies that bring the epidemic rapidly under control require significantly more animals to be culled early in the epidemic than those on the known infected premises. Such strategies are only viable if there are sufficient logistical resources to implement them and if there are adequate means of disposing of carcases. This is a key practical issue (see Chapter 9).

(iii) Many of the farms culled before becoming infected under strategies 2 and 3 would probably have become infected later under a strategy that failed to bring the disease under control (strategy 1).

(iv) Although strategy 3 culls more premises per infected premises than strategy 2, it is the strategy that leads to a shorter epidemic with fewer premises culled in total. Thus the ratio of premises culled per infected premises is not a good performance indicator when comparing different programmes of control. Indeed, performance measures are difficult to define.

6.20 It should also be noted that it is quite possible for an individual farm that is spared a proposed extended cull to remain subsequently uninfected, but this could well be because the sacrifice of its neighbours prevented second- or higher-generation transmission. One spared farm might not disable a 'firebreak', but too many exceptions waste the sacrifice of the culled farms.

6.21 Fewer resources are required to terminate an epidemic in its early stages, before the number of infected premises and associated high-risk premises has grown too large. Thus, a decision to bring in harsh control measures is easiest to implement if it is made very early on in the development of an epidemic, but requires a rapid mobilisation of resources.

6.22 The course of the epidemics outlined qualitatively in figures 6.1 and 6.4 has been greatly simplified by the assumption that each outbreak has only one epicentre. As has already been noted, at the start of the 2001 epidemic the disease was spread around the country and epidemics were widespread. The nationwide situation is therefore the sum of the epidemics within all these regions. It is important for these separate outbreaks to be investigated in detail, to explore whether it is appropriate to have different control strategies based on local circumstances.

6.23 The control procedures considered so far have assumed the use of culling as the main method of control combined with movement restrictions and current biosecurity measures. The prospects for involving emergency vaccination early in the outbreak are considered in Chapters 8 and 9. It is worth noting here that, because vaccination takes time to provide protection, vaccination strategies need to involve significantly more animals than culling-only strategies if they are to be equivalently effective. A key factor is therefore the ultimate fate of the vaccinated animals.

(c) Management and analysis of the data

6.24 It may be necessary to implement harsh control strategies early in the course of an epidemic, and such decisions might have to be made with incomplete information. Data analysis and modelling can assist decision making in such difficult circumstances.

(i) What can analyses offer?

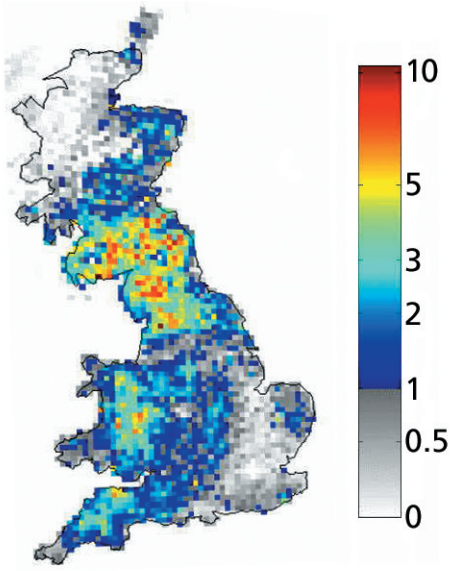
6.25 The effective control of any epidemic requires an accurate and up-to-date assessment of the factors governing its spread. Thus, the management and analysis of data gathered in the field are crucial. Before listing the data required, we consider the uses that those data will be put to.

- First, and possibly most importantly, up-to-date tables and plots of numbers of new cases per day or per week should be prepared, on a national, regional or local basis, distinguishing between confirmed and

suspected cases. It should be easy to produce maps showing this information and the positions of individual cases.

- Simple statistical methods are needed that will help in the interpretation of the above material and avoid over-interpretation when numbers are small. These should include estimates of the apparent doubling time and checks of whether the epidemic is still in an initial phase of exponential expansion.
- Assessments of geographical spread and maps or indicators of spatial incidence and spread, adjusted for the numbers of animals at risk, are crucial.
- The data provide vital information for tuning models, for testing their adequacy and for their further development. These models are essential tools if comparisons are to be made of the likely impact of different new control programmes.
- One succinct way of summarising the output of models is an 'R_0 map' (figure 6.5), which indicates the areas of the country at highest risk for the rapid dissemination of FMD.[4] The map is based on more information than just the densities of different livestock species in different areas, because it includes the transmission risks arising from the spatial arrangement of farms of different types. An obvious example is that a high-risk farm poses a much greater risk if it lies close to several other high-risk farms than if it is isolated in a sea of low-risk farms.
- Finally, data are needed for operational planning, for example for estimating the numbers of animals likely to be slaughtered or vaccinated in a particular geographical area in, say, the next one-week or two-week period. If the control strategy is being modified, modelling to take account of such changes is needed. In other cases simpler methods of forecasting, based on an empirical extrapolation of current trends by using statistical methods, may be as good as or better than the complex analyses of transmission dynamics.

Figure 6.5. R_0 map from the 2001 FMD epidemic.



Source: M Keeling, University of Warwick.

6.26 To offer these types of analyses a broad range of data have to be gathered, some in the teeth of an epidemic, but much of it beforehand. Those data types are easily classified as answers to the following five questions.

- Where are the cases?
- Where are all the other animals?
- How does the infectious agent spread?
- What control options are there?
- What are the logistical constraints?

(ii) Data quality and data management

6.27 The criteria for data might be easy to state, but they can be difficult to achieve. It is vital that the information recorded is simply and unambiguously defined and is accurate and timely, and that the burden on the farmer of collecting the data is minimised (for example by the use of sampling rather than a complete census). The collection, checking and storage of all these data is a major task, but it can be greatly aided by automatic data checking and other techniques developed for data validation in the commercial sector, for example. Furthermore it is a continuing task that requires continuous updating. In other areas of government, Britain has a good reputation for the excellence of its records. The expertise of bodies outside DEFRA should be called in at all stages of this data collection exercise, for example the Office of National Statistics could be asked to organise the auditing of the data.

6.28 Data should be stored in databases allowing speedy and flexible access. Ideally there should only be one database for all the information relevant to disease control, the 'infection risk database'. If this is not practicable, the different databases must be compatible and readily accessible in a transparent manner by all relevant parties, including researchers in the UK and elsewhere. The practicality of developing a comprehensive unified 'infection risk database' needs urgent exploration.

6.29 At the end of an epidemic a large quantity of new data has typically been accumulated. This might contain valuable new information about risk factors for disease. For example, what are the

influences on why some farms are affected and other, apparently similar, farms escape? Data protection issues are clearly important, but need to be interpreted in a manner consistent with protecting the public good. In the immediate future it is vital that information latent in the records of the recent FMD outbreak should be made widely available forthwith, subject to sensible but not over-burdensome confidentiality constraints, and studied thoroughly.

(d) Data requirements

6.30 The five questions posed in paragraph 6.26 define a large array of data that need to be gathered, checked and stored. Some of the data have to be collected during an outbreak, but most can be collected in advance. This section deals sequentially with the five classes of data required: case finding and contact tracing; livestock demography and farm geography; epidemiology and transmission; control options and their likely impact; and logistic constraints and capacity.

(i) Case finding and contact tracing

6.31 The process of tracing where an animal has been potentially infectious begins as soon as infectious disease has been diagnosed. Immediate enquiries by field epidemiologists involve obtaining from the livestock keeper a detailed history of the infected animal, its cohorts and other associated animals. Information on movements is routinely obtained from records held by markets, dealers and abattoirs, all of which have a statutory requirement to be kept. A careful examination is undertaken of individual animals and animal groups on the farm and further samples are collected. Identification of a dangerous contact depends on a good understanding of the routes of transmission of the disease. This understanding indicates which risk factors for onward transmission are associated with animals already identified as harbouring the disease. Much of the information on human and animal movements can be obtained only from interviews with livestock keepers and others in the locality. A knowledge of normal farming practices in that region is essential when gathering the relevant information and gaining the trust of interviewees.

6.32 Tracing dangerous contacts is difficult if the livestock keepers misconstrue the motives behind the questions that are put to them by field epidemiologists. The implications of a livestock owner admitting to having moved stock, or having had contact with potentially infected animals, can be severe and perceived as being against their own interests. In the early stages of the 2001 FMD epidemic it seems that on average only 0.8 dangerous contacts were identified per infected premises. That suggests that when infection was still spreading a significant number of infected premises were being missed and that the definition of dangerous contacts was not sufficiently sensitive.

6.33 An important step in contact tracing from an infected farm is to know how long that farm has been infected. In some infections, including FMD, this can be estimated from the appearance of the lesions harboured by infected animals. This can be a difficult task, particularly when the lesions have just developed or are healing. Some experience of clinical signs and pathology is necessary, or at least an ability to describe the lesions accurately. Ideally a small team, which should include personnel with experience, should perform this task to give consistency, but field staff might not be available, particularly early in an epidemic when this work is most important.

6.34 Once a farm has been identified as infected, its continuing status with regard to measures for infection risk must be monitored, recorded and input, with suitable checks, into the infection risk database, on which is also recorded the demographic and geographical properties of all the country's farms.

(ii) Livestock demography and farm geography

6.35 Information about a developing epidemic can be understood only in the context of a proper description of the livestock population and farming landscape in which it is taking place.

6.36 During the 2001 FMD epidemic in the UK it proved difficult to identify individual farms. A system that ought to have identified each farm by a unique 'county-parish-holding' (CPH) number failed in several respects. It will be necessary to establish a robust database of farms and their land that will permit a proper assessment of the lay-out of farms and hence of the risks of farms near to infected premises. Ideally, the results of formal analyses of the 2001 epidemic will be used in drawing up a list of those facts about farms that are relevant to predicting the likely spread of highly infectious viruses.

6.37 Animal demography is a crucial factor in the spread of an outbreak of infection. Routine annual census data provide the bedrock of

livestock demography, but they are not sufficient. More detailed population size data are needed that can account for fluctuations in population size and distribution during the course of a year and give a more detailed breakdown about the composition of the livestock population, for example by breed and age. It should be possible, through carefully structured surveys, to gather this more detailed information from only a sample of farms. Knowing where the animals are is one important aspect of livestock demography; another is the movement data that describe how they reached there and identify which other animals they mixed with on their way. Animal movements through trade (both through markets and by other routes) need to be described. Equally, the seasonal movements of animals that are a traditional part of the husbandry of our livestock need to be described quantitatively.

6.38 It should be possible to specify the location of animals much more finely than simply the address of their owner's holding. It is important to investigate whether this would make all analyses significantly more accurate (some holdings are very large, so the livestock could be many miles from the farmhouse) and a system to record fields rather than farms should be piloted. The updating of such a database at the time of an epidemic would be a massive task but, with sufficient input from local veterinary practises, it is conceivable. Models driven by such a system would have the advantage of proper spatial location of the livestock.

(iii) Epidemiology of transmission

6.39 The third component of understanding the spread of infection is a knowledge of the routes and rates of transmission of the agent.

6.40 An understanding of the factors determining the spread of infectious diseases is the essential first step towards devising effective control strategies. The factors determining the spread of the diseases under review are: the infectious process in an individual animal; the spread of infection within a herd or flock; the survival of the infectious agent outside the host; the spread of infection between flocks or herds by direct contact or indirectly via vectors; and the role of other host animals, particularly wildlife.

6.41 It is these biological processes that determine the routes (and rates) of transmission of infection. Although much is known about the basic biology of many of the pathogens considered here, detailed quantitative information about the probability and rates of spread by different pathways is scarce. One of the best sources of such information comes from the analysis of past epidemics. One classical design for such analyses is the case-control study in which farms that became infected are compared with farms that escaped infection, in the hope of finding a list of attributes that can predict which farms are most likely to become infected. This and other methods of formal statistical analysis offer the best hope of developing a rigorous definition of premises that are genuinely at high risk of being infected. These would represent 'evidence-based dangerous contacts'. The aim in identifying the factors that define such farms would be to find criteria for contact tracing that are more sensitive than those used until now.

6.42 In the 2001 FMD epidemic 80% of transmissions were classified as 'local spread'[5] without the actual mechanism of transmission being known. This high proportion of cases attributed to such vague causation reflects the limited knowledge base about the quantitative epidemiology of FMD**.** More research is required into the modes of transmission, both by experimental studies and by retrospective analysis of past epidemics.

(iv) Control options, and their likely impact and logistical requirements

6.43 The options for controlling an epidemic depend on the modes of transmission of the infectious agent. The possibilities always include biosecurity and culling of infected premises. As discussed above, it might be necessary to cull farms that are simply at high risk of having been infected. For many infectious agents vaccines are available, and vaccination (either routinely or as an emergency measure) becomes a possibility.

6.44 If the available control options are to be assessed in a rational way, the likely impact of each needs to be known. A combination of experimental investigation and retrospective analysis of past epidemics is required. The aim is to know how quickly and with what efficacy each control method can block onward transmission from infected farms or protect susceptible farms from becoming infected.

6.45 Although modelling can give some indication of the effectiveness of different control strategies, these cannot be pursued if adequate resources are not available. In addition to the estimates from the models of the numbers of animals affected by various control procedures, the necessary operational research models require basic logistic data. It is therefore necessary to collate fundamental logistic information about the personnel and equipment required to

perform a given infection control task at a given rate (such as the number of animals that can be vaccinated or culled by a team each day). Equally, the whereabouts and availability of personnel and equipment need to be known. This latter information changes during the course of an epidemic, so it needs to be stored in a manner that can easily be updated.

(e) Mathematical modelling

6.46 By their nature mathematical models are simplified abstractions of complex processes. The degree of that simplification varies. The very word 'model' implies an idealised and simplified representation of a complex process. Any model is at best a good approximation developed for a particular purpose. The level of simplification varies between models: some are deliberate oversimplifications (caricatures, aimed to capture essentials); others are more elaborate and complex (aimed at practical planning). The advantage of a well-chosen model is that it allows the essential features of a complex issue to be explored.

6.47 Models make abstractions of the real world in two ways. On the one hand, they must describe the *type* of interactions that can take place. This is reflected in the form of the different terms of the model. On the other hand, models have to specify the *rate* at which each interaction takes place; this is achieved by specifying numerical values for a small number of terms called the parameters.

6.48 Mathematical models of epidemics are sets of equations that describe the spread of infection. In most cases these are equations describing the rate of change in the number of individuals in each of a variety of groups. For the diseases considered here appropriate groups might include 'the susceptible farms', 'the infected farms that are not yet infectious' and 'the infectious farms that are not yet showing clinical signs'.

6.49 So, for example, a simple assumption is that for a single susceptible individual the current chance of becoming infected is proportional to the current number of infectious individuals. This is represented in a model by writing a term for the rate at which new cases are generated, which is equal to the product of three quantities: the number of susceptible individuals, the number of infectious individuals and the transmission rate between them. The whole term represents the generality of the assumption, and the transmission rate is the parameter, which is a large number for highly infectious agents and a smaller number for less infectious agents. The real transmission rate is also dependent on many other factors such as the distance between the two farms and the species mix on each farm.

6.50 By keeping track of the number of individuals in each group, models can calculate the predicted epidemics that are the logical consequence of the biological assumptions inherent in their equations and parameters. Models used to design real control programmes tend to be more complex than is implied by the simple examples described here. They need, for example, to keep track of the size and species mix of the farms in each group and their spatial location.

(i) Types of model

6.51 Mathematical models can be used to understand complex situations, plan interventions and predict future events; see figure 6.6 for some well-known examples. Of these three, accurate prediction is always the hardest objective. Mathematical models of the spread of infectious disease have a long history of fruitful application. Until recently these models have mostly been in human health, initially in connection with malaria (figure 6.6) and subsequently, for instance, in studies of the cyclical behaviour of measles epidemics and in finding suitable vaccination strategies for childhood and other diseases. Mathematical modelling in infectious diseases is a vibrant area of interdisciplinary research that is increasingly applied to the design of control strategies for a wide range of diseases.[6–10]

6.52 Models of epidemics received much public attention during the 2001 FMD outbreak. The models were used to guide policy decisions on the control of the disease through regular meetings with the Chief Scientific Adviser's science group. This was the first time that such models had been used for the control of FMD. Because they are likely to make an important contribution to the management of future epidemics, their nature, strengths and limitations should be broadly understood by a wide community of users.

6.53 Simple models have been designed to establish the broad features of an epidemic, namely the interaction between infected and susceptible individuals, and the dependence on the distribution of incubation periods and periods of infectivity. Such models often make drastic simplifications, for example by omitting specifically spatial aspects.

Figure 6.6. Case histories of the use of models of infectious disease for understanding, planning and predicting.

Modelling for understanding: the Ross–MacDonald malaria model

Sir Ronald Ross won the 1902 Nobel Prize in medicine for his discovery that mosquitoes spread malaria. In addition to this important practical discovery, Ross laid the foundations of the mathematical modelling of malaria. His mathematical models are described in a series of papers published about the time of World War I.[21] In the 1950s George MacDonald took the early work of Ross and developed it into what is now known as the Ross–MacDonald malaria model.[22] In 1952 MacDonald described Ross's analytical work in the following words.

> *Ross was working on a background of a study of epidemic malaria in Mauritius and set out to analyse probable happenings by mathematical means, trying to see how changes in the factors responsible would influence the amount of disease. He produced a general statement of epidemic happenings, and the theory of the critical level, which stated that for any given set of malariological circumstances some minimum number of mosquitoes, above zero, was needed to keep transmission going. If the numbers fell below this level, the amount of disease would progressively decrease to ultimate extinction, and if they were above, it would be maintained or exacerbated.*

The essential practical implication of Ross's theoretical work was that malaria could be controlled by reducing the number of mosquitoes, and that it could be eradicated without eliminating every last mosquito.

MacDonald took this idea of a threshold level of the mosquito population below which malaria could not persist and generalised it into the basic reproduction ratio of malaria, a single summary number defined as 'the number of infections distributed in a community as the direct result of the presence in it of a single primary non-immune case'. This single summary statistic combines descriptors of the biology and behaviour of mosquito, human and parasite. It is the direct precursor of the summary parameter called the basic reproduction ratio, R_0, used in recent models of the epidemiology of FMD.

Modelling for planning: the control of fox rabies

The control of rabies in the fox populations of Western Europe is one of the great current success stories of the control of veterinary infectious diseases. It has been made possible by the development of a new vaccine that is safe, cheap and can be delivered in bait that the foxes eat. Part of planning the control programme was calculating the proportion of foxes that had to be immunised.[23] Just as the Ross–MacDonald malaria model predicted that malaria transmission would cease below a threshold density of mosquitoes, simple rabies models predicted that, below a threshold density of susceptible foxes, rabies transmission would cease. The rabies models were based upon the important biological observation that foxes are the major reservoir species in Western Europe. Thus, if the fox population were so heavily vaccinated that it could not continue to support rabies transmission, rabies should die out. In large parts of Western Europe this is indeed what has happened.

But how many foxes must be vaccinated? Theory predicts that rabies transmission will be interrupted if the proportion, p, of immunised foxes exceeds

$$p = 1 - K_T/K.$$

Here, K_T is the threshold density of unvaccinated foxes that will allow continuing rabies transmission and K is the density of foxes that would be supported in the area targeted for vaccination if rabies were absent. The formula is derived from the simple idea that under vaccination, the density of unimmunised foxes (equal to $(1 - p)K$) must be at, or below, the threshold density for continuing transmission, K_T.

The density of foxes below which rabies fades away (K_T) can be estimated from epidemiological observation. In the calculations used to plan the control programme a value of $K_T = 0.4$ per square kilometre was used. In the largely rural regions targeted for vaccination the fox density is somewhere below 2 per square kilometre. Put together, these two estimates give a target level of immunisation of 80%.

What actually happened? A large-scale trial of fox immunisation, which achieved 81% coverage, led to the eradication of rabies from the trial area. The success of that trial led to the widespread adoption of the strategy of oral vaccination of wild fox populations across Western Europe[24] and, as a result, Belgium and Luxembourg became rabies-free during 2001, just part of a broad picture of dramatic reductions in rabies incidence across Western Europe.

Figure 6.6. *continued*

Modelling for prediction: New Zealand's measles epidemic

In 1996 the New Zealand Ministry of Health assisted by AgResearch (an independent research and development organisation in New Zealand) developed a mathematical model of measles transmission that predicted that New Zealand should expect a new measles epidemic (the first since 1991). In 1997, the predicted epidemic arrived.

The model was based on a standard description of the spread of childhood infectious disease.[25] It included different patterns of mixing between children of different ages, and seasonal variation in the rate of spread. The model was supported by excellent data provided by the Ministry of Health. The prediction was made on the basis of a calculation of the accumulated numbers of measles-susceptible children.

Although the predicted epidemic arrived a few months ahead of schedule, its anticipation meant that the spread of infection could be rapidly brought under control with obvious benefits for the population of New Zealand.

This case history provides an example of how a robust mathematical model, based upon high-quality data and developed in collaboration between civil servants and academic scientists, can be a useful tool for controlling an infectious disease.

6.54 The simplest models are to be contrasted with more elaborate 'quasi-realistic' models, one of whose main objects is to include as many as possible of the likely material factors influencing the process. Quasi-realistic models themselves vary in complexity. It is not necessarily true that the bigger and more complex (and hence superficially more realistic) the model the better. To obtain useful results each feature has to be specified numerically, typically by assigning values to one or more parameters. For example, infection from one geographical area to another requires specifying not only infection rates but also how they vary with distance. This requires suitable data or background biological knowledge. The performance of a model can be made worse if numbers have to be given to parameters about which little is known. Indeed, a critical aspect of the application of models to a particular epidemic is the availability of timely and accurate data to permit the fitting of key parameters, especially those characteristic of that particular epidemic and, where appropriate, their updating as the epidemic proceeds.

6.55 Simple models can sometimes be analysed by purely mathematical methods, so that the relations between assumptions and conclusions are fully understood. Quasi-realistic models require the use of modern computational methods. Some very complex models, such as those used in weather forecasting, can stretch even large computing facilities to their limits. The reliance on computers, rather than mathematical arguments, has the disadvantage that many separate runs of the computer might be needed to make comparisons, which in mathematical answers are captured in a single formula. However, computer-based answers do have a powerful advantage, especially with the use of specially designed graphical displays, because they can show the evolution in time and space of model epidemics and this can in principle enhance understanding, in particular of the comparative impact of different control measures. The counterbalancing concern is that, in the absence of an intuitive understanding of how the model's assumptions and parameters relate to the precise conclusions, detailed quantitative output from the models cannot always be trusted and needs to be thoroughly tested against data from a real epidemic.

6.56 Another classification of models is into those in which the element of chance enters specifically and those that give only average behaviour. The technical terms often used for these are stochastic and deterministic, respectively. Even though at a large-scale level, for example for a large region, the course of an epidemic can be quite predictable, at a very detailed level a strong element of chance is involved. Given two very similar farms in an area of high incidence, one may escape, the other not, for reasons that might be impossible to specify, certainly in any model.

6.57 Generally, the stochastic model is the more realistic, but the inclusion of chance in the model represents an additional level of complexity and sometimes compromises some other aspect of realism. Broadly, the inclusion of chance is important when small numbers of cases are involved, such as when attempting to predict the end of the epidemic or when predictions are required for very small geographical areas. In particular, the introduction of chance into the

Figure 6.7. Some uses of models in understanding disease

Before epidemics, models can be used

- to formulate needs for data collection;
- for performing 'what if' modelling, e.g.
  - comparing different control strategies,
  - predicting the spread of infection if introduced at different times of year,
  - assessing the necessary scale of emergency vaccination for different scenarios;
- as the basis for contingency planning and disease control exercises;
- for training vets and policy makers in the behaviour of epidemics.

During an epidemic, models can be used:

- to determine the risk of transmission in the area of identified infected premises on the basis of known risk factors;
- to compare the predicted impact of control options;
- to assess the operational requirements of different control options;
- to predict, with an assessment of uncertainty, future events such as the total number of infected premises.

model forces a recognition of the massive uncertainty involved. Otherwise, deterministic models might be adequate, provided always that the possibility of statistical fluctuation around the predicted outcomes is recognised; often the amount of this chance variation can be estimated roughly by simple statistical analysis. In principle all such predictions should have limits of error attached to them as a recognition of essential uncertainty.

6.58 Some of the uses of mathematical models for disease transmission are listed in figure 6.7.

6.59 Although most consideration has been given here to disease control models, it is important to recognise that models can also provide important insights in other areas. Animal disease epidemics can have an effect on more than just the farming community. A group at Wageningen University have developed an economic module to interface with the InterSpread package[11] to model the effect of disease on the economic activity of the country. Similarly, it is possible to provide other modules or to develop new models to explore other aspects of the effect of disease.

6.60 Specialist models can provide quantitative help at a local level**.** For example, under certain circumstances the FMD virus can be spread on the wind, sometimes over long distances; wind direction and speed, temperature, and level of moisture are all important factors in this spread. IAH Pirbright, together with the Meteorological Office and collaborators from Denmark, has developed a model for airborne dissemination of the virus over short and longer distances depending on the weather conditions[12]. Such models bring together meteorological analyses and estimates of the quantities of virus that are being released by infected animals before they have been slaughtered, and are tools in predicting where the infection might spread.

6.61 Because livestock live in relatively isolated and static groups (especially after the imposition of movement bans), spatial aspects of the spread of their infections are particularly important. There are many different approaches to making mathematical models of the spread of infection across a landscape, and this is a research area at the forefront of mathematical epidemiology. The modelling groups that contributed to the Chief Scientist's Advisory Group employed the following range of methods.

- At the most complex end of the scale was the simulation model called InterSpread.[13] This model specifies locations of farms and routes of transmission in great detail, although its precise workings are not published. The package had been purchased by the VLA, but not been fully implemented at the start of the 2001 epidemic. It was used throughout to keep track of the disease and to estimate the future progress of the epidemic. This model has been used by the Wageningen Group, for example in its study of the outbreak of CSF in The Netherlands in 1997.[14]
- The Cambridge group's model[4] also specified the exact location of all farms in a micro-simulation where the rate of spread from farm to farm was directly estimated from field data.
- Kao[15] made an abstraction of farming landscapes consisting of a hexagonal lattice that allowed the detailed investigation of the likely impact of local burnout on ending the epidemic.
- The Imperial College group does not include spatial structure explicitly in its models[16,18], but does make allowance for spatially localised disease transmission by modelling spatial contacts and tracking pairs of infected sites[17].

6.62 The first three of these models permit a stochastic element in their prediction. The Imperial College model was deterministic. A review by Kao[19] gives an account of the benefits and shortcomings of the different approaches.

(ii) Developing and testing models

6.63 If models are to deliver reliable forecasts in a timely manner they need to be developed and tested in advance of the next outbreak. It is not satisfactory to rely on the development of models during an outbreak, or even to make other than minor modifications to existing research tools. Mathematical models have many uses (see figure 6.7) and the quality of a model can be judged only in the context of the question that it sets out to address. Several different models are normally needed for a full understanding of the spread of any one pathogen. That is not to say, however, that all models are worth using. If models are to be used to support decisions on control policies, DEFRA needs to develop a process that highlights their strengths and weaknesses for use in disease control.

6.64 In so far as possible, the models need to be validated. This is a process in which a model's predictions are compared with a set of data different from that used in the original construction and fitting of the model. Because outbreaks of List A infectious diseases are rare, totally independent validation from first principles is not often possible, but some checks of model suitability remain very important. International collaborations that make models available for the analysis of infectious disease outbreaks in other countries offer an important forum for continuing validation and parameter estimation. There is scope for much more work here.

6.65 The models also need to have undergone substantial sensitivity analysis so that their dependence on uncertain parameters is well understood. A full account of this analysis, the assumptions underpinning the models and the validation of those assumptions should be published in the peer-reviewed scientific literature, together with the computer code for the models, so that their workings can be subjected to full analysis. *The computational implementation of each model needs to be kept up to date and functioning, to be properly documented, and to have an easily used interface.*

(iii) Use of models before the next outbreak

6.66 The main role of modelling before an outbreak is to analyse a wide range of possible control measures and so lay the foundation for a series of policy options to be included in contingency plans. But equally important is the role of modelling in enhancing the intuitive understanding of complex situations.

6.67 A great strength of mathematical models of infectious disease is their ability to address 'what-if' questions; for example, what will happen if all the animals within 3 km of an infected farm are culled? How does this compare with culling half the animals within 6 km or the emergency vaccination of all cattle within 10 km? If such questions are addressed with the use of well-tested models that are driven by reliable data, the models can be a powerful tool in the development of control strategies.

6.68 In this context it is important for the data on the 2001 FMD epidemic to be checked as far as possible, including reviewing the epidemiological tracings, and for this information to be made available to modelling teams, including those outside the UK. Only then will it be possible to check the basic assumptions used by the various modelling teams during the outbreak and to refine future strategies.

6.69 Further value can be obtained from models by adding the ability to handle information about the cost and feasibility of different interventions to make predictions that include economic indications.[14,20] Not surprisingly, such models frequently indicate that the earlier that infection is controlled, the cheaper the control will eventually be. Early intervention is therefore economically advantageous, and a delay of only a few days in the initiation of control measures can substantially increase the total cost.

6.70 A different style of 'what-if' question is 'What if infection gains access to this part of the country?' Models that include a spatial element can produce 'risk maps' as a very natural output. Such maps (for example the R_0 map for the 2001 UK FMD epidemic shown in figure 6.5) indicate the likely consequences of the spread of infection to different regions.

6.71 Models also have an important use in providing realistic scenarios for the testing and rehearsing of contingency plans.

(iv) Use of models during an outbreak

6.72 At the start of an outbreak there are few data on the spread of infection, and hence the control policies must be based on strategies determined beforehand for particular circumstances. Pre-planned scenarios could be devised that

investigated the impact of epidemics arising in different locations or at different times of the year. An appropriate R_0 map would be of value here, for example based on the animal population and husbandry situation for the particular time of year. It is also important to assess the likelihood of airborne spread and whether the relevant models should be activated. Finally, it is crucial to ensure that the data collection and integration into the infection risk database is set in train and is proceeding satisfactorily.

6.73 As far as possible, models should be established for each infectious disease of livestock of relevance to the UK, including checking the sensitivity of the model to the range of existing strains of the infectious agent. However, if an outbreak were to occur, it would be necessary to tune the model to the particular strain or sub-strain. This would require information from experiments undertaken at the OIE reference laboratories, with standard procedures or protocols.

6.74 An important role for models is to estimate the number of farms likely to be affected by particular control activities, such as culling or vaccination; this information is required for input into operational research models used to determine the necessary logistics.

6.75 As the epidemic progresses, more information becomes available, and careful data analysis and models can start checking on the progress of the disease and whether the control measures are working. At this stage they can also be used to test the effect of tailoring the control measures to local circumstances and the characteristics of the outbreak.

(f) Future requirements

6.76 It is essential to have available sufficient staff of field epidemiologists trained and experienced in the relevant disease. Improved technological support in the field would aid in the task of tracking infection, including better tools for molecular epidemiology to allow genomic tracing; improved communications technologies to permit the electronic transfer of images for viewing centrally by experienced pathologists, which would be beneficial both for second-opinion diagnosis and for determining the age of lesions; and improved and quicker diagnostics as discussed in chapter 7.

6.77 It is crucially important to have a soundly based method of determining those premises that have traditionally been defined as 'dangerous contacts'. Research is needed to investigate whether more formal data analysis and mathematical modelling can assist field epidemiology in this endeavour. This could generate broad rules for defining 'local farms at risk'. The aim of such a definition would be to achieve a greater sensitivity than current contact tracing (i.e. to detect a larger proportion of secondary infections) and greater specificity than simple contiguity and 3 km definitions (i.e. to condemn a smaller number of uninfected farms).

6.78 In the past, infectious diseases of livestock have attracted relatively little attention in the world of mathematical modelling of infection, lagging behind advances in the field of human infections. However, because it is possible to perform experimental infections on animals, it should eventually be possible to make models of livestock infectious disease that are more reliable than those in human epidemiology because the models can be properly parametrised and then tested. However, to do this even for one infectious agent is a major undertaking, and the OIE's List A contains 15 different agents.

6.79 A library of mathematical models needs developing that can be called upon when making policy decisions. The UK is well supplied with modellers of infectious diseases, with links to colleagues elsewhere in Europe and worldwide. However, their expertise must be engaged in developing and validating the appropriate models.

6.80 One way of encouraging modellers to develop this library is to give them access to the necessary data. The data sets collected in the 2001 FMD epidemic in the UK can be expected to encourage the theoretical study of spatio-temporal aspects of epidemiological processes, including the associated important problems of statistical fitting and interpretation. With some careful steering, some of that theoretical work may turn into useful tools for policy planning. It is of paramount importance that a range of research groups, with different modelling approaches and different types of expertise, be engaged in the development of new models, collaborating where possible with practising veterinarians. The establishment of a new Epidemiology Laboratory in Denmark is worth noting as one route forward. The laboratory is funded jointly by the Danish Government and the livestock industry. Within this laboratory, all academic researchers can propose research projects to gain access to raw data on livestock infectious disease surveillance, on condition that they make their results available in the peer-reviewed literature. Funds are available to support such research. In the UK it

might be appropriate for there to be a 'virtual laboratory' for modelling that can encompass a range of groups (see chapter 10). We also stress the need for DEFRA or their agencies to develop their own expertise in this area.

6.81 We would emphasize again that it would be wrong to assume that mathematical models of FMD are now 'finished' or 'ready'. Uncertainties still exist about many of the important underlying processes that such models represent. As these uncertainties are tackled the models can be expected to move towards becoming increasingly useful tools for defining disease control strategies. Because FMD infects so many species of livestock, good FMD models will be useful as starting templates for developing models of other infections. Experience from human infections gives cause for genuine optimism that mathematical models can have an important role in understanding the epidemiology of infectious diseases of livestock. If they can be combined with high-quality, relevant data that are available in a timely manner, they ought to become a welcome weapon in the armoury of those charged with protecting our livestock from these devastating events.

6.82 The purpose of this chapter is to set out the quantitative dimension to infectious disease control. We believe that this has considerable potential, which now needs to be introduced systematically throughout veterinary medicine. We recommend that DEFRA should:

- **establish a review to determine the data required for informing policy both before and during epidemics of infectious diseases. This review should involve all those likely to be involved with disease control, including modelling teams, and cover:**
  - **information to be collected on a routine basis, and how this can be kept up to date;**
  - **information to be collected during the outbreak;**
  - **incorporation of the data into a central database;**
  - **use of modern techniques for real time data capture and verification; (R6.1)**
- **commission research to improve the methodology used to identify dangerous contacts; (R6.2)**
- **undertake a major research programme into the potential of mathematical modelling for understanding the quantitative aspects of animal disease. Mathematical models can be used both in preparing for outbreaks (including evaluating alternative strategies) and during the course of controlling an epidemic; (R6.3)**
- **ensure that the data from the 2001 epidemic are checked and then made widely available, while ensuring that any data protection issues are resolved. (R6.4)**

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7 Diagnosis

(a) Introduction

7.1 Rapid local diagnosis using the latest scientific techniques could help to reduce the scale of future outbreaks of infectious diseases and should permit the improved targeting of scarce resources (such as slaughter or vaccination teams). National diagnostic services capable of an immediate response to outbreak situations, supported by automated high-throughput diagnostic systems, are essential. Development of tests applicable to on-farm diagnosis and linked to a central database could improve diagnostic accuracy as well as speed, thereby reducing the extent of culling or emergency vaccination needed. It is necessary to diagnose samples from the index case at the OIE reference laboratory, but during an outbreak the emphasis must be on moving the rapid diagnosis of subsequent cases closer to outbreak sites and onto farms (pen-side tests). Medical needs and now the threat of malicious release have driven research into new ways of detecting microbial agents; the animal disease research community must follow these methods and seek to apply them in combating diseases such as foot-and-mouth disease (FMD). The international bodies must collaborate to find quicker ways of validating the best of these new tests for animal diseases, including providing proper resources for those organisations charged with the task.

7.2 This chapter describes the general principles of diagnosis, taking the case of FMD to address the phases of clinical diagnosis, laboratory testing, diagnosis during an outbreak and surveillance after an outbreak. We look at the scope for improved diagnostics, the potential for pen-side tests, and the prospects of novel approaches in biosensors and medical diagnostics. We raise the general issues of maintaining a state of preparedness and of integrating diagnosis to rapid response, and we consider the issue of intensifying surveillance in high-risk periods for detecting impending disease outbreaks. Finally, we briefly cover diagnostic issues relating to other diseases in the OIE's List A, and draw some general conclusions.

(b) The general principles

7.3 The essential elements of diagnosis in the context of infectious disease control are sensitivity, specificity and speed. This requires excellent communication between farmers, veterinarians, diagnostic scientists in the laboratory, and pathologists, as well as an understanding of each other's roles in the phases of:

- immediate reporting of disease to the veterinarian by the farmer;
- clinical examination to provide a presumptive diagnosis, and the immediate collection and submission of appropriate specimens to the laboratory; and
- rapid processing of specimens in the laboratory and immediate reporting.

7.4 There are many notifiable diseases (see Chapter 3) and their clinical diagnosis is often challenging. In an outbreak situation the need to act on suspicion is crucial, but suspected clinical diagnoses require laboratory confirmation. Diagnosis itself involves several steps:

- an understanding of the husbandry system, as well as an understanding of the specific farm;
- an assessment of the number of animals affected, their epidemiological groups, and the speed and nature of the signs described;
- a thorough clinical examination; and
- a thorough understanding of the lesions in the particular disease and a knowledge of the 'normal' situation in uninfected livestock.

7.5 There is no substitute for clinical experience, but the very rarity of these notifiable List A diseases (and their consequences) means that diagnosis is dependent upon the laboratory's identifying the specific microorganism (or their consequential effects) and a pathological analysis of tissue. Occasionally, of course, the overt lesions or signs are so unmistakeable that a diagnosis is immediate. If a sick animal dies, pathological and laboratory investigations are essential. Because the diseases are notifiable, the State Veterinary Service (SVS) must be notified immediately that there is a suspicion of their presence, and instructions will be issued for the submission of appropriate samples to the reference laboratories.

7.6 Laboratory diagnosis still rests partly upon showing the presence of the infecting microorganism – virus or bacterium – after culture, and partly on detecting antibodies in the blood of the host. Culture is undertaken from specimens taken early in infection when the organism is invading and replicating. Antibody

Figure 7.1. Methods for virus detection used in human and veterinary medicine.

Method	Time	Sensitivity (minimum no. of particles per ml or no. of nucleic acid molecules per ml)	Specificity
Cell culture	2–21 days	High ($10^{1.5}$–10^{3})	Low (high after typing)
Electron microscopy (EM, IEM, SPIEM)	<30 minutes	Low (10^{6})	Low (higher after IEM or SPIEM)
Immunofluorescence test	1 hour	Medium (10^{4}–10^{5})	High (depending on fluorescence in labelled antibody used)
Enzyme-linked immunosorbent assay (ELISA) for antigen	1.5–2 hours	Medium (10^{5})	Medium (not for subtypes)
PCR/RT-PCR (qualitative) (single, multiplex, nested)	6–16 hours	High (particularly nested PCR) (10^{1}–10^{2})	High (particularly nested PCR)
PCR/RT-PCR (quantitative) (real-time)	1–2 days	High	High
PCR/RT-PCR followed by sequencing of amplicon	2–5 days	High (10^{2}–10^{3})	High

Abbreviations: IEM, immunoelectron microscopy; SPIEM, solid-phase IEM; RT-PCR, Reverse transcriptase polymerase chain reaction.

cannot be detected until the animal has mounted an immune response in the convalescent phase of disease, and it therefore provides a retrospective diagnosis. Culture techniques are usually highly sensitive, theoretically requiring only one infectious particle in the sample to replicate under suitable growth conditions. Bacteria grow in a nutrient agar, whereas viruses require living cells within which to replicate. The infectious agent might be detectable within 24 hours or less but if the organism grows slowly or is present in only very small amounts, it might be detectable only after multiple cycles of replication, which could take several days or weeks. Thus, although positive results are sometimes achievable within 24 hours, negative results might not be confirmed for a week or more, and this has a great impact on disease control measures such as the isolation of high-risk groups of animals and restrictions on movement. This problem has stimulated the application of new scientific methods to speed up detection and to increase sensitivity and specificity. Examples of tests developed for the detection of human viruses are given in figure 7.1, which illustrates the variation in time, sensitivity and specificity of various approaches.

7.7 Two main approaches have been applied to viral diseases:

(i) *Detection of the nucleic acid* that makes up the genetic material of the organism. This can be achieved by amplifying minute amounts of the pathogen's nucleic acid by an enzyme so that the amplified product, now consisting of millions of copies, can be detected and characterised. This technique is known as polymerase chain reaction (PCR) when applied to DNA and RT (reverse-transcription)-PCR when applied to RNA. It is RT-PCR that is required for detecting FMD virus (FMDV). The technique is so sensitive that fewer than 10 molecules of DNA (or 20 molecules of RNA) in the original sample can be detected by this method and it is widely used in medical diagnosis, routine screening of blood donations and in forensic DNA tests.

(ii) *Direct detection of the protein antigens* with the use of specific antibodies, which recognise and capture the antigens. There are a variety of techniques to visualise the captured material, involving enzyme-induced colour changes to permit amplification of the signal. These tests are known as antigen-capture enzyme-linked immunosorbent assays (ELISAs).

7.8 Both approaches have been refined to suit the characteristics of particular diseases and the samples to be investigated. However, the overriding objectives remain:

- sensitivity—the ability to detect very small numbers of microorganisms within a specimen;
- specificity—to identify pathogens accurately, avoiding false positives or negatives;
- speed—to ensure that disease control strategies can be implemented with minimum delay.

Both approaches have their advantages and disadvantages, which affect the choice of test for particular circumstances (figure 7.1). PCR is extremely sensitive and ideal for samples containing very little virus, which might or might not be infectious. However, unless stringent measures are adopted, cross-contamination with amplified nucleic acid can occur in laboratories handling large numbers of samples, and this can result in false positive results. Similar problems would be encountered in a contaminated field environment. Until recently the technology of PCR has been exclusively laboratory based, but modern developments are now overcoming some of the contamination problems; portable field equipment for PCR tests has been designed to allow 'patient-side' or 'on-farm' testing.[1] the reliability and quality assurance issues of such systems are being addressed. ELISAs are less sensitive for virus detection but are adaptable to easily used 'dipstick' technologies, which facilitate pen-side testing and can give very rapid (less than 30 minutes) results, albeit within the limits of the sensitivity and specificity of the test. They are very attractive to veterinarians. Costs also need to be taken into account and related to the benefits.

7.9 In spite of the development of these methods, the culture and characterisation of disease-causing agents remain important for some diseases and are performed in parallel with other rapid diagnostic measures. For example, when human influenza occurs, new isolates are examined to check for mutation (antigenic drift) and ascertain whether the strain can be controlled by the vaccines available. The need to update vaccine strains is therefore recognized. When Newcastle disease outbreaks occur in chickens, it is important to define the pathogenicity of the isolate, because different control measures are activated depending on the properties of the virus. With FMDV, the current approach to ensure that the best match of vaccine strain is selected for emergency vaccination is to conduct ELISAs with a range of specific antisera against vaccine strains within the same serotype.

7.10 Scientific advances have also been made in developing rapid serological tests to measure the antibodies produced later in the disease. Classically, neutralisation tests have been conducted to detect the presence of antibodies against viruses, but they require the growth of virus in cells and the measurement of inhibition of virus growth by antibody. Such tests are technically demanding and take several days to complete, but they remain the 'gold standard' for some microorganisms. In general, however, they have been replaced by ELISAs in which viral antigen of a known identity is used to capture antibody in the blood sample; and the antibody's presence is detected by measuring enzyme-induced colour changes. This test is effectively the converse of the antigen-detection ELISA. Alternatively, in competition ELISAs the test sample displaces an enzyme-tagged reference antiserum. Antibody tests are useful for screening large numbers of blood samples to discover whether infection has occurred in herds in the absence of observed clinical signs and are essential in the final phase of disease control, post-disease surveillance.

7.11 Many of these modern techniques lend themselves to automation, allowing large numbers of tests to be conducted rapidly. This development greatly enhances our capacity for surveillance and disease control, particularly in detecting incursions of new diseases into a population or in monitoring the efficacy of vaccination programmes. Investment in capital equipment, staff training and quality assurance schemes are essential if the veterinary world is to benefit from these advances, particularly the increased sensitivity and speed of diagnosis provided by automated PCR systems.

7.12 A vital aspect of diagnosis is the standardisation of technical approaches within and between laboratories so that the resulting data are reliable and their sensitivity and specificity can be compared. For veterinary work this is particularly important with regard to international disease control, for which regulations affecting the movement of animals and trade are predicated on the serological status of animals to List A diseases. The Standards Commission of the OIE has a key role in this, prescribing internationally accepted tests and facilitating the preparation of international reference reagents, but it needs to be better resourced if the processes are to be speeded up.

(c) The specific diagnosis of foot-and-mouth disease (FMD)

7.13 This section deals with the diagnosis of FMD in detail. This involves the four distinct phases mentioned previously, some of which are laid down in internationally agreed regulations. We look at each phase in turn before considering the prospects for faster laboratory testing, the use of pen-side tests during an outbreak, and continuous monitoring systems applicable to post-outbreak surveillance and periods of imminent risk.

(i) Clinical diagnosis in the field

7.14 Recognition of the disease among stock remains the most important step and depends crucially on disease awareness by the farmer and good communications between farmer and veterinarian. For FMD it requires examination of the visible mucous membranes of the conjunctiva, nose, mouth, tongue and eyes and the external surface of the body and limbs. Recognition in cattle and pigs is usually relatively easy but is more difficult in sheep, in which infection can be sub-clinical. Diagnosis has to differentiate between lesions in cattle caused by FMD, mucosal disease, malignant catarrhal fever, trauma, tooth eruptions, and so on. Similarly, in sheep, it must differentiate between FMD, contagious ecthyma (also known as Orf), staphylococcal mouth lesions, traumatic injuries, foot disease, and so on. Host-specific adaptations of FMD occur and recognition problems can arise with mixed-species exposure. For example, type O Taiwan/97 FMDV was very virulent for pigs but did not cause reported cases in cattle or sheep and failed to infect experimental cattle by contact.[2] During the 2001 UK outbreak, 'classical' FMDV-like signs were observed in deer that were subsequently not considered to be infected, thus underlining the need for laboratory diagnosis.[3] A far better understanding of the causes of vesicular lesions would greatly assist differential diagnosis and improve the targeting of resources to genuine FMDV outbreaks.

7.15 In FMD, cattle develop fever, severe depression, anorexia and a sudden cessation in milk production; after 1 or 2 days they develop lesions on the tongue, lips, gums, dental pads and the interdigital spaces. Stomatitis is painful and causes excessive salivation, while foot lesions result in lameness. The morbidity rate is high but, except in young calves, the mortality rate is low. Pigs become febrile, anorexic, acutely lame and recumbent. Vesicle development on the feet is pronounced and in severe cases there may be sloughing of the hoof. Vesicles may occur on the snout. The mortality rate can be high in young animals. Sheep become lame in increasing numbers as infection moves through the flock, but other signs might not be readily noticed. Affected animals are febrile and the feet are hot. Vesicle formation in the mouth is rare because the superficial epithelium is thin and easily ruptured; however, erosions may be found especially on the dental pad.

7.16 Successful laboratory diagnosis is dependent on the collection of appropriate samples in the acute phase of the disease, and rapid transport to the laboratory on transport medium under cool conditions is the ideal. Epithelium, vesicular and throat fluid and blood may all yield virus; however, the concentration of virus is lower from aged lesions or blood. Skill in recognising and sampling acute lesions is a cornerstone of virus detection and, when fully developed, specific pen-side tests would increase the detection rate.

(ii) Laboratory diagnosis of the index case

7.17 Once an initial case is suspected on a farm, the next step is the rapid confirmation or negation of the putative clinical diagnosis of FMDV by detecting (or failing to detect) virus in vesicular fluid, epithelial tissue or blood. If the result is positive the 'index case' must be characterised to determine the strain type for the purposes of emergency vaccination and later diagnoses. These investigations must be performed in an OIE reference laboratory (in the UK this is the IAH Laboratory at Pirbright) using internationally agreed techniques. The traditional and most sensitive method for the detection of FMD is virus isolation in primary bovine thyroid cell cultures, but it can take up to 4 days for virus growth to develop. Virus is confirmed by using a type-specific ELISA,[4] which relies on the use of a type-specific antibody to trap antigen (virus) in the sample specimen. The trapped antigen is then detected with the use of type-specific antisera and indicated by an enzyme-induced colour change. The ELISA, which detects all seven serotypes in parallel, takes about 3 hours to complete and is relatively rapid. The ELISA can be used directly on pathological samples but not on blood or milk, and although highly specific it is somewhat insensitive, particularly if material from aged lesions is submitted. For bovine samples some 10–20% of positive samples are not detected with the direct ELISA, whereas for sheep this increases to about 40%.[5]

7.18 In practice, the Pirbright Laboratory undertakes an immediate antigen-detection ELISA and follows this with virus isolation on 'negative-in-ELISA' samples. This requires maintaining large-scale tissue culture facilities during an outbreak. Positive confirmatory results become available at any time between 3 hours and 4 days after receipt of the sample, with negative results being declared after 4 days. Fortunately, at the outset of the 2001 outbreak, the index samples gave a positive ELISA result without the need for amplification in cell culture. It is obvious that rapid diagnosis would greatly enhance our ability to control the spread of infection.

7.19 International back-tracing is required after an outbreak, so the genetic sequence of part of the

VP1 gene of the FMDV is analysed immediately. The sequence is compared with a database of previously sequenced viruses of known serotype and origin. Within a serotype, viruses can be allocated to topotypes, which represent independent genetic lineages occurring within different geographical regions. This helps to determine the possible geographical origin of the particular strain of virus involved in an outbreak. For serotype O there are eight topotypes.[6]

7.20 Although it is recognised that the diagnostic techniques used for confirmation of the index case must follow international standards and link to trade regulatory matters and decisions on compensation, there are new techniques (as yet unvalidated by the OIE) that hold the prospect for more rapid diagnosis and therefore the ability to reduce secondary spread. In particular a variety of RT-PCR systems have been developed (see below) and their refinement and implementation constitute one way of improving the handling of future outbreaks.

(iii) Diagnosis during an outbreak

7.21 During an outbreak many suspected clinical cases (particularly in sheep) require laboratory confirmation, for which a variety of virus detection systems can be used. In the 2001 outbreak the antigen ELISA and virus isolation techniques described above were used routinely, but RT-PCR was also applied on a limited scale for critical samples and for research purposes. There is a strong case for using RT-PCR on a larger scale in future FMDV outbreaks, and this is considered in paragraph 7.29. In particular, RT-PCR has the potential to transform the diagnostic rate in sheep by testing blood samples in the absence of suitable epithelial lesions.

7.22 Infected herds can also be identified by detecting antibodies that develop 5–8 days after initial infection. In situations when the infection spreads slowly and might be sub-clinical, such as among grazing sheep, this approach can be valuable in identifying infected flocks. The reference test is the type-specific neutralising antibody test, but more rapid ELISAs are now widely used.

7.23 Until the end of 2001 the liquid-phase blocking ELISA[7] was the only OIE-prescribed test for certifying livestock free from infection for the purposes of international trade, or for providing legal evidence relating to the status of livestock within the UK. Because this test does produce a significant number of false positive results (up to 4%), any positive liquid-phase blocking ELISA has to be confirmed by a virus neutralisation (VN) test. However, this VN test can also produce results in an inconclusive range between positive and negative if the antibody titre is too low, or if the laboratory strain of FMDV used in the test is not identical to the field strain. In view of these limitations a more specific solid-phase competition ELISA for antibody was developed[8] and validated jointly by the IAH, the Veterinary Laboratories Agency (VLA) and DEFRA during 2001.[9] This test has now been accepted by the OIE Standards Commission as an additional approved test for international trade. The test has sensitivity of 100% with experimental sheep samples collected 8 days after infection and when the cut-off point is set to 50–60% inhibition. The test specificity was 97.46% at 50% inhibition, and 99.8% specific at 60% inhibition.

(iv) Surveillance after an outbreak

7.24 After an outbreak has ostensibly been brought to an end, a period of surveillance is required under international regulations, to ensure that no further pockets of infection remain. This requires both clinical surveillance and laboratory testing, and rapid diagnosis is essential to stamp out flare-ups. The solid-phase competition ELISA was used extensively to screen sheep flocks during 2001 and 2002. Diagnostic needs will be different if a 'vaccination to live' policy is introduced as part of the control strategy (Chapters 8 and 9), as the solid-phase competition ELISA, based on virus structural capsid proteins, does not differentiate between vaccinated and infected animals. A differential test, which measures antibodies against non-structural proteins as opposed to capsid antigens, will be required, and such tests have been developed but not fully validated.[10] In South America similar tests are used routinely for the surveillance of infection in vaccinated populations.[11] These issues are covered further in Chapters 8 and 9.

(d) Improved diagnostics and their potential application to the decentralisation of diagnosis

(i) The need for speed

7.25 Many of those who gave evidence emphasised the need to speed up diagnosis in an outbreak situation and pointed out the value of introducing rapid, reliable diagnosis on farms, to reduce and in some cases avoid delays associated with the process of referral to DEFRA headquarters. At present, *'Confirmation of the presence of FMD (on the farm) is made by veterinary staff at the SVS headquarters and*

leads to a declaration that the holding is an IP [infected premises]. This is based on discussion with the reporting veterinarian, including a detailed description of the clinical signs, and a review and agreement of a second veterinary surgeon at SVS headquarters. Laboratory tests are used for confirmation of the first case identified and cases with an equivocal clinical picture'.[12] This process inevitably takes time, and at the height of an outbreak such as that in the UK in 2001, time becomes a limiting factor in control. Meanwhile, virus is spreading from the infected animals. This process needs to be speeded up while ensuring reliability and maintaining the security of diagnosis and overall control. One potential way of improving confidence and speed of decision-making would be to transmit digital photographic images between farms and DEFRA. Of even more value, however, would be portable diagnostic tests on farms.

(ii) PCR methods for the detection of nucleic acid

7.26 *Automated PCR in human medicine.* In human diagnostic laboratories, PCR is replacing culture techniques for virus detection. Quantitative PCR machines such as the TaqMan and LightCycler are used in medicine, and for some pathogens they give results in less than an hour. LightCycler assays are in routine use in several human diagnostic laboratories for pathogens including cytomegalovirus, tuberculosis, HIV and herpes simplex virus. A LightCycler assay for enterovirus (also a picornavirus, like FMDV) is being evaluated by the Public Health Laboratory Service (PHLS). Robotic nucleic acid extraction machines that can feed directly into a LightCycler system can make the process faster and more reliable, and are also in routine use in some PHLS laboratories.[13] With the development of automated PCR for RNA and DNA,[14] it has been possible to apply it routinely to screening blood donated in the transfusion service for blood-borne viruses such as hepatitis B, hepatitis C and HIV.[15] The ability to screen simultaneously the nucleic acids of several different organisms in a mixture by using multiple PCR assays[16] is particularly exciting and potentially revolutionises our surveillance capabilities. It is undoubtedly true that PCR and antigen ELISAs are replacing virus culture as key techniques for pathogen detection.[17] Provision of such automated systems will require substantial investment in the veterinary sector but would provide a step improvement in surveillance capacity.

7.27 *Laboratory based RT-PCR for FMDV.* The antigen-detection ELISA used for FMDV diagnosis is acceptably rapid but has low sensitivity, and the combined ELISA–virus isolation method is too slow (up to 4 days) for use in emergency situations. The technique of RT-PCR, which allows the detection of minute amounts of viral nucleic acid and can provide a diagnosis within the same day, is an excellent alternative. Recent developments offer good prospects for its application to FMD. A highly sensitive fluorogenic PCR test has become available as a research tool,[18] and preliminary tests have shown that it detects virus in epithelial suspensions with a greater sensitivity than both the ELISA and earlier RT-PCR methods.[19] The current RT-PCR used at Pirbright is generic and so detects RNA from all seven serotypes. If required, PCR product from positive samples can be sequenced immediately to define the serotype of an index case. For PCR to be used efficiently in an outbreak situation, automated equipment, sufficient trained staff and quality assurance schemes need to be in place.

7.28 *Pen-side PCRs.* Another highly specific and sensitive RT-PCR method (using a Cepheid Smart Cycler machine) was shown to be more sensitive than virus isolation for detecting infection in experimental sheep.[1] The authors conclude that the assay could be used in a variety of field contexts, including post-outbreak surveillance, to identify carrier animals. In a second study the Cepheid Smart Cycler machine provided a rapid and accurate method for the detection of FMD when optimal reagents were used, and it might also be suitable for the rapid diagnosis of FMD in the field. Sensitivity seems to be highly dependent on the reagents used.[20] Although opportunities to validate a portable RT-PCR test were not taken during the 2001 outbreak, this should not delay further work to explore this promising technology, perhaps in collaboration with countries where FMD is endemic. The assay methods should be investigated thoroughly by DEFRA for their suitability for on-farm testing or in biosecure mobile or regional laboratories. PCR systems need to be assessed for their potential for false positive results, and for speed and reliability. Significant optimisation of assay conditions and extensive validation of the techniques will be required to produce a robust assay that can be relied upon in a crisis.

7.29 *Diagnosis by PCR during the incubation period.* Additionally, there should be an exploration of PCR's potential contribution to providing a diagnosis earlier in the course of infection by detecting virus in samples before clinical signs develop. This opportunity exploits a time window when virus is present in the circulation of an

infected animal but before lesions develop. Clinically normal animals on high-risk farms could be sampled to determine whether transmission of infection has occurred. If a pen-side portable RT-PCR test were capable of delivering a diagnosis ahead of the veterinarian, this could enhance stamping-out measures in both speed and confidence. We fully recognise that the use of PCR under field conditions will be technically demanding and quality assurance of on-farm testing will need to be supported by reliable and standard reagent supplies involving central or regional laboratories. However, PCR has become routine in medical diagnostics and must surely have a greater role in veterinary diagnostics.[17]

7.30 *Continuous monitoring by PCR.* New adaptations of the PCR might enable the continuous monitoring, at reasonable cost, of animal products (such as milk or carcasses), or even the air in highly intensive livestock sheds. Such techniques could act as an additional line of defence in picking up the spread of infection during an outbreak. In principle they could be introduced in a defined region around an outbreak, to help determine the scale and spread of the disease, but this would demand capacity and trained staff. Although their routine use at all times would put an undue burden on the livestock industry (at least until costs reduced substantially), their application to surveillance – particularly when outbreaks might be considered imminent – should be considered, thus applying the precautionary principle.

(iii) Detection of viral antigen and antibody by ELISA

7.31 *'Patient-side' and pen-side ELISAs.* A range of 'patient-side' tests have been developed to detect viral infections (such as influenza and respiratory syncytial virus (RSV)) in humans. These tests are rapid (15 minutes) and require no specialist equipment and only minimal training.[13,17] A similar pen-side antigen detection test has been developed for FMD[21] that is applicable to suspensions of epithelium, nasal swabs and probang samples and could allow the animal-side confirmation of a clinical suspicion. In its present form the activated device works by using the lateral flow of an FMD group-reactive monoclonal antibody in a chromatographic strip; a reaction develops a visible blue line of 'precipitation' in positive cases. Results are visible within a few minutes and are of comparable sensitivity to the laboratory-based ELISA. Although not tested in the 2001 outbreak, efforts to assess its usefulness on field samples should be pursued vigorously. With rinderpest a similar test has been found to assist field-service veterinarians in the diagnosis of subacute atypical cases,[22] and it could be equally valuable in FMD outbreaks. The prospects for developing a similar pen-side test for FMDV antibody detection should also be explored because this would be particularly useful for detecting FMD in sheep flocks, in which clinical signs are less obvious.[23]

7.32 Differential diagnosis of the various vesicular diseases in FMDV-susceptible species would be very valuable and this might be possible with PCR (mentioned above) and biosensor technology. With the use of multiplex systems (or, in the interest of maintaining the greatest sensitivity, duplex systems) PCR can detect several distinct microorganisms simultaneously. For instance, if vesicular disease were found in pigs, in principle the portable PCR system could diagnose whether it was FMD, classical swine fever, African swine fever or vesicular stomatitis within a short period.

(e) The prospect of novel approaches applied to diagnosis and disease control

7.33 Progress in diagnostic technology was reviewed by the Director of the PHLS Central Public Health Laboratory, who stated that '*A revolution is occurring in the detection, identification, and characterisation of pathogens by the combining of the seemingly disparate fields of nucleic acid analysis, bioinformatics, data storage and retrieval, nanotechnology, physics, microelectronics and polymer, solid state and combinatorial chemistry. The scenario of taking a drop of blood, urine, or saliva and within an hour knowing whether a pathogen is present and its anti-microbial resistance potential is no longer science fiction but will soon be reality.*'[24] Veterinary diagnostic science and technology can and must keep pace with this vision and build on the advances that are taking place in human diagnostics. This is well understood by the scientists who work on animal disease diagnostics, but their capacity to respond is limited by resources and the managerial will to develop new diagnostic methods. Without the best diagnostics, the ability to manage disease outbreaks is significantly impaired. This is evident not only in FMD but also in the spongiform encephalopathies.

7.34 In this era of heightened concern about national security on a range of fronts, it is reasonable for society to expect that significant national resources will be spent on developing innovative ways of detecting biological agents of all sorts. Those efforts will have to be led by governments

and will need to be coordinated internationally. To ensure that the field of animal disease control benefits from these likely advances, DEFRA must ensure that its scientists and commissioned research teams are well connected to these international efforts.

(i) Biosensors—general

7.35 Modern biosensors exploit the selective binding capabilities of biological molecules such as antibodies, nucleic acids, enzymes and receptor molecules. The basic principle is to convert a biologically induced recognition event (such as the binding of antibody to antigen, or of enzyme to substrate) into an electronic signal by using a chemical or physical transducer. They have the potential to be both sensitive and specific and can be used in the laboratory or under field conditions. There is an international consortium of R&D organisations and suppliers dedicated to developing microminiaturisation strategies – the 'Lab-on-a-chip' concept – with a wide range of applications, including patient testing.[25–27] At present, most sensors are in the R&D phase, with issues of sensitivity, calibration and linked processing to be overcome. But they hold promise for the rapid on-site testing of infectious diseases and can generate easily transmissible data.[25-27]

7.36 Recent research on biosensors for viral diagnosis includes the use of protein micro-arrays to detect the presence of antibodies (e.g. against rubella and herpes viruses), rupture scanning events for the detection of HSV1;[28] immunochips for the detection of dengue virus viraemia; optical sensors for the detection of influenza;[29,30] and DNA arrays for the rapid detection and typing of viral nucleic acids and the characterisation of virulence factors.[31,32] Biosensors have also been developed to detect bacteria, including the use of immunomagnetic capture and time-resolved fluorescence for the simultaneous detection of *Escherichia coli* and *Salmonella* in ground meats; conductimetric immunosensors to detect *E. coli*, and surface plasmon resonance immunosensors to detect *Legionella*. Other devices are being investigated as 'breathalyser' tests for evidence of infection or disease.[33] For example, exhaled air from cattle with ketosis is monitored for acetone with a biosensor, and a similar gas method can detect infection with *Helicobacter pylori* in the human stomach. In these cases the substance detected is not a component of the infectious microorganism itself but a chemical reaction product (metabolite) specific to the infection. The simultaneous testing of various antigens or nucleic acids of microorganisms in parallel by multiplexed microsphere-based assays and flow cytometry is another promising development.[34]

(ii) Biosensors and FMD

7.37 In the field of FMD, biosensors have the potential to replace ELISAs for antigen and antibody detection, just as ELISA tests began to replace radioimmunoassays twenty years ago. Could not biosensor membranes coated with antibody against FMDV detect small amounts of viral antigen in blood or vesicles early in infection? Equipment using surface plasmon resonance to detect and quantify minute amounts of specific antigens has been described,[28] and in principle viral RNA could also be detected by hybridization to specific DNA sequences arrayed on biosensor membranes, particularly if linked to an integrated PCR amplification step.[31]

7.38 Monitoring with sensitive biosensors might permit routine screening for a range of infectious agents simultaneously, among animals gathered together in abattoirs, auction lairages and livestock units. This would be particularly useful in the face of a new infectious disease outbreak. Pigs in particular can release enormous amounts of infective virus in exhaled breath. Biosensors might have a particular future role in helping to prevent such spread by detecting virus, before clinical signs develop, in pig units or pig abattoirs. It would also be extremely useful to monitor other high-risk groups of animals, for example dairy herds and in lambs housed indoors.

7.39 There are undoubtedly many technical problems to be resolved before biosensors have a role in veterinary medicine; however, to capitalise on this technology and provide the clinician with reliable pen-side tests and early warning systems, multidisciplinary groups of molecular biologists, veterinarians and physical scientists are required. Although medical biosensors might provide a large market to encourage private sector innovation, research in the specifically veterinary area is unlikely ever to be supported by the industry itself because of the relative smallness of the market in normal times. The demand for novel detection devices particularly for exotic diseases will – we hope – be highly intermittent. Governments must therefore accept that, given such market weakness, they will have to support such R&D with public funds.

(f) Maintaining a state of preparedness

7.40 The 2001 outbreak spotlighted the difficulties in mobilising sufficient numbers of trained diagnostic staff to respond to an outbreak situation. As part of its contingency planning, DEFRA need to address how to maintain their laboratory diagnostic readiness. This could include:

- contracts with other laboratories with suitable containment facilities;
- training of staff, perhaps aided by an annual retainer, employed in other areas and institutes who could be diverted to emergency testing;
- maintenance of large stocks of diagnostic reagents for use in an outbreak;
- contracts for access to additional automated machinery;
- suitable validated diagnostic tests available online, with standards;
- as many common procedures across methods as possible.

7.41 There are obviously special problems when diseases are rare, but this type of situation cannot be unique and DEFRA needs to plan now how to scale up rapidly to meet the demands of an outbreak situation. If on-farm testing is to be introduced, regional technical support and quality-assurance infrastructure of the highest order will be required to maintain security and control.

7.42 One significant rate-limiting factor in the introduction of new diagnostic techniques and reagents for notifiable List A diseases is the need for their international validation. Such validation is essential if the results of such tests are to be accepted internationally for trade purposes. It is in the interests of all Member States of the OIE to provide that organisation and its reference laboratories with the resources it needs to conduct such validation as rapidly and professionally as possible. It would be unacceptable for the introduction of a new technique to be delayed for the lack of relatively small resources.

(g) Integrating diagnosis to rapid response

7.43 Our expectation is that it will soon become possible to integrate rapid molecular diagnostic technologies with engineering and informatic technologies so as to respond rapidly to suspected outbreaks. Such a 'joined-up' response mode has been proposed[35] for a global, virtual laboratory against human influenza, and for the United States Department of Agriculture in the case of a suspected FMD outbreak in the USA.[36] Telemedicine systems are being considered in parts of America and Canada and have been initiated in the UK for human medicine. The development of diagnostic systems for notifiable diseases in the UK has to take account of the benefits and drawbacks of having a system linked to a central laboratory or regional centres. Important issues will be the maintenance of reagents and test kits under suitable conditions, quality assurance of the reagents and kits, regular training of operators at disease locations, rapid transport systems to sites of disease outbreaks, disease security, good communications between laboratories or testing sites and DEFRA, and quality assurance of pen-side testing schemes, particularly during outbreak conditions.

7.44 The vision offered to us by several individuals for controlling a disease outbreak combines local diagnosis with robust technologies linked to a geographic information system (GIS) that automatically provides information to the disease control system. We believe that DEFRA should be seeking solutions along these lines: as emphasised repeatedly, the two major EU outbreaks of classical swine fever and FMD have each cost low billions of pounds in compensation.

(h) General conclusions on diagnosis of other List A diseases

7.45 Aspects of diagnosis of the eight List A diseases are summarised in Figure 9.3 and the following general conclusions are possible.

7.46 Having reviewed the diagnostic techniques available for classical swine fever, African swine fever (ASF), avian influenza, Newcastle disease, bluetongue and African horse sickness, we are broadly satisfied that acceptable technologies do exist for each, although there is scope for more development of pen-side technologies. In most cases (and with the exception of FMD), the speed with which a laboratory result can be produced is acceptably brief. Group-specific RT-PCR tests are needed to improve the diagnostic armoury for bluetongue and African horse sickness to overcome the inability of ELISA to detect group antigen in the blood. An antigen ELISA and PCR need to be completed and validated for the initial diagnosis of ASF.

7.47 With the increasing application of PCR for rapid diagnosis in the future, positive and negative standards will be required for many diseases (including FMD). It is also noted that antisera for bluetongue virus are more than 20 years old and existing stocks are low. In view of the current situation, where this virus is establishing itself in Greece, Italy and the Balkans, this deficit should be rectified.

7.48 Because of the relative smallness of the UK, samples can reach either of the reference

laboratories within a few hours of collection and we accept the view that under normal (i.e. non-outbreak conditions) it is better to concentrate the necessary techniques in a single national reference laboratory rather than in several regional centres. This avoids the need for maintaining specialisations in more than one location and the need for cross-standardisation exercises. The availability of reliable pen-side tests will alter this. The position changes during a major outbreak (such as FMD in 2001), when the focus has to shift to local diagnosis after the index case has been identified and characterised, and staff from regional centres have to provide additional assistance. Subsequently during the concluding serological surveys, several regional laboratories also need to be involved in testing (see 7.40).

7.49 We wonder whether any justification exists for continuing to divide responsibility for disease diagnoses between the IAH and the VLA, and would suggest that consideration be given to bringing the responsibility for all List A diseases under a single organisation.

(i) Recommendations

7.50 Given the major potential impact that improvements in diagnostics could have on the prevention and control of infectious disease outbreaks in the future, we make a number of recommendations in this area, some of which are quite detailed and cover areas in which we know that some action is already in hand.

We recommend that DEFRA should:

- **consult with other member states to ensure that the OIE is appropriately constituted to validate new diagnostic techniques and reagents as rapidly as possible; and that OIE reference laboratories are supported politically and financially, so that they can better undertake their national and international obligations, including the development of diagnostic tests; (R7.1)**
- **ensure that sufficiently specific and sensitive pen-side antigen detection ELISAs are developed for FMD and other major diseases, are validated as quickly as possible, and are available on a large scale for use in the field, and that a similar ELISA is developed especially for detecting antibodies in sheep; (R7.2)**
- **explore the potential for portable RT-PCR machines for use in the field or at regional laboratories; (R7.3)**
- **develop advanced telecommunications between the field and central control; (R7.4)**
- **consider the benefits of bringing responsibility for all List A diseases under a single organisation. (R7.5)**

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8 Vaccination

(a) Introduction

8.1 Vaccines offer powerful defence against infectious disease in humans and animals. In this chapter we consider the vaccination options for the control of infectious diseases of livestock in the light of new developments in our scientific understanding of the immune response, vaccines and strategies for their deployment. We focus on the two ways in which vaccines can be used: routine or preventative vaccination of livestock (e.g. cattle and pigs), and emergency vaccination of livestock in the face of an epidemic.

8.2 Routine vaccination is used widely and successfully to control foot-and-mouth disease (FMD) in countries where the virus is endemic or poses recurrent threats of virus incursions from neighbouring countries. Intensive vaccination of livestock over decades eventually allows such countries to reduce the incidence of FMD to the point at which they are able to eradicate infection, allowing them to acquire disease-free status. In turn this brings considerable economic gains and entry into world markets for animals and animal products.

8.3 In FMD virus-free countries such as the UK the use of routine vaccination faces the same problems as elsewhere of having to vaccinate against many strains with vaccines that give a relatively short period of immunity, requiring half-yearly or yearly vaccination of susceptible species. Routine vaccination also brings a further complication in that its use deprives a country of the 'disease-free without vaccination' status (Chapter 4) essential for universal free trade. The UK has never used vaccination, either routinely or in emergency against FMD and during an epidemic has adopted a policy of movement restrictions and 'stamping out'. At present the UK is not a country with endemic FMD and given the limitations of current routine vaccines we do not consider that the use of routine vaccination to control FMD is appropriate, but only so long as the country's ability to respond to outbreaks is commensurate with a low level of risk. Circumstances could change, however, and alter the cost–benefit analysis in favour of vaccination, and accordingly we recommend that research to develop better vaccines that could be used for preventive vaccination should be strongly supported at an international level.

8.4 Emergency vaccination to counter an outbreak already underway in a country where entire populations of unimmunised cattle, pigs and sheep may be at risk raises different considerations, notably the selection of vaccines that specifically match the incoming strain and strategies for vaccination. We discuss these. The scientific questions raised by the use of emergency vaccination in a disease-free country centre on three major issues: the infectiousness of carrier animals; discrimination between vaccinated and infected animals; and efficacy of emergency vaccines and speed of delivery. The economic and political questions are concerned with the consequences of emergency vaccination for temporary embargoes on trade in animals and animal products through a loss of disease-free status without vaccination.

8.5 The situation regarding FMD vaccination is changing. The member countries of the OIE have agreed to reduce the trading penalties caused by vaccination (Chapter 4). This decision is, in part, the result of a greater understanding of the risks attached to vaccination, particularly the risk of carrier animals and the development of tests that distinguish between vaccinated and infected animals. Ultimately the aim is to use emergency vaccination (still combined with culling of IPs and DCs) to contain and eradicate the epidemic with a post-vaccination exit strategy.

8.6 We examine the scientific issues that lie at the heart of the emergency vaccination question. Here recent scientific developments, both in emergency vaccines and in tests for discriminating between vaccinated and infected animals, offer new approaches that allow emergency vaccination to be considered as a tool of first rather than last resort. Accordingly we recommend that emergency vaccination, together with other control measures, has an essential role in the control of future epidemics of FMD virus (FMDV), as discussed further in Chapter 9.

(b) Elimination of infectious diseases by vaccines

8.7 Vaccination to control and eliminate infectious diseases of humans and animals has had many successes (figure 8.1). In humans, smallpox infection has been eradicated. At present wild-type poliovirus remains endemic in only 10 countries, with fewer than 1 000 cases being reported in 2001. This is to be compared with the

situation in 1988, when at the start of the global vaccination scheme there were more than 350 000 cases worldwide.[1] The incidence of measles has been dramatically reduced, and many life-threatening bacterial infections such as diphtheria and whooping cough have been brought under control. In cattle and buffalo, rinderpest has been eradicated from large parts of Asia and Africa by vaccination programmes[2] and the FAO now plans for global eradication by 2010. In the UK, vaccines against *Brucella abortus* and classical swine fever (CSF) were used in the 1950s and 1960s to reduce the level of endemic infection to the point where 'stamping out' could be applied and final pockets of infection eradicated. In pigs, vaccination against Aujeszky's disease[3] – a herpes virus infection of pigs (known as pseudorabies) – and parvovirus have had dramatic effects on reducing infections by these viruses. Control of bacterial diseases of sheep by vaccination against clostridial toxins has yielded significant economic gains for sheep farming. In dogs, vaccination against canine distemper virus is routine. Rabies is now under control in many parts of the EU by a combination of vaccinating persons at risk, dogs and, by releasing baits containing vaccine into the wild, a large proportion of the wild fox population.[4]

8.8 When applied successfully, vaccination has significantly improved many aspects of agriculture, including international trade, animal movements and food safety. Thus, rinderpest vaccine has greatly reduced the threat of large-scale losses of animals in Asia and Africa. Rabies vaccination has allowed European countries such as France, Italy, Switzerland, Luxembourg and Belgium to declare that they are 'rabies free' and, as a result, this has led to the UK abolishing strict quarantine regulations for rabies and replacing it with the Pet Travel Scheme. The European pig industry has successfully controlled, and in places eradicated, pseudorabies in commercial pig units by using an attenuated virus with a defined gene deletion as a vaccine[5]. The viability of the poultry industry in the UK, and elsewhere in the world, is dependent on vaccination against a number of diseases, which if left unchecked would result in high levels of mortality. Newcastle disease has been successfully controlled in commercial poultry establishments by the routine use of vaccines[6]. Finally, *Salmonella* vaccines, together with adherence to strict biosecurity and good flock management, have led to a 90% decrease in the incidence of this pathogen in poultry products.[7]

8.9 Although vaccines have worked well in the control of many diseases, not all attempts prove successful. Some vaccines fail to give good protection and a few have had harmful consequences. For example, vaccination against certain poultry herpes viruses (such as Marek's disease virus (MDV)), although initially highly successful, has apparently led to the emergence of more virulent strains that cause serious outbreaks of disease, which cannot now be controlled with the original vaccine.[8] In this situation different vaccine strains of MDV must then be used to restore vaccine cover. In a minority of cases in humans, inappropriate immune responses to inactivated respiratory syncytial virus in children after vaccination has been linked with an exacerbation of respiratory disease induced by the virus rather than with protection.[9]

(i) Experience of routine vaccination for FMD

8.10 In countries where FMD is normally endemic, a primary aim of routine vaccination[10,11] is to reduce productivity losses, whether that be milk and meat production in cattle or the death of piglets in pig production. Thus, in South America, Africa and India vaccination focuses upon cattle, while in South East Asia the focus is on pigs and cattle. In other countries the priorities are different. For example, in Israel – an advanced agricultural country that has to be on constant alert for FMD, being located within a heavily infected region – there is routine annual vaccination of all cattle with a trivalent (O, A22, Asia 1) vaccine and all sheep and goats with a monovalent type O vaccine. As a result there has been no FMD on dairy farms in Israel during the past 10 years. Although there have been outbreaks, most have been in unvaccinated small ruminants.[12] FMD eradication has been perceived as the ultimate aim because it permits widespread international trade and removes the health hazards to the indigenous herds and flocks. As outlined in Chapters 1 and 4, Europe decided to eradicate FMD in the decades after 1945, and the nationally coordinated programmes involved the routine annual vaccination of cattle and sometimes pigs. The improvements were dramatic and by the 1980s the very occasional outbreaks were apparently associated either with virus escapes from laboratories or vaccine plants, or with residual live virus in some formaldehyde-inactivated vaccines. The average number of outbreaks between 1952 and 1975 fell from around 30 000 per annum to less than 30. From 1962 France used a policy of vaccination and slaughter of infected animals. In 1991 the EU abandoned FMD vaccination and moved to being 'disease free without vaccination'. Very extensive long-term vaccination programmes in the meat-exporting areas of South America

Figure 8.1. Examples of successful human and veterinary vaccines.

Vaccine type	Human examples	Notes	Veterinary examples	Notes
Live related virus.	Vaccinia for smallpox.	The first vaccine; introduced in 1794 and used to eradicate smallpox by 1979.	Turkey herpes virus for Marek's disease.	Highly effective when first introduced but now less effective owing to the emergence of virulent strains of Marek's disease virus.
Live attenuated virus.	MMR for measles, mumps and rubella.	Very effective vaccines, widely used.	Rinderpest vaccine.	Highly effective disease suppression in Africa (rinderpest).
	Sabin oral vaccine for polio.	Three serotypes are used. Rare possibility of reversion to virulence of serotype 3 in the polio vaccine.	Canine distemper vaccine.	Routine vaccine for dogs.
			Newcastle disease virus vaccine.	Effective poultry vaccine.
			Aujesky's disease vaccine in pigs.	Gene-deleted marker vaccine for pigs.
Killed (whole) virus.	Salk injectable vaccine for polio.	Used in many countries and exclusively in some in the final stages of polio elimination. Very safe.	Equine herpes virus.	Gives short-lived protection.
	Inactivated vaccines for influenza.	Very effective if they match the virus strain.	Bovine viral diarrhoea virus.	Protection for six to nine months.
Subunit vaccines.	Tetanus toxoid.	Prevents disease, not infection.	Leukogen for feline leukaemia.	Cancer vaccine for virus-induced feline leukaemia.
	Influenza haemagglutinin.	Very effective if matches prevalent strain.	Toxoids for clostridial disease in sheep.	Cheap and effective reduction of disease burden.
	Hepatitis B surface antigen.	Generates effective neutralising antibody.		
Live attenuated bacterium.	BCG for tuberculosis.	Efficacy varies worldwide.	*Bordetella bronchoseptica* vaccines.	Control of kennel cough in dogs.
			Brucella abortus.	Greatly reduced brucellosis in cattle.
Killed bacteria.	*Bordetella pertussis.*	Very effective in reducing whooping cough in children.	Leptospiral vaccines for cattle and dogs.	Dog vaccine extremely effective and has reduced incidence of canine leptospirosis by 90%.
			Escherichia coli for mastitis.	Gives short-lived protection.
			Salmonella in chickens.	Reduced *Salmonella* infection in birds.

eventually eradicated the disease in Argentina – about 50 million cattle are vaccinated twice per year on 300 000 farms – but unfortunately the disease re-enters all too often owing to incursions from neighbouring states. Although parts of Argentina and other countries are 'disease free with vaccination', their livestock industry can export only deboned beef to FMD-free countries including the EU. The struggle continues and typically an eradication programme – as in the Philippines – has to be measured in decades, not years. We received a valuable summary of the current situation in evidence from the IAH.[13]

8.11 Vaccination has never been used to control FMD in the British Isles (the UK and Ireland). Instead, great efforts went into removing the most dangerous livestock diseases altogether; this was achieved completely for rinderpest and contagious bovine pleuropneumonias by movement control and the slaughter of infected herds. The scale of FMD infections was reduced but during the past century there were regular outbreaks every 2 years between 1924 and 1960 and five epidemics, in 1922–24, 1937–38, 1952, 1967 and 2001. Although vaccines eventually became available the slaughter policy is maintained to the present day. Vaccination was considered during the 1967/68 epidemic. The subsequent Northumberland report[14], although supporting a continuation of the slaughter-only policy, suggested that ring vaccination could be a useful adjunct in certain conditions. It went on to recommend that *'contingency plans for the application of ring vaccination should be kept in constant readiness'* should the slaughter policy not be successful in limiting the number of outbreaks. We understand that vaccination was considered during the 2001 epidemic in the UK but was rejected for various reasons.

8.12 The European non-vaccination policy since 1991 was considered a success until the UK epidemic of 2001. Through the 1990s the only epidemics occurred in Italy (1993) and Greece (1994, 1996 and 2000) and the total savings to EU agricultural costs in avoiding routine vaccination costs were estimated at €1 billion (by calculation from ref. 15), whereas the cost of the four outbreaks has been estimated at €30 million. Under such conditions the public accepted that the control of epidemic diseases in livestock was a matter for the industry and the authorities, but the situation has been changed by the outbreak of CSF in The Netherlands and that of FMD in the UK. Not only were the costs of these two epidemics enormous but the many other changes in society (summarised in paragraph 1.21) also mean that future control strategies must be justifiable in the public domain. Indeed, it should be a primary aim of exotic infectious disease research to improve the available control strategies.

8.13 The arguments against using routine vaccination in the UK have always rested upon a combination of scientific factors relating to the drawbacks of available vaccines (see below, but including strain specificity, efficacy in the main target species, masking of field virus infection in vaccinated populations, carrier animals, no knowledge of the proportion of animals to be vaccinated, and logistics of vaccinating large numbers) bolstered by important commercial factors: trade freedom in animals. Furthermore FMD was successfully eradicated in the UK before vaccines were available and this country was able to maintain freedom due in part to its island status. Cost–benefit analyses have demonstrated the economic advantages of sustaining a no-vaccination policy for FMD and CSF.[16] We have concluded that many of the technical issues are amenable to scientific solutions although we freely accept that some (such as adequate multivalent vaccines) remain significant challenges.

(ii) The immune responses to viral infections

8.14 At the onset of most viral infections there is a period of virus replication, in which the amount of virus in the blood (viraemia) and tissues rises sharply and during which the animal may be highly infectious but shows no signs of the disease (see figure 6.2). In FMD, animals are infectious 1–4 days after infection and before clinical disease, and that is one reason why FMD spreads so widely before detection. By the time the first clinical cases have been diagnosed, infection may already have been transmitted and it may be too late to protect by vaccination. Thus speed of action is paramount in FMD control. With FMD, infection is established when virus enters, either via the oropharynx – as in pigs fed with contaminated swill – or by aerosol or droplet infection from infectious animals. During this pre-clinical phase, pigs can shed more than 400 million virus particles in their breath every day and thus act as a massive source of rapid infection. In contrast, sheep produce much less virus in the pre-clinical period: up to one million virus particles per day.

8.15 Two separate arms of the immune response are induced by viral infection: T lymphocytes (T-cells) attack virus-infected cells, and B lymphocytes (B-cells) produce antibodies. Both are necessary for effective immunity. Antibodies block the ability of the virus to enter cells and establish infection. A

huge variety of antibodies are made by B-cells, and the presence of these antibodies in the serum, tissues or mucosal surfaces neutralises infectious virus and recruits the inflammatory response that helps to eliminate viral infections. T-cells do not prevent the infection of cells by a virus but are essential in limiting the initial infection because they provide a range of mechanisms for eliminating virally infected cells. If such cells are killed during the early stages of infection, the amount of new virus produced is markedly reduced, because viruses replicate only inside cells. Therefore, the combination of T-cells and the different types of antibody are largely responsible for the recovery from infection. In some viral infections, the immune system is unable to eliminate the virus completely but does control any persistent infection quite effectively. A good example is the Epstein–Barr virus, which causes infectious mononucleosis in humans and infects more than 85% of the human adult population in the UK. It is harmless as long as T-cell immunity is maintained.

8.16 The disappearance of characteristic lesions in FMD coincides with the rapid increases in antibody levels. The first, protective, virus-neutralising antibodies are detected in cattle 3–5 days after infection and peak at about 28 days after infection.[17] Cattle also mount a strong mucosal antibody response[18] with an early peak of antibody in oropharyngeal secretions between 7 and 14 days after infection. In some animals mucosal antibody is produced continuously over several months, whereas in others production can be detected only sporadically. In cattle recovering from live FMD infection, levels of neutralising antibodies – sufficient for immunity – can be found in the serum for several years. It is claimed that some cattle are protected against disease from the same strain for up to 4½ years after infection.[19,20]

8.17 In convalescing cattle, virus can be recovered from the pharynx for several months. This is the so-called carrier state, which is considered further below. In pigs the kinetics of the immune response is similar but the pig seems able to clear the virus completely: four weeks after infection no virus can be recovered from the pharynx. This is consistent with evidence that the pig does not become a carrier of infectious virus after recovery from infection.

8.18 Recovery from a viral infection leaves the individual primed to make a rapid secondary response if it should be re-exposed to the same infection. This is known as 'immunological memory' and results in an enhanced immune response, which controls the virus and eliminates virally infected cells. Sufficient serum or mucosal antibodies can prevent the infection from developing at all by neutralising the incoming pathogen before replication occurs. Mucosal antibodies may be particularly important in FMD because they block infection at epithelial surfaces such as the mouth, respiratory tract and gut—the usual routes of entry of FMD. Inhalation of as little as 10 infectious units of FMDV is enough to infect cattle, but pigs require at least 100 times as many infectious units to establish infection by inhalation (see Chapter 3). If a repeat infection does take hold with the homologous virus it results only in a mild illness with reduced shedding of virus and lower transmission rates. If infection does occur in an occasional animal in an otherwise immunised population, an epidemic cannot occur because the single infected animal is surrounded with immune animals.

8.19 A classic difficulty is that some viruses, such as those causing the common cold, are very adept at evading established immunity by evolving different strains through genetic changes or small mutations. Accumulated mutations can eventually result in an escape from immunity induced by the original virus strain. Unfortunately, this occurs with FMDV, which has many variant strains grouped into seven serotypes: O, A, C, SAT1, SAT2, SAT3 and Asia1. This classification is based on the observations that infection with one serotype does not confer protection against another serotype and that serum from animals infected with one serotype does not neutralise viruses of other serotypes. The strains within each FMD serotype also vary antigenically with a spectrum of antigenic differences existing between strains, ranging from some that show minor differences and completely cross-protect to others that show substantial differences and fail to cross-protect. The reason that FMD viruses are capable of constantly generating multiple variants within a particular serotype is because errors occur in virus replication, which results in mutations. In immunised populations these variants can escape the immune response, become dominant in the immunised populations and give rise to new rounds of infection against which there is no immunity. An essential requirement for successful vaccination in this situation is to identify the new endemic strain through good surveillance and to vaccinate accordingly.

(iii) The immune response to viral vaccines

8.20 Normally, vaccines are deployed routinely to protect the individual and population against

possible disease threats in the future. Measles and poliomyelitis vaccination in humans, and distemper vaccination in dogs, are typical examples of routine vaccination. Ideally, such vaccines should provide solid, lifetime protection against all known strains of the infectious agent. Vaccination protects the vaccinated animal (*individual immunity*) and, by so doing, reduces the risk to the population in general by diminishing the pool of susceptible animals (*herd immunity*). Both are important components of a vaccination strategy. The actual degree of protection provided to the individual depends on the efficacy of the vaccine, which varies widely. Rinderpest, a live attenuated vaccine, gives lifelong immunity after a single course of vaccination, which is one of the reasons why rinderpest vaccination is successful. Others give immunity for a finite period of years (e.g. feline leukaemia), and still others give much shorter immunity of a year or less (e.g. equine influenza and contagious bovine pleuropneumonia) and require repeated booster injections. All current FMDV vaccines fall into the third category.

8.21 For routine vaccination against FMD it is usual to employ standard-potency vaccines of about 3 PD_{50} (where PD_{50} is the dose that protects 50% of susceptible animals). Generally a primary course of vaccination requires two doses of vaccine. The first dose primes the animal's immune system within 7–10 days and the second booster vaccination, given after three or four weeks, results in high levels of immunity within a week. This gives high levels of neutralising antibodies in the serum but, unlike the situation with FMD infection, mucosal antibodies appear transiently in the pharyngeal fluids of such vaccinated cattle and do not persist to the same level as in convalescent animals. In vaccinated animals the overall immunity declines after a variable period (3–12 months) and maintenance requires booster vaccinations, usually at 6-month intervals in the first few years of life. Thereafter, annual vaccinations seem to give adequate levels of immunity. Cattle vaccinated repeatedly have been shown to be protected against virus challenge for up to 17 months after the previous vaccination. Moreover, a recent study has reported high titres of anti-FMDV antibodies in a proportion of French cattle sampled 6 years after the cessation of FMDV vaccination in Europe.[21] In general, however, the duration of immunity to homologous virus after a single vaccination is short lived compared with that after infection, in which immunity against infection with the identical (homologous) virus can persist for years.

8.22 At the population level, the protection afforded depends not only upon the efficacy of the vaccine but also upon the proportion of the population vaccinated. This is a well-established phenomenon for all vaccines[22] (see Chapter 6). Ideally, every member of a population at risk should be vaccinated, but failing that the proportion vaccinated must be high enough to ensure that the infectious agent cannot circulate and precipitate an epidemic.

8.23 With regard to FMD, immunity at the level of the herd is rather easily compromised by the short duration of immunity and by the variation in the immune response between individuals. Effective protection is also greatly influenced by the demography of the livestock and in particular by the density of animals, the structure and size of the herds or flocks, and the patterns of losses and replacements. Large, intensive pig herds provide ample opportunity for rapid spread within the pig unit and for the release of airborne FMDV, which then spreads to other susceptible species. A very high proportion of the pigs must therefore be vaccinated. Sheep in hill flocks are far more dispersed, except when they are brought in for lambing or shearing, and the infection might die out of its own accord owing to a lack of contact between susceptible animals. This is an area in which mathematical modelling of vaccination strategies based on demography and population density of flocks and herds at risk, together with epidemiological knowledge, can and should be used to develop vaccination strategies. We believe that this is an important and timely area for research.

8.24 Once vaccinated, a population's immunity must be maintained by vaccinating new susceptible animals. Herds or flocks are not static populations; livestock in breeding units are replenished by births, and those in fattening or dairy units by purchases. Both situations dilute vaccine cover in the herds. Animals born into vaccinated herds or flocks are provided with a measure of maternal or 'passive' protection through antibodies in the colostrum (first milk). This maternal protection against FMD lasts for two or three months but it must then be replaced by the protection conferred by vaccination. If the young animal is vaccinated with live attenuated virus while it is still protected by colostral antibody, the live vaccine might be neutralised by those same antibodies. Although maternal protection of the newborn can be boosted by giving the dam a booster dose near the time of parturition, calves, lambs and piglets require vaccination after passive immunity from the dam has waned. Mature susceptible animals entering

a vaccinated population, usually as purchased additions to herds and flocks, should be vaccinated at or before entry.

8.25 A final issue, which is particularly important for FMD, is which species should be vaccinated in routine vaccination. The vaccines available are effective in protecting cattle, sheep and pigs, and the risks would clearly be minimised by vaccinating all three species. However, this might not be necessary, and financial and logistics might argue against vaccinating all three species. The case for vaccinating the three main livestock species is as follows (the costs are dealt with in the next section).

- *Cattle*. Experience in other countries (such as Argentina and Uruguay) suggests that routinely vaccinating cattle alone can minimise the risk of major epidemics. Vaccinating and maintaining herd immunity in cattle populations is relatively straightforward: one course of vaccination of young stock when they lose maternal immunity, followed by twice-yearly vaccination of adults, eventually becoming annual vaccination in repeatedly vaccinated animals (see above, in paragraph 8.20).
- *Pigs*. The presence of large populations of pigs would risk the failure of a vaccination policy focused only on cattle. Pigs remain the most likely species to be infected in an index outbreak (as happened in the UK in 2001) as they might be fed with infected meat products. In the UK the recent ban on swill feeding to pigs will decrease the risk in the commercial pig sector, but feeding waste food to non-commercial (i.e. pet) pigs remains prevalent despite the swill-feeding ban. Pigs are also the species that present the greatest threat to other livestock; if they become infected they shed huge quantities of FMDV particles. For these reasons the case for vaccinating pigs as part of a routine vaccination programme is strong. However, maintaining herd immunity in pig breeding populations has to take into account the logistics involved in administering the vaccine, especially in very large piggeries where there may be a need to vaccinate cohorts of new offspring frequently, if not daily. Breeding sows can be vaccinated annually, but in young animals vaccination would need to be given when colostral immunity had declined; otherwise the vaccine would be ineffective. However, the pig industry routinely vaccinates pigs for other diseases and so these logistical difficulties are well understood and coped with.
- *Sheep.* For sheep the case is arguable. When kept extensively there is not a strong case for vaccinating sheep in a routine vaccination programme, but when brought together through repeated markets, closely mixed and then transported great distances they present a huge risk for the spread of FMD, as was seen in the UK in 2001. If this remains the pattern for the sheep industry in the UK, vaccination for sheep would seem sensible in a routine vaccination programme. Logistically, vaccinating sheep flocks should be straightforward because sheep are routinely gathered for shearing and for other vaccinations.

(iv) The economics of routine vaccination

8.26 Relatively little research has been undertaken upon how different control strategies affect the overall economic costs of a disease such as FMD, taking into account the impact not only on the agricultural industry but also on other sectors of the economy, including tourism and the food industry. The most comprehensive published studies have been conducted on CSF, which include the consequential losses for farmers and related industries subjected to control measures.[23]

8.27 After the 1967 FMD epidemic, an economic analysis[24] was conducted by two MAFF economists. They approached the problem by assessing the costs that would be incurred if the disease became endemic and then measured the benefit over a 17-year period if the disease were controlled by slaughter, or alternatively by vaccination. They concluded that *'on the basis of purely quantifiable factors the slaughter policy is the more acceptable on any realistic set of assumptions. The difference between the two policies is, however, probably much less marked when allowance is made for non-quantifiable effects such as stress and uncertainty to farmers'*. The study was one of the earliest essays into animal health cost–benefit analysis and it has been criticised[25]. The lack of estimates of the direct cost of the disease based on recorded mortality and morbidity data remain a major obstacle to an economic analysis of FMD. A further consideration is that in 1967 the rural economy was greatly different from that in 2001.

8.28 A cost–benefit analysis of alternative policies[26] was performed by the European Commission in 1987. The analysis compared the costs of two sets of control measures: slaughter without vaccination, and vaccination backed up by the slaughter of infected herds. The two policies were costed over a period of a future 10 years and the expected number of epidemics, based on the

Figure 8.2. Estimated annual costs (£ millions) of routine FMD vaccination in the UK.

Item	Cattle only	Cattle and pigs	Cattle, pigs and sheep
Vaccination costs			
Cattle	24	24	24
Pigs	0	19	19
Sheep	0	0	92
Total	24	43	135
Production losses			
Milk	1.6	1.6	1.6
Campaign costs	3.0	3.0	3.0
Serological surveys	3.2	5.7	8.2
Grand total	31.8	53.3	147.8

Figures taken from VEERU (2002).[28]

record of the previous 10 years, in the eight Member States with a vaccination policy, and in the four Member States with a stamping-out policy. It was this 1987 analysis that led the EU Commission to recommend that the EU should henceforward rely on slaughter rather than on vaccination. In 1997 the EC conducted a review[27] of this policy in the light of increasing global trade and the small number of outbreaks that had occurred in the EU (Italy and Greece) since 1992. The conclusion was, on the basis of an economic assessment and for the benefits of global trade, that the non-vaccination policy should continue.

8.29 To assess the costs of different FMD control strategies we commissioned an outline analysis by the Veterinary Economics and Epidemiology Unit (VEERU) at Reading University.[28] This report argues that FMD can have serious effects on livestock production in the UK. A brief analysis shows the most severe impact on farms to be on dairy and pig systems, and it is likely that FMD would quickly put such farm enterprises out of business. However, in beef and sheep systems, which have lower variable costs and lower capital investments and are supported by subsidies, the impact of FMD on farms is much less severe.

8.30 The VEERU report also addressed routine vaccination as a method of keeping British livestock free of disease. The calculations were based on the use of currently available inactivated vaccines, with two doses administered to young stock and one per year to adults and assuming a cost per administered dose of £1.50. The cost of three scenarios, vaccinating (i) cattle only, (ii) cattle and pigs, and (iii) cattle, pigs and sheep, are shown in figure 8.2.

8.31 On the basis of present knowledge and for the reasons given in paragraph 8.25 it is considered necessary to vaccinate cattle and pigs, but not sheep, if the intention is to reduce the risk of disease interfering with production. At current prices, the annual cost of vaccinating cattle and pigs would be in the order of £50 million per year, assuming that young cattle receive two doses of vaccine, and adults and pigs one dose per year.

(v) Key design features of vaccines

8.32 Poliovirus and measles, mumps and rubella vaccines in humans, and distemper vaccine in dogs, are good examples of live attenuated vaccines, which replicate in their hosts without causing disease but prime the immune system to give long-term protection against disease. Tetanus vaccine is the inactivated toxin from the tetanus microorganism (*Clostridium tetani*), and although it does not replicate in the host it gives good protection for about 3–5 years after the first course of vaccination. Inactivated typhoid vaccines give limited protection, and equine flu vaccines require repeated boosters and seldom protect for more than a year. Attenuation of wild-type viruses does not always result in a successful vaccine. An over-attenuated vaccine might be ineffective and an inadequately attenuated organism might revert to virulence and cause disease. For example, a poorly attenuated equine herpes virus can cause paralysis and death,[29] and a recent report[30] indicates the dangers that can arise from polio vaccines. Polio vaccines themselves give disease at very low frequency.

8.33 Most FMDV vaccines that have been used globally in routine vaccination are inactivated whole-virus vaccines grown in cell culture. Modern regulated procedures of inactivation use ethyleneimine compounds to give high-order inactivation of FMD vaccines. The vaccines are also batch tested *in vitro* and *in vivo* to exclude any residual infectivity. This eliminates the risk of spreading

FMD through vaccination, although the hazard of potential residual infectivity is always present unless very strict quality control and batch testing for infectivity are undertaken. Currently, the use of live attenuated FMD vaccines is actively discouraged by the OIE because of possible residual pathogenicity and the risk of reversion to virulence with such vaccines.

8.34 Potency is a critical feature for a vaccine. It is a measure of the concentration of the active ingredient in the vaccine and indicates vaccine efficacy in the field against challenge with the homologous strain. For live attenuated vaccines it is related to the number of infectious particles in the vaccine. For inactivated vaccines it is measured by chemical or immunochemical means during production and, indirectly, as a response in animals to the final product. For example, equine influenza vaccine potency is assessed by the levels of antibody stimulated in horses or guinea pigs, whereas FMDV vaccine potency is assessed in terms of the number of protective doses (PD_{50}) measured by infectious challenge of vaccinated cattle. The standards are laid down in the OIE's Manual of Standards. In Europe the requirements for licensing are set out in the European Pharmacopoeia and EU legislation. FMD vaccines used for routine vaccination, for which there is less urgency to stimulate antibodies as soon as possible, contain far less antigen than those used in emergency vaccination, and a minimum potency of about 3 PD_{50} is accepted for routine vaccination, in comparison with potency levels of up to about 100 PD_{50} for emergency vaccines.[31]

8.35 The level and duration of immunity can also be dependent on whether the vaccine is attenuated or inactivated. Live attenuated vaccines (e.g. rinderpest, polio) and recombinant vector vaccines give prolonged levels of immunity (years) after a single course of vaccination. To boost the immunogenicity of inactivated vaccines, such as the current FMDV vaccines, adjuvants are usually incorporated, which are non-specific inflammatory agents that enhance the specific immune response. Adjuvants work by activating cytokines – essentially 'cell messengers' that amplify immune responses – *in vivo*. For example, in pigs the use of one injection of FMD vaccine containing an oil-based adjuvant gives good immunity, including good mucosal antibody levels, until a production pig reaches its slaughter weight. Sows can be boosted annually to maintain immunity. In sheep and cattle, oil-adjuvanted vaccines give at least 12 months of high antibody levels.

8.36 As discussed in paragraph 8.18, one of the major challenges to routine vaccination in FMD is strain variation. Optimising the virus chosen as a vaccine candidate is a professional task, and constant surveillance of the predominant antigenic variants and their comparison with vaccine strains are essential.[32] In FMD, with its large number of serotypes, if vaccination uses the 'wrong' strain there will be no protection. Rapid identification of FMD strain is undertaken by the OIE Reference Laboratory at Pirbright, which receives 300–400 virus isolates from all around the world each year. We understand that about half of these viruses are characterised antigenically and their RNA sequenced to provide information on serotype and genetic relatedness to other isolates. Once characterised it is possible to determine whether the isolate is a new strain and, if so, it is designated as such. Vaccine manufacturers and control authorities are then alerted to the appearance of new strains, and viruses are made available to manufacturers for them to determine whether new vaccine master seeds are required or whether existing vaccine viruses will provide adequate immunity. Submission of viruses from endemically infected countries is voluntary, and there are often financial and logistical difficulties in shipping these dangerous viruses overseas. The absence of submissions from other countries seriously undermines horizon scanning for FMD and hides potential new threats. This is a serious deficiency in global surveillance. The EU/FAO should take the lead within OIE in establishing a subsidised shipping and testing service for developing countries associated with its reference laboratories.

8.37 The role of the Pirbright laboratory in FMDV characterisation is quite essential. If the strain is not in the vaccine bank and has to be prepared from scratch, the lead-in time to develop the new vaccine strain could be one to three months, depending on how it grows *in vitro* and its yield of antigens.[13] All countries should be encouraged and supported (by the OIE and FAO) to collect and submit FMD viruses; laboratories must have adequate resources and the political support to characterise strains rapidly, to maintain stocks of virus suitable as vaccine candidates and to communicate speedily and widely with all governments, vaccine manufacturers and control authorities on changing epidemiological patterns, new risks and the potential need to modify vaccine strains. We recommend that an analysis be undertaken of the financial and political support needed by Pirbright and other OIE Reference Laboratories so that they are properly equipped to undertake their

international obligations. They may well need to expand their capabilities for surveillance, for refining virus strain identification and for ensuring that they have a central role in communicating emerging risks to the Government.

(c) Improving routine vaccines for FMD

8.38 Although existing inactivated vaccines have been successfully used in the control of FMD, they are not without certain limitations related to protection against different strains, duration and type of immunity. As the IAH emphasised in their evidence[13], *'there is a fundamental obstacle to broad spectrum vaccines and that is the dependence of protective immunity on the antibody arm of the immune system. More research is needed to understand the contribution that cellular (T cell) responses make to protection'*. Currently the answer is to use multivalent vaccines (i.e. those containing mixtures of FMDV strains). The ideal FMD vaccine would have the following characteristics:

- It would give protection against all isolates of the virus in cattle, pigs and sheep and prevent virus carriage and the possibility of shedding and transmission.
- It would stimulate a broad level of T-cell immunity necessary to drive an effective and long-lasting antibody response.
- It would be cheap to manufacture and simple to administer.
- It would be safe to use, have a long shelf life and be stable without refrigeration.
- It would not give rise to vaccine-induced epidemics due to improper inactivation.
- It would allow discrimination between vaccinated and infected animals.
- It would give good levels of maternal immunity.

8.39 Vaccine research in both human and veterinary vaccines currently offers exciting new opportunities for improving on existing FMD vaccines. Genetic engineering is now widely used to create recombinant viruses that carry the key antigenic structures of pathogens. These are generally safer because they do not expose the recipient to the whole infectious organism. This approach has been successfully used in the control of fox rabies, in which a safe human vaccine strain (vaccinia) was used as a vector for the major antigenic protein of the rabies virus. Use of recombinant FMD vaccines is now in the experimental stage for FMD and studies so far have demonstrated proof of principle. A recombinant human adenovirus carrying the capsid antigens of an FMD strain has been used to vaccinate pigs inducing neutralising antibodies and protection against live homologous virus challenge 7 days after a single vaccination.[33,34] Another novel recombinant approach, which generates virus capsid 'particles' that mimic whole virus but are free of viral genetic material (empty particles) and are hence non-infectious, has been developed by Abrams et al[35]. Crystallographically these 'natural', RNA free, empty particles have an identical surface structure (and hence presumably antigenicity) to that of full virions. Antibody and other tests show that they are identical to the 'natural' capsid structure of FMDV infection.[36] Because they also completely lack the non-structural proteins these particles could be used in emergency vaccination as they would allow discrimination between vaccinated and infected animals.

8.40 So-called DNA vaccination is an even more recent strategy. Naked DNA that encodes one or more antigen genes of the targeted microbe can be injected, enter a few cells and prime the immune system for an enhanced secondary response to the corresponding protein antigens (prime-boost strategy). This approach obviates the need to immunise with an entire microorganism, whether live, live attenuated or killed. This prime-boost strategy has proved successful in experimental situations with primate immunodeficiency viruses[37] and is currently being tested in Phase II clinical trials for HIV vaccines in humans.[38] Experimental studies with FMD in mice have shown that the prime–boost strategy can induce neutralising antibodies.[39]

8.41 The challenge for routine vaccination in FMD will be to see whether any of these novel strategies can be developed to the stage where they are as successful as the rabies example. We do not believe that it is a daunting scientific task to develop novel FMD vaccines because this has already been achieved on many occasions for other viruses. The creation of such a vaccine will require a significant (international) research effort but FMD remains a global problem of great concern to both disease-free and FMD-endemic countries. Given the trends outlined in Chapter 5 we believe that it is in the UK and the EU's interests to move the vaccine research forward so that when they become available it would overcome current regulatory and practical obstacles, which stigmatise vaccination. We are firmly of the view that vaccination should be considered to be a heightened level of security and not a sign of inadequate disease control policies. One of our major recommendations is that the Government

act to prepare a research programme with the express intention of developing a vaccine against FMD that would permit the routine and global vaccination of livestock.

(d) Emergency vaccination against FMD

8.42 Emergency vaccination is performed in the face of an epidemic in a localised area. For FMD, emergency vaccines are formulated to contain higher levels of antigen than in conventional, routine vaccines, so making them more potent and maximising the rate at which immunity develops. The vaccine is designed to be optimal for the invading virus by matching the vaccine strain as nearly as possible to the outbreak strain. Ideally it should be delivered quickly and it must provide rapidly developing immunity within days against the virus causing the epidemic. Smallpox vaccine was used in this way in the UK in the 1960s and 1970s, when there were relatively few outbreaks. Influenza vaccines can be deployed in this way.

8.43 Several outbreaks of FMD in recent years have been suppressed using emergency vaccination usually coupled to rapid culling (Albania, 1996; Korea, 2000; South Africa, 2000; Uruguay, 2001; The Netherlands, 2001). Uruguay used an intensive routine vaccination strategy together with stamping out, and by the early 1990s was declared disease free without vaccination. An epidemic then occurred in 2001 possibly owing to the incursion of virus from neighbouring countries because a market gradient had been created by being disease free, which led to illegal imports of animals. In 2001 there were 1200 separate outbreaks despite the slaughter of some 7000 cattle, sheep and pigs. The authorities, faced with a widespread and overwhelming epidemic, suspended culling and initiated the vaccination of 10 million cattle (80% of the cattle population). Sheep and pigs were not vaccinated. The epidemic was extinguished within 15 weeks of the first animals being vaccinated.[40]

8.44 Emergency vaccination has never been used in the UK during any FMD epidemic. We understand that doses were formulated from the vaccine bank at Pirbright and that some plans were drawn up during the 2001 epidemic in the UK to use emergency vaccination selectively to protect cattle herds in Cumbria, but they were not implemented. As Chapter 4 indicates, the EU recognises the value of emergency vaccination and has legislation to allow its use where FMD threatens to become extensive or other Member States are at risk.

8.45 The use of emergency vaccination is not without its penalties and is therefore regarded by some countries, including the UK, as a tool of last resort. We are not persuaded by this view. Some of the arguments relate to restriction on trade, which have now been reduced (see Chapter 4), and some relate to the fact that little effort has been invested in determining precisely how emergency vaccination can be employed and ensuring that the institutional, cultural and technical issues have been circumvented *before* an outbreak occurs. The *scientific* arguments against emergency vaccination focus on three issues: the question of carrier animals; discrimination between vaccinated and infected animals; and the efficacy and speed of deployment of emergency vaccine. We focus on these issues.

(i) The carrier state

8.46 The term 'carrier state' is much used in discussions on FMD, and it is important to be precise in understanding the meaning of the term. In the context of disease transmission it means an individual person or animal that exhibits a high probability of passing on an infection while seeming to be clinically normal**.** Classic examples of the carrier state are seen in AIDS, in which infected individuals, who have yet to develop clinical disease, are chronic carriers of HIV and are highly likely to pass on HIV infection to others. In FMD a proportion of convalescent animals (20–70%) that have been infected by FMDV are said to become 'carriers' in the sense that it is possible to recover virus from them 28 days or more after infection. This may not be a permanent feature of FMD-recovered animals. Mere demonstration of viral persistence is, in itself, insufficient to fulfil the requirements of a carrier in the epidemiological sense and it does not mean that such animals are contagious to others (see below). Labelling all animals as persistently infected with FMD as carriers has unfortunately resulted in the assumption that any persistently infected animal is potentially able to transmit the disease. This type of FMD carrier state is well recognised in cattle[41] and sheep[42] but not in pigs[43,44]. For comprehensive reviews see Salt[45] and Thomson[46].

8.47 When antibodies are produced in the bloodstream after infection, the virus is cleared in a few days. Recovery from FMD is usually complete 14 days after infection, at which time virus has been cleared from most tissues. If it persists thereafter the virus seems to be confined to certain sites in the pharynx. There is no clear evidence for the persistence of virus in other parts of the body, nor is there any evidence for a

persistent or even occasional recurrent viraemia; in that respect the carrier state in FMD must be distinguished from sub-clinical infection (which implies that the infectious agent circulates in the host and multiplies without giving rise to clinical disease).

8.48 Carrier animals seem to have a normal immune system and some have very high titres of circulating antibody against the virus. Virus can be detected in samples of secretions and cellular debris collected from the pharyngeal cavity and demonstrated either by the isolation of virus in cell culture or by quantitative polymerase chain reaction (PCR).[47,48] The frequency with which virus can be isolated from the pharyngeal tissues and the amount of virus that can be recovered decline with time, and detection of virus is often intermittent. In general the number of animals that remain carriers decreases after 6 months and only a small proportion remain carriers after 1 year.[46]

8.49 The virus seems to persist in the basal epithelial cells of the soft palate and pharynx.[49] Unusually for a highly cell-damaging virus there is no inflammation, suggesting that the virus replicates differently and/or has different pathological effects on the epithelial cells in these tissues. Alexandersen et al[50] have suggested that the pharyngeal and soft palate tissues of cattle contains a region of specialised cells (not prominent in pigs) that can harbour virus.

8.50 The ability of FMDV to persist after infection is poorly understood but several explanations have been proposed: (i) the virus might have found immunological sanctuary by residing in a subset of specialised cells that are not susceptible to immune recognition; (ii) infectious virus might have mutated to a less virulent and less infectious form; or (iii) it might have escaped immune recognition in infected cells by disrupting the infected cells' ability to present viral antigens to the immune system, thus avoiding T-cell and antibody-mediated immune recognition (see ref. 45 for a review).

8.51 Carriers arise in a vaccinated population because current vaccines do not provide sterile immunity, and sub-clinical infections, with low levels of virus replication, can occur in a few animals. Because the FMD vaccines do not contain live virus it is, of course, not the vaccination itself that causes a carrier state to develop, but the infection with wild-type virus. It is likely that during emergency vaccination, when the overall availability of infective virus at a population level is lowered, the number of carrier animals may be significantly decreased.[51]

8.52 This type of carrier state is not unique to FMD viruses, and in other diseases live virus can also persist after symptoms have disappeared and an immune response has developed. For example, polio virus continues to be shed from the gut for 8 weeks after vaccination,[52] and measles virus can persist for several weeks. Some 30–50% of stallions recovered from equine arteritis can be healthy persistent carriers and continue to shed infectious virus in the semen for their breeding life, passing on infection to mares by venereal transmission.[53]

(ii) Are carrier animals infectious?

8.53 The carrier animal has achieved iconic status in the international regulations governing the trade in live animals. The possibility that vaccinated animals encountering a field challenge might become carriers is always raised as an objection to trading animals from a nation using vaccination and hence as an argument against using emergency vaccination to stamp out an outbreak. The key question is whether carrier animals, vaccinated or not, are able, *even occasionally*, to transmit the infection to other animals.

8.54 Although virus that has been recovered from carriers and artificially inoculated into susceptible animals can provoke infection,[54] many experiments performed in containment facilities have failed to demonstrate the transmission of FMDV from carriers to susceptible animals in close contact with them. Why this should be so is unclear. The decline in titre of virus in probang samples taken from the oropharynx during the period of persistence[55] might reduce the level of virus below that necessary for disease transmission to susceptible animals. In addition, the carrier state is normally associated with the presence of significant titres of neutralising antibody in oropharyngeal secretions, some of which might be complexed with virus (thus preventing the transmission of infection to susceptible animals). Other experimental studies[56] have shown that vaccinated cattle challenged with infectious virus can transmit it to in-contact animals up to 14 days after infection, but by 21 days fail to transmit infection. The authors concluded that, during emergency vaccination programmes, it is advisable to vaccinate all FMD-susceptible animals within the vaccination zone and that they should be separated from non-vaccinated animals at the boundaries for at least three weeks.[56] Having movement restrictions for a short period (3–4 weeks) after emergency vaccination may also be a valuable risk reduction measure for carriers during an emergency vaccination strategy. The numbers of animals involved in all these

experiments are necessarily small and so they cannot reveal an infectious state if it occurs rarely or is dependent on other factors such as co-infection with other pathogens (such as parainfluenza) that might cause suppression of the animal's immune system.

8.55 Field evidence for the infectiousness of carriers is largely historical and derives from observations during epidemics in the UK in the early 20th century, more recent observations in Africa, and the outcome of the post-war European vaccination campaigns. However, the early reports of UK outbreaks of FMD attributed to suspect carriers were made before techniques were developed to characterise virus isolates, so it was impossible to say that the virus isolated from one animal was identical to that isolated from another that had become infected after being in contact with it. The more recent reports from Africa show that carrier buffalo occasionally transmit SAT strains of FMDV to in-contact cattle and there is strongly suggestive evidence of transmission of SAT strains from carrier cattle. This long-term persistence and transmissibility might be a unique feature of the SAT strains in the buffalo and does not prove that the same situation exists for non-SAT viruses.[46]

8.56 We conclude that detailed scientific evidence for the infectiousness of carriers is weak. If transmission of infection from carriers does occur it is at very low frequencies and under a particular set of circumstances that are as yet undefined, from either field or experimental studies. Although it is impossible to exclude the possibility that a very small number of vaccinated and challenged animals might transmit infection, the fact that vaccination was used to eradicate FMD in Europe and parts of South America, as well as recent outbreaks in Albania, Korea, Uruguay and South Africa, argues against the contention that the carrier animal is a significant risk factor in spreading or maintaining the disease.

8.57 This issue of the carrier state is so important in a regulatory sense that we are surprised the issues remain unresolved and that no *quantitative* risk assessment ever seems to have been undertaken. We do not consider that risk of the carrier state precludes the use of emergency vaccination, although it does demand a clearly defined strategy for monitoring vaccinated animals after the cessation of a FMD epidemic. Clearly, more research is required upon these specific issues and a study of the lack of the carrier state in the pig might provide valuable clues. We recommend that more specific research be performed on the mechanisms underlying FMDV persistence in cattle (and also in sheep), the state of the virus and its infectivity for other species.

(iii) Discriminating between vaccinated and infected animals

8.58 If emergency vaccination is to be used during an FMD epidemic it is essential to discriminate unequivocally between animals that have been vaccinated and those that have been infected. This discrimination is essential for disease control, but it also permits a more rapid return to disease-free status and would hence make an emergency 'vaccination to live' policy practicable. It would also enable authorities to monitor the presence and circulation of viruses in countries that use routine vaccination.

8.59 Recent experiments indicate that it is now possible to differentiate between the two types of animals by testing serum for the presence of antibodies that are unique markers of infection, namely antibodies against the viral polyprotein (3ABC) that gives rise to these non-structural proteins (NSPs). The principle behind this important development is that, during virus replication, NSPs are synthesised in cells, and infected animals develop antibodies against them. However, these proteins are not incorporated into virus particles to any great extent and are therefore not present in vaccines that consist of inactivated virus particles that have been purified from cellular material. Thus, purified vaccines do not stimulate antibody against NSPs. Antibodies against structural proteins (i.e. those in the viral capsid) cannot be used to differentiate infected from vaccinated animals because both vaccines and infection stimulate antibody against these proteins.

8.60 The confidence with which infected versus uninfected vaccinated animals can be discriminated depends on a number of factors that affect both sensitivity and specificity. These include:

- the degree of viral replication that occurs during a mild infection in a vaccinated animal;
- the amount and duration of antibody against NSPs in infected animals;
- the timing of the blood sample in relation to previous infection (which affects sensitivity);
- the purity of the vaccine preparations and the number of doses administered (which affect specificity).

8.61 The potential practical benefits of such a test resulted in a Concerted Action (CT93) sponsored by the European Community. This assessed the performance of several different assays that detect antibody against NSPs and reached

conclusions about their potential application.[58] There was general agreement, based on testing several thousand experimental and archived sera from outbreaks, that the detection of antibodies against NSPs is the single most reliable marker for discriminating between vaccinated and convalescent animals. Several groups have now developed sensitive enzyme-linked immunosorbent assays (ELISAs) for detecting antibodies against NSPs and report 99.8–100% specificity in sheep and cattle.[59] In unvaccinated infected animals, detectable antibody persists in 90% of convalescent animals for at least 1 year.[60] Repeatedly vaccinated but uninfected animals have been shown to be completely free of antibody against NSPs. ELISA-based NSP assays can discriminate between infected and vaccinated cattle, sheep and pigs.[61–63]

8.62 These studies on the use of NSP assays are a watershed in resolving the important question of distinguishing infected from vaccinated animals. At present these tests are extremely valuable in detecting infected herds exposed to infection and have sufficient specificity and sensitivity to be applied at the overall herd level. Infections within a herd result in a significant proportion of the animals testing positive for NSP, and this would indicate infection within the herd. Such a herd would then be culled as being on infected premises. Commercial kits based on these techniques are being developed and it should be mandatory that only purified vaccines free from NSPs be used in an emergency vaccination campaign in which differential diagnosis based on NSPs is required. It is most encouraging that the OIE has changed the FMD code to permit a shorter period for regaining FMD-free status if NSP antibody tests are used as part of surveillance. What is now needed is for candidate tests that have been independently validated by an OIE reference laboratory to be tested on large panels of reference sera from outbreaks. This would allow a sampling framework with sufficient statistical power for cattle, sheep and pigs to be set with 95% confidence limits on a percentage of animals to be screened in a herd or flock. This could be done fairly rapidly because the technology and field sera exist. The NSP test should be seen as part of a process whereby the risk of vaccinated populations containing animals that might be infectious is diminished to the point at which animals can be moved with safety. This process should start with accurate records of outbreaks, marking of all vaccinated animals, post-infection serological surveys including tests for antibodies for NSPs, and finally tests for virus. Thus, the NSP tests permit risk reduction as part of an exit strategy after emergency vaccination (see below).

8.63 In addition to NSP serological tests, other methods that look directly for virus by sensitive PCR-based analysis would give further levels of assurance about whether any virus were present in the emergency-vaccinated herd or flock. When a small number of borderline positives are detected in the NSP tests there might be a case for follow-up virus detection tests to establish the presence of infection (and therefore carriers).

8.64 A novel method of determining whether an animal is infected might be to look for $CD8^+$ T-cell responses, which (in other infections) are reliably stimulated by live virus infection but less readily by inactivated virus or subunit vaccines. There are now simple methods for monitoring $CD8^+$ T-cell responses to a virus and these can be automated. The surge of interest in developing human vaccines for infections such as HIV, tuberculosis and malaria is stimulating the invention of methods to measure these responses efficiently and cheaply; such methods have the potential to be transferred to FMDV, if it can be shown that FMDV induces a $CD8^+$ T-cell response of sufficient magnitude and duration for routine detection.

8.65 These scientific developments in discriminatory tests mark a turning point in FMD science. We acknowledge the uncertainty regarding the surveillance strategy for NSP tests in an outbreak, which will require official validation. However, the strategies for statistical sampling required for NSP surveillance are not difficult to define, given all the information now available on the specificity and sensitivity of the NSP tests, and validation should be completed in the short term.

(iv) Efficacy of emergency vaccines in an outbreak

8.66 If FMD vaccines are to be effective under field conditions, there are several imperatives. First, international standards (OIE) for efficacious vaccines[64] need to be applied, and in some countries they have not been universally adopted or even imposed by international authorities. As a consequence in some situations emergency vaccination has failed and these examples are quoted as general proof that emergency vaccination does not work. This is a technical matter, which requires resolution at an international level.

8.67 Potency of the vaccines is critical.[65] FMD vaccines used in emergency vaccination are of high potency and protection against FMD can be achieved as early as 3–4 days after vaccination in cattle, sheep and pigs with inactivated high-potency vaccines using oil-based adjuvants.[66,67]

Under certain conditions, adjuvants can speed up the early immune responses to give protective antibody levels within 3–4 days. This is important in emergency vaccination, when speed of immune response is crucial. Another imperative is a good match between the vaccine strains used and the field viruses circulating. In this regard, prior knowledge of circulating strains of the virus through international surveillance is essential (see Chapter 5).

8.68 In emergency vaccination against FMD, delivery of potent vaccines to a high proportion of the livestock must occur within a short period. This requires robust vaccines capable of withstanding unfriendly field conditions.

(v) The role of vaccine banks

8.69 Several FMD-free countries have established vaccine reserves, which are either ready-formulated vaccine of limited shelf life, or concentrated inactivated antigens maintained over liquid nitrogen for many years and can be formulated in response to an emergency. There are four international banks: the North American Bank supported by Canada, the USA and Mexico; the International Vaccine Bank (IVB, housed at IAH, Pirbright) funded by seven countries (the UK, Australia, Finland, New Zealand, Norway, the Republic of Ireland, and Sweden), the European Community Vaccine Bank (EUVB) established and maintained by the EU, and the All-Russian Research Institute for Animal Health vaccine bank. In addition, some countries maintain national banks, often through private arrangements with manufacturers.[68] The international banks hold a range of vaccine antigens that are largely in line with the strains recommended as priority vaccine strains by the OIE's Reference Laboratory at Pirbright[69] and taking account of information from the OIE and FAO. The antigens held by the vaccine bank at Pirbright are purchased from commercial sources but can be formulated on site under Good Microbiological Practice (GMP) conditions to provide 500 000 high-potency cattle doses of each of seven strains. This facility is not available at all vaccine storage sites, and antigen would have to be shipped internationally to licensed production sites for final vaccine formulation. The EU vaccine bank holds stocks at Institutes in Brescia, Lyon and Pirbright of more than 500 000 doses of 13 strains constituting in excess of 30 million doses in total. Antigens from these stocks were formulated into vaccines and made available for use during emergency situations in the Balkans in 1996, Algeria and Morocco in 1999, and Japan, South Korea and Turkey in 2000. Including national supplies, it is belived that more than 67 million doses of vaccine are held in Europe covering the major serotypes.[69] The range held reflects the priority given to virus strains by the Reference Laboratory at Pirbright and also the location and local hazards of the countries participating in support of the banks.

8.70 Most of the vaccine viruses held have been selected on the basis of their broad antigenic cross-reactivity and ability to provide highly potent products. However, it is recognised that continued monitoring of contemporary viruses is essential for responding to changing global threats. The suitability of the strains held at Pirbright has been reviewed by Barnett et al[70], who identified a need for vaccine strains providing better protection against A variants isolated in Iran and Turkey in 1996 and 1997, and in Thailand and Malaysia in 1997. It was recognised that the criteria used for vaccine strain selection were still largely intuitive and that further studies are required on the correlation between tests *in vitro* and protection *in vivo*. The strengths and weaknesses of the EU vaccine banks were also considered in an EU Report of the Scientific Committee on Animal health and Welfare[71], which endorsed the inclusion of further strains into vaccine banks and recommended regular reviews of the quality and suitability of vaccine antigens by an EU-designated institute.

8.71 If emergency vaccination during an outbreak becomes a normal part of disease control policy – as we recommend – vaccine banks must hold both ready formulated vaccine of limited shelf life for *immediate* use in a crisis, backed up by larger quantities of concentrated antigens that can be formulated within a few days as a follow-up supply. This should be feasible, possibly through cooperation between commercial and government organisations. The amount of vaccine stored would need to be constantly reviewed and there would have to be a concerted rapid response to update vaccine banks as risks from virus strains changed, as well as an appropriate budget to do so. The shelf life of licensed commercial vaccines in use is currently 12–18 months, but recent work at Pirbright suggests that this can be extended considerably by serially freezing the diluents/adjuvant separately from the antigen but in the same ampoule, and keeping them at very low temperatures. Vaccine for injection can then be prepared immediately by thawing the adjuvant and antigen, and mixing them by agitation.[72] Research is needed to improve the thermostability of diluted vaccines. In the meantime, the costs of holding (say) one or two

million doses of vaccines of the strains most likely to invade (i.e. A, O, Asia 1 and SATs1 and 2), diluted and formulated, need to be estimated. Compared with the cost of a major epidemic, we surmise that the costs would not be excessive and would enable emergency vaccination in an outbreak to begin immediately (Chapter 9). If the costs of carrying readily available stocks are deemed burdensome to governments, arrangements could be made for using these doses elsewhere in the world well before their shelf life expired. Finally, a system of international quality assurance is needed to monitor the quality of antigens stored.

8.72 If an emergency vaccination-to-live policy is to be adopted in the future it will be absolutely essential that the vaccines used are licensed for use in the UK by the Veterinary Medicines Directorate. This is a necessary step in using any vaccine on animals destined for the food chain. Currently, the Pirbright aluminium-hydroxide-adjuvanted emergency vaccine holds a market authorisation (licence) for use in cattle and sheep but so far the oil-adjuvanted version, which will be required for pigs, is not licensed. We also understand that the vaccines from only one manufacturer are licensed for use in the UK. We would encourage Pirbright to press ahead with a market authorisation for its oil-adjuvanted vaccine as soon as possible and ask DEFRA to encourage the other manufacturers to seek UK market authorisations.

8.73 When emergency vaccination is undertaken during an extensive epidemic, the proportion of the animals at risk that have to be protected needs to be close to 100%. Such levels of vaccination coverage attainable in the UK: cattle and pig herds are confined, and even extensively reared sheep flocks can be gathered. It may be less easy in countries with more extensive livestock systems. Some initial modelling work[73] indicates that rapid and intensive mass vaccination of cattle, combined with culling IPs and DCs could reduce the main body of the epidemic and its tail. More targeting of the vaccination, such as selecting large cattle farms, which are particularly susceptible to infection, does not reduce significantly the main body of the infection, but can reduce the tail by cutting key links in the transmission network. These simulations also illustrate that a strain of FMD much more transmissible in pigs than the 2001 strain would require much higher levels of vaccine uptake to control. It is an urgent task to refine the logistical and biological assumptions of these models and to test them in real world situations; collaboration between theoretical and empirical epidemiologists is essential to achieve this.

(vi) Exit strategies

8.74 We believe that the advances in tests to identify whether there are infected animals in a herd of vaccinated animals has progressed to the stage at which they can be used to determine when a country that had used emergency vaccination should regain its normal trading situation as a country free from FMD. Once these tests have been fully validated and accepted, there should be no reason in principle why there need be a minimum time before they can be used to support an application for a return to normal trading status. Thus, if emergency vaccination were used in a small outbreak and involved only relatively few farms, the surveillance and testing should not be too onerous and the return to normal status would be quick: for an extensive outbreak the return to normal status would take longer. Until such a flexible procedure can be agreed, the recent reductions in the minimum period before resumption of full trading status is an important step forward. Thus in the long term we consider that emergency vaccination should be considered, even for small outbreaks, to damp down local spread, and that its implementation in an outbreak should be immediate.

8.75 We stress that we do not see the necessary changes to trading regulations and the validation of the necessary surveillance tests as a question of 'if they happen' but rather a question of 'when they will be implemented'. Hence, DEFRA should now be exploring possible strategies, together with likely requirements for vaccines and vaccinators. In the meantime, emergency vaccination still has a much to offer to control outbreaks. It is therefore essential for DEFRA to discuss with the relevant stakeholders the development of regional strategies for the use of emergency vaccination with suitable safeguards or compensation/insurance arrangements for those involved. This should include mechanisms by which vaccinated but not infected animals can enter the food chain and the milk can be used for human consumption.

8.76 The use of emergency vaccination as part of an overall control strategy is considered further in the next chapter.

(e) Vaccines against other exotic viral diseases of livestock

8.77 The other viral diseases, in addition to FMD, that pose a threat to UK livestock are listed in figure 8.3.

(i) High-risk diseases

8.78 Four of these diseases, classical swine fever,

Figure 8.3. Exotic viral diseases that pose a threat to UK livestock.

Category	Disease	Species affected	Arthropod vector	Type of vaccine available
High-risk* diseases	Classical swine fever	Pigs	—	Live attenuated
	Newcastle disease	Poultry/birds	—	Live attenuated and inactivated
	Avian influenza	Poultry/birds	—	Inactivated
	Swine vesicular disease	Pigs	—	None
Medium-risk diseases, vector-borne	Bluetongue	Cattle, sheep, goats	*Culicoides* species	Live attenuated (multiple serotypes)
	African horse sickness	Horses	*Culicoides* species	Live attenuated (multiple serotypes)
	African swine fever	Pigs	*Ornithodorus*, species of soft tick	None
	West Nile fever†	Birds, man, animals	*Culex*, species of mosquito	Inactivated‡
Low-risk diseases	Rinderpest	Cattle	—	Live attenuated
	Peste des petits ruminants	Sheep, goats	—	Live attenuated
	Sheep and goat pox	Cattle, sheep, goats	—	Live attenuated

*All of these diseases have been introduced into the UK in the recent past.
†Although West Nile fever virus infects a range of animal species, wild birds are believed to be the principal animal reservoir, and among domestic livestock only horses suffer from overt clinical disease.
‡Available for horses only, in the USA, under a conditional licence.

swine vesicular disease, Newcastle disease and avian influenza, have been introduced into the UK on one or more occasions in the past 30 years. These four diseases are either present or occur sporadically within other countries of the EU. Wild boar and migratory birds act as wildlife reservoirs for infection with classical swine fever virus and Newcastle disease virus, respectively. These diseases are therefore considered to pose a high risk to livestock in the UK.

- Classical swine fever (CSF) can cause large outbreaks of disease on a similar scale to those caused by FMDV. The available vaccines use a single live attenuated strain of the virus, the best characterised strain being the Chinese C strain.[74] The vaccine is safe and highly effective, a single dose giving rapid and long-lasting immunity, which is effective against all strains of the virus. Routine vaccination against CSF is practised in many parts of the world and was originally used in EU countries to assist in the eradication of the disease. EU legislation permits emergency vaccination as a last resort, but this has not been implemented in the recent outbreaks in the UK and mainland Europe. One of the main reasons for the reluctance to employ emergency vaccination is the lack of reliable diagnostic assays to distinguish infected from vaccinated animals. Considerable effort is being devoted to the development of alternative vaccines (either subunits or molecularly modified attenuated strains) that would allow the identification of infection in vaccinated populations.[75,76]
- Newcastle disease virus has caused several large outbreaks of disease in the UK over the past 30 years.[77,78] A live attenuated vaccine is available, which gives good protection against disease and is effective against all strains of the virus. An inactivated vaccine is also available. Vaccination is used extensively in parts of the world where Newcastle disease is endemic. In Europe, vaccination policy varies between different countries: Norway, Sweden and Denmark practice a non-vaccination policy, The Netherlands has compulsory vaccination, and in other countries, including the UK, vaccination is voluntary. A recombinant Newcastle disease virus vaccine that allows discrimination between vaccinated and infected animals has been developed.[79]
- Avian influenza causes sporadic outbreaks of disease in poultry, usually associated with high mortality.[80] Several different serotypes of the virus have been responsible for outbreaks in Europe. In the EU, control of disease caused by virulent strains of the virus relies primarily on the slaughter of affected flocks, but provision is made for emergency vaccination.

Vaccination has been employed to control a recent outbreak in Italy.[81] The vaccine consists of inactivated viral antigen similar to that used in humans and horses. Because different serotypes of the virus can cause disease, the viral antigen used in the vaccine must be matched with the serotype of the virus strain responsible for the outbreak. The vaccine needs to be administered by injection, which in poultry is a significant disadvantage because of the time and cost involved in vaccinating birds individually. For these reasons, and because of the sporadic nature of the outbreaks, routine preventive vaccination is considered not to be justifiable.

- Swine vesicular disease virus belongs to the same broad family of viruses as FMDV and produces similar, but less severe, clinical signs. It is also readily transmitted in meat products. The virus consists of a single serotype although it exhibits some antigenic variability. The disease was present in several European countries including the UK during the 1960s and 1970s and was introduced again into The Netherlands, Italy and Spain in the early 1980s. Subsequently it has been confined to Italy, where it now causes much milder disease than when it was initially introduced. There is no vaccine, and control of the disease in the EU relies on diagnosis and slaughter.

(ii) Medium-risk diseases

8.79 The diseases in this category (African swine fever, bluetongue, African horse sickness and West Nile fever) have not previously been introduced into the UK but for different reasons represent a significant threat. They are all vector-borne diseases but most can also readily be transmitted from animal to animal. All four diseases are either present or have recently been present in countries of the EU. Global warming could significantly increase the risk from these diseases (particularly those transmitted by midges and mosquitoes) by allowing the northerly spread of vector species capable of transmitting the viruses.

- African swine fever is currently present in Sardinia and was present in Portugal and Spain in the 1980s and early 1990s. Tick species capable of transmitting the virus occur in southern Europe. Affected pigs are highly infectious, and the persistence of virus in animals that recover from the disease provides a further source of infection. The virus can also be transmitted in meat products. There are no vaccines against African swine fever.
- Bluetongue and African horse sickness are caused by related viruses (Orbivirus), both of which are transmitted by *Culicoides* midges. Bluetongue virus occurs in southern Europe and its distribution has extended northwards in the past few years. It is currently present in Greece, Spain, France and Italy. Although Europe is free of African horse sickness, the virus was detected in Portugal and Spain in the early 1990s and because of the extensive international movement of horses the risk of reintroducing the virus is considered to be high. Both viruses occur as multiple serotypes: there are 24 serotypes of bluetongue and 9 of African horse sickness.[82] Live attenuated vaccines containing multiple serotypes of the viruses have been produced in South Africa for use in regions where the diseases are endemic. However, there are serious concerns about the use of these vaccines in Europe. They produce transient viraemia in vaccinated animals, which might allow transmission to midges, and because of the segmented nature of the virus genomes, recombination could occur between vaccine and field strains of the virus. Moreover, the bluetongue vaccines have been tested adequately only for use in sheep. Current research seeks to produce alternative vaccines based on the use of subunit antigens or subviral particles.[83,84]
- West Nile fever virus has a wide host range, including both birds and mammals. Although it usually does not cause serious disease in domestic livestock (a small proportion of infected horses develop clinical disease), infections in animals could have a role in the epidemiology of human disease. In the past decade the virus has become more widely distributed and there is evidence that species of mosquito capable of transmitting the virus are extending northwards in Europe. Several other mosquito species in Europe have not been tested for their ability to transmit the virus. Within the EU the virus is currently found only in France. There are no West Nile fever vaccines for use in human beings, although a killed virus vaccine has been available in the USA for horses under a conditional licence since August 2001. However, technologies that are showing promise for development of vaccines for related viruses (these are flaviviruses), such as tick-borne encephalitis, might be applicable to West Nile fever.

(iii) Low-risk diseases

8.80 The viruses in this category, namely rinderpest, *peste des petits ruminants* and sheep and goat pox, occasionally encroach into southeast Europe but pose a relatively low risk to the rest of

Europe. Effective live attenuated vaccines are available for all three diseases. A concerted international vaccination programme is continuing for rinderpest, the ultimate aim of which is to achieve global eradication of the disease.[85] So far this programme has been successful in eradicating the disease from many countries in Africa and Asia.

(f) Recommendations

8.81 This chapter explains the background to our recommendations.

These are:

- **The Government should take the lead in developing an international research programme aimed at an improved vaccine that would permit routine and global vaccination of livestock against FMD and other List A diseases. (R8.1)**
- **Emergency vaccination should be seen as a major tool of first resort, along with culling of infected premises and known dangerous contacts, for controlling FMD outbreaks. This policy should be vaccinate-to-live, which necessitates acceptance that meat and meat products from vaccinated animals enter the food chain normally. (R8.2)**
- **In determining the arrangements for deploying emergency vaccination, DEFRA should:**
  - **take account of the urgent need to achieve a proper validation for field use of the tests that discriminate infected from vaccinated animals;**
  - **develop emergency vaccination strategies that integrate theoretical and empirical epidemiology and the logistics of delivery of vaccine cover;**
  - **establish an exit strategy that takes account of the need for ongoing surveillance, safeguards for those involved and agreement that products from vaccinated animals can enter the normal human food chain; (R8.3)**
- **DEFRA should explore with the EU and OIE what improvements to vaccines and surveillance tests are required to allow disease free status to be based entirely on surveillance results without the requirement for a minimum waiting period. (R8.4)**

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9 Dealing with an outbreak: control measures and relevant wider issues

(a) Introduction and background

9.1 In this chapter we consider how the various factors discussed earlier should be brought together when developing strategies for controlling and eradicating an outbreak. The key control measures are biosecurity, culling and emergency vaccination, but each must be viewed in the light not only of ethical, environmental, health and resource constraints but also of their relative effectiveness in ending an outbreak. It is appropriate to use foot-and-mouth disease (FMD) as the illustrative case because many of the issues are generic and can be transferred, with suitable modification, to the control of other exotic diseases as outlined in section (c). The final step – developing contingency plans – is outlined in the final section. we recognize that our recommendations set out at the end of this chapter concerning control measures, and in particular those associated with emergency vaccination, will require further work. However, provided this is put in hand without delay and with sufficient resources, we believe that this work could be completed in about twelve months.

9.2 The choice of control strategies is far more difficult than some observers claim. Even apparently 'easy' steps, such as movement controls and other forms of biosecurity, can cause considerable problems. Not least are those associated with animal welfare if animals are trapped by movement restrictions in unsuitable or overcrowded conditions. In developing the overall strategy the aim is to minimise as many as possible of the following effects of the disease or the control arrangements:

- the severity and duration of the outbreak (upon which many of the other effects depend);
- the total number of animals culled;
- the adverse effects on the welfare of livestock;
- the adverse effects on the economics of farming (e.g. the duration of movement bans, and any consequences of vaccination);
- the adverse effect on other parts of the rural economy (e.g. tourism);
- the loss of unique or especially valuable genetic material;
- the spread of the infection by the control procedures; and
- the adverse effect on international trade in animals and animal-based food products.
- the potential impact on human health;

Usually, it will not be possible to minimise all of them simultaneously, and it will be necessary for those in charge of the operation to decide on priorities. Optimising the strategy is dependent upon the expertise and training of staff within DEFRA, the availability of appropriate scientific advice, and the formulation of clear instructions that empower persons regionally and centrally.

(i) Ethics and welfare issues

9.3 The highly infectious nature of List A diseases means that it is totally impractical to keep herds or flocks of infected animals in high-security containment facilities (isolation 'wards') while they recover, except perhaps for very valuable animals. Neither would this reduce the impact of the disease on subsequent production. In countries wishing to remain 'disease free' there is therefore no alternative to culling infected animals to prevent them from infecting other animals.

9.4 The views expressed at various meetings suggest that it is ethically acceptable to cull a 'reasonable number' (undefined, but relatively small) of uninfected animals provided that this is the only way of reducing the overall number of animals destroyed. Because in most cases, apart from breeding stock, the animals culled would have been slaughtered for food often a few weeks or at most months later, the ethical issues are largely concerned with the scale of the waste of natural resources, and the welfare of farmers and their families as well as their animals. Hence it is important:

- to examine other ways of bringing epidemics under control that reduce the numbers culled;
- to ensure that any control measure, not just culling, is conducted in such a way so as to ensure the highest possible standards of animal welfare, including reducing the level of stress caused by the various control procedures;
- to develop acceptable and high-quality standards for the on-farm slaughter of all species of farm animals, including relevant arrangements for young animals; and
- to recognise that it is unacceptable merely to keep animals alive if they are then denied access to food or acceptable living conditions by animal movement bans or a reduction in their economic value.

9.5 The welfare issues connected with the control of infectious diseases were considered in a report to us and other inquiries from the Farm Animal Welfare Council[1]. We endorse the recommendations, which include the following (numbered as in the report):

(5) An audit of slaughtermen and killing equipment immediately available to deal with a disease outbreak, as well as the ability of manufacturers to increase production, must form part of the annual review of contingency plans.
(10) Detailed strategies for killing in the field of all species and ages should be available as part of contingency plans. These strategies should be based on sound scientific research.
(11) Field slaughtermen should be issued with an Army style 'Green Card' setting out the minimum standards required of them.
(12) Research is needed to assess the effectiveness of captive bolt stunners as a killing method for sheep.
(13) Government should consider the establishment of a scheme of recognised standards for slaughter/killing equipment.
(15) There should be a specific licence for field killing and incentives for slaughtermen to be trained and take up this option. Slaughter teams should not be paid piece rates.
(16) The organisational principles of large scale killing under field conditions need defining and setting out clearly to provide operational guidelines for those having to set up and implement procedures on farms having widely different facilities.
(17) In the event of a disease outbreak leading to ring-fencing of a region by vaccination, there must be adequate capacity to provide for animal welfare and to cope with the number of livestock requiring slaughter or disposal.
(20) Welfare schemes should in future address all avenues available to enable producers to sustain the welfare of their animals, not just disposal. In particular, Government should consider a system of 'welfare vouchers' to assist with the provision of fodder or other resources.
(21) Government funding of fodder support schemes should be given greater priority.
(22) Management and veterinary advice should be made available to farmers whose animals are subject to lengthy movement restrictions.
(23) Consideration of any proposed method of individual animal identification must include an assessment of the impact on animal welfare.

(ii) Environmental issues

9.6 Controlling a major epidemic places a burden on the environment, and measures have to be put in place to reduce the short-term and long-term effects. The most obvious issues are those associated with the disposal of carcasses, although significant problems can arise with the use and disposal of disinfectants and the disruption of normal arrangements for disposing of farm effluent.

9.7 The advice from the Environment Agency[2] is that their preference for the disposal of carcasses that cannot enter the food chain is the following, in increasing order of risk to the environment and human health:

- rendering;
- commercial incinerating;
- licensed landfill;
- on-site burning; and
- on-site burial.

9.8 There is, however, a limit to the rendering capacity and we note that the interim DEFRA contingency plan reverses the order of the first two options in the list. It is essential and urgent for DEFRA and the Environment Agency to examine and agree upon the future arrangements. Of the above, the use of licensed landfill sites is probably the most appropriate way forward when the number of carcasses is large, and it would ensure that the disposal is undertaken professionally (including ensuring long-term maintenance of the disposal arrangements). This will require the arrangements to be agreed in advance and the reasons explained to the general public. For small numbers of carcasses, on-site burial may still be the most effective and quickest way forward and reduce the need for transport of potentially infected carcasses. On-site burial is not, of course, appropriate where watercourses or groundwater might become contaminated, and ways of ascertaining this rapidly in a given region need to be organised in advance. EC limitations imposed on-site burial a maximum of 8 tonnes for, but the Environmental Agency indicated that the quantified scientific basis for this does not appear strong. We recommend that research be commissioned by DEFRA to explore the risks of on-site burial, where it is appropriate, with a view to raising the 8 tonnes limit.

9.9 During an epidemic additional biosecurity measures must be implemented as quickly as possible, and some have environmental impacts. For example, sites for disinfection need to be agreed in advance and incorporated into

contingency plans, and those responsible need to be aware and trained in using them. Arrangements also have to be made for identifying where movement restrictions or other disease control measures might lead to disruption in the normal methods of disposing of farm effluent, so that these do not lead to the pollution of watercourses or groundwater. Although less time critical, arrangements need to be made for the safe disposal of used and unwanted disinfectants (we understand that more than a million litres of undiluted disinfectant was used during the 2001 epidemic). The relatively few incidents reported during the 2001 epidemic suggest that arrangements were generally satisfactory, but again it is important for them to be clear in contingency plans.

9.10 As far as possible, contingent biosecurity measures need to be planned and agreed in advance with the Environment Agency and incorporated into the contingency plans.

(iii) Human health considerations

9.11 FMD virus is not a significant health risk to humans, but they can be vectors of infection on clothing, hair and even via the upper respiratory tract for up to 28 hours after contact.[3]

9.12 Concerns were raised during the 2001 epidemic about the safety of animal products from vaccinated animals, especially dairy products, for human consumption. These concerns have no scientific foundation. Virtually all food animals are vaccinated against a wide range of diseases, and the Food Standards Agency issued a statement that it was satisfied that vaccination had no implications for food safety. The use of clostridial vaccines in sheep is widespread and in recent years the vaccination of poultry against *Salmonella enteritidis* has been used to reduce the level of risk to humans of *Salmonella* in eggs and poultry meat. Modern FMD vaccines do not contain live virus and all the available evidence indicates that no component of any vaccine is toxic and that neither vaccinated animals nor their products carry any health risk. Many European countries routinely used vaccination for FMD and classical swine fever (CSF) for decades without any human health concerns. All vaccines licensed for use in the UK for livestock carry a nil withdrawal period, which indicates that the European and national medicine licensing authorities are satisfied that they pose no risk to human health.

9.13 Carcasses should not remain exposed in fields, and care has to be taken to ensure that the disposal of culled animals through on-site burial or burning on pyres does not cause problems for human health, especially through the contamination of watercourses or groundwater. The possibility of the emission of pollutants (including sulphur dioxide, particulates, polycyclic aromatic hydrocarbons, and dioxins) from pyres was modelled and tested, but levels of pollutants in air were found to be lower than air quality standards or within the range of urban background levels. Levels of dioxins in soil, herbage and food were mostly within the expected range and/or similar to levels at control farms. However, the same report makes recommendations of distances beyond which populations downwind of pyres should remain.[4] The one area that remains a theoretical risk is in the disposal of cattle over 30 months old, through the dispersal of prions, particularly in the groundwater, in pyres and in ash. Prions are implicated as the infectious agent for variant Creutzfeldt–Jakob disease and are particularly resistant to heat. Any residual risk from these sources will disappear as BSE is finally cleared from the UK cattle herd.

(iv) Resources

9.14 The resources required to implement various control strategies are critical when deciding on the strategies to be included in the contingency plans. These include veterinary personnel for surveillance and field epidemiology, teams for slaughter and emergency vaccination, equipment and vehicles, the appropriate vaccines, and methods of disposing of carcasses. The deployment of such resources in a major epidemic requires input from operational research techniques, and there must be appropriate management and communications facilities. We assume that the *Lessons Learned Inquiry* of Dr Iain Anderson will consider this matter in considerable depth.

(v) Permanent standstill periods for all livestock

9.15 Although a permanent feature rather than an emergency measure, permanent standstill period arrangements for all livestock, discussed in Chapter 5, would significantly decrease the chance of long-distance dissemination of the disease before it is detected. Indeed, it is highly unlikely that an epidemic of similar proportions to the 2001 epidemic would occur in the future if appropriate permanent standstill arrangements were in place. If a standstill period of less than about 20 days is in place, it might be appropriate to bring in a temporary extension if the risk of a disease outbreak increases, for example if there is an outbreak elsewhere in the EU.

(vi) Increased levels of surveillance on farm

9.16 Once an outbreak of an exotic or notifiable disease

has been suspected or confirmed, the intensity of surveillance increases; this can involve regular veterinary visits to high-risk premises, the inspection of all animals and the recording of recent history. The relative risks and benefits of this must be assessed. Veterinary visits, and clinical examination of sheep in particular, can identify disease sooner than daily stock-keeping, purely from the discipline of careful inspection. In addition, contact with farmers is beneficial, providing a chance to advise on biosecurity issues, on signs to watch for in stock, and on changes in regulations. However, these benefits must be weighed against the risks of veterinarians entering closed units with regular mixing and handling of animals (often against the wishes of the owner). It is also arguable whether this type of surveillance is using veterinary resources as effectively as possible, because the logistics of such an exercise, especially in extensive upland areas, are complex. If it is to be undertaken it should be by veterinarians who understand the nature of farming in that region, and the same veterinarians should survey the same livestock units so that the veterinarian understands both farmer and animals, and a trusting relationship can develop.

9.17 It is important for clinicians to recognise the clinical characteristics of the disease, and it is imperative to build up a library of images as quickly as possible in any outbreak because lesions might not be 'typical'; it is also important for practitioners to build up a collective experience of lesions likely to be seen. As explained in Chapter 7, the development of reliable, sensitive and specific pen-side tests is important because it resolves diagnoses. For sheep in particular, few diagnoses are unequivocal without a test.

9.18 A substantial advance in disease control would come from the ability to identify incubating farms during the viraemic phase before the appearance of clinical signs. This might be scientifically feasible (see Chapter 7) but will still require the taking of a large number of samples, because without clinical signs the animals that might be incubating the disease are unknown. Especially for housed animals on high-risk farms, the regular testing of a statistically appropriate sample should be a feasible proposition. It might also prove possible to detect virus in the air within buildings housing the animals. Furthermore, as explained in Chapter 3, dairy cattle excrete virus in their milk several days before clinical signs appear. Milk from all farms in areas at risk could be tested daily for the presence of virus by using RT-PCR (reverse-transcription polymerase chain reaction) technology; this would be a significant advance in identifying infected premises (IPs). In any outbreak of FMD or any exotic disease where the virus can be detected in milk, DEFRA must ensure that the contingency plan includes arrangements for milk to be sampled at the time of collection and tested in the laboratories of the milk-processing companies.

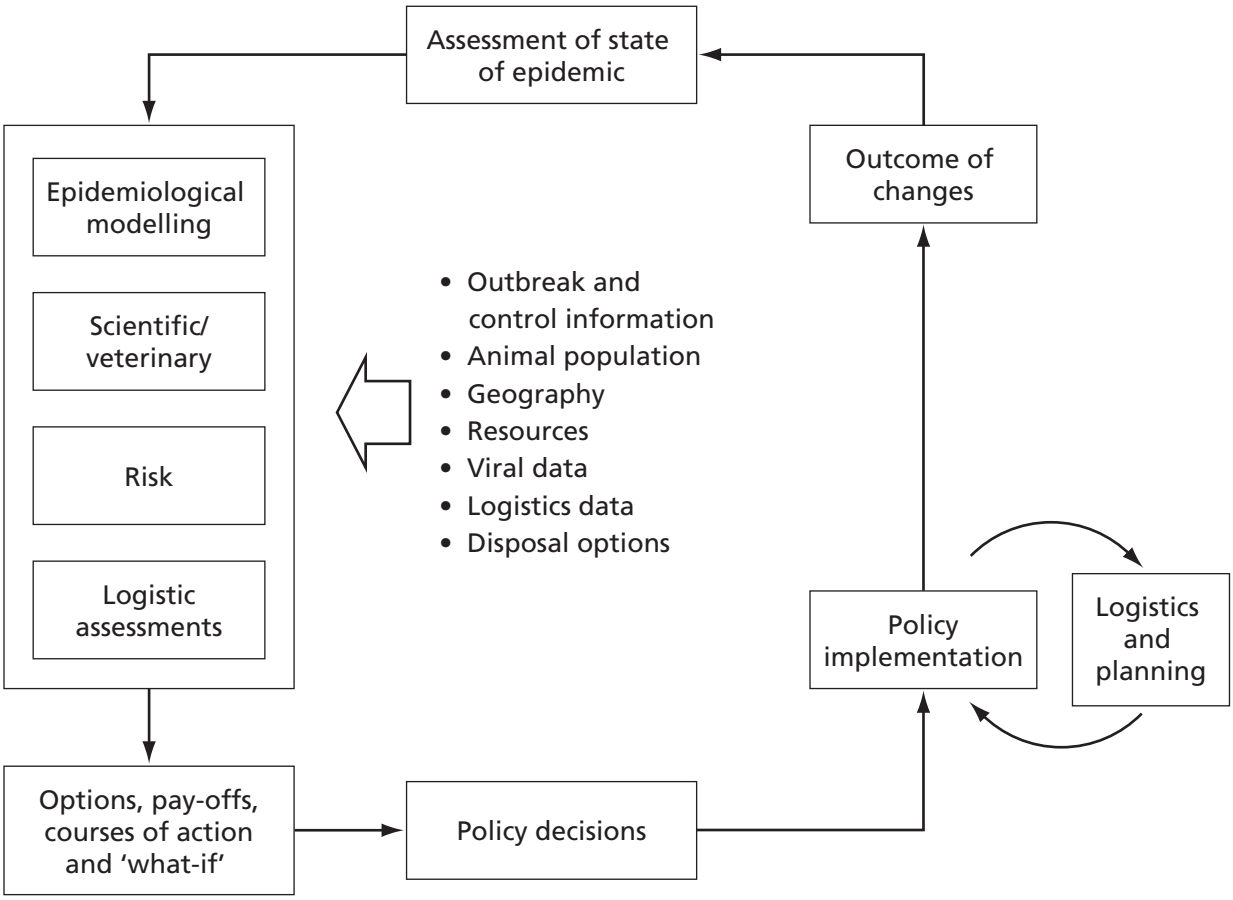
(vii) Technical input to the control of disease

9.19 A wide range of both professional and scientific input needs to be combined for successfully tackling an outbreak of an infectious disease in livestock. With regard to professional assistance in the field, the main issue is the rapid expansion of the front-line complement to the numbers necessary to handle an epidemic, with the associated management and communications structure to ensure that they are deployed effectively. Although this is included in the interim contingency plan for FMD, we believe that the plan needs to be strengthened especially in the areas of communications. Again we assume this will be considered in the Anderson Inquiry.

9.20 The other area of concern is the input of more specialist technical advice at the strategic level, such as risk analysis, data analysis, modelling and operational research. DEFRA's interim contingency plan has provision for a high-level committee to determine overall policy (DEFRA's "Gold team"), but lacks machinery for technical advice. We strongly recommend the creation of a high-level technical advisory committee, covering at least the issues set out in figure 9.1, which is activated along with all the other machinery upon confirmation of the first case To a large extent this function was fulfilled during the 2001 epidemic by the Chief Scientific Adviser's Science Group, but ideally such a group needs to be integrated into the DEFRA structure. We suggest that it be chaired by the Chief Scientific Adviser in DEFRA and involve senior officials from the other relevant Departments (including the Chief Scientific Adviser, The Cabinet Office Civil Contingency Unit the Department of Health and the Ministry of Defence). It should also contain experts from outside the Government, including the universities, and from other EU countries.

9.21 It is essential that those taking the decisions understand the advice being offered and, although it is incumbent on the technical advisors to ensure that their advice is in an appropriate form, this will demand a level of commitment from the policy makers. Furthermore, such an advisory committee is no substitute for DEFRA, or its agencies, having sufficient in-house expertise in all of the relevant

Figure 9.1. The technical input to the decision-making process.



technical areas and having arrangements for supplementing these very rapidly in the event of an outbreak. These staff need to have sufficient resources to maintain close contact with teams in universities in the UK and abroad and also with their opposite numbers in other Member States within the EU. Indeed it might be appropriate to consider whether some of these teams within DEFRA and its agencies should be considered as part of an overall EU resource.

(b) Key control measures that can be applied during an outbreak

9.22 Three main measures are available for controlling epidemics: further biosecurity, culling, and emergency vaccination. This section considers the strengths and weaknesses of these measures.

(i) Enhanced biosecurity

Emergency transport movement bans from the first detection of an outbreak

9.23 Movement bans are a key measure in reducing spread of the disease and are imposed locally when a first case is suspected. As soon as a first case has been confirmed, this local movement ban is extended (see below) and an immediate national ban on animal movements must be imposed until the extent of the outbreak is determined. It is essential to decide in advance how animals already in transit are to be treated. There are many possibilities (the stage of transportation should be completed; the animals should be returned to their last premises of embarkation; the animals should be diverted to the nearest abattoir.) DEFRA must decide which of these would be appropriate and to provide unequivocal advice.

9.24 Although emergency movement bans are valuable in reducing the spread of infection, the problems they cause should not be underestimated. In particular, prolonged movement restrictions cause considerable welfare problems, most obviously if animals are trapped in bare, waterlogged or otherwise unsuitable fields. The natural breeding cycles can also result in large numbers of newly born

animals being trapped in unsuitable accommodation, especially if farms normally sell-on young animals for growing or finishing, often in other parts of the country from the breeding farms. This illustrates again the importance of trying to reduce the length of the epidemic.

Emergency increases in biosecurity

9.25 Although 20% of foot-and-mouth spread in 2001 was 'long distance' and led to the disease jumping significantly, one of the most telling statistics (as in 1967) was the extent of local spread, which was about 80% (figure 3.3). Therefore, in addition to the ban on animal movements, a 72-hour total ban should be imposed on movements on or off all farms in an area 10 km surrounding the IP. This would includes feed lorries, milk tankers and all people (except for those on genuine emergency calls, who must take extra biosecurity precautions). This would allow time for the initial epidemiological tracings to be undertaken.

9.26 For FMD, quite mildly acidic (below pH 6) disinfection is sufficient to kill the virus (Chapter 3). However, mere disinfection might not be enough. A study of the effectiveness of footbaths in removing bacterial infection found that effective disinfection was achieved only after total removal of all organic contamination, which including scrubbing the boots in the disinfectant and then standing them in the bath for 5 minutes (or for the period recommended on the disinfectant label).[5] The authors concluded that 'most on-farm boot washing procedures do not disinfect boots' and that *'improper boot cleaning methods waste time and money and may place the herd at risk of pathogen spread'*. While these studies were conducted using mean bacterial counts, and this might not relate directly to the reduction of other pathogens, it should be noted that when disinfectants are being tested to achieve DEFRA approval, the requirement is for there to be a 10 000-fold reduction in FMD virus titre after 30 minutes.

9.27 Similarly, disinfectant mats on the road might not be effective. For vehicle wheels the surfaces of the tyres become hot enough during use to kill any virus; it is wheel arches that are much more important. It is therefore important to have provision of disinfection stations with the ability to power-wash all parts of the vehicles to remove organic matter and apply disinfectant.

9.28 To reduce the likelihood of veterinarians and other official personnel physically transmitting virus from an infected farm to another (apart from the normal biosecurity arrangements over clothing and boots), it is usual for there to be a minimum period of 3 days before a visit can be made to another livestock farm. This can cause logistical problems and further work needs to be put in hand to investigate the transfer of virus by humans, including the effectiveness of mouthwashes and nasal sprays.

9.29 The UK countryside has a large number of footpaths, and this is one basis of rural tourism. As explained in Chapter 3, we have not been able to find sufficient quantitative evidence that would enable a definitive risk assessment to be undertaken over the use of footpaths or the cancellation of horse races and rural sports outside restricted areas. We note the guidance in the interim contingency plan, which indicates that there would not be wholesale closure, and we would not argue against this provided that farms maintain adequate levels of biosecurity and adequate guidance is given to those on footpaths, with diversions to avoid livestock farmyards and other concentrations of animals.

9.30 There is no evidence to suggest that wildlife can act as a reservoir of infection for FMD (other than buffalo in Africa). Indeed, the successful elimination of FMD from European countries over the past decade, with long time gaps between infections, argues against wildlife forming any reservoir of infection. Nevertheless, we believe that further work needs to be put in hand to investigate the possible role of wildlife in local transmission, as part of a wider study of local modes of transmission.

(ii) Culling

9.31 The traditional mechanism for handling an outbreak of FMD is to cull the IP and all identified dangerous contacts (DCs) as soon as possible. Because infected farms can infect other farms before clinical signs appear, it is essential to perform pre-emptive culls of high-risk premises before they display clinical signs. If these steps can be conducted rapidly enough, epidemics are usually contained, but this is not necessarily the most effective strategy. More sophisticated strategies that might, for instance, involve harsher culling at the start of the epidemic could be more effective in some circumstances, both in terms of an earlier end to the epidemic and fewer farms culled in total. The only certainty is that determining an optimal culling strategy is exceedingly difficult and requires local knowledge combined with the tools of epidemiology and modelling (Chapter 6).

9.32 Whether IP/DC culling is sufficient to bring an epidemic rapidly under control depends crucially

on identifying a sufficiently high proportion of the secondary infections from IPs, and then culling them quickly. As explained in Chapter 6, the identification of all DCs is difficult, even if veterinary input is not limiting, as it is still not possible to identify all of the transmission routes or their probability. During the early stages of the 2001 epidemic (the exponential phase of the outbreak) on average only 0.8 DCs were identified per IP, and only a proportion of these would actually have been infected. Because of the great difficulty in detecting where the disease has already spread from the IPs, other measures have to be introduced concomitantly with culling IPs and DCs. These include one or more of the following:

- rapid increases in biosecurity to decrease 'local spread';
- earlier and fast diagnosis, particularly during the viraemic phase, with the use of modern techniques (see Chapter 7);
- better identification of DCs;
- implementing culling strategies that are more sophisticated; and
- employing emergency vaccination very early in an epidemic.

9.33 Improved biosecurity would reduce the amount of infectivity escaping from an IP, but significant improvements are hampered by the lack of knowledge of transmission routes, and this needs to be addressed urgently. The possibility of improved identification of DCs was considered in Chapter 6. It is unlikely that this will be totally successful in identifying all of the incubating premises. Although, as Chapter 7 indicates, it is now possible to detect pre-clinical infection during the viraemic phase, the logistical problems of continually testing large numbers of herds and flocks around an IP or a known DC are formidable and require resolution. Unless a higher proportion of incubating premises can be identified, further control action will be required, especially in high-density animal areas. The next sections consider the optimal further culling strategies and the use of emergency vaccination.

Optimal further culling arrangements

9.34 As explained in Chapter 6, it is essential that before the next outbreak of FMD (or any other infectious livestock disease), a range of possible strategies will have been explored and decisions already taken as to the optimal strategy for different disease outbreaks. In principle the appropriate strategy will depend on the following:

- the species infectivity of a particular strain of virus, along with its transmission characteristics and survivability;
- the mix of animals, their density and distribution in the region around the IP;
- the dynamics of livestock activities at that particular time of year; and
- meteorological conditions, including the likelihood of significant airborne spread.

9.35 The major strategies based upon culling include the following.

- Creating a large firebreak around the IP by culling up to a certain distance. This will involve killing many animals. Certain circumstances might favour this model (e.g. an IP that created other IPs in an area of very dense susceptible animals such as pigs or dairy herds).
- Targeting high-risk farms rather than removing all farms within a particular area:
  - population size—large farms, especially dairy farms, seem to be at higher risk;
  - species mix—mixed cattle and sheep farms seem to be at higher risk;
  - proximity to an IP—during the 2001 epidemic, 50% of all infected farms were within 1.5 km of the possible index farm;
  - the possibility of spread in particular directions by airborne plumes of virus.

9.36 It was from considerations such as the above that the strategy of culling contiguous premises during 2001 was developed with the aid of models. It is an example of a selective cull designed both to take out additional farms where there is incubating disease (first generation of transmission from an infected farm) not identified as DCs, and also to reduce the density of farms susceptible to second and later generations of transmission of infection. The contiguous culling strategy had the additional practical advantage of providing a simple definition of farms to be culled, which enabled more rapid culling of those premises suspected of incubating the disease. Although this strategy might be optimal in certain circumstances, it is likely that there will be other circumstances in which it will not be the best, either because it is excessively harsh (e.g. in low-density farm areas, where less costly culling strategies might be more appropriate) or possibly in more extreme circumstances (e.g. high-density pig or cattle areas) because it is an insufficient measure to control the epidemic. The detailed exploration of the most appropriate culling strategies for particular circumstances is a vital research area, which should begin forthwith.

9.37 Any culling strategies more extensive than IPs and

DCs depend upon great logistical resources to cull the animals and dispose of the carcasses. It appears unlikely that they could be implemented by DEFRA alone. The modelling research therefore needs to be linked to operational research techniques that establish the logistical requirements of a particular strategy. Further processes of optimisation could then be required to establish the resource constraints and how they might be overcome.

9.38 Furthermore, it is important to ensure that any such arrangements do not themselves increase the risk of further spread because of lax biosecurity, either on the part of those undertaking the culling or through the personnel or transport involved with the disposal of the carcasses. Unless biosecurity can be guaranteed, the strategy will at best be less effective and at worse counterproductive. For diseases that can be spread by wildlife, although we do not yet fully understand the significance of this mode of transmission, it is important to recognise that the disturbance of culling and cleansing a farm, and the associated removal of feed sources, will displace potential vectors and drive the disease outwards.

9.39 It is particularly important to have determined in advance the strategy for dealing with the first few cases, before the extent of the outbreak is clear, because early control measures can have such a major impact on the eventual size of the epidemic. We note that the interim contingency plan proposes the culling of IPs and DCs plus "contiguous premises informed by field epidemiology" within 24 and 48 hours respectively, and we believe that this should be studied further in the light of the data from the 2001 epidemic to determine under what circumstances this would be appropriate. Furthermore, it is clear that any initial strategy would need to be reassessed at the end of the first week.

9.40 Even when optimised and when logistical resources are not limiting, in an extended epidemic a control strategy based on extensive culling of contiguous premises to create firebreaks, as applied in 2001, involves the slaughter of very large numbers of animals (although we are reminded that movement controls in the 1997 CSF epidemic in The Netherlands led to welfare culls much larger than those killed for disease control purposes). Attempts to minimise culling at the start could be counterproductive, resulting in the eventual culling of even more animals. Furthermore, with a large number of cases, it is difficult to effect the required speed of slaughter on IPs and other high-risk farms while maintaining a high level of biosecurity.

9.41 Emergency vaccination offers an alternative additional control strategy, which can avoid extensive culling, is likely to be less disruptive to the farming and tourist economies, runs less risk of spread of the virus by the culling operation, and can be a more humane and ethically acceptable approach to disease control.

(iii) Emergency vaccination

9.42 We entirely accept that, in view of the highly contagious nature of FMD, there is no alternative to culling all livestock on IPs and those premises where a direct contact with the IP can be established. The rapid culling of IPs and DCs is the cornerstone of any control programme. However, as explained in Chapter 8, emergency vaccination offers an alternative to the contiguous or wider neighbourhood cull of large numbers of animals.

9.43 As explained in Chapter 4, there was until recently a mandatory 12-month wait before a country could apply for disease-free status after the use of emergency vaccination, in comparison with three months if culling only has been used. This significant trade penalty of an additional nine months is one reason why emergency vaccination has hitherto been viewed as a measure of last resort. Indeed, it has never been used in the British Isles and there remains a great reluctance even to contemplate its introduction, despite the fact that a strategy already exists for the use of emergency vaccination under current OIE regulations (as set out in a report of the EU Scientific Committee on Animal Health and Welfare[6]), which states that emergency vaccination can be a useful tool in the control of FMD if there is a risk or tendency towards uncontrolled spread. Although we understand this reluctance, and do realise that some issues have yet to be resolved, we believe most strongly that a *prima facie* case exists for using emergency vaccination and that the details of how it should be used require establishing as a Government priority.

9.44 With the recent scientific developments of assays that discriminate vaccinated from infected animals, the scientific arguments that underpin the relevant OIE regulations have lost much of their force and at its meeting on 28 May 2002 the OIE agreed to amend the Code to reduce the trade penalty to three months more than that for using a culling-only strategy. Although, as explained in Chapter 8, some work remains to validate the tests and the procedures that should be adopted for surveillance after emergency

vaccination, we believe that we should be exploring emergency vaccination strategies now in anticipation of the successful validation. Furthermore, we believe that the recent change to the Code is only a first step, and that we should be working to ensure that in the future further changes could be made to the OIE Code so that emergency vaccination is treated on a par with culling-only strategies. When this has been achieved, emergency vaccination could be considered for use as part of the control strategy even for small outbreaks.

Strategies for the use of emergency vaccination, and comparison of its effectiveness compared with extended culling

9.45 The rationale for emergency vaccination during an outbreak is that it protects susceptible animals against the infection, and, if implemented effectively and promptly, has been shown to halt the spread of infection quickly. A nation wishing to use emergency vaccination early in an epidemic must of course have the necessary resources to implement the strategy. Emergency vaccination is not a viable strategy – and neither is any other – if plans have to be laid *during* an epidemic. For that reason we argued in Chapter 1 that the nation needs to have accepted the principles behind the contingency plans before they are needed and agreement exists with the key stakeholder. As regards emergency vaccination this not only requires the trade issues to have been resolved satisfactorily but also a clear acceptance that products from vaccinated animals will enter the food chain normally.

9.46 There are two main strategies for emergency vaccination in the face of an epidemic.

(i) *Area vaccination*, in which all susceptible animals at risk in an area are immunised to reduce the weight of infection and to protect susceptible herds. The area can take the form of a ring, normally centred on the initial outbreak, or a zone, county or region. The area is determined after epidemiological investigation of the potential spread of infection.

(ii) *Barrier vaccination*, in which herds that border an infected zone are immunised to prevent infection from spreading out of the zone. This measure is appropriate only if an epidemic is out of control and it is necessary to prevent it from moving into new areas. Because vaccination takes time to provide immunity, the barrier needs to be some distance from the nearest IP.

9.47 There is a delay before vaccinated animals acquire immunity (see Chapter 8). Cattle and sheep are protected against airborne challenge after 4–5 days of vaccination.[8] With oil-adjuvanted and high-potency vaccines, pigs can be protected from airborne challenge at 3–4 days after vaccination.[9,10] Although immunised cattle can shed virus, if challenged by infection 7 days or less after vaccination,[7] the excretion of virus in breath, vesicle fluids, saliva, milk, urine and faeces is reduced.[7] Culling infected animals immediately curtails the excretion of virus. Although this advantage of speed of effect might be offset somewhat if vaccination can be performed faster than culling, the vaccination zone has to be wide enough to take account of the delay, and hence more animals have to be involved in a vaccination strategy than in an equivalent strategy based on culling. The fate of the vaccinated animals is therefore crucial.

9.48 The major problem with a culling-only strategy is that, as occured in 2001, it is difficult to determine the optimal extent of slaughter required to bring the epidemic quickly under control with the minimum total number of animals destroyed. It can develop into a process of attrition, as occurred in Cumbria last year. However, provided that emergency vaccination is associated with only minimal economic or other penalties (there is no strategy that is cost-free), it is possible to err on the side of safety and vaccinate larger areas, because of the relatively small cost of vaccinating additional farms. This is true even if one takes into account the larger number of animals involved in vaccination strategies than in the equivalent culling strategies.

9.49 Both vaccination and culling involve the movement of personnel on and off farms, and in an infected zone this risks the further spread of infection. Fewer personnel are required for vaccination, and, provided that the appropriate precautions are taken, the risk of spreading infection should be less. Furthermore, if the vaccination starts outside the expected infected area and works inwards (the strategy used for emergency vaccination in the 2001 epidemic in The Netherlands) the risk of spread due to these activities is further reduced.

9.50 Culling requires personnel and equipment to slaughter animals, to dispose of their carcasses and to disinfect and cleanse premises. The resources required are considerable; if they are insufficient for the task, the delays in the operations risk a further spread of infection. The resources required for vaccination are significantly less, but the logistical requirements must not be ignored and require thorough planning and rehearsal within the overall

Figure 9.2. Criteria to be taken into account when considering emergency vaccination

(a) The outbreak

- The location within the country, the species affected in the primary cases and the stocking density.
- The characteristics of the virus, e.g. extent of any likely airborne spread, and virulence in the different species.
- Extent of any likely spread by direct contacts before the index case was identified.

(b) National level

- Export markets for different livestock products.
- The relative effect of different control strategies on the rural economy.

(c) In the region or area affected

- Rural economy, jobs, rural community stability relating to the principal activities.
- The possibility of freeing up movement within the restricted and vaccinated zone (e.g. movement to abattoirs or other grazings; opening up footpaths).
- The exit strategy.

contingency plan. During the FMD epidemic in The Netherlands each vaccination team (one veterinarian supported by two lay persons) was able to vaccinate 1500 pigs a day.

9.51 Comprehensive vaccination in an area or region results in a population that is immune, and this might facilitate a limited relaxation of movement restrictions, particularly to abattoirs, within the infected or vaccinated area, thus reducing the need for 'welfare' culls. The need for such measures is also reduced if vaccination results in a substantial reduction of the length of the epidemic. Hence, we believe that the science of vaccination has advanced to such an extent that there is now a real prospect that emergency vaccination, without the subsequent premature slaughter of vaccinated animals, is a viable control measure in addition to culling IPs and DCs. Further work is required to validate the tests to distinguish between infected animals in a vaccinated herd, and to develop accepted strategies for surveillance after vaccination.

Strategies involving emergency vaccination

9.52 Speed will be as important, if not more so, in using emergency vaccination as it is in culling. The decision to vaccinate will depend on many factors, including those set out in figure 9.2.

9.53 Under the OIE Code up to the end of May 2002, emergency vaccination leads to significant trade penalties, and the EU has suggested criteria for using vaccination. They include:

- infection in a dense population,
- infection predominantly in pigs,
- evidence of movement of infected animals out of the area of the index case,
- evidence or prediction of airborne spread, and
- evidence of rapidly spreading infection.

9.54 Now that the Code has been amended, to reduce the trade penalties it is possible to consider emergency vaccination and extended culling as alternative strategies, with the choice based on the one most likely to achieve the best balance of the issues set out in paragraph 9.2. It could be, for example, that even a small outbreak of FMD in a densely populated area should, in addition to an IP/DC cull, trigger ring vaccination of all farms within, say, 5 km working inwards, rather than a cull of contiguous premises.

9.55 As a part of contingency planning it is essential to develop strategies for alternative emergency vaccination scenarios and to determine how to prioritise the vaccination programme. It will be important to set up appropriate models that test the various scenarios to take into account the variability of virus strains, the demography and distribution of susceptible animals and the high-risk modes of transmission. If the virus strain is one for which airborne spread is a significant feature, then dispersal models using weather, terrain and biological data will be valuable in helping to predict the areas requiring vaccination as well as those for which targeting of laboratory-based surveillance is needed.

9.56 Until the OIE Code has been changed to remove all of the trade penalties associated with emergency vaccination, as explained in Chapter 8, it will be necessary to decide in advance what regional zone arrangement needs to be put in place to ensure that the UK retains its overall trading status, with an agreed and published exit strategy. These agreed plans must be drawn up in collaboration with farmers, veterinarians, local industry and others with an interest so that the consequences of deploying emergency vaccination in a region are fully understood. Although vaccination was not used, it is noteworthy that, in the 2001 epidemic in

Northern Ireland, restricted areas were designated outside which movements and rural activities went on as normal.

Practical considerations for the delivery of emergency vaccination

9.57 The virus strain can be identified within a few hours after confirmation of the index case by the reference laboratory, and arrangements for the supply and distribution of vaccine should begin once this is known. As explained in Chapter 8, it should be possible to have at least 500 000 doses available by day 4, and significantly more in succeeding days. It is therefore realistic to plan on being able to have the vaccine available, if necessary, for use in the designated areas by day 5. A far faster delivery (within 24 hours) of at least 100 000 doses is possible if the vaccine banks are routinely prepared to hold strategic reserves of already formulated vaccine, or if it proves to be practical to hold significant amounts of frozen antigen/diluent already prepared. We recommend that DEFRA explore ways of ensuring that at least 100 000 doses of the required serological type of vaccine would be available within 2 days of confirmation of an outbreak and that over the subsequent 3–8 days five million doses could be made available.

9.58 We have considered the logistical arrangements for applying a vaccinated zone of not less than 10 km around all IPs or DC premises, and the practicality of the vaccination process. One model is that used in The Netherlands in 2001, when private practitioners assisted by lay vaccinators undertook the task.

9.59 Because the number of farm animal veterinarians is broadly related to the number of farm animals, the size of the area to be vaccinated should not significantly affect the length of time it will take to complete the vaccination programme. Using the above model, we estimate that it should be possible, with farmers' assistance and compliance, to vaccinate at least 90% of the cattle or all the cattle on the larger farms within 6 days in an area of any size. Because of their numbers, sheep will present more of a logistical problem. However, because the vast majority of farmers regularly vaccinate their animals against other diseases, many could administer the FMD vaccine themselves, under the supervision of the local private veterinarians and their vaccination teams.

9.60 The species to be vaccinated will need to be prioritised depending on the species mix in the affected areas.

9.61 We recommend that DEFRA draw up contingency plans to enable a wide-scale cattle vaccination programme, with specified target times for the completion of the programme in the three major species. We also recommend that, as a part of the contingency plan, DEFRA contract with private practitioners to be available to train and supervise suitable lay persons to perform emergency vaccination, under veterinary supervision or direction.

(iv) Special arrangements—zoos and rare breeds

9.62 Measures for the prevention and control of animal diseases are usually directed towards animals kept for food production and pet animals. Animals susceptible to FMD that do not fall into these two categories include domesticated species belonging to rare breeds, and wild species held in zoos. When the control of an epidemic does not include the use of emergency vaccination as one of the control strategies, these categories of animal need special treatment. Any arrangement requires a process of prior registration and decision because they cannot be decided during an outbreak.

Rare breeds

9.63 The demand for high production targets and the success of genetic improvements have led the livestock industry to concentrate food production on a small number of breeds such as the Holstein–Friesian or on highly developed genetic crosses. The commercial importance of many other breeds has declined, although they might well contain genetic material that could be of importance in the future. Some rare breeds are now represented by small numbers of animals, making them very vulnerable to the effects of disease outbreaks in which extensive culling is used.

Zoo animals

9.64 Zoological gardens and safari parks keep animals susceptible to FMD. In general, zoological gardens adhere to well-established biosecurity systems; the stock is kept under close veterinary supervision and is rarely in contact with domestic livestock.

9.65 In recent decades, zoological gardens have become involved in captive breeding programmes that are increasingly important for the survival of species threatened in the wild. Most of these programmes are long term and internationally coordinated, and involve the movement of animals between zoos (e.g. the okapi breeding programme). The UK and other EU Member States have accepted an obligation under international conventions to conserve global biodiversity. The slaughter of endangered species

as a part of FMD and other animal disease control could be held to be a breach of those obligations.

Protection of rare breeds and zoo animals against FMD

9.66 In April 2001 the OIE reviewed the protection against FMD and the use of vaccination in special cases in relation to rare breeds, zoos, wildlife parks, rare genetic material, endangered species and animals in special research programmes. The outcome of this review concluded that the OIE Code should be modified, where appropriate, to permit the emergency vaccination of certain rare or valuable animals without prejudice to the 'FMD free without vaccination' status of the country or zone. This was conditional on such animals' being individually identified, maintained in a location that had physical barriers, zoo-sanitary procedures adequate to prevent contact with any susceptible animals that might be situated beyond the confines of the location, and measures in place to prevent the spread of infection by fomites. This location could be considered as an 'FMD-free zone where vaccination is practised', where all the attendant 'Code restrictions' will apply to the vaccinated animals, their progeny, embryos, ova and semen, and other products derived from these animals.

9.67 Likewise, EU examined in April 2001 the potential use of emergency vaccination of endangered species. In this context the preambles of Commission Decision 2001/303/ made it possible for Member States to use vaccination, under specified conditions, as an additional instrument to protect species defined as threatened in the Red List published by the International Union for Conservation of Nature and Natural Resources (IUCN; the World Conservation Union). Threatened species include those in four subcategories: Extinct in the Wild; Critically Endangered; Endangered; and Vulnerable. However, none of the Member States made use of the provisions for the emergency vaccination of endangered species during the 2001 FMD epidemic.

9.68 The case for protecting zoological collections and, by extension, certain collections of rare breeds by vaccination is clear cut in that they are genetically important, are held in secure locations and do not participate in normal trading movements. However, for protective vaccination to be acceptable a number of detailed conditions would need to be met, for example:

- the groups of animals concerned should be designated in advance of an outbreak;
- bio-sanitary precautions must be agreed in advance, subject to inspection, and approved as part of the designatory process (for zoos, such arrangements could be defined in the Secretary of State's Standards of Modern Zoo Practice); and
- the locations would be accepted under EU law as 'FMD-free zones where vaccination is practised'.

Individual zoos or owners of rare breeds should be responsible for applying for permission to vaccinate: it should not be compulsory. We recommend that, as a matter until the OIE regulations have been changed, we recommend that, as a matter of urgency, DEFRA draw up arrangements for a regulation process for the prior registration of zoos and rare breed collections.

(v) Requirements at end of outbreak

9.69 At the end of the epidemic, serological and/or virological surveillance will be required to ensure that there are no animals likely to be carrying the virus. If vaccination has been used this needs to include the differential test for non-structural viral proteins (Chapter 8).

9.70 The Disease Control System database contains valuable information to allow epidemiologists to review the steps taken to control the epidemic and to see where improvements can be made. Other studies of the epidemic might need to be undertaken and the results archived for future use.

9.71 The control measures should be reviewed regularly to determine what improvements can be identified in the light of emerging scientific discovery. The data should be made available to modelling teams in the UK and abroad so that they can contribute to the scientific debate.

(c) Control of other diseases

9.72 So far we have considered the treatment of an outbreak in terms of FMD, but the surveillance and much of the forward planning is common to all of the List A infectious diseases and many of those in list B. However, detailed control arrangements will differ and we outline here the main differences here for the six diseases highlighted in Chapter 3. Despite these differences we believe that there needs to be an overarching contingency plan for all infectious livestock diseases, with separate sections for specific diseases where required. We need to stress that we have not been able to spend as much time on these other diseases as we would

have wished and therefore are only able to make general points. However, it is essential for the country to be prepared for outbreaks of these diseases, and in particular:

a. bluetongue and African horse sickness because of the relentless northward movement of this disease, possibly because of climate change, and because of the close relationship between its current midge vectors and UK midges;
b. classical swine fever, because of the continuing outbreaks elsewhere with the EU exacerbated by it now being endemic in the wild boar population and the possibility that it might infect the growing number of UK wild boar;
c. strict contingency plans are required for highly pathogenic avian influenza following the outbreak in Hong Kong, where all flocks were culled and several people died;
d. evidence was given to us that routine vaccination had changed the situation over Newcastle Disease and that it should no longer be classified as a List A disease[13]. We believe that this possibility requires careful investigation.

9.73 There are other List A diseases that warrant attention including swine vesicular disease, and African swine fever. In considering other diseases the criteria to be considered include:

- The degree of mortality and morbidity in both adult and young animals.
- The methods available to achieve rapid diagnosis with high sensitivity and specificity.
- Whether the disease is likely to cause a threat to human health.
- The degree of infectiousness and whether there are special vectors that are the main mechanism for transmission, such as insects or wildlife.
- The species of livestock infected.
- Whether vaccines are available and suitable for routine or emergency vaccination.
- The availability of effective vaccines and tests that will allow discrimination between infection and vaccination.

We summarise these and other factors in Figure 9.3 on page 126, for the six diseases.

Control measures

9.74 For all of the diseases in Figure 9.3 the current policy is to retain disease-free status, and this is fully justified by their high infectiousness and mortality rates, which in some cases approaches 100%. Furthermore, with the exception of Newcastle Disease, where a satisfactory vaccine is available, this status is achieved without vaccination.

9.75 In all cases stringent biosecurity measures together with rapid culling are the control measures currently used to stamp out outbreaks of these diseases in Figure 9.3.

9.76 As far as emergency vaccination is concerned the current situation is set out in section (e) of Chapter 8. There is no effective vaccine available for African swine fever, and only a poor vaccine for swine vesicular disease. With bluetongue and African Horse Sickness there are problems. In view of the northward spread of Bluetongue, however, the existing vaccines need to be tested for safety and efficacy and a research programme supported to develop a safe non-replicating vaccine for eventual commercial production by a European manufacturer. For classical swine fever emergency vaccination appears to be an option as a marker vaccine is under development, although it is not currently as effective as the available live attenuated vaccines. Unfortunately serological tests to differentiate infection from vaccination antibodies are yet to be configured to provide both high sensitivity and specificity. Current research to develop alternative marker vaccines needs to be fully supported and until this research produces acceptable results emergency vaccination as an aid to controlling a CSF outbreak is unlikely to be practicable.

9.77 A considerable amount of work needs to be done on these other diseases, and DEFRA should undertake a quantified risk assessment exercise to determine the priorities for this work, and then to put this in hand.

(d) Contingency planning

9.78 At various places within this report we have stressed the need for adequate prior planning and the drawing together of this work into a formal contingency plan. Since many of the management, administrative arrangements, underpinning data and communications requirements are common to all of the diseases in livestock, we believe that there should be an umbrella plan of these common issues, and then disease specific components for each of the diseases, which should include the alternative control strategies, and the arrangements for taking decisions during an epidemic.

9.79 We welcome the publication of the interim contingency plan for controlling FMD, published by DEFRA in March 2002, and after we had completed our work we also received a draft contingency plan from the Scottish Executive. We particularly welcome the fact that both

bodies were actively seeking comments on these plans, as we believe that it is essential for such contingency plans to be discussed openly, and widely promulgated so that all stakeholders know what would be expected of them in the event of an outbreak. Our first recommendation was that this should involve Parliament. At the very least the detailed plan needs to be presented to the Environment Food and Rural Affairs Select Committee, but the Secretary of State may wish to consider presenting the outline plan for debate in the House.

9.80 The situation over these diseases and the options available for their control is highly dependent on a range of factors including changes to the agricultural processes, the level of external threat, and the advances in underpinning science and technology, particularly in vaccines and diagnostics. It is essential for there to be regular reviews of the contingency plans to see whether changes are required in the light of the developing situation. We have therefore also recommended a formal review process.

9.81 It is clear that contingency plans, especially those associated with intermittent events, need to be tested regularly, through annual practical fire drills, not just paper exercises. These should involve all of the organisations inside and outside Whitehall that would be required to play a role in controlling an outbreak.

Development of the control policy component within the contingency plan

9.82 The interim contingency plan covers the management and administrative issues, but explicitly does not cover matters of policy. We believe that further work is required to strengthen a number of areas including: the input of technical advice; the establishment of appropriate communications at all levels and; the arrangements required to deliver quickly formulated emergency vaccines and to mobilise vaccination teams.

9.83 In earlier parts of this report we have stressed the need for much further work on the question of underpinning information, information collection during the outbreaks and studies using modelling as well as the insights from experienced field epidemiologists of various strategies that could be adopted to combat outbreaks of these diseases. Even with the extensive experience of culling, there is still much that needs to be explored, and there is very little quantitative work on the possible strategies for emergency vaccination.

9.84 It is therefore essential for DEFRA to put in place the work required to establish the database and contingent data collection arrangements during an outbreak. The latter should take account of best practice over the collection and validation of real-time information, and should not, as we understand happened during 2001, require multiple entries of the same data.

9.85 Similarly, work needs to be put in hand to explore further control measures beyond culling infected premises and dangerous contacts. In particular the urgent need to explore the potential of targeted emergency vaccination strategies for combating outbreaks of FMD and possibly CSF. We are also concerned that work be put in hand immediately to develop a strategy for dealing with an outbreak of bluetongue.

9.86 Significant effort is required to develop the overall strategy even for a single disease such as FMD, including the work associated with developing a viable strategy for using emergency vaccination as part of the control arrangements. Hence work on this should begin immediately and be appropriately resourced. We understand that following the classical swine fever epidemic in 1997–98, the Dutch Government set up a dedicated team of experienced officials and advisers to develop and draft a revised contingency plan. Realistically it should be possible to complete the short-term work for FMD, including that associated with emergency vaccination, before the end of 2003. We discuss in the next chapter the longer-term research that is required.

(e) Recommendations

9.87 Our main recommendations are

- **that the main objective in dealing with an outbreak must be to ensure that it does not develop into an epidemic. This requires the following basic measures:**
  - **i. on suspicion of an outbreak the immediate imposition of strict local movement restrictions and biosecurity measures, including the culling of the animal with clinical signs;**
  - **ii. on confirmation of an outbreak by an OIE Reference Laboratory:**
    - **the mobilization of the full emergency arrangements including interdepartmental coordination and scientific advisory structure;**
    - **imposition of a total country-wide**

ban on animal movement with unambiguous and widely publicised advice on the fate of any animals in transit;
- **rapid culling of all infected premises;**
- **identification and rapid culling of all premises where there is a high risk of the disease.**

where these measures are insufficient to guarantee that the outbreak will be contained, we recommend in addition the early deployment of emergency vaccination; (R9.1)

- **as a matter of urgency, DEFRA draw up arrangements for a process for the prior registration for vaccination of zoos and rare breed collections; (R9.2)**
- **DEFRA should review its arrangemnets for other diseases, and in particular the developments required to enable emergency vaccination to be used for CSF and Bluetongue; (R9.3)**
- **the detailed strategies for controlling outbreaks of livestock diseases be included in the published contingency plan, which should consist of an umbrella plan for matters that are common to all diseases, with specific modules for each disease. These plans should be rehearsed in an annual 'fire drill' that must be realistic and invole DEFRA and all other relevant bodies including MoD. (R9.4)**

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Figure 9.3. Biological properties of List A viruses threatening the UK.

Disease	Foot and mouth (FMD)	Classical swine fever (CSF)	African swine fever (ASF)	Avian Influenza (AI)	Newcastle Disease (ND)	Bluetongue (BT)	African Horse sickness (AHS)
Causative agent	*Aphthovirus* (Picornaviridae)	*Pestivirus* (Flaviviridae)	*Asfivirus* (Iridoviridae)	*Influenza virus* (Orthomyxoviridae)	(Paramyxoviridae)	*Orbivirus* (Reoviridae)	*Orbivirus* (Reoviridae)
Number of serotypes	7 (A, O, C, Asia, SAT1-3)	1	1	2 (H5, H7 HPAI) (15x11 LPAI)	1 (8 other avian PMVs)	25	9
Domestic livestock affected	Cattle, pigs, sheep, goats, deer, camelids.	Pigs	Pigs	Poultry, possibly swine.	Poultry	Sheep, goats, deer, cattle.	Horses, donkeys, mules, dogs (rare).
Wild/exotic hosts	Deer, some zoo animals e.g. okapi, elephants.	Wild Boar	Wild boar, warthogs.	Water fowl and sea birds.	Many bird species, esp. water fowl.	Deer, pronghorn antelope.	Zebras
Carrier animals	Cattle, sheep, buffalo.	Swine infected in utero (2.5 yr)	Warthogs , ticks.	Many avian species esp. waterfowl.	Psittacine birds (>1 year). Convalescent chickens 4 wk.	Cattle (20 weeks)	Zebras?
Routes of transmission	Direct contact, fomites, aerosol and ingestion.	Ingestion, direct contact, fomites.	Ticks, ingestion, direct contact, aerosol.	Ingestion, aerosol.	Ingestion, aerosol, dust or direct contact.	Insect vector, transplacental or via semen.	Insect vectors
Arthropod vectors	No	No	Soft ticks	No	No	Culicoides spp. (midges)	Culicoides spp. ticks, mosquitoes.
Environmental stability	Stable up to 6 mo. in slurry, 3–28 days on the ground.	Stable in cold conditions. Survives curing and smoking.	Stable in blood, faeces and tissues.	Stable in tissue faeces and cold water.	Stable, especially in faeces.	Extremely stable (several years in blood @ 20°C).	Stable at @37°C.

Figure 9.3. continued

Disease	Foot and mouth (FMD)	Classical swine fever (CSF)	African swine fever (ASF)	Avian Influenza (AI)	Newcastle Disease (ND)	Bluetongue (BT)	African Horse sickness (AHS)
Zoonotic threat	Insignificant	No	No	Potentially serious	Insignificant	No	V. rare
Clinical features	Fever, anorexia, reduced lactation. Lameness. Vesicles or blisters on oral mucosa, nostrils, teats, coronary bands and interdigital spaces. Claw loss in pigs. Myocarditis (often fatal) in young animals. Milder signs in sheep.	Fever, anorexia, lethargy. Multifocal skin haemorrhage. Cyanosis of extremities. Ataxia, paresis, convulsion. Death within 7 days. (Clinically identical to ASF) Button ulcers in ileum for sub-acute infections.	As for CSF	Severe depression and anorexia. Drastic reduction in egg laying. Facial swelling. Petechial haemorrhages. Sudden death.	Velogenic form: Severe depression and anorexia. Drastic reduction in egg laying. Facial swelling. Petechial haemorrhages Paralysis. Sudden death. Milder mesogenic and lentogenic forms exist.	Fever Inflammation, ulceration and necrosis of oral mucosa. Swollen, cyanotic tongue. Lameness. Abortion. Emaciation. Death.	Fever, swelling of supraorbital fossa and tissue of head and neck. Death in 4–8 days (cardiac form). Acute respiratory distress, frothy exudates from lungs. Death in 2–24 hr due to anoxia (pulmonary form).
Incubation period	2–8 days (cattle)	2–14 days	5–15 days	3–5 days	4–6 days	5–20 days	3–14 days.
Morbidity and mortality rate	100% morbidity (cattle). 5% mortality in adults, ≤75% in piglets or lambs.	100% morbidity 30–90% mortality	100% morbidity 30-100% mortality	100% morbidity 100% mortality	100% morbidity 100% mortality (velogenic strains)	80% morbidity 30% mortality Sub-acute form more common in European breeds.	50–95% mortality
Differential diagnosis	Swine vesicular disease Vesicular stomatitis virus Mucosal disease Infectious bovine rhinotracheitis Bovine mammillitis Bovine papular stomatitis	African Swine fever PDNS BVDV Salmonellosis Erysipelas Acute pasteurellosis Leptospirosis Coumarin poisoning	CSF PDNS BVDV Salmonellosis Erysipelas Acute pasteurellosis Leptospirosis Coumarin poisoning	Acute fowl cholera Velogenic NDV Infectious laryngotracheitis	Acute fowl cholera HPAI Infectious laryngotracheitis Fowlpox (diphtheritic form) Psittacosis Mycoplasmosis Infectious bronchitis	Contagious ecthyma FMD Photosensitisation Pneumonia Polyarthritis Plant poisonings PPR	Anthrax EIAV EVA Hendra Trypanosomosis Equine encephalosis Piroplasmosis Purpura-haemorrhagica

Figure 9.3. continued

Disease	Foot and mouth (FMD)	Classical swine fever (CSF)	African swine fever (ASF)	Avian Influenza (AI)	Newcastle Disease (ND)	Bluetongue (BT)	African Horse sickness (AHS)
Last UK outbreak	2001	2000	Never	1992	1997	Never	Never
UK/EU/World reference lab.	Pirbright	VLA Pirbright Hanover (EU)	VLA	VLA	Pirbright Onderspoort VI (S.Africa)	Pirbright	Onderspoort VI (S.Africa)
Virus detection methods	Ag-ELISA, RT-PCR, virus isolation.	Immuno-staining on tissue or cell culture. PCR (developmental).	Cell culture. Immuno-staining, PCR (developmental).	HA, HAI and AGIT tests using virus from infected embryonated chicken eggs and type specific sera. Intravenous pathogenicity index test (IVPI) or sequencing of HA cleavage site to confirm pathogenicity.	As for HPAI. Sequence analysis of F2 protein cleavage site predictive for velogenic strains (test under development).	Virus culture in eggs followed by Ab typing. Ag-ELISA (VP7) (10^3 $TCID_{50}$ sensitivity. Not suitable for blood) RT-PCR (developmental).	As for BTV
Antibody tests	ELISA, VNT, NSP ELISA (for differentiating vaccinated from convalescent animals) . .	ELISA, VNT (Note antibodies appear after 21 days, therefore only useful for low virulence strains).	ELISA, Immunoblotting.	HAI test.	HAI test.	ELISA, VNT.	ELISA, CFT Immunoblotting.
Preventative measures (UK)	Import restrictions, quarantine.	Import restrictions, quarantine.	Import restrictions, quarantine.	Biosecurity	Routine vaccination Biosecurity	Import restrictions, quarantine.	Import restrictions, quarantine.
Current UK/EU vaccination policy	Prohibited in UK.	Prohibited in EU.	N/A	Prohibited in UK.	Universal	Prohibited in UK.	Prohibited in UK.
Current control measures (UK)	Culling IP, DC and CP. Movement restrictions.	Culling IP and DC. Movement restrictions.	Culling IP and DC. Movement restrictions.	Culling IP. Movement restrictions.	Culling IP. Movement restrictions.	Culling infected animals.	Culling infected animals.

Figure 9.3. continued

Disease	Foot and mouth (FMD)	Classical swine fever (CSF)	African swine fever (ASF)	Avian Influenza (AI)	Newcastle Disease (ND)	Bluetongue (BT)	African Horse sickness (AHS)
Current vaccines	Killed virus (strain matched).	Live attenuated (indistinguishable from natural infection by serology. Can cause abortion) .	No vaccine available.	Killed virus. Recombinant fowlpox vectors.	Live attenuated (B1 and La Sota strains). Killed virus.	Multivalent live attenuated (may cause abortion).	Live attenuated polyvalent (S.Africa) Killed virus (AHS 4) used in Portugal.
Developmental vaccines	Heterologous recombinant viral (e.g. Ad5). Synthetic peptide. Live attenuated.	Heterologous recombinant viral (e.g. baculovirus or CSFV/BVDV chimera based)	Antibodies to both p54 and p30 required for protection. Combined expression vectors under development.	Baculovirus and ILTV based recombinants.	Recombinant fowlpox vectors.	Recombinant baculovirus expressed VP3 and VP7.	Recombinant baculovirus.
Problems and future needs.	Need for pen-side test. Improved marker vaccines desirable.	Need for pen-side test that can differentiate CSF from BVD and Border disease virus. Marker vaccines and differential tests desirable.	Validation of Ag-ELISA. Completion of RT-PCR test development.	Elimination of LPAI H5 and H7 strains from flocks to prevent evolution of virulence. Monitoring program yet to be started.	No serious deficiencies. Constant monitoring and vigilance .	BTV specific RT-PCR for detection of virus in blood is a priority.	AHS specific RT-PCR for detection of virus in blood is a priority. Improved polyvalent vaccines desirable.

10 Research and development, education and training

(a) Research and development

(i) Introduction

10.1 Our Inquiry contains many recommendations relating to specific requirements for research and development. Their implementation depends upon the existence of a high-quality research base that can be applied to infectious diseases and immunity in livestock, and this chapter asks whether the current arrangements – dominated in terms of funding and policy by the BBSRC, DEFRA and the universities – are optimal and what changes could be introduced to improve the situation.

10.2 This year the Royal Agricultural Society of England has launched its Year of Science and this reflects how important the farming community consider the research and development that underpins their industry. This view was also highlighted by Curry[1]: *'To stay competitive, businesses need to know about the latest developments and be able to apply them if appropriate. Information gained from research needs to be readily available in a usable format…'*. These responses reflect unease at the current levels of investment in agricultural research and at the quality of the direction given by Government to the research efforts themselves. Meanwhile, expenditure on dealing with problems such as bovine spongiform encephalopathy (BSE), foot-and-mouth disease (FMD) and classical swine fever has been at least £15 billion, whilst the ongoing annual costs of endemic diseases amount to 17% of the annual turnover of the livestock industry. Had Britain and its partners invested substantially over the past 15 years in developing new vaccines or making the most modern diagnostics available, the cash savings could have been vast, let alone the benefits to livestock farming from better animal health. We seem to have forgotten the importance of technology in generating and maintaining efficient British agriculture (the motto of the Royal Agricultural Society is 'Practice with Science'). We received evidence[2] reminding us that the research and development budget in agriculture (Ministry of Agriculture, Fisheries and Food (MAFF)) decreased by 44% between 1986 and 2001.

10.3 Resources, including manpower resources, are a key factor and these are currently being addressed in the Government's Spending Review. Later we consider the resource issue in more detail, but we note that President Bush proposes to enhance research into bioterrorism within the USA by $1.5 billion in 2003 alone. These extra funds will be invested in precisely the areas of research mentioned below that hold the key to controlling animal or human diseases in the future.[3]

10.4 The UK's contribution to animal disease research compares well with that of other countries but, as will be evident later, the size of the research endeavour worldwide is small relative to that in human medicine. Because infectious diseases do not respect national borders and pose a risk to all EU countries, it is appropriate for regulations governing animal health and trade to be agreed at EU level. For the same reason, national research efforts into livestock diseases should be coordinated across Europe, and we cannot see why the Common Agricultural Policy should not fund research into exotic diseases of livestock within the EU so that it works to a largely common agenda. An alternative would be to ensure that the EU's Framework Programme (number 6) includes livestock under the theme that covers genomics, biotechnology, food quality and food safety.

10.5 As regards the UK, we support the Curry Commission in recommending that the Government should establish a new 'priorities board' for research into farming and food matters. Such a board should set the national agenda for publicly supported research covering animal disease, animal welfare, crop improvements, farm practices, economics and the environment.

(ii) Animal disease research in Britain

10.6 In the context of our specific remit the Government should develop a 'national strategy for research in animal disease and surveillance'. The issue is of strategic importance for the livestock industry, and short-, medium- and long-term vision is required, encompassing research and surveillance on all livestock diseases—endemic and exotic, old and new. The broad areas where we believe research and development offer opportunities to improve disease control include:

- livestock management practices,
- biosecurity,
- pathogenesis of infectious diseases,
- viral and bacterial biology,

- predictive capacity, risk and surveillance,
- modelling and epidemiology,
- veterinary clinical research and diagnosis of disease,
- vaccination,
- zoonotic disease transmission to humans through food.

10.7 In all these areas it is no longer appropriate to separate 'basic' from 'applied' research, 'research' from 'development', and 'research' from 'surveillance'. These are arbitrary divisions of R&D and impede the flow from basic research into application, at least insofar as the biological sciences are concerned. The drive within the Office for Science and Technology (OST) and the Department of Trade and Industry (DTI) is towards scientists who not only make discoveries but are also committed to their development and application, and work in an environment that supports this. In our view the area of animal disease research is one in which the continuum from basic research to application should be strongly encouraged.

10.8 Over time the UK has created a number of artificial boundaries for responsibility for animal disease and surveillance, and no one single organisation has overall responsibility. In our view this is a crucial point since it is unacceptable for the R&D system in the relatively small area of animal disease to work sub-optimally when it is of such importance to the future of the livestock industry. The difficulties can be overcome by creating a national strategy and then ensuring proper coordination of the delivery system. We believe that the resources for research funding in infectious diseases of animals (both endemic and exotic), currently separated within England across DEFRA, BBSRC and the Food Standards Agency, should be brought under a single joint arrangement and the funds made available to the body organising and implementing the national strategy for animal diseases and surveillance.

10.9 Opportunities are currently particularly favourable for an overhaul. DEFRA has been formed recently with responsibility for both the environment and agriculture and is developing its overall strategy. The Research Councils have created a body to coordinate their own efforts (RCUK) under the Director-General of the Research Councils. Three recent appointments have been made to important positions, notably the Chief Executive at BBSRC (Professor Julia Goodfellow), DEFRA's Chief Scientific Adviser (Professor Howard Dalton) and the Director of the Institute of Animal Health (Professor Paul-Pierre Pastoret).

(iii) Current provision and issues

10.10 Research on animal diseases in the UK takes place largely in the following locations:

- The Institute for Animal Health (IAH, with laboratories at Compton, Pirbright and Edinburgh), which is a BBSRC-sponsored institute, funded mainly by votes from the DTI/OST, and by commissions from DEFRA. Its turnover is £25 million p.a., of which some £16 million is spent on endemic diseases and £9 million on exotic diseases (largely at Pirbright).
- The Veterinary Laboratories Agency (VLA, with headquarters at Weybridge and with regional laboratories), which is sponsored by DEFRA and largely funded from this source. It has a turnover of some £80 million p.a., of which £58 million is devoted to surveillance and £22 million to research. Research focuses primarily upon endemic diseases (the current spend on research and surveillance on transmissible spongiform encephalopathies (TSEs) is about £40 million p.a.) but about £3 million is devoted to statutory exotic viruses and bacteria. The VLA contains a large epidemiology group (more than 40 staff), which underpins all disease issues.
- University departments, including the veterinary schools, which are supported by research grants and contracts from BBSRC, the Wellcome Trust, DEFRA and others, along with their core Higher Education Funding Council allocations of research funds (QR).
- The Food Standards Agency, which supports research on food safety in connection with zoonotic diseases.
- The Veterinary Science Division of the Department of Agriculture and Rural Development in Northern Ireland, which supports work at Stormont and in Queen's University, Belfast, on endemic diseases with a particular focus upon cattle tuberculosis.
- The Moredun Research Institute in Edinburgh, with its focus upon infectious diseases in livestock, and along with the Veterinary Science Division of the Scottish Agricultural College (which is responsible for disease surveillance in Scotland) carries out research on related topics. Both are supported by the Scottish Executive Environment and Rural Affairs Department.
- Private research institutes such as the Animal Health Trust at Newmarket. This trust has a total turnover of £8.3 million and devotes just over £1 million to infectious diseases of horses.

10.11 Reviews and audits have been undertaken recently by the BBSRC on the IAH (BBSRC Institute Assessment Exercise of 2001, followed by the establishment of a review panel under Professor Keith Gull); by DEFRA on the VLA (Science Audit 2001/2002) and on all university departments through the Funding Councils' 2001 Research Assessment Exercise.

10.12 Given the quality of the research in the universities and the institutes, the UK has the potential for world-leading research and biotechnology expertise in animal disease research and its application, but we believe this position is endangered by the absence of a coherent and integrated national strategy. We seek less fragmentation and better overall coordination between the component parts in delivering the national strategy.

10.13 It is not within our remit to recommend a particular model for delivering the national strategy but an attractive option could be to create a virtual 'Centre for Animal Disease Research and Surveillance' which would include the IAH, the VLA and the universities as the primary members. Ideally, it would extend across the UK to include the publicly funded research on animal diseases in Northern Ireland and Scotland, and might invite privately funded institutes such as the Animal Health Trust to be members. It is the Board of this 'Virtual National Centre' that we envisage setting the national strategy, having access to the overall resources, establishing the mechanisms to approach each disease problem, and taking responsibility for the ultimate delivery of the programme. A key development would be the establishment of Research Units or Groups within universities to complement and strengthen the research base available in the VLA and IAH and the other institutes. The other models to which we would draw attention are the successful virtual centres on catalysis, and on mobile communications, created by the Engineering and Physical Sciences Research Council (EPSRC).

10.14 We have noted with interest the response by the Department of Health to their own analysis of the risks from human infectious disease outlined in *Getting ahead of the curve*[4]. They plan a new Health Protection Agency that will bring together the functions currently held by the Public Health Laboratory Service, the National Radiological Protection Board, the Centre for Applied Microbiology and Research, and the National Focus for Chemical Incidents. This will integrate both surveillance and the underpinning research, and we believe that DEFRA should investigate this model and its relevance for our suggested virtual national centre.

10.15 We were made aware that the BBSRC has submitted a strong submission to the 2002 Spending Review for enhanced research investment on 'animal infectious diseases and epidemiology' aimed at strengthening the infrastructure (containment facilities) and stimulating new research into exotic and endemic diseases in their institutes and the universities. In terms of research areas suggested, the submissions from the BBSRC, IAH and the VLA accord well with our thoughts in paragraph 10.5 above:

- pathogen biology and host–pathogen interactions,
- faster strain characterisation of viruses,
- rapid diagnosis and more efficient serological testing, including the ability to distinguish infected from vaccinated stock,
- vaccine design and testing emanating from a better understanding of livestock animal immunology,
- a search for antiviral drugs,
- biomathematical modelling,
- surveillance in risk assessment.

10.16 The Inquiry also received submissions from university research groups and from veterinary schools. Essential expertise lies within the universities and they should be involved from the outset in developing the new national strategy for animal disease research and surveillance. They bring the following skills:

- medical research and the capacity to understand how it can complement and strengthen work on animal biomedical research;
- specific research expertise, such as the world-leading modelling and epidemiology groups at Imperial College, Oxford, Edinburgh, Cambridge, Warwick and Liverpool;
- the veterinary schools, which are crucial to the veterinary profession in this country as well as having considerable strengths in funded infectious diseases research with international publications in the leading journals (as recognised by the Funding Councils' Research Assessment Exercise).

10.17 In 1997 Lord Selborne chaired a committee (set up by the Royal College of Veterinary Surgeons) on the future of research in the veterinary schools; the report[5] was published in 1997. It was the fourth report to spell out the

Figure 10.1. Average number of research publications per year on livestock diseases during 1991–2001.

Disease	World	UK
Livestock diseases		
Foot-and-mouth	117.7	27.6
Classical swine fever	83.5	8.5
African swine fever	35.3	8.2
Avian influenza	37.8	5.8
Newcastle disease	131.6	11.5
Bluetongue	75.2	17.5
Bovine tuberculosis	43.9	13.3
Rabies	229.3	18.3
TSEs	209.8	63.1
Human diseases		
Hepatitis B	1811.4	165.6
Hepatitis C	2496.8	181.7
HIV	9682.8	1035.5
Influenza	1229.3	151.5
Malaria	1387.4	285.4
Tuberculosis	2250.2	304.7

inadequacies of arrangements for supporting research and to contrast them with those in the medical schools. Progress since then has been slow. The schools produced 'Veterinary Research within the UK Veterinary Schools: a Strategy for Development' in March 2001, which is still under consideration by an implementation group that includes the Higher Education Funding Council for England and the Scottish Higher Education Funding Council. These proposals argue for deeper collaboration between the six veterinary schools and other stakeholders to produce a national research base in veterinary infectious diseases.

10.18 The first of the three main aims in the proposals is: *'To increase the quality, quantity, and international competitiveness of research in infectious diseases in the UK veterinary schools by developing in each school one of the platform technologies that together will constitute a national research base in this area'*. We would wish to see the Selborne Report acted upon by the Funding Councils.

10.19 A major reason for ensuring the necessary linkages both within and beyond the UK is the relatively small size of the world research effort on animal diseases. We commissioned a brief bibliometric study[6] on the number of research papers published per year during the period 1991–2001 for various diseases. The measure of papers published is used only as a proxy for research volume; it says nothing about the quality of research. The results are summarised in figure 10.1.

10.20 In general any area of research publishing only 50–100 articles a year would be considered small and probably translates into a worldwide population of lead scientists of between 10 and 20. The UK's animal disease research community is clearly still a significant world player and the figures would indicate that this is a national expertise. However, the funding of statutory and exotic diseases remains small. A recent series of data from DEFRA[7] indicate that the current expenditure on exotic disease (all in the institutes) is £3.9 million in 2001–02. Recalculating the series of published figures to 2002 pounds it is clear that expenditure from DEFRA has been effectively constant during the 1990s. (The overall expenditure by DEFRA on disease and welfare increased by just over 20% in real terms, with most of the increase going towards TSEs and tuberculosis.) We draw attention to these figures because they argue strongly for closer links between research into infectious diseases in humans and animals, both for staff at the institutes and for any staff in the new Research Units that we recommend below.

10.21 Government-funded R&D in agriculture has faced a difficult period over the past 20 years. Central government regarded basic research in agriculture as over-supported in the 1970s, whilst in the 1980s some areas were also regarded as too 'near market' to be appropriate for Government support.

10.22 The result has been that the BBSRC (previously the AFRC) research institutes have faced an extremely difficult 20 years and had to struggle against annual decreases in budgets, particularly for 'applied' research commissioned by the then MAFF under the Rothschild 'customer–contractor' principle. The number of permanent staff in the institutes has halved since 1980 and although the individual institutes remain strong, they are no longer as significant in the overall national system of biological research. Many of the research-intensive university schools in the biological sciences and in medicine have grown substantially, doubling in size since the late 1980s and containing 300–400 researchers. This growth has been driven by three factors: a doubling in undergraduate numbers; relatively buoyant research funds available to support postgraduate students, postdoctoral fellows and research projects; and professionalisation of the entire university research enterprise so that departments focus in the long term upon

research specialities and construct their infrastructure accordingly.

10.23 An important issue within livestock veterinary medicine is the relative smallness of the market for many treatments. This applies particularly to exotic diseases and especially to vaccine and diagnostic developments. The recent effect of creating a market for BSE diagnostics is an example in which commercial developments have been triggered rapidly. Because market pull is unlikely to be sufficient to stimulate product development for rare exotic diseases, we believe that the Government, working with the EU, should consider how public funds might procure such materials from the commercial sector.

(iv) Resources

10.24 Finally, we comment upon the financial investment needed to improve animal disease research in Britain. Earlier we emphasised the huge expense—at least £15 billion—that has fallen upon the taxpayer as a result of the three unpredicted crises of the last decade. We strongly believe that Britain is failing to invest adequately in infectious animal disease research (both exotic and endemic) and while this continues it will be ill equipped with the technologies and personnel to fight infectious diseases. We noted, for example, that cattle tuberculosis, which infected nearly one-half of British cattle herds in the 1930s, was reduced to 0.1% by 1979 by a combination of science, surveillance using science, and slaughter of infected animals. In the year 2000 new infections affected 1.5% of cattle herds. Other instances could be given of our failings to face up to existing and potential animal diseases and to undertake the research and development that would allow them to be combated effectively.

10.25 The Government must increase their investment in animal disease research, with the extra investment intended to produce a step change in the national research capacity. We believe that an additional sum of £250 million will be required over the next 10 years—the issues are long term, not short term. In all cases the aim should be for basic research which follows through into application.

10.26 We do not make detailed recommendations upon how these extra funds should be spent but believe the following elements are critical:

- *IAH and VLA.* Increased funds are needed at the IAH and the VLA to strengthen both the underlying research capacity, which is exceedingly small, in all the exotic disease areas, and to invest in translational research whereby fundamental discoveries are developed to improve surveillance, diagnosis and treatment.
- *University-based units.* A number of university-based research units should be created that would focus upon research areas complementary to work within the institutes, as well as opening up new opportunities. These should be based upon the well-tried models of MRC centres or the (old) AFRC Research Groups and should be established on a rolling five-year programme with a minimum life of a decade (subject to satisfactory peer review). They must be embedded within research-rich university departments. Preferably a number would be located in those universities with veterinary schools in order to ensure knowledge transfer of basic research into clinical solutions to diseases. The units must interact freely and continuously with the disease researchers in the institutes, and with relevant disciplines in medicine and other fields. Particular areas we believe to be of great importance are:
  - livestock management practices to reduce disease and enhance welfare (see Chapter 5),
  - epidemiological modelling (see Chapter 6),
  - animal disease pathogenesis (see Chapter 6),
  - immunology in livestock (see Chapter 8),
  - understanding diseases of the future,
  - food safety issues.
- *Infrastructure*. Without modern large animal containment facilities it is not possible to undertake research upon many infectious diseases since it must be carried out on the target species (such as cattle, pigs and sheep). In many instances it has been a relative lack of such facilities that has been an impediment to understanding key research questions raised in this report (such as the carrier state, the survival of exotic viruses and the ability to test vaccines thoroughly). We believe that a small number of new containment facilities are required, to ensure their availability to university research groups and to improve even further those available at the institutes. We were not equipped to cost these accurately but suspect that an investment of £25 m to £50 m will be required.
- *Research grants*. A targeted programme of research grants is required that will stimulate novel ideas in key areas such as diagnostics, novel antimicrobials, vaccine development and understanding the molecular basis of disease, with the aim of approaching disease

control genetically. An important feature will be to ensure the bringing together of research on human and animal medicine.
- *The need for a career structure*. The key to the above will be to attract extremely talented individual persons into animal disease research. For this reason we believe that funding outstanding young talent is the primary requirement. A key aspect of this is to create a research career pyramid for promising investigators so that the entry-level PhD, particularly those whose first degree has been in veterinary science, can see a clear career path in incremental stages to a Senior Principal Research Fellowship, with long-term funding and security.

10.27 In conclusion we note that in the past decade the UK has faced a series of major problems with animal disease, health and welfare. These have caused a national crisis of confidence in our ability to solve and manage these problems, and although research is only one component it is a most important one. For this reason we do not believe that matters can be allowed to remain as they are: we consider that nothing less than a major overhaul of the present system will satisfy either the Government or the public.

10.28 We recommend that the Government should:

- **undertake a thorough overhaul of research into animal disease, and in particular develop a national strategy for research in animal disease and surveillance; (R10.1)**
- **draw together the current research funding in infectious diseases of animals (both endemic and exotic) within England into a single joint arrangement, the funds being made available to implement the national strategy; (R10.2)**
- **create a virtual National Centre for Animal Disease Research and Surveillance, the Board of which would be responsible for delivering the National Strategy; (R10.3)**
- **increase investment in animal disease research and development by the order of £250 million over the next 10 years. (R10.4)**

(b) Education and training

10.29 This Inquiry has placed much emphasis upon the linkages between the livestock farmer and the veterinarian, which we see as the bedrock upon which good surveillance occurs. This section considers the training requirements for the farmer and the livestock keeper, and for the veterinarian in livestock practice.

(i) Farmers and livestock keepers

10.30 We are pleased to see that DEFRA will review the effectiveness of training and education provision for farmers and other land managers.[8] This is needed not only for exotic diseases, which strike rarely, but also to reinvigorate the broader skills of farmers as they face a challenging future. It is worth recalling paragraphs 5.52–5.63 describing some of the important advances being undertaken to improve livestock management practices and disease prevention: their introduction requires a high level of skills on the farm.

(ii) Undergraduate veterinary education

10.31 The FMD outbreak of 2001 brought into sharp focus the role of the veterinary surgeon. Indeed, many have been jolted into reassessing their profession and the underlying vocational basis of the majority who enter veterinary careers. Surveys indicate that most students enter veterinary school with their sights set on general veterinary practice. That remains the prime role of a veterinarian, but greater efforts should be devoted to attracting a proportion of the graduates into public health, state veterinary medicine and research. For example, the difficulties in retaining young veterinarians within research impoverishes the enterprise of a key group of individuals whose research focus is devoted to the whole animal and its health and welfare.

10.32 An underlying problem – described in detail in the Selborne Report[5] – is that whereas the Department of Health has a crucial role in supporting the universities in the training of medical students (e.g. through SIFT (the Service Increment for Teaching and Research)) and the provision of research facilities, no Government Department has an equivalent role with regard to university veterinary education. This means that the veterinary expertise in DEFRA and the VLA is uncoupled from the expertise in the veterinary schools. If they were brought together through joint funding, or even if a joint standing committee in education and research were created, it could do much to improve our national capability in the surveillance, diagnosis and control of infectious diseases in animals.

10.33 Demand for places at veterinary schools remains considerable and most admit students with straight 'A' qualifications. The curriculum is a

Figure 10.2. Postgraduate qualifications in selected veterinary subjects, as at 31 December 2001.

	Certificate		Diploma	
Subject area	Enrolled	Holders	Enrolled	Holders
Cattle health and production	52	85	12	8
Pig medicine	13	37	3	12
Sheep health and production	12	56	2	9
Equine subjects	179	177	17	21
Small animal subjects	523	179	52	42
State veterinary medicine	8	4	0	0
Total for all subjects	**1265**	**1468**	**151**	**338**

The table gives the numbers of those who were currently studying for the quakifications at the end of last year. The number of holders at that date represents all the certificates and diplomas awarded since the qualifications were introduced, and are therfore cumulative year on year.
Source: Royal College of Veterinary Surgeons.

professional training and faces demands covering practical learning, leaving little room for other topics. This is a challenge for all professional curricula, and the risk for veterinary science graduates is that the requirements for producing professional 'omnicompetence' on graduation squeezes out the essential need and requirement for a scientific education that should provide the intellectual tools for the veterinarian in many different career paths. Veterinary undergraduates need to be equipped with the skills of the future, including those of modern molecular sciences, quantitative epidemiology (mathematical modelling) and risk assessment, and their application to the diagnosis and control of infectious disease.

10.34 The Royal College of Veterinary Surgeons (RCVS) has begun to address this issue in its current review of veterinary education and training. In its draft consultative document on this it states, *'The notion of "omnicompetence" at the point of registration with the RCVS has been at the heart of much soul searching amongst veterinary educators and the profession over the years. We believe this concept to be unrealistic and fundamentally misguided in its assumptions. No other profession, to our knowledge, requires its final year undergraduates to be examined in everything there is to know, or to be equally competent across all species and disciplines.'* We encourage the RCVS to press ahead urgently with its review of veterinary education, and the veterinary schools to put in place now the necessary curriculum changes that address the future requirements mentioned above.

(iii) Continuing professional development

10.35 In the context of this Inquiry we are particularly concerned about the attractiveness of the State Veterinary Service (SVS) as a career. Views were expressed that the recruitment of high-quality veterinarians was proving difficult. The reasons go far beyond such issues as salary. Because a significant element in the success or otherwise of an overhaul of animal health and welfare depends upon the SVS, we place a high priority upon the quality of the SVS.

10.36 Continuing professional development or lifelong learning is now well accepted within the veterinary profession. Because the veterinary degree is broad based it is important that graduates undertake further training in their chosen branch of veterinary work, and the RCVS is proposing that in future, legislation permitting, a period of professional training should take place after graduation but before registration, similar to that which operates in medicine and dentistry.

10.37 We are particularly concerned about the continuing professional development available for those veterinarians who join the SVS and for large-animal practitioners in general. The SVS currently prefers, but does not insist, that applicants have spent time in veterinary practice, preferably farm animal practice. Further training is provided by DEFRA for all veterinary officers which includes a short period at the IAH, Pirbright. Experience in other career structures suggests that postgraduate training and a formal qualification at masters level in the control and management of endemic and exotic diseases should become a normal part of an SVS veterinarian's professional training. We believe that career progression within the SVS should be dependent upon the gaining of postgraduate qualifications, and that means should be found to encourage and support large-animal practitioners to extend their professional knowledge base.

10.38 As figure 10.2 indicates, this is a serious problem. The numbers attracted to state veterinary medicine are minimal and to the main livestock courses are relatively small.

10.39 Some veterinary schools also offer relevant diploma and master's courses in areas of importance to the livestock industries (for example the Royal Veterinary College and the University of London have diploma and master's courses in Livestock Health and Production, Veterinary Public Health and Epidemiology, Veterinary Microbiology and Veterinary Epidemiology). Such courses have many strengths but do not attract large numbers of students. The Royal Veterinary College (University of London) informs us that it has requested DEFRA to ensure the viability of these courses by sending staff members to take them.

10.40 Demand for one-year residential courses within the UK is minimal. For example, the University of Edinburgh offered a Diploma in State Veterinary Medicine (DVSM) but it closed in 1975. It is likely that its Diploma in Tropical Veterinary Medicine (DTVM) will cease in the current academic year. Again, the difficulties have arisen because the Government have withdrawn funding for the participation of UK and overseas students.

10.41 It does seem that these models of postgraduate training are no longer appropriate, whether for young persons who leave university with not inconsiderable debts, for veterinarians already in their professional careers or for veterinarians overseas. In the business, engineering, legal and education professions, new forms of continuing professional development have taken the place of the traditional residential master's degree. Courses are delivered in modules that build over time to different levels of qualification: certificate, diploma, master's and doctorate. The best courses combine distance learning at the place of employment with short residential periods. Such a model is used at Liverpool University for the Diploma in Bovine Reproduction. It is also important that Europe should maintain regular contact with the veterinary services and the RCVS in the rest of the world so as to ensure that we aid countries to develop high-quality disease surveillance, diagnosis and control. DEFRA, the Department for International Development and the EU should play a key role in shaping such professional training and linkages: the Government have done this recently where they perceive a requirement for enhanced continuous professional development (e.g. the training of head teachers).

10.42 The training of Temporary Veterinary Inspectors (TVIs) and Local Veterinary Inspectors (LVIs) is crucial. In any major outbreak of infectious disease the SVS will need to call on outside veterinarians to work as TVIs from the control centres. In the recent FMD outbreak more than 2000 TVIs were employed. A survey conducted by the British Veterinary Association (BVA) confirmed that many of these came from small-animal practice and were inexperienced in the differential diagnosis of FMD, while 1000 came from overseas and were not entirely knowledgeable in UK farming practices (there are 10 000 registered veterinarians in the UK). The amount of training that TVIs received was minimal (range 1–21 hours, average 3 hours). Clearly, the crisis in 2001 made formal training on a large scale difficult to implement but we have been impressed by the number of submissions describing the need for a trained veterinary reserve force who would be available, in disease emergencies, to leave their places of work at short notice and work as TVIs for DEFRA. The British Cattle Veterinary Association (BCVA) has submitted suggestions that a network of farm veterinary practices working in partnership with the SVS could offer a range of services such as health planning, risk assessment and management, infectious disease surveillance and the education of farmers and stockmen, as well as being available as a reserve force of TVIs. Such a network must be an organised professional service with adequate funding, training and logistical support. The contractual arrangements for such a force are not within the remit of our Inquiry but it is important for this issue also to address the training requirements.

10.45 In terms of education and training **we recommend that DEFRA should take rapid action to investigate and improve:**

- **the continuous professional development of farmers and stock keepers;**
- **postgraduate training in livestock health and welfare;**
- **the attractiveness of careers within the State Veterinary Service;**
- **the training of temporary and local veterinary inspectors by DEFRA, with the RCVS, the BVA and its species divisions, investigating the feasibility of the BCVA proposals. (R10.5)**

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