

Studies on the 1967–68 foot and mouth disease epidemic: incubation period and herd serial interval

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SUMMARY

The incubation period during this epidemic was studied using both a spectral analysis-cum-filtering method and analysis of case histories. Using spectral analysis, the modal herd serial interval was estimated to be 8–10 days based on the record of the daily number of outbreaks and an adjusted cattle series. The case histories tended to confirm these estimates but indicated that the serial interval varied considerably between species. The filtering method revealed that the herd serial interval apparently changed during the epidemic. For the first 4 weeks the interval was 8 days, while in the latter stages it was about 2 weeks.

INTRODUCTION

This epidemic of foot and mouth disease started officially on 25 October 1967 and finished the following June 1968, by which time disease had been diagnosed on some 2300 farms. Its origins and spread are described in the first part of the Northumberland Report (1969), Hugh-Jones & Wright (1970) and in Tinline (1972). A basic step in the study of foot and mouth disease (and any other infectious disease) is the estimation of the incubation period and serial interval under field conditions. If we regard an epidemic as a network of infections, of donor-recipient pairs, the temporal length of the strand is the serial interval, and between herds or flocks the herd serial interval. The classical methods of Pickles (1939) and Sartwell (1966) can be used with some case histories, but under field conditions with a multitude of cases it is extremely difficult to determine when a donor was infective or when an infective dose of virus was acquired by the recipient. In our studies of the 1967–8 foot and mouth epidemic we were only able to identify the donor-recipient pairings in a few special cases and hence our confidence in the estimates obtained from these pairings was necessarily limited. Our need, then, was to derive an independent set of estimates in some other way. This we have done by examining the daily record of outbreaks for cyclical fluctuations on the assumption that

the most important cyclical fluctuations in the record of outbreaks will reflect the serial interval. The technique chosen to perform this investigation is based on a combination of spectral analysis and filtering techniques.

It is essential to point out that, no matter which of the above methods we use, we are seldom measuring a 'true' period. There are two reasons for this. First, both methods depend on records of the onset of clinical disease and, as Burrows (1968) has shown, animals can excrete infective amounts of virus for several days before apparent disease. Secondly, finding one animal with legally defined lesions condemns all the animals on the farm and subsequent slaughter cuts short a full expression of the infection on the herd or flock. Thus the apparent incubation period will depend on those animals with the most rapid response. It appears, however, that while the first complication mentioned above tends to lengthen the apparent incubation period the second complication tends to shorten it.

MATERIALS AND METHODS

Source data

For the case history method it was necessary to obtain estimates of the time of onset of symptoms and the time of infection. Because of the size of the epidemic it was not possible to obtain many estimates by personal farm visits. However, because of the necessity of tracing and checking all animal, vehicle and human contacts with infected animals it was incumbent on the veterinary officer to collect as complete a history and clerical record as possible. Since these reports were collected for every outbreak at the actual time of disease and since experience has shown that the factual parts of these reports, if complete, agreed with one's own observations when interviewing the farmer later, it seemed possible to obtain the necessary estimates from their reports. In using these reports clinical disease has been assumed to have begun on a calendar day when an animal later diagnosed to have FMD was first noted to be 'ill at ease', inappetent, dull or not its normal self, irrespective of whether vesicles had yet been found. Lacking this history, an estimate was made based on the animal's temperature and the extent of vesication, as described in Hugh-Jones & Wright (1970). Altogether this allows the dates of onset of clinical disease on the individual farms to be used, and corrects the errors inherent in using the dates of disease notification or confirmation. The official dates were not randomly distributed throughout the week and their use would have introduced spurious results. For the spectral analysis we used: (i) the series of daily numbers of all confirmed outbreaks for days 1-103 of the epidemic; and (ii) a weighted series of initial disease in cattle (cattle formed about 82% of all outbreaks) for days 1-97 of the epidemic. The cattle series was based on the number of herds with clinical disease. Each herd was multiplied by the number of days it had been affected up to a limit of a factor of 6; the sum of all such weighted 'emitters' became the number in our cattle series for the day in question. This weighting scheme approximated the actual build-up of infected animals within a herd as determined from the veterinarians' reports on infected holdings. In this way we hoped to eliminate noise in the data caused by an apparent 2-3 day

variability in reporting outbreaks. The length of these series was constrained by the need to have a continuous record of outbreaks for the spectral analysis.

Method, spectral analysis-cum-filtering

A time series can be considered as the sum of a number of separate series each with a different frequency. Spectral analysis provides a way of decomposing a given series into small bands of component frequencies and assessing the contribution of these frequencies to the variance of the original series. The technique is described in Granger & Hatanaka (1964). The output of spectral analysis is known as a 'spectrum' and is a plot of variance (power) versus frequency or wavelength which is the reciprocal of frequency (see Fig. 3).

In conjunction with spectral analysis, we have used another technique known as filtering to remove the growth trend from the series to be analysed, since it is an assumption of spectral analysis that the series to be analysed is trend free (stationary). We defined trend as all fluctuations with periods greater than 15 days or less.

A mathematical filter works by creating a new series, the terms of which are the weighted sum of a specified number of terms of the original series. For a symmetric filter the i th term of the new series is given by:

$$Y_i = \sum_{k=-m}^m w_k x_{i+k},$$

where Y_i is a term of the new series, x_{i+k} is a term of the original series and the w_k are appropriate weights chosen by the filter designer so that the filter will pass or suppress the desired frequencies. A problem in filter design is that in order to increase the discrimination of a given filter the number of weights must be increased but increasing the number of weights also increases the number of terms that are distorted at the ends of the new series. As there are no set rules for making this trade-off, we first plotted the response curves for many filters of different lengths and with different weights. From this catalogue we were able to pick a trend removing filter that maximized response to wavelengths longer than 15 days and minimized response to wavelengths less than 15 days. The response curve of the chosen filter and its weights are given in Table 1.

The same technique was employed to design a band pass filter to pass wavelengths between 7 and 11 days. This filter was used to investigate the possibility of a change in serial interval over the course of the epidemic. The difficulty in preparing such a filter is shown in Fig. 4 which compares the desired or 'ideal' filter response with the response of the filter actually used. The major design constraint here was to minimize the number of terms used (m) and therefore minimize distortion in the ends of the filtered series. The filter's response curve and its weight are given in Table 1. Holloway (1958) provides an excellent further discussion of the design and use of filters.

Table 1. *Filter response curves*

Wavelength (days)	Trend removing filter*	Band pass filter†
Infinity	1.00	0.00
72.0	0.97	0.01
36.0	0.90	0.05
24.0	0.77	0.11
18.0	0.58	0.17
14.4	0.37	0.23
12.0	0.16	0.28
10.3	-0.02	0.30
9.0	-0.13	0.30
8.0	-0.16	0.28
7.2	-0.13	0.25
6.5	-0.03	0.21
5.5	-0.01	0.16
5.1	-0.01	0.09
< 5.0	-0.10 approx.	< 0.06 approx.

* Filter weights were: 0.0634 (central), 0.1228, 0.1122, 0.0957, 0.075, 0.0535, 0.0296, 0.0072, -0.0079, -0.01973.

† Filter weights were: 0.0758 (central), 0.9547, 0.0048, -0.0257, -0.0335, -0.0236, -0.0108, -0.0032, -0.0004.

Note that since both filters are symmetric only the right side weights are given.

RESULTS

Case histories

In a few circumstances it has been possible to obtain estimates of the time of onset of symptoms and the time of infection based on the veterinary officers' reports. Several of these circumstances are reported below, for not only do they provide a means of verifying our previous estimates but they enable us to indicate species and age specific variations which may occur.

(a) *Fomite infections*

A few outbreaks occurred following known exposure times. A cattle truck was the common link between an affected pig farm and two other farms. The lorry that transported pigs from this farm to a slaughter house was used to carry at least 36 cattle on two successive days. One of these cows became affected with FMD 5 days later and the other 7 days later; the reporting officer felt that the former cow had been carried in the lorry on both days.

In another case infective skim milk delivered to three farms appeared to be responsible for a series of outbreaks in pigs. Between 4 and 8 days after the pigs had eaten this skim milk, 28 pigs were diagnosed as having FMD. The median incubation period was 7 days (Hugh-Jones & Wright, 1970).

(b) *Intrafarm*

Clear examples of animal to animal spread on the farm are infrequent. However, two examples are presented in which there was a history of introducing apparently healthy stock incubating disease or where the primary single infected animal was not diagnosed and the infection spread to the rest of the herd.

Table 2. *Incubation period of eleven recrudescence cattle outbreaks (13 February-22 March 1968)*

	First slaughter date	Stock activity		Second outbreak initial disease	Possible incubation period (days)
		Movement	Date		
1	29 Nov. 67	Welfare	27 Jan. 68	7 Feb. 68	11
2	22 Nov. 67	Restock	9 Feb. 68	16 Feb. 68	7
3	16 Nov. 67	Welfare	16 Feb. 68	20 Feb. 68	4
4	3 Dec. 67	Welfare	11 Mar. 68	17 Mar. 68	6
5	20 Jan. 68	Restock	16 Mar. 68	21 Mar. 68	5
6	26 Nov. 67	Restock	13 Mar. 68	22 Mar. 68	9
7	5 Dec. 67	Restock	16 Mar. 68	25 Mar. 68	9
8	10 Dec. 67	Restock	15 Mar.-5 Apr. 68	6 Apr. 68	< 8
9	2 Feb. 68	Restock	1 Apr. 68	6 Apr. 68	5
10	6 Dec. 67	Restock	29 Mar. 68	9 Apr. 68	11
11	22 Nov. 67	Restock	25-26 Mar. 68	15 Apr. 68	21

In the first case an apparently healthy heifer from a farm in Darley Dale was brought to Edale. Two days later FMD was noticed in the heifer and simultaneously at the Darley Dale farm. Three days later, seven animals on the Edale farm had FMD vesicles representing an incubation period of 3-5 days.

At Baschurch a housed cow had a temperature of 105° F., was 'off-colour' and tender on her feet, but had no vesicles; FMD was not diagnosed. The next morning the index cow was moved into a loose-box and a heifer from the loose-box put in her standing. During the evening of the third day, five cows clustered about the heifer's standing were inappetent and lifting and shaking their feet. At mid-day on the fourth day, 48 hr. after being moved, the heifer had a temperature of 104.5° F. and ruptured and unruptured vesicles in her mouth and feet. The index cow had a temperature of 101.8° F., extensive separation of the coronary band on all feet, one teat vesiculated and no mouth lesions. A second cow sharing the loose-box was unaffected. Hence the incubation period for the five cows about the heifer was about 3 days and 36-48 hr. for the heifer (Hugh-Jones & Wright, 1970). Thus, in these examples, the incubation period is between 36+ hr. and 5 days. It is of interest to note that the shortest interval of 36-48 hr. was in an animal which would have been exposed to a very heavy environmental contamination.

(c) *Recrudescence outbreaks*

When the re-stocking of farms began and the welfare movement of cattle from outlying fields into home farms was allowed, eleven farms became affected with FMD for a second time *soon* after the stock were moved. These were considered to be recrudescences and not infected a second time by further nearby outbreaks (Table 2). The possible incubation periods, with one exception, were between 4 and 11 days, with a median value of 7-8 days.

Table 3. *Minimum inter-farm serial intervals*

Area	Source date(s)	Minimum inter-farm intervals (days)						
		3	4	5	6	7	8	9
Bosbury	22-23 Nov.						*	
Carnforth	20-30 Oct.				*	*		
	1 Nov.							
Darley Dale	6-9 Nov.				*			
Lincoln	7-9 Dec.	*		*				
Longridge	24-26 Nov.						*	
Winchcombe	16-17 Nov.	*		*				
Worcester (1)	15-17 Nov.	*						
(2)	17 Nov.							*

(d) Interfarm interval

The interfarm interval appears to be very variable for cattle (Table 3). Examples have been taken to demonstrate only a minimum disease interval of local outbreaks in areas which had been without disease. Later outbreaks have been ignored as a second source might have become available and the extra time taken by the animal to find the virus had become significant. The minimum possible disease interval was between 3 and 9 days with a median of 6 days. Of the eight source farms, seven had live animals with clinical disease for 2-3 days, and therefore even if we assume for convenience that the 'serial interval' is the incubation period, the latter period can be at least 2-3 days longer than the apparent minimum.

(e) The Worcester epidemic

The Worcester epidemic began on 10 November 1967, when 1800 gallons of infected skim milk were delivered to three farms near Worcester and were fed to pigs. Over the course of the next few weeks some 28 further outbreaks were confirmed in the immediate vicinity of these farms. Because the Worcester area was isolated from the main infected area to the north and because of the limited duration of the epidemic it is certain that these outbreaks were the result of spread from the three original outbreaks. Hence we had an opportunity not only to obtain an estimate of the mean incubation period but of the shape of the frequency distribution of incubation periods.

Figure 1 summarizes the spatial distribution of all affected herds and flocks in the Worcester area. Since proximity and wind direction (Smith & Hugh-Jones, 1969; Wright, 1969; Tinline, 1969) can be the most important factors in the spread of FMD, we were able to establish that the spread of disease on 15 and 16 November from farm 1 was probably responsible for the majority of subsequent outbreaks; those on farms 4-17, 19-24, 26 and 27. The temporal distribution of first noted disease in these flocks and herds is given in Fig. 2. The median herd incubation period was seven days, and nine days for flocks. Taken as a whole the distribution is approximately normal and has a mean, median and mode of about 8 days.

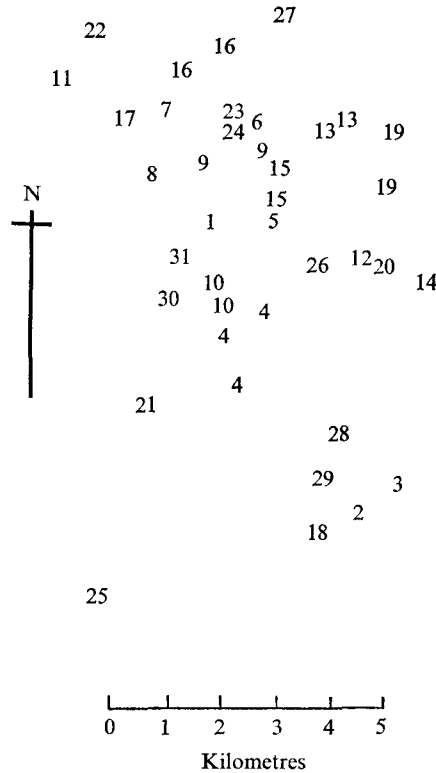


Fig. 1. FMD outbreaks in the Worcester area. The identifying number for each farm indicates the order farms were affected. It is repeated for as many separate groups of clinically affected stock on the farm and also indicates their positions.

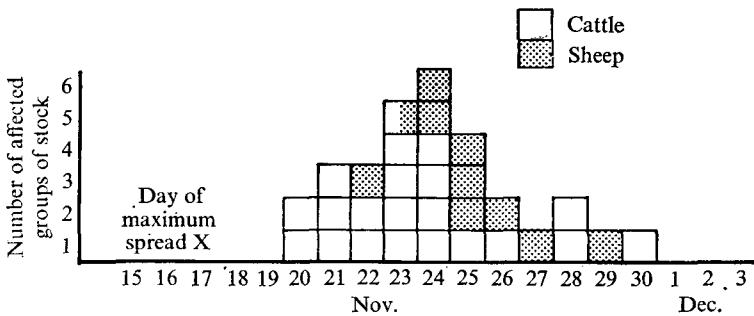


Fig. 2. Groups of cattle and sheep affected by FMD near Worcester, probably spread from farm 1 by date of initial disease.

By considering the number of animals becoming clinically affected each day (Table 4) we were able to obtain complementary estimates of the incubation period. The bimodal cattle incubation period evident in Table 4 was probably due to the internal spread of disease in two herds on farms 14 and 21. If the secondarily affected animals are excluded, only eleven cattle in three herds were affected on 26 November and none on 27 November and the median incubation period is still 7 days; if they are included, ten days. The median is unaffected by the inclusion

Table 4. *Numbers of stock affected with clinical disease probably spread from farm 1 (Worcester epidemic) on 16 November*

Date	Cattle	Sheep
20 Nov.	2	—
21	9	—
22	12	1
23	21	11
24	9	6
25	2	12
26	44	12+
27	12	2
28	3	0
29	0	2
30	9	1
1 Dec.	0	1

(as a result of using the initial wind tracks) or exclusion (using late wind tracks) of outbreaks 23 and 24 on 28 November and 26 on 30 November. Using Sartwell's estimation (1966) the estimated median is 7.3 days with a dispersion factor of ± 1.4 .

Spread from farm 2 on 17 November was probably responsible for disease in cattle on farm 18 (9 days) and sheep on farm 25 (10 days). After seven days disease appeared in sheep on farm 28, probably as a result of spread from farm 18. The date and therefore origin of first disease on farm 29 could not be estimated because of the very large number of sheep found to be affected at diagnosis. Finally, spread on 27/28 November from farm 21 was probably responsible for cattle disease on farms 30 and 31 9–12 days later.

The Worcester data thus suggest that the incubation period for cattle appears to be in the range 4–14 days with a median value of about 7 days. The incubation period for sheep appears to be in the range 6–15 days with a median value of 9 days. The Sartwell estimate for sheep is 8.0 days with a dispersal factor of ± 1.3 . From the recorded history of disease on farms 1, 2 and 3 the incubation period for sows was 4–6 days, and for weaners and stores, 6–8 days.

(f) *Conclusions*

From the case histories presented, it would appear that the incubation period varies with age, species and amount of exposure to infection. For cattle with a massive exposure to infection, the incubation period might be as short as 36+ hr. but under usual field conditions the minimum incubation period was between 3 and 5 days inside a herd and 3 and 8 days between farms; in the Worcester outbreaks the incubation period was between 4 and 14 days, with a median of 7 days. This longer period for the Worcester epidemic might have been the result of lower initial exposure to infection since infection was probably due to a viral aerosol dissipated somewhat after a downwind journey. For pigs the incubation period was between 4 and 9 days, with a tendency for the incubation period in younger pigs to be in the longer part of this range. In sheep the incubation period seems to have been between 6 and 13 days with a median of 9 days.

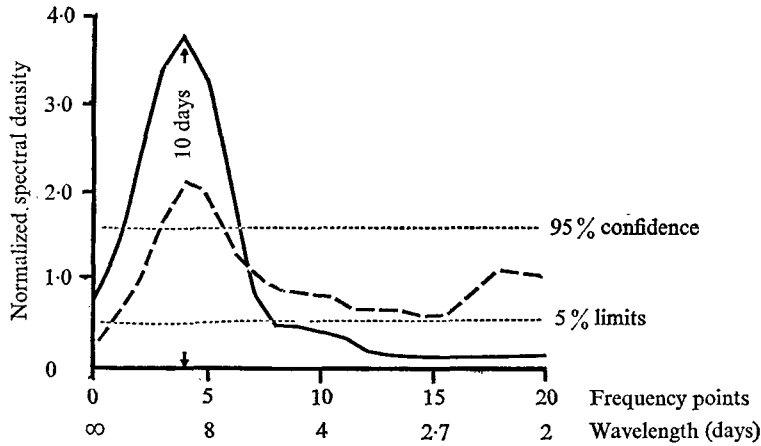


Fig. 3. Spectra of weighted cattle series (solid line) and outbreak series (dashed line).

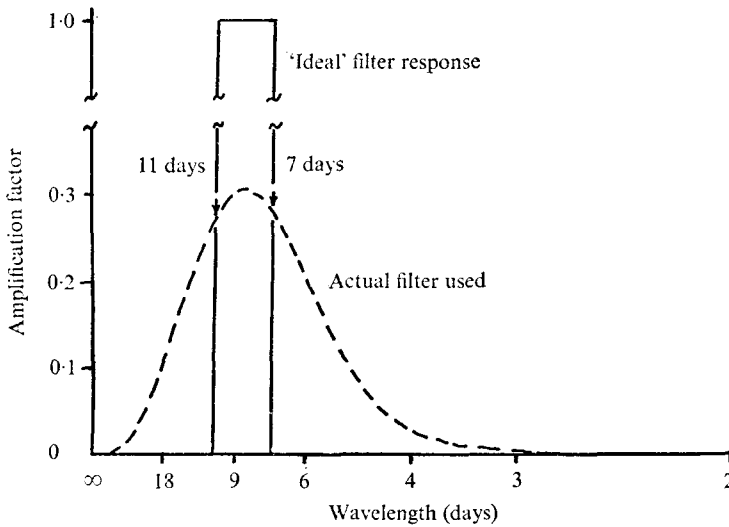


Fig. 4 Band-pass filter response curves.

Spectral analysis-cum-filtering

(a) *Modal herd serial interval*

The resulting spectra for the analysis of the series of the daily number of outbreaks and the cattle series are given in Fig. 3. The confidence limits shown in Fig. 3 are for the cattle series only, but since in terms of the outbreak series they are conservative they also perform for this series as well. The limits were calculated by the method outlined in Granger & Hughes (1968). Both series contained significant cyclical components with wavelengths (periods) ranging from approximately 5-15 days and with a mode at 10 days.

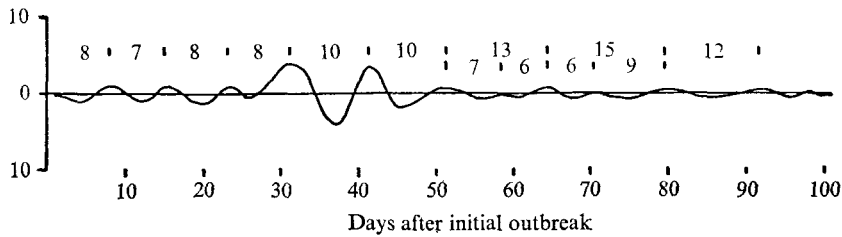


Fig. 5. Filtered outbreak series.

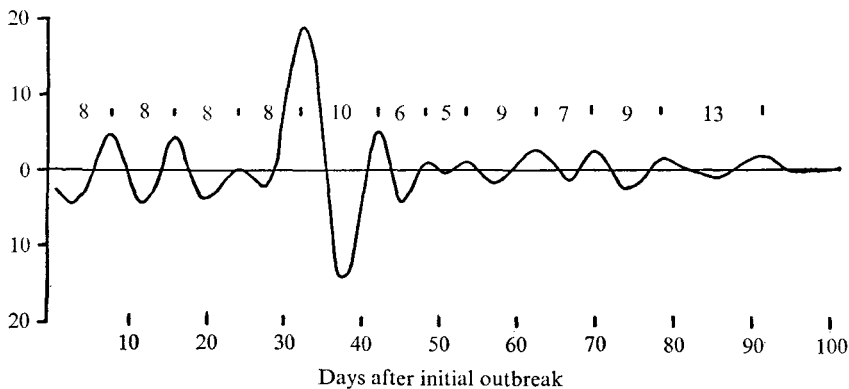


Fig. 6. Filtered cattle series.

(b) *Change in herd serial interval*

The spectral analysis estimate of 10 days for the herd serial was 1–2 days longer than estimates from the previous section. Since the spectral analysis used data from the whole time span of the epizootic, it seemed that this anomaly could be explained by assuming that the herd serial interval had lengthened during the epidemic.

To investigate this possibility we could have split the series into two portions and conducted separate analysis on both portions. However, as the following paragraph will describe, the logical division point was around day 30, making the first portion of the series rather short for reliable estimates from spectral analysis. Consequently, we used a band-pass filter to extract wavelengths of the order of 5–15 days from both the cattle and the outbreak data series, since we knew from the spectral analysis of the entire series that if changes had occurred it would be in this range of wavelengths. The results are shown in Figs. 5 and 6. The amplitude of the peaks on this graph indicates the relative importance of the indicated wavelengths, bearing in mind that with the filter shown in Fig. 4, wavelengths less than 7 days and greater than 11 days are not amplified to the same extent as those between 7 and 11 days. The total amplitude of the cattle series was greater than the outbreak series since our weighting system apparently removed the high frequency noise components such as the apparent 2–3 day variability in reporting outbreaks already mentioned.

The wavelengths in both series were very similar up to days 41–42. For the

interval from days 1 to 31–32 the series displayed a wavelength of close to 8 days. The wavelength suddenly lengthened to 10 days between days 31–32 and 41–42. After 41–42 and up to days 78–79 the outbreak series tended to show that the wavelength increased to 2 weeks. In contrast the cattle series showed that the wavelength varied between 5 and 9 days. After days 78–79 both series showed a wavelength of 12–13 days.

DISCUSSION

Two methods, case histories and a combination of spectral analysis and filtering have been presented as means of estimating the incubation period of the disease. Each method has its own specific advantages and disadvantages depending on the situation in which it is used. A method based on case histories, is, of course, the ideal method since, if the proper data were available, excellent estimates can be obtained for both age and species groups. However, without a great mass of accurate data that pinpoints both donor and recipient, case studies have to rely on those fortuitous circumstances in which this information is known. Thus the need for a method, such as spectral analysis, which can extract information from the daily record of outbreaks.

Unfortunately spectral analysis cannot provide age or species specific estimates unless there is a continuous record of outbreaks derived from an area in which an age group or species predominates. The close correspondence of the results from this method and the case history method increases our confidence that the incubation period and the herd serial interval were of similar length. Since the values of the filtered series are reliable over the entire series (the stationary assumption is not necessary) and the results are complimentary to the spectral analysis results, filtering appears to be a very useful follow-up to spectral analysis as well as a necessary first step for non-stationary series. The case history and spectral analysis-cum-filtering methods are best used in tandem with the former producing species specific estimates of the incubation and with the latter providing supporting evidence from the entire epidemic and allowing investigation of changes during the epidemic. With appropriately long and continuous records from isolated areas it would be possible to investigate regional variations as well as using spectral analysis.

We have noted that the serial interval suddenly lengthened between days 30 and 40 and then continued to lengthen if the outbreak series only was considered. We have considered three possible explanations.

First, the character of the virus might have changed during the epidemic. It has been suggested that the virus may lose its 'virulence' at the end of an epidemic. However, field specimens collected throughout the epidemic revealed no change in antigenic or pH stability characteristics (Brooksby, personal communication). Passaging of a virus in a single species host is as likely to increase its virulence as decrease it, and cattle continued to be the apparent host of choice throughout the epidemic.

Secondly, our data suggests that sheep appear to have a longer incubation period. We know that the percentage of confirmed outbreaks in sheep gradually

increased during weeks two to twelve from 6 to 12% while confirmed outbreaks in cattle declined from 90 to 86% (pigs changed from 4 to 2%). Since the cattle series (Fig. 6) showed no evidence of a longer interval except from days 30 to 40 it is possible that the apparent lengthening of the cycle in the outbreak series was due to increasing numbers of confirmed outbreaks in sheep. However, the small numbers involved and the fact that the sudden lengthening at day 30 in both series is not accounted for implies that this is a rather weak possibility.

Thirdly, it seemed possible that the remaining susceptible animals were exposed to less virus as the epizootic progressed. At the widest extent of the epidemic the outbreaks became relatively further apart and though the absolute amount of virus in the air would be high, its concentration per unit volume of air would decrease. Cottral (1968) has confirmed that the incubation period varies inversely with the initial dose of virus as we previously implied in an 'intrafarm' example. Since the major diffusing mechanism is by wind, the amount of airborne virus would be reduced during periods of dry calm anticyclonic weather and the mean infecting dose would drop. Such a period of dry calm weather preceded the peak of the epidemic (day 30) and we have already noted the lengthening of the serial interval immediately after 30, the period when 'strikes' made during the calm dry weather would begin to show up. Returning to the Worcester epidemic, one could argue that the apparently longer incubation period for spread from farm 2 was the result of such a process, since spread from farm 2 was assumed to have taken place on 17 November, the beginning of the dry calm weather. If our hypothesis is correct, then, for other epidemics where airborne virus is the major source of infection, longer serial intervals after anticyclones can be expected.

Parenthetically, it must be noted that as any epidemic wanes the smaller and smaller numbers available for analysis will result in increasingly diffuse results. This increasing lack of definition can make it more difficult to judge the later periods with as much confidence as the earlier ones.

Finally, it must be noted that the herd serial interval and the median incubation period for an individual cow were of similar length (7-10 days). Thus it would seem that the roles which the diseased herd will play in the epidemic, of being just a 'receptor' of infection or of also being a 'source', is largely determined at the time of initial infection. This emphasizes that in controlling FMD there should be no delay in slaughtering once a single diagnosis is made, since many others in the herd are also likely to have been infected at the same time as the diagnosed case. The spread of infection inside the herd is not only rapid but the shortened incubation period noted in these circumstances would radically increase any 'source' potential of the herd.

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