Predicting the level of herd infection for outbreaks of foot-and-mouth disease in vaccinated herds

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SUMMARY

Foot-and-mouth disease (FMD) is a highly contagious virus infection of sheep, goats, cattle, pigs and other, non-domesticated species of artiodactyls, and causes both clinical and sub-clinical infection according to the natural or acquired immunity of the host. Within vaccinated dairy herds FMD may appear as an acute, mild or subclinical infection, dependent upon the immune status of the herd, the level of challenge and the efficacy of the vaccine used. In the large dairy herds of Saudi Arabia, sub-clinical FMD was on a number of occasions, found to have spread amongst the cattle before signs of disease were seen. Such undetected transmission resulted in a large incidence on the first day of diagnosis and curtailed the impact of post-outbreak vaccination (PoV). First day incidence (FDI) for these herds was found to correlate with the final cumulative incidence of clinical disease. Since FDI is available at the start of an outbreak it can be used as a predictive tool for the eventual outcome of an FMD outbreak. During the past 11 years 47% of dairy herds examined in Saudi Arabia have experienced FMD initially as sub-clinical disease. For the remaining 53%, waning vaccinal protection did not suppress clinical disease in the initially infected animals, and these showed severe rather than mild signs. Hence, in such herds there was a very low initial level of subclinical infection, so PoV was more effective, and the timing of PoV was found to give a good correlation with cumulative herd incidence: an early PoV resulted in low prevalence of clinically infected animals whilst late PoV permitted high prevalence. PoV timing can thereby be used in tandem with FDI as a predictive tool for future outbreaks, estimating the final cumulative incidence (or prevalence) of clinical FMD cases.

INTRODUCTION

A significant feature of FMD epidemiology is that the infectious period begins before the appearance of clinical signs [1]. Consequently at the onset of an outbreak, the disease may already have spread within the herd prior to it becoming apparent. The delay in detection can be further prolonged where the signs in

initially infected animals are mild or sub-clinical, so that when clinical signs are identified the number of infected animals may be high. This is evident in outbreaks within the large, vaccinated dairy farms of Saudi Arabia [2, 3]. Amongst the Saudi farms that have kept epidemiological records approximately half record a relatively large incidence on the first day of diagnosis, and these outbreaks showed only mild signs for the initially infected animals [2–4]. Mild signs can be defined as a drop in milk yield, transient pyrexia and a few lesions. These herds are more likely to be

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ones with high vaccinal protection that consequently suppress the disease into a relatively mild form.

When disease is first recognized in a sub-clinically infected herd the first day incidence (FDI) is likely to be high. At this time many animals will be infected and non-responsive to vaccinal protection, although some will still be uninfected and therefore responsive to a boost in vaccinal protection. The impact of post-outbreak vaccination (PoV) or vaccination after discovery of disease will be reduced by the presence of sub-clinically infected and incubating animals.

The occurrence of sub-clinical disease is not only dependent upon the level of herd immunity provided by vaccination but also upon the level of viral challenge mounted by the outbreak source [2]. A high challenge mounted against animals with high immunity or a low challenge in herds with low vaccinal titre, may both initially produce sub-clinical disease. Animals that have specific antibody titres against FMD virus (as measured by ELISA using homologous virus as antigen) are considered susceptible to FMD below 45; at titres between 45 and 100 they are considered partially-immune and titres over 100 are considered to provide good immunity [5]. However, these values are not absolute, and there is considerable individual variation. In addition, if the outbreak strain of FMD virus is antigenically different from that used in the vaccine, the protection provided by vaccination is reduced (relative to the antigenic difference).

Although it is not possible to quantify the challenge experienced by the farms under study, the level of farm security would have prevented entry of infected animals. Hence, initial challenge would most likely have resulted through aerosols from infected animals outside the perimeter fence, or from feed or bedding contaminated with FMD virus [6, 7].

First day incidence is an indication of the sub-clinical disease that has already occurred before diagnosis and thereby represents the success of initial challenge against herd immunity. Since it is available at the time of diagnosis, it precedes the spread of clinical infection. Hence, for herds with sub-clinical infection, FDI potentially holds predictive value.

For herds without sub-clinical disease, the timing of PoV (rather than FDI) may become the means of predicting a likely level of disease prevalence. Amongst the Saudi farms, herds with low vaccinal protection showed early evidence of clinical disease following challenge and initially infected animals showed acute rather than mild signs [2]. Acute signs

were exhibited by animals with serum antibody titre below 45 by ELISA [5]. These signs included numerous severe lesions of the mouth, tongue and teats, acute lameness, swollen tongue, fever, anorexia and if in milk, a loss of yield. Without sub-clinical FMD, infection cannot spread across the farm before diagnosis, so an early administered PoV would be effective in controlling an outbreak [2]. Moreover, the timing of PoV could give an accurate estimation of cumulative herd incidence (or prevalence), where an early PoV maintains low prevalence and late PoV permits high prevalence. PoV timing is available at the start of an outbreak and would therefore become a predictive tool for future outbreaks when FDI was not appropriate.

In summary, sub-clinical epidemics can be identified by a large number of animals showing mild signs at the onset of an outbreak, and FDI may offer a mode of predicting cumulative disease incidence (or prevalence). Herds without sub-clinical disease are identified by a few initially infected animals showing acute signs, and PoV timing may become the predictive parameter.

This paper examines the evidence for a relationship between FDI or PoV, and cumulative disease incidence, using field data from large dairy herds in Saudi Arabia.

METHODS

Extensive field data from FMD outbreaks in Saudi Arabia has been made available to the FAO/OIE World Reference Laboratory (WRL) at Pirbright and Table 1 lists details of 17 outbreaks collated from 12 dairy farms. The herds formed closed populations of Friesian cattle.

Whilst not all Saudi farms have kept epidemiological records, for those that were examined the herd populations ranged from 150–20 000 animals and hence the sample size was statistically large. Furthermore each farm was divided into managed pens of similar dimension and population, with no free-mixing of individuals between them [2]. Consequently herd size and population density were assumed and have already been shown not to be a relevant factor in determining disease prevalence [2].

Each farm had a similar and regular vaccination policy in operation, and when FMD was seen in the herd, the entire herd was re-vaccinated within 1–2 days [8, 9]. Post-outbreak vaccination was taken as the interval (in days) between the first day of diagnosis

Table 1. *Data from 17 FMD outbreaks on 12 Saudi farms (in chronological order)**

No.	Farm	Pre-outbreak vacc	Post-outbreak vacc	First disease	Herd size	No. affected	% affected	Type	Duration	FDI
1	Al-Safi		9.i.86	7.i.86	12000	265	2	O	42 days	19
2	Al-Zeid	12.vii.88		28.ix.88	2050	1081	53	O		1
3	Janadria	6.iii.88	10.x.88+	5.x.88	160	65	39	O		1
4	Al-Kharj	12.vii.88	19.x.88	20.x.88	2090	56	3	O	57 days	1
5	Wadi Birk	23.x.88	17.xi.88	17.xi.88	1927	6	0·3	O		6
6	Ben Amar	25.x.88		16.xii.88	2683	453	17	O		2
7	Aziziah	11.x.88	15.i.89	15.i.89	3747	457	12	O	75 days	1
8	Al-Safi	Dec 88/Jan 89	19.iii.89	15.iii.89	18000	3200	18	O	25 days	1
9	Todhia	14.vi.89	25.viii.89	25.viii.89	3095‡	440	14	O	26 days	19
10	Medyan	15.xii.90	19,20.ii.91	19.ii.91	2013	312	15	O	70 days	1
11	Al-Kharj	11.vi.92	28.ix.92	26.ix.92	1845	709	38	A	33 days	1
12	Bandria	13.viii.93	1.xi.93	27.x.93	3249	143	4	A	19 days	13
13	Abu Saba	15.xi.93	11.ii.1994†	13.ii.94	2609	152	6	O	54 days	8
14	Todhia	15.xi.93	7.iii.94	7.iii.94	2999	831	28	O	56 days	37
15	Al-Kharj	15.xi.93	8.iii.1994†	10.iii.94	2303	47	2	O	42 days	1
16	Al-Safi	19–24.iii.94§	13–29.iv.94	13.iv.94	8782	3061	35	O	102 day	67
17	Nakheel	26.vii.94	9.x.94	9.x.94	6852	1274	19	O	99 days	37

* This table is adapted from a table devised by Samir M. Hafez [8, 9].
† Listed as post-outbreak since challenge preceded vaccinal boost to immunity.
‡ Also recorded as 2895.
§ Vaccination is post-challenge (see Hutber, 1997) so previous vaccination taken for PoPv period (Table 2a).
FDI, first day incidence.

Table 2. *Herds with (a) sub-clinical and (b) acute FMD infection*

No.	Farm	% infected	FDI	PoV/days	PoPv/days	Clinical signs at FDI
(a) Herds with sub-clinical FMD infection						
1	Al Safi	2	19	3		
5	Wadi Birk	0·3	6	1	25	Mild
9	Todhia	14	19	1	71	Pneumonia, pre-FDI
12	Bandria	4	13	6	75	
13	Abu Saba	6	8	−1	88	
14	Todhia	28	37	1	112	
16	Al Safi	35	67	1–16	90+	
17	Nakheel	19	37	1	75	
(b) Herds showing acute FMD infection						
2	Al Zeid	53	1		77	Severe – teat, tongue lesions
3	Janadria	39	1	6+	212	Mouth, teat vesicles
4	Al Kharj	3	1	0	100	Severe – teat vesicles
6	Ben Amar	17	2		51	Severe – lesions
7	Aziziah	12	1	1	96	Teat, tongue, foot vesicles
8	Al Safi	18	1	5	45–75	Mouth, teat, tongue vesicles (slaughtered)
10	Medyan	15	1	1	65	
11	Al Kharj	38	1	3	107	
15	Al Kharj	2	1	−1	113	

and the administration of re-vaccination following diagnosis. The pre-outbreak post-vaccinal (PoPv) period (in days) was measured from the date of the last pre-outbreak vaccination to the first case(s) of clinical disease. It was assumed that the most recent vaccine administration will heighten antibody levels beyond any previous immunization [10], and that the level of herd immunity at the time of challenge, would be directly related to the time of the last pre-outbreak vaccination. PoPv was therefore used in this analysis
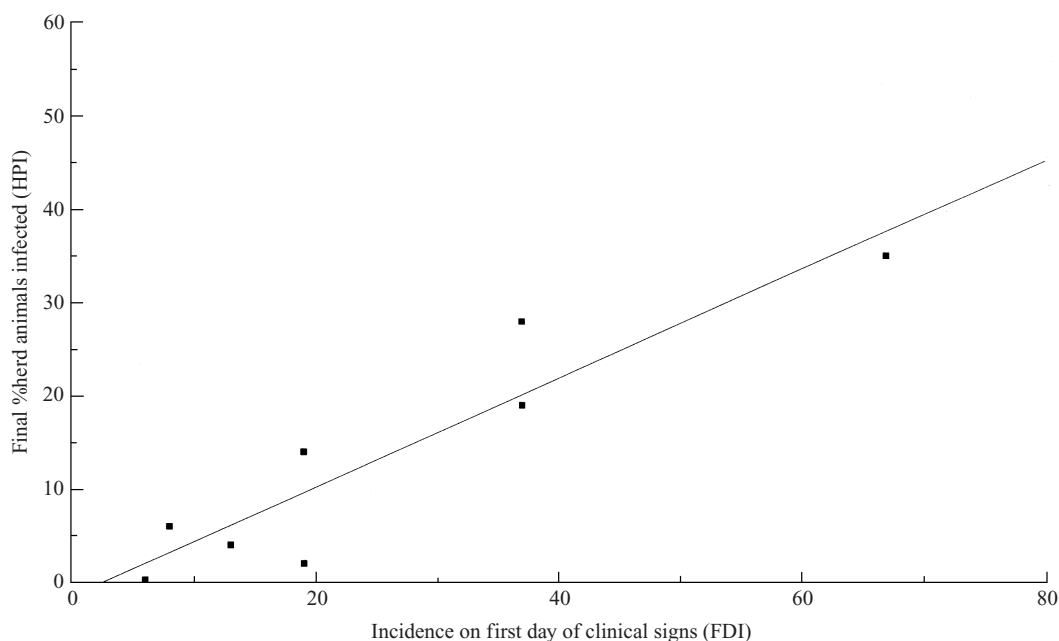
Fig. 1. The effect of FDI upon disease prevalence for Saudi herds with sub-clinical FMD infection.

as a measure of herd immunity at the time of challenge.

First day incidence was measured as the number of clinical cases counted in the herd on the first day of disease diagnosis, or in other words on day 1 of clinical (rather than sub-clinical) disease.

The outbreaks listed in Table 1 were divided into two groups. Herds in the first group contained > 2 initially infected animals with mild clinical signs (Table 2a). Mild signs were denoted by a drop in milk yield, transient pyrexia and a small number of lesions. The second group collated herds with < 3 initially affected animals showing acute clinical signs. Acute signs were lameness, swollen tongue, fever, anorexia and if in milk, a loss of yield (Table 2b).

The two groups were then subjected to a statistical analysis to examine the following relationships:

(i) the correlation between FDI and disease prevalence for herds with initially mild infections;

(ii) the correlation between FDI and disease prevalence for herds with initial acute clinical signs;

(iii) the correlation between PoV and disease prevalence for herds with initially mild infections;

(iv) the correlation between PoV and disease prevalence for herds with initial acute clinical signs;

(v) the correlation between PoPv and disease prevalence for herds with initially mild infections;

(vi) the correlation between PoPv and disease prevalence for herds with initial acute clinical signs.

Disease prevalence was measured in terms of the final cumulative number of clinically infected animals within a herd/herd population size, or in other words herd % infected (HPI). A regression analysis and Pearson correlations were computed for the above relationships using the MiniTab software package and a general linear model.

RESULTS

Herds showing initial mild clinical disease (Table 2a)

There was a highly significant correlation ($F_{1,6} = 36.61$, $r = 0.927$, $P < 0.01$) between FDI and herd % infected, where the relationship explained 83.6 % (adjusted r^2) of the observed variance (Fig. 1). Correlation coefficients for HPI against PoV/PoPv were not significant ($r = 0.297/r = 0.677$). These findings were substantiated by a multiple regression analysis of FDI, PoV and PoPv on HPI. Multiple regression indicated that PoV and PoPv did not have significant effects independent of the other variables, whilst the impact of FDI upon HPI approached significance ($F_{3,2} = 15.06$, $P < 0.06$). Repeating the regression with the least significant variable (PoV) removed, the significance of FDI upon HPI was high
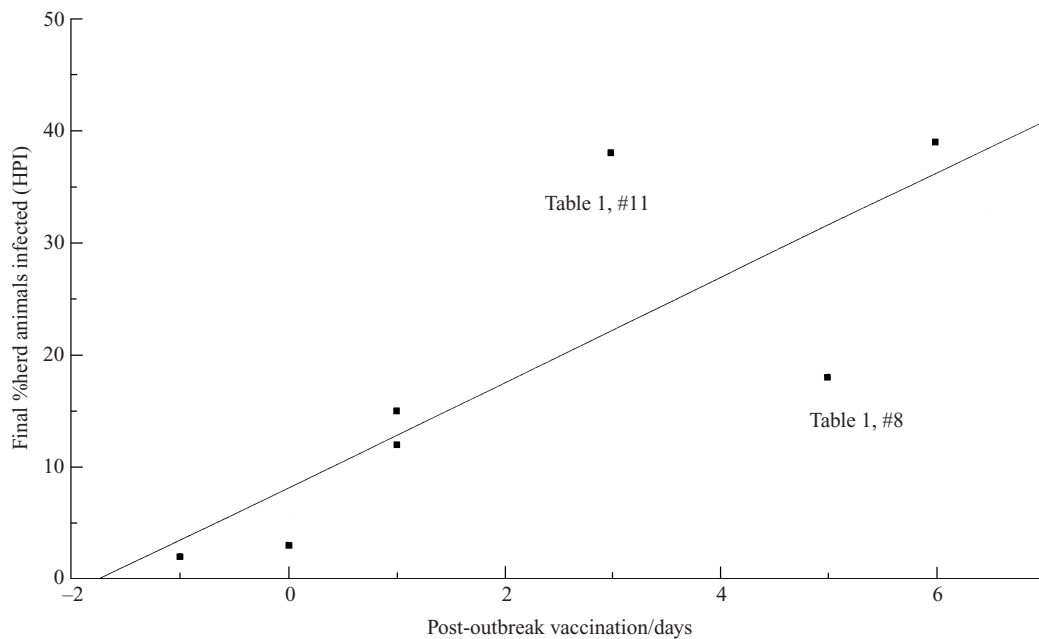
Fig. 2. The effect of post-outbreak vaccination upon disease prevalence for Saudi herds showing acute FMD clinical signs. The points labelled Table 1, no. 11 and Table 1, no. 8 in this figure refer respectively to the outbreaks numbered 11 and 8 listed in Table 1.

($P < 0.01$) but the effect of PoPv remained below significance. Hence, for herds showing initial mild disease FDI was a highly significant factor in determining herd % infected and can be used to estimate disease prevalence.

Herds showing initial acute clinical signs (Table 2 b)

There is no significant relationship between FDI and herd % infected for herds showing acute infection (Table 2 b) ($r = 0.105$). However, there is a significant correlation between PoV and herd % infection ($F_{1,5} = 9.38$, $r = 0.808$, $P < 0.05$), where the relationship explained 61 % (adjusted r^2) of the observed variance (Fig. 2). The correlation coefficient for HPI against PoPv was not significant ($r = 0.244$). Since FDI was practically a constant it was not included as a variable within the multiple regression analysis. Multiple regression indicated that PoPv did not have a significant effect, whereas the impact of PoV upon HPI was significant ($F_{2,3} = 17.39$, $P < 0.05$). Hence, for herds with initial acute clinical signs, PoV was a significant factor in determining herd % infected and can be used to estimate disease prevalence.

DISCUSSION

For infected herds showing initially mild disease, the linear relationship between FDI and herd % infected provides a measurable parameter at the start of an FMD epidemic, and one that can predict the likely level of cumulative disease incidence (or prevalence). FDI has been applicable to 47 % (9/17) of the recorded Saudi outbreaks in the past 11 years.

The remaining 53 % of herds examined in Saudi Arabia were not infected sub-clinically and the initially affected animals showed acute clinical signs. For these herds a linear relationship was evident between PoV and HPI. PoV therefore replaces FDI as a predictive parameter since it is also available at the start of an outbreak.

Epidemiologically, PoV will have a larger effect on HPI for herds without sub-clinical infection (Table 2 b, $P < 0.05$). In these herds FDI represents the start of the outbreak, and PoV can therefore heighten protection for large portions of the farm that have not as yet been challenged. Conversely PoV has less effect on sub-clinically infected herds (Table 2 a, $r = 0.297$) because FDI does not coincide with the start of sub-clinical disease, and many animals will already be infected before PoV is administered.

Disease prevalence is not dependent on herd immunity alone but also on the level of viral challenge, and it is the combined result of challenge against herd immunity that determines prevalence. Moreover, virus challenge levels are not easily measured in the field environment, so it is not possible to estimate prevalence by measuring challenge and herd immunity separately. Thus, for sub-clinically infected herds it is

FDI that reflects the success of a virus challenge in overcoming herd immunity, and ultimately this produces the observed level of disease prevalence.

The fact that the correlation coefficient for PoPv against HPI is high in sub-clinically infected herds ($r = 0.677$), suggests that their level of herd immunity is waning as the PoPv period increases. PoPv period has less relevance for herds showing acute infection because PoV is administered at the start of the outbreak (when clinical signs are expressed) and this will heighten vaccinal titre above previous PoPv levels.

Both FDI and PoV are useful predictive parameters for herds that have a regular vaccination programme. Cleland and colleagues [11] have pointed out that sensitized animals respond more readily (compared to susceptible individuals) in any subsequent vaccinations. As such the applicability is not known of FDI or even PoV, to unvaccinated herds with little if any immunity.

Hafez [8, 9] records that in 4 of the 17 outbreaks (Table 1, nos. 2, 3, 11, 12) the antigenic closeness of the vaccine strain to the infecting virus was poor, resulting in a subsequent modification of the vaccines in use. The impact of the poor antigenic match (between vaccine and outbreak strains) upon FDI and herd HPI is not apparent (Fig. 1). However, the poor matching for the Al Kharj outbreak (Table 1, no. 11) does appear to inflate herd infection (Fig. 2) and similarly, the slaughter of infected animals at the start of the Al Safi outbreak (Table 1, no. 8) indicates a deflation of herd infection (Fig. 2) FDI incorporates factors such as the antigenic closeness of vaccine and outbreak strains, the slaughter of infected animals and other control measures. The relative contributions of these factors to FDI are not easily measured, but their collective impact (or FDI) can be measured.

Both FDI and PoV can become useful parameters for predicting FMD prevalence in vaccinated herds. They may in the long term be useful for other diseases that fail to show initial clinical signs or exhibit a mild form of disease in the presence of waning vaccinal immunity.

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