Protection against direct-contact challenge following emergency FMD vaccination of cattle and the effect on virus excretion from the oropharinx

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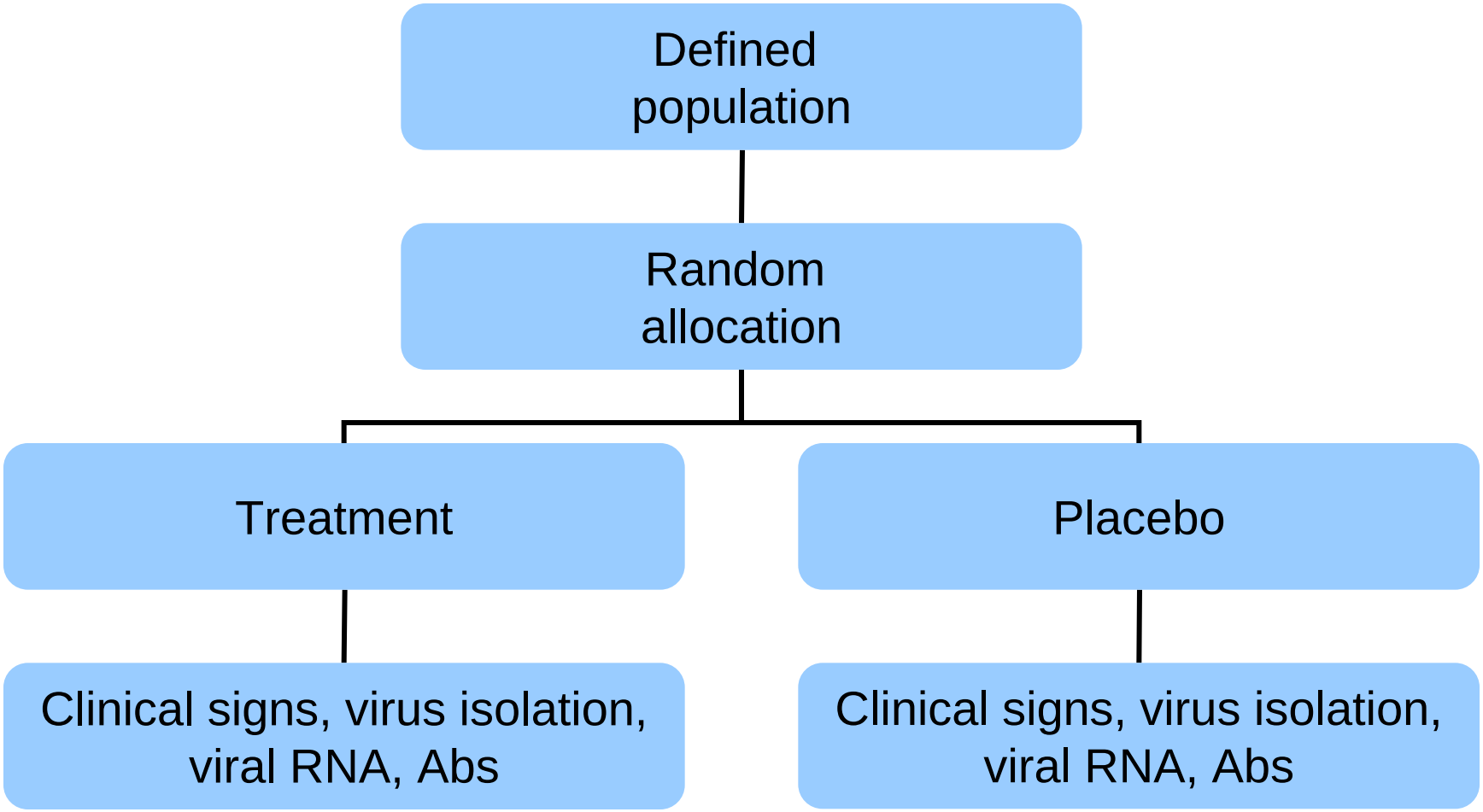
Study limitations

Prophylactic field trial



Phase I, II, or III ?

Phase I
The safety of the product is tested on a limited number of animals

Phase II
A limited number of animals are vaccinated and then challenged with the micro-organism being evaluated

Phase III
A large number of animals in the field are vaccinated to estimate both the efficacy and effectiveness against the disease and infection

Field Trials requirements

- the experiment is planned
- comparison of a treatment group and a control group
- study groups are comparable
- animals are followed up …… outcome

Clinical Trials steps

1 Background information
2 Study objective
3 Outcome
4 Study population
5 Inclusion & exclusion criteria
6 Sample size
7 Enrollment of animals
8 Intervention
9 Bias control
10 Data collection
11 Data analysis
12 Report of results

3 Outcome was efficacy defined?

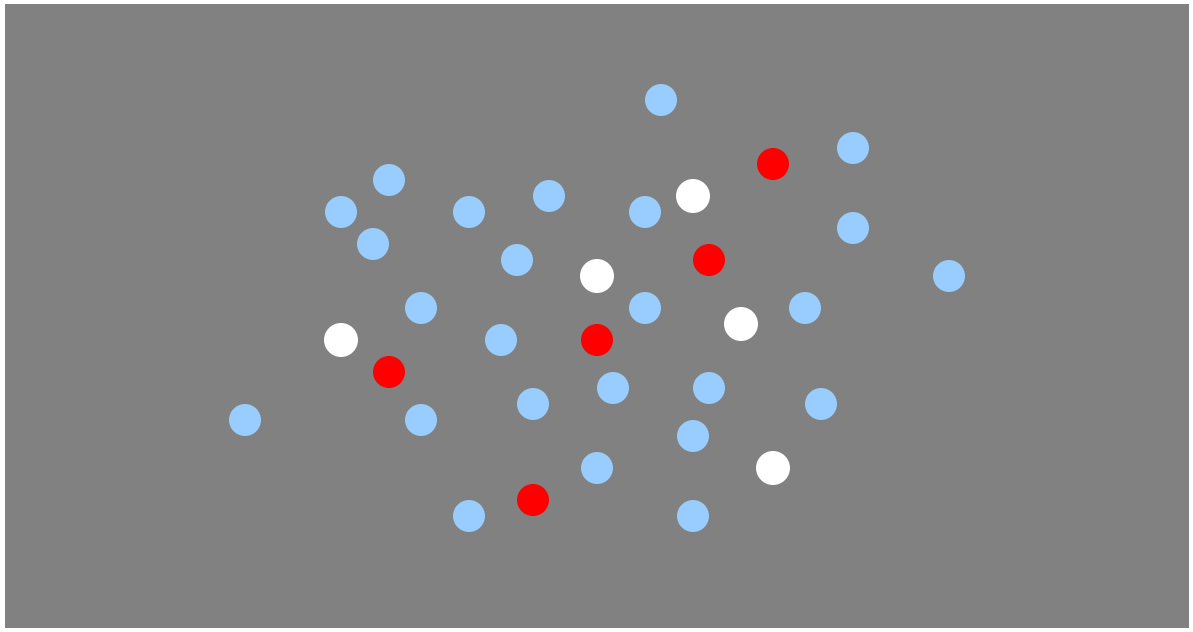
Clinical signs of FMD (%)
Viremia (%)

Local virus replication (%)

FMD viral RNA (mean, %)

Neutralizing Abs (mean, %)
NSP Abs (mean, %)

6 Sample size was it explained and justified?



9 Bias control

- Randomization
- Standardization
- Masking

11 Data analysis is it relevant to compare means?

Clinical signs of FMD (%)
Viremia (%)

Local virus replication (%)

FMD viral RNA (mean, %)

Neutralizing Abs (mean, %)
NSP Abs (mean, %)

Conclusions

- 9/20 vaccinated cattle became PI at 28 dpc. However, since live virus was not isolated, the risk of these animals transmitting disease was probably very low.

- Use of an emergency vaccine will prevent or reduce local virus replication, virus released in the environment in early post-exposure period.

Table 1
Virus isolation (VI) and PCR results from probang samples and non-structural antibody (NSAb) results from cattle which either had no or very limited local virus replication which was cleared by 28 days post-initial contact with infected donor cattle (Group 1)

Animal reference	Test	Days post challenge									
		Pre	2	4	7	10	12	14	16	21	28
UV 3	VI	–	–	–	–	–	–	–	IS	–	–
	PCR	–	–	–	–	–	–	–	–	–	–
	NSAb*										–
UV 4	VI	–	–	+	–	–	–	–	IS	–	–
	PCR	–	–	+	–	–	–	–	–	–	–
	NSAb*						–				–
UV 6	VI	–	–	–	+	–	–	–	IS	–	–
	PCR	–	–	–	–	–	–	–	–	–	–
	NSAb*										–
UV 7	VI	–	–	–	–	–	IS	–	IS	–	–
	PCR	–	–	–	–	–	–	–	–	–	–
	NSAb*										–
UV 8	VI	–	–	–	–	–	–	–	IS	–	–
	PCR	ND	–	–	–	–	–	–	–	–	–
	NSAb*										–
UV 12	VI	–	–	+	+	+	–	–	IS	–	–
	PCR	–	+	+	–	–	–	–	–	–	–
	NSAb*										–
UV 15	VI	–	–	–	–	–	–	–	IS	–	–
	PCR	–	–	+	–	–	–	–	–	–	–
	NSAb*										–
UV 16	VI	–	+	–	–	–	–	–	IS	–	–
	PCR	–	–	+	–	–	–	–	–	–	–
	NSAb*										–
UV 18	VI	–	IS	–	–	–	+	–	IS	+	–
	PCR	–	IS	–	–	–	–	–	–	–	–
	NSAb*										–
UV 20	VI	–	+	+	–	–	–	–	IS	–	–
	PCR	–	+	+	–	–	+	–	–	–	–
	NSAb*										–
UV 21	VI	–	+	+	–	–	–	–	IS	–	–
	PCR	–	+	+	–	–	–	–	–	–	–
	NSAb*										–

Virus isolation and viral RNA and Abs

Group 1: vaccinates

28 dpc, 11/20 vaccinates showed no evidence of viral recovery

11 + 2 = 13/20 vaccinates showed no evidence of NSP Ab development

Table 2
Virus isolation (VI) and PCR results from probang samples and non structural antibody (NSAb) results from cattle which either had local virus replication or FMDV RNA still evident at 28 days post challenge (Group 2)

Animal reference	Test	Days post challenge									
		Pre	2	4	7	10	12	14	16	21	28
UV 2	VI	–	–	+	+	+	–	–	IS	–	–
	PCR	–	+	+	+	–	–	–	+	–	+
	NSAb*										–
UV 5	VI	–	–	+	–	+	+	+	IS	+	–
	PCR	–	–	+	+	+	+	+	+	+	+
	NSAb*										+
UV 9	VI	–	+	+	+	+	+	+	IS	+	–
	PCR	–	+	–	+	+	+	+	+	+	+
	NSAb*										+
UV 10	VI	–	+	–	+	+	+	+	IS	+	–
	PCR	–	+	–	+	+	+	+	+	+	+
	NSAb*										+
UV 11	VI	–	+	+	+	+	–	+	IS	+	+
	PCR	–	–	+	+	+	+	+	+	+	+
	NSAb*										+
UV 13	VI	–	+	+	+	+	+	+	IS	+	–
	PCR	–	+	+	+	+	+	+	+	+	+
	NSAb*										+
UV 14	VI	–	+	+	+	+	+	+	IS	+	–
	PCR	–	–	+	+	–	+	–	–	+	+
	NSAb*										–
UV 17	VI	–	IS	+	+	+	+	+	IS	+	–
	PCR	–	IS	+	+	+	+	+	+	+	+
	NSAb*										+
UV 19	VI	–	+	+	+	+	–	+	IS	+	–
	PCR	–	+	+	+	+	+	+	+	+	+
	NSAb*										+

Virus isolation and viral RNA and Abs

Group 2: vaccinates

NSP seropositive animals (7) with persistent local virus replication/detection

Table 3
Virus isolation (VI) and PCR results from probang samples and non-structural antibody (NSAb) results from unvaccinated control cattle

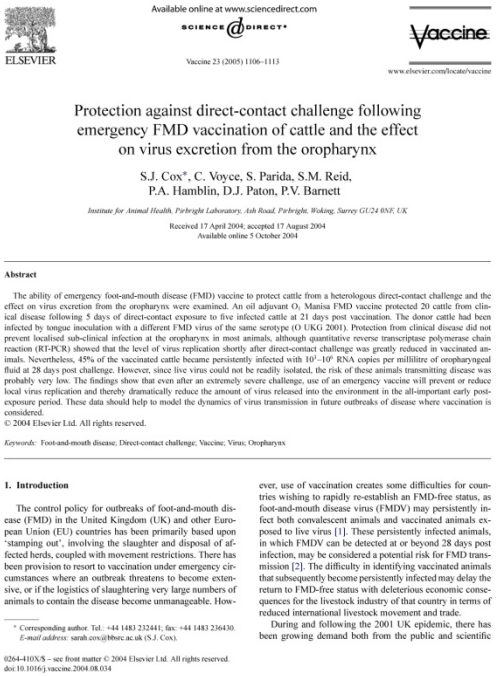
Animal reference	Test	Days post challenge								
		Pre	2	4	7	10	12	14	16	21	28
UV 22	VI	–	+	IS	+	–	–	–	IS	–	–
	PCR	–	+	+	+	+	–	–	+	–	–
	NSAb*										+
UV 23	VI	–	+	+	+	+	–	–	IS	–	–
	PCR	–	–	+	+	+	+	–	–	+	–
	NSAb*										+
UV 24	VI	–	–	+	+	–	–	–	IS	+	–
	PCR	–	+	+	+	+	+	–	–	–	–
	NSAb*										+
UV 25	VI	–	+	+	+	+	–	+	IS	+	–
	PCR	–	+	+	+	+	+	+	–	+	+
	NSAb*										+
UV 26	VI	–	+	+	+	+	–	+	IS	+	–
	PCR	–	+	+	+	+	+	+	+	–	–
	NSAb*										+

Virus isolation and viral RNA and Abs

Group 3: non-vaccinates

NSP seropositive animals (5) with persistent local virus replication/detection

12 Report of study results research for policy making



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Protection against direct-contact challenge following emergency FMD vaccination of cattle and the effect on virus excretion from the oropharynx

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Abstract

The ability of emergency foot-and-mouth disease (FMD) vaccine to protect cattle from a heterologous direct-contact challenge and the effect on virus excretion from the oropharynx were examined. An oil adjuvant O, Manisa FMD vaccine protected 20 cattle from clinical disease following 5 days of direct-contact exposure to five infected cattle at 21 days post vaccination. The donor cattle had been infected by tongue inoculation with a different FMD virus of the same serotype (O UKG 2001). Protection from clinical disease did not prevent localised sub-clinical infection at the oropharynx in most animals, although quantitative reverse transcriptase polymerase chain reaction (RT-PCR) showed that the level of virus replication shortly after direct-contact challenge was greatly reduced in vaccinated animals. Nevertheless, 45% of the vaccinated cattle became persistently infected with 10^1–10^6 RNA copies per millilitre of oropharyngeal fluid at 28 days post challenge. However, since live virus could not be readily isolated, the risk of these animals transmitting disease was probably very low. The findings show that even after an extremely severe challenge, use of an emergency vaccine will prevent or reduce local virus replication and thereby dramatically reduce the amount of virus released into the environment in the all-important early post-exposure period. These data should help to model the dynamics of virus transmission in future outbreaks of disease where vaccination is considered.

Keywords: Foot-and-mouth disease; Direct-contact challenge; Vaccine; Virus; Oropharynx

1. Introduction

The control policy for outbreaks of foot-and-mouth disease (FMD) in the United Kingdom (UK) and other European Union (EU) countries has been primarily based upon 'stamping out', involving the slaughter and disposal of affected herds, coupled with movement restrictions. There has been provision to resort to vaccination under emergency circumstances where an outbreak threatens to become extensive, or if the logistics of slaughtering very large numbers of animals to contain the disease become unmanageable. However, use of vaccination creates some difficulties for countries wishing to rapidly re-establish an FMD-free status, as foot-and-mouth disease virus (FMDV) may persistently infect both convalescent animals and vaccinated animals exposed to live virus [1]. These persistently infected animals, in which FMDV can be detected at or beyond 28 days post infection, may be considered a potential risk for FMD transmission [2]. The difficulty in identifying vaccinated animals that subsequently become persistently infected may delay the return to FMD-free status with deleterious economic consequences for the livestock industry of that country in terms of reduced international livestock movement and trade.

During and following the 2001 UK epidemic, there has been growing demand both from the public and scientific

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Data should help to model the dynamics of virus transmission in future outbreaks of disease where vaccination is considered.