Administration of an immunocontraceptive vaccine to Kaimanawa mares

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Abstract

A population of 29 bands of wild horses were identified. Bands were divided into three treatments (receive vaccine - 9 bands with 26 mares; receive placebo - 2 bands with 8 mares; control - 18 bands with 63 mares). The initial vaccine and placebo was injected into 24 mares from 9 bands and 8 mares from 2 bands, respectively, during the muster in June 1995. A booster vaccine was successfully administered to at least 13 mares. The vaccine failed to prevent conception and all but one vaccinated mare had a foal in the spring of 1996. The reason why the vaccine failed is unknown. It is unlikely that Kaimanawa mares could not mount an immune response to the vaccine and we are confident that the vaccine was successfully administered to at least 13 horses. It is most likely that the vaccination programme failed because the vaccine was inactive for some reason or other. It is possible that the vaccine deteriorated during transit from the USA to the individual mare. Retrospectively the vaccine should have been tested in domestic mares before its use in wild mares.

1. Introduction

Immunocontraceptive vaccines are being used worldwide to control the population of a number of captive and free-living species (Kirkpatrick et al. 1997; McCallum 1996). There are several types of immunocontraceptive vaccines available, but a vaccine based on porcine zona pellucida, which has been used successfully in wild horses previously (Kirkpatrick et al. 1997; Willis et al. 1994: Kirkpatrick et al. 1990), was chosen for this trial.

These vaccines must be administered systemically as oral administration does not work. Several techniques for administration are available, namely by intramuscular injection, by dart or by the Ballista-Vet system (Herriges et al. 1991; Jessup et al. 1991) in which a biobullet containing the vaccine is shot into a muscle mass by airgun. The latter was selected as it had been used successfully in previous trials (Willis et al. 1994) and initial indications were that biobullets might be more useful for long-distance administration than darts. In addition we did not want to have horses dropping darts in the army exercise area and felt it would be too difficult and time-consuming to follow the mares and wait for the darts to drop off. Darts with a radio transmitter to facilitate collection were available but considered too expensive.

Biobullets packed with the vaccine or a placebo were imported from the laboratory of Dr. Richard Fayrer-Hosken at the College of Veterinary Medicine, University of Georgia, Athens, Georgia, USA. To be effective the vaccine had to be administered twice, an initial biobullet followed four or more weeks later by a booster.

The initial biobullet would be administered whilst the target mares were held in yards during the May/June 1995 muster, the second given to them while they were free on their range. If a target mare was not mustered, both initial and booster vaccine or placebos were given to her while she was free.

A focal population of 29 breeding groups (bands) were identified by freeze brands or by documented and photographed variations in the colour markings of individuals. The population inhabited a study area of 53 km^2 including the Argo Basin and Westlawn Plateau of the southern Kaimanawa Ranges.

These animals have been under regular observation since 1992 and have become habituated to the presence of humans, and so it was thought that administering the second vaccine or placebo should not be too difficult.

2. Vaccination of mares

2.1 SELECTION OF MARES

Analyses suggested that mare age, band social structure and the presence of more than one stallion influenced mare fecundity (Linklater et al. 1996a, 1996b). Therefore the fecundity of individual mares in the same bands were not independent. Consequently bands and not mares were assigned to vaccination, placebo and control treatments. All the mares in bands assigned to vaccination or placebo treatment received the appropriate biobullets. Control bands were not interfered with.

There were 9 bands with 26 mares in the vaccination treatment, 2 bands with 8 mares in the placebo treatment and 18 bands with 63 mares as controls (Linklater 1996c). Mares in the three treatments varied similarly in age, and in average pregnancy and foaling rates during 1994 and 1995 prior to vaccination (Table 1; Figure 1).

2.2 ADMINISTRATION OF VACCINE AND PLACEBO

The Ballista-Vet system was tested on a firing range and found to be accurate up to 30 metres at air pressures greater than 950 psi (DeNicola et al. 1996). However, field conditions, particularly wind, reduced accuracy and response to air pressure so 1200 - 1500 psi was used with a maximum target distance of 20 metres. Consequently most booster biobullets were administered to target mares standing at a maximum distance of 20 m and often within 5-10 m of the shooter.

The administration of the vaccine and placebo was easily and effectively carried out in the yards where the mares were well within range (<5 m). The biobullet was shot into the thigh or rump muscles. It was easy to determine whether the biobullet had pierced the skin and entered the muscles in the yards because a small trickle of blood or a small wound was seen at the entry site.

Administration of the biobullet was much more difficult in the field, where a long period of time was required to get within range of the target mares. It was also more difficult to determine whether the shot had been successful, as the hair, particularly wet hair, often camouflaged the target area and made seeing the blood smear difficult. Binoculars (< 15X) and a spotting scope (<60X) were used when necessary to search for evidence of biobullet impact.

2.3 SUCCESS OF ADMINISTRATION OF VACCINE AND PLACEBO

Mares were given their first vaccination or placebo in the yards after the muster on 7 June 1995. Two of the mares identified to be vaccinated were not mustered or could not be identified in the yards (Table 1). These mares were given their first vaccination on 12 and 29 August 1995 whilst free-ranging. Booster vaccine and placebos were administered between 4 and 15 weeks after the first vaccination (Table 1), between 12 July and 27 September 1995.

It was not always possible to confirm successful delivery of the booster biobullet due to mare disturbance, poor visibility due to rain or snow, or absence of visible bleeding. However, visible wounding and or bleeding similar to that seen after the first administration and documented in previously successful penetration by biobullet (Willis et al. 1994) was observed in 17 vaccinated and 4 placebo mares (Table 1).

After impact, the mares often kicked with one or both of their rear legs, jumped and walked or trotted up to 40 m. This response varied between mares and could not be distinguished from their response to the sound of the shot. Limping for a few steps after impact was also observed.

During the experimental period one placebo and 3 control mares died and 4 vaccinated, one placebo and one control mare were killed by army live firing on 5 November 1995. Mortalities reduced the number of target mares to 22 for vaccination and 7 for placebo administration. Of these 17 vaccine and 4 placebo mares received booster biobullets.

2.4 EFFECT OF VACCINE

The vaccination programme failed and only one of the vaccinated mares failed to conceive in the spring of 1995. She (number 132) may not have got the booster vaccine (Table 1). Vaccination did not reduce pregnancy or foaling rates (Figure 1). Indeed pregnancy and foaling rates were higher in 1996 than previously recorded in 1994 and 1995 for vaccinated, placebo and control mares (Figure 1).

2.5 REASON FOR FAILURE

This type of immunocontraceptive vaccine produced from porcine zona pellucida proteins and packed with an adjuvant into biobullets for delivery via the Ballista-Vet system has been demonstrated to prevent conception in domestic mares (Willis et al. 1994).

It obviously failed in this experiment and although the cause of failure may not be determined it is important to identify areas where failure could have occurred.

1. Vaccine manufacture. This is possible but unlikely as the method of manufacture had been used many times previously without reported failure. However, failures occur and the vaccine should have been tested on domestic mares before shipment from the USA or on receipt in New Zealand.

   Surplus vaccine was held and will be used on domestic mares in 1998. The vaccine is now nearly 3 years old and if it does not cause an antibody response it will not help define the problem area. To test the vaccine, the mares' antibody response will be monitored after vaccination.

2. Biobullet packing. It is possible that the vaccine was not securely packed into the biobullet. Tests on the stability of the biobullet have been carried out using a dead horse. The vaccine component remained securely in the biobullet after administration, but it may have leaked out after administration.

3. Transport. The vaccine is not a live vaccine but it might deteriorate, as conditions changed and the temperature rose during transport.

   The vaccine should have been tested on arrival in New Zealand to ensure its efficacy. This would have entailed using domestic horses and collecting blood before and after vaccine administration and sending them to the USA for analysis.

   The vaccine used is an experimental vaccine produced by two laboratories in the USA. It is available when either of these laboratories are producing it and we obtained vaccine too late in 1995 to test it on domestic mares. The vaccine was made up in March or April of 1995, tested for infectious agents and arrived just before the muster began. The shelf life of the vaccine was thought to be around 3 to 6 months and we did not want to store it for any unnecessary time. It had not been expected that the vaccine would deteriorate during transport.

4. A failure to deliver the vaccine effectively We are confident that the initial and booster biobullets were administered successfully to at least 13 mares as they were seen to bleed at the entry wound on both occasions (Table 1). However, the conditions under which the booster biobullet was administered were sometimes difficult. Luckily these

mares had become habituated to humans and could be approached to within 5-10 m.

The time between first and booster vaccination varied but was usually around 4 to 6 weeks (Table 1) and it is expected that the booster should have been effective. However, it has to be said that the Ballista-Vet delivery system did not live up to expectations, and retrospectively a modern dart gun would have been much more effective.

The one mare that did not conceive (number 132) may not have received the booster vaccine.

5. Biobullet penetration and stability in the mare. The biobullet may not have penetrated far into the mares' muscle mass and may have fallen out or it may have shattered either immediately after administration or due to muscle movement or enzyme activity and thereafter fallen out piecemeal. A trial in which biobullets were shot into a dead horse indicates that air pressure of 1200 to 1400 psi is necessary to propel the biobullet through the skin, fascia and into the underlying muscles. The maximum range for successful penetration of muscle is 20 m but even at that range some biobullets lodged just under the skin. Biobullets which had lodged under the skin leaked back out through the skin as they softened, within 12 hours of administration. This leakage would include the vaccine component of the biobullet. However a range of 5-10 m and air pressure of 1200 -1400 psi resulted in deep penetration of the muscles.

6. The Kaimanawa horses do not mount an immunological response to the vaccine. This is unlikely given that the vaccine has worked in animals as diverse as seals, deer and elephants (Kirkpatrick et al., 1997; Bertschinger et al., 1996; Brown et al. 1996). This possibility will be tested in a study during February 1998. Brown et al. (1996) expressed concern that there may be some interaction between the biobullet casing and one or more components of the vaccine causing a decrease in the vaccine's efficacy. However, Willis et al. (1994) found that the vaccine packed in a biobullet was quite effective at preventing conception in domestic mares.

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Table 1. The resident band, band type, identification number, age and treatment history of mares that received vaccine (a) and placebo (b) biobullets.

(a)

				FIRST TREATMENT		BOOSTER 1		BOOSTER 2		FECUNDITY	
Band ID	Band type	Mare ID	Mare age	Date	Evidence of successful administration	Date	Evidence of successful administration	Date	Evidence of successful administration	Preg.	Foal
C-band	S	2	3	7.06.95	muster†	25.07.95	Trickle of blood			M	M
Ally's	S	39	7	7.06.95	muster†	3.09.95	Kicked and trickle of blood			+	+
Mary's	S	50	9	7.06.95	muster†	12.07.95	Trickle of blood			+	+
Alaskans	S	58	9	29.08.95	Kicked, open wound, no blood	26.09.95	Kicked, open wound, no blood			+	+
Ally's	S	65	2	7.06.95	muster†	14.07.95	Hair tuft and wet trickle from it			+	+
Mule's	S	70	4	7.06.95	muster†	24.07.95	Kicked, favoured leg, no blood	24.07.95	Startled, no blood.	+	+
Rust	M	91	2	7.06.95	muster†	14.07.95	Trickle of blood			+	-
Ally's	S	100	7	7.06.95	muster†	11.08.95	Trickle of blood			+	+
C-band	S	107	3	7.06.95	muster†	10.08.95	Kicked, no blood			+	-
C-band	S	112	3	7.06.95	muster†	27.08.95	Kicked, limped, drop of blood			M	M
Electra's	S	113	7	7.06.95	muster†	30.08.95	Kicked, trickle of blood			+	+
C-band	S	115	3	7.06.95	muster†	13.07.95	No response, trickle of blood			+	+
Ally's	S	117	4	7.06.95	muster†	11.08.95	Open wound, trickle of blood			+	+
Ally's	S	118	8	7.06.95	muster†	24.07.95	Trickle of blood			+	+
Ally's	S	119	9	7.06.95	muster†	2.09.95	Kicked, no blood seen (heavy rain)			+	+
Electra's	S	120	4	7.06.95	muster†	30.08.95	Kicked, hair tuft, no blood			+	-
W-band	S	121	7	7.06.95	muster†					+	+
Ally's	S	122	7	7.06.95	muster†	24.07.95	Trickle of blood			+	+
C-band	S	123	8	7.06.95	muster†	13.07.95	Trickle of blood			M	M
Electra's	S	124	5	7.06.95	muster†	12.08.95	Kicked, trickle of blood			+	+
Electra's	S	126	3	7.06.95	muster†	12.08.95	Kicked, trickle of blood			+	+
Ally's	S	127	8	7.06.95	muster†	25.07.95	No response, hair tuft, no blood	3.09.95	Kicked, open wound	+	+
Ally's	S	130	5	7.06.95	muster†	25.07.95	Kicked, open wound, no blood			+	+
C-band	S	132	4	7.06.95	muster†	13.07.95	No response, no blood			-	-
C-band	S	137	1	7.06.95	muster†	13.07.95	No response, no blood	10.08.95	Kicked, no blood	M	M
Rust	M	154	adult	12.08.95	Kicked, trickle of blood	3.09.95	Kicked, no blood			+	+

NOTES: Band type: S=single stallion band, M=multi-stallion band (Linklater et al. 1996a, 1996b).

†=all mares treated in the muster received a biobullet at less than 5 meters and wounding and/or a trickle of blood were observed in all cases.

+=positive test for pregnancy or mare observed with a foal, M=mortality of mare in Spring-Summer 1995-96 before results could be obtained.

				FIRST TREATMENT		BOOSTER 1		BOOSTER 2		FECUNDITY	
Band ID	Band type	Mare ID	Mare age	Date	Evidence of successful administration	Date	Evidence of successful administration	Date	Evidence of successful administration	Preg.	Foal
Imposters	S	6	3	7.06.95	muster†					M	M
Raccoon's	M	16	3	7.06.95	muster†					+	+
Henry's	S	18	1	7.06.95	muster†	27.09.95	no blood			M	M
Hillbillys	S	62	6	7.06.95	muster†					+	+
Henry's	S	64	7	7.06.95	muster†	25.09.95	Kicked, open wound			+	-
Henry's	S	67	9	7.06.95	muster†	25.09.95	Trickle of blood			+	+
Henry's	S	74	8	7.06.95	muster†	27.09.95	no response	27.09.95	Trickle of blood	+	+
Henry's	S	92	2	7.06.95	muster†	25.09.95	Open wound, trickle of blood			+	+

NOTES: Band type: S=single stallion band, M=multi-stallion band (Linklater et al. 1996a, 1996b).

†=all mares treated in the muster received a biobullet at less than 5 meters and wounding and/or a trickle of blood were observed in all cases.

+=positive test for pregnancy or mare observed with a foal, M=mortality of mare in Spring-Summer 1995-96 before results could be obtained.

Table 2. Penetration of the muscles of the hind leg of a dead horse by biobullets fired using the Ballista-Vet system.

Range (meters)	Air Pressure (PSI)	Effect
25	12-1400	Biobullet bounced off skin
25	12-1400	Biobullet bounced off skin
25	12-1400	Biobullet stuck in skin (2/3 of biobullet visible outside skin)
25	12-1400	Biobullet stuck in skin (½ of biobullet visible outside skin)
25	12-1400	Biobullet lodged just under skin - leaked out after 12 hours
25	12-1400	Biobullet lodged just under skin - leaked out after 12 hours
20	12-1400	Biobullet cut skin but bounced off
20	12-1400	Biobullet lodged just under skin - leaked out after 12 hours
20	12-1400	Biobullet lodged just under skin - leaked out after 12 hours
20	12-1400	Biobullet through skin and 5 mm into muscle
20	12-1400	Biobullet through skin and 5 mm into muscle
20	12-1400	Biobullet through skin and 5 mm into muscle
20	12-1400	Biobullet through skin and 10 mm into muscle
10	12-1400	Biobullet through skin and 10 mm into muscle
10	12-1400	Biobullet through skin and 20 mm into muscle
5	12-1400	Biobullet through skin and 40 mm into muscle
5	12-1400	Biobullet through skin and 30 mm into muscle
5	12-1400	Biobullet through skin and 30 mm into muscle
5	12-1400	Biobullet through skin and 20 mm into muscle
10	8-900	Biobullet lodged under skin and leaked out after 12 hours
10	8-900	Biobullet lodged under skin and leaked out after 12 hours
10	8-900	Biobullet through skin and 5 mm into muscle
10	8-900	Biobullet through skin and 5 mm into muscle

* When biobullet pierced the muscle fascia it did not leak out.

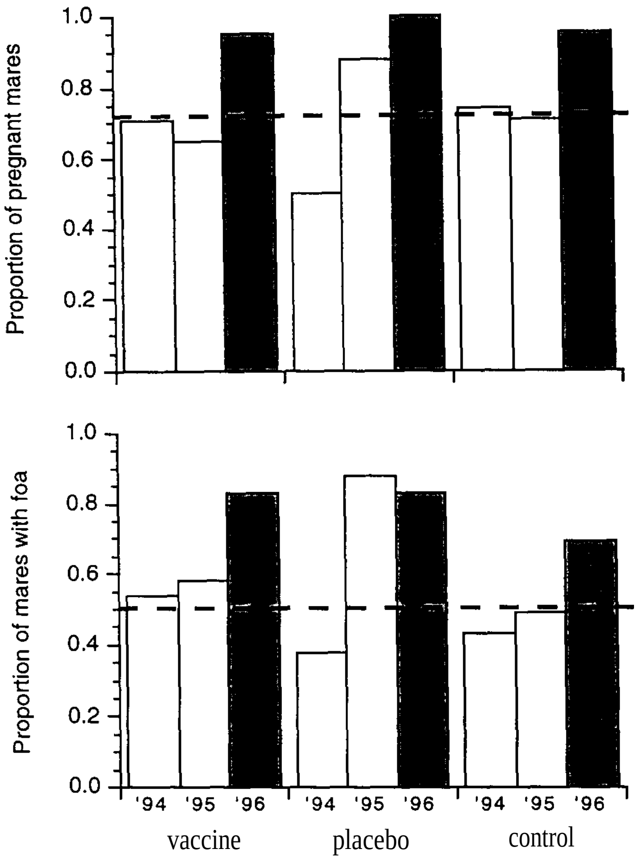

Figure 1. The proportion of mares administered vaccine (n=26), a placebo (n=8), or in the control group (n=63) who were pregnant (a) and who subsequently foaled (b) in 1994 and 1995 breeding seasons prior to vaccination (☐) and in 1996 after vaccination (■). Dashed lines represent the average pregnancy and foaling rates for the entire focal population from 1994 and 1995 breeding seasons.