



## **GnRH VACCINE**

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Mares come into heat or estrus due to rising estrogen levels produced by developing ovarian follicles. Mares typically do not show heat during the winter when they have small inactive ovaries. Heat is also not exhibited after ovulation when mares have a corpus luteum producing progesterone. Ultimately, expression of behavioral estrus occurs in the presence of estrogen and the absence of progesterone. Absence of estrus is a function of low estrogen levels and/or elevated progesterone levels.

In previous issues, we have discussed the effectiveness (or lack thereof) of cattle implants, human contraceptive agents, and even marbles for suppression of estrus in mares. Now we will review the use of a vaccine to prevent heat in mares.

Reproductive events in mares, such as development of follicles and ovulation, are initiated by hormonal signals from the brain. Gonadotropin-releasing hormone (GnRH) is produced by the hypothalamus and secreted in pulses into the blood stream. The anterior pituitary gland is situated near the base of the brain and receives the GnRH signals from the hypothalamus. The pituitary secretes follicle stimulating hormone (FSH) which stimulates follicular growth and luteinizing hormone (LH) which causes follicle maturation and induces ovulation.

Vaccines have been developed which target the initial player in this cascade of events (GnRH). A vaccine is traditionally used to stimulate the immune system to produce antibodies against one or more specific infectious disease agents. However, vaccines can also be developed against other substances, including hormones. Vaccination against GnRH results in production of anti-GnRH antibodies by the immune system. These antibodies bind to GnRH circulating in the blood stream and block the biological activity of the GnRH molecule. As a consequence, the lack of bioactive GnRH results in a reduction of FSH and LH production by the anterior pituitary and ultimately a reduction of ovarian follicular development. The absence of follicular growth is associated with estrogen levels that are insufficient to cause behavioral estrus.

Equity™ is the name of a commercial vaccine licensed in Australia 'for use in the control of estrus and estrus-related behavior in fillies and mares not intended for breeding'. The vaccine is administered as a two-dose series, with the second dose given 4 weeks after the initial dose. Research studies have reported that vaccinated mares develop an antibody response that peaked approximately 2 weeks after the second vaccination. Immunization resulted in a reduction of ovarian activity, with the

ovaries in most mares resembling those of seasonally anovulatory mares with 4 weeks after the second dose. Vaccination also was associated with a reduction in estradiol levels and an attenuation of behavioral heat.

An increase in ovarian activity and a return to estrus was observed in most mares as the concentrations anti-GnRH antibodies in circulation decreased over time. It has also been reported that live foal rates were similar between mares receiving a placebo treatment and vaccinated mares in subsequent years after the effects of the vaccine had disappeared.

However...anecdotal accounts have also surfaced suggesting that some young mares vaccinated against GnRH when they were in training have subsequently failed to develop follicles or ovulate when their performance career is over. The incidence rate of this issue has not been determined. A risk of any vaccine is the inability to predict either the magnitude or duration of the immune response. Mares that fail to develop a significant antibody response after vaccination may continue to cycle and exhibit behavioral estrus. Conversely, mares that have a prolonged duration of elevated antibody levels may not have normal reproductive cycles for an extended period of time.

The Australian vaccine is clearly labeled for fillies and mares not intended for breeding. Holding to that principle would negate any adverse effects on ovarian function. However, the future use of a horse may change over time and as horses are bought and sold. In addition, one cannot necessarily predict the end of an athletic career and the start of a breeding career.

In summary, vaccines against GnRH offer great potential for a medically safe and straightforward means of blocking estrus or inducing contraception in mares. Horse owners, trainers, and veterinarians must realize that there may be serious issues regarding future reproductive performance in a limited percentage of vaccinated fillies or mares. Currently there are no vaccines against GnRH approved for use in horses in the United States.