

A Review of Contemporary Contraceptives and Sterilization Techniques for Feral Horses

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Porcine zona pellucida immunocontraceptives have received the most attention and use over the past 40 years, but other treatments such as a gonadotropin-releasing hormone (GnRH) vaccine^a are also available. Optimization of these treatments as well as the development of other molecular approaches, intrauterine devices, and surgical techniques are ongoing. Author's address: U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, 2150 Centre Ave., Bldg B MS2E6, Fort Collins, CO 80526; e-mail: albert.j.kane@aphis.usda.gov. © 2018 AAEP.

1. Introduction

Since the late 1970s, researchers have sought a safe and effective equine contraceptive to help reduce population growth rates of feral horses (*Equus ferus caballus*) and burros (*E. asinus*). A treatment that is safe, practical, effective, and long lasting has not yet been developed. Even after a treatment is developed that is effective for individual animals, there remain significant hurdles at the population level that must be overcome to reduce population growth rates.¹ This commentary provides a brief review of past research efforts to develop contraceptives for feral horses as well as a discussion of the contraceptives and sterilization techniques currently available.

2. Review

Early fertility control efforts focused on both male and female contraception. However, as early as 1980, scientists with the National Research Council, part of the National Academies of Science, recommended that wild horse contraceptive efforts should focus on reducing fertility in mares.² They recognized the polygynandrous nature of feral horses

where multiple males may breed the same or multiple females. Although it is true that wild horses live in harems that include a dominant stallion, much of the breeding may also be done by other stallions, and harem structures are fluid over time. It has been demonstrated that up to one third of foals may be sired by stallions that are not affiliated with a mare's band.³

Steroid Hormones to Vaccines

Early contraceptive studies in stallions and mares used steroid hormones to alter fertility. Although there was some success in mares, the treatments were cumbersome to administer, and there were concerns about the potential for persistence of the hormones in the food chain and the environment. At approximately the same time, studies were done with surgical vasectomies applied to harem stallions. There was a small effect noted in one of the two groups studied, but it was short lived. The researchers concluded that, although it may be effective at the individual horse level, the efficacy of vasectomizing males for population growth suppression over time was doubtful.

This work first appeared in *Human-Wildlife Interactions*. Kane AJ. A review of contemporary contraceptives and sterilization techniques for feral horses. 2018;12:111–116. Available at: <https://digitalcommons.usu.edu/hwi/vol12/iss1/12>. Reprinted here with permission.

NOTES

As attention turned away from using steroid hormones to alter fertility, porcine zona pellucida (PZP) vaccines were developed in laboratory rodents and later applied to horses.^{4,5} The PZP vaccine contains a glycoprotein antigen harvested from pig (*Sus scrofa domesticus*) ovaries. When mixed with a powerful adjuvant (in most cases, it is emulsified with Freund's adjuvant), it stimulates the mare's immune system to make antibodies to ZP proteins. These antibodies block fertilization of the egg and over time bind to zona proteins in the ovary, causing it to shrink and become nonfunctional. The most widely used PZP vaccine is Zonastat-H®. This liquid immunocontraceptive can be hand injected or darted into mares. When a booster shot is also administered about 30 days later and about 1–2 months prior to the breeding season, it is highly effective at preventing conception for one year, with only about 10 to 20% of treated mares foaling each year. In smaller herds where the number of animals is at or very close to the appropriate management level (AML), Zonastat-H can successfully reduce or even eliminate the need to gather and remove animals over time.

The Bureau of Land Management (BLM) is currently using this approach in several herds.⁶ The biggest limitation to this treatment is that it must be administered every year. Most animals on BLM ranges cannot be approached closely enough to allow darting, and repeated annual roundups to allow hand injecting the treatment get more difficult with each repetition, usually becoming impractical and ineffective after two or three iterations. Another limitation of this approach is how long it takes to achieve desired population numbers, called the AML by BLM, when herds are even modestly above the desired numbers. The so-called "Assateague prescription," where the majority of mares were darted every year,⁷ was eventually effective at achieving population targets on a small barrier island, but it took 13 years before a decline in numbers was achieved and several additional years before AML was achieved. That population of 156 horses started in 1993 only 30% over the desired AML of 120 horses, had 143 horses after 13 years, and today has about 90 horses. For comparison, many wild horse herds managed by the BLM in the west are currently at levels more than 100% greater than AML.

The quest for a longer-lasting PZP treatment began about the same time that Zonastat-H was being developed. An early study of the pelleted "PZP-22"^{cc} treatment was most promising, with only 6–18% of mares with reported foaling in the first two years of the Clan Alpine study and 30–40% foaling in years 3 and 4.⁸ Unfortunately, this level of success has never been repeated with several captive and free-ranging trials reporting 25, 30, or even 70% foaling in the first two years following treatment. The reasons for this poor performance mostly remain a mystery. Recently success of 15–40% foaling over a

three year period was reported with reformulated PZP-22 after additional booster treatments,⁹ but whether or not this can be repeated remains to be seen. Currently, PZP-22 is the treatment used most frequently by the BLM, because, at the very least, it usually provides one year of good efficacy without requiring a 30-day booster shot, and when boosted a year or two later, efficacy should improve.

SpayVac®,^d another formulation of PZP developed to offer longer lasting efficacy, uses similar PZP antigens with a unique liposome technology expected to provide several years of efficacy. As with PZP-22, an initial study of the treatment was promising.¹⁰ However, subsequent trials aimed at demonstrating long term efficacy in a captive pasture breeding setting could not duplicate the same results and, in fact, showed reasonable efficacy in one year (15% foaling) but poor efficacy over time, with up to 70% of treated mares foaling.¹¹ Although this vaccine is not commercially available at this time, the proponents of the product have regrouped and hope to conduct testing of a new formulation of SpayVac in the future.¹² Although this product shares the same limitations inherent to the PZP antigen as Zonastat-H and PZP-22, in some species, including occasionally horses, it seems like it could be long lasting or even permanent. The reliability of the newly formulated product will need to be established in captive breeding trials with horses before one might have the confidence needed for field applications.

Gonacon

At this time, there is only one other contraceptive product available for use in horses. Gonacon-Equine® is a vaccine that acts against gonadotropin-releasing hormone (GnRH), a hormone critical to fertility. The vaccine was formulated and registered with the Environmental Protection Agency as a one-shot treatment that was thought to provide good multiyear efficacy. Captive pen trials resulted in good efficacy (6% foaling) the first year,¹⁰ but, again, the efficacy of a single treatment in field trials conducted with feral horses at Theodore Roosevelt National Park never reached that level of effectiveness, with about 50% of animals foaling the first and second years.¹³ Fortunately, with a booster treatment as much as three years following the initial shot, efficacy improved dramatically, with 0% of mares foaling a year later and around 15% foaling in the following two years. Like PZP vaccines, Gonacon can be hand injected or darted. It has two advantages in that it does not require mixing in the field and is more stable when stored. The longer term efficacy of Gonacon seems more promising than the PZP vaccines at this time; however, optimal booster schedules are still being investigated. The BLM has used Gonacon in one small pilot project on the range, and the early results are encouraging. Gonacon treatment that includes a

booster may be one of the best options currently available for the contraception of feral horses.

Intrauterine Devices

After many years of focusing primarily on PZP and GnRH technologies, other contraceptive approaches are now being investigated for feral horses, with support from the BLM.⁶ In addition to injectable treatments, new intrauterine devices (IUDs) are being tested. Early studies of IUDs were promising, with reports of over 80% retention and efficacy with no negative effects on mare health.¹⁴ However, once again, when additional captive breeding trials were done with the same design (as well as other more sophisticated designs that was promoted as effective with 100% retention), the results were disappointing, with 60–100% of the devices falling out soon after stallions were allowed to breed the mares. A current BLM-supported study of a new IUD has had some success with a redesigned product that seems to offer better retention in the presence of stallions. Data are still being obtained at this time to demonstrate retention, efficacy, and safety over a period of years. IUDs have the advantage of being almost 100% effective as long as they are retained. They appear to have no long-term negative effects on the mare's health or the uterus, and they could be 100% reversible if removed. They do have the distinct disadvantage that they can only be inserted into nonpregnant mares and most feral horse mares of breeding age are pregnant for most of the year.

Surgical Sterilization

Surgical sterilization, once considered taboo for feral horses because it is permanent, is also again being considered as a means of reducing population growth rates. For stallions, the same limitations of polygynandry that became apparent back in the 1980s are still present. It seems unlikely that castrating or vasectomizing only some portion of the more dominant males in a herd will significantly slow population growth over a period of several years, because enough stallions will still be present to eventually breed all the mares present. However, a saturation approach where some high percentage (e.g., 80–95%) of stallions are sterilized remains untested.

In their most recent review of the science behind feral horse contraception, the National Academy of Sciences recommended chemical vasectomy as a promising technique.¹⁵ Despite acknowledging that it was not yet proven, they felt that it should not be difficult to adapt to feral horses. Unfortunately, this does not seem to be the case. When chemically vasectomized horses were reexamined after a recent study performed on the Sheldon Wildlife Refuge,¹⁶ it was revealed that the chemical vasectomies failed to block sperm transport in any of the dozens of animals treated.¹⁷ Although it should be possible to develop and use a technique for chemical vasectomy, it seems to offer little advan-

tage over the surgical procedure, which has been done with individual horses but remains unproven at the population level. The fact that a small number of fertile stallions can impregnate many mares suggests that any form of vasectomy is unlikely to be an effective means of long-term population growth suppression.

The consideration of surgical sterilization is not limited to stallions but also extends to spaying and tubal ligation procedures for mares. There is no established procedure for tubal ligation in mares. It is not something that is called for among domestic horses and has not been developed or tested for feral horses. Spaying, although not as common as castration, is done in domestic horses and has been done with feral horses. The procedure in horses is much more difficult than it is in cattle and not as routinely practiced as spaying dogs and cats, for example. It is almost never done to pregnant domestic horses, so the safety and practicality of spaying feral horses on a large scale, particularly while pregnant, remain mostly untested.

Feral mares were spayed on the Sheldon Wildlife Refuge, with a report of fewer foals born to harems that included spayed mares and vasectomized stallions,¹⁶ but it remains to be seen if similar results could be obtained in other places when spaying alone is done on a large scale in the context of typical BLM roundups. Yes, individual mares can be spayed, but can practitioners do it safely on a large scale with pregnant mares and will it help achieve the goal of controlling population growth rates? The BLM has attempted to answer some of these questions with applied research, but these questions remain unanswered largely due to litigation that prevented the projects from getting started.

3. Discussion

We are often asked, why hasn't anyone developed the ideal contraceptive for feral horses when BLM has been supporting this research for over 40 years? The answer is perhaps that an ideal contraceptive is an unreasonable expectation, for any species. Safety for mares, unborn colts, and the environment are paramount, but is it really reasonable to expect a one-shot, long-lasting, predictably reversible contraceptive that has no behavioral effects for horses when modern science has never even developed such a treatment for dogs, cats, or people? The emphasis for reproductive research in the domestic horse world has always been getting mares pregnant, not trying to prevent pregnancy. Until the last few years, there has been very limited funding for contraceptive research for horses, with more funding obligated by BLM to research projects in the last few years than the previous 40 years combined. From where we started in the 1970s, researchers have made significant discoveries and improvements in contraceptives for feral horses.

The desperate need for results in the field and the limited funding available have meant that several

treatments were advanced to field trials or management use in the field after only one test under more limited conditions in captivity. It is not uncommon for treatments that work in controlled laboratory or clinical settings not to work as well when applied on a larger scale in the field. Unfortunately, we have seen this with feral horse contraception on several occasions. Were the early studies flawed by unblinded, biased outcome assessments? What about the blinded (SpayVac) studies that also could not be replicated? Was it the biological variation in the PZP itself, changes in the adjuvants, or preparation of the vaccines? All of these factors are the reason that research science prefers to look for replication of results by different investigators under expanded conditions before taking treatments to management application in the field. However, these are luxuries that feral horse contraceptive research did not have.

The pressure and the push have been to take treatments to the field as soon as they offer some legitimate promise of success. The upside would have been faster results where they were needed most. The down side was several treatments did not work as well as expected when applied on a large scale. These challenges were added to the practical limitations and expectations of trying to apply darting programs to the typically vast western rangelands that span not thousands of acres but hundreds of thousands of acres. Darting programs can work on a small scale where a hundred or so named animals can be approached to within 30 or 40 yards. However, where 10 times as many horses might roam on land areas 30 times larger and the horses cannot be recognized as individuals because they mostly look alike, this approach is not practicable. Most often these animals cannot be approached to less than hundreds of yards. Under these more typical conditions, darting programs are not likely to succeed. Despite all this, there have been small scale successes on some BLM lands; the Pryor Mountains Wild Horse Range and the Little Book Cliffs, McCullough Peaks, and Spring Creek Basin Herd Management Areas come to mind.

4. Conclusion

The history of feral horse contraception research is one of desperate need, ambitious (perhaps sometimes unreasonable) goals, and the passionate pursuit of a solution by a handful of investigators challenged by limited resources as well as the biology of the endeavor. Unfortunately, despite the many advances that have been made, a contraceptive solution that is safe, practical, and effective for most herds on typical western herds is not in hand. Right now, feral horse contraception research has better levels of funding than ever before, with major universities more engaged than ever and new, never previously conceived molecular techniques being investigated. Nevertheless, progress will likely be slow. For every idea that advances to the next level

of investigation, two or three others will fail. Despite the desperate need, if we can maintain current research funding levels, we are years, likely more than a decade, away from a contraceptive solution to the challenge of significantly reducing feral horse population growth rates on western rangelands. The good news is it is still conceivable, and there are still some very bright and passionate scientists working on solutions that will make a difference.

Acknowledgments

The Author is grateful to Drs. Butch Roelle and Paul Griffin for their assistance in preparing this work. The information, ideas, and opinions expressed are those of the author and do not necessarily represent those of the U.S. Department of Agriculture or the U.S. Department of Interior, or endorsement of the products described herein.

Declaration of Ethics

The Author has adhered to the Principles of Veterinary Medical Ethics of the AVMA.

Conflict of Interest

The Author is an employee of the U.S. Department of Agriculture, Animal and Plant Health Inspection Service (APHIS), Veterinary Services and serves as an advisor to the APHIS/BLM Wild Horse and Burro Partnership that is supported by funding provided from the BLM to the USDA APHIS. Gonacon is manufactured and sold by the USDA APHIS Wildlife Services, but the author has no financial or employment involvement with this branch of the USDA APHIS or any other companies that manufacture or sell products that figure prominently in this review.

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^cPZP-22 John Turner, Univ of Toledo, Toledo, OH 43606.

^dSpayVac® SpayVac for Wildlife Inc, Sidney, BC Canada.