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Commentary

A review of contemporary contraceptives and sterilization techniques for feral horses

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Abstract: This commentary provides a brief review of the history of contraceptive research efforts for feral horses (*Equus ferus caballus*) as well as the contraceptives and sterilization techniques currently available for feral horses. Porcine zona pellucida (PZP) immunocontraceptives have received the most attention and use over the past 40 years, but other treatments such as the GnRH vaccine Gonacon™-Equine are also available. Optimization of these treatments as well as the development of other molecular approaches, intrauterine devices, and surgical techniques is ongoing.

Key words: contraceptive, *Equus ferus caballus*, feral horse, fertility control, sterilization

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 good 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 (Garrott 2018).

Early fertility control efforts focused on both male and female contraception. However, as early as 1980, scientists with the National Research Council (NRC), part of the National Academies of Science, recommended that wild horse contraceptive efforts focus on reducing fertility in mares (NRC 1982). They recognized the polygynandrous nature of feral horses where multiple males may breed the same or multiple females. While 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 (Bowling and Touchberry 1990).

Steroid hormones to vaccines

Early contraceptive studies in stallions and mares used steroid hormones to alter fertility. While 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. About this same time, studies were done with surgical vasectomies applied to harem stallions. There was a small effect noted in 1 of the 2 groups studied, but it was short lived. The researchers concluded that, while it may be effective at the individual horse level, the efficacy of vasectomizing males for population growth suppression over time was doubtful.

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 (Liu et al. 1989, Kirkpatrick et al. 1992). 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 1 year, with only about 10–20% of treated mares foaling each year. In smaller herds where the number of animals is at or very close to the desired population numbers, or 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 (BLM 2017). 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 2 or 3 iterations. Another limitation of this approach is how long it takes to achieve the AML when herds are even modestly above the desired numbers. The so-called Assateague prescription, where the vast majority of mares was darted every year (Kirkpatrick and Turner 2008), 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 >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" treatment was most promising with only 6–18% of mares reported foaling in the first 2 years of the Clan Alpine study (Turner et al. 2007) and 30–40% foaling in years 3 and 4. 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 2 years following treatment. The reasons for this poor performance mostly remain a mystery. Recently, success of 15–40% foaling over a 3-year period was reported with reformulated PZP-22 after additional booster treatments (Rutberg et al. 2017), but whether or not this can be repeated remains to be seen. Currently, PZP-22 is the treatment used most frequently by the BLM; at the very least, it usually provides 1 year of good efficacy without requiring a 30-day booster shot, and when boostered 1–2 years later, efficacy should improve.

Spay Vac®, 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 (Killian et al. 2008). 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 1 year (15% foaling) but poor efficacy over time with up to 70% of treated mares foaling (Roelle et al. 2017). 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 Spay Vac in the future (Bechert and Fraker 2018). 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 1 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 1-shot treatment that was thought to provide good multiyear efficacy. Captive pen trials resulted in good efficacy (6% foaling) the first year (Killian et al. 2008), 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 (Baker et al. 2017). Fortunately, with a booster treatment as much as 3 years following the initial shot, efficacy improved

dramatically with 0% of mares foaling a year later and around 15% foaling in the following 2 years. Like PZP vaccines, Gonacon can be hand injected or darted. It has 2 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 a small pilot project on the range, and the early results are encouraging. Gonacon treatment that includes a booster may be among 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 (BLM 2017). In addition to injectable treatments, new intrauterine devices (IUDs) are being tested. Early studies of IUDs were promising, with reports of >80% retention and efficacy with no negative effects on mare health (Daels and Hughes 1995). However, once again, when additional captive breeding trials were done with the same design (as well as other more sophisticated designs 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 good 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. The 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 non-pregnant 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 (NRC 2013). Despite acknowledging that it was not yet proven, they felt that it should not be difficult to adapt to feral horses. Unfortunately, this doesn't seem to be the case. When chemically vasectomized horses were reexamined after a recent study performed on the Sheldon Wildlife Refuge (Collins and Kasbohm 2016), it was revealed that the chemical vasectomies failed to block sperm transport in any of the dozens of animals treated (Scully et al. 2015). While it should be possible to develop and use a technique for chemical vasectomy, it seems to offer little advantage 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 just is not something that is called for among domestic horses and has not been developed or tested for feral horses. Spaying, while 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, remains

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 (Collins and Kasbohm 2016), but it remains to be seen if similar results could be obtained in other places when spaying 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.

What is the ideal contraceptive?

We are often asked, why hasn't anyone developed the ideal contraceptive for feral horses when the BLM has been supporting this research for >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 1-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 the 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 1 test under more limited conditions. 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 (Spay Vac) 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 didn't 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 downside was several treatments didn't 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 100 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 can't be recognized as individuals because they mostly look alike, this approach is not practicable. Most often these animals can't be approached to less than hundreds of yards. Under these more typical conditions, darting programs aren't 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.

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, today, 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 2 or 3 others will fail. Despite the desperate need, if we can maintain current research funding levels, we are years or 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 that it is still conceivable, and there are still some very bright and passionate scientists working on solutions that will make a difference.

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Literature cited

Baker, D., J. Powers, J. Ransom, B. McCann, M. Oehler, J. Bruemmer, N. Galloway, D. Eckery, and T. Nett. 2017. Gonadotropin-releasing hormone vaccine (GonaCon-Equine) suppresses fertility in free-ranging horses (Equus caballus): limitations and side effects of treatment. Proceedings of the 8th International Conference on Wildlife Fertility Control 8:12.

Bechert, U. S., and M. A. Fraker. 2018. Twenty years of SpayVac® research: potential implications for regulating feral horse and burro populations in the United States. Human–Wildlife Interactions 12:117–130.

Bowling, A. T., and R. W. Touchberry. 1990. Parentage of Great Basin feral horses. Journal of Wildlife Management 54:424–429.

Bureau of Land Management (BLM). 2017. Wild horse and burro: science and research. U.S. Department of the Interior, Washington, D.C., USA, <https://www.blm.gov/programs/wild-horse-and-burro/herd-management/science-and-research>. Accessed February 21, 2018.

Collins, G. H., and J. W. Kasbohm. 2016. Population dynamics and fertility control of feral horses. Journal of Wildlife Management 81:289–296.

Daels, P. F., and J. P. Hughes. 1995. Fertility control using intrauterine devices: an alternative for population control in wild horses. Theriogenology 44:629–639.

Garrott, R. A. 2018. Wild horse demography: implications for sustainable management within economic constraints. Human–Wildlife Interactions 12:46–57.

Killian, G., D. Thain, N. K. Diehl, J. Rhyan, and L. Miller. 2008. Four-year contraception rates of mares treated with single injection porcine zona pellucida and GnRH vaccines and intrauterine devices. Wildlife Research 35:531–539.

Kirkpatrick, J. F., I. M. K. Liu, J. W. Turner, R. Naugle, and R. Keiper. 1992. Long-term effects of porcine zonae pellucidae immunocontraception on ovarian function in feral horses (*Equus caballus*). Journal of Reproduction and Fertility 94:437–444.

Kirkpatrick, J. F., and A. Turner. 2008. Achieving population goals in a long-lived wildlife species (*Equus caballus*) with contraception. Wildlife Research 35:513–519.

Liu, I. K. M., M. Bernoco, and M. Feldman. 1989. Contraception in mares heteroimmunized with pig zonae pellucidae. Journal of Reproduction and Fertility 85:19–29.

National Research Council. 1982. Wild and free-roaming horses and burros: final report. National Academies Press, Washington, D.C., USA.

National Research Council. 2003. Using science to improve the BLM Wild Horse and Burro Program: a way forward. National Academies Press, Washington, D.C., USA.

Roelle, J. E., S. S. Germaine, A. J. Kane, and B. S. Cade. 2017. Efficacy of SpayVac® as a contraceptive in feral horses. Wildlife Society Bulletin 41:107–115.

Rutberg, A., K. Grams, J. W. Turner, and H. Hopkins. 2017. Contraceptive efficacy of priming and boosting does of controlled-release PZP in wild horses. Wildlife Research 44:174–181.

Scully, C. M., R. L. Lee, L. Pielstick, J. Medlock, K. M. Patton, G. H. Collins, and M. A. Kutzler. 2015. Comparison of chemical and surgical vasectomy on testicular activity in free-roaming horses (*Equus caballus*). Journal of Zoo and Wildlife Medicine 46:815–824.

Turner, J. W., I. K. Liu, D. R. Flanagan, A. T. Rutberg,

and J. F. Kirkpatrick. 2007. Immunocontraception in wild horses: one inoculation provides two years of infertility. Journal of Wildlife Management 71:662–667.

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