

Just because I can, doesn't mean I should: the application of evidence-based medicine to small animal theriogenology

Melissa Goodman

Veterinary Reproductive Services, West Chester, PA

“You ask of my companions. Hills, sir, and the sundown, and a dog..... They are better than beings, because they know, but do not tell.”

Emily Dickinson

Introduction

The stresses and demands of modern American society have triggered an increase in dog ownership; as stated by the American Veterinary Medical Association, our canine counterparts provide companionship, joy, unconditional love, a sense of safety, and often a service. This same trend has caused pet owners to become careful consumers, desiring a healthy, stable dog with traits compatible with an individual's way of life. A pedigreed dog that is carefully bred and raised is the best guarantee that a rewarding and long lasting relationship will develop, and likewise the best guarantee that fewer animals end up unwanted, in shelters or on the street.

As the importance of purebred dog ownership is increasingly appreciated, dog breeders are challenged to produce quality animals. The veterinary profession, however, had largely neglected the field of canine reproduction; despite progress in the study of reproduction in human medicine and livestock since the 1960's, little technical progress was made on behalf of dog breeders. Recent years, however, have seen a dramatic change. Proper reproductive management is recognized as the foundation of a successful breeding program; genetic screening is seen to be an important factor in planned breedings; technologically advanced breeding systems have been developed to give dog breeders wider options; the pathology and treatment of canine infertility is better understood. Most importantly, the veterinarian has become an active participant in the dog breeding process.

Keywords: Evidence-based medicine, artificial insemination, vaginal insemination, transcervical insemination, surgical insemination

The importance of evidence

While the field has grown, and the demand has increased exponentially, training and information have remained limited. The time sensitive and multidisciplinary nature of small animal theriogenology is difficult to fit into the practical limitations of an academic system; as a result veterinary students, interns and residents have limited exposure to the type of cases that are routinely managed in a practice setting. Logistical, financial and ethical constraints severely restrict the amount and quality of research performed, and with it the evidence available to aid in clinical decision making. Nonetheless, it remains our obligation to recognize these inherent limitations, and to use the best available resources in a disciplined, science-based approach, to determine both the benefits and potential adverse effects of the procedures and treatments we recommend. By combining our collective knowledge and reasoning and maintaining the “science based” approach available to us, we can do justice to our clients and patients. By ignoring them, we risk succumbing to quackery.

Veterinary medicine offers some unique ethical challenges not faced by other health professionals. We must serve the needs of both the animals and the humans who own them, in areas as diverse as the beloved pet being given medical care as sophisticated as that provided to their human counterparts, as well as cattle in the feedlot, and laboratory animals used in biochemical research. The leaders of the profession are just beginning to learn how to address these issues.

Today we come together as veterinarians who work specifically with purebred dog breeders. Our society wants and demands healthy pets who fit a specific lifestyle and are both mentally and physically sound, but at the same time unwanted pets fill our shelters. Purpose-bred dogs are needed for military service, guide dogs and service dogs. Wealthy pet owners want to clone a beloved pet. Anti-dog and

anti-dog breeding legislation is on the rise at the same time that “designer breeds” are flooding the consumer market. Veterinarians must use the advancing technology in reproduction and genetics to help their clients make good breeding decisions to achieve their goals but not neglect the health and well-being of the individual animals or their offspring.

Evidence based medicine has been described as “the conscientious, explicit and judicious use of the best scientific evidence to inform clinical judgments with a view to improving clinical outcome at the level of the individual case.”¹ In small animal reproduction, “best scientific evidence” is often absent or lacking. A recent review of the quality of current literature in theriogenology found that only 7 % of publications in canine reproduction were graded adequate to draw sound conclusions.² An earlier review found that only 31 % could be classified as clinical trials, with the remaining 69 % being case reports or personal opinion. Meta-analysis (the integration of data from a number of independent studies to increase the statistical relevance) could not be found in the literature of canine reproduction, and in half, generally accepted and science-based conclusions could not be legitimately drawn from the collected data.³ Nonetheless, although they are few and far between, quality research studies that are both critically designed and statistically evaluated are the best predictors of the results likely to occur in our patients. As clinicians, we are forced to make decisions regarding treatment options without significant randomized and controlled scientific studies to guide us. To deal with these limitations, it is helpful to rank the information available into categories that reflect the relative strength of the evidence, and to use this type of methodical and systematic approach to formulate clinical decisions. Several reasonable scoring systems have been described, with an example shown below:⁴

- Grade I: At least one properly designed randomized controlled clinical study performed in patients of the target species
- Grade II: Evidence from properly designed randomized controlled studies in animals of the target species with spontaneous disease in a laboratory or research colony setting
- Grade III: Appropriately controlled studies without randomization
Appropriately designed case-controlled epidemiologic studies
Studies using models of disease or simulations in the target species
Dramatic results from uncontrolled studies
Case series
- Grade IV: Studies conducted in other species
Reports of expert committees
Descriptive studies; Case reports
Pathophysiologic justification/rationale
Opinions of respected experts

Many treatment modalities and techniques have become commonplace in small animal reproduction based on anecdotal information, and without proof of efficacy or a critical evaluation of potential risks and benefits. While dog breeders and veterinarians clamor for “newer, better, cheaper”, we must resist the temptation to embrace unproven treatments “just because we can”.

Applying evidence based reproduction: choosing an insemination method

Three insemination techniques are widely used in canine artificial insemination, namely (1) vaginal, (2) intrauterine deposition via surgical insemination, and (3) intrauterine deposition via a transcervical approach, either through the use of a rigid catheter or with endoscopic guidance. The techniques involved are well described elsewhere; the specifics will not be discussed here. The choice of insemination technique should be made based on the clinical history of the animals, the quality of the semen being used, the goals of the client, the safety of the procedures, and the skills of the operator. A

technique should be chosen that is likely to give the desired results using the method that is the least invasive, the least expensive, and safest. How to decide? First evaluate the evidence and grade it according to scientific standards. Then apply the evidence to your patient. Are the outcomes of the study applicable to your circumstance? Are there differences between your patient and the animals in the study that may alter the expected response? Are there differences in the semen quality or available insemination dose from that used in the study that may alter the expected response? Will the patient's behavior, breed, or history influence the decision? How will the owner's values or financial situation affect your decision? What are the patient's likely benefits and risks from the various options? Does the patient have other health conditions that alter the potential benefits and risks of each option?

Vaginal Insemination involves deposition of semen into the cranial portion of the vagina, essentially approximating the site of semen deposition that occurs in a natural mating. This method is indicated for most instances of artificial insemination. This simple technique requires minimal equipment, experience and training, and is relatively noninvasive, with little risk to the bitch regardless of her degree of cooperation (or lack thereof). Since it is as close as possible to natural breeding, it will appeal to owners who desire a more natural approach. Studies have shown efficacy with fresh, chilled-extended and frozen semen of high quality, with conception rates of between 60 and 95%. Relatively large numbers of healthy sperm are required, when available this should be the method of choice.

Surgical intrauterine insemination involves deposition of semen into the cranial uterine horns, close to the site of fertilization in the oviducts, which should maximize conception. This method is indicated when using semen of low quality (either in motility, count, longevity and/or vigor), or in females in which fertility is expected to be compromised. The procedure is quick and simple, and easily performed safely by a veterinarian with basic surgical skills. It can be assumed that only bitches in good general health are voluntarily bred, and with the safe and short acting anesthetics available today, the risks of general anesthesia are low. The procedure is performed using sterile technique, so the risk of bacterial introduction into the uterus is eliminated. A surgical approach allows reliable access to the uterus, so that deposition of semen into the cranial uterine horns is done with confidence, regardless of volume, and without tissue trauma to the vagina, cervix or uterus. Visualization and gentle palpation of reproductive organs can be performed to assess possible pathology in subfertile bitches. General anesthesia will minimize stress in nervous, excitable or pain sensitive bitches. However, a surgical approach for an elective procedure may be morally objectionable for some clients. Studies and anecdotal reports give the highest success rates with this method.

Transcervical insemination (TCI) involves deposition of semen into the uterine body, avoiding general anesthesia and surgery, although sedation is sometimes necessary. This method is indicated when it is desirable to get past the cervix but not necessary to get close to the site of conception in the oviducts. The procedure requires specialized equipment and can be difficult and time-consuming to learn, as well as frustrating and time-consuming to perform. The size and anatomy of some bitches create challenges that may be difficult to overcome. Since the uterine body is small and the myometrium of the uterus has significant resistance, only a small volume of semen can be used without backflow through the cervix into the vagina. This small volume may limit the insemination dose unless semen is concentrated by centrifugation, which will frequently lower sperm quality, especially in samples that are already compromised, or by lowering extender to semen dilution ratios which may also decrease sperm quality. Since the cervix is not directly accessible to the operator, TCI has an increased risk of trauma of the reproductive tract, especially with the rigid catheter technique. In addition, since the catheter is taken from the nonsterile vagina through the cervix into the uterus, the procedure should be used with caution in bitches who are at increased risk of pyometra. Studies have shown acceptable conception rates with fresh, chilled and frozen semen, although results have been somewhat contradictory from study to study.

What is the evidence?

A literature search showed no properly designed randomized controlled clinical studies performed in dogs comparing insemination techniques.

There were three properly designed studies performed in laboratory or research animal colony settings. In one study, both fresh semen and frozen/thawed semen were used, with both vaginal and surgical intrauterine insemination methods. The semen parameters for all groups were in range of what would be considered adequate numbers and quality. Conception rates were similar to other studies of fresh semen (100%) and frozen/thawed semen (60%). No significant difference was found between vaginal and surgical insemination.⁵ In another study, two different semen freezing extenders were compared with both intravaginal and transcervical inseminations. Again, generally accepted adequate semen parameters for both sperm numbers and quality were used. No significant differences in pregnancy rate or number of fetuses were found between the two insemination methods.⁶ The third study used a cross-over design to evaluate vaginal vs. surgical intrauterine insemination technique in bitches with decreased fertility. Surgical insemination showed a significant increase in conception over vaginal insemination when female fertility was compromised.⁷ Several other experimental studies looking at conception with varying insemination methods were found in the literature, but other variables affecting fertility were not controlled. As a result, these studies could not be used to give evidence concerning the choice of insemination technique.

Numerous cohort studies, both prospective and retrospective, evaluating canine conception rates were found in the literature. Some of these compared insemination techniques, and some evaluated conception using fresh, chilled or frozen/thawed semen using one insemination method. The usefulness of these studies was limited by the number of variables that were poorly controlled or uncontrolled. For example, factors such as ovulation timing methods, number of inseminations performed per cycle, numbers of viable sperm per insemination dose can and do have a profound effect on conception. Even still, when evaluating the data of these studies, insemination method appeared to have little effect on conception providing adequate numbers of viable sperm were used. This held true for fresh, chilled and frozen/thawed semen inseminations.

Studies in other species (equine, porcine and human)⁸⁻¹⁰ comparing site of deposition of compromised semen largely show an increase in conception with “deep uterine insemination” into the anterior portion of the uterine horns or close to the oviducts. Similar results may be expected in the dog, suggesting that surgical insemination might be expected to yield superior results over transcervical and intravaginal insemination when compromised sperm numbers or semen quality is used.

Safety and side effects with different insemination techniques have not been studied but are discussed as points to consider in several reports. These include the risk of anesthesia and/or surgical complications with surgical insemination, as well as the risk of bacterial introduction, trauma, pain and stress with transcervical insemination. Interestingly, in spite of voicing these concerns, several authors suggested doing transcervical inseminations for all breedings, so that the veterinarian could become competent in performing the procedure.^{11,12}

Pathophysiologic knowledge may also be used as evidence and rationale to justify the choice of insemination method. Since it is known that conception occurs in the oviducts, it follows that the goal of any insemination would be to place semen in a location such that adequate numbers of sperm are present in the oviducts at a time that conception can occur. The anatomy of the bitch presents limitations that must be dealt with when approaching this challenge. In a properly performed vaginal insemination, semen is deposited in the cranial vagina, close to the site nature intended with natural mating. Sperm will then travel through the cervix, the uterine body, the uterine horns, and into the oviducts. The canine uterine horns are long, and the lumen is often tortuous, greatly increasing the length the sperm must traverse to reach the oviducts. Nonetheless, normal dogs have an extremely high efficiency of reproduction with natural mating, and it should be assumed that vaginal insemination would be successful as well. However, when the fertility of the dogs is compromised, it would also follow that the goal of the insemination technique chosen would be to place the semen as close to the site of conception in the oviducts as is necessary for the individual case. At the same time, insemination method should not further compromise any pathology that exists. For example, transcervical insemination and to a lesser extent surgical insemination, limit insemination volume. To achieve this small volume, centrifugation of the semen may be required, which has a high chance of causing further damage and/or loss of sperm

numbers in an already compromised semen sample. Bitches with decreased fertility may be more susceptible to trauma to the reproductive tract, which is difficult to control with transcervical insemination. Likewise these bitches may be less able to clear bacteria that are introduced via transcervical insemination. Another consideration might be a negative effect of mild trauma, that may occur with transcervical insemination, to cervical competence.

Recommendations

Vaginal insemination should be used for all cases involving normal fertile males and females to minimize risks but maintain high efficacy. This should hold true for chilled and frozen/thawed semen breedings, providing adequate numbers of normal sperm are available.

Surgical insemination should be used in cases involving dogs and/or bitches with compromised fertility, or when sperm numbers and/or quality is limited.

Transcervical insemination should be used in cases involving normal fertile bitches but semen quality is not good enough to expect success with vaginal insemination, but not poor enough to require surgical insemination.

For ethical considerations, the safest and least invasive method with the lowest risk of side effects, that is likely to achieve the desired results, should be chosen.

Conclusion

As veterinarians, we strive to achieve the best results for our clients. When making therapeutic decisions, we must consider the quality of the evidence available to support our options. Improvement in the quality of the studies performed in small animal theriogenology is necessary for our field to legitimately progress.

References

1. Cochrane AL: Effectiveness and efficiency : random reflections on health services. London: Nuffield Provincial Hospitals Trust: 1972.
2. Simoneit C, Heuwieser W, Arlt S: Evidence-based medicine in bovine, equine and canine reproduction: quality of current literature. *Theriogenology*. 2010;76:1042-1050.
3. Arlt S, Dicty V, Heuwieser W: Evidence based medicine in small animal reproduction: current available literature. *Proc 6th Int Symp Canine Feline Reprod*; 2008.
4. Roudebush P, Allen TA, Dodd CE, et al: Application of evidence-based medicine to veterinary clinical nutrition. *J Am Vet Med Assoc* 2004;224:1766-1771.
5. Silva LD, Onclin K, Lejeune B, et al: Comparisons of intravaginal and intrauterine insemination of bitches with fresh or frozen semen. *Vet Rec* 1996;138:154-157.
6. Rota A, Iguer-Ouada M, Verstegen J, et al: Fertility after vaginal or uterine deposition of dog semen frozen in a tris extender with or without Equex STM paste. *Theriogenolgy* 1999;51:1045-1058.
7. Brittain D, Concannon PW, Flanders JA, et al: Use of surgical insemination to manage infertility in a colony of research German Shepherd Dogs. *Lab Anim Sci* 1995;45:404-407.
8. Roca J, Rodríguez-Martínez H, Vázquez JM, et al: Strategies to improve the fertility of frozen-thawed boar semen for artificial insemination. *Soc Reprod Fertil Suppl* 2006;62:261-275.
9. Samper JC: Management and fertility of mares bred with frozen semen. *Anim Reprod Sci* 2001;68:219-228.
10. Merviel P, Heraud MH, Grenier N, et al: Predictive factors for pregnancy after intrauterine insemination (IUI): an analysis of 1038 cycles and a review of the literature. *Fertil Steril* 2010;93:79-88.
11. Wilson MS: Endoscopic transcervical insemination in the bitch. In: Concannon PW, England G, Verstegen J, et al, editors. *Recent advances in small animal reproduction*. Ithaca (NY): International Veterinary Information Service; 2003. A1232.1203. Available at: www/ivis.org.
12. Linde-Forsberg C: Intra-uterine insemination in the dog using the Scandanavian trans-cervical catheter and a comparison with other methods. In: Concannon PW, England G, Verstegen J, et al, editors. *Recent advances in small animal reproduction*. Ithaca (NY): International Veterinary Information Service; 2001. A1207.0201. Available at: www/ivis.org.

