

# Current concerns about veterinary product use and cow-calf fertility

Bob L. Larson, DVM, PhD

College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506

## Abstract

Monitoring and ensuring the fertility of breeding cattle and protecting them from pregnancy-wasting disease are key veterinary services provided to beef cattle clients. Questions about the effect of insecticides, vaccines, and other technologies to improve or compromise bovine reproduction require a thorough investigation of the available evidence to supply clients with informed recommendations.

**Key words:** cattle, breeding, fertility, pregnancy

## Résumé

Surveiller et s'assurer de la fertilité des bovins reproducteurs tout en les protégeant des maladies qui affectent la gestation sont des services vétérinaires clés fournis aux clients de bovins de boucherie. Les questions concernant l'effet des insecticides, les vaccins et les technologies qui améliorent ou compromettent la reproduction bovine demandent une enquête approfondie des données disponibles pour pouvoir fournir aux clients des recommandations éclairées.

## Introduction

The practice of high-quality veterinary medicine to significantly reduce disease and production risk to the benefit of our clients and their cattle requires knowledge and skill in the realms of both art and science. In my opinion, the aspect of high-quality veterinary practice that is “art” is the ability to observe animals and their surroundings very well. The “science” aspect of veterinary practice includes: 1) the accurate measurement of all the important animal and environment risk factors, as well as all of the important outcome variables, 2) the appropriate comparison of outcome variables between groups of similar cattle in similar situations that do or do not receive a management intervention of interest while controlling for potentially biasing or confounding factors, and 3) the best allocation of resources based on evaluation of competing intervention options. The complete and accurate observation of cattle and their environment (i.e. art of veterinary medicine) serves important roles in the science of veterinary medicine by providing a source of questions or hypotheses to be

tested, and as the basis for measuring both risk factors and outcomes. The science of veterinary medicine builds on accurate observations to identify and limit “truths” about biology and animal production within the complexity of biological homeostasis, positive and negative feedback, substitution, confounding, and interactions.

Both the art and science of veterinary medicine have limitations, and either one used without the benefit of the other severely limits our ability to provide clients with high-quality service and advice. Because of the complexity of biology and ecology, accurately observing animals and their environment without utilizing the skills and expertise of appropriate experimental design and statistical interpretation carries a high risk of biasing or confounding factors leading an observer to false conclusions about the cause-and-effect relationships and interactions he/she is observing. In addition, because of the same complexity, carefully designed and interpreted studies that are not based on valid and important questions or accurate observations of cattle and their environment will lead to conclusions that are either inaccurate or inconsequential.

Basing conclusions and client advice based solely on observations or well-controlled studies is not practicing veterinary medicine at a high quality level. Because of the need for **both** of these skills to be mastered in order to provide high-quality advice, the level of expertise required of veterinarians is not easily replaced by searching the Internet or other sources of publically available or proprietary information. To provide the best possible information to cattle-producing clients, practicing veterinarians and veterinary researchers must observe animals and their environments very well, and must appropriately account for the complexity of biology that can distort observations away from useful “truths”.

### *The Effect of Commercially-available Vaccines on Cattle Fertility*

Diseases that negatively impact reproductive efficiency either reduce the likelihood that gametes (sperm or egg) are produced, released, or can participate in successful fertilization, or they increase the risk that a growing embryo or fetus dies or is delivered prematurely. Because pregnancy loss is a relatively rare event at the individual level and the risk of catastrophic losses (e.g. abortion storms) at the herd level is also rare, evalua-

tion of strategies that reduce this risk requires a large number of cattle or herds to detect true differences. Because of the complexity of pregnancy maintenance and the many rule-outs associated with pregnancy loss, careful attention to control for potential sources of bias or confounding is also necessary.

A recent publication about the comparison of vaccination with a modified-live viral (MLV) vaccine, an inactivated viral vaccine, and unvaccinated controls prior to synchronized breeding of immunologically naïve beef heifers raises questions for veterinary practitioners about appropriate vaccination recommendations for their clients.<sup>5</sup> The experimental protocol included randomized allocation of heifers to treatment to effectively control for selection bias, and the statistical tests used to evaluate the data were appropriate. The authors do not state whether or not blinding to control observation bias was employed, but it would have been simple to blind the assessment of pregnancy status and hormonal concentrations. Therefore, the conclusion that vaccination with a MLV vaccine 8 days prior to artificial insemination (AI) breeding resulted in a lower percentage of naïve heifers in this group becoming pregnant to 1 AI exposure following estrous synchronization and 14 days of exposure to bulls, compared to unvaccinated controls and heifers vaccinated with 2 doses of inactivated vaccine administered 36 and 8 days prior to AI breeding, seems very defensible.

Based on this published study, if a client has yearling heifers that are naïve to the pathogens targeted by commercially available viral vaccines, you may recommend avoiding vaccination with MLV vaccines within 8 days of breeding unless other studies refute the finding. A search using CAB and PubMed and a hand-search of the references cited by the article revealed no studies to support or refute the results of this study situation (vaccination of naïve heifers with a commercially available MLV vaccine via the labeled route of administration shortly before breeding).

However, if your client is seeking advice regarding vaccinating unknown serostatus or previously exposed cattle with MLV viral vaccines, several articles from peer-reviewed journals were identified<sup>1,2,4,6</sup> that showed either no effect or a positive effect of vaccination on reproductive success.

Herd-level data is often used to evaluate the benefit or harm of veterinary interventions. Herd-level reproductive performance data can be very helpful for veterinarians advising their clients, but may also be completely biased or confounded and inappropriate, to use for decision making. Records from a single herd comparing 1 year (or other time frame) to another year cannot be used to compare any change in management (e.g. adding or removing a specific vaccine from the herd vaccination protocol) because the study is not replicated

and any factor of interest will be confounded by countless other factors that are associated with that time frame. In contrast, herd-level records from a random sampling of herds with a management change of interest, compared to a random sampling of control herds may be helpful for decision-making, if enough herds are enrolled to ensure valid conclusions. Describing the outcome over time of several herds that make similar management changes without a clear description of how that sample of herds was chosen from all herds making the management change, or how that sample of herds compares to other control herds is not appropriate, due to high risk of bias and confounding of the results.

#### *The Effect of Pyrethroid Insecticides on Cattle Fertility*

Another topic concerning beef herd reproductive efficiency that has gained interest in the lay press and on internet list-serves recently has been the potentially negative role of pyrethroid insecticides on bull fertility. A thorough search of the literature did not reveal any research on bulls that supported a causal relationship between bulls observed to have a high percentage of sperm with morphologic abnormalities and appropriate treatment with commercially available pyrethroid insecticides. There are studies in the published literature that demonstrate effects of pyrethroids on mouse sertoli cell culture on gene expression that differed from estradiol 17B,<sup>7</sup> and negative effects of high doses of cypermethrin on testis weight and sperm numbers in laboratory rats.<sup>3</sup> Other *in vitro* and *in vivo* studies using mice and rats reported negative effects of various pyrethroids on cell function of various tissues.

For veterinary practitioners, the question is whether the well-documented effect of high doses of pyrethroids on reproductive tissues raises clinically relevant concerns about the appropriate use of commercially available products to control external parasites on bulls. Uncontrolled observations, as in the case with the observations presented in lay press articles and list-serve postings, have the appropriate function of providing a subject for a testable hypothesis. Therefore, a hypothesis that states “use of pyrethroids on bulls results in measurable reductions in successful pregnancies” could be used to design a controlled experiment that would provide evidence to support or not support the hypothesis. All veterinarians and researchers should recognize that making a hypothesis should never be confused with stating evidence for a conclusion; one is made at the beginning of the scientific process, the other at the end.

#### *Strategies to Evaluate New Claims / Products / Management Interventions*

Because of the desire to provide services and advice that reduce reproductive or disease risk or increase herd productivity, veterinarians are under the obligation to

evaluate numerous claims about products and management interventions that may impact their clients' herds. Claims can be made that a new intervention will enhance productivity or reduce risk, that an existing or alternate intervention increases risk or reduces productivity, or that an intervention that is either less expensive, easier to implement, or provides other advantages results in equivalent productivity or risk compared to existing management.

The first step in evaluating a claim is to determine exactly what the information source is asserting. What type of cattle is the intervention claimed to benefit (or harm)? That is, is the claim directed at dairy cattle, beef cattle, calves, adults, feedlot cattle, stocker calves, or all classes of cattle? Also, clarify in your own mind what type of enhanced production or reduced risk is claimed. Is the outcome claimed of direct or indirect importance to you and your client? Examples of direct benefits include more efficient production of beef or milk, and reduced number of cases of disease or death; while indirect benefits include higher or lower serologic titers for pathogens, lower fecal egg counts for parasites, and lower clinical illness score. Then, based on the claim, clarify the question you have for a particular client's herd and find articles that report studies that address the same or very similar claim in as similar a production setting as possible to your client's situation. To find studies that address the aspects of the claim that directly affect your client, use literature search engines on the internet such as CAB, PubMed, or Google scholar. In addition, you may have access to the veterinary library of the school where you graduated; many veterinary college libraries provide article search and retrieval support for alums. And finally, determine exactly what the articles report.

As you summarize your findings, if you have several high-quality articles based on a production setting that is similar to your clients' then ignore all other papers with the greatest limitations (lack of control for bias or low applicability). If you have to base your clinical decision on studies that were done in other species or in cattle populations that are very different from your clients' herds, or if the studies did not control for important sources of bias or confounding, then you should act with an appropriate degree of uncertainty. That means that if you choose to implement the new management advocated by the claim, you should be willing to reverse your decision once more information is available. Similarly, if you choose not to make the change advocated by the claim, you must be prepared to implement the new management at a later date if sufficient additional evidence supports the claim.

Regardless of the type of claim, large effects are easier to detect than small effects. Therefore, a management change that results in large positive or negative effects can be detected using relatively few valid observa-

tions. In contrast, subtle improvements or harm require a large number of valid observations. If factors that bias or confound the outcome are present, then even large apparent differences can be a distortion of biologic truths, and conclusions based on these distortions are not valuable to cattle-producing clients. Claims of equivalence between products or management interventions require many more animals than claims of superiority (or inferiority) to arrive at the same level of certainty.

## Conclusions

In this age of rapid and constant introduction of new products, services, and management ideas, coupled with almost instantaneous communication among large numbers of people using the internet and other technology, veterinarians must develop sound methods for assessing the claims that bombard their clients and themselves. Acquiring literature-search and -evaluation abilities is as important for today's veterinarian as other time-honored veterinary services such as physical examination, diagnostic interpretation, and delivering medical and surgical interventions. A thorough understanding of the scientific method of hypothesis testing, coupled with a high level of skepticism for untested claims, as well as an appreciation of the ability of well-designed studies to detect even subtle improvements or harms are necessary skills for veterinarians wanting to protect their clients from needless risk, expense, or missed opportunities for improved efficiency.

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