# 50 Years of Applying Reproductive Technology to Breeding Cattle

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Prior to the mid 20th century, reproductive management of both beef and dairy cattle consisted primarily of purchasing a bull every 2 years from a neighbor thought to have a herd with above average genetics. That description is still embarrassingly close to the truth for the majority of beef cattle herds in North America. The one striking difference is that bulls being purchased currently are, in fact, usually above average genetically. One result is that the amount and quality of beef produced per cow or per unit input of feed, labor, etc. have increased dramatically, at least partly due to continual genetic change.

Why bother with superimposing reproductive technology on management of cattle? At least in some situations, the following can be accomplished more efficiently or rapidly with aid of reproductive technology:

- The first priority is simply to get the cow or heifer pregnant as close to the optimal time as possible. For most herds, non-pregnant and late pregnant cows are the most costly problem in the operation.

- A second priority is genetic improvement to meet goals of the herd, e.g. profitability.

- A third set of priorities, especially relevant as larger numbers of cattle are managed per person, include convenience/efficiency objectives such as shortening the calving season, introducing the polled trait, decreasing dystocia, especially in heifers, etc. Note that many of these also have animal welfare benefits.

- Experimenting with new approaches. This can be a low or high priority. Trying new things can maintain interest of high value employees and the younger generation. This also can rejuvenate oldsters!

## A Foundation Is Required

Most reproductive technology is of value only in well managed herds characterized by factors such as a herd health program (even a modest one consisting of two or three systematically administered vaccines) and good nutrition. Good management also includes some means of identifying individual animals and keeping and using at least minimal records. Computers are an enormously useful technology.

Nutrition cannot be over-emphasized when considering applying reproductive technology. In most cases, it is essential to monitor nutritional status by weighing and/or condition scoring animals for reproductive technology to be effective. There are interactions between nutrition and application of some reproductive technologies, and in some situations, technology can partially substitute for inadequate nutrition, e.g. use of progestins to induce puberty or estrous cycles post-partum. However, the more extreme the reproductive technological intervention (e.g. use of sexed semen with superovulated cows) the more important that nutritional status be optimized.

A few other foundational issues need mentioning. Nearly every reproductive endpoint is positively affected by crossbreeding. Suckled beef cows are very different from yearling heifers from a reproduction standpoint; similarly, Bos taurus and Bos indicus cattle differ. There are climate X breed X reproductive technology interactions. Some approaches such as 48-hour calf removal to induce post-partum estrous cycles are efficacious but impractical except in niche situations.

I am emphasizing applying reproductive technology in production herds, but another perspective is applying technology for research purposes. While purposes differ between these two applications, almost all research technologies eventually end up being applied in production herds, sometimes after a few months and sometimes after a few decades. Sometimes these are niche applications, and sometimes they are widely applied.

## The Past 50 Years Record

To analyze the significant reproductive technologies of the past 50 years, I'll start by considering the technologies themselves. These are listed in Table 1 under two headings: 1) those in routine use in most progressive commercial herds, and 2) those used more in niche applications and for research purposes. However, those in the second list tend to migrate to the first list over time, and those in the first list originally were in the second list. I have picked the top 10 in each list, arranged in roughly chronological order of being used.

**Table 1.** Reproductive Technology Tools

| | Tools in Routine Use | | Tools for Research and Niche Applications |
|---|---|---|---|
| 1 | Artificial insemination | 1 | Hormone assays |
| 2 | Electroejaculation | 2 | Superovulation |
| 3 | Vaccination | 3 | Nonsurgical embryo recovery and transfer |
| 4 | Cryopreservation of sperm | 4 | Cryopreservation of embryos and oocytes |
| 5 | Readily available hormones: progesterone, GnRH, prostaglandin F-2-alpha, FSH, others | 5 | In vitro fertilization and sperm injection |
| 6 | Body condition scoring | 6 | Splitting embryos |
| 7 | Expected progeny differences (EPDs) | 7 | Transvaginal oocyte aspiration |
| 8 | Ultrasound: ovarian status, pregnancy, sexing, pathology of uterus, ovary, testis | 8 | Cloning by nuclear transplantation |
| 9 | Sexing embryos, fetuses, sperm | 9 | Preimplantation genetic diagnosis |
| 10 | Genomics | 10 | Transgenic procedures |

The first item on List 1 is artificial insemination (AI), easily the most powerful tool for most applications, and the oldest, dating back nearly a century in applications and several centuries on an anecdotal basis. Many other technologies either depend on AI or are synergistic with AI. Electroejaculation, the second item on the list, is essential for breeding soundness examinations, important for buying and selling bulls.

Vaccinations for brucellosis have so effectively eliminated that disease that some veterinarians no longer recommend it. Vaccination for vibriosis also has been exceedingly effective, and a number of other disease organisms can be controlled effectively via relatively inexpensive, but systematic vaccination strategies.

Cryopreservation of sperm completely changed the bovine AI industry in the late 1950s. Similarly, cryopreservation of embryos changed the Embryo Transfer (ET) industry in the 1980s.

Availability of relatively inexpensive standardized hormonal preparations was invaluable for research, as well as the applications that ensued. There are numerous exceedingly interesting stories concerning discovery, synthesis, or unraveling the function of reproductive hormones; several of these discoveries led to Nobel prizes. Interestingly, development of some hormones made others obsolete, e.g. gonadotropin-releasing hormone (GnRH) has replaced human chorionic gonadotropin (hCG) for nearly all applications with cattle.

We could argue about whether the next two items listed, body condition scoring and expected progeny differences (EPDs) are reproductive technological tools, but their importance in managing reproduction is indisputable. In my own herd, we sort off the thinner cows at weaning and feed them a bit extra during the fall; the excellent research by James Wiltbank and other showed convincingly that it is almost impossible to add weight to cows economically during early lactation if they are thin at parturition, with the result being long periods of post-partum anestrus.

The development of EPDs to guide breeding decisions not only enables rational use of reproductive technologies for genetic improvement for traits such as weaning weight and carcass characteristics, but even more important in my opinion is use of EPDs for reducing dystocia in heifers.  Dead calves are the ultimate reproductive failure, as the entire investment over the period of gestation is lost.

Ultrasonography is an excellent example of a technology first used for research, which then migrated to practical applications.  It is invaluable for rapid early pregnancy diagnosis, and also can be used to evaluate ovarian status as well as uterine pathology.

Sex is the most important genetic trait, and being able to choose sex at conception is the most sought-after reproductive technology of all time, as attested by Greek documents nearly 2500 years old.  Commercially available sexed bovine semen at 90% accuracy is now a reality, although fertility is clearly lowered somewhat with current procedures.  Embryos also can be biopsied and sexed with nearly 99% accuracy, and 2- to 3-month-old fetuses can be sexed accurately using ultrasound.  Biopsying embryos to determine sex is a special case of preimplanation genetic diagnosis, and this can be used to determine the allelic status of almost any gene of interest, especially for genetic diseases.

The newest technology on my top 10 list, genomics, has had an exceedingly rapid rate of introduction to commercial use.  For virtually any trait that can be measured, including many reproductive traits, genomics procedures promise to speed up the rate of genetic progress over use of EPDs alone.  See Seidel (2010) for an explanation of how this technology works.

I will not discuss List 2 of Table 1 on a tool-by-tool basis, but rather refer the reader to readily available references discussing these tools in detail (Seidel and Seidel, 1991; Seidel et al., 2003).  I will point out that nearly all of these tools already are in use for niche applications in seedstock herds, and therefore, do affect most beef producers via the resulting bulls purchased.  Almost always some animals in the pedigrees of breeding bulls were produced via AI and increasingly via ET.  I also point out that while transgenic technology, (direct genetic engineering via adding, deleting, or correcting genes) currently is unpopular with the public and faces huge regulatory barriers, it is one of the most potent tools available for improving cattle, and likely will be used routinely in the coming decades.

While there is some redundancy with Table 1, I next will discuss the practices that the tools in Table 1 enable, which are summarized in top-10 fashion in Table 2.  Numbers 1, 2, and 3 already have been touched on in discussing tools.  I again emphasize that AI will be a powerful component of most progressive cow/calf operations.

**Table 2.** Reproductive Technology Procedures

1. Breeding soundness examinations
2. Increasing rate of genetic change via AI/frozen semen
3. Herd health programs – reproductive diseases
4. Crossbreeding
5. Ovulation synchronization
6. Inducing parturition
7. Improving calving ease
8. Inducing post-partum reproductive cycles and puberty
9. Sexing semen
10. Fetal programming

Number 4, crossbreeding, is another practice with benefits that are difficult to over-state. The benefits are for traits complementary to those that are readily modified using EPDs. EPDs are great for dealing with calving ease, weight traits, and carcass traits, but not so useful for traits such as health, fertility, and longevity, which are greatly bolstered by crossbreeding. The conclusion is obvious: use both EPDs and crossbreeding. Amazingly, the theoretical/molecular basis of hybrid vigor due to crossbreeding remains unclear. There are theories, but limited consensus.

Next to come along chronologically is estrus synchronization, which frankly needs renaming to ovulation synchronization. There have been literally thousands of papers and reports written on synchronization of bovine reproduction, and one would logically think that there is nothing new in this area worth studying. However, there certainly have been advances in the past few years, and rather remarkable pregnancy rates can now be achieved with timed AI using frozen semen, and with no estrus detection. These procedures generally require two trips through the chute prior to AI, and still have the nuisance component of having to sort off the calves. The optimal procedures require use of three naturally occurring hormones: progesterone (via a CIDR), GnRH, and prostaglandin-F-2-alpha. Combining ovulation synchronization with AI, EPDs, genomics, and crossbreeding greatly increases reproduction and production efficiencies compared to practices of only a few years ago.

Number 6 on the list, inducing parturition is a practice that may be under-utilized. Toward the end of gestation, calves increase in weight at the rate of nearly a pound a day, and those gestations that go a bit long in heifers likely result in increased dystocia. In certain situations such as when heifers were inadvertently bred to difficult calving bulls, inducing the calves to be born a few days immature, with parturition fairly precisely timed could decrease dystocia more effectively than waiting for random calving times. One cost of induced parturition is more retained placentas, best handled with prophylactic antibiotic use. This is an opportune point to indicate that all technologies have costs, and it is the benefit-to-cost ratio that should be considered.

Reducing dystocia, number 7 on this list, has progressed markedly over the past few decades. Dystocia is easily kept to a minimum by using AI with semen from bulls with easy calving EPDs. A caveat is that about 1 in 10 bulls with low accuracy EPD (e.g. less than 0.5 accuracy) will not in fact be easy calving. Calving difficulty can be reduced further by making pelvic measurements on heifers and culling the few percent with the smallest pelvic measurements. Adequate nutrition and paying attention to age and weight at breeding are obviously essential to minimizing dystocia in heifers. Putting all these practices together enables selecting for high weaning weights while keeping dystocia levels low, and eliminates wasteful practices such as calving at 3 rather than 2 years of age or breeding heifers to breeds such as Jerseys.

In an ideal world, all females will be having regular estrous cycles at the start of the breeding season, but this is rarely the case, which brings up item 8 in Table 2. A major benefit of ovulation synchronization programs using progestins is to initiate reproductive cycling in some of the pre-pubertal heifers or post-partum cows that otherwise might not have such cycles for another month. Progestins also can be used prior to the synchronization programs for the same purpose. Temporary weaning of calves for 48 hours also is very effective for inducing reproductive cycling post-partum. Of course these practices are not appropriate substitutes for inadequate nutrition or poor management of post-partum interval, but they are appropriate tools for use in certain situations.

Item 9, sexed semen, has resulted in a paradigm shift for some dairy herds, that could have implications for beef producers as more dairy cows are bred with semen of beef breeds because fewer cows need to be bred to produce replacements. For the majority of matings in beef cattle, one sex of calf will be more valuable than the other. However, this difference in value due to gender usually will be considerably less than $100 for most herds, the exception being certain matings for seedstock producers. There are three issues with currently available sexed semen: accuracy generally is only 90%; cost per semen dose is on the order of $15-20 more than unsexed semen; and fertility is about 10 percentage points lower than with unsexed semen with ideal management, and even lower with poor management of nutrition, AI programs, etc. However, even with these "warts," there is one situation in which sexed semen will fit many beef producers: breeding heifers to have heifer calves for the first service AI. This has two advantages: 1) heifers are an excellent source of replacement genetics; in any good breeding program the youngest animals have the best genetics, and 2) heifer calves average about 5 lbs lighter than bull calves, so there will be less dystocia. The lower fertility with sexed semen will have minimal effect if used only for the initial AI, especially if heifers are rebred AI for second services.

The final concept in Table 2, fetal programming, occurs as a function of the health and nutritional status of the mother during gestation. Much additional research is required to understand and manage this phenomenon in cattle. For example, it is likely that nutrition between 1 and 3 months of gestation will be more critical in programming the fetus for adult life than at other times, but this requires more research. However, extensive data from other species and preliminary data from cattle leave no doubt that fetal programming explains some of the non-genetic differences that we see in adults, e.g. in feed efficiency. Furthermore, it is likely that fetal programming can be managed to increase efficiency of beef production with somewhat minor interventions. It is likely that phenomena such as disease resistance, susceptibility to conditions causing brisket disease, and concepts such as easy fleshing also are explained partly by fetal programming.

I want to re-emphasize that the order of items in the tables is roughly chronological. The most important items in Table 2 are the first 5, and items 1, 3, and 4 are critical for any cow/calf herd. I also point out that reproductive technologies and factors that interact or synergize with reproductive technologies are the main subject of this article. Great improvements in other aspects of successful cow/calf production also have been made over the past 50 years, such as nutrition, herd health for non-reproductive diseases, carcass characteristics, resistance to heat stress, and marketing, just to mention a few obvious ones.

## The Future

The near future, e.g. next 5-10 years, can be predicted rather confidently with respect to reproductive technology. Procedures such as ovulation synchronization and sexing semen will be further refined. Fetal programming will be understood more fully and used to advantage. Genomics will be used to improve rates of genetic gain for numerous traits, including some that have not really been tackled previously, such as health traits, longevity, and fertility. Technology will continue to displace labor, such as eliminating detection of estrus and minimizing dystocia. Animal welfare issues, both perceived and real, will demand increased attention. Record keeping at all levels will become more thorough, and there will be more regulation by government. Almost everyone reading this would have correctly predicted these outcomes during this timeframe. I find little merit in attempting to predict the distant future, say 50-100 years hence. The intrinsic unpredictability makes this an almost meaningless exercise for current purposes.

It is the 10-25 year time horizon that is most interesting to consider. I have made such predictions years ago with respect to embryo transfer technology (Seidel, 1991). I predict that genetics, particularly relating to reproduction, will turn out to be even more complicated than we currently imagine. Especially complex will be genotype X environmental interactions, exacerbated by epigenetic effects (Seidel, 2002). Epigenetic examples include why identical twins differ from each other, gametic imprinting (genes inherited from mothers have different effects than the same alleles inherited from the father), and fetal programming.

Another prediction is that transgenic manipulations will be commonplace, just as genetically modified crops have become dominant, at least in North America. These tools are so powerful that they can not be ignored indefinitely for production purposes.

I predict huge emphasis in optimizing the whole system rather than piecemeal approaches used these days. This will be done in two senses: 1) optimizing the production system, and 2) optimizing the genetics, particularly in producing bulls (semen factories). In the first sense, systematic changing of environment, such as levels of energy intake during gestation, will be combined with genetics and reproductive technologies to nearly double beef production per unit of feed, labor, $CO_2$ produced, etc. over the lifetime of the animal. A bold extension of this is dispensing with the cow herd entirely by having each heifer have a heifer calf to replace herself. Weaning might occur 3 months after calving, after which the dam will be placed on a fattening ration for 3 months and then slaughtered. This system would require only slightly more nutrients per animal than what is needed currently for raising replacements, and there is no cow herd to maintain. Of course, this would not be 100% efficient and would require use of accurately sexed semen, so a few head would need to be kept for second calves . . . unless some of the heifers would have twin calves, either via hormonal treatment or using cattle selected to have twins genetically.

We still would need bulls, but not very many, and none in herds using all AI. No matter what the system, optimizing bull genetics will really become interesting. First, bulls will be selected based on their genomic profiles in the following way, even before they become embryos. Embryos will be produced by in vitro fertilization, screened genomically from biopsies, to produce thousands of new genotypes each week. In some cases, cells of selected embryos will be multiplied in vitro, and further modified transgenically. Nuclei from these genetically improved cells will be used for cloning procedures to produce new embryos for transfer to recipients to produce bulls needed for semen production. We might eventually dispense with the bull altogether via in vitro spermatogenesis, but that likely will not occur within a 25-year time horizon, at least not so that it can be used routinely at reasonable cost.

The above system relies on screening new combinations of alleles resulting from the crossing over and random assortment of chromosomes that occur naturally during meiosis. A completely different approach is to make new genetic combinations by directly modifying genomes using recombinant DNA technology. My suspicion is that this will not be feasible for decades, simply because the information to optimize will be so complex that our minds can not deal with it, and similarly we will not be able to write computer programs to deal with tens of thousands of alleles of genes on a gene-at-a-time basis. That does not mean that we can not optimize a few dozen alleles and select for specific traits such as sex, polled condition, color, etc. in manufacturing genomes to produce the bulls. Also, we may be able to optimize allelic combinations to maximize heterosis, circumventing the need for crossbreeding.

I have tried not to get too theoretical or wildly imaginative with the ideas presented. For an even more wide-ranging discussion, but focused on equine reproduction, see Seidel (2011).

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