TECHNOLOGY AND ANIMAL BREEDING: APPLICATIONS AND CHALLENGES FOR DAIRY CATTLE BREEDING

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INTRODUCTION

The last 40 years of dairy cattle breeding have been marked genetically by the impact of what may prove to have been the economically most efficient biotechnology--artificial insemination. The last few years have been marked by biological developments that are absolutely amazing. The next few years are likely to be marked by even more amazing developments. The impact of these developments may require some time for implementation. The challenge to animal breeders is to design strategies for the integration of these developments with more conventional breeding strategies and to analyze the interactions between the new biotechnology, the animal, and its environment. The following paragraphs consist primarily of speculation on possible potential as well as challenges to dairy cattle breeders of various new and old biotechnologies. These will include growth hormone, artificial insemination, embryo transfer with multiple ovulation, embryo splitting and sexing of embryos, sexing of semen and in vitro fertilization, and nuclear cloning.

Growth Hormone

A product of genetic engineering that may have a major impact on dairy cattle breeding is growth hormone. The most immediate impact is likely to be from bovine growth hormone (bGH) produced by bacteria and administered to lactating cows (Bauman et al., 1982; Bauman et al., 1985; Peel et al., 1983) rather than growth hormone produced by insertion of additional genes for producing growth hormone normally associated with the bovine or other species (Hammer et al., 1985; Palmiter et al., 1982; Palmiter et al., 1983).

Administered growth hormone presents many challenges similar to those that animal breeders have faced in the past and as well as presents many questions that as yet have no answers. The questions, however, need to be asked.

A most critical question is whether selection for milk production is possible if animals are administered an optimal dosage of bGH; i.e., if production is not limited by bGH, are there any genetic differences among cows for milk production? Speculation can run from the extreme of none to little genetic variation to the extreme of additional genetic variation due to higher production levels.

If sufficient genetic variation for effective selection exists, then many questions still remain. Certainly added production from relatively inexpensive genetic selection is likely to be as good a bargain as in the past.

One issue is whether there is any genetic variation in how cows respond to bGH. Can cows be selected to improve response to bGH? Can cows be selected to respond maximally to dosages that are less than those now thought to be optimal? Underlying the last question is the question of whether cows respond differently to the same dosage of bGH.

If bGH can be considered simply as a management tool that increases production but allows expression of genetic variation, then usual genetic evaluations will be needed. Models and record keeping may need to be modified especially if evaluations are made with records of combinations of "treated" and untreated cows. Dosage as well as duration of treatment and in what stages of lactation may need to be known. Is response proportional to overall management or additive to other management effects? Is genetic and phenotypic variation the same or different in treated and untreated cows? What is the genetic correlation between response of a genotype in the bGH and no-bGH environments? If the correlation is much less than unity, then multiple trait evaluation procedures that account for the genetic and phenotypic variances and genetic covariance will be indicated.

Artificial insemination units may need individually or jointly to establish bull sampling herds in order to standardize effects of bGH on proofs obtained from daughter records. These herds may include treated and untreated cows in some optimum proportionality consistent with optimizing gain in populations of both treated and untreated cows.

Selection of bull dams may be even more difficult than evaluation of bulls. Bull dams are typically chosen from "outliers" of a population. Selecting for outliers is hoped to result in genes that determine high production but unfortunately outliers may also be due to favorable temporary random environmental effects. Outliers can also be created by deliberate preferential treatment. The opportunity for preferential treatment with bGH which may increase production by 20% or more is obvious. Safeguards may need to be set up if standards for fair comparisons are regularly violated. A safeguard such as blood testing of a herd with a potential bull dam to determine whether all cows are receiving equivalent dosages of bGH may be necessary although such a procedure seems a rather extreme and awkward requirement and may not be workable because cows may be taken on and off treatment at different times and stages of lactation.

The current situation with dairy cattle evaluation with regard to exogenous bGH is that many questions are unanswered and that the answers are going to require considerable effort and innovation.

A more desirable way of increasing circulating levels of active growth hormone would appear to be the insertion of extra copies of the gene responsible for growth hormone. Even though transgenic copies of growth hormone genes have been inserted into genomes of many mammalian species, the difficulties of obtaining meaningful improvement in milk production in the dairy cow are not trivial but are probably manageable within a few years. Progress in such fields of research in the past few years is amazing and will no doubt accumulate at an even greater rate in the future. Some obvious difficulties are:

1) siting extra copies in locations which are appropriate,
2) inserting the optimum number of copies,
3) regulating the actions of these copies by turning the "genes" on and off at the correct time in the life or production cycle,
4) making certain the extra copies are transmitted to offspring, and
5) making certain that the extra copies do not disrupt the, perhaps, delicately balanced genetic makeup of the modern dairy cow.

At some stage economic analyses may need to compare whether administered growth hormone or growth hormone from inserted gene copies is more efficient. Such an analysis may need to consider the possibility of combining both in a production system.

Artificial Insemination (AI)

AI was and remains the biotechnology that has had the largest impact of any technology on genetic improvement for milk production. The gain in milk yield because of AI has been slower than theoretically possible (Robertson and Rendel, 1950) for single trait selection but the cumulative effect has been substantial. One reason for the less than optimal gain has been the use of too large a fraction of proved bulls--not just the top bulls.

A way to increase the selection intensity on proved bulls is to reduce the number of sperm per breeding unit (R. H. Foote, personal communication, 1985). The genetic gain from increased selection intensity on proved bulls must, however, be compared to the increased costs of reduced conception rate per service due to a larger number of services per conception and a longer open period per conception. If, for example, increasing from 50,000 to 100,000 breeding units per bull per year reduces first service conception rate by only 2% the result is a halving of the fraction of sampling bulls returned to service. Under U.S. conditions, the extra cost per cow per year will be $4 to $5 but value over feed costs of the genetic gain in a few years from the increased selection intensity will be $40 to $70 per cow per year. Implementation of such a strategy would require considerable understanding between the buyers and sellers of proved bull semen. Nevertheless, analysis of the economics of reduced conception rate and increased use of superior proved bulls may show a way to provide for greater gain than will be possible by more recent technological developments.

Embryo Transfer (ET)

ET, a more recent reproductive technology (Seidel, 1981), has become the center of several related developments which can increase the rate of genetic gain for milk production. For example, successful embryo splitting and in vitro fertilization are dependent on embryo collections from the donor and delivery to the recipient.

Multiple ovulation and embryo transfer (MOET) can increase genetic gain per year substantially over that possible by AI alone through increased genetic selection intensity for dams of bulls and dams of cows (Christensen and Liboriussen, 1985; Land and Hill, 1975; McDaniel and Cassell, 1981; Nicholas and Smith, 1983; Smith, 1984; Van Vleck, 1981). Although the proportional increase in gain due to the dam of cow path is greater than through the dam of bull path, the cost is many times greater. Economic benefits from MOET applied to the dam of cow path are highly dependent on reducing the cost of a successful transfer to near that for a successful conception from artificial insemination. The number of successful transfers is the number of cows in the population. Inexpensive and successful sexing of embryos can not only increase selection intensity and genetic gain but also can essentially halve the cost. Low cost and successful embryo splitting has similar potential. The combination of embryo splitting (Ozil et al., 1982; Willadsen, 1979; Willadsen et al., 1981; Williams et al. 1982) and sexing (Betteridge et al., 1981; White et al., 1984) may reduce the costs to economic feasibility.

MOET for the dam of bull path is relatively inexpensive requiring only about three times the number of transfers as the number of bulls to be sampled. Reliable embryo sexing can further reduce the ratio of number of transfers to number of bulls to sample. The increase in selection intensity will depend on the success of multiple ovulation, sexing and splitting. Whether more than one son should be obtained from a single cow has been questioned. At least two other concerns should be addressed.

Theoretical genetic response from selection assumes a normal distribution. That assumption may be quite good for moderate intensity of selection but may not be accurate for selection of only a fraction of one percent. Of perhaps more concern is the possibility of preferential treatment to make a merely good cow appear to be an outlier that would qualify as an embryo donor. Methods may be needed to detect these false outliers if the economic potential of MOET is to be achieved.

Embryo splitting might appear to be a method of extending the semen production of a superior genotype. One-half of a split embryo would be stored until, or until shortly before, a daughter proof is available from test matings to the other half of the embryo. The original sperm producer would have been slaughtered to save costs. The stored embryo would be implanted and allowed to grow to semen producing age. The genotype and sperm of the stored half would duplicate that of the deceased half.

Some cautions, however, should be considered before attempting such a strategy. The survival rate of embryos through splitting, freezing, thawing, implantation, and gestation is much less than 100%. Secondly, although the genotypes of the two halves are identical, their potential to produce semen is not identical. For many characteristics of semen production, repeatability is much greater than heritability, which is quite small (Taylor and Everett, 1985). Heritability, not repeatability, is the measure of correlation between semen traits of identical genotypes.

Sexing semen and in vitro fertilization

Despite occasional claims, separating semen into male and female determining sperm has not proven successful. Nevertheless the potential of accurately sexed semen for increasing genetic gain is substantial because of increases in selection intensity for the dam paths of selection (Foote and Miller, 1971). Sexed semen also would complement embryo transfer. The promise of sexed semen is that the technology may prove relatively inexpensive to apply. Because half of all sperm (Y-carriers) could not produce heifers calves the same number of bulls would be required. In fact, if much X-carrying sperm was lost in the separation process then more bulls would be needed and intensity of selection would decrease for the sire of cow selection path.

Even if most sperm are lost in separation and if the separated sperm are male determining, then successful in vitro fertilization (Brackett et al., 1982) may make the separation process worthwhile (R. H. Foote, personal communication, 1985). The assumption is that only a few sperm will be needed for in vitro fertilization. Again, the potential for genetic gain will come primarily in the dam of sire path but could be combined with MOET and embryo splitting to make embryo transfer more economically efficient for the dam of cow path.

Gene Insertion

The production of more copies of a desirable gene for the same animal or from another species is being discussed in another symposium (Krausslich, 1986; Robertson, 1986; Wagner, 1986; Ward, 1986) and, except for the previous discussion of the gene for growth hormone, will not be discussed here. The exception is to speculate that genes controlling specific disease resistance or general immune response such as the major histocompatability complex are likely to be the first to provide improved productivity.

Nuclear Cloning

Infinite splitting of embryos that would lead to genetic immortality will be referred to as nuclear cloning (Illmensee and Hoppe, 1981; McGrath and Solter, 1983). Nuclear cloning seems less likely to succeed if completely differentiated adult tissue is the starting point. Technology for nuclear cloning, however, would have immediate and major impact on genetic gain. As with other technologies the costs must be balanced against the gain. The challenges to animal breeders will be, 1) to identify the superior genotypes for cloning, and 2) to find a way to continue genetic gain after the initial superior genotypes are disseminated.

One method (Hulle and Van Vleck, 1984; Nicholas and Smith, 1983) of initiating such a breeding program would be to identify the foundation cows and bulls. For example, the best 10 or more cows based on estimated transmitting ability could be superovulated and bred with the best 10 or so bulls based on progeny proofs. An arbitrary number of these genotypes (e.g., 50 or more of each sex) would be produced and the female genotypes cloned. With infinite splitting, female copies would be distributed to the whole population; other copies would be tested, perhaps 20 per genotype; and still other copies would be stored to provide further copies when needed. Male genotypes would undergo a standard progeny test by mating to enough cows to produce 50 to 60 daughters. After testing, a fraction of the female genotypes would be selected, perhaps 5 to 20 genotypes. The second major increase in genetic value would come when copies of the selected female genotypes replace the initial genotypes. Other copies of the selected female genotypes would be grown and mated to the selected males to produce another generation of 50 or more male and female embryos. The process would then be repeated. Each generation could result in twice the progress of conventional AI program (Hulle and Van Vleck, 1984; Nicholas and Smith, 1983).

Will the initial intense selection and succeeding generations of intense selection so drastically reduce genetic variation that progress will be impossible or slow after selection of the foundation genotypes? Simulation studies or studies with laboratory species may provide a guide to the answer.

Random mating of the foundation females and males and testing of the resulting genotypes should reduce the risk of faulty evaluations of some of the foundation cows and bulls.

CONCLUSIONS

Administration of growth hormone to dairy cows poses many questions for dairy cattle breeders: 1) will cows exhibit genetic variation if growth hormone is no longer limiting, and 2) what will be the effect on genetic evaluation and selection programs?

Improvement of conception rate from artificial insemination or even reduced conception rate from fewer sperm per service to increase selection intensity from fewer bulls being required both may be economically effective in increasing average genetic value for milk production.

Embryo transfer can substantially increase genetic gain from the dam of cow path of selection but the gain is likely not to be as valuable as the cost of the gain unless extra costs are reduced to about the cost of artificial insemination. Costs might be reduced by embryo splitting and sexing. Embryo transfer can be economically effective for the dam of bull path of selection if normality is valid for predicting selection response and if bull dams are unbiasedly evaluated.

Sexing of semen, possibly together with in vitro fertilization, might be valuable for increasing selection intensity for the dam paths of selection.

Nuclear cloning, if possible to implement, can result in a dramatic initial increase in genetic value for production. Testing of the initially highly selected genotypes can result in a second dramatic increase. Further increases may be possible by a combination of traditional progeny testing of bulls and testing of female genotypes by cloning if genetic variation is not exhausted by the intense selection.

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