Future trends in dairy reproduction

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SUMMARY

- Research in the next 100 years will focus on improving existing technologies so that they are more effective, less expensive, and easier to use on large farms.

- Important areas for research will aim to improve cow fertility, semen fertility, synchronization of estrus, detection of estrus, embryo technologies and early pregnancy diagnosis.

- Genetic selection will lead to high milk producing dairy cows with superior fertility.

- Now is the time to identify the traits that define "high fertility" in dairy cows.

Introduction

The birth of artificial insemination (AI) within the dairy industry occurred about 75 years ago (Foote, 2002). The hurdles associated with AI were overcome so that the technology became commonplace in the dairy industry. Initial scepticism and rejection of AI were followed by acceptance and finally widespread implementation of AI in the dairy industry. The future will be the same for all new technology as it is tested and decisions about commercial utility are made. If the next 100 years are as innovative as the past 100 years then the future of dairy reproduction is very promising.

Predicting what will happen in the next 100 years is nearly impossible. It is safe to assume that there will be continued pressure on greater milk production per cow. The carbon footprint per unit of milk of a high production dairy cow is less than that of a low production cow (Capper et al., 2009). This fact along with the need to produce more food per unit land area will drive milk production per cow to greater levels. More milk production per cow will place greater stress on the cow which will create strain that is manifest through the reproductive system. This review discusses several areas for technological improvement in dairy reproduction.

Potential Improvements to Cow Fertility and AI

Cow Fertility. The smooth transition from the dry to lactating cow is absolutely essential for good fertility postpartum. A major focus of the future will be ensuring that the cow's immune system is highly functional so that diseases like metritis are minimized. The development of Imrestor™ (pegbovigrastim) from Elanco is one example of a new product designed to stimulate immune function of early postpartum dairy cows. Although Imrestor is labelled to prevent mastitis, stimulating the immune system with Imrestor may improve uterine health as well or prevent depressed milk production associated with metritis (Ruiz et al., 2017).

The use of antibiotics in the dairy industry is being discouraged. There is a need for innovative treatments of uterine disease so that fertility is fully restored in cows that have metritis postpartum. These treatments will probably not involve the antibiotics that are typically used on dairy farms. An immunomodulatory feed ingredient, for example, was shown to benefit uterine health and milk production when fed to postpartum cows (Brandão et al., 2016).

There continues to be considerable interest in understanding how feeds can affect the fertility of the cow. “Functional foods” are defined as foods that serve a dual purpose. The first purpose is nutritional and the second purpose is functional to improve animal biology. Feeding specific fatty acids that are tailored to affect endocrine function is an example of a functional food (Thatcher et al., 2011). Although the concept or functional foods has been in the literature for a long time there is a need to do further work to define the best ingredients in dairy cow diets. The best ingredients will serve unique functions with respect to the biology of the cow.

Improvements in sperm viability. There is the need to increase sperm production per bull or to develop methods to dilute semen further without compromising fertility. A two-fold greater dilution, for example, would double the number of units coming from an elite sire and double the rate of genetic progress if fewer bulls were used in breeding programs. The second challenge is to increase the lifespan of bovine sperm in the female reproductive tract (Saacke, 2008). This would greatly facilitate the use of AI because cows could be inseminated long before ovulation without a decrease in fertility. Third, liquid nitrogen and a liquid nitrogen tank provide safe storage of semen for an indefinite period of time. A simpler and effective method for long term storage of semen on farm, however, would certainly be an important innovation.

Better Methods for Gender Selection of Semen. The usefulness of gender selected semen within the dairy industry has been demonstrated but the current method to generate the product (flow cytometry) is slow and inefficient (Seidel, 2014). New methods to sex semen are clearly needed and will theoretically be achieved in the next century. It is also necessary to develop methods that are less damaging to the sperm cell. Current methods damage the cells in a non-compensable manner. Future methods will be less damaging and give better fertility when gender selected semen is used in both heifers and cows.

Estrous detection and timed AI detection

New technology for estrous detection. Farmers detect cows in estrus because estrus is the best predictor of ovulation. Timed AI programs are used because they do essentially the same thing (enable farmers to know when ovulation will occur). There is the possibility that consumers will increase their control over methods used in dairy production and force legal practices out of existence. Consumer concerns could arise for $PGF_{2\alpha}$, GnRH, and progesterone particularly when they are applied to all cows in timed AI programs. If timed AI programs are forced out of existence then farmers will need to be detect cows in estrus or, alternatively, be able predict when they will ovulate.

Automated methods for detection of estrus will come of age in the next 100 years. Surprisingly, the requirements for automated estrous detection systems have not changed a lot since they were first proposed by Senger (1994). Specifically there is a need for: 1) continuous surveillance of the cow; 2) accurate and automatic identification of the cow 3) lifetime operation 4) minimal labour; and 5) high accuracy in identifying the physiologic or behavioural events that correlate with ovulation. An additional requirement that the author will add is 6) the system needs to be inexpensive and seamlessly integrated into the herd management software.

Automated systems for activity monitoring meet many of these criteria (Nebel et al., 2000). Although the new monitors are technologically superior to the old systems, they essentially rely on a premise that cows in estrus are more active. High production cows, however, are less active compared with low production cows in estrus (Wiltbank et al., 2006). This fact may blunt the utility of these programs in the next century.

Automated milk progesterone systems (DeLaval Herd Navigator System) provide an alternative for dairy producers. Estrus is preceded by a drop in milk progesterone concentrations. By monitoring milk progesterone, therefore, it is possible to predict when a cow will be in estrus and ovulate. The question is whether this system based on progesterone will predict ovulation for routine AI. In addition to potential application for timing of AI, milk progesterone systems offer a unique opportunity to perform pregnancy diagnosis. A sustained elevated concentration of progesterone after day 21 indicates that the cow is pregnant after AI.

New Products for Estrous Synchronization and Timed AI. The products that we currently use for estrous synchronization ($PGF_{2\alpha}$, GnRH, and progesterone) were developed over 40 years ago. Each of these products has challenges that will theoretically be overcome in the next 100 years. For example, $PGF_{2\alpha}$ is not 100% effective for regressing the corpus luteum at all times during the estrous cycle. The challenge can be over-come somewhat by giving two injections of $PGF_{2\alpha}$ at a 24 hour interval. Indeed, a system in now in place that uses a second injection of $PGF_{2\alpha}$ at the end of an Ovsynch program (Santos et al., 2016). Anecdotal evidence suggests that the second injection of $PGF_{2\alpha}$ is widely used in the United States. A superior solution would be to develop a new formulation to increase the efficacy of $PGF_{2\alpha}$ so that a single injection would achieve equal response to the two-injection system. GnRH is less-effective for causing ovulation during the mid-luteal phase. This fact limits the utility of GnRH in some programs. Luteinizing hormone would theoretically be superior to GnRH because an LH injection does not depend on the cow's pituitary to release LH. Recombinant bovine LH is not available for use in dairy cattle. A related product - hCG that is isolated from human placenta is used because it has LH-like activity in cattle. It is very likely that both LH and FSH that are made using recombinant DNA technology will be available to the dairy industry in the near future. The recombinant LH could replace GnRH for synchronizing a follicular wave and inducing ovulation during timed AI. The recombinant FSH may achieve similar superovulatory responses with fewer injections when compared with Folltropin (Vetoquinol) that is extracted from porcine pituitaries (Carvalho et al., 2014). Progesterone-releasing devices are used to treat non-cycing and cystic cows. Progesterone encased in silicone within an intravaginal implant is a simple and effective method of delivery. Nonetheless, there is progesterone remaining in the device after use and the delivery of progesterone from the device is too low for large metabolically active dairy cows. Better methods to delivery progesterone to the cow (electronic pumps, etc.) should be developed in the future.

New Methods for pregnancy diagnosis

If a cow is not pregnant to first insemination then the shortest interval to second insemination is best (Giordano et al., 2013). If non-pregnant cows are not observed in a return estrus then approximately 5 weeks are lost from AI to pregnancy diagnosis (day 35) and additional time is lost when cows are resynchronized for AI. If pregnancy could be diagnosed earlier then this would save time. Genes are up-regulated during maternal recognition of pregnancy in cattle (day 16 to 20; Green et al., 2010) and specific genes (ISG15, OAS1, and MX2) can be used to detect pregnancy within the first 3 weeks after AI. The challenge is that the gene-based pregnancy test is difficult to do in the laboratory (requires at least 8 hours). If a simple test could be developed then testing cows for pregnancy within 16 days after AI is possible given today's knowledge. Regardless of when it is applied, an ideal pregnancy test would be usable on the farm and could be completed rapidly alongside the cow. This would enable efficient management of non-pregnant cattle. One of the current limitations of blood tests for pregnancy associated glycoproteins (PAG) is that they cannot be completed cow side. The most-recent versions of the tests, however, can be completed within 30 minutes (Mayo et al., 2016) which is superior to older versions of the tests that required several hours.

Genetic Testing and Genetic Selection for Fertility in Dairy Cattle

Genome-based selection will rapidly improve many traits in the dairy cow (Pryce et al., 2016). It is extremely important that the dairy industry define "high fertility" and adopt a genetic selection program that yields the desired "high fertility" cow. The current fertility trait (DPR) is a function of days open (interval from calving to pregnancy). For dairy systems that do not intervene with reproduction (i.e., do not use $PGF_{2\alpha}$, GnRH, and(or) progesterone treatment at any time and do not use timed AI) then DPR is an excellent fertility trait. Cows that are healthy, cycling, come into estrus, are observed in estrus (intense signs), are inseminated and become pregnant during the early postpartum period have the most desirable DPR. Cows that are not cycling or do not come into estrus (silent ovulation) or have subtle signs of estrus or do not become pregnant after insemination will have longer days open and a poor DPR. They are infertile because their reproductive system does not function when placed under lactation stress.

Timed AI programs mask infertility by enabling otherwise infertile cows (non-cyclers, etc.) to become pregnant. These infertile cows may have a desirable DPR because they were timed AI and become pregnant early postpartum. Their reproductive system may not function well independent of external intervention. A genetic recording system must be developed that can account for the breeding interventions used in postpartum cows. Otherwise our population of "fertile" cows may only be "fertile" when treated with $PGF_{2\alpha}$, GnRH, and (or) progesterone and timed AI. The abrupt disappearance of synchronization programs could trigger a reproductive crisis in dairy cows. It is necessary to develop robust fertility phenotypes that are suitable for dairy cow of the future.

Embryo technologies

Seidel (2016) summarized emerging new technology within the gamete and embryo transfer industry. He stated 10 areas for future research that included gametes (both sperm and egg), embryos, and stem cells. There continues to be a need for improvements in superovulation (number of embryos produced per cow). In vitro production of embryos is possible but in vitro produced embryos do not freeze well and are not equal in quality when compared with a fresh in vivo produced embryo. If commercial scale production of high-quality low-price frozen embryos can be achieved then this would revolutionize dairy reproduction particularly during the summer when embryo transfer is superior to AI in terms of pregnancy rates (Stewart et al., 2011). Genetically modified embryos (CRISPR/Cas9 gene editing technology) hold tremendous promise in future agricultural systems but their fate may lie with consumers who will decide if they want to consume food from this type of animal.

Summary

The next 100 years will be a rapid period of change in dairy reproduction. Improved cow fertility and better semen are obvious targets for future research. There will be more effective products for synchronization that will replace the ones that we use today. New methods for pregnancy diagnosis will detect pregnancies sooner after AI and allow for more efficient resynchronization of non-pregnant cows. Genetic selection for fertility will lead to high milk producing dairy cows with high fertility. Now is the time to define “high fertility” within our genetic selection programs. The new era of genetic selection will give rise to high milk producing dairy cows with a fully functional reproductive system that requires minimal intervention to achieve pregnancy.

References

Brandão AP, Cooke RF, Corrá FN, Piccolo MB, Gennari R, Leiva T, Vasconcelos JL. 2016. Physiologic, health, and production responses of dairy cows supplemented with an immunomodulatory feed ingredient during the transition period. J. Dairy Sci. 99:5562-5572.

Capper JL, Cady RA, Bauman DE. 2009. The environmental impact of dairy production: 1944 compared with 2007. J. Anim. Sci. 87:2160-2167.

Carvalho PD, Hackbart KS, Bender RW, Baez GM, Dresch AR, Guenther JN, Souza AH, Fricke PM. 2014. Use of a single injection of long-acting recombinant bovine FSH to superovulate Holstein heifers: a preliminary study. Theriogenology 82:481-489.

Foote RH. 2002. The history of artificial insemination: Selected notes and notables. J. Anim. Sci. 80 (E Suppl 2):1-10.

Giordano JO, Fricke PM, Cabrera VE. 2013. Economics of resynchronization strategies including chemical tests to identify nonpregnant cows. J. Dairy Sci. 96:949-961.

Green JC, Okamura CS, Poock SE, Lucy MC. 2010. Measurement of interferon-tau (IFN-tau) stimulated gene expression in blood leukocytes for pregnancy diagnosis within 18-20d after insemination in dairy cattle. Anim. Reprod. Sci. 121(1-2):24-33.

Mayo LM, Moore SG, Poock SE, Silvia WJ, Lucy MC. 2016. Technical note: Validation of a chemical pregnancy test in dairy cows that uses whole blood, shortened incubation times, and visual readout. J. Dairy Sci. 99:7634-7641.

Nebel RL, Dransfield MG, Jobst SM, Bame JH. 2000. Automated electronic systems for the detection of oestrus and timing of AI in cattle. Anim. Reprod. Sci. 60-61:713-723.

Pryce JE, Parker Gaddis KL, Koeck A, Bastin C, Abdelsayed M, Gengler N, Miglior F, Heringstad B, Egger-Danner C, Stock KF, Bradley AJ, Cole JB. 2016. Invited review: Opportunities for genetic improvement of metabolic diseases. J Dairy Sci. 99:6855-6873.

Ruiz R, Tedeschi LO, Sepúlveda A. 2017. Investigation of the effect of pegbovigrastim on some periparturient immune disorders and performance in Mexican dairy herds. J Dairy Sci. (in press)

Saacke RG. 2008. Insemination factors related to timed AI in cattle. Theriogenology 70:479-484.

Santos VG, Carvalho PD, Maia C, Carneiro B, Valenza A, Crump PM, Fricke PM. 2016. Adding a second prostaglandin F2α treatment to but not reducing the duration of a PRID-Synch protocol increases fertility after resynchronization of ovulation in lactating Holstein cows. J Dairy Sci. 99:3869-3879.

Seidel GE Jr. 2014. Update on sexed semen technology in cattle. Animal 8 (Suppl 1):160-164.

Seidel GE Jr. 2016. Assisted reproduction with gametes and embryos: what research is needed and fundable? Reprod. Fertil. Dev. 28(1-2):125-129.

Senger PL. 1994. The estrus detection problem: new concepts, technologies, and possibilities. J. Dairy Sci. 77:2745-2753.

Stewart BM, Block J, Morelli P, Navarette AE, Amstalden M, Bonilla L, Hansen PJ, Bilby TR. 2011. Efficacy of embryo transfer in lactating dairy cows during summer using fresh or vitrified embryos produced in vitro with sex-sorted semen. J Dairy Sci. 94:3437-3445.

Thatcher W, Santos JE, Staples CR. 2011. Dietary manipulations to improve embryonic survival in cattle. Theriogenology 76:1619-1631.

Wiltbank, M., Lopez, H., Sartori, R., Sangsritavong, S., Gümen, A. 2006. Changes in reproductive physiology of lactating dairy cows due to elevated steroid metabolism. Theriogenology 65:17-29.