J. Dairy Sci. 104
https://doi.org/10.3168/jds.2021-20281

Invited review: Use of assisted reproduction techniques to accelerate genetic gain and increase value of beef production in dairy herds

Alan D. Crowe,[1,2] Pat Lonergan,[1*] and Stephen T. Butler[2*]
[1]School of Agriculture and Food Science, University College Dublin, D04 N2E5 Ireland
[2]Teagasc, Animal and Grassland Research and Innovation Centre, Moorepark, Fermoy, Co. Cork, P61 C996 Ireland

ABSTRACT

The contribution of the calf enterprise to the profit of the dairy farm is generally considered small, with beef bull selection on dairy farms often not considered a high priority. However, this is likely to change in the future as the rapid rate of expansion of the dairy herd in some countries is set to plateau and improvements in dairy herd fertility combine to reduce the proportion of dairy breed calves required on dairy farms. This presents the opportunity to increase the proportion of beef breed calves born, increasing both the value of calf sales and the marketability of the calves. Beef embryos could become a new breeding tool for dairies as producers need to reassess their breeding policy as a consequence of welfare concerns and poor calf prices. Assisted reproductive technologies can contribute to accelerated genetic gain by allowing an increased number of offspring to be produced from genetically elite dams. There are the following 3 general classes of donor females of interest to an integrated dairy-beef system: (1) elite dairy dams, from which oocytes are recovered from live females using ovum pick-up and fertilized in vitro with semen from elite dairy bulls; (2) elite beef dams, where the oocytes are recovered from live females using ovum pick-up and fertilized with semen from elite beef bulls; and (3) commercial beef dams (≥50% beef genetics), where ovaries are collected from the abattoir postslaughter, and oocytes are fertilized with semen from elite beef bulls that are suitable for use on dairy cows (resulting embryo with ≥75% beef genetics). The expected benefits of these collective developments include accelerated genetic gain for milk and beef production in addition to transformation of the dairy herd calf crop to a combination of good genetic merit dairy female calves and premium-quality beef calves. The aim of this review is to describe how these technologies can be harnessed to intensively select for genetic improvement in both dairy breed and beef breed bulls suitable for use in the dairy herd.

Key words: dairy-beef integration, assisted reproductive technology, in vitro fertilization, embryo transfer

Received February 10, 2021.
Accepted August 2, 2021.
*Corresponding authors: stephen.butler@teagasc.ie and pat.lonergan@ucd.ie

INTRODUCTION

"Beef on dairy" is currently a hot topic. Traditionally, in a dairy herd, all cows and heifers were bred to a dairy breed bull; the required number of heifer calves were kept as replacements, with the remaining surplus (mostly male) dairy calves being sold for a low value. This traditional situation has evolved such that it is now possible to target only the top elite females in the herd to generate replacements, allowing new approaches to increase the value of the nonreplacement calves for beef production.

Dairy and beef production are inextricably linked. Although the main source of revenue in dairy herds is from milk sales, beef output from the sale of cull cows and surplus calves represents 10 to 20% of the gross income in most production systems (van der Werf et al., 1998). Gestation and parturition are prerequisites for the initiation of lactation, but in all dairy herds, the total number of calves born is greater than the required number of replacement females. Hence, in most herds, ≥60% of the calves born are destined for beef production, despite the fact that their genetics have been selected for dairy production. This results in animals of low economic value, in turn leading to welfare and environmental concerns. As a strategy to increase calf value, many dairy producers are increasingly mating dairy dams not required to generate replacement females (either surplus to requirements or genetically inferior) to beef sires.

For the small proportion of dairy herds with elite genetic merit dams, male dairy calves are also of potential value as future bulls to be used for AI. The next generation of AI bulls can be identified shortly after birth using genomic testing, allowing elite bulls to be purchased by animal breeding companies, producing semen for sale from as young as 12 mo of age (Murphy et al., 2018). Use of conventional (i.e., not sex-sorted) semen results in approximately 52:48 male-to-female sex ratio at birth (Xu et al., 2000; Roche et al., 2006; Berry and Cromie, 2007), resulting in a large surplus of male dairy calves. Thus, animal breeding companies can screen large numbers of potentially elite male dairy calves of interest using genomic testing. Although this has provided long-term genetic gain, there are unintended consequences of this approach that present welfare, social, and environmental concerns (Ritter et al., 2019; Shivley et al., 2019; Haskell, 2020).

Biological and physiological constraints limit the speed at which animals can reproduce. Young bulls must reach 9 to 12 mo of age before they achieve puberty and produce fertile sperm. Similarly, although female calves are born with all of their oocytes in their ovaries, they too must wait until puberty to ovulate a fertile oocyte. Albeit attainment of puberty can be accelerated somewhat in both males (Dance et al., 2015; Bollwein et al., 2016; Byrne et al., 2018; Kenny and Byrne, 2018) and females (Perry, 2016; Cardoso et al., 2020; Heslin et al., 2020) by judicious early-life nutritional management, the time taken to reach this developmental milestone nonetheless restricts the speed at which generations can turnover. For instance, the current generation intervals for Holstein cattle in the United States are ~2.5 yr for sires and dams of bulls, and ~4.5 and ~5 yr for sires of cows and dams of cows, respectively (García-Ruiz et al., 2016). However, the biological boundaries to generation interval are currently being pushed; it is now possible for a heifer calf to be the mother of a bull destined to become an AI sire before she herself has reached puberty or ever lactated. Holstein calves can now be born from oocytes aspirated from prepubertal females as young as 2 mo and fertilized in vitro by the sperm of 10-mo-old bulls. This process, known as velogenetics, discussed later, was first described in 1991 (Georges and Massey, 1991), but it was not until the development of low-cost, high-density genotyping chips (SNP chips) and genomic selection that it became practicable. Now, instead of waiting until a bull is approximately 7 yr old for progeny test results, semen from bulls is routinely made available at 1.5 to 2 yr old.

Several generations of assisted reproductive technologies (**ART**) have been applied to dairy cattle breeding. The more "traditional" ART such as AI, multiple ovulation embryo transfer (**MOET**), in vitro embryo production (**IVP**), precise pharmaceutical regulation of estrus and ovulation to facilitate timed AI and timed embryo transfer, and sex-sorting of sperm to produce offspring of the desired sex are already well established in the toolbox accessible to farmers. Others, including in vitro gametogenesis (Hayashi, 2019; Hayashi et al., 2021) have undergone rapid development in association with stem cell biology, opening many possibilities in this field. However, future global regulation and public acceptance of some of the newer technologies, particularly modern molecular techniques such as genome editing, remains uncertain (Van Eenennaam et al., 2020).

In this review, we briefly outline dairy breeding goals, the integration of the beef and dairy industries, and the historical development of ART in cattle and describe how these techniques can be harnessed to intensively select for genetic improvement in both dairy breed and beef breed bulls suitable for use in the dairy herd. In an era with ever-increasing focus on maximizing efficiency and reducing waste (Place and Mitloehner, 2014; Burggraaf et al., 2020), an exciting new development is the potential to produce and transfer 100% beef breed embryos into surrogate dairy dams that are not suitable for generating replacements. The expected benefits of these collective developments include accelerated genetic gain for milk and beef production, and transformation of the dairy herd calf crop to a combination of high genetic merit dairy female calves and premium-quality beef calves. This structural change takes advantage of the new tools mentioned above that are now easily available to producers for animal breeding (in particular, sex-sorted sperm and IVP embryos), and will help to increase the efficiency of dairy and beef production.

DAIRY CATTLE BREEDING GOALS

For centuries, animal breeders have intentionally selected the parents of the next generation based on their concept of the "ideal" or "best" animals in the current generation. The rate of genetic improvement is controlled by the following 4 main factors: (1) the selection intensity, a measure of how choosy breeders are in selecting the best animals; (2) the selection accuracy, a measure of the confidence that the selected animals are indeed the best; (3) the genetic variation in the trait under consideration (the greater the variation is, the greater the scope is to select animals that are well above the population average); and (4) the generation interval, a measure of how quickly the superior genes of the selected parents in the current generation can be propagated into the next generation.

Genetic selection has been a very successful tool for the long-term improvement of livestock. The rapid adoption of genomic selection, first postulated in 2001 (Meuwissen et al., 2001) and first introduced in 2008 with the development of the first high-density genotyping chip for agricultural species (Matukumalli et al., 2009), has doubled the rate at which some dairy cattle populations are improving (García-Ruiz et al., 2016). By avoiding the delays associated with progeny testing and phenotypic measures, genomic selection leads to an increase in genetic gain due to shorter generational intervals, as well as savings in cost. The rate of genetic gain through genomic selection is doubled by using bulls at 2 yr of age instead of 5, with a decrease in cost of up to 92% by avoiding progeny testing (Schaeffer 2006). As such, genomic selection is the most important technology adopted by the dairy industry since the introduction of AI about 75 yr ago, playing a critical tool in addressing declining Holstein cow fertility associated with intensive selection for milk in the previous decades (García-Ruiz et al., 2016; Taylor et al., 2016).

Selection indices for different dairy production systems and breeding strategies vary from country to country. Historically, selection within the global dairy industry focused exclusively on increasing milk production, but negative associations with fertility prompted a move away from single-trait selection to more balanced breeding objectives (Berry et al., 2016). Nowadays, selection emphasis has shifted away from traits focused on animal productivity toward those related to efficient resource utilization and improved health, welfare, and resilience. Cole and VanRaden (2018) summarized traits included in 21 total merit indices from the United States and 16 other countries. Although current selection indices differ within and across countries due to variations in economic conditions including payment schemes, traits recorded, and breeds used, common trait groups include yield (e.g., milk volume, fat and protein yield), longevity (e.g., productive life), fertility (e.g., nonreturn rate, days open, calving interval), udder health (e.g., SCC, clinical mastitis), calving traits (e.g., calving difficulty, stillbirth), milking traits (e.g., milking speed), and conformation (e.g., udder conformation, feet and leg score; Cole and VanRaden, 2018).

In terms of genetic improvement, genes can flow through 1 of 4 different pathways in a population as follows: (1) sires of bulls, (2) sires of cows, (3) dams of bulls, and (4) dams of cows (Rendel and Robertson, 1950). The aim of breeding companies is to maximize selection intensity of paths (1) and (3), whereas the farmer controls (2) and (4) when making breeding decisions. More than 70% of all US dairy cows are bred by AI, and because approximately all of the female calves produced have historically been retained as herd replacements, selection differentials and generation intervals for pathways of the sires of bulls and sires of cows have contributed the most to selection response (García-Ruiz et al., 2016). García-Ruiz et al. (2016) measured the effect of genomic selection on selection differential and generation interval in US Holstein cattle using this 4-path model, and compared the observed results with those predicted by theory (Schaeffer, 2006). This analysis demonstrated that rates of annual genetic improvement in US Holstein dairy cows had increased from 50 to 100% for moderately heritable yield traits and from 300 to 400% for lowly heritable fitness traits.

Good reproductive performance in the dairy herd is essential to improve the integration of the dairy and beef sectors, as it ensures a greater proportion of dairy cows are not required to produce dairy replacements and are available to increase beef production from the dairy herd. This can be further accelerated when sexed dairy semen is used to generate replacements (Murphy et al., 2016; Ettema et al., 2017). There is a growing body of evidence that using bulls with greater genetic merit for fertility traits can improve herd fertility phenotypes and reproductive performance (Cummins et al., 2012; O'Sullivan et al., 2020; Rojas Canadas et al., 2020a,b). In addition, the availability of low-cost high-density genetic marker panels (SNP chips) as well as the emergence of low-cost whole genome sequencing has provided marked improvement in our understanding of the biology of fertility in the dairy cow by allowing identification of genes associated with large effects on fertility and the dissection of the biology of gametogenesis, fertilization, and embryo development and maternal-embryo interaction (Cole and VanRaden, 2018).

Since about 2000, balanced breeding objectives have been implemented that incorporate fertility and longevity traits, and phenotypic fertility performance in the Holstein breed has recently begun to improve (Butler, 2013; García-Ruiz et al., 2016). The trend worldwide is to move toward more rounded selection indices, and in many cases, breeding cows to have reduced costs of production is as important as improving total income (VanRaden, 2004; Miglior et al., 2005; Coleman et al., 2010; Ramsbottom et al., 2012; Byrne et al., 2016). In Ireland, since 2001, the Economic Breeding Index (**EBI**) has evolved to combine milk production, fertility and health, and management traits (Veerkamp et al., 2002; Berry et al., 2007). Animals with greater EBI produce less total milk (kg/yr), but greater milk solids (i.e., fat and protein) reflecting the importance of milk solids in the Irish payment scheme (Ramsbottom et al., 2012; O'Sullivan et al., 2020). Cows with greater EBI, and specifically greater EBI fertility subindex, maintain greater body condition throughout lactation (Coleman et al., 2010; Cummins et al., 2012; O'Sullivan et al., 2020), which is a key phenotype that facilitates superior fertility performance and greater longevity in the herd. The current EBI places a strong emphasis (35%) on fertility traits, reflective of the economic importance of phenotypic fertility performance, particularly in a seasonal pasture-based production system (Roche et al., 2018).

In the United States, fertility traits and calving ease have been included in the US Department of Agriculture national genetic index (Net Merit Index; **NM$**) since 2003, with the aim of increasing the total profitability of US dairy cows (VanRaden, 2004). The latest revision includes milk traits (with a negative value for milk volume but a positive value for milk solids), health traits (e.g., SCS, udder health, lameness), fertility (daughter pregnancy rates, cow and heifer conception rates), calving traits (e.g., calving ease), and cow longevity (livability and survival in a productive herd; VanRaden et al., 2018). It is likely that the NM$ of the future will continue to select cows that are efficient producers of milk, are healthy and have long productive lives, and have good fertility (Cole and VanRaden, 2018).

Welfare Concerns Arising from Current Breeding Strategies—A Driver for Change

The health and welfare of unwanted male calves is a significant issue in the dairy industry worldwide, and represents a major reputational risk to the industry (Ritter et al., 2019; Haskell, 2020). The value and fate of male dairy calves varies significantly between countries (e.g., bobby calves in New Zealand and Australia, veal, finished beef). Furthermore, as mentioned above, the carcass characteristics and meat quality in finished dairy breed steers is inferior compared with beef breed steers (Berry et al., 2018).

Due to their low economic value, early rearing and health management practices are less stringently implemented for male dairy calves compared with more valuable female dairy calves. This presents animal welfare risks and damages to the public perception of dairy production (Renaud et al., 2017). In New Zealand and Australia, seasonal calving and the absence of a well-established industry for raising male dairy calves means the majority of calves are transported long distances to be slaughtered within days of birth (Cave et al., 2005; Thomas and Jordaan, 2013; Boulton et al., 2020). In Ireland, a substantial proportion of male dairy calves are transported to mainland Europe for either veal or beef production. For example, in 2019, the total number of calf births registered to a dairy sire was 798,926. Of these, 115,885 dairy breed calves under 6 wk of age were exported live to continental Europe, of which 114,063 (98%) were bull calves. This amounted to 28% of the dairy bull calves born in 2019 being live exported under 6 wk of age (Department of Agriculture, Food and The Marine, 2019b). Even though these animals could all potentially enter the human food chain and provide a source of high-quality animal protein, long distance travel is a welfare concern, and slaughter of young calves is unacceptable to most consumers.

Solutions to this issue are likely to vary between regions and may include using sexed semen to generate replacements and beef semen for all other inseminations (i.e., to markedly reduce the number of male dairy calves), using dual-purpose breeds (i.e., where male dairy calves have a recognized beef merit), targeting premium meat products, and ensuring high welfare standards. In addition, it is likely that new systems of beef production will be required, especially in countries with seasonally concentrated spikes in dairy calf births in late winter and early spring. For example, in New Zealand, the potential to finish male calves of dairy origin at 8 to 12 mo is being explored (Pike et al., 2019). Of note, economic modeling has indicated that the resulting beef would need to command a price premium to break even with existing conventional steer or bull beef enterprises (Hunt et al., 2019). Pike et al. (2019) reported that meat quality attributes related to tenderness scores were good, suggesting that there may be options to explore specialized premium markets.

Beef from the Dairy Herd—Integrating Beef and Dairy

The global dairy market was valued at US$718.9 billion in 2019 and is projected to grow to $1,032.7 billion by 2024 (Global Dairy Market, 2020). One of the primary factors supporting the market growth is the rising demand for milk and milk-based ingredients, which can be attributed to population growth, rising incomes, and health consciousness. Expanding dairy herds, particularly in some European countries following the removal of the EU milk quota regimen in 2015, coupled with improved fertility performance brought about through changes in selection indexes (Ma et al., 2019) and improvements in management practices (Carvalho et al., 2018), means that a greater proportion of cattle slaughtered for beef production originate from dairy herds. Thus, revenue attainable from the sale of surplus calves can significantly affect dairy farm profitability.

Use of sexed dairy semen to generate replacement females and beef semen on the remaining animals not required for replacements is growing in popularity (Ettema et al., 2017; Bérodier et al., 2019), facilitating genetic gain in the dairy industry while enhancing the beef value of surplus calves (Bittante et al., 2020). For example, in the United States, the number of matings between beef bulls and dairy cows more than doubled in the period from 2015 to 2019 (McWhorter et al., 2020). Similarly, in 2018, 45% of Irish calves from Holstein-Friesian dams were sired by beef bulls (Depart-

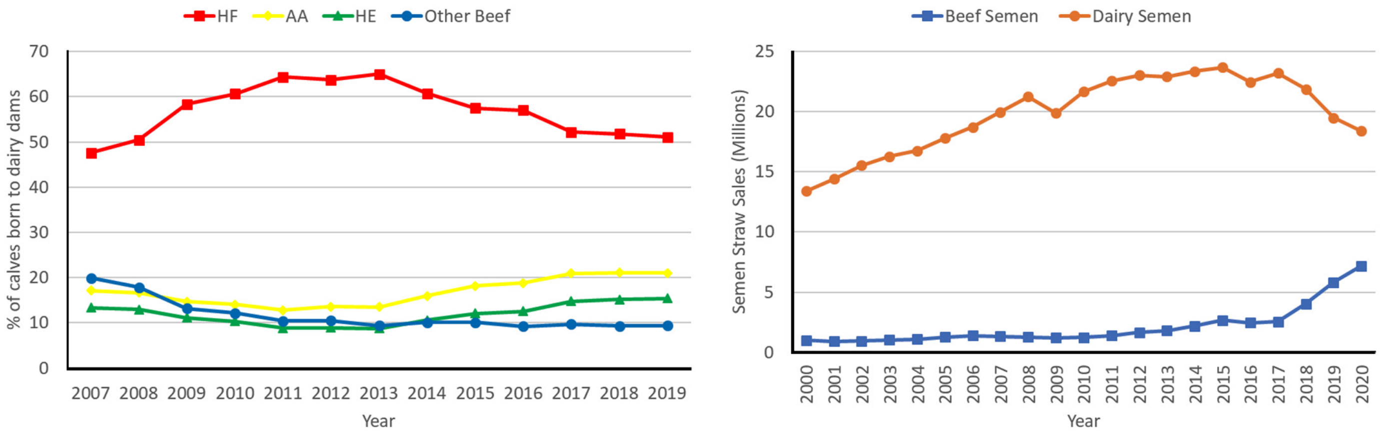

Figure 1. (A) Percentage of calves born from Holstein-Friesian dairy dams in Ireland between 2007 and 2019 displayed by sire breed (HF = Holstein Friesian; AA = Aberdeen Angus; HE = Hereford). Data are from the Animal Identification and Movement (AIM) System: Bovine Statistics Annual Reports (https://www.gov.ie/en/publication/467e3-cattle-aim/#aim-bovine-statistics-annual-reports). (B) Total domestic semen sales in units (straws) in the United States between 2000 and 2020. Data is from National Association of Animal Breeders (www.naab-css.org/semen-sales).

ment of Agriculture, Food and The Marine, 2019a), an increase from 32% in the 5 yr previously (Department of Agriculture, Food and The Marine, 2014; Figure 1). Although beef-cross calves have greater economic value than dairy bred calves, further gains can be made by using 100% beef breed genetics through embryo transfer (see below).

The 2 key traits of interest to dairy farmers when selecting beef bulls for use on their herds are calving ease and gestation length. Conversely, beef farmers that purchase these calves are interested in terminal traits such as age at finishing, carcass weight, and carcass conformation. Berry et al. (2019) described the introduction of a dairy-beef index (**DBI**) to rank beef bulls for use on dairy females, based on genetic potential to efficiently produce a high-value carcass while having minimal repercussions on milk, health, and reproductive performance of the dairy female. This index helps dairy farmers to select the most appropriate beef bulls, but is also used by beef bull breeders that breed the next generation of beef bulls to meet the demands of dairy producers. Some 65% of the emphasis in the index relates to calving performance (calving difficulty, gestation length, and calf mortality), reflecting the needs of the dairy farmer; the remaining weighting is on carcass merit (26%), feed intake (8%), and docility (1%), reflecting characteristics desired by the beef farmer and processor.

Superior growth performance and carcass traits are achievable with appropriate selection of beef bulls for use on dairy females, with only a very modest increase in collateral effects on cow performance (2–3% greater dystocia and 6-d longer gestation length; Berry et al., 2019). Although the DBI evaluates traits related to calf growth and dam performance, it does not include traits related to bull fertility. McWhorter et al. (2020) evaluated sire conception rate for beef breed sires, predominantly Angus, used to inseminate dairy cows and heifers. Mean conception rates were similar in cows (33.8 vs. 34.3%) and heifers (53.0 vs. 55.3%) for insemination events with beef versus Holstein sires, respectively. Beef sires were used more frequently in problem cows, which may explain some of the minor differences in conception rate. Hence, greater usage of beef bulls is possible without detriment to timing of pregnancy establishment.

Controlled studies have consistently demonstrated superior carcass characteristics from beef × dairy crossbred animals compared with dairy breed contemporaries (Keane and Drennan, 2008; Campion et al., 2009). In an analysis of 53,838 calves (<12 wk of age) born to dairy cows, Mc Hugh et al. (2010) reported that male calves with a beef breed sire had greater value relative to male calves with a dairy breed sire (Mc Hugh et al., 2010). For example, each 1% increase in the proportion of Belgian Blue or Charolais breed composition was worth an extra €1.86 and €1.99, respectively. Similarly, based on an analysis of 117,593 carcass records from the progeny of dairy cows, Berry et al. (2018) reported a greater carcass value of Angus × dairy crosses compared with purebred dairy animals or dairy × dairy crosses. Using field data, Berry and Ring (2020a) quantified the physical and financial performance of male progeny from different sires as follows: (1) a dairy sire; (2) a sire that exceled in a total merit index encompassing calving performance and beef performance traits (DBI); or (3) a sire that exceled in a subindex based solely on calving performance (**CLV**). The authors concluded that sires that were highly ranked on DBI produced progeny that had heavier and better confirmation carcasses compared with the progeny from both high CLV beef sires and dairy sires, and that using highly ranked DBI sires could increase dairy herd profit by 3 to 5% compared with CLV.

Beef-sired calves are more prone to dystocia, which can have consequences for subsequent dairy cow performance. Berry and Ring (2020b) used field data to examine the potential repercussions of the beef-cross pregnancies on subsequent performance of the dairy female in the absence of calving difficulty. A total of 1,764,075 singleton calving events from 896,629 Holstein-Friesian dairy cows in 7,353 herds were used in the analysis to quantify the associations between sire beef merit (sire breed and genetic merit for carcass weight and conformation) and subsequent cow milk production and phenotypic reproductive performance (Berry and Ring, 2020b). Although some significant associations were detected, the actual size of the associations was biologically small (Berry and Ring, 2020b). For example, service sire accounted for only 1% of the phenotypic variation in kilograms of milk, fat, and protein, and service sire had negligible effects on phenotypic reproductive performance.

ART: Effect on Genetic Gain

The idea of using ART to accelerate genetic gain in dairy breeds and improve the beef quality of nonreplacement offspring in dairy herds is not new (Bekman et al., 1994; Hanekamp, 1999). The technologies and strategies available to accelerate genetic gain in dairy breeds and in beef breeds suitable for crossing with dairy breeds are summarized in Figure 2A and 2B. Although insemination with beef semen will result in the generation of a calf with an expected 50% beef breed composition, the opportunity also exists to generate embryos with 100% beef breed composition (using slaughterhouse ovaries from beef heifers to provide oocytes for IVP-embryo transfer; **IVP-ET**) to maximize the value of the calf surplus to replacement requirements (Figure 2C).

Several generations of ART have been applied to domestic animal breeding and can affect one or more of the factors affecting the rate of genetic improvement (Lonergan, 2007). As mentioned earlier, many of these technologies are already well established in the toolbox accessible to farmers and breeding companies and have potential value for dairy genetic gain (more calves per elite donor, more dam-sire combinations). Although the rate of improvement could be accelerated using newer technologies (cloning, genome editing), both approval to use these technologies by regulatory authorities and public acceptance currently remains uncertain (Van Eenennaam, 2019; Bishop and Van Eenennaam, 2020).

The application of reproductive technologies in dairy cattle breeding has been recently reviewed (Moore and Hasler, 2017; Ferré et al., 2020). Artificial insemination has revolutionized dairy cattle breeding since its widespread adoption. Artificial insemination, however, has only resulted in increased selection intensity in the sire-to-progeny selection pathway. Considerable gains in selection intensity, and thus accelerated genetic gain, could be achieved by applying similar principles to the dam to progeny selection pathways. In contrast to high genetic merit sires, which produce billions of fertile gametes at each ejaculation and can sire thousands of offspring during (and even after) their lifetime, the contribution of genetically superior cows to a breeding program is limited by the fact that they are (usually) monovulatory, have a 9-mo gestation followed by a necessary period of uterine involution, and that they have a relatively short (~5 yr) productive herd life span.

Superovulation

Manipulating reproduction by repeated superovulation of the donor animal, recovery of the resulting embryos, and their transfer to surrogate recipients provides an opportunity to substantially increase the effect of superior females on a breeding program. Embryo transfer is growing in importance in US dairies. It can be used to mitigate the adverse effects of summer heat stress on cow fertility, and can increase the number of genetically elite female calves born. However, the costs of embryo production must decrease and pregnancy rates must increase to drive greater adoption (Hansen 2020).

Techniques for superovulation and ET for cattle were developed in the 1940s and 1950s (Casida et al., 1943; Rowson, 1951; Willett et al., 1951; Dziuk et al., 1958); however, large-scale ET operations were not established in North America until the 1970s, in Europe until the 1980s, and in South America until the 1990s (Hasler, 2014). Despite sustained research focused on methods to increase the number of ovulations and viable embryos recovered from the donor female, the average yield of transferable embryos produced per superovulatory cycle (6–8) has not changed markedly during the last 50 yr. The incidence of embryo death by d 7 after estrus and insemination can be as high as 50% in high-producing dairy cows (Sartori et al., 2010). Given that all of the myriad biological and technical reasons for embryo death by d 7 are avoided when a blastocyst-stage embryo is transferred into the recipient female, one would expect that pregnancy success would be greater for ET than for AI. Pregnancy suc-

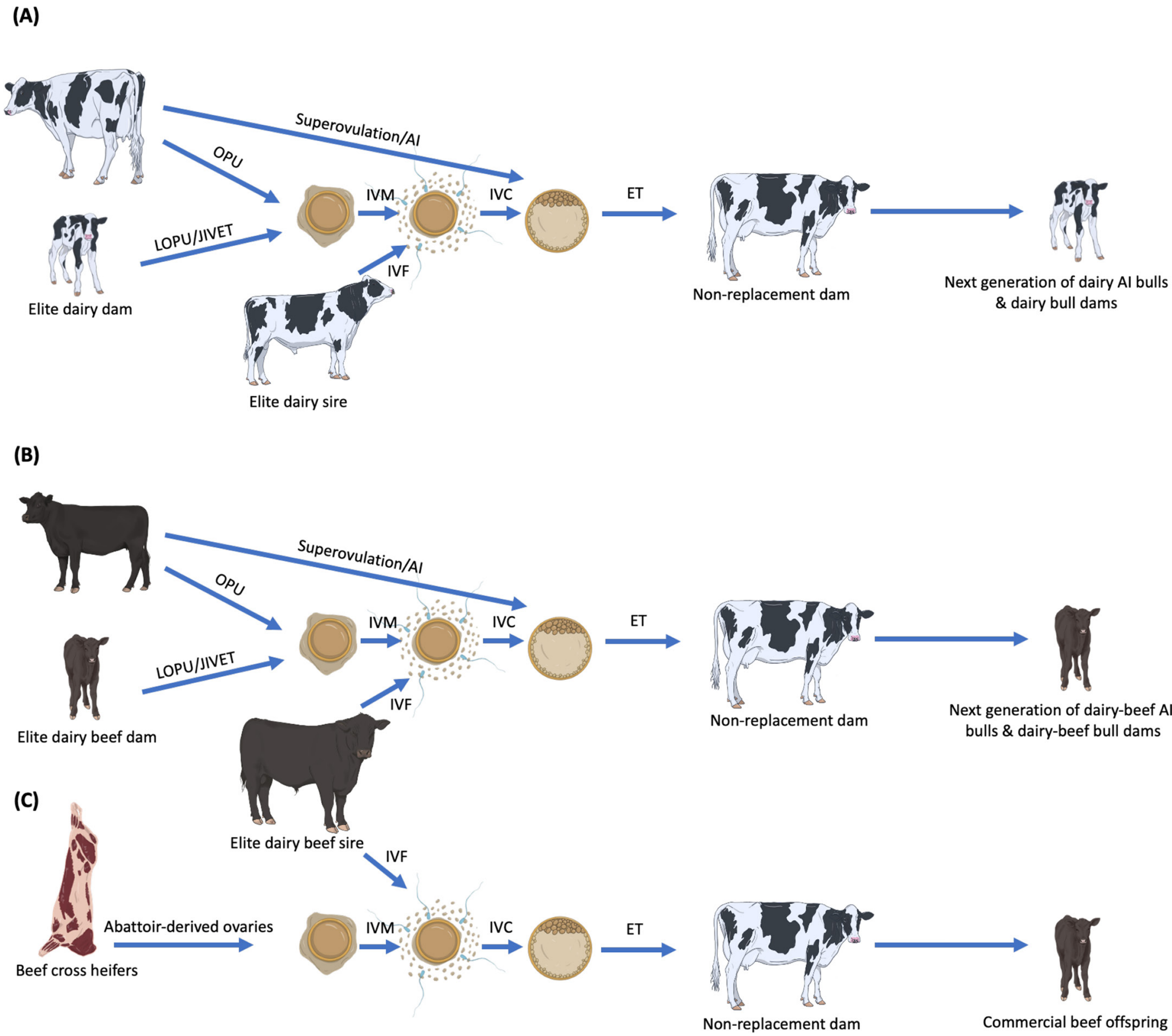

Figure 2. Use of assisted reproductive technologies to generate the next generation of elite dairy, elite dairy-beef, and commercial beef calves. (A) To create the next generation of dairy AI bulls and dairy bull dams, embryos are generated from elite dairy dams by superovulation and AI or by using ovum pick-up (OPU) or laparoscopic OPU (LOPU) or juvenile in vitro fertilization and embryo transfer (JIVET) to collect oocytes followed by in vitro maturation (IVM), fertilization (IVF) with semen from elite dairy bulls, and culture (IVC) to produce embryos for transfer (ET) to recipient dairy dams not required to generate replacement females (either surplus to requirements or genetically inferior). (B) To create the next generation of dairy-beef AI bulls and dairy-beef bull dams, superovulation and AI or OPU and LOPU followed by IVF with semen from elite dairy-beef bulls (e.g., Angus) is conducted on elite dairy-beef dams to generate embryos for transfer to recipient dairy dams. (C) To produce commercial beef animals, ovaries collected postslaughter from beef-cross heifers are used as a source of low-cost oocytes. These oocytes are fertilized with semen from elite dairy-beef bulls (different breed to maximize heterosis), resulting in embryos suitable for transfer to recipient dairy dams. The male and female offspring are all commercial beef animals, with female offspring also being a potential source of oocytes after slaughter.

cess is generally similar for both technologies, however, implying that either technical aspects of ET have yet to be optimized or that underlying female fertility associated with embryo death before d 7 also cause it to die later in pregnancy (Hansen, 2020). Success of ET is under some degree of genetic control (Jaton et al., 2016; Parker Gaddis et al. 2017), implying that it is possible to select for better outcomes.

The association between the size of the ovarian reserve and fertility in female cattle has recently attracted attention due to the validation of 2 reliable markers of the reserve as follows: (1) the number of follicles recruited during waves of follicular development (antral follicle count; **AFC**); and (2) circulating concentrations of anti-Müllerian hormone (**AMH**). Using ultrasonography, the peak number of follicles recruited per wave has been shown to be highly variable between animals but highly repeatable within individual animals (Burns et al., 2005; Gobikrushanth et al., 2017). Similarly, growing evidence indicates that AMH concentrations vary minimally during estrous cycles in cattle, implying that AMH concentrations can be reliably determined with a single blood sample on a random day of the cycle (Gobikrushanth et al., 2017). This allows accurate phenotypic evaluation of the ovarian reserve in cattle based on a single assessment of either AFC or blood concentrations of AMH. Furthermore, a strong positive correlation has been demonstrated between the variation in AFC, AMH, and total number of morphologically healthy follicles and oocytes in ovaries of young adult cattle (Ireland et al., 2011). In addition, peripheral concentrations of AMH are positively correlated with response to superstimulation and number of collected embryos (Rico et al., 2009). Hence, prior identification of dams that are most likely to have a strong response to ovarian superstimulation by measuring either AFC or AMH can aid identification of the best candidate donors for MOET. Other markers may arise in time. For instance, recently, heifers with divergent ovarian responses exhibited differential expression of plasma extracellular vesicle-miRNAs, which may prove useful as a potential biomarker to predict superstimulation response (Gad et al., 2020).

IN VITRO EMBRYO PRODUCTION

The techniques and challenges associated with IVP have been the subject of numerous comprehensive reviews (Bavister, 2002; Hansen, 2006; Lonergan and Fair, 2008; Sirard, 2018). Developments in in vitro oocyte maturation and sperm capacitation, fertilization, and embryo culture during the 1970s and 1980s led to the birth of calves following the transfer of blastocysts produced completely in vitro in 1987 (Lu et al., 1987; Gordon, 2003). In the early days of IVP, the sole source of oocytes was from ovaries collected from heifers or cows postslaughter. Although this was an excellent resource for research, these female cattle represented the commercial tier of the population, and were typically of average genetic merit; hence, the application of IVP in breeding programs was limited. The development of transvaginal ovum pick-up (**OPU**) during the late 1980s by Pieterse et al. (1988) allowed repeated oocyte recovery from live (elite) donor females and opened up the possibility of carrying out in vitro fertilization (**IVF**) with semen from elite males to produce genetically valuable embryos in large numbers, thus providing an alternative to MOET by combining OPU, IVP, and ET (Kruip et al., 1991). The practice of IVP has grown rapidly since the 2000s, with large-scale commercial operations established primarily in South and North America. Data collated annually by the International Embryo Technology Society indicate that around 1.1 million bovine embryos were transferred worldwide in 2019, the latest year for which figures are available (Figure 3). Approximately one-third of these were in vivo–derived embryos from MOET, whereas the remaining two-thirds were produced in vitro (Viana, 2020). Of all the IVP embryos transferred in 2019, the majority were in South America (50%) and in North America (40%) (Viana, 2020).

The use of embryo technologies in Brazil increased dramatically in the past 20 yr, and the country is the largest producer of bovine IVP embryos where it has almost fully replaced superovulation (MOET) as the technique of choice for embryo production (Viana et al., 2017). There are several reasons for this marked increase, including the following: (1) the willingness to rapidly adopt new technologies and develop the logistics required for use on a commercial scale; (2) the large number of antral follicles available for aspiration in many Zebu breeds (Nelore) and Zebu-hybrids (Brahman), effectively balancing the relatively poor overall efficiency of OPU-IVP; (3) poor and inconsistent ovarian response to exogenous FSH stimulation commonly observed in Zebu breeds; and (4) the scale effect. Although IVP has high fixed costs, it facilitates optimization of the use of high-cost semen straws, as well as an improvement in the logistics of recipient synchronization and management, due to a better predictability of oocyte yield per donor. Consequently, when used on a large scale, the cost per pregnancy from IVP can be lower than from conventional ET (Viana et al., 2012). Furthermore, the increase in dairy IVP in Brazil was mainly driven by the commercial availability of sex-sorted semen (Pontes et al., 2010).

According to data collected by the American Embryo Transfer Association Statistical Committee (Demetrio et al., 2020a), dairy cows yield an average of 15.5 oocytes and 3.2 viable embryos per OPU session. Approximately 80 to 90% of immature bovine oocytes undergo nuclear maturation in vitro, about 80% undergo fertilization, 30 to 40% develop to blastocyst stage, and around 50% of the transferred embryos establish a pregnancy. Although issues with cryotolerance (i.e., freezability) of IVP embryos, embryo loss, and calf birth weight remain to be fully resolved (Ealy et al., 2019), IVP embryos are here to stay as a tool for genetic improvement in dairy

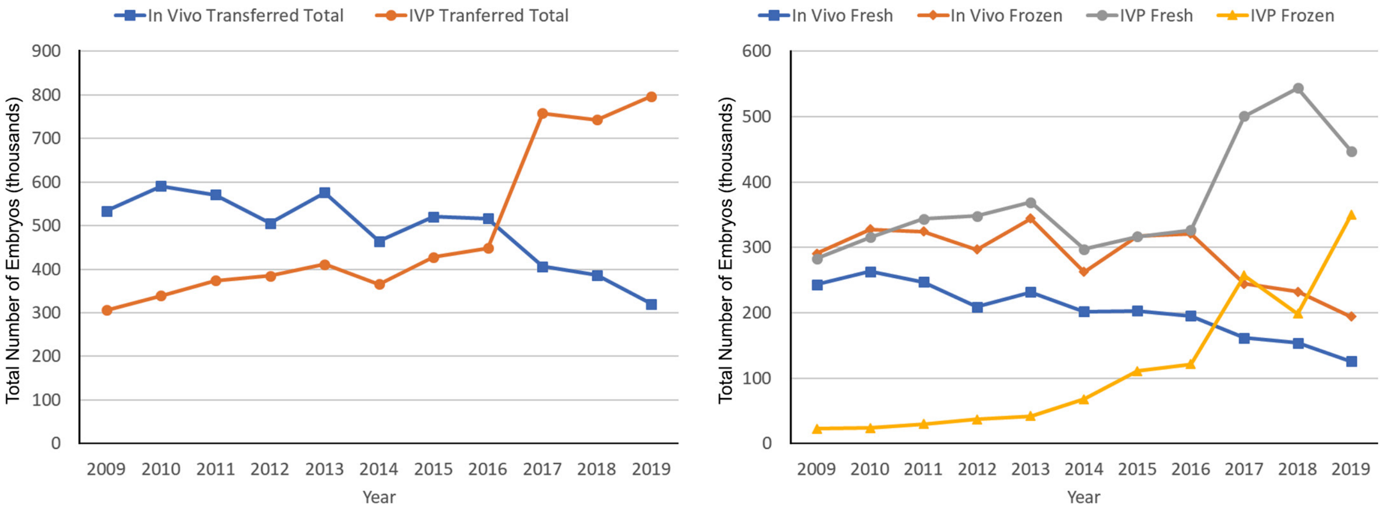

Figure 3. Number of in vivo and in vitro produced bovine embryos transferred in the years 2009 to 2019. (A) Total number of in vivo and in vitro embryo production (IVP) embryos transferred. (B) Total numbers of in vivo and IVP embryos transferred fresh or frozen. Data collated by the International Embryo Technology Society (www.iets.org).

herds (Sanches et al., 2019). Over the past decade, the success of commercial IVP has significantly improved, as greater blastocyst rates, better cryotolerance, greater pregnancy rates, reduced pregnancy loss, and decreased incidence of offspring with large birthweights have been reported (Demetrio et al., 2020b). Nevertheless, embryos generated in vitro still differ from their in vivo produced counterparts (Hansen, 2020). The quality of the oocyte at the start of the process is the key factor determining the proportion of oocytes developing to the blastocyst stage (Lonergan and Fair, 2016). Continual refinement of post-IVF culture media, known to have a major effect on blastocyst quality (Rizos et al., 2002; Lonergan et al., 2003), will undoubtedly improve success rates in the future.

Use of Juvenile In Vitro Embryo Production and Transfer to Shorten Generation Interval

The use of genomic selection allows for the identification of genetically elite dams at birth, resulting in growing interest in producing embryos from calves that are too immature to respond to traditional superovulation and flushing protocols. One of the main differences between MOET and OPU-IVP-ET is that the latter can be performed earlier in the life of the heifer than MOET, leading to shorter generation intervals. In addition, OPU-IVP allows the potential for each oocyte to be fertilized by a different sire, whereas MOET typically involves insemination with semen from a single sire per flushing.

The ovaries of young animals are characterized by much greater numbers of antral follicles compared with older donors (Desjardins and Hafs, 1969), and hence more oocytes are typically recovered from young animals per OPU session (Landry et al., 2016). Although viable embryos can be produced, the success rate of OPU-IVP with prepubertal heifer donors is generally poorer compared with that achieved with postpubertal and mature female donors (Baruselli et al., 2016).

Laparoscopic OPU (**LOPU**) in calves followed by in vitro embryo production and transfer into adult recipients—to produce "calves from calves"—has great potential for accelerated genetic gain through significant shortening of the generation interval. This allows the production of progeny from prepubertal females as young as 2 to 6 mo of age, yielding an average of ~22 viable oocytes, ~20% transferable blastocyst rate, and >50% pregnancy rate (reviewed by Baldassarre, 2021). This technique, sometimes referred to as juvenile in vitro embryo production (**JIVET**), exploits the fact that, although prepubertal females are incapable of ovulation, waves of follicular growth occur and the recruited follicles can be stimulated with exogenous gonadotropins to produce competent oocytes for aspiration, followed by in vitro embryo production (Currin et al., 2017; Baldassarre and Bordignon, 2018; Baldassarre et al., 2018).

Hormonal stimulation of prepubertal donors is critical given the fact that their hypothalamus-pituitary-ovary axis is not yet fully functional. Oocytes collected from 2- to 6-mo-old Holstein calves exhibited greater rates of development to the blastocyst stage following longer gonadotropin stimulation (3 d) compared with either shorter duration (2 d) or no stimulation, which was associated with a greater proportion of larger follicles

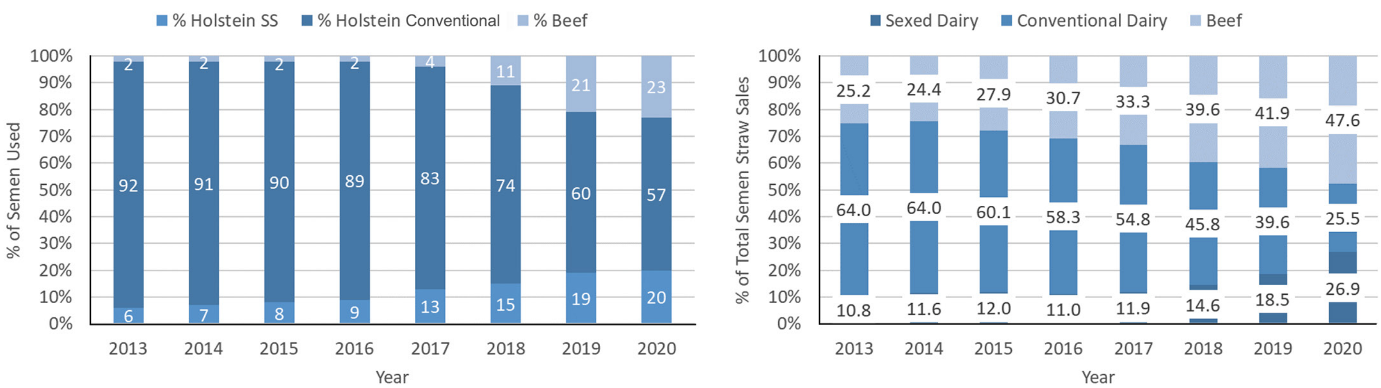

Figure 4. (A) Relative proportions of Holstein sexed semen (SS), Holstein conventional semen, and beef semen used to inseminate Holstein dams in Wisconsin from 2013 to 2020 (Li and Cabrera, 2019). (B) Breakdown of semen sales in the United Kingdom from 2013 to 2020 (% of total semen sales). Sexed dairy semen, conventional dairy semen, and beef semen are included. Data from the Agriculture and Horticulture Development Board (AHDB, 2020; https://www.thecattlesite.com/news/55869/jump-in-use-of-sexed-dairy-beef-semen/).

(Currin et al., 2017) yielding more competent oocytes (Baldassarre et al., 2018).

Sex-Sorted Semen

Sexed semen involves the sorting of X and Y sperm cells by flow cytometry and reliably produces a 9:1 female-to-male sex ratio, reducing the number of male dairy calves (Holden and Butler, 2018). As farmers move toward greater usage of sex-biased semen on genetically superior females to generate replacements, there is a corresponding increase in beef semen usage (to produce crossbred beef calf offspring) or perhaps an opportunity to further increase calf value by beef ET (to produce offspring with ≥75% beef breed genetics). Increasing the dam-side selection pressure by breeding replacement females from only genetically superior heifers and cows in the herd could accelerate herd genetic gain by up to 15% (De Vries et al., 2008). This is only feasible, however, with widespread uptake of sexed semen from the best bulls.

Once the finite requirement for female offspring pregnancies has been achieved using sex-sorted sperm for insemination, there is increased scope for beef AI or beef ET. This resulting increase in the number of beef-bred calves from the dairy herd (Murphy et al., 2016; Ettema et al., 2017) increases the marketability of the nonreplacement calf crop, and these calves have greater likelihood of achieving desired market specifications at slaughter (Wolfová et al., 2007; Berry and Ring, 2020a; Twomey et al., 2020). The usage of sexed semen has steadily increased during the last decade, especially in systems with year-round calving. Hutchinson and Bickhart (2016) reported that usage of sexed semen in heifers in the United States increased from 9% in 2007 to 31% in 2015. More recently, similar trends have been reported by Li and Cabrera (2019) highlighting increases in the use of both sexed Holstein semen and beef semen on US dairy farms (Figure 4A). Even more striking, a recent survey of UK breeding companies indicated that first-time farmers buy more sexed dairy semen than conventional semen (AHDB, 2020; Figure 4B). In the 12 mo preceding March 2020, sales of sexed semen made up 51.3% of all dairy semen sales, up from 31.9% the previous year, and only 17.9% in 2017. This rapid change is likely due a combination of improving pregnancy per AI (**P/AI**) with sexed semen, more competitive pricing of sexed semen relative to conventional semen, and greater scrutiny and monitoring of the welfare and fate of dairy breed bull calves.

There are several drivers of these changes. Sexed semen availability is now much greater than it was in the early 2000s and, importantly, the best bulls are now generally available sexed (and sometimes exclusively available as sexed). This was not always the case. Genomics has facilitated earlier identification of elite sires since 2009, and is now increasingly applied to dam selection also. About 40% of the semen used on dairy cattle nowadays is either beef semen or sexed semen. The sudden surge in popularity potentially comes from low value for dairy bull calves, large dairy heifer inventories, and the high cost of raising replacement animals.

The drivers of the use of sex-sorted semen differs among countries. The reasons for adoption of sexed semen and beef semen for use in lactating cows in the United States include strategies to right-size replacement inventories, set lower culling rates, and add value to calves not needed as replacements in a scenario where increases in reproductive efficiency through improved management, adoption of technology, and the development and implementation of hormonal fertility programs lead to an overproduction of replacement heifers. In Europe, although the attractiveness of sexed semen is still associated with being able to breed replacement females from the elite dams, its use, in combination with beef semen, to overcome the over production of unwanted low-value male dairy calves is a major driver. Usage of hormonal fertility programs for whole-herd reproductive management is much less common in Europe compared with North America, but yet the uptake of sexed semen is steadily increasing. In the United Kingdom, for example, the Agriculture and Horticulture Development Board and National Farmers Union published a national dairy calf strategy in 2020, which aims to eliminate calf euthanasia by 2023 and increase the number of male calves entering the beef supply chain (https://ahdb.org.uk/GB-calf-strategy; accessed July 7, 2021). A recent survey conducted in Ireland examined the attitude of Irish dairy farmers to male dairy calves (Maher et al., 2021). In that study, the 3 highest ranked options for managing the number of male dairy calves were to increase exports, encourage greater use of sexed semen, and improve the beef merit of these calves. Of note, the majority of respondents (85%) indicated that dairy farmers had a responsibility to reduce the number of male dairy calves.

At present, the P/AI achieved with frozen-thawed conventional semen continues to be better than sex-sorted sperm (Drake et al., 2020; Maicas et al., 2020), although the gap has been reported to be considerably smaller if the sex-sorted sperm is distributed as fresh liquid semen (i.e., not cryopreserved; Xu, 2014). It is likely that the gap in P/AI between conventional and sex-sorted sperm will continue to close as the technologies for creating sex-biased semen improve in the years to come, fostering greater uptake and usage of sex-sorted sperm.

Sexed beef semen is now becoming increasingly available, and is being actively marketed in some countries for use on dairy cows (e.g., UK; https://www.cogentuk.com/news/sexed-male-beef-semen-an-industry-game-changer; accessed July 7, 2021). We are not aware of any detailed economic appraisal of the merits of this approach, and whether this will gain traction remains to be seen. The big driver of future uptake will depend on the price differential between male and female beef-cross calves, and hence greater ability to market the nonreplacement calves.

Use of ART to Reduce (Avoid) Generation Intervals: In Vitro Breeding

A bottleneck of genomic selection is that the generation intervals are still reliant on the mating of individual animals, and thus on the amount of time required for the individuals to reach puberty. Large increases in genetic gain can be achieved when reproductive technologies (MOET, JIVET) are combined with genomic selection (Granleese et al., 2015). These technologies allow increased selection intensity on females while reducing the age at which animals are selected and thus decrease generation intervals.

Thirty years ago, Georges and Massey (1991) introduced the concept of "velogenetics." This comprised use of IVF of prepubertal or even fetal (Betteridge et al., 1989) oocytes, using sperm from (progeny-tested) bulls to rapidly introgress markers for important traits into new genetic backgrounds by using repeated backcrossing. The proposed strategy presented the following 2 main advantages over the status quo at that time: (1) markedly reduced dam generation interval; and (2) ability to monitor the segregation of markers in each backcross without a requirement for phenotypic expression of the trait of interest. Velogenetics could be used for several generations without adult animals and without recording the phenotype of interest until an animal with the desired marker configuration was developed. Eight years later, this concept was further developed by Haley and Visscher (1998), who proposed 2 modifications. The first was termed "nuclear velogenetics," which relied on in vitro culture of embryos, selection of embryos based on markers, and the use of nuclear transfer from cultures of interest to generate embryos for transfer to recipients; fetal oocytes could be harvested in utero and matured, fertilized, and cultured in vitro to repeat the cycle. The second was termed "whizzogenetics," which also relied on in vitro culture of embryos and selection of embryos based on markers, but then selected cultures of interest were induced to undergo meiosis, and the resulting cells were fertilized in vitro and the cycle of embryo culture repeated until the desired marker configuration was achieved. Then, nuclear transfer from selected cultures could be used to generate new embryos for transfer to recipients (Haley and Visscher, 1998). If strategies such as velogenetics and whizzogenetics can reduce the generation interval by a factor X, then they can also increase the genetic gain by the same factor X, but only if accuracy of selection is not affected (Meuwissen, 2003). At that time, however, selection strategies relied on measures of phenotypic performance, and genetic markers only explained a part of the genetic variance.

The velogenetics and whizzogenetics concepts were developed before high-density QTL maps were available and before widespread use of genomic information in genetic selection programs. In the years since, SNP arrays and next-generation sequencing have allowed identification of thousands of QTL linked to traits of economic importance and facilitated the development and successful implementation of genomic selection in dairy cattle (Meuwissen et al., 2001; Hayes et al., 2009). Nevertheless, successfully increasing the frequency of favorable alleles for large numbers of QTL, even with the advent of genomic selection, will remain slow.

The emerging technology of in vitro gametogenesis, where the entire germline can be recapitulated in vitro (Hikabe et al., 2016), is expected to eliminate the bottleneck in genomic selection (Hou et al., 2018; Goszczynski et al., 2019). The successful in vitro generation of germ cells from embryonic stem cells in mice (Hikabe et al., 2016; reviewed by Hayashi, 2019; Hayashi et al., 2021) and the recent efficient derivation of embryonic stem cells from bovine blastocysts (Bogliotti et al., 2018) will potentially enable a paradigm shift in livestock breeding in the near future. Building on the concepts of velogenetics and whizzogenetics, Goszczynski et al. (2019) outlined a potential methodology, which they termed in vitro breeding, that may soon be feasible to leverage the new ART and genomic tools to accelerate genetic gain. This strategy uses genomic selection to identify elite sires and dam combinations, from which large numbers of embryos are generated. Embryonic stem cell cultures are derived from the blastocyst inner cell mass (Bogliotti et al., 2018), and the embryonic stem cells are genotyped to allow estimation of genomic merit of each cell line for the traits of importance for a particular breeding objective. After identifying the best cell lines, functional oocytes are derived from the embryonic stem cells through germ cell differentiation, and these are used in repeated rounds of IVF, generation of embryonic stem cells, selection of the best cell lines, and germ cell differentiation. Assuming the time required for germ cell differentiation in cattle (procedure not yet developed) is similar to mice (2–3 mo), the authors estimated that a complete breeding cycle could be completed in 3 to 4 mo. It is noteworthy that the in vitro breeding strategy is amenable to combination with genome editing to promote favorable alleles and with gene drive to generate homozygosity for the edited allele. Simulation studies have indicated that both genome editing (Jenko et al., 2015) and gene drive (Gonen et al., 2017) can markedly accelerate genetic gain. The use of established, new, and emerging ART combined with genetic and genomic tools will soon revolutionize dairy and beef cattle breeding.

Implications of ART for Inbreeding

The use of any reproductive technology to selectively focus on a limited pool of (elite) genetics could result in an increase in inbreeding rate, and this includes existing commercially available technologies including AI (with or without sexed semen), MOET, and IVP-ET that have already been in use for some time. A simulation study conducted by Thomasen et al. (2016) examined how genomic selection of dams (0 or 2,000 genotyped heifers per year) interacted with reproductive technologies (0 or 50 selected donors) with different reliability values for genomic prediction (0.36 or 0.50). Stochastic simulation was used to vary the following key inputs: (1) the number of donors (25, 50, 100, 200); (2) the number of calves born per donor (10 or 20); (3) age of donor (2 or 14 mo); and (4) number of sires (25, 50, 100, 200). Greater reliability for the genomic prediction estimates and use of greater numbers of donors and sires limited the inbreeding rates. It is important that use of ART for generating breeding stock is appropriately implemented to provide sustainable breeding schemes for the future.

ECONOMICS OF IN VITRO EMBRYO PRODUCTION

Sanches et al. (2019) concluded that IVF is becoming an economically viable practice in large-scale dairy programs. Nonetheless, only a few studies are available that have examined the economics of the use of IVP-ET in dairy herds. Compared with a straw of semen, IVP embryos are costly, and transfer of IVP embryos, particularly frozen-thawed embryos, can lead to lower reproductive performance compared with AI through increased pregnancy losses. The economic incentive to implement IVP-ET in a dairy herd is based on the ability to generate offspring with superior genetic merit compared with use of AI, but the cost to produce a pregnancy with an IVP embryo is significantly greater than the cost of AI. De Vries and Kaniyamattam (2020) reviewed estimates of the net benefit of using IVP-ET versus AI in dairy herds, and reported that the most profitable use of AI and IVP-ET is often a combination of both technologies; more IVP should be used when the value of the surplus calves is greater and the cost of IVP-ET is lower. Benefits are maximized when superior donors and recipients are accurately identified, reducing the generation interval and achieving greater embryo production efficiency.

Regarding the potential gains that might be achieved, use of IVP-ET can greatly decrease the genetic lag (difference in genetic merit between the average cow in the herd and the best available sires). Use of IVP-ET results in a high selection intensity (a small number of genetically elite animals provide many calves for the next generation), a short generation interval (donors are typically heifers or young cows), and may have increased accuracy through the use of genomic testing for donor and recipient selection.

One major disadvantage of IVP-ET is the greater cost per breeding and pregnancy compared with AI. Ribeiro et al. (2012) calculated a difference in the cost of a female pregnancy to be $329 higher for IVP-ET than for AI using sexed semen. That study did not include additional genetic gain benefits from IVP-ET, however. Thomasen et al. (2016) reported that the greatest increase in economic value of genetic gain in a closed population was achieved when JIVET was used along with genomic selection in the bull-dam part of the population. Combining IVP-ET with genomic testing was profitable in almost all scenarios examined when the cost of producing a calf (potential future sire) by IVP-ET ranged from $500 to $1,500.

Kaniyamattam et al. (2017) compared an exclusive (100%) IVP-ET system and AI for genetic, technical, and financial herd performance. For the IVP-ET system to be at least as profitable as the comparable AI system during a 15-yr investment period, the surplus calves from the IVP-ET system needed to be sold at premium prices. The break-even price of fresh embryos was estimated to be $84 for the exclusive IVP-ET system, which is significantly lower than the current market price for IVP-ET. This resulted in the same profit as the AI system, which maximized NM$ for a 15-yr investment period and in which heifer calves were sold at a premium price. In a subsequent study (Kaniyamattam et al., 2018), the percentage of pregnancies derived from IVP-ET was varied from 0 to 100% to find the optimal proportion of pregnancies from IVP-ET and AI to maximize profitability across a range of prices for embryos and surplus dairy heifer calves. Importantly, some use of IVP-ET was profitable in many realistic combinations of embryo prices and surplus dairy heifer calf values. The profit at yr 15 after the start of the IVP-ET program was maximized when 40% of the total pregnancies in the herd came from IVF-ET. Lower prices for IVP-ET or greater value of surplus dairy heifer calves increased the optimal proportion of IVP-ET that should be used.

Although not assessed directly in those studies, the use of IVP-ET to generate a calf with increased beef merit would also contribute to farm profitability and add to the justification for using the technology. Ettema et al. (2017) reported that the potential returns from increasing beef semen usage is herd-specific. In herds with above-average management levels for calf survival, longevity, and reproductive performance, economic performance can be improved by combining the use of sexed dairy semen and beef semen, but only when the effect of the changes in the genetic merit of the female dairy calves was included in the calculations. In reality, a combination of technologies will likely be most profitable in a given scenario. For example, Clasen et al. (2021) reported that a combination of genomic testing, sexed semen, beef semen, and terminal cross breeding improved the total economic return in simulated Swedish Red and Swedish Holstein herds. In that study, the greatest total economic returns were achieved in scenarios where the breeding tools were used most, whereas the greatest genetic returns depended on phenotypic reproductive performance.

SUMMARY

Because of their poor future beef value, the majority of male dairy calves have low economic value. This is now leading to major concerns regarding the welfare and survival of these calves. In addition, ruminant production is being placed under increasing scrutiny for the environmental impact of milk and meat production. The suite of ART tools that are now available can be harnessed to provide a step change in the efficiency, environmental footprint, and public image of milk and beef production.

Assisted reproductive technologies can contribute to accelerated genetic gain by allowing an increased number of offspring to be produced from genetically elite dams. There are 3 general classes of donor females of interest to an integrated dairy-beef system as follows: (1) elite dairy dams, from which oocytes are recovered from live females (potentially multiple times) using OPU and fertilized in vitro with semen from elite dairy bulls; (2) elite beef dams, where the oocytes are recovered from live females using OPU and fertilized with semen from elite beef bulls; and (3) commercial beef dams (≥50% beef genetics), where ovaries are collected from the abattoir postslaughter and oocytes are fertilized with semen from elite beef bulls that are suitable for use on dairy cows from (2) above (resulting embryo ≥75% beef genetics). For (1) and (2), the embryos can be genotyped to calculate the genomic merit, the best embryos transferred to surrogate dams, and the best male and female offspring retained to sustain the cycle of continued genetic gain. For (3), the major challenge will be to be economically competitive versus beef AI (pregnancy establishment, embryo loss, calf value). For a dairy farmer to switch from using beef AI to beef ET, the resulting calf would need to attract a greater economic value at 2 wk of age. For the beef farmer to spend more money on an ET calf versus an AI calf, either the slaughter value needs to be greater (larger carcass, better conformation, premium price) or the cost of getting to slaughter needs to be less (e.g., finished at an earlier age, better growth rates, better feed efficiency). What phenotype differences can be expected between calves that have 50% beef breed + 50% dairy breed genetics versus 100% beef breed genetics? How much selection intensity can be placed on the oocyte donor? Can beef bulls be selected that are specifically suited for IVP and ET into surrogate dairy dams? There are many gaps in our current knowledge. Research on the cost-benefit of using beef ET versus beef AI is required, incorporating comparative data on pregnancy establishment, calving performance, postnatal growth rates, postslaughter carcass characteristics, and meat quality attributes.

In an ideal scenario, future AI bulls are generated by design, relying on OPU from elite dairy dams and IVF to generate blastocysts suitable for transfer to recipients. Within commercial dairy herds, only elite dairy sexed semen would be used to generate female replacements. Collectively, this would account for approximately one-third of the pregnancies in the dairy herd. The remaining two-thirds of the dairy herd would either be (1) inseminated following observed estrus using suitable beef bulls (50% beef genetics in resulting offspring); or (2) have an embryo transferred (≥75% beef genetics) on d 7 after estrus. This scenario would change the face of dairy and beef production, removing the male dairy calf as a major welfare concern and increasing the value of beef output from the dairy herd.

ACKNOWLEDGMENTS

The authors' work is funded by the Teagasc Walsh Scholarships Programme, The Department of Agriculture, Food and the Marine (Dublin, Ireland) Research Stimulus Fund (grant 15/S/732), Science Foundation Ireland (grant 16/IA/4474), as well as funding from a research grant from Science Foundation Ireland and the Department of Agriculture, Food and Marine (grant 16/RC/3835; VistaMilk). The authors also thank Beatriz Fernandez-Fuertes, Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (INIA), Madrid, for help with the artwork for Figure 2. The authors have not stated any conflicts of interest.

REFERENCES

AHDB (Agriculture and Horticulture Development Board). 2020. Jump in use of sexed dairy semen. Accessed Jul. 8, 2021. https://ahdb.org.uk/news/jump-in-use-of-sexed-dairy-semen.

Baldassarre, H. 2021. Laparoscopic ovum pick-up followed by in vitro embryo production and transfer in assisted breeding programs for ruminants. Animals (Basel) 11:216.

Baldassarre, H., and V. Bordignon. 2018. Laparoscopic ovum pick-up for in vitro embryo production from dairy bovine and buffalo calves. Anim. Reprod. 15:191–196. https://doi.org/10.21451/1984-3143-AR2018-0057.

Baldassarre, H., L. Currin, L. Michalovic, A. M. Bellefleur, K. Gutierrez, R. G. Mondadori, W. G. Glanzner, Y. Schuermann, R. C. Bohrer, N. Dicks, R. Lopez, F. X. Grand, C. Vigneault, P. Blondin, J. Gourdon, and V. Bordignon. 2018. Interval of gonadotropin administration for in vitro embryo production from oocytes collected from Holstein calves between 2 and 6 months of age by repeated laparoscopy. Theriogenology 116:64–70. https://doi.org/10.1016/j.theriogenology.2018.05.005.

Baruselli, P. S., E. O. S. Batista, L. M. Vieira, R. M. Ferreira, B. G. Guerreiro, B. M. Bayeux, J. N. S. Sales, A. H. Souza, and L. U. Gimenes. 2016. Factors that interfere with oocyte quality for in vitro production of cattle embryos: Effects of different developmental & reproductive stages. Anim. Reprod. 13:264–272. https://doi.org/10.21451/1984-3143-AR861.

Bavister, B. D. 2002. Early history of in vitro fertilization. Reproduction 124:181–196. https://doi.org/10.1530/rep.0.1240181.

Bekman, H., T. H. E. Meuwissen, and J. K. Oldenbroek. 1994. Increasing beef-production from dairy-cows by implanting embryos from moet nucleus breeding schemes for beef-cattle. Livest. Prod. Sci. 37:271–282. https://doi.org/10.1016/0301-6226(94)90122-8.

Bérodier, M., M. Brochard, D. Boichard, C. Dezetter, N. Bareille, and V. Ducrocq. 2019. Use of sexed semen and female genotyping affects genetic and economic outcomes of Montbéliarde dairy herds depending on the farming system considered. J. Dairy Sci. 102:10073–10087. https://doi.org/10.3168/jds.2018-16041.

Berry, D. P., P. R. Amer, R. D. Evans, T. Byrne, A. R. Cromie, and F. Hely. 2019. A breeding index to rank beef bulls for use on dairy females to maximize profit. J. Dairy Sci. 102:10056–10072. https://doi.org/10.3168/jds.2019-16912.

Berry, D. P., and A. R. Cromie. 2007. Artificial insemination increases the probability of a male calf in dairy and beef cattle. Theriogenology 67:346–352. https://doi.org/10.1016/j.theriogenology.2006.08.003.

Berry, D. P., N. C. Friggens, M. Lucy, and J. R. Roche. 2016. Milk production and fertility in cattle. Annu. Rev. Anim. Biosci. 4:269–290. https://doi.org/10.1146/annurev-animal-021815-111406.

Berry, D. P., M. J. Judge, R. D. Evans, F. Buckley, and A. R. Cromie. 2018. Carcass characteristics of cattle differing in Jersey proportion. J. Dairy Sci. 101:11052–11060. https://doi.org/10.3168/jds.2018-14992.

Berry, D. P., and S. C. Ring. 2020a. Observed progeny performance validates the benefit of mating genetically elite beef sires to dairy females. J. Dairy Sci. 103:2523–2533. https://doi.org/10.3168/jds.2019-17431.

Berry, D. P., and S. C. Ring. 2020b. Short communication: The beef merit of the sire mated to a dairy female affects her subsequent performance. J. Dairy Sci. 103:8241–8250. https://doi.org/10.3168/jds.2020-18521.

Berry, D. P., L. Shalloo, A. R. Cromie, R. F. Veerkamp, P. Dillon, P. R. Amer, J. F. Kearney, R. D. Evans, and B. Wickham. 2007. The economic breeding index: a generation on. in Technical report to the Irish Cattle Breeding Federation. Accessed Jul. 8, 2021. https://www.icbf.com/wp/wp-content/uploads/2013/06/The_Economic_breeding_a_generation_on_Dec_2007.pdf.

Betteridge, K. J., C. Smith, R. B. Stubbings, K. P. Xu, and W. A. King. 1989. Potential genetic improvement of cattle by fertilization of fetal oocytes in vitro. J. Reprod. Fertil. Suppl. 38:87–98.

Bishop, T. F. and A. L. Van Eenennaam. 2020. Genome editing approaches to augment livestock breeding programs. J. Exp. Biol. 223(Pt Suppl 1):jeb207159. https://doi.org/10.1242/jeb.207159.

Bittante, G., R. Negrini, M. Bergamaschi, A. Cecchinato, and H. Toledo-Alvarado. 2020. Short communication: Pure-breeding with sexed semen and crossbreeding with semen from double-muscled sires to improve beef production from dairy herds: Weight and value of calves. J. Dairy Sci. 103:5258–5262. https://doi.org/10.3168/jds.2019-18011.

Bogliotti, Y. S., J. Wu, M. Vilarino, D. Okamura, D. A. Soto, C. Zhong, M. Sakurai, R. V. Sampaio, K. Suzuki, J. C. Izpisua Belmonte, and P. J. Ross. 2018. Efficient derivation of stable primed pluripotent embryonic stem cells from bovine blastocysts. Proc. Natl. Acad. Sci. USA 115:2090–2095. https://doi.org/10.1073/pnas.1716161115.

Bollwein, H., F. Janett, and M. Kaske. 2016. Impact of nutritional programming on the growth, health, and sexual development of bull calves. Domest. Anim. Endocrinol. 56(Suppl):S180–S190. https://doi.org/10.1016/j.domaniend.2016.02.006.

Boulton, A. C., N. J. Kells, N. Cogger, C. B. Johnson, C. O'Connor, J. Webster, A. Palmer, and N. J. Beausoleil. 2020. Risk factors for bobby calf mortality across the New Zealand dairy supply chain. Prev. Vet. Med. 174:104836. https://doi.org/10.1016/j.prevetmed.2019.104836.

Burggraaf, V. T., G. M. Lucci, S. F. Ledgard, D. L. Antille, V. O. Snow, and C. A. M. de Klein. 2020. Application of circular economy principles to New Zealand pastoral farming systems. J. N. Z. Grasslands 82:53–59. https://doi.org/10.33584/jnzg.2020.82.426.

Burns, D. S., F. Jimenez-Krassel, J. L. H. Ireland, P. G. Knight, and J. J. Ireland. 2005. Numbers of antral follicles during follicular waves in cattle: Evidence for high variation among animals, very high repeatability in individuals, and an inverse association with serum follicle-stimulating hormone concentrations. Biol. Reprod. 73:54–62. https://doi.org/10.1095/biolreprod.104.036277.

Butler, S. T. 2013. Genetic control of reproduction in dairy cows. Reprod. Fertil. Dev. 26:1–11. https://doi.org/10.1071/RD13304.

Byrne, C. J., S. Fair, A. M. English, M. Cirot, C. Staub, P. Lonergan, and D. A. Kenny. 2018. Plane of nutrition before and after 6 months of age in Holstein-Friesian bulls: I. Effects on performance, body composition, age at puberty, and postpubertal semen production. J. Dairy Sci. 101:3447–3459. https://doi.org/10.3168/jds.2017-13719.

Byrne, T. J., B. F. S. Santos, P. R. Amer, D. Martin-Collado, J. E. Pryce, and M. Axford. 2016. New breeding objectives and selection indices for the Australian dairy industry. J. Dairy Sci. 99:8146–8167. https://doi.org/10.3168/jds.2015-10747.

Campion, B., M. G. Keane, D. A. Kenny, and D. P. Berry. 2009. Evaluation of estimated genetic merit for carcass weight in beef cattle: Live weights, feed intake, body measurements, skeletal and muscular scores, and carcass characteristics. Livest. Sci. 126:87–99. https://doi.org/10.1016/j.livsci.2009.06.004.

Cardoso, R. C., S. M. West, T. S. Maia, B. R. C. Alves, and G. L. Williams. 2020. Nutritional control of puberty in the bovine female: Prenatal and early postnatal regulation of the neuroendocrine system. Domest. Anim. Endocrinol. 73:106434. https://doi.org/10.1016/j.domaniend.2020.106434.

Carvalho, P. D., V. G. Santos, J. O. Giordano, M. C. Wiltbank, and P. M. Fricke. 2018. Development of fertility programs to achieve high 21-day pregnancy rates in high-producing dairy cows. Theriogenology 114:165–172. https://doi.org/10.1016/j.theriogenology.2018.03.037.

Casida, L. E., R. K. Meyer, W. H. McShan, and W. Wisnicky. 1943. Effects of pituitary gonadotropins on the ovaries and the induction of superfecunity in cattle. Am. J. Vet. Res. 4:76–79.

Cave, J. G., A. P. Callinan, and W. K. Woonton. 2005. Mortalities in bobby calves associated with long distance transport. Aust. Vet. J. 83:82–84. https://doi.org/10.1111/j.1751-0813.2005.tb12203.x.

Clasen, J. B., M. Kargo, S. Østergaard, W. F. Fikse, L. Rydhmer, and E. Strandberg. 2021. Genetic consequences of terminal crossbreeding, genomic test, sexed semen, and beef semen in dairy herds. J. Dairy Sci. 104:8062–8075. https://doi.org/10.3168/jds.2020-20028.

Cole, J. B., and P. M. VanRaden. 2018. Symposium review: Possibilities in an age of genomics: The future of selection indices. J. Dairy Sci. 101:3686–3701. https://doi.org/10.3168/jds.2017-13335.

Coleman, J., K. M. Pierce, D. P. Berry, A. Brennan, and B. Horan. 2010. Increasing milk solids production across lactation through genetic selection and intensive pasture-based feed system. J. Dairy Sci. 93:4302–4317. https://doi.org/10.3168/jds.2009-2591.

Cummins, S. B., P. Lonergan, A. C. Evans, D. P. Berry, R. D. Evans, and S. T. Butler. 2012. Genetic merit for fertility traits in Holstein cows: I. Production characteristics and reproductive efficiency in a pasture-based system. J. Dairy Sci. 95:1310–1322. https://doi.org/10.3168/jds.2011-4742.

Currin, L., L. Michalovic, A. M. Bellefleur, K. Gutierrez, W. Glanzner, Y. Schuermann, R. C. Bohrer, N. Dicks, P. R. da Rosa, M. P. De Cesaro, R. Lopez, F. X. Grand, C. Vigneault, P. Blondin, J. Gourdon, H. Baldassarre, and V. Bordignon. 2017. The effect of age and length of gonadotropin stimulation on the in vitro embryo development of Holstein calf oocytes. Theriogenology 104:87–93. https://doi.org/10.1016/j.theriogenology.2017.08.011.

Dance, A., J. Thundathil, R. Wilde, P. Blondin, and J. Kastelic. 2015. Enhanced early-life nutrition promotes hormone production and reproductive development in Holstein bulls. J. Dairy Sci. 98:987–998. https://doi.org/10.3168/jds.2014-8564.

De Vries, A., and K. Kaniyamattam. 2020. A review of simulation analyses of economics and genetics for the use of in vitro produced embryos and artificial insemination in dairy herds. Anim. Reprod. 17:e20200020. https://doi.org/10.1590/1984-3143-ar2020-0020.

De Vries, A., M. Overton, J. Fetrow, K. Leslie, S. Eicker, and G. Rogers. 2008. Exploring the impact of sexed semen on the structure of the dairy industry. J. Dairy Sci. 91:847–856. https://doi.org/10.3168/jds.2007-0536.

Demetrio, D., C. Looney, H. Rees, and M. Werhman. 2020a. 2020 Statistical Information Committee Report (2019 Data). Accessed Jul. 8, 2021. https://www.aeta.org/docs/2019_Stats.pdf.

Demetrio, D. G. B., E. Benedetti, C. G. B. Demetrio, J. Fonseca, M. Oliveira, A. Magalhaes, and R. M. Dos Santos. 2020b. How can we improve embryo production and pregnancy outcomes of Holstein embryos produced in vitro? (12 years of practical results at a California dairy farm). Anim. Reprod. 17:e20200053. https://doi.org/10.1590/1984-3143-ar2020-0053.

Department of Agriculture, Food and The Marine. 2014. AIM Bovine Statistics Report. Accessed Jul. 8, 2021. https://assets.gov.ie/101734/02930db2-d291-4eff-b3a0-b7c22cd9c495.pdf.

Department of Agriculture, Food and The Marine. 2019a. AIM Bovine Statistics Report 2018. Accessed Jul. 8, 2021. https://assets.gov.ie/101724/cb6fa3d1-097b-47f1-b43e-f9a4d9f98506.pdf.

Department of Agriculture, Food and The Marine. 2019b. AIM Bovine Statistics Report 2019. Accessed Jul. 8, 2021. https://www.gov.ie/en/publication/467e3-cattle-aim/#aim-bovine-statistics-annual-reports.

Desjardins, C., and H. D. Hafs. 1969. Maturation of Bovine Female Genitalia from Birth through Puberty. J. Anim. Sci. 28:502–507. https://doi.org/10.2527/jas1969.284502x.

Drake, E., S. A. Holden, V. Aublet, R. C. Doyle, C. Millar, S. G. Moore, C. Maicas, F. Randi, A. R. Cromie, P. Lonergan, and S. T. Butler. 2020. Evaluation of delayed timing of artificial insemination with sex-sorted sperm on pregnancy per artificial insemination in seasonal-calving, pasture-based lactating dairy cows. J. Dairy Sci. 103:12059–12068. https://doi.org/10.3168/jds.2020-18847.

Dziuk, P. J., J. D. Donker, J. R. Nichols, and W. E. Petersen. 1958. Problems Associated with the Transfer of Ova Between Cattle. University of Minnesota Agricultural Experiment Station.

Ealy, A. D., L. K. Wooldridge, and S. R. McCoski. 2019. Board invited review: Post-transfer consequences of in vitro-produced embryos in cattle. J. Anim. Sci. 97:2555–2568. https://doi.org/10.1093/jas/skz116.

Ettema, J. F., J. R. Thomasen, L. Hjorto, M. Kargo, S. Ostergaard, and A. C. Sorensen. 2017. Economic opportunities for using sexed semen and semen of beef bulls in dairy herds. J. Dairy Sci. 100:4161–4171. https://doi.org/10.3168/jds.2016-11333.

Ferré, L. B., M. E. Kjelland, L. B. Strobech, P. Hyttel, P. Mermillod, and P. J. Ross. 2020. Review: Recent advances in bovine in vitro embryo production: reproductive biotechnology history and methods. Animal 14:991–1004. https://doi.org/10.1017/S1751731119002775.

Gad, A., J. M. Sanchez, J. A. Browne, L. Nemcova, J. Laurincik, R. Prochazka, and P. Lonergan. 2020. Plasma extracellular vesicle miRNAs as potential biomarkers of superstimulatory response in cattle. Sci. Rep. 10:19130. https://doi.org/10.1038/s41598-020-76152-9.

García-Ruiz, A., J. B. Cole, P. M. VanRaden, G. R. Wiggans, F. J. Ruiz-Lopez, and C. P. Van Tassell. 2016. Changes in genetic selection differentials and generation intervals in US Holstein dairy cattle as a result of genomic selection. Proc. Natl. Acad. Sci. USA 113:E3995–E4004. https://doi.org/10.1073/pnas.1519061113.

Georges, M., and J. M. Massey. 1991. Velogenetics, or the synergistic use of marker assisted selection and germ-line manipulation. Theriogenology 35:151–159. https://doi.org/10.1016/0093-691X(91)90154-6.

Global Dairy Market. 2020. Global Dairy Market: Industry Trends, Share, Size, Growth, Opportunity and Forecast 2020–2025. Accessed Feb. 3, 2021. https://www.imarcgroup.com/global-dairy-market.

Gobikrushanth, M., P. A. Dutra, T. C. Bruinje, M. G. Colazo, S. T. Butler, and D. J. Ambrose. 2017. Repeatability of antral follicle counts and anti-Mullerian hormone and their associations determined at an unknown stage of follicular growth and an expected day of follicular wave emergence in dairy cows. Theriogenology 92:90–94. https://doi.org/10.1016/j.theriogenology.2017.01.018.

Gonen, S., J. Jenko, G. Gorjanc, A. J. Mileham, C. B. Whitelaw, and J. M. Hickey. 2017. Potential of gene drives with genome editing to increase genetic gain in livestock breeding programs. Genet. Sel. Evol. 49:3. https://doi.org/10.1186/s12711-016-0280-3.

Gordon, I. 2003. Laboratory Production of Cattle Embryos. 2nd ed. CABI Publishing.

Goszczynski, D. E., H. Cheng, S. Demyda-Peyras, J. F. Medrano, J. Wu, and P. J. Ross. 2019. In vitro breeding: Application of embryonic stem cells to animal production dagger. Biol. Reprod. 100:885–895. https://doi.org/10.1093/biolre/ioy256.

Granleese, T., S. A. Clark, A. A. Swan, and J. H. J. van der Werf. 2015. Increased genetic gains in sheep, beef and dairy breeding programs from using female reproductive technologies combined with optimal contribution selection and genomic breeding values. Genet. Sel. Evol. 47:70. https://doi.org/10.1186/s12711-015-0151-3.

Haley, C. S., and P. M. Visscher. 1998. Strategies to utilize marker-quantitative trait loci associations. J. Dairy Sci. 81(Suppl. 2):85–97. https://doi.org/10.3168/jds.S0022-0302(98)70157-2.

Hanekamp, W. J. A. 1999. Transfer of beef embryos in dairy cows: Influence of recipient and embryo quality on pregnancy rate and calving performance. Reprod. Domest. Anim. 34:459–463. https://doi.org/10.1111/j.1439-0531.1999.tb01404.x.

Hansen, P. J. 2006. Realizing the promise of IVF in cattle–An overview. Theriogenology 65:119–125. https://doi.org/10.1016/j.theriogenology.2005.09.019.

Hansen, P. J. 2020. The incompletely fulfilled promise of embryo transfer in cattle-why aren't pregnancy rates greater and what can we do about it? J. Anim. Sci. 98:skaa288. https://doi.org/10.1093/jas/skaa288.

Haskell, M. J. 2020. What to do with surplus dairy calves? Welfare, economic, and ethical considerations. Landbauforschung 70:45–48.

Hasler, J. F. 2014. Forty years of embryo transfer in cattle: A review focusing on the journal Theriogenology, the growth of the industry in North America, and personal reminisces. Theriogenology 81:152–169. https://doi.org/10.1016/j.theriogenology.2013.09.010.

Hayashi, K. 2019. In vitro reconstitution of germ cell development. Biol. Reprod. 101:567–578. https://doi.org/10.1093/biolre/ioz111.

Hayashi, K., C. Galli, S. Diecke, and T. B. Hildebrandt. 2021. Artificially produced gametes in mice, humans and other species. Reprod. Fertil. Dev. 33:91–101. https://doi.org/10.1071/RD20265.

Hayes, B. J., P. J. Bowman, A. J. Chamberlain, and M. E. Goddard. 2009. Invited review: Genomic selection in dairy cattle: Progress and challenges. J. Dairy Sci. 92:433–443. https://doi.org/10.3168/jds.2008-1646.

Heslin, J., D. A. Kenny, A. K. Kelly, and M. McGee. 2020. Age at puberty and pregnancy rate in beef heifer genotypes with contrasting nutritional intake from 8 to 13 months of age. Anim. Reprod. Sci. 212:106221. https://doi.org/10.1016/j.anireprosci.2019.106221.

Hikabe, O., N. Hamazaki, G. Nagamatsu, Y. Obata, Y. Hirao, N. Hamada, S. Shimamoto, T. Imamura, K. Nakashima, M. Saitou, and K. Hayashi. 2016. Reconstitution in vitro of the entire cycle of the mouse female germ line. Nature 539:299–303. https://doi.org/10.1038/nature20104.

Holden, S. A., and S. T. Butler. 2018. Review: Applications and benefits of sexed semen in dairy and beef herds. Animal 12:s97–s103. https://doi.org/10.1017/S1751731118000721.

Hou, Z., L. An, J. Han, Y. Yuan, D. Chen, and J. Tian. 2018. Revolutionize livestock breeding in the future: an animal embryo-stem cell breeding system in a dish. J. Anim. Sci. Biotechnol. 9:90. https://doi.org/10.1186/s40104-018-0304-7.

Hunt, J. J., P. R. Tozer, P. R. Kenyon, N. M. Schreurs, S. J. Pike, R. E. Hickson, H. T. Blair, and D. J. Garrick. 2019. Brief communication: Relative cost of producing carcasses from dairy-origin steers slaughtered at 8 – 12 months of age in New Zealand. N. Z. J. Anim. Sci. Prod. 79:153–155.

Hutchinson, J. L., and D. M. Bickhart. 2016. Sexed-semen usage for Holstein AI in the United States. J. Dairy Sci. 99:176.

Ireland, J. J., G. W. Smith, D. Scheetz, F. Jimenez-Krassel, J. K. Folger, J. L. H. Ireland, F. Mossa, P. Lonergan, and A. C. O. Evans. 2011. Does size matter in females? An overview of the impact of the high variation in the ovarian reserve on ovarian function and fertility, utility of anti-Mullerian hormone as a diagnostic marker for fertility and causes of variation in the ovarian reserve in cattle. Reprod. Fertil. Dev. 23:1–14. https://doi.org/10.1071/RD10226.

Jaton, C., A. Koeck, M. Sargolzaei, C. A. Price, C. Baes, F. S. Schenkel, and F. Miglior. 2016. Short communication: Genetic correlations between number of embryos produced using in vivo and in vitro techniques in heifer and cow donors. J. Dairy Sci. 99:8222–8226. https://doi.org/10.3168/jds.2016-11356.

Jenko, J., G. Gorjanc, M. A. Cleveland, R. K. Varshney, C. B. Whitelaw, J. A. Woolliams, and J. M. Hickey. 2015. Potential of promotion of alleles by genome editing to improve quantitative traits in livestock breeding programs. Genet. Sel. Evol. 47:55. https://doi.org/10.1186/s12711-015-0135-3.

Kaniyamattam, K., J. Block, P. J. Hansen, and A. De Vries. 2017. Comparison between an exclusive in vitro-produced embryo transfer system and artificial insemination for genetic, technical, and financial herd performance. J. Dairy Sci. 100:5729–5745. https://doi.org/10.3168/jds.2016-11979.

Kaniyamattam, K., J. Block, P. J. Hansen, and A. De Vries. 2018. Economic and genetic performance of various combinations of in vitro-produced embryo transfers and artificial insemination in a dairy herd. J. Dairy Sci. 101:1540–1553. https://doi.org/10.3168/jds.2017-13475.

Keane, M. G., and M. J. Drennan. 2008. A comparison of Friesian, Aberdeen Angus × Friesian and Belgian Blue × Friesian steers finished at pasture or indoors. Livest. Sci. 115:268–278. https://doi.org/10.1016/j.livsci.2007.08.002.

Kenny, D. A., and C. J. Byrne. 2018. Review: The effect of nutrition on timing of pubertal onset and subsequent fertility in the bull. Animal 12(s1):s36–s44. https://doi.org/10.1017/S1751731118000514.

Kruip, T. A., M. C. Pieterse, T. H. van Beneden, P. L. Vos, Y. A. Wurth, and M. A. Taverne. 1991. A new method for bovine embryo production: A potential alternative to superovulation. Vet. Rec. 128:208–210. https://doi.org/10.1136/vr.128.9.208.

Landry, D. A., A. M. Bellefleur, R. Labrecque, F. X. Grand, C. Vigneault, P. Blondin, and M. A. Sirard. 2016. Effect of cow age on the in vitro developmental competence of oocytes obtained after FSH stimulation and coasting treatments. Theriogenology 86:1240–1246. https://doi.org/10.1016/j.theriogenology.2016.04.064.

Li, W., and V. E. Cabrera. 2019. Dairy x beef: Fad or sustainable future? Pages 32–40 in Proc. Dairy Cattle Reproduction Council Conf.

Lonergan, P. 2007. State-of-the-art embryo technologies in cattle. Soc. Reprod. Fertil. Suppl. 64:315–325.

Lonergan, P., and T. Fair. 2008. In vitro-produced bovine embryos: Dealing with the warts. Theriogenology 69:17–22. https://doi.org/10.1016/j.theriogenology.2007.09.007.

Lonergan, P., and T. Fair. 2016. Maturation of oocytes in vitro. Annu. Rev. Anim. Biosci. 4:255–268. https://doi.org/10.1146/annurev-animal-022114-110822.

Lonergan, P., D. Rizos, J. Kanka, L. Nemcova, A. M. Mbaye, M. Kingston, M. Wade, P. Duffy, and M. P. Boland. 2003. Temporal sensitivity of bovine embryos to culture environment after fertilization and the implications for blastocyst quality. Reproduction 126:337–346. https://doi.org/10.1530/rep.0.1260337.

Lu, K. H., I. Gordon, M. Gallagher, and H. McGovern. 1987. Pregnancy established in cattle by transfer of embryos derived from in vitro fertilisation of oocytes matured in vitro. Vet. Rec. 121:259–260. https://doi.org/10.1136/vr.121.11.259.

Ma, L., J. B. Cole, Y. Da, and P. M. VanRaden. 2019. Symposium review: Genetics, genome-wide association study, and genetic improvement of dairy fertility traits. J. Dairy Sci. 102:3735–3743. https://doi.org/10.3168/jds.2018-15269.

Maher, J. W., A. Clarke, A. W. Byrne, R. Doyle, M. Blake, and D. Barrett. 2021. Exploring the opinions of Irish dairy farmers regarding male dairy calves. Front. Vet. Sci. 8:635565.

Maicas, C., S. A. Holden, E. Drake, A. R. Cromie, P. Lonergan, and S. T. Butler. 2020. Fertility of frozen sex-sorted sperm at 4×10^6 sperm per dose in lactating dairy cows in seasonal-calving pasture-based herds. J. Dairy Sci. 103:929–939. https://doi.org/10.3168/jds.2019-17131.

Matukumalli, L. K., C. T. Lawley, R. D. Schnabel, J. F. Taylor, M. F. Allan, M. P. Heaton, J. O'Connell, S. S. Moore, T. P. L. Smith, T. S. Sonstegard, and C. P. Van Tassell. 2009. Development and characterization of a high density SNP genotyping assay for Cattle. PLoS One 4:e5350. https://doi.org/10.1371/journal.pone.0005350.

Mc Hugh, N., A. G. Fahey, R. D. Evans, and D. P. Berry. 2010. Factors associated with selling price of cattle at livestock marts. Animal 4:1378–1389. https://doi.org/10.1017/S1751731110000297.

McWhorter, T. M., J. L. Hutchison, H. D. Norman, J. B. Cole, G. C. Fok, D. A. L. Lourenco, and P. M. VanRaden. 2020. Investigating conception rate for beef service sires bred to dairy cows and heifers. J. Dairy Sci. 103:10374–10382. https://doi.org/10.3168/jds.2020-18399.

Meuwissen, T. H. 2003. Genomic selection: The future of marker assisted selection and animal breeding. Accessed Jul. 8, 2021. http://www-naweb.iaea.org/NaFa/news/Meuwissen.pdf.

Meuwissen, T. H., B. J. Hayes, and M. E. Goddard. 2001. Prediction of total genetic value using genome-wide dense marker maps. Genetics 157:1819–1829. https://doi.org/10.1093/genetics/157.4.1819.

Miglior, F., B. L. Muir, and B. J. Van Doormaal. 2005. Selection indices in Holstein cattle of various countries. J. Dairy Sci. 88:1255–1263. https://doi.org/10.3168/jds.S0022-0302(05)72792-2.

Moore, S. G., and J. F. Hasler. 2017. A 100-Year Review: Reproductive technologies in dairy science. J. Dairy Sci. 100:10314–10331. https://doi.org/10.3168/jds.2017-13138.

Murphy, C., L. Shalloo, I. A. Hutchinson, and S. T. Butler. 2016. Expanding the dairy herd in pasture-based systems: The role of sexed semen within alternative breeding strategies. J. Dairy Sci. 99:6680–6692. https://doi.org/10.3168/jds.2015-10378.

Murphy, E. M., A. K. Kelly, C. O'Meara, B. Eivers, P. Lonergan, and S. Fair. 2018. Influence of bull age, ejaculate number, and season of collection on semen production and sperm motility parameters in Holstein Friesian bulls in a commercial artificial insemination centre. J. Anim. Sci. 96:2408–2418. https://doi.org/10.1093/jas/sky130.

O'Sullivan, M., S. T. Butler, K. M. Pierce, M. A. Crowe, K. O'Sullivan, R. Fitzgerald, and F. Buckley. 2020. Reproductive efficiency and survival of Holstein-Friesian cows of divergent Economic Breeding Index, evaluated under seasonal calving pasture-based management. J. Dairy Sci. 103:1685–1700. https://doi.org/10.3168/jds.2019-17374.

Parker Gaddis, K. L., S. Dikmen, D. J. Null, J. B. Cole, and P. J. Hansen. 2017. Evaluation of genetic components in traits related to superovulation, in vitro fertilization, and embryo transfer in Holstein cattle. J. Dairy Sci. 100:2877–2891. https://doi.org/10.3168/jds.2016-11907.

Perry, G. A. 2016. Factors affecting puberty in replacement beef heifers. Theriogenology 86:373–378. https://doi.org/10.1016/j.theriogenology.2016.04.051.

Pieterse, M. C., K. A. Kappen, T. A. Kruip, and M. A. Taverne. 1988. Aspiration of bovine oocytes during transvaginal ultrasound scanning of the ovaries. Theriogenology 30:751–762. https://doi.org/10.1016/0093-691X(88)90310-X.

Pike, S. J., N. M. Schreurs, R. E. Hickson, J. J. Hunt, P. R. Kenyon, D. J. Garrick, H. T. Blair, and S. T. Morris. 2019. Brief communication: Meat quality of light-weight, yearling steers of dairy origin. N. Z. J. Anim. Sci. Prod. 79:156–158.

Place, S. E., and F. M. Mitloehner. 2014. The nexus of environmental quality and livestock welfare. Annu. Rev. Anim. Biosci. 2:555–569. https://doi.org/10.1146/annurev-animal-022513-114242.

Pontes, J. H., K. C. Silva, A. C. Basso, A. G. Rigo, C. R. Ferreira, G. M. Santos, B. V. Sanches, J. P. Porcionato, P. H. Vieira, F. S. Faifer, F. A. Sterza, J. L. Schenk, and M. M. Seneda. 2010. Large-scale in vitro embryo production and pregnancy rates from *Bos taurus*, *Bos indicus*, and *indicus-taurus* dairy cows using sexed sperm. Theriogenology 74:1349–1355. https://doi.org/10.1016/j.theriogenology.2010.06.004.

Ramsbottom, G., A. R. Cromie, B. Horan, and D. P. Berry. 2012. Relationship between dairy cow genetic merit and profit on commercial spring calving dairy farms. Animal 6:1031–1039. https://doi.org/10.1017/S1751731111002503.

Renaud, D. L., T. F. Duffield, S. J. LeBlanc, D. B. Haley, and D. F. Kelton. 2017. Management practices for male calves on Canadian dairy farms. J. Dairy Sci. 100:6862–6871. https://doi.org/10.3168/jds.2017-12750.

Rendel, J. M., and A. Robertson. 1950. Estimation of genetic gain in milk yield by selection in a closed herd of dairy cattle. J. Genet. 50:1–8. https://doi.org/10.1007/BF02986789.

Ribeiro, E. S., K. N. Galvão, W. W. Thatcher, and J. E. P. Santos. 2012. Economic aspects of applying reproductive technologies to dairy herds. Anim. Reprod. 9:370–387.

Rico, C., S. Fabre, C. Medigue, N. di Clemente, F. Clement, M. Bontoux, J. L. Touze, M. Dupont, E. Briant, B. Remy, J. F. Beckers, and D. Monniaux. 2009. Anti-Müllerian hormone is an endocrine marker of ovarian gonadotropin-responsive follicles and can help to predict superovulatory responses in the cow. Biol. Reprod. 80:50–59. https://doi.org/10.1095/biolreprod.108.072157.

Ritter, C., A. Beaver, and M. A. G. von Keyserlingk. 2019. The complex relationship between welfare and reproduction in cattle. Reprod. Domest. Anim. 54:29–37. https://doi.org/10.1111/rda.13464.

Rizos, D., F. Ward, P. Duffy, M. P. Boland, and P. Lonergan. 2002. Consequences of bovine oocyte maturation, fertilization or early embryo development in vitro versus in vivo: Implications for blastocyst yield and blastocyst quality. Mol. Reprod. Dev. 61:234–248. https://doi.org/10.1002/mrd.1153.

Roche, J. R., D. P. Berry, L. Delaby, P. G. Dillon, B. Horan, K. A. Macdonald, and M. Neal. 2018. Review: New considerations to refine breeding objectives of dairy cows for increasing robustness and sustainability of grass-based milk production systems. Animal 12(s2):s350–s362. https://doi.org/10.1017/S1751731118002471.

Roche, J. R., J. M. Lee, and D. P. Berry. 2006. Climatic factors and secondary sex ratio in dairy cows. J. Dairy Sci. 89:3221–3227. https://doi.org/10.3168/jds.S0022-0302(06)72597-8.

Rojas Canadas, E., M. M. Herlihy, J. Kenneally, J. Grant, F. Kearney, P. Lonergan, and S. T. Butler. 2020a. Associations between postpartum fertility phenotypes and genetic traits in seasonal-calving, pasture-based lactating dairy cows. J. Dairy Sci. 103:1002–1015. https://doi.org/10.3168/jds.2018-16000.

Rojas Canadas, E., M. M. Herlihy, J. Kenneally, J. Grant, F. Kearney, P. Lonergan, and S. T. Butler. 2020b. Associations between postpartum phenotypes, cow factors, genetic traits, and reproductive performance in seasonal-calving, pasture-based lactating dairy cows. J. Dairy Sci. 103:1016–1030. https://doi.org/10.3168/jds.2018-16001.

Rowson, L. E. 1951. Methods of inducing multiple ovulation in cattle. J. Endocrinol. 7:260–270. https://doi.org/10.1677/joe.0.0070260.

Sanches, B. V., A. F. Zangirolamo, and M. M. Seneda. 2019. Intensive use of IVF by large-scale dairy programs. Anim. Reprod. 16:394–401. https://doi.org/10.21451/1984-3143-AR2019-0058.

Sartori, R., M. R. Bastos, and M. C. Wiltbank. 2010. Factors affecting fertilisation and early embryo quality in single- and superovulated dairy cattle. Reprod. Fertil. Dev. 22:151–158. https://doi.org/10.1071/RD09221.

Schaeffer, L. R. 2006. Strategy for applying genome-wide selection in dairy cattle. J. Anim. Breed. Genet. 123:218–223. https://doi.org/10.1111/j.1439-0388.2006.00595.x.

Shivley, C. B., J. E. Lombard, N. J. Urie, D. M. Weary, and M. A. G. von Keyserlingk. 2019. Management of preweaned bull calves on dairy operations in the United States. J. Dairy Sci. 102:4489–4497. https://doi.org/10.3168/jds.2018-15100.

Sirard, M. A. 2018. 40 years of bovine IVF in the new genomic selection context. Reproduction 156:R1–R7. https://doi.org/10.1530/REP-18-0008.

Taylor, J. F., K. H. Taylor, and J. E. Decker. 2016. Holsteins are the genomic selection poster cows. Proc. Natl. Acad. Sci. USA 113:7690–7692. https://doi.org/10.1073/pnas.1608144113.

Thomas, G. W., and P. Jordaan. 2013. Pre-slaughter mortality and post-slaughter wastage in bobby veal calves at a slaughter premises in New Zealand. N. Z. Vet. J. 61:127–132. https://doi.org/10.1080/00480169.2012.734374.

Thomasen, J. R., A. Willam, C. Egger-Danner, and A. C. Sørensen. 2016. Reproductive technologies combine well with genomic selection in dairy breeding programs. J. Dairy Sci. 99:1331–1340. https://doi.org/10.3168/jds.2015-9437.

Twomey, A. J., S. C. Ring, N. McHugh, and D. P. Berry. 2020. Carcass and efficiency metrics of beef cattle differ by whether the calf was born in a dairy or a beef herd. J. Anim. Sci. 98:ska321. https://doi.org/10.1093/jas/skaa321.

van der Werf, J. H. J., L. H. van der Waaij, A. F. Groen, and G. de Jong. 1998. An index for beef and veal characteristics in dairy cattle based on carcass traits. Livest. Prod. Sci. 54:11–20. https://doi.org/10.1016/S0301-6226(97)00167-X.

Van Eenennaam, A. L. 2019. Application of genome editing in farm animals: Cattle. Transgenic Res. 28(Suppl 2):93–100. https://doi.org/10.1007/s11248-019-00141-6.

Van Eenennaam, A. L., F. F. Silva, J. F. Trott, and D. Zilberman. 2021. Genetic engineering of livestock: The opportunity cost of regulatory Delay. Annu. Rev. Anim. Biosci. 9:453–478.

VanRaden, P. M. 2004. Invited review: Selection on net merit to improve lifetime profit. J. Dairy Sci. 87:3125–3131. https://doi.org/10.3168/jds.S0022-0302(04)73447-5.

VanRaden, P. M., J. B. Cole, and K. L. P. Gaddis. 2018. Net merit as a measure of lifetime profit: 2018 revision. United States Department of Agriculture.

Veerkamp, R. F., P. Dillon, E. Kelly, A. R. Cromie, and A. F. Groen. 2002. Dairy cattle breeding objectives combining yield, survival and calving interval for pasture-based systems in Ireland under different milk quota scenarios. Livest. Prod. Sci. 76:137–151. https://doi.org/10.1016/S0301-6226(02)00006-4.

Viana, J. H. 2020. 2019 Statistics of embryo production and transfer in domestic farm animals. Accessed Jul. 8, 2021. https://www.iets.org/Portals/0/Documents/Public/Committees/DRC/IETS_Data_Retrieval_Report_2019.pdf.

Viana, J. H. M., A. C. S. Figueiredo, and L. G. B. Siqueira. 2017. Brazilian embryo industry in context: Pitfalls, lessons, and expectations for the future. Anim. Reprod. 14:476–481. https://doi.org/10.21451/1984-3143-AR989.

Viana, J. H. M., L. G. B. Siqueira, M. P. Palhao, and L. S. A. Camargo. 2012. Features and perspectives of the Brazilian in vitro embryo industry. Anim. Reprod. 9:12–18.

Willett, E. L., W. G. Black, L. E. Casida, W. H. Stone, and P. J. Buckner. 1951. Successful transplantation of a fertilized bovine ovum. Science 113:247. https://doi.org/10.1126/science.113.2931.247.

Wolfová, M., J. Wolf, J. Kvapilik, and J. Kica. 2007. Selection for profit in cattle: II. Economic weights for dairy and beef sires in crossbreeding systems. J. Dairy Sci. 90:2456–2467. https://doi.org/10.3168/jds.2006-615.

Xu, Z. Z. 2014. Application of liquid semen technology improves conception rate of sex-sorted semen in lactating dairy cows. J. Dairy Sci. 97:7298–7304. https://doi.org/10.3168/jds.2014-8507.

Xu, Z. Z., D. L. Johnson, and L. J. Burton. 2000. Factors affecting the sex ratio in dairy cattle in New Zealand. Proc. N.Z. Soc. Anim. Prod. 60:301–302.

ORCIDS

Alan D. Crowe https://orcid.org/0000-0001-6108-9254
Pat Lonergan https://orcid.org/0000-0001-5598-5044
Stephen T. Butler https://orcid.org/0000-0003-1542-8344