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A 100-Year Review: Reproductive technologies in dairy science[1]

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ABSTRACT

Reproductive technology revolutionized dairy production during the past century. Artificial insemination was first successfully applied to cattle in the early 1900s. The next major developments involved semen extenders, invention of the electroejaculator, progeny testing, addition of antibiotics to semen during the 1930s and 1940s, and the major discovery of sperm cryopreservation with glycerol in 1949. The 1950s and 1960s were particularly productive with the development of protocols for the superovulation of cattle with both pregnant mare serum gonadotrophin/equine chorionic gonadotrophin and FSH, the first successful bovine embryo transfer, the discovery of sperm capacitation, the birth of rabbits after in vitro fertilization, and the development of insulated liquid nitrogen tanks. Improved semen extenders and the replacement of glass ampules with plastic semen straws followed. Some of the most noteworthy developments in the 1970s included the initial successes with in vitro culture of embryos, calves born after chromosomal sexing as embryos, embryo splitting resulting in the birth of twins, and development of computer-assisted semen analysis. The 1980s brought flow cytometric separation of X- and Y-bearing sperm, in vitro fertilization leading to the birth of live calves, clones produced by nuclear transfer from embryonic cells, and ovum pick-up via ultrasound-guided follicular aspiration. The 20th century ended with the birth of calves produced from AI with sexed semen, sheep and cattle clones produced by nuclear transfer from adult somatic cell nuclei, and the birth of transgenic cloned calves. The 21st century has seen the introduction of perhaps the most powerful biotechnology since the development of artificial insemination and cryopreservation. Quick, inexpensive genomic analysis via the use of single nucleotide polymorphism genotyping chips is revolutionizing the cattle breeding industry. Now, with the introduction of genome editing technology, the changes are becoming almost too rapid to fully digest.
Key words: artificial insemination, multiple ovulation and embryo transfer, in vitro embryo production, sexed semen

INTRODUCTION

Artificial insemination was the first reproductive technology applied to cattle, initially in Russia and Denmark during the early 1900s (Ivanoff, 1922; Perry, 1945). The primary driving force behind AI was its potential to increase the rate of genetic gain in livestock populations by widespread use of sires with elite genetic merit. Cooperative AI centers began in Denmark in 1936 and were replicated internationally (Perry, 1945). Not since the invention of the milking machine has a technology had such an effect. For farmers, transition away from natural service breeding required changes in herd reproductive management. In addition to genetic gains, AI breeding avoided the need to have bulls on each farm and contributed to improved safety for farm employees. Today, use of AI has grown to the extent that internationally approximately 130 million cattle are submitted for AI annually (Vishwanath, 2003).

Birth of the first calves from the use of frozen–thawed semen (Polge and Rowson, 1952) and embryos (Wilmut and Rowson, 1973) represented important milestones during the past century. Both developments were critical to the feasibility and growth of large-scale AI and embryo transfer (**ET**) operations globally because it became no longer essential to use only unfrozen (fresh) semen and embryos. Today, the vast majority of inseminations and transfers are performed with frozen–thawed semen and embryos, respectively (Vishwanath, 2003; Hasler, 2014).

Techniques for multiple ovulation 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). In vitro developments in oocyte maturation and sperm capacitation, fertilization, and embryo

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Table 1. Key events in our understanding of reproductive biology before the early 1900s[1]

Event	Year
de Graaf describes testis structure.	1668
de Graaf describes follicle structure.	1672
Van Leuwenhoek and Ham describe spermatozoa.	1678
Spallanzani reports AI of a bitch followed by birth of pups.	1784
Spallanzani reports that sperm survived chilling.	1803
Von Baer describes oocytes.	1827
Kölliker demonstrates that the testes produce sperm.	1841
Barry observes the fusion of sperm and oocyte.	1843
Leydig describes Leydig cells.	1851
Sertoli describes Sertoli cells.	1865
Waldeyer describes the ovary and oocyte formation.	1870
Von Ebner describes spermatogenesis.	1871
Dreisch demonstrates artificial embryo twinning in the sea urchin (an invertebrate).	1885
Heape performs the first mammalian embryo transfer.	1890
Spemann demonstrates artificial embryo twinning in the salamander (a vertebrate).	1902

[1]Data from Marshall (1910); Genetic Science Learning Center (2014).

culture during the 1970s and 1980s led to the birth of the first completely in vitro embryo produced calves in 1987 (Lu et al., 1987). The ovum pick-up (**OPU**) method for repeated oocyte recovery from live donor females was developed during the late 1980s by Pieterse et al. (1988). Protocols for in vitro embryo production (**IVP**) were further developed in the 1990s as an alternative to multiple ovulation and ET by combining OPU, in vitro fertilization (**IVF**), and ET (Looney et al., 1994). The practice of IVP has grown rapidly since the 2000s, with large-scale commercial operations established primarily in South America (Hasler, 2014).

Cloning techniques for production of identical sheep began in the 1970s, first by embryo splitting (Willadsen, 1979) and subsequently replaced by nuclear transfer (Willadsen, 1986; Prather et al., 1987). A far more powerful technology, however, involved what is referred to as somatic cell nuclear transfer (**SCNT**), allowing the cloning of an animal whose genetics and morphology were already known. Dolly the sheep was the first example of success with SCNT (Wilmut et al., 1997). The technique was also applied to the production of transgenic cattle (Cibelli et al., 1998) and has so far found its greatest use in production of transgenic and gene-edited animals for research or pharmaceutical use. Examples include development of cattle with mastitis resistance (Liu et al., 2014) and polled traits (Carlson et al., 2016). Nuclear transfer can be combined with genomic selection to further accelerate genetic gain by reducing the generation interval (Kasinathan et al., 2015).

Production of offspring of predetermined sex has been long sought after by livestock producers. Sorting of X- and Y-chromosome-bearing sperm by flow cytometry has been possible since the 1980s (Garner et al., 1983), but the initial procedures killed sperm. It was not until 1989 that the first offspring (rabbits) from sexed semen were born (Johnson et al., 1989), and it was 1993 before the first calf from sex-sorted semen was born (Cran et al., 1993). In recent years, the use of sexed semen has grown internationally to the extent that bovine semen is currently being sex sorted in approximately 15 countries.

It is a credit to the many scientists, farmers, veterinarians, and breeding organizations that have translated the basic science to on-farm and laboratory technologies. In this review, we highlight the scientific advances that contributed to the development of reproductive technologies in dairy science. To put the advances of the past century in perspective, key events in reproductive biology preceding the early 1900s are summarized in Table 1. The review begins with the development of AI and continues chronologically with each advancement (see Appendix Table A1).

DEVELOPMENTS IN AI

Before the development of AI, cows were bred by natural service and bulls were often shared among farms. It was in Denmark in 1936 that the first large-scale bovine AI organization was established before similar organizations were established in the United States and worldwide (Perry, 1945). Some producers and breeders initially opposed the use of AI because early procedures for collection, handling, and insemination were cumbersome (Polge, 2007; Wilmot, 2007). The benefits of AI over natural service, however, soon became obvious. Artificial insemination was critical to increasing the reproductive potential of sires with elite genetic merit. The reduction in disease transmission between animals and the opportunity to evaluate sperm production and characteristics provided additional importnant benefits (Ivanoff, 1922; Perry, 1945). Most important, AI enabled precise genetic evaluation of bulls via hundreds