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40th Anniversary Special Issue

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

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ABSTRACT

After the first successful transfer of mammalian embryos in 1890, it was approximately 60 years before significant progress was reported in the basic technology of embryo transfer (ET) in cattle. Starting in the early 1970s, technology had progressed sufficiently to support the founding of commercial ET programs in several countries. Today, well-established and reliable techniques involving superovulation, embryo recovery and transfer, cryopreservation, and IVF are utilized worldwide in hundreds, if not thousands, of commercial businesses located in many countries. The mean number of embryos produced via superovulation has changed little in 40 years, but there have been improvements in synchrony and hormonal protocols. Cryopreservation of in vivo-derived embryos is a reliable procedure, but improvements are needed for biopsied and in vitro-derived embryos. High pregnancy rates are achieved when good quality embryos are transferred into suitable recipients and low pregnancy rates are often owing to problems in recipient management and not technology per se. In the future, unanticipated disease outbreaks and the everchanging economics of cattle and milk prices will continue to influence the ET industry. The issue of abnormal pregnancies involving in vitro embryos has not been satisfactorily resolved and the involvement of abnormal epigenetics associate with this technology merits continued research. Last, genomic testing of bovine embryos is likely to be available in the foreseeable future. This may markedly decrease the number of embryos that are actually transferred and stimulate the evolution of more sophisticated ET businesses.

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1. Introduction

It is widely recognized that the first documented live birth resulting from the transfer of mammalian embryos was achieved by Walter Heape in 1890 [1]. In a subsequent paper, Heape described his technique for handling rabbit embryos, which involved spearing them on the tip of a needle and transferring them to a recipient without an intermediary step of placing them in holding medium [2]. Heape's varied discoveries and successes in the field of reproduction were described in detail by John Biggers, who was awarded the Pioneer Award (*PA*) by the International Embryo Transfer Society (IETS) in 1990 [3]. Thirty years then passed before another success in producing mammalian offspring from embryo transfer (ET) was reported and it again involved rabbits [4]. The first birth of a calf resulting from ET is credited to E.L. Willet, et al., at the University of Wisconsin [5] and occurred 63 years ago. The research by Willet and the other early workers that led up to this first success in cattle is elegantly described by Keith Betteridge (2003 IETS-*PA*) in a paper published in *Theriogenology* in 2000 [6].

Protocols for the superovulation of cattle [7–9], appropriate media (for review see [10,11]), and the

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surgical recovery and transfer of embryos [9,12] were developed primarily starting in the late 1940s and into the 1960s. These procedures, which led to the establishment of the modern ET industry in the early 1970s, are covered in a number of reviews, including some especially thorough contributions by Betteridge [13,14], Adams [15], Foote (2002 IETS-PA) and Onuma [10], and Seidel (2008 IETS-PA) [16].

In cattle, ET on a commercial basis has grown into a mature industry that is active today on a worldwide basis. Coincident with this 40th anniversary edition of *Theriogenology*, the commercial ET industry is today just a few years past 40 years of age. Also, the 40th anniversary of the IETS will be celebrated at the annual meeting in Reno, Nevada, in January 2014.

The modern livestock ET industry is a result of the pioneering efforts of two groups: The scientists who initially developed the procedures and techniques of ET, and the commercial ET practitioners who modified this technology, making it practical and available first to the cattle industry and then to other livestock species. When possible, the contribution of practitioners will be acknowledged. However, a fair amount of technology and ET improvements from the private sector have not been published and are available only in verbal, anecdotal form.

Seeking to provide comprehensive coverage of ET in cattle, whether on the basis of the historical development of the technology, the development and growth of the commercial industry, or the research applications that are utilized, is simply not possible in a short review paper. While preparing this manuscript, I sat in my home office surrounded by reprints of at least 1000 published papers dealing with some aspect of bovine ET, not including a number of books and published proceedings. A recent survey of PubMed showed a total of 2051 references on bovine ET, 609 on bovine superovulation, and 877 on bovine IVF.

The invitation to write this review for Theriogenology represents a daunting challenge; I was afforded a good deal of freedom and I have chosen to emphasize the following: to briefly cover the early history and development of bovine ET; outline the growth of the commercial ET industry, primarily in North America; and describe personal experiences in the growth and evolution of the commercial ET industry. However, my experiences in the ET industry are not particularly unique or unusual, but they span approximately 40 years, and I believe a personal view may sometimes be more interesting and informative than limiting coverage to published scientific papers, although I will emphasize key studies published in Theriogenology. Because of the breadth of the subject and space limitations, it is not possible to include all relevant references. Using IVF as an example, there are 170 pages of references in Ian Gordon's (1998 IETS-PA) 1994 comprehensive review of cattle IVF [17]. Consequently, many fine studies published in journals other than Theriogenology, and many that have appeared in Theriogenology are not included in this review. I offer a sincere apology to any authors whose work I may have covered superficially or outright failed to include.

2. The early days of commercial ET

A large degree of recognition must be extended to Tim Rowson (1985 IETS-PA) and his colleagues at the Agricultural Research Council Unit of Animal Reproduction in Cambridge, Great Britain, for contributing much of the technology that got commercial bovine ET started in early 1970s. The Animal Research Council unit initiated surgical recovery and transfer of bovine embryos, which led to the establishment in the early 1970s of some of the first ET units in North America, including Alberta Livestock Transfer in Calgary Alberta; Modern Ova Trends in Norval, Ontario; Colorado State University (CSU) in Ft. Collins; Carnation Genetics in Hughson, California; and Codding Embryological Science, Inc., in Foraker, Oklahoma. All of these units built and operated expensive surgical facilities for both the donors and recipients that underwent aseptic surgery under general anesthesia. These early commercial programs greatly extended and improved the work started by research programs such as the station in Cambridge. During this period of time there were also significant contributions being made from the growing ET industry in other areas of the world.

As technology rapidly improved and commercial ET units rapidly came on line, there were two noteworthy meetings of academicians and practitioners involved with both ET research and commercial services. In December 1975, a group of scientists and practitioners representing both North America and Europe met at Cambridge. A book edited by Rowson detailing the presentations at this meeting was published by the European Commission of the European Communities [18]. In July 1976, many of the participants in the Cambridge conference, plus a number of additional persons met to discuss ET during the 8th International Congress on Animal Reproduction in Krakow, Poland. The resulting monograph [19] detailing the papers and discussions from this meeting and the Rowson publication from the Cambridge meeting [18] were enormously helpful in advancing ET science into the commercial realm, and much of the science described remains accurate and relevant today. A few years later, in 1982, an excellent review edited by Cyril Adams of both the history and the current status of ET procedures was published [15].

In addition to development of technology, a second factor strongly influenced the early growth of the ET industry in North America. The legal importation of so-called exotic cattle from Europe was approved by the Canadian government [14,20]. These cattle, initially representing several breeds including Simmental, Limousin, and Charolais, could not be imported directly into the United States, but once they were in Canada, they could qualify for movement into the United States. Three-quarter and even half-blood females sold for very high prices and these cattle fueled the early ET industry in North America.

Starting in 1973 through 1975, the rapid increase in the number of Simmental calves born in the United States as a result of ET is shown in Table 1. Although more than 1500 Simmentals were reported born during this period, no Angus and only 21 Holsteins were recorded by their respective breed associations. Of the 33 cattle breeds

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