Embryo transfer as a reproductive management tool

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Introduction – embryo transfer is more than just a tool for genetic selection

Regardless of whether generated by superovulation (otherwise called multiple ovulation – embryo transfer; MOET) or by in vitro production (IVP), the most common purpose of transfer of cattle embryos today is for genetic improvement. The advent of genomics means that genetically-superior females can be identified with acceptable accuracy and these females can be used to produce up to 100 or more embryos from a cow or heifer each year. Embryo transfer can also be used to rapidly establish a herd of high-producing animals, as exemplified by the large numbers of embryos exported from North America to other countries to establish high-yielding dairy herds. Production of embryos in vitro is also an effective means of utilizing sexed semen because one straw of sexed semen can be used to produce multiple embryos in vitro. The pregnancy rates following transfer into recipients is similar between cows receiving embryos produced sexed semen and those receiving embryos produced with conventional semen (Xu et al., 2006; Rasmussen et al., 2012).

A less well appreciated use of the bovine embryo is as a tool for improving pregnancy rates. In general, the percent of cows pregnant after receiving an embryo is not appreciably higher than pregnancy success following artificial insemination (AI). However, embryo transfer can improve fertility of cow populations when reproduction is suboptimal because of heat stress. There is also some evidence in dairy cattle that embryo transfer can improve pregnancy rates of lactating cows classified as repeat breeders.

The physiological basis for improvement in fertility using embryo transfer

Pregnancy rates can be improved in infertile cows by embryo transfer because the procedure bypasses certain causes of pregnancy failure that occur before the time when an embryo is typically transferred into cows (day 7-8 after ovulation). Among the reasons why a cow fails to become pregnant after AI are anovulation, fertilization failure and early embryonic death. For an embryo transfer recipient, these causes are reduced because most embryos used for transfer are the product of a successful fertilization (with the exception of a few parthenotes) and the embryo has been capable of developing to the morula stage or blastocyst stage when it is typically transferred.

Embryo transfer during heat stress

The best documented example of the use of embryo transfer to improve fertility is for the heat-stressed cow. Much of the negative effect of heat stress on pregnancy establishment involves negative effects on the oocyte or the developing embryo. The oocyte can be damaged by heat stress as early as 105 days before ovulation (Torres-Júnior et al., 2008) and remains sensitive to heat stress through oocyte maturation on the day of ovulation (Putney et al., 1989b). Development of the early embryo is also inhibited by heat stress but it becomes resistant to elevated temperature by about the 8-cell stage of development (Hansen, 2013). Experimentally, heat stress at Day 1 after estrus reduced embryonic development but heat stress at Days 3, 5, and 7 had no effect (Ealy et al., 1993). What this means is that the morula and blastocyst stage embryos that are typically transferred into recipients are largely resistant to damage by maternal hyperthermia and subsequent development is unlikely to be compromised by heat stress.

The effectiveness of embryo transfer for improving pregnancy rate during heat stress is shown by representative experiments depicted in Figure A. The improvement in fertility with ET as compared to AI has been seen when embryos were produced by MOET (Putney et al., 1989a; Drost et al., 1999; Rodrigues et al., 2004; Vasconcelos et al., 2011) or by IVP (Ambrose et al., 1999; Al-Katanani et al., 2002; Block et al., 2010; Stewart et al., 2011). The poor cryosurvival of IVP embryos means, however, that pregnancy rate was improved during heat stress when IVP embryos were transferred fresh but not when transferred after conventional freezing or vitrification (see data from Drost et al., 1999; Block et al., 2010 and Stewart et al., 2011 presented in Figure A).

Using embryo transfer, the summer decline in fertility of lactating cows can be largely eliminated. This idea is shown graphically for an experiment in Brazil in Figure 1B (Rodriques et al. (2004) and there are other examples in the literature (Putney et al., 1988; Chebel et al., 2008; Vasconcelos et al., 2011; Ferraz et al., 2016).

One important consideration when carrying out embryo transfer during heat stress is that estrous behavior is reduced in cows exposed to heat stress. Accordingly, the technique is usually performed using fixed-time embryo transfer based on one or more ovulation synchronization protocols such as Ovsynch. In such systems, the day of ovulation (i.e., day of insemination for timed AI protocols) is considered day 0 when calculating synchrony with the embryo. Not every cow responds successfully to ovulation synchronization protocols so an embryo is transferred only into those recipients with a functional corpus luteum as determined by rectal palpation or ultrasonic examination.

Repeat breeder cows

Another possible use for embryo transfer is to improve fertility of the repeat-breeder cow. These animals are defined as those that have not become pregnant after multiple inseminations (usually three). There are three experiments supporting the idea that embryo transfer can increase fertility for these type of animals as compared to fertility after AI (Table). Each of these studies involved small numbers of animals and further work is warranted. Moreover, it is unlikely that embryo transfer will prevent all sources of infertility associated with the repeat-breeding condition. Ribeiro et al. (2016) observed that negative effects of disease incidence (uterine or non-uterine) before breeding on fertility was apparent in cows subjected to either AI or embryo transfer.

Can embryo transfer be used to improve pregnancy rates in the absence of infertility?

Based on what was stated at the beginning of this paper, one would expect that pregnancy rate following embryo transfer would usually be higher than pregnancy after AI because failure of achieve pregnancy because of oocyte defects, anovulation, misdiagnosis of estrus, errors in insemination, poor semen quality, fertilization failure, and disruptions in early embryonic development would be prevented. Surprisingly, however, there is not usually a fertility advantage for embryo transfer as compared to AI unless there is some underlying cause of infertility such as heat stress or the repeat-breeder condition. This phenomenon is illustrated in the experiment of Rodrigues et al. (2004) depicted in Figure B. Although pregnancy rates were much higher for embryo transfer than AI in the warm months, pregnancy rates were similar for embryo transfer and AI in cool months of the year. Similar results were seen in studies with lactating cows in Wisconsin (Sartori et al., 2006) and Florida including one performed in cool months (Rasmussen et al., 2012) and one using data collected year-round (Ribeiro et al., 2016). The reason why ET does not meet the promise of improving fertility in most situations is not known. It may be that technical limitations in embryo production or transfer limit the expected improvement in pregnancy rate.

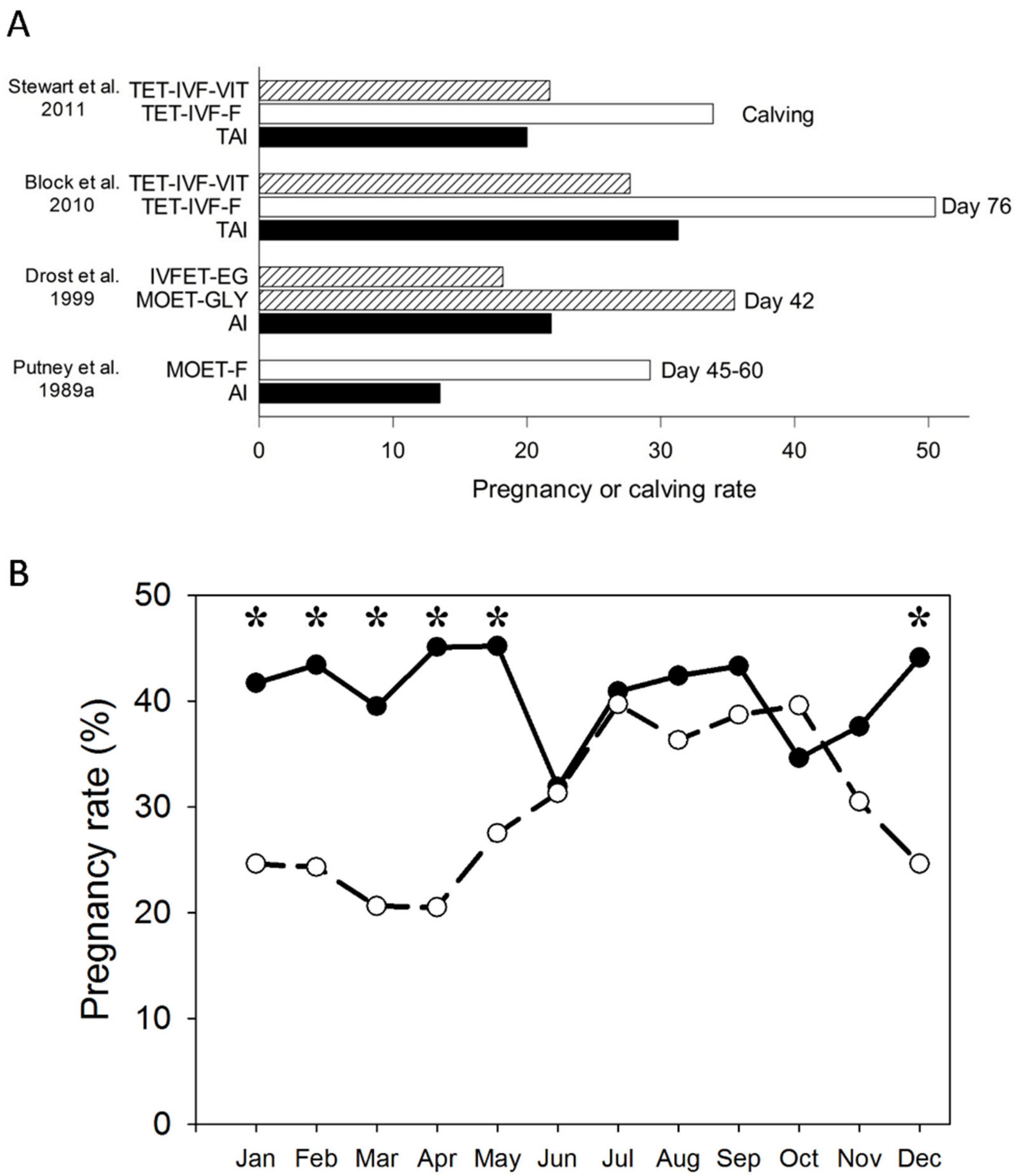

Figure. Enhancement of pregnancy rates during heat stress using embryo transfer. Data in Panel A represent results from various experiments in the summer in Florida. Abbreviations are as follows: AI: artificial insemination; EG, frozen in ethylene glycol; F, fresh; Gly, frozen in glycerol; IVFET, embryo transfer with an in vitro produced embryo; MOET, multiple ovulation embryo transfer; TAI, timed artificial insemination; TET-IVF, timed embryo transfer with an in vitro produced embryo; VIT, vitrified. The numbers in the graph represent the day of gestation at which pregnancy diagnosis was carried out. Panel B represents data from a commercial dairy in Brazil in which cows were either inseminated or received an embryo produced by superovulation (Rodriques et al., 2004). Asterisks represent months in which pregnancy rate was different between AI and ET. The figure is reproduced from Hansen (2013).

Table. Improvement in fertility in repeat-breeder dairy cows by embryo transfer (ET) as compared to artificial insemination (AI).

Study	Location	Embryo type	Definition of repeat-breeder	Treatment	Number of animals	Pregnancy rate, percent
Tanabe et al., 1985	USA-Pennsylvania	MOET	>3 infertile services	AI at estrus	22	50
				ET at estrus	23	70
Son et al., 2007	South Korea	MOET	3 or more infertile services	AI at estrus	27	18.5
				Timed AI	13	7.7
				Timed ET	13	53.8
Block et al., 2010	USA – Florida	IVP	> 3 infertile services	Timed AI	33	21.1
				Timed ET-fresh	25	60.0
				Timed ET-vitrified	31	29.0

Conclusion

Based on the experiments conducted to date, there is a high degree of confidence that embryo transfer can improve pregnancy rate when heat stress is a factor. Although the evidence is less clear, there may also be an improvement in fertility using embryo transfer for repeat-breeder cows. The decision to use embryo transfer for fertility enhancement depends on an individual cow's fertility, the expected improvement in pregnancy rate caused by using embryo transfer, the cost of the embryo available for transfer, and the economic value of getting a cow pregnant. For a discussion of the economic value of embryo transfer, see papers by Ribeiro et al. (2012) and Kaniyamattam et al. (2018).

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