

Impact of Heat Stress on Female Fertility

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The Nature of the Problem

Heat stress has two major actions on physiology of the female that reduce the probability of a cow becoming pregnant. First, heat stress reduces ability to detect estrus. On one dairy in Florida, only about 18-24% of estruses in hot months were detected by herdsmen while 45-56% of estrus periods were detected in cool months (Thatcher and Collier, 1986). The reduction in estrus detection is the result of effects of heat stress on cow behavior (for example, reduced walking time; López-Gatiús et al., 2005) and on reduced circulating concentrations of the hormone estradiol-17 β that causes estrous behavior (Gilad et al., 1993). Secondly, heat stress causes a large reduction in fertility. In lactating dairy cows, pregnancy rates per insemination in the summer can be as low as 10-20% (Hansen and Aréchiga, 1999). Fertility is reduced because heat stress can damage both the oocyte and early embryo (Hansen, 2013). The oocyte can be compromised by heat stress as early as 105 days before ovulation (Torres-Júnior et al., 2008) and as late as the peri-ovulatory period (Putney et al., 1989b). The early embryo is also initially sensitive to heat stress but quickly becomes resistant so that heat stress on day 1 after estrus reduced embryonic development whereas heat stress at day 3 had no effect (Ealy et al., 1993). The times in the reproductive cycle in which the cow is sensitive to heat stress are illustrated in Figure 1.

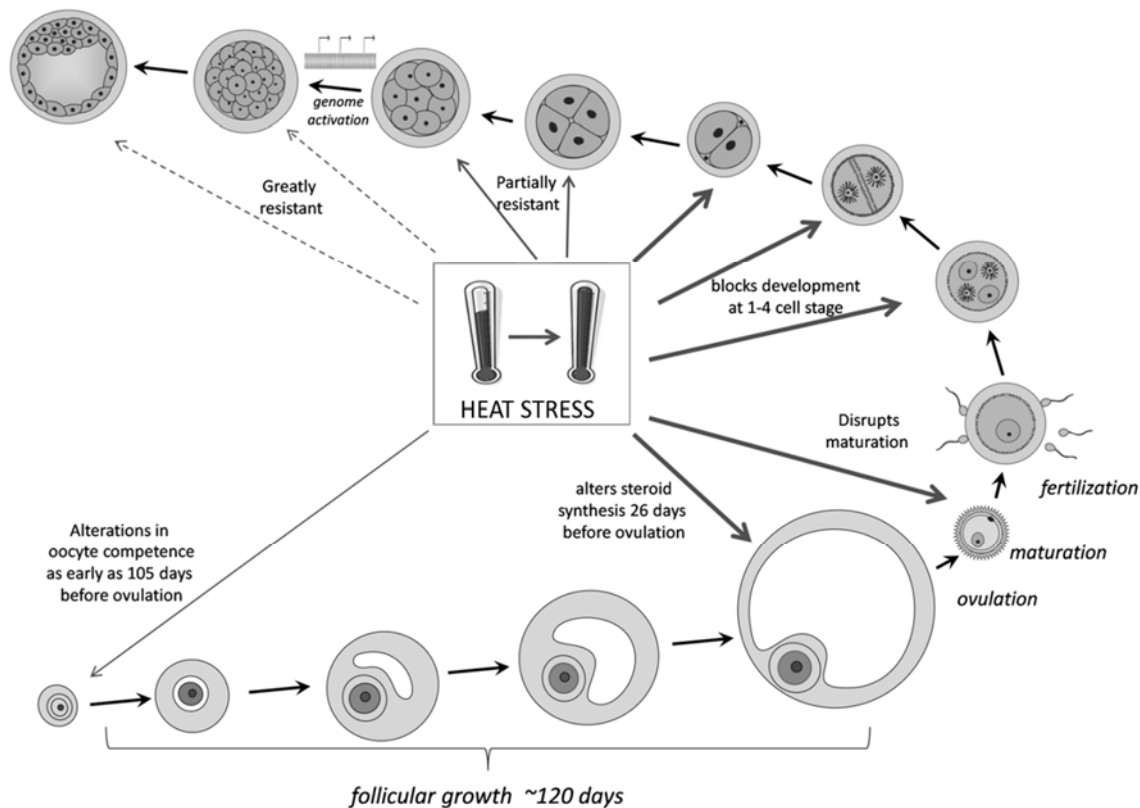


Figure 1. Diagram illustrating the timing of effects of heat stress on reproductive events that affect fertility. Heat stress during follicular growth can affect oocyte competence for fertilization and development. It is not known how early in the process of folliculogenesis that heat stress is disruptive to oocyte development but it could be as early as 105 days before ovulation. Oocyte maturation around the time of estrus is also compromised by heat stress. The early cleavage-stage embryo remains susceptible to heat stress during the first 1-2 days after estrus (1-cell to 4-cell stage) but the embryo then begins gaining resistance to maternal heat stress. By the blastocyst stage at Day 7 after estrus, the embryo is largely resistant to heat stress.

Heat stress is largely a problem of the lactating dairy cow. Non-lactating dairy animals and beef cattle are much less likely to experience infertility during heat stress. In Florida, for example, conception rates in Holsteins declined in the summer for lactating cows but not for non-lactating heifers (Badinga et al., 1985). The lactating cow is very susceptible to heat stress because the large amounts of heat produced as a result of lactation makes it difficult to regulate body temperature during heat stress. Hyperthermia (elevated body temperature) in lactating cows can occur at air temperatures as low as 77-84°F (Berman et al., 1985; Dikmen and Hansen, 2009).

Beef cattle can also be affected by heat stress, particularly in feedlot situations (Mitlöhner et al., 2002) or when grazing fescue-infected pastures (Caldwell et al., 2013), but several factors mitigate against large effects on reproduction in beef cattle. An example of the lack of seasonal effects on reproductive function of beef cattle is shown in Figure 2 for beef cattle in Oklahoma. The factors that limit the impact of heat stress on beef cattle reproduction include the existence of beef breeds that are genetically resistant to heat stress (Gaughan et al., 2010), seasonal breeding patterns that ensure that cows are not bred at the warmest time of year, and relatively low amounts of metabolic heat production as compared to lactating dairy cows.

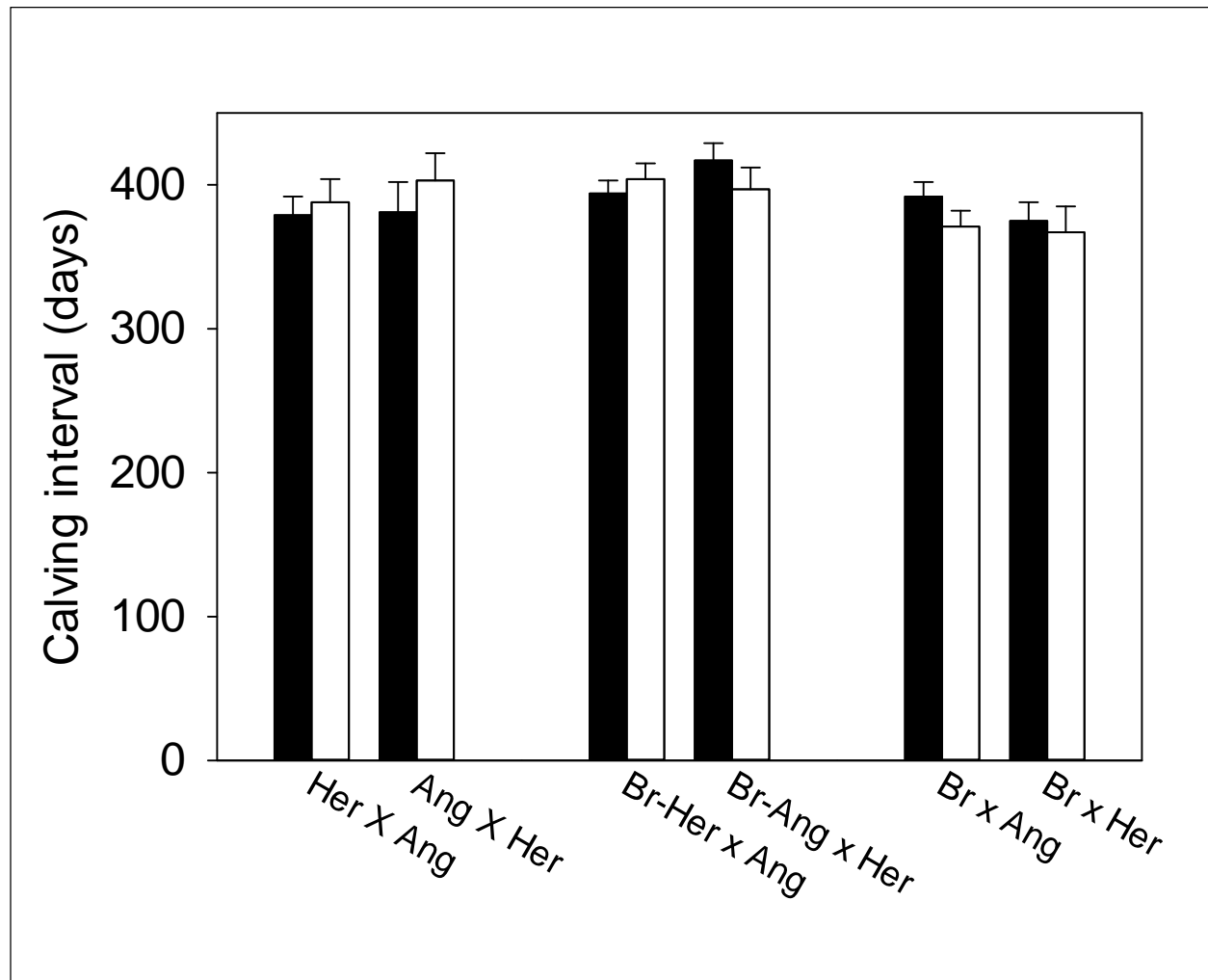


Figure 2. Lack of seasonal effect on calving interval in Oklahoma. Shown are calving intervals for cows calving in spring (black bars) and fall (white bars) for various types of cattle. Abbreviations: Ang, Angus, Br, Brahman, Her, Hereford. Data are from McCarter et al. (1991).

Despite the fact that beef cattle are much more resistant to heat stress than dairy cattle, it is important not to be complacent about the problem but rather to be aware of approaches to reduce the negative consequences of heat stress. Global climate change may well increase the severity of heat stress in many regions of the world where beef cattle are currently raised. Genetic selection for increased growth could also result in cattle being more susceptible to heat stress because of the associated increase in heat production.

Alleviating actions of heat stress on reproductive function is difficult. The most common approach for dairy cattle is to provide housing that minimizes heat stress. Incorporation of features such as shade structures, fans, and sprinklers, and misters or foggers can be seen in many dairies in hot regions of the world. While very important, cooling cows does not totally prevent reduced reproductive function during heat stress. In Florida, for example, seasonal variation in pregnancy rate persisted in a herd where cows were cooled with sprinklers and fans (Hansen and Aréchiga, 1999). In Israel, pregnancy rate per insemination in intensively-cooled herds was 19% in summer vs 39% in winter for high-producing herds and 25% in summer vs 40% in winter for low-producing herds (Flamenbaum and Ezra, 2006). Cooling is not a very attractive option for cattle managed on pasture.

In this paper, I will put forward two methods for reducing the impact of heat stress that can be applied to cattle managed intensively or on pasture. The first method, incorporation of timed artificial insemination (AI) protocols, eliminates the need for estrus detection and therefore prevents loss of reproductive performance caused by poor estrus detection. The second method is embryo transfer. While not always practical economically, this technique bypasses pregnancy losses caused by effects of heat stress on the oocyte and early embryo.

Timed AI

Protocols for timed AI can completely bypass problems associated with detecting estrus during heat stress because timing of ovulation is synchronized and insemination can be implemented at a fixed time without the need for estrus detection. What timed AI does not do is reverse damage to the oocyte or embryo caused by heat stress. Nonetheless, implementation of timed AI programs during heat stress can increase the rate at which cows get pregnant after calving because of an increase in the number of eligible cows that are inseminated.

The effectiveness of timed AI during heat stress can be examined by looking at results from two experiments with dairy cows conducted in the summer (Table 1). The first experiment was conducted in south Florida by Aréchiga et al. (1998). Cows were assigned to either be bred at first detected estrus after the voluntary waiting period of 70 days or were subjected to the Ovsynch timed AI procedure to be inseminated at 70 days after calving. Implementation of timed AI reduced the interval from calving to first service by 10 days. There was no difference in the proportion of cows that became pregnant after first insemination between treatments. Moreover, few animals became pregnant, undoubtedly because of the high degree of heat stress. Nonetheless, more cows were pregnant by 90 days postpartum in the timed AI group, presumably because more cows had been inseminated.

Table 1. Effectiveness of timed insemination protocols for increasing pregnancy rates of lactating Holsteins when implemented during periods of heat stress in Florida and Kansas.

Experiment ^a	Treatment ^b	No. of cows	Interval, calving to first service, days	Cows bred within 7 d after PGF	Pregnancy rate at first service	Pregnancy rate at 90-d postpartum
Florida	Estrus	184	82.4	--	12.5%	9.8%
	TAI	169	72.4***	--	13.6%	16.6%*
Kansas	SS	128	--	57%	32.0%	17.9%
	TAI	207	---	100%	33.3%	33.3%**

^a Florida: Aréchiga et al. (1998); Kansas: Cartmill et al. (2001).

^b Estrus = breeding at each observed estrus beginning at Day 70 postpartum; TAI = timed artificial insemination followed by breeding at all observed estrous periods thereafter; SS=Select Synch; GnRH followed by prostaglandin F-2 α (PGF) 7 d later and breeding at detected estrus for the next 21 d .

* $P < 0.05$ ** $P < 0.01$ *** $P < 0.001$

Similar results were obtained in Kansas by Cartmill et al. (2001). In this experiment, one group of cows were subjected to an estrous synchronization regimen (Select Synch) whereas another group was inseminated using the Ovsynch protocol. The overall level of fertility was higher than for the Florida study. Like for the Florida experiment, timed AI did not increase the percent of cows pregnant at first insemination after calving. However, more cows were inseminated within 7 days after the TAI treatment than after the estrous synchronization treatment. As a result, the percent of cows pregnant at 90 days postpartum was almost twice as high for the timed AI group (Table 1).

While timed AI can increase the number of heat-stressed cows that are inseminated, it cannot increase the percent of inseminated cows that become pregnant. Unfortunately, no pharmacological treatment has been identified that can consistently increase pregnancy rate per AI during heat stress (see Hansen, 2011 for review). Among the treatments that have been examined are treatment with human chorionic gonadotropin at day 5 of the estrous cycle to increase circulating progesterone concentrations, treatment with bovine somatotropin to increase secretion of the embryoprotective molecule insulin-like growth factor-1 and treatment with gonadotropin releasing hormone to extend lifespan of the corpus luteum. The ineffectiveness of hormonal treatments is probably related to the broad period of time in which the oocyte and early embryo are susceptible to disruption by heat shock. Treatments that might reverse effects of heat stress at one physiological window cannot reverse effects at others. Consider, for example, use of chorionic gonadotropin to increase output of progesterone by the corpus luteum. Such a treatment might be effective at reversing effect of heat stress on circulating progesterone concentrations after ovulation (Wolfenson et al., 2000) but this effect would not improve fertility in a cow whose oocyte was already damaged by heat stress occurring at some time before ovulation.

Embryo Transfer

Embryo transfer was developed as a tool to increase the number of offspring from genetically-superior females. This technology can also be used for improving fertility during heat stress (Figure 3). Embryo transfer is, in fact, the best method available for increasing pregnancy rate in lactating cows exposed to heat stress.

As shown in Figure 1, fertility is low in the summer largely because of damage to the growing follicle, oocyte and embryo caused by exposure to maternal hyperthermia. 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 on the day of ovulation (Putney et al., 1989b). The early embryo, too, can be damaged by heat stress but soon acquires biochemical mechanisms that protect it from elevated temperature (Hansen, 2013). Thus, 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).

In embryo transfer protocols, the only embryos typically transferred are those that have developed normally. Thus, the embryo that is transferred into a heat-stressed recipient has, for one reason or another, escaped effects of heat stress. In addition, embryos have become resistant to heat stress by the time they reach the stage of development where they are ready to be transferred into a recipient (the morula or blastocyst stage). Thus, it is unlikely that maternal hyperthermia will kill an embryo after day 7 of pregnancy.

Embryos can be produced by either superovulation or in vitro fertilization. For superovulation, cows are injected with follicle stimulating hormone to cause the growth and ovulation of multiple follicles. For in vitro fertilization, oocytes are harvested either from growing follicles using transvaginal, ultrasound guided aspiration (called oocyte pickup or OPU) or from ovaries recovered at slaughter or ovariectomy. Oocytes are then fertilized with sperm and the resultant embryos allowed to develop in the laboratory until transferred into recipients. Embryos produced by superovulation are superior to those produced in vitro in terms of ability to establish pregnancy after transfer and survive cryopreservation for long-term storage. As shown in Figure 3, transfer of superovulated embryos improves fertility during heat stress regardless of whether embryos are cryopreserved or transferred fresh. However, the poor survival of in vitro produced embryos to cryopreservation means that transfer of in vitro produced embryos improved fertility only when embryos were transferred without cryopreservation.

Despite the problems caused by poor embryo freezability, in vitro production systems are superior to superovulation in terms of the maximum number of embryos that can be produced from a cow per year. In addition, sexed semen can be used very efficiently for in vitro fertilization since one straw can be used to inseminate dozens of oocytes. Production of in vitro produced embryos using oocytes collected at a slaughterhouse is much less expensive than production of embryos by superovulation or by in vitro fertilization of oocytes harvested using OPU.

The decision as to whether to use embryo transfer during the summer depends on the magnitude of the reduction in fertility caused by heat stress, the degree of improvement in fertility caused by embryo transfer and the cost of the embryo available for transfer. Ribeiro et al. (2012) estimated the cost to produce a female pregnancy in lactating cows as a function of the pregnancy rate per AI or embryo transfer. As an example, consider the case where pregnancy rate in the summer is 15% to AI using conventional semen and 25% using embryo transfer with sexed semen. In this scenario, embryo transfer would be profitable. It would cost \$1,157 to produce a female pregnancy using timed AI, \$1,042 to produce an embryo using an oocyte harvested by ultrasound, and \$820 to produce an embryo using an oocyte recovered from a slaughterhouse ovary.

Embryo transfer will become more profitable during heat stress as improvements in the process increase the competence of the embryo to establish pregnancy and survive cryopreservation. In addition, cost advantages of using embryos derived from oocytes recovered from the slaughterhouse should not be overlooked. Embryos of high genetic merit can be produced by using elite bulls because one straw of semen can produce dozens of embryos. Improvements in cryopreservation will also make embryo biopsy for genotyping more practical.

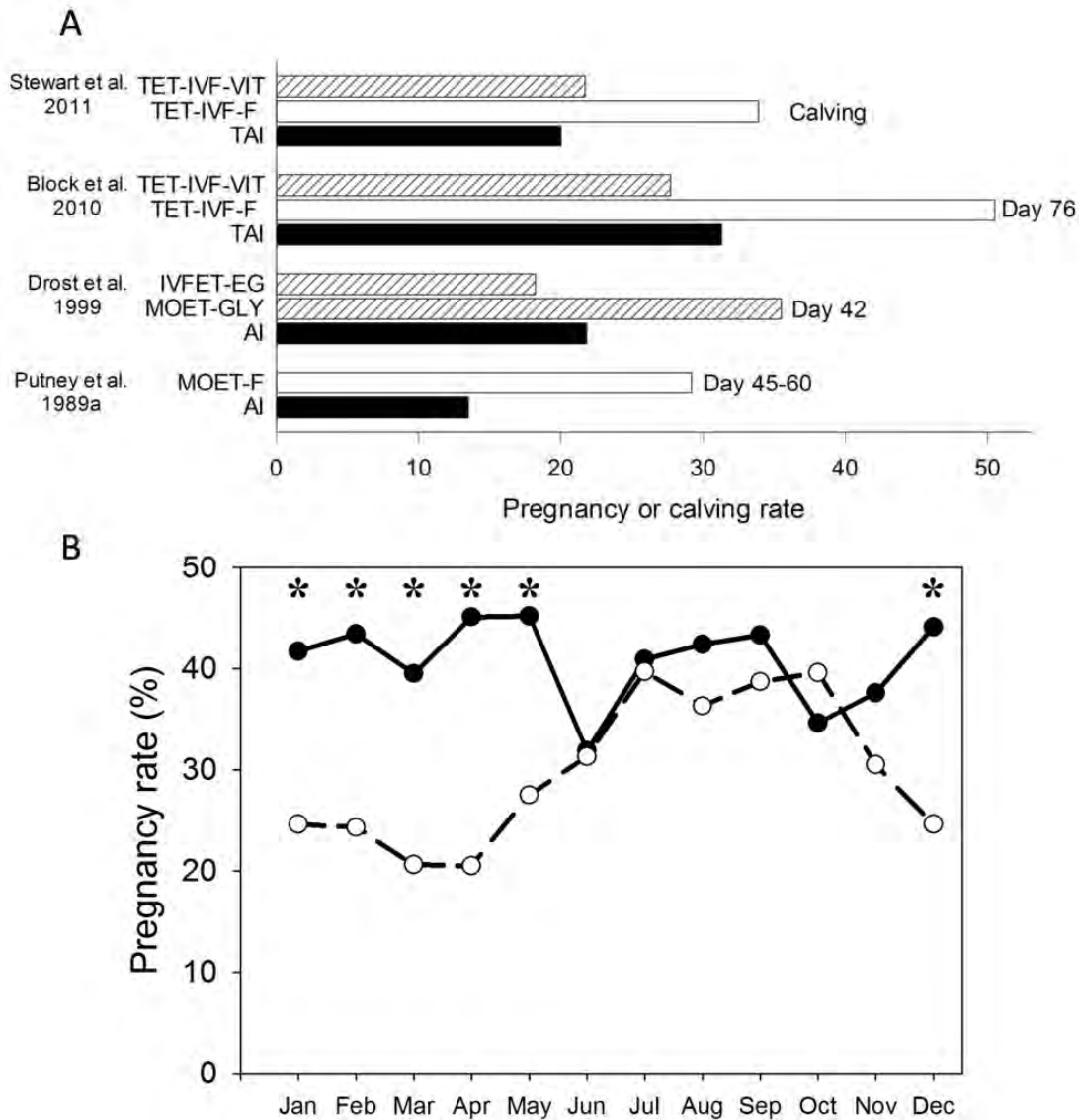


Figure 3. Enhancement of pregnancy rates during heat stress using embryo transfer. Data in Panel A represent results from various experiments in the summer in Florida. Abbreviations are as follows: AI: artificial insemination; EG, frozen in ethylene glycol; F, fresh; Gly, frozen in glycerol; IVFET, embryo 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 (Rodrigues et al., 2004). Asterisks represent months in which pregnancy rate was different between AI (open circles) and ET (filled circles). The figure is reproduced from Hansen (2013).

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