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Physiological Bases for Understanding Estrous Cycle Differences Between *Bos taurus* and *Bos indicus*

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ABSTRACT

Background: Although there is some information in the literature discussing differences of the estrous cycle of *Bos taurus* and *Bos indicus* cattle, most of the data derive from studies performed in temperate climate countries, under environmental and nutritional conditions very different than those found in tropical countries. Moreover, the physiological basis for understanding the differences between *Bos taurus* and *Bos indicus* estrous cycles are still unknown. This review explores the physiological and metabolic bases for understanding the key differences between the *Bos taurus* and *Bos indicus* estrous cycle. Moreover, it presents recent results of studies that have directly compared reproductive variables between Zebu and European cattle.

Review: The knowledge of reproductive physiology, especially the differences between *Bos taurus* and *Bos indicus*, is important for the development and application of different techniques of reproductive management in cattle. In this regard, overall, *Bos indicus* have a greater number of small ovarian follicles and ovulatory follicles are smaller as compared to *Bos taurus*. Consequently, Zebu cattle also have smaller corpus luteum (CL). Nevertheless, circulating concentrations of steroid and metabolic hormones are not necessarily higher in European cattle. In fact, some studies have shown that despite ovulating smaller follicles and having smaller CL, *Bos indicus* cows or heifers have higher circulating concentrations of estradiol, progesterone, insulin and IGF-I compared to *Bos taurus* females. In addition, there are also substantial differences between *Bos indicus* and *Bos taurus* cattle in relation to follicle size at the time of selection of the dominant follicle.

Conclusion: Data from very recent studies performed in Brazil have corroborated results from previous reports that have observed substantial differences in the estrous cycle variables of *Bos indicus versus Bos taurus* cattle. Those differences are probably related to distinct metabolism and metabolic hormone concentrations between Zebu and European cattle. This increased knowledge will allow for the establishment of more adequate reproductive management protocols in both breeds of cattle.

Keywords: reproductive physiology, *Bos taurus*, *Bos indicus*, steroid hormones, metabolic hormones, heat stress.

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I. INTRODUCTION

Many researchers have studied the reproductive physiology of *Bos indicus* and *Bos taurus* females. However, consistent information related to those genetic groups of cattle managed in tropical and subtropical environments still are necessary because most of the data generated from those studies were produced under different conditions than those observed in a tropical environment, like Brazil. Furthermore, alterations in reproductive variables of *Bos indicus* and *Bos taurus* cattle may happen when nutritional and metabolic conditions of these animals change.

The purpose of this article is to discuss physiological and metabolic bases for understanding the differences between the estrous cycle of *Bos indicus* and *Bos taurus* cattle.

II. FOLLICLE RECRUITMENT AND DEVIATION

Many studies have reported that the number of ovarian antral follicles is greater in *Bos indicus* than *Bos taurus* breeds [10,47]. Similarly, when comparing nonlactating Zebu and European cows under the same environmental and nutritional conditions, Bastos et al. [6] observed a greater number of small follicles (2-5 mm) in the ovaries of Nelore (42.7 ± 5.9) than Holstein (19.7 ± 3.2) cows at the time of wave emergence. This difference in number of small follicles between those breeds persisted throughout the estrous cycle.

It is very likely that factors directly involved in the recruitment of small antral follicles are related to circulating FSH concentrations and the Insulin/IGF-I system [54]. Recent studies have shown that *Bos indicus* females have lower circulating FSH [1], but higher plasma insulin [6] and IGF-I [1,50, M.R. Bastos, unpublished data] concentrations than *Bos taurus* cows or heifers.

The beginning of follicular growth and development through the preantral phase seems to be dependent on growth factors [54]. At that time, follicle development is gonadotropin-independent. Nevertheless, FSH receptor mRNA was detected in follicles with only one or two granulosa layers (primary follicles), even before the formation of theca interna [5,54]. *In vivo* and *in vitro* studies have shown that FSH at the preantral phase increases follicle development, but is not essential for this phenomenon to occur. However, after recruitment (diameter e"4 mm), follicles become gonadotropin-dependent and growth factors are less relevant and exert a permissive role, since during the antral phase follicles grow only up to 4 mm in diameter in the absence of gonadotropins [9,22,54].

Studies have demonstrated that IGF-I is important for the early stages of follicle development, because knockout of the IGF-I gene led to a severe impairment of preantral and early antral follicle growth in mice [reviewed by 8]. Besides, changes in circulating insulin and IGF-I concentrations induced by nutrient management affect follicle recruitment [54]. Moreover, small follicles in overfed heifers had a significant reduction in the expression of IGFBP-2 and -4 mRNA, increasing the bioavailability of IGF-I. This is probably a critical factor for preantral follicle developmental control. In agreement, other studies have shown that most of the non-recruited follicles expressed IGFBP-2 mRNA [13,65], suggesting that follicles with IGFBP-2 mRNA expression are the ones that undergo atresia.

In our recent study [6] we have observed that the plasma insulin concentrations before feed consumption were higher in the follicular phase as compared to the luteal phase in Nelore (11.9 ± 2.05 *vs.* 8.3 ± 1.47 μIU/mL) as well as in Holstein (4.2 ± 1.05 *vs.* 2.2 ± 0.64 μIU/mL) cows. It is known that serum insulin concentrations change during the day, but these changes also occur during the estrous cycle, with a significant increase during the preovulatory period [54]. Estradiol is a strong candidate to mediating these changes, because the increase in serum concentrations of insulin occurs with the increase in circulating estradiol produced by the dominant follicle. It has been shown that estradiol stimulates both the expression of insulin mRNA as well as its secretion by the pancreas cells [54].

Insulin is one of the main factors that control the release and bioavailability of IGF-I [2,21]. Therefore, we speculate that higher concentrations of insulin, as well as IGF-I are responsible for the greatest number of small follicles in *Bos indicus* than *Bos taurus* cattle, especially because these metabolic hormones are increased during the periovulatory period, when follicle recruitment occurs.

Another main difference between *Bos indicus* and *Bos taurus* is the diameter of the greatest growing follicle at the time of follicle deviation. Follicle deviation has been used to refer to the time at which differences in the growth rate between the future dominant and the future subordinate follicles become apparent [20]. The average diameter of the future dominant follicle at the time of deviation was 8.5 to 8.9 mm in Holstein females [6,20,45], whereas follicular deviation occurred when the greatest growing follicle reached 5.4 to 6.2 mm in diameter in Nelore heifers [11,18,44] and 7.0 mm in diameter in nonlactating Nelore cows [6]. Despite those differences in follicle size, the time of the estrous cycle in which deviation occurs does not differ between *Bos taurus* and *Bos indicus*. On average, deviation occurred between 2.3 and 2.8 days after wave emergence or ovulation in Holstein and Nelore females [6,11,18,20,44,45]. This fact is only possible because follicle growth rate in Nelore (0.8 to 1.2 mm/day) [18] is lower than in Holstein (1.2 to 1.6 mm/day) [45] cattle.

Studies [16,36] have shown that there is also a strong involvement of the IGF system in the selection of the dominant follicle. The synergism between IGF-I and FSH promotes estradiol synthesis in antral follicles. There is a negative association between estradiol concentration and low molecular weight IGFBP in follicular fluid [16,36] and this association was already present on Day 2 of the first follicular wave in cattle [36]. At that moment, the diameter difference between the dominant follicle and the largest subordinate follicle was only 1 mm. However, estradiol concentration was four times greater and the levels of IGFBP-4 were 2.5 times lower in follicular fluid of the dominant follicle than the largest subordinate one. According to that study, follicles with a greater responsiveness to FSH, acquire IGFBPase-4 earlier, increasing free IGF-I concentrations in follicular fluid which, in synergism with FSH, stimulates steroidogenesis increase. Then, estradiol exerts a negative feedback on FSH secretion, preventing other follicles of the same wave to acquire IGFBPases and become dominant.

As mentioned above, Zebu cattle have higher circulating concentrations of IGF-I and insulin than European cattle. It is believed that follicle diameter at deviation in Nelore is smaller than in Holstein cows and heifers, because these metabolic hormones increase the follicle responsiveness and sensitivity to FSH.

III. SIZE OF THE DOMINANT/OVULATORY FOLLICLE, CORPUS LUTEUM AND REPRODUCTIVE HORMONES

Studies have demonstrated that the maximum size of the dominant follicle and CL are greater in *Bos taurus* than *Bos indicus* breeds. For example, the maximum diameter of the ovulatory follicle were, on average 14 to 17 mm in Holsteins [19,46] and 11.3 to 12.3 mm in Nelore cattle [15,44]. Similarly, the maximum CL diameter was between 20 and 30 mm in *Bos taurus* [19,46] and between 17 to 21 mm in *Bos indicus* [15,35,47] females.

Despite those differences in size favoring European cattle, Zebu have greater circulating concentrations of steroid and metabolic hormones than *Bos taurus* cattle. In relation to circulating estradiol, studies that have directly compared *Bos taurus* and *Bos indicus* are scarce. In one of those studies [1], circulating estradiol peak concentrations (8.9 ± 1.6 *vs.* 9.1 ± 1.4 *vs.* 8.7 ± 1.4 pg/mL in Brahman, Angus and Senepol cows, respectively) did not differ among breeds. However, this is the only study that we are aware of that have observed a greater diameter of the ovulatory follicle in *Bos indicus* than in *Bos taurus* cattle (15.6 ± 0.5 *vs.* 12.8 ± 0.4 *vs.* 13.6 ± 0.4 mm in Brahman, Angus and Senepol cows, respectively).

According to Randel [33], *Bos indicus* females and crossbreds have lower progesterone concentration per gram of luteal tissue than *Bos taurus* cattle. However, Segerson et al. [47] found no difference in progesterone production by the CL between Brahman and Angus cows (75.8 ± 11.3 and 65.9 ± 5.3 mg progesterone/g of CL, respectively; P > 0.10). In contrast, studies performed in Brazil did not corroborate those reported above. A study with *Bos indicus* (Nelore and Gir), *Bos taurus* (Angus and Holstein) and *Bos indicus* x *Bos taurus* (Angus x Nelore and Gir x Holstein) heifers has detected higher circulating progesterone concentrations in *Bos indicus* females during the time in which they received an intravaginal progesterone-releasing device [10]. Similarly, although in our recent study [6], the maximum diameter of the ovulatory follicle (15.8 ± 1.4 *vs.* 13.4 ± 1.4mm) as well as CL volume on Day 14 of the estrous cycle (7890.90 ± 1752.40 *vs.* 4916.64 ± 1733.40 mm^3) were greater in Holstein cows, plasma estradiol, progesterone, insulin and IGF-I concentrations were higher in Nelore cows.

In relation to higher circulating progesterone concentration, the authors [6,10] speculate that this finding may be due to a higher liver metabolism of this steroid hormone in European as compared to Zebu cattle. It is known that the liver metabolism of steroid hormones is correlated with the dry matter intake [42,53]. However, in our study [6], all cows were fed the same maintenance diet and dry matter intake per kg of body weight was 1.37% for Nelore and 1.54% for Holstein cows, according to NRC (2000) recommendation. Therefore, based on these results, we speculate that a possible higher steroid metabolism in Holstein cows may be inherent to the breed and not only a consequence of higher feed intake. Moreover, Nelore cows may also have lower hepatic metabolism and/or increased steroid production by the ovaries than Holstein cows. Finally, heat stress can be another important factor related to lower circulating estradiol and progesterone in Holstein cows. These hypotheses will be discussed in more detail at the following sessions.

IV. EFFECT OF METABOLIC HORMONES ON PRODUCTION AND METABOLISM OF STEROID HORMONES

It is speculated that *Bos indicus* have lower steroid metabolism than *Bos taurus* females and this may be due to the higher circulating insulin in Zebu cattle. The greatest amount of circulating progesterone is inactivated or catabolized in hepatocytes by cytochrome P450 2C (CYP2C) and cytochrome P450 3A (CYP3A) enzymes. The main metabolites are 21-hydroxyprogesterone and 6â-hydroxyprogesterone, respectively [30,31]. Some studies have shown that insulin alters the expression of these enzymes. Studies [41,48] in which hepatocytes of rodents were cultured *in vitro*, observed a decrease in expression of CYP3A mRNA when physiological doses of insulin were added to the media. They also observed an insulin dose-dependent decrease in 6â-hydroxyprogesterone. Recently, Lemley et al. [28] showed that insulin alters the expression of these enzymes in dairy cows. These authors first induced the increase of insulin by propylene glycol infusion and detected lower expression of CYP3A. Subsequently, insulin and glucose were infused to promote a hyperinsulinemic-euglycemic curve. It was observed that insulin caused a dose-dependent decrease in expression of both CYP2C and CYP3A enzymes.

Moreover, results from recent studies in which Zebu have higher circulating insulin and IGF-I concentrations than European cattle, allow us to hypothesize that Nelore cows or heifers have a higher steroid production and lower steroid metabolism than Holstein females. Both insulin and IGF-I act as potent stimulators of granulosa cells proliferation and steroidogenesis in cattle [54]. IGF-I acts in synergism with FSH on steroidogenesis by increasing the P450 aromatase activity [14]. *In vitro* culture of bovine granulosa cells with 100 ng/ml of insulin stimulated mRNA expression and P450 aromatase activity, and increased estradiol secretion by these cells [49].

Recently, bovine granulosa cells were cultured under different concentrations of IGF-I (1, 50 and 100 ng/mL) in a serum-free system without insulin [29]. The authors observed that cells cultured with IGF-I (50 or 100 ng/mL) had a significant increase in 17β-estradiol production, in cell number, in mRNA expression of genes related to steroidogenesis (CYP11A1, HSD3B1, and CYP19A1) and of genes that encode receptors for IGF-I and FSH (FSHR and IGF-IR). Cells cultured only with FSH did not have any significant effect. Besides, it was reported that CL also has IGF-I receptors, and that IGF-I may increase gonadotropin activity and progesterone synthesis [43].

Another important action of insulin was shown by Armstrong et al. [2]. The authors found that higher circulating insulin concentrations induced by high feed intake decreased IGFBPs expression, increasing the bioavailability of IGF. It was also cited that nutritional status, i.e., higher circulating insulin, can alter the amount and type of circulating IGFBPs [21]. Lower circulating IGFBPs, may indicate higher free IGF-I concentration.

Thus, based on the data presented above, we must consider the possibility that steroid hormones production in follicles and CL is, in fact, greater in *Bos indicus* than in *Bos taurus*, and insulin and IGF-I may be responsible for that. However, to date, there are no reports that have evaluated and directly compared steroid production and metabolism in *Bos taurus* vs *Bos indicus* females.

V. EFFECT OF HEAT STRESS ON CIRCULATING CONCENTRATIONS OF STEROIDS HORMONES

Heat stress during summer substantially contributes to lower fertility and production, especially in *Bos taurus* breeds. In contrast, *Bos indicus* breeds are known for their adaptation to adverse conditions at tropical environments, especially due to their higher thermo tolerance as compared to European breeds. However, the impact of heat stress on Zebu breeds should not be ignored [25,51].

The effects of environmental temperature on animal performance can be measured by establishing a critical temperature [7] or through an index of equivalent temperature, which incorporates temperature and humidity of the air (THI) [32].

According to the literature, milk production and dry matter intake decrease when the maximum THI reaches 77. Subsequent researches have determined maximum, intermediate and minimum THI of 76, 72 and 64, respectively, for *Bos taurus* females. In fact, THI can be used as an estimative for predicting the effects of heat stress on cattle performance [reviewed by 55].

In relation to the heat stress influence on neuroendocrine and reproductive physiology of *Bos taurus* and *Bos indicus*, few studies have reported that FSH plasma concentrations are increased in cows under heat stress, probably because circulating inhibin concentrations are reduced by the impairment of follicular development [34].

Data regarding plasma LH concentrations in animals under heat stress are controversial. Studies have shown that cows under heat stress have reduced amplitude and frequency of LH pulses. However, the preovulatory LH peak was reduced in heifers but not in cows [reviewed by 34]. It is suggested that these differences are related to the preovulatory circulating estradiol concentrations found in these studies, in which cows with lower plasma estradiol concentrations had less LH pulses, or vice-versa [17]. The growth of the dominant follicle is regulated by LH pulse frequency. If heat stress decreases LH pulses, there is an impairment in follicle development, and consequently on its estradiol production and secretion. In fact, several studies have shown that plasma estradiol concentrations are reduced in dairy cows or heifers under heat stress [17,40,56,57,60,63]. According to the majority of the studies that have reported reduced LH concentrations in animals under heat stress, the dominant follicle develops at low LH concentrations, resulting in decreased estradiol secretion, what directly affects estrus expression. In this case, even high FSH concentrations are not able to overcome the deleterious effect of the LH decrease on estradiol synthesis by the preovulatory follicle. Moreover, the decrease in steroidogenic capacity of follicles in cows or heifers under heat stress may be related to lower activity of aromatase in granulosa cells that has been reported, decreasing estradiol concentration in follicular fluid of dominant follicles [3].

A seasonal study has evaluated the function of dominant follicles on Day 7 of the estrous cycle. Estradiol concentrations in follicular fluid were lower during the summer. This decrease was due to a drastic reduction in the production of androstenedione by theca cells during summer (4.1 ± 0.5 and 1.1 ± 0.3 ng/10^5 of viable cells for winter and summer, respectively). Thus, the production of estradiol by granulosa cells decreased around 50% during the warmer months (12.6 ± 1.7 and 6.6 ± 0.9 ng/10^5 of viable cells for winter and summer, respectively) [60]. Moreover, the percentage of viable granulosa cells from follicles during the summer decreased ~60%, contributing to the reduced blood estradiol concentration [61]. Theca cells incubated at elevated temperatures or from follicles collected in the winter of cows under acute heat stress in chambers have also shown reduced androstenedione production [60].

In contrast to other studies, no difference in serum or follicular concentrations of estradiol and progesterone was detected in lactating [12] or nonlactating [23] Holstein cows under acute heat stress and the control group.

The effect of heat stress on blood progesterone concentration is even more controversial. Studies have reported that circulating progesterone concentrations were increased, not influenced or decreased (majority of the studies) by heat stress (Table 1). Two of these studies did not detect effect of heat stress on plasma progesterone concentrations [23,24]. However, in another study, progesterone concentrations increased after Day 16 of the estrous cycle and luteolysis was delayed in lactating cows under heat stress (29.1 ± 2.4 *vs.* 20.4 ± 2.4 days) [56]. The controversial results reported in the literature, may be due to interference of many uncontrolled factors, such as: type of heat stress (acute or chronic), dry matter intake, liver metabolism, age and stage of lactation [61].

Table 1. Influence of acute or chronic heat stress on plasma progesterone concentration. Adapted from Rensis & Scaramuzzi [34] and Wolfenson et al. [62].

Reference	Progesterone concentration	Type of stress
[52,56]	Increased	Acute (warming chambers)
[23,24]	Not altered	Acute (warming chambers)
[37]	Increased	Acute (solar radiation)
[39]	Not altered	Acute (solar radiation)
[27,38,51,58,59,64]	Decreased	Chronic

Most of the authors suggest that plasma progesterone concentrations are reduced in animals under chronic heat stress, typically observed in natural conditions of summer. However, under acute heat stress, such as exposure to direct solar radiation or use of warming chambers, increases in circulating progesterone have been reported [26,62]. This higher progesterone concentration in cows under acute heat stress may be related to a higher progesterone secretion by the adrenal gland [26], and not necessarily by the CL. *In vitro* studies support this hypothesis, because progesterone production by luteinized theca cells obtained from cows during summer was lower than during winter [62].

The study performed by Alvarez et al. [1] that was mentioned previously, in which Brahman cows had greater follicles and CL than Angus cows, was performed during summer in Florida. These unexpected results possibly reflect a more pronounced effect of heat stress on follicular dynamics of Angus (*Bos taurus*) than Brahman (*Bos indicus*) cows. However, those differences in size between breeds were not reproduced on circulating steroid concentrations, since there was no difference in plasma estradiol or progesterone concentrations between Brahman and Angus cows.

A study performed in Brazil [51] found no immediate effect of heat stress on reproductive function of Gir cows, possibly due to the higher thermo tolerance and rusticity of Zebu breeds. However, the extended heat stress those cows underwent promoted deleterious effects on follicular growth by increasing the number and diameter of large follicles, through an ineffective mechanism of selection and follicle dominance. Indeed, Sartori et al. [46] observed that lactating dairy cows during summer, had a higher incidence of follicular codominance than heifers, resulting in a higher percentage of multiple ovulations. Delayed ovulation or failure to ovulate was also more frequent in lactating cows than in nulliparous heifers.

In our recent study, performed during the summer of 2010 in Brazil, the maximum diameter of the ovulatory follicle, as well as the CL volume was greater in nonlactating Holstein than Nelore cows, as mentioned above [6]. However, plasma progesterone concentrations on Day 7 and 14 of the estrous cycle and peak estradiol were higher in *Bos indicus* than *Bos taurus* cows. Besides potential differences in steroid metabolism between breeds, as discussed before, it is possible that estradiol and progesterone production and secretion by the ovaries of Holstein cows may have been negatively influenced by heat stress, given that the maximum and minimum THI recorded were 87.5 and 64.5, respectively. Probably, although THI was high during that period of study, Nelore cows may still have been in thermal comfort zone due to their greater adaptation to the tropical environment, differently than Holstein cows.

Finally, the mechanisms involved in gonadotropins and steroid hormones secretion in animals under heat stress are poorly understood. However, it seems that the main action of heat stress is at the hypothalamic-pituitary-gonadal axis, decreasing GnRH and LH release and, consequently, estradiol production by the preovulatory follicle. Moreover, plasma progesterone concentrations are influenced by multifactorial factors; being the reason why data presented in the literature are so controversial.

VI. CONCLUSIONS

After extensive literature review, it was observed that there are still few studies that have effectively and directly compared the reproductive physiology of *Bos taurus* and *Bos indicus* subspecies. Some information regarding the differences in the estrous cycle are known, however, the vast majority of the work was not developed in the tropical climate conditions found in Brazil. In this regard, very recent studies performed in Brazil with direct comparisons between Zebu and European cattle have provided important facts that can be used to optimize reproductive management and enable the development of specific biotechnologies for *Bos taurus* or *Bos indicus* cattle.

REFERENCES

1 **Alvarez P., Spicer L.J., Chase Jr. C.C., Payton M.E., Hamilton T.D., Stewart R.E., Hammond A.C., OlsonT.A. & Wetteman R.P. 2000.** Ovarian and endocrine characteristics during the estrous cycle in Angus, Brahman and Senepol cows in a subtropical environment. *Jounal of Animal Science*. 78: 1291-1302.

2 **Armstrong D.G., Mcevoy T.G., Baxter G., Robinson J.J., Hogg C.O., Woad K.J. & Webb R. 2001.** Effect of dietary energy and protein on bovine follicular dynamics and embryo production *in vitro*: associations with the ovarian insulin-like growth factor system. *Biology of Reproduction*. 64: 1624-1632.

3 **Badinga L., Thatcher W.W., Diaz T., Drost M. & Wolfenson D. 1993.** Effect of environmental heat stress on follicular development and steroidogenesis in lactating Holstein cows. *Theriogenology*. 39: 797-810.

4 **Bao B., Garverick H.A., Smith G.W., Smith M.F., Salfen B.E. & Youngquist R.S. 1997.** Changes in messenger ribonucleic acid encoding luteinizing hormone receptor, cytochrome P450-side chain cleavage, and aromatase are associated with recruitment and selection of bovine ovarian follicles. *Biology of Reproduction*. 56: 1158-1168.

5 **Bao B. & Garverick H.A. 1998.** Expression of steroidogenic enzyme and gonadotropin receptor genes in bovine follicles during ovarian follicular waves: A review. *Journal of Animal Sci*ence. 76: 1903-1921.

6 **Bastos M.R., Mattos M.C.C., Meschiatti M.A.P., Surjus R.S., Guardieiro M.M., Ferreira J.C.P., Mourão G.B., Pires A.V., Biehl M.V., Pedroso A.M., Santos F.A.P. & Sartori R. 2010.** Ovarian function and circulating hormones in nonlactating Nelore versus Holstein cows. *Acta Scientiae Veterinariae*. [in press].

7 **Berman A., Folman Y., Kaim M., Mamen M., Herz Z., Wolfenson D., Arieli A. & Graber Y. 1985.** Upper critical temperatures and forced ventilation effects for high-yielding dairy cows in a subtropical climate. *Journal of Dairy Science*. 68: 1488-1495.

8 **Buratini Jr. J. 2006.** Foliculogênese em bovinos. Biotecnologia da Reprodução em Bovinos. In: *2º Simpósio Internacional de Reprodução Animal Aplicada*. (Londrina, Brasil).

9 **Campbell B.K., Scaramuzzi R.J. & Webb R. 1995.** Control of antral follicle development and selection in sheep and cattle. *Journal of Reproduction and Fertility*. 49: 335-350.

10 **Carvalho J.B., Carvalho N.A., Reis E.L., Nichi M., Souza A.H. & Baruselli P.S. 2008.** Effect of early luteolysis in progesterone-based timed AI protocols in *Bos indicus*, *Bos indicus x Bos taurus*, and *Bos taurus* heifers. *Theriogenology*. 69: 167-175.

11 **Castilho C., Garcia J.M., Renesto A., Nogueira G.P. & Brito L.F. 2007.** Follicular dynamics and plasma FSH and progesterone concentrations during follicular deviation in the first post-ovulatory wave in Nelore (*Bos indicus*) heifers. *Animal Reproduction Sciencie*. 98: 189-196.

12 **Castro e Paula L.A., Andrzejewski J., Julian D., Spicer L.J. & Hansen P.J. 2008.** Oxygen and steroid concentrations in preovulatory follicles of lactating dairy cows exposed to acute heat stress. *Theriogenology*. 69: 805-813.

13 **Chandrashekar V., Zaczek D. & Bartke A. 2004.** The consequences of altered somatotropic system on reproduction. *Biology of Reprod*uction. 71: 17-27.

14 **Echternkamp S.E., Howard H.J., Roberts A.J. & Grizzle W.T. 1994.** Relationships among concentrations of steroids, insulin-like growth factor-I and insulin-like growth factor binding protein in ovarian follicular fluid of beef cattle. *Biology of Reproduction*. 51: 971-981.

15 **Figueiredo R.A., Barros C.M., Pinheiro O.L. & Sole J.M.P. 1997.** Ovarian follicular dynamics in Nelore breed (*Bos indicus*) cattle. *Theriogenology*. 47: 1489-1505.

16 **Fortune J.E., Rivera G.M. & Yang M.Y. 2004.** Follicular development: the role of the follicular microenvironment in selection of the dominant follicle. *Animal Reproduction Science*. 82-83: 109-126.

17 **Gilad E., Meidan R., Berman A., Graber Y. & Wolfenson D. 1993.** Effect of heat stress on tonic and GnRH-induced gonadotrophin secretion in relation to concentration of oestradiol in plasma of cyclic cows. *Journal of Reproduction and Fertility*. 99: 315-321.

18 **Gimenes L.U., Sá Filho M.F., Carvalho N.A.T., Torres-Junior J.R.S., Souza A.H., Madureira E.H., Trinca L.A., Sartorelli E.S., Barros C.M., Carvalho J.B.P., Mapletoft R.J. & Baruselli P.S. 2008.** Follicle deviation and ovulatory capacity in *Bos indicus* heifers. *Theriogenology*. 69: 852-858.

19 **Ginther O.J., Knopf L. & Kastelic J.P. 1989.** Temporal associations among ovarian events in cattle during oestrous cycles with two or three follicular waves. *Journal of Reproduction and Fertility*. 87: 223-230.

20 **Ginther O.J., Wiltbank M.C., Fricke P.M., Gibbons J.R. & Kot K. 1996.** Selection of the dominant follicle in cattle. *Biology of Reproduction*. 55: 1187-1194.

21 **Gong J.G., Armstong D.G., Baxter G., Hogg C.O., Garnsworthy P.C. & Webb, R. 2002.** The effect of dietary intake on superovulatory response to FSH in heifers. *Theriogenology*. 57: 1591-1602.

22 **Gong J.G., Campbell B.K., Bramley T.A., Gutierrez C.G., Peters A.R. & Webb R. 1996.** Suppression in the secretion of follicle-stimulating hormone luteinizing hormone, and ovarian follicle development in heifers continuously infused with a gonadotropin-releasing hormone agonist. *Biology of Reprod*uction. 55: 68-74.

23 **Guzeloglu A., Ambrose J.D., Kassa T., Diaz T., Thatcher M.J. & Thatcher W.W. 2001.** Long term follicular dynamics and biochemical characteristics of dominant follicles in dairy cows subjected to acute heat stress. *Animal Reproduction Science*. 66: 15-34.

24 **Gwazdauskas F.C., Thatcher W.W., Kiddy C.A., Paape M.J. & Wilcox C.J. 1981.** Hormonal patterns during heat-stress following PGF2á salt induced luteal regression in heifers. *Theriogenology*. 16: 271-285.

25 **Hammond A.C., Olson T.A., Chase Jr. C.C., Bowers E.J., Randel R.D. & Murphy C.N. 1996.** Heat tolerance in two tropically adapted *Bos taurus* breeds, Senepol and Romosinuano, compared with Brahman, Angus, and Hereford cattle in Florida. *Journal of Animal Science*. 74: 295-303.

26 **Howell J.L., Fuquay J.W. & Smith A.E. 1994.** Corpus luteum growth and function in lactating Holstein cows during spring and summer. *Journal of Dairy Science*. 77: 735-739.

27 **Jonsson N.N., McGowan M.R., McGuigan K., Davison T.M., Hussain A.M., Kafi M. & Matschoss A. 1997.** Relationships among calving season, heat load, energy balance and postpartum ovulation of dairy cows in a subtropical environment. *Animal Reproduction Science*. 47: 315-326.

28 **Lemley C.O., Butler S.T., Butler W.R. & Wilson M.E. 2008.** Short communication: insulin alters hepatic progesterone catabolic enzymes cytochrome P450 2C and 3A in dairy cows. *Journal of Dairy Science*. 91: 641-645.

29 **Mani A.M., Fenwick M.A., Cheng Z., Sharma M.K., Singh D. & Wathes D.C. 2010.** IGF-I induces up-regulation of steroidogenic and apoptotic regulatory genes via activation of phosphatidylinositol-dependent kinase/AKT in bovine granulose cells. *Reproduction*. 139: 139-151.

30 **Murray M. 1991.** Microsomal cytochrome P450-dependent steroid metabolism in male sheep liver. Quantitative importance of 6â-hydroxylation and evidence for the involvement of a P450 from the IIIA subfamily in the pathway. *The Journal of Steroid Biochemistry and Molecular Biology*. 38: 611-619.

31 **Murray M. 1992.** Participation of a cytochrome P450 enzyme from the 2C subfamily in progesterone 21-hydroxylation in sheep liver. *The Journal of Steroid Biochemistry and Molecular Biology*. 43: 591-593.

32 **NOAA. 1976.** Livestock hot weather stress. United States Dept. of Commerce, Natl. Oceanic and Atmospheric Admin., Natl. Weather Service Central Region. Regional Operations Manual Letter C-31-76.

33 **Randel R.D. 1976.** LH and ovulation in Brahman, Brahman x Hereford and Hereford heifers. *Journal of Animal Science*. 43: 300.

34 **Rensis F.D. & Scaramuzzi R.J. 2003.** Heat stress and seasonal effects on reproduction in the dairy cow - a review. *Theriogenology*. 60: 1139-1151.

35 **Rhodes F.M., De'ath G. & Entwistle K.W. 1995.** Animal and temporal effects on ovarian follicular dynamics in Brahman heifers. *Animal Reproduction Science*. 38: 265-277.

36 **Rivera G.M., Chandrasekher Y.A., Evans A.C.O., Giudice L.C. & Fortune J.E. 2001.** A potential role for insuluin-like growth factor binding protein-4 proteolysis in the establishment of ovarian follicular dominance in cattle. *Biology of Reproduction*. 65: 102-111.

37 **Roman-Ponce H., Thatcher W.W. & Wilcox C.J. 1981.** Hormonal interrelationships and physiological responses of lactating dairy cows to shade management system in a tropical environment. *Theriogenology*. 16: 139-154.

38 **Rosenberg M., Herz Z., Davidson M. & Folman J. 1977.** Seasonal variations in post-partum plasma progesterone levels and conceptions in primiparous and multiparous dairy cows. *Journal of Reproduction and Fertility*. 51: 363-367.

39 **Roth Z., Meidan R., Braw-Tal R. & Wolfenson D. 2000.** Immediate and delayed effects of heat-stress on follicular development and its association with plasma FSH and inhibin concentration in cows. *Journal of Reproduction and Fertility*. 120: 83-90.

40 **Roth Z. 1998.** Immediate and delayed effect of heat stress on ovarian follicular development and function in dairy cows. MSc. Thesis, Faculty Agriculture, Hebrew University, Rehovot, Israel, in Hebrew, with English abstract.

41 **Saad B., Thomas H., Schawalder H., Waechter F. & Maier P. 1994.** Oxygen tension, insulin, and glucagon affect the preservation and induction of cytochrome P450 isoforms in cultured rat hepatocytes. *Toxicology and Applied Pharmacology*. 126: 372-379.

42 **Sangsritavong S., Combs D.K., Sartori R., Armentano L.E. & Wiltbank M.C. 2002.** High feed intake increases liver blood flow and metabolism of progesterone and estradiol 17 beta in dairy cattle. *Journal of Dairy Science*. 85: 2831-2842.

43 **Santos J.E.P. & Amstalden M. 1998.** Effects of nutrition on bovine reproduction. *Arquivo da Faculdade de Veterinária UFRGS*: Porto Alegre. 26(1): 19-89.

44 **Sartorelli E.S., Carvalho L.M., Bergfelt D.R., Ginther O.J. & Barros C.M. 2005.** Morphological characterization of follicle deviation in Nelore (*Bos indicus*) heifers and cows. *Theriogenology*. 63: 2382-2394.

45 **Sartori R., Fricke P.M., Ferreira J.C.P., Ginther O.J. & Wiltbank M.C. 2001.** Follicular deviation and acquisition of ovulatory capacity in bovine follicles. *Biology of Reproduction*. 65: 1403-1409.

46 **Sartori R., Haughian J.M., Shaver R.D., Rosa G.J. & Wiltbank M.C. 2004.** Comparison of ovarian function and circulating steroids in estrous cycles of Holstein heifers and lactating cows. *Journal of Dairy Science*. 87: 905-920.

47 **Segerson E.C., Hansen T.R., Libby D.W., Randel R.D. & Getz W.R. 1984.** Ovarian and uterine morphology and function in Angus and Brahman cows. *Journal of Animal Science*. 59: 1026-1046.

48 **Sidhu J.S. & Omiecinski C.J. 1999.** Insulin-mediated modulation of cytochrome P450 gene induction profiles in primary rat hepatocyte cultures. *Journal of Biochemical and Molecular Toxicology*. 13: 1-9.

49 **Silva J.M. & Price C.A. 2002.** Insulin and IGF-I are necessary for FSH-induced cytochrome P450 aromatase but not cytochrome P450 side-chain cleavage gene expression in oestrogenic bovine granulosa cells *in vitro*. *Journal of Endocrinology*. 174: 499-507.

50 **Simpson R.B., Chase Jr. C.C., Spicer L.J., Vernon R.K., Hamond A.C. & Rae D.O. 1994.** Effect of exogenous insulin on plasma and follicular insulin-like growth factor I, insulin-like growth factor binding protein activity, follicular estradiol and progesterone, and follicular growth in superovulated Angus and Brahman cows. *Journal of Reproduction and Fertility*. 102: 483-492.

51 **Torres-Júnior J.R.S., Pires M.F.A., de Sá W.F., Ferreira A.M., Viana J.H.M., Camargo L.S.A., Ramos A.A., Folhadella I.M., Polisseni J., Freitas C., Clemente C.A.A., Sá Filho M.F., Paula-Lopes F.F. & Baruselli P.S. 2008.** Effect of maternal heat-stress on follicular growth and oocyte competence in *Bos indicus* cattle. *Theriogenology*. 69: 155-166.

52 **Trout J.P., McDowell L.R. & Hansen P.J. 1998.** Characteristics of the estrous cycle and antioxidant status of lactating Holstein cows exposed to heat-stress. *Journal of Dairy Science*. 81: 1244-1250.

53 **Vasconcelos J.L.M., Sangsritavong S.J., Tsai S.J. & Wiltbank, M.C. 2003.** Acute reduction in serum progesterone concentrations after feed intake in dairy cows. *Theriogenology*. 60: 795-807.

54 **Webb R., Garnsworthy P.C., Gong J.G. & Asrmstrong D.G. 2004.** Control of follicular interactions and nutritional influences. *Journal of Animal Science*. 82: 63-74.

55 **West J.W. 2003.** Effects of Heat-Stress on Production in Dairy Cattle. *Journal of Dairy Science*. 86: 2131-2144.

56 **Wilson S.J., Marion R.S., Spain J.N., Spiers D.E., Keisler D.H. & Lucy M.C. 1998a.** Effect of controlled heat stress on ovarian function in dairy cattle: I. Lactating cows. *Journal of Dairy Science*. 1(21): 24-31.

57 **Wilson S.J., Kirby C.J., Koenigsfeld A.T., Keisler D.H. & Lucy M.C. 1998b.** Effects of controlled heat stress on ovarian function of dairy cattle: 2. Heifers. *Journal of Dairy Science*. 81: 2132-2138.

58 **Wise M.E., Rodriguez R.E., Armstrong D.V., Huber J.T., Wiersma F. & Hunter R. 1988.** Fertility and hormonal responses to temporary relief of heat-stress in lactating dairy cows. *Theriogenology*. 29: 1027-1035.

59 **Wolfenson D., Flamenbaum I. & Berman A. 1988.** Hyperthermia and body energy store effects on estrous behavior, conception rate, and corpus luteum function in dairy cows. *Journal of Dairy Science*. 71: 3497-3504.

60 **Wolfenson D., Lew B.J., Thatcher W.W., Graber Y. & Meidan R. 1997.** Seasonal and acute heat stress effects on steroid production by dominant follicles in cow. *Animal Reproduction Science*. 47: 9-19.

61 **Wolfenson D., Roth Z. & Meidan R. 2000.** Impaired reproduction in heat-stressed cattle: basic and applied aspects. *Animal Reproduction Science*. 60-61: 535-547.

62 **Wolfenson D., Sonego H., Bloch A., Shaham-Albalancy A., Kaim M., Folman Y. & Meidan R. 2002.** Seasonal differences in progesterone production by luteinized bovine thecal and granulosa cells. *Domestic Animal Endocrinology*. 22: 81-90.

63 **Wolfenson D., Thatcher W.W., Badinga L., Savio J.D., Meidan R. & Lew B.J. 1995.** The effect of heat stress on follicular development during the estrous cycle dairy cattle. *Biology of Reproduction*. 52: 1106-1113.

64 **Younas M., Fuquay J.W., Smith A.E. & Moore A.B. 1993.** Estrous and endocrine responses of lactating Holsteins to forced ventilation during summer. *Journal of Dairy Science*. 76: 430-436.

65 **Yuan W., Bao B., Garverick H.A., Youngquist R.S. & Lucy M.C. 1998.** Follicular dominance in cattle is associated with divergent patterns of ovarian gene expression for insulin-like growth factor (IGF)-I, IGF-II and IGF binding protein-2 in dominant and subordinate follicles. *Domestic Animal Endocrinology*. 15: 55-63.