

# ENERGY BALANCE AND OVARIAN FOLLICLES

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## INTRODUCTION

Ovarian follicles have multiple roles in successful reproduction of dairy cattle. From several months before puberty in heifers to aged cows, follicles grow continuously in successive waves. Pituitary and ovarian hormones regulate follicular growth. Most follicles that initiate growth degenerate and die by a process of atresia. Few follicles actually experience growth that proceeds to ovulation. Follicles that ovulate, avoid atresia by achieving dominance. Dominant follicles have the greatest function and largest size of all other follicles in the same growth group or cohort. These dominant follicles also suppress growth and function of other follicles in the same cohort and ultimately cause their atresia. Function of follicles, measured by estradiol secretion, is critical to growth, survival and ovulation opportunity of follicles. All follicles contain an oocyte that remains dormant until the follicle is committed irreversibly to ovulation. So, if a follicle survives to ovulate, there is no current evidence that the welfare of the oocyte is affected by the hormonal or metabolic circumstances before ovulation.

At least 80 percent of dairy cows experience negative energy balance (**NEB**) in early lactation. The magnitude and duration of NEB is highly variable among cows. Negative energy balance extends the interval from calving to first ovulation, increases the number of medium but decreases the number of large follicles, and reduces function of corpora lutea (**CL**). Thus, energy balance affects follicular growth and function. However, there is no evidence that energy balance affects fertilizability of oocytes.

Compared to positive energy balance, the metabolic and hormonal status of cows is altered substantially during NEB. Among the differences due to NEB, luteinizing hormone (**LH**) is a likely mediator of the effects of NEB on follicles.

To resolve the adverse effects of NEB on follicles, the major challenges are:

- 1) understand regulation of follicles independent of energy balance,
- 2) identify the factors that mediate the adverse effects of NEB on follicles, and
- 3) minimize the magnitude and duration of NEB without limiting yield of milk in early lactation.

## WHY ARE FOLLICLES IMPORTANT?

Ovarian follicles have multiple but critical roles in successful reproduction. In non-pregnant cows follicles are the major source of estradiol, which is imperative for the physical and behavioral signs of estrus. Thus, function of follicles is necessary for detection of estrus and the opportunity for insemination. In addition, growth and function of follicles capable of ovulation determines the interval from calving to ovulation. After ovulation, the recently ovulated follicle differentiates to form a CL. Subsequent development and function of the CL is affected positively by the size and function of the follicle that ovulated, which becomes the parent tissue to the CL. If the ovulatory follicle has limitations, these limit the CL (Villa-Godoy et al., 1988) and presumably reduce fertility by increasing embryonic death. Another reason follicles are important is that follicles control their resident oocyte. The current model explaining oocyte maturation is that oocytes remain dormant until the associated follicle commits irreversibly to ovulation. Based on available evidence, oocytes are protected or shielded from the hormonal and metabolic environment in and around the follicle. Except for aging of females, factors that might affect fertility of oocytes or survival of subsequent embryos have not been examined rigorously. Whether hormones or metabolites that characterize NEB have direct effects on oocytes is not known.

Success of reproduction depends on multiple variables. It is impossible to establish any single variable as critical or most limiting. But, it should be clear that growth and function of ovarian follicles has major influence on reproductive performance of postpartum cows.

## **REGULATION OF FOLLICLES**

At birth a heifer has at least 100,000 ovarian follicles. All of these follicles are very simple with an oocyte surrounded by a few granulosa cells. These primordial follicles are in a maintenance existence and do not grow, secrete little or no hormones, and do not require hormones for survival. Several months before puberty cohorts of 10 to 15 primordial follicles start growth. This process of growth initiation is called recruitment. Its regulation is not understood. Among those follicles recruited, one follicle becomes bigger after a few days, suppresses growth of the other members of the cohort and achieves dominance. The subordinate follicles experience atresia and die. If the dominant follicle is not exposed to a pre-ovulatory surge of LH, it will experience atresia. In the absence of the suppressive effects of a dominant follicle, another cohort of follicles experiences accelerated growth and a single follicle achieves dominance. This pattern of follicular growth and demise is described as waves (Sunderlund et al., 1994). During an estrous cycle cows will have two or three follicular waves and the last wave will end with ovulation.

Waves of follicular growth are regulated by LH and follicle stimulating hormone (**FSH**). An increase in FSH during atresia of a dominant follicle is believed to accelerate growth of follicles in the next cohort (Sunderlund et al., 1994). After follicles develop theca they become responsive to LH. Continued growth and increased function depends on frequent pulsatile secretion of LH with continued stimulation by FSH. Concurrent with effects of LH and FSH, estradiol is important to increase the number of granulosa cells and to sustain physical growth. Estradiol is a key measure of function and affects growth and health of a follicle. Dominant follicles are largest, have the most granulosa cells, and produce the most estradiol. That dominant follicles suppress growth and cause atresia of subordinate follicles is established. Numerous intrafollicular peptides are under investigation but the

mechanism of this atretogenic effect of dominant follicles is not understood (Sunderlund et al, 1996).

Waves of follicular growth occur continuously from before puberty, during estrous cycles, and throughout gestation and the postpartum period. Most of these waves end with atresia because the dominant follicle does not experience an ovulatory stimulus. A few dominant follicles ovulate. Cows that have short anovulatory periods postpartum start waves early after calving and have frequent pulses of LH.

## **REGULATION OF OOCYTES**

Each diploid cell in a bovine embryo has 60 chromosomes. To achieve this number, the spermatozoa and oocyte that joined at fertilization must each have half of that number. This is haploid. Oocytes are diploid until immediately before ovulation. In fact, the nucleus of oocytes does not complete the reduction division so long as the follicle avoids ovulation or atresia. Thus in healthy follicles the nucleus of oocytes is viewed as arrested or quiescent. But, there is some transcription and translation to sustain maintenance, metabolism and accumulation of ooplasm.

In healthy follicles, the current model for regulation of oocyte maturation is that the reduction division of meiosis is blocked by follicular products so oocytes stay diploid. Furthermore, during this period of nuclear quiescence, metabolic activity in the ooplasm is minimal. In follicles that never ovulate or do not experience atresia, these oocytes are quiescent and the nuclei are arrested for years. This potent regulatory influence of a follicle on the resident oocyte appears to be quite resistant to influence from outside the follicle. In contrast to some previous suggestions (Hoard's Staff, 1994), there is no evidence that development or post-ovulatory fertility of oocytes is affected by the hormones or metabolites that characterize cows in early lactation.

## **ENERGY BALANCE ON FOLLICLES**

The most compelling observation that energy balance affects ovarian follicles is that duration of postpartum anovulation is correlated positively with the magnitude of NEB (Canfield and

Butler, 1991; Beam, 1996; Zurek, 1995). Delayed ovulation after calving is caused in part by delayed resumption of pulsatile secretion of LH. It is not known if a metabolite or hormone unique to NEB has direct adverse effects on ovarian follicles.

Among the metabolites and hormones that establish the milieu of NEB (Zurek et al., 1995) and suckling (Stevenson, 1997), few have been tested rigorously for direct effects on growth or function of ovarian follicles. Many possible mediators of energy balance on ovarian follicles have not been examined or at least not reported (Short et al., 1990; Bell, 1995).

Concentrations of growth hormone (**GH**) in blood are increased by NEB and exogenous GH augments NEB transiently. These observations have led to several investigations of the effects of exogenous GH on ovarian morphology and function. Compared to cows injected with saline; exogenous GH increased the number of medium size follicles and decreased the number of large follicles (Lucy et al., 1992). Although significant, these effects of exogenous GH on inventory of follicles are probably not a direct endocrine action of GH. To date, no receptor for GH has been detected in granulosa cells. So, the mechanism by which exogenous GH affects inventory of follicles is not clear. The overall effect is that GH reduces the functional significance of a dominant follicle.

It is well established that NEB will decrease pulsatile secretion of LH (Schillo, 1992). Independent of the mechanism for decreased secretion of LH, the effect is decreased follicular growth and reduced opportunity for ovulation because no preovulatory surge of LH occurs. If the effects of GH on follicles are not direct and not mediated by other messengers like insulin like growth factor-I (**IGF-I**), the effects of GH on follicles may be due to augmented NEB and subsequent decreased secretion of LH.

## SUMMARY

Growth and development of ovarian follicles occurs continuously throughout the reproductive life of dairy cattle. In fact, folliculogenesis is so consistent that there is virtually always a follicle present that is capable of ovulation.

A major limiting factor for ovulation is a adequate secretion of LH. But, just because a follicle is capable of ovulation does not mean that reproduction will be successful after ovulation. Follicles that grow during NEB are less likely to achieve dominance. With NEB there may be: less hormonal stimulation for estrus, increased incidence of multiple ovulation and(or) reduced function of CL formed by smaller ovulated follicles. There is no single hormone that has effects on follicles that are predominant to effects of other hormones. But, the fact that NEB reduces pulsatile, mean, and peak secretion of LH is the strongest explanation available for altered follicular dynamics and delayed ovulation postpartum.

## IMPLICATIONS

Among cows in NEB, there are no obvious or biologically reasonable hormonal therapies to convert follicular dynamics to those observed in cows at or above energy balance. The best available approach is to manage prepartum nutrition so that at parturition body condition is slightly above moderate. Then, manage postpartum nutrition to minimize loss of body condition and to minimize the magnitude and duration of NEB. Early and minimal NEB will initiate a wave of follicular growth soon after calving, which is key to resumption of estrous cycles and the opportunity for timely insemination and conception. I am not a nutritionist, so it would be irresponsible, and likely humorous, if I tried to describe nutritional management to achieve these goals. Thus, I will leave that to others. But, the principle is this, the most effective therapy for reproductive performance is maximal appetite and maximal consumption of dietary calories. With a background of NEB there are very few recorded successes of therapy for reproduction that can be delivered by syringes.

## LITERATURE CITED

- Beam, S.W. 1996. Energy balance, follicular growth and first ovulation in postpartum dairy cows. *J. Dairy Sci.* 79(1): 127.
- Bell, A. 1995. Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. *J. Anim. Sci.* 73: 2804.
- Canfield, R.W. and W.R. Butler. 1991. Energy balance, first ovulation and the effects of naloxone on LH secretion in early postpartum dairy cows. *J. Anim. Sci.* 69: 740.

- Hoard's staff. 1994. Here's the theory on why early breeding works. *Hoard's Dairyman* 139(Aug): 599.
- Lucy, M.C., J.D. Savio, L. Badinga, R.L. DeLaSota and W.W. Thatcher. 1992. Factors that affect ovarian follicular dynamics in cattle. *J. Anim. Sci.* 70: 3615.
- Schillo, K.K. 1992. Effects of dietary energy on control of luteinizing hormone secretion in cattle and sheep. *J. Anim. Sci.* 70: 1271.
- Short, R.E., R.A. Bellows, R.B. Staigmiller, J.G. Berardinelli and E.E. Custer. 1990. Physiological mechanisms controlling anestrus and infertility in postpartum beef cattle. *J. Anim. Sci.* 68: 799.
- Stevenson, J.S., G.C. Lamb, D.P. Hoffman and J.E. Minton. 1997. Interrelationships of lactation and postpartum anovulation in suckled and milked cows. *Livestock Prod. Sci.* In press.
- Sunderland, S.J., M.A. Crowe, M.P. Boland, J.F. Roche, and J.J. Ireland. 1994. Selection, dominance and atresia of follicles during the oestrous cycle of heifers. *J. Reprod. Fert.* 101:547.
- Sunderland, S.J., P.G. Knight, M.P. Boland, J.F. Roche and J.J. Ireland. 1996. Alterations in intrafollicular levels of different molecular mass forms of inhibin during development of follicular-and luteal-phase dominant follicles in heifers. *Biol. Reprod.* 54:453.
- Villa-Godoy, A., T.L. Hughes, R.S. Emery, L.T. Chapin and R.L. Fogwell. 1988. Association between energy balance and luteal function in lactating dairy cows. *J. Dairy Sci.* 71:1063.
- Zurek, E., G.R. Foxcroft and J.J. Kennelly. 1995. Metabolic status and interval to first ovulation in postpartum dairy cows. *J. Dairy Sci.* 78: 1909.