CHAPTER II
LITERATURE REVIEW

1. General aspect of growth and reproductive performance in goats

Growth is one of the main attributes of living things and is such an obvious process that it hardly seems to justify any particular formal definition. The simple concept of growth meaning getting bigger is perhaps ratter better than many of the complicated attempts to formalize something of such extraordinary complexity. In general, it is most helpful to use a descriptive word or phrase to quality growth to identify the broad aspect with which one is concerned. For example, within one individual animal, one may speak about cell growth, organ growth, fetal growth, prepubertal growth, bone growth, chemical growth or negative growth and so on. In farm animals the main interest lies in the growth of specific parts of the animal such as bone, muscle, fat or the development of the mammary gland. These aspects of growth are readily appreciated and can be easily subjected to quantification either by weighing or by linear measurement. In this age of dramatic advances in the high technology of biochemistry and genetic engineering, it is helpful to remind ourselves of the biological significance of the size and physical form of animals (Lawrence and Fowler, 2002).

1.1 Growth pattern in Thai-native goats

Thai native goats are similar to the Katjang breed of Malaysia. The major colors of goats were brown, (49-60%) followed by cream, black and the combination of brown, black and white (Saithanoo and Milton, 1988). Estimates on the average body weights of adult indigenous goats also varied. Songprasert et al. (1979) studied indigenous goats 5.1 months old with a body weight of 11.3 kg, Anekawiang (1982) reported that a group of young indigenous bucks (1-3 years old) had an average body weight of 23.4±0.8 kg, while a group of young does (1-2 years old) averaged 22.6±1.4 kg. The same results were also reported by Suthiwanich (1983) working on indigenous goats who found that female goats (1-3 years old) had an average body weight as 21-25 kg and males goat, 22-27 kg.

Songprasert et al. (1979) reported that grazing refer to goats on natural grasses under longan trees for 53 days during the dry season (October-December) yielded average daily gains of 63±7.1 g for the 8-12 months of age. Pashaa and Saithanoo (2000) estimated an average daily gain of only about 57 g for Kambing Katjang goats in Malaysia during their first year of life.

Kuprasert et al. (2001) studied the effects of energy and protein levels in concentrate on post-weaning growth of Thai native-Anglo-Nubian crossbred. Twenty-four weaners (12 males and 12 females) were used. These goats were fed 50 g/day of hay and ad libitum concentrate. Energy levels in concentrate were 2,700 and 2,900 kcal/kg ME and protein levels in concentrate were 10, 12, and 14%. Goats consumed 371-442 g of concentrate daily and male goats consumed more concentrate than did female (442 and 350 g/d, $P<0.01$). However, growth rate of male goats (47.3 g/d) was significantly greater than that of female goats (31.2 g/d).

Sripongpun et al. (2001) conducted a study of growth rates and carcass characteristics compaired among Thai local entire male, entire male castrated and female goats. The mean initial weight of goats was 14.8 kg with 199 days of age. Growth rate for these treatments were 49, 53, and 39 g/d, respectively.

1.2 Reproductive performance in Thai-native goats

Puberty is generally considered to be related more to growth than age in tropical goats (Devendra, 1981), with first estrus occurring with the attainment of 60-70% of adult live weight. Thai-native does can be used for breeding when they reach 8-10 months of age or 20-25 kg in body weight (Pralomkarn et al., 1996). Goats in Thailand are not seasonal breeders unlike those in the temperate zone and show estrus with ovulation in all months of the year. Indigenous does first come into estrus as early as 5-6 months of age. Does can be use for breeding when they reach 8-10 months of age or 20-25 kg in body weight. The estrous cycle in general ranges from 18-22 days (Pralomkarn et al., 1996).

Anekawiang et al. (1983) reported the average estrous cycle of indigenous Thai goats was 20.2±2.4 days, ranging from 17 to 22 days. Jansakul et al. (1982) studied indigenous goats in southern of Thailand 10-16 months of age, with a body weight of 20-26 kg and found the estrous cycle to be 17.9±4.0 days. The survey of

village goats (Saithanoo et al., 1991) showed that 60% of does conceived before 7 months, with an average age at first kidding of 12.4 months.

Young bucks 6-8 month old, in good bodily condition and weighing approximately 30-25 kg, can be used for breeding with a group of 6 or 8 does. However, older bucks of 18-20 months can service a group of 25-30 does (Saithanoo et al., 1991).

2. Folliculogenesis and Ovarian dynamics in goats

2.1 Follicular development

Follicular dynamics during the estrous cycle of the goat were first reported by Ginther and Kot (1994) using real-time ultrasonography (UTR). These authors frequently found four follicular waves in the estrous cycle and suggested that follicular dominance occurred in the first and last waves. These results have been confirmed by other reports (De Castro et al., 1999; Gonzalez-Bulnes et al., 1999; Padilla and Holtz, 2005), and are similar to the follicular dynamics observed in other ruminant species (Ireland et al., 2000; Mihm and Bleach, 2003). The occurrence of reduced, or lack, of follicular dominance in some waves in the middle of the estrous cycle of polyovular species (sheep and goats) has been reported by some authors (Schrick et al., 1993; Orita et al., 2000), but there is no agreement on this point (Bartlewski et al., 1999; Gibbons et al., 1999; Evans et al., 2000). In cows, the pattern of hormonal and follicular dynamic of waves with co-dominant follicles or one dominant follicle had some differences (Kulick et al., 2001) to small ruminants. Recent studies linking the morphological and functional characteristics of ovarian structures have provided an understanding of the relationships between progesterone (P4), estradiol, FSH or inhibin to goat ovarian dynamics (De Castro et al., 1999; Schwarz and Wierzchos, 2000; Menchaca and Rubianes, 2002; Medan et al., 2003).

Rubianes and Menchaca (2003) suggested that when ovulation is induced by luteolysis the ovulatory follicle could be a dominant follicle of an existing wave in either the growing or static phase. The ovulatory follicle was present at the time of the induced luteolysis in a significant proportion of the goats in the study of Gonzalez-Bulnes et al. (2005). Studies of follicular dynamics in the natural estrous cycle of goats (Ginther and Kot, 1994; De Castro et al., 1999; Medan et al., 2003)

show that there are no significant differences between the last two waves of the cycle or between these waves and the previous ones. However, these studies show a great variability in the number of follicular waves and it may be important to characterize them in relation to the number of waves present in the estrous cycle. The data of these studies were analyzed by combining the waves of each ovary, since both ovaries receive the same hypophyseal-pituitary signal, although the asymmetry of the follicular dynamics between right and left ovary has been recognized (Driancourt, 2001).

In domestic ruminants, ovarian follicular development occurs in waves of growth and regression of antral follicles (Adams, 1999; Webb et al., 2003). Best characterized in cattle, two or three successive waves of follicular growth occur in most estrous cycles (Adams, 1999; Townson et al., 2002); the duration of the inter-wave interval being a function of follicular dominance (Fortune et al., 1991; Ko et al., 1991; Adams, 1999). Recent ultrasonographic studies also confirm that there is a distinct wave-like pattern of follicular development in sheep and goats (Ginther and Kot, 1994; Bartlewski et al., 1999; De Castro et al., 1999), although follicular dominance is less pronounced than in cattle (Ginther and Kot, 1994; Souza et al., 1997; De Castro et al., 1999).

The results of daily ultrasonographic studies indicate that the interovulatory cycle of goats is characterised by a wavelike pattern of follicular development (Ginther and Kot, 1994; De Castro et al., 1999; Gonzalez-Bulnes et al., 1999) as was report for other ruminant species (Sirois and Fortune, 1988; Ginther et al., 1995). A follicle wave involves the emergence of a group of small antral follicles from which commonly one or two follicles are selected to grow to more than 5 mm in diameter. According to different authors the number of follicular waves ranges between two and five waves per cycle, but the predominant pattern for goats that developed an interovulatory cycle of normal length (19–22 days) is of four waves (Ginther and Kot, 1994; Schwarz and Wierzchos, 2000; Menchaca and Rubianes, 2002). The emergence of waves 1, 2, 3 and 4 (the ovulatory wave) occurs on day 0, 5–6, 10–11, and around day 15 post-ovulation, respectively (Figure 2.1). Some of the more frequently observed characteristics of the follicular waves are: (1) the diameter of the largest follicle of a wave differs between waves; commonly the largest follicles of

waves 2 and 3 attain smaller maximum diameters than both, the largest follicle of wave 1 and the ovulatory follicle (Ginther and Kot, 1994; Menchaca and Rubianes, 2002); (2) two or more follicles per wave frequently attain 5 mm or more in diameter (Ginther and Kot, 1994; Schwarz and Wierzchos, 2000). (3) the growth rate between the day of emergence (i.e. first day with a size of 3 mm) and the day of maximum diameter is around 1mm per day (Ginther and Kot, 1994; Gonzalez de Bulnes et al., 1999; Schwarz and Wierzchos, 2000); (4) as the luteal phase progresses, follicular turnover increases and the inter-wave intervals are shorter than during the early luteal phase (Ginther and Kot, 1994; De Castro et al., 1999); (5) during the mid-late luteal phase the follicles that do not grow beyond 4 mm often are not part of the wave phenomenon and it is suggested that they represent a dynamic underlying pool (Ginther and Kot, 1994; De Castro et al., 1999); (6) most of the ovulatory follicles are the largest follicles on the day of luteolysis (Ginther and Kot, 1994; De Castro et al., 1999); (7) in most double ovulatory goats the ovulatory follicles emerged as part of the same follicular wave but in a few cases also as a part of different waves (Ginther and Kot, 1994); and (8) the double ovulations occur on the same day in most cycles (Ginther and Kot, 1994).

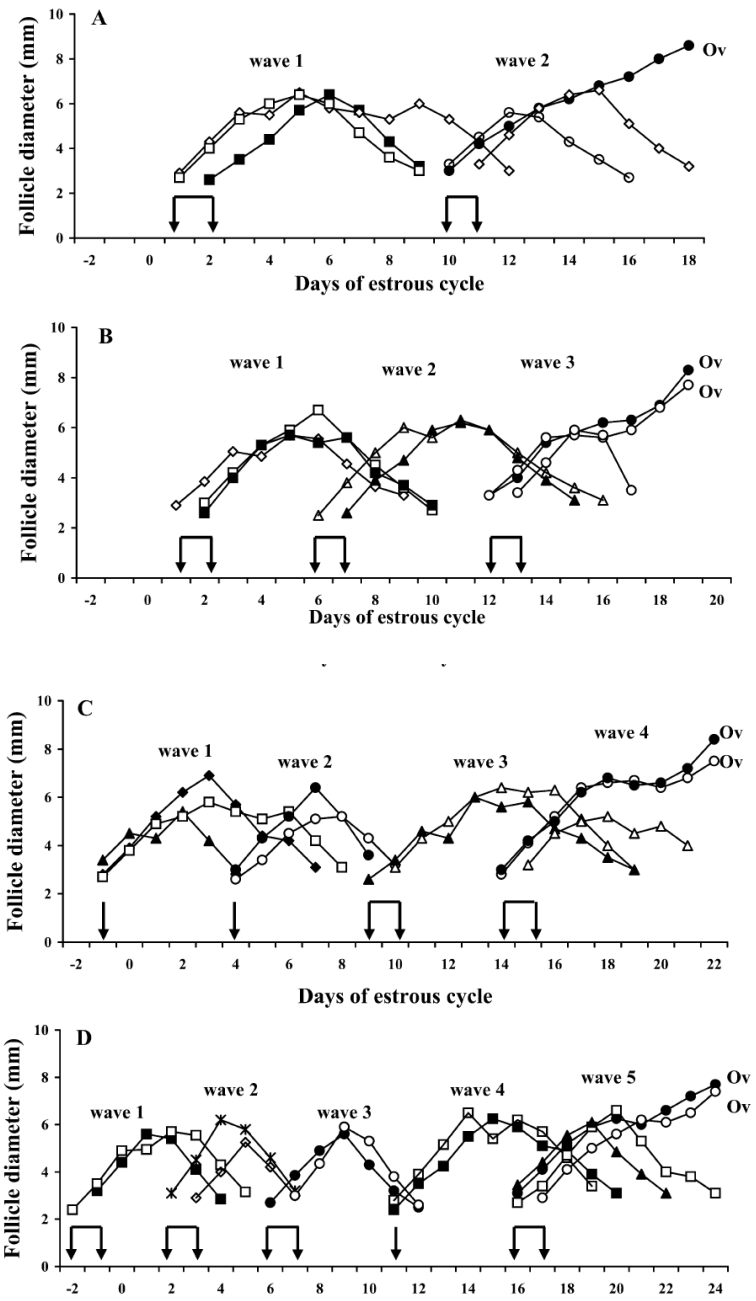


Figure 2.1 Representation patterns of growth and regression of individual follicles during the estrous cycle in goats with two (A), three (B), four (C), and five (D) waves of follicular development. Arrows indicate the emergence of follicular waves, and different symbols indicate a different follicle in each follicular wave (Ov = ovulation)

Source: Medan et al. (2005)

2.2 Corpus luteum in small ruminant

The corpus luteum (CL) is a transient endocrine gland formed from the wall of the Graffian follicle after the release of the egg, by a complex mechanism involving morphological and biochemical changes. It is a dynamic endocrine gland showing variations in size, structure and steroidogenic activities in different stages of the estrous cycle and pregnancy (Fields and Fields, 1996). The CL consists of two types of luteal or steroidogenic cells, viz. granulosa lutein and theca lutein cells and several types of cells such as endothelial cells, pericytes, smooth muscle cells, macrophages, leucocytes and occasional plasma cells (Alila and Hansel, 1984). It secretes progesterone as the principal steroid hormone and small quantities of oestradiol-17β, prostaglandins and a number of peptide hormones such as relaxin, oxytocin, oxytocin related neurophysin-I, vasopressin and inhibin (Fields, 1991). Information on structure (including ultrastructure), histochemistry, biochemistry, endocrinology, immunology, in vitro manipulation by growth factors and regulatory mechanisms (including apoptosis), has been elaborated specially in rodents and large ruminants (Guraya, 2000). However, relatively less attention has been paid to the cellular and molecular biology of CL of small ruminants especially goat and sheep which are of great economic importance in developing countries (Smith et al., 1994).

2.2.1 Development of corpus luteum

The follicle wall after ovulation becomes loose and the vascularization of membrane a granulosa occurs simultaneously with the degeneration of basal lamina under the influence of various angiogenic factors (Redmer and Reynolds, 1996; Reynolds and Redmer, 1998). The luteinization of granulosa cells is known to be controlled by luteinizing hormone (LH) and blood vascularity, transporting oxygen, nutrients, hormones and various factors (Niswender and Nett, 1994; Milvae et al., 1996; Guraya, 2000). The sprouting blood capillaries invade the granulosa cells and form an extensive network within CL of the goat (Sharma, 2000). The rate of luteal vascular growth is greatest in the early estrous cycle and by midcycle the mature CL are highly vascular. The luteinized granulosa cells, the surrounding theca-interstitial cells and invading vasculatures intermingle to form a CL which secretes progesterone during the postovulatory phase. Hypertrophy of luteinized granulosa cells, hyperplasia of fibroblasts of the connective tissues and vascularity contribute to an

increase in size of CL. The maximum diameter of CL is reached 6-9 days after ovulation and then regression starts between Days 13 and 16 in ewes (Jablonka-Shariff et al., 1993). During the tremendous growth of CL there occur dramatic changes in tissue remodeling, including cell hypertrophy, hyperplasia and migration. These cellular changes occur in unison with changes in extracellular matrix, affecting specific cellular processes such as mitosis, migration, differentiation and gene expression (Getzenberg et al., 1990). Two families of proteins that are involved in extracellular matrix remodeling include metaloproteinases and plasminogen activator/plasmin. Protease inhibitors (TIMP and α2 macroglobulin) may play a role in regulating the activity of metaloproteinases preceding follicular rupture and in the regulation of tissue remodeling during CL development (Smith et al., 1994).

The shape, size and structure of granulosa luteal cells in goats and sheep are various (Brar, 1993). The differences in the degree of hypertrophy or luteinization in different granulosa cells can be attributed to the heterogeneity in granulosa cells of the maturing follicle and granulosa cells surrounding the antrum that possibly do not differentiate (or do not develop sufficient LH receptors to luteinize), immediately after ovulation (Guraya, 2000). The differentiation of theca and granulosa cells into steroidogenic luteal cells is well accepted. However, the idea that small luteal cells originate exclusively from theca cells and large luteal cells from granulosa cells remains controversialist (Sangha et al., 2002).

In domestic ruminants there is morphological and immunological evidence for small theca-derived luteal cells differentiating into large luteal cells (Cran, 1983; Alila and Hansel, 1984; Farin et al., 1988). As stated by O'Shea et al. (1986) there is still no compelling evidence supporting the hypothesis that small luteal cells differentiate into large luteal cells during the mid-luteal phase of the estrous cycle. It is not feasible to obtain large and small luteal cell populations in CL between Days 1 and 6 of the estrous cycle in sheep. The size distribution of steroidogenic cells actually overlaps and forms populations (Schwall et al., 1986). The number of steroidogenic cells increases in the first half of the cycle while the number of non-steroidogenic cells tend to increase in the later part of the cycle (Farin et al., 1988).

3. Physiology of the estrous cycle in goat

3.1 Estrous cycle

The estrous cycle consists of all morphological and physiological changes in the ovaries and genital tract leading to estrus expression (phase of receptivity towards males) and ovulation and the preparation of the genital tract for copulation, fertilization and embryo implantation. During the course of the breeding season, females can undergo several estrous cycles successively and the number of successive cycles is dependent on the length of the breeding season and the breed of goat. The length of estrous cycle is defined by the interval between two successive expressions of estrus or two successive ovulations. While the average duration of the goat estrous cycle is of 21 days (Figure 2.2), its length is highly variable. A study with Alpine goats during the breeding season recorded 77% cycles of normal in duration (17–25 days), 14% were short cycles (8 days in average) and 9% were long cycles (39 days in average; Baril and Saumande, 2000). The relative high frequency of short cycles is characteristic of goats and increases when ovulation is induced either just before or during breeding season. This proportion can be modulated by environmental factors such as photoperiod and nutrition.

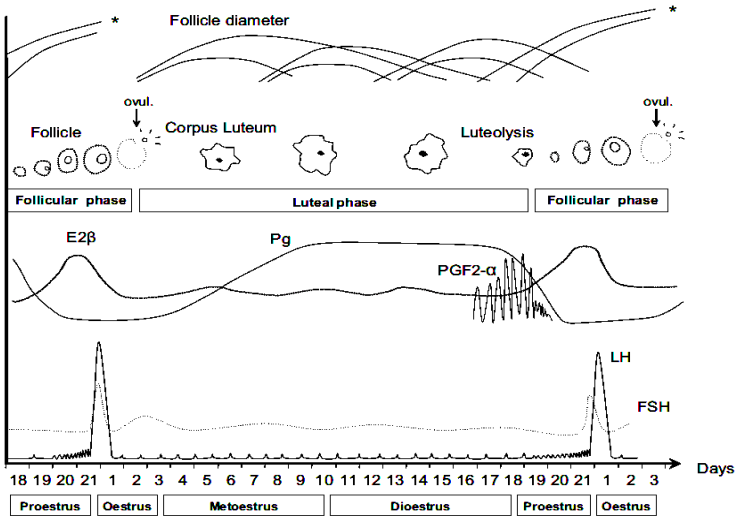


Figure 2.2 Schematic representation of the different physiological events occurring during oestrous cycle in goat: pattern of follicle development, ovarian cycle and endocrine regulations. *Ovulatory follicle(s)

Source: Adapted from Baril et al. (1993) and Evans (2003)

3.2 Ovarian cycle and hormonal change

Recent studies linking the morphological and functional characteristics of ovarian structures have provided an understanding of the relationships between progesterone (P4), estradiol, FSH or inhibin to goat ovarian dynamics (De Castro et al., 1999; Schwarz and Wierzchos, 2000; Menchaca and Rubianes, 2002; Medan et al., 2003). Rubianes and Menchaca (2003) suggested that when ovulation is induced by luteolysis the ovulatory follicle could be dominant follicle of an existing wave in either the growing or static phase. The ovulatory follicle was present at the time of the induced luteolysis in a significant proportion of the goats in the study of Gonzalez-Bulnes et al. (2005). Studies of follicular dynamics in the natural estrous cycle of goats (Ginther and Kot, 1994; De Castro et al., 1999; Medan et al., 2003) show that there are no significant differences between the last two waves of the cycle or between these waves and the previous ones. However, these studies show a great variability in the number of follicular waves and it may be important to characterize them in relation to the number of waves present in the estrous cycle.

During the estrous cycle, ovaries undergo a number of morphological (follicular recruitment and growth), biochemical (follicular maturation) and physiological (endocrine regulations) changes leading to the ovulation. These cyclical changes in the gonads are referred to as the ovarian cycle. Follicular growth evolves in a wave-like manner throughout the cycle (Figure 2.2). A follicular wave is characterised by the sequence of three gonadotropin-dependent events in follicular growth: recruitment, selection and dominance (Driancourt, 2001). Studies using repeated ultrasonography suggest that there are between two and six waves of follicle development during estrous cycles in goats with three or four waves being the most prevalent (Evans, 2003; Simoes et al., 2006). The last wave provides the ovulatory follicle. When double ovulations occur they are usually of follicles derived from the same wave, but in a few cases they derive from two consecutive follicle waves (Ginther and Kot, 1994). The ovarian cycle is classically divided in two phases: the follicular phase and the luteal phase (Figure 2.2). The follicular phase corresponds to the wave of follicle development providing the ovulatory follicle and involves maturation of gonadotropin-dependant follicles until ovulation (terminal growth).

During the follicular phase, FSH secreted by the pituitary gland stimulates follicular growth. A cohort of gonadotropin-dependant antral follicles of 2–3 mm of diameter is recruited and follicles enter their terminal growth. Only 2–3 of these follicles reach 4 mm diameter and are selected to enter the dominance phase. Under the influence of LH, they reach the pre-ovulatory stage (6–9 mm), while subordinate follicles degenerate (follicular atresia). The increase in peripheral concentrations of estradiol 17 β, secreted by bigger follicles, induces estrous behavior and acts as a positive control on the gonadotropic axis. The consequent increase in GnRH secretion induces the pre-ovulatory LH surge which induces ovulation 20–26 h later and subsequently luteinization of follicular cells. The beginning of the follicular phase, before overt estrous behavior is observed, is also referred to as the proestrus. The estrous phase includes events from overt estrous behavior to ovulation (Figure 2.2).

Both season and nutrition are known to affect the ovulation rate, especially in the Angora breed. Angora goats typically have a single ovulation under most production conditions but may have two under very good nutritional conditions. Average ovulation rate is reported as 1.7 in Boer goat (Greyling, 2000), 1.5 in local Maure goat and probably much higher in Chinese Matou goat, which have an average litter size of 2.1 (Moaeen-ud- Din et al., 2008).

The luteal phase starts from the time of ovulation. About 5 days after the onset of oestrus, cells of the ovulating follicle turn into luteal cells and form the corpus luteum (CL). They secrete progesterone causing its concentrations to increase and remain at a high level (>1 ng/ml) during 16 days. During this luteal phase, gonadotropin-dependant follicular growth continues in a wave-like manner but progesterone inhibits ovulation. At the end of the luteal phase, 16–18 days after estrus, prostaglandin F2α secreted by the non-gravid uterus induces the CL regression called luteolysis and the decrease of progesterone secretion. The decrease of plasma concentrations of progesterone gradually removes the inhibition of gonadotropic hormones secretion and a new follicular phase then commences (Baril et al., 1993). The luteal phase is also called the post-estrous period, which can be divided in metestrus, when peripheral concentrations of progesterone begin to rise, and diestrus, when peripheral concentrations of progesterone are high up to the start of luteolysis.

3.3 Cyclical changes in the cytology and secretions of the genital tract

During the estrous cycle, changes occur in the genital tract in order to facilitate sperm transport and fertilization and then to prepare for embryo implantation. Vaginal, cervical and uterine mucosa congest and become edematous at the time of estrus due to high estrogen levels (Hamilton and Harrison, 1951). In addition, uterine, cervical and vaginal glands secrete important quantities of aqueous mucus, clear at the beginning of estrus then becoming more viscous and compact as the period of estrus continues.

The cervical mucus plays a central role in cervical function by controlling and directing sperm migration. Estrogens stimulate the secretion of sialomucin by mucus cells located at the bottom of the large cervical folds within the cervix. Sulfomucins are also secreted in smaller quantities by mucus cells on the upper parts of the cervical folds (Heydon and Adams, 1979). At estrus, the cervical mucus becomes more watery and penetrable to sperm, allowing their migration through the cervix. Cervical secretion is inhibited by the post-ovulation rise in peripheral progesterone.

Different studies have recorded cytological changes in the genital tract of the female goat during the estrous cycle. The relationships between vaginal exfoliated cells and ovarian steroids secretion cycle have been well established in goats. This pattern of exfoliation of vaginal cells could be used to determine the estrous cycle status. In this respect, superficial cells appear to be associated with the proestrus, estrus and early metestrus (Hulet and Shelton, 1980). Intermediate and parabasal cells are observed in larger quantities during the progesterone dominated luteal phase. Exfoliated cells in the vaginal lumen are the result of rising peripheral estrogen which causes the vaginal wall to thicken. As the outermost layer moves further from the vascular supply, the cells keratinise and detach from the wall (Perez-Martinez et al., 1999).

Distribution of mast cells also varies depending on physiological changes during the estrous cycle in the goat reproductive tract and ovarian tissues. The numbers of mast cells in the ovary, uterus, uterine cervix and uterine tubes are highest on proestrus and lowest on metestrus (Karaca et al., 2008). Mastocytes are derived from haematopoietic precursors and represent critical effecter cells in allergic

diseases. It is assumed that these cells might operate as sentinel cells to help mediate the uterine host defense systems and might have a role in the uterus with regard to the embryo implantation.

3.4 Estrous behavior

Estrous behavior includes into two phases: proceptivity and receptivity. Proceptivity consists in seeking out and stimulating the male partner. Receptivity consists in the expression of the immobilization reflex in response to male nudges, inducing serial mounting and copulation. At the beginning of estrus, proceptivity always precede receptivity, then both behavior components are expressed simultaneously (Figure 2.3).

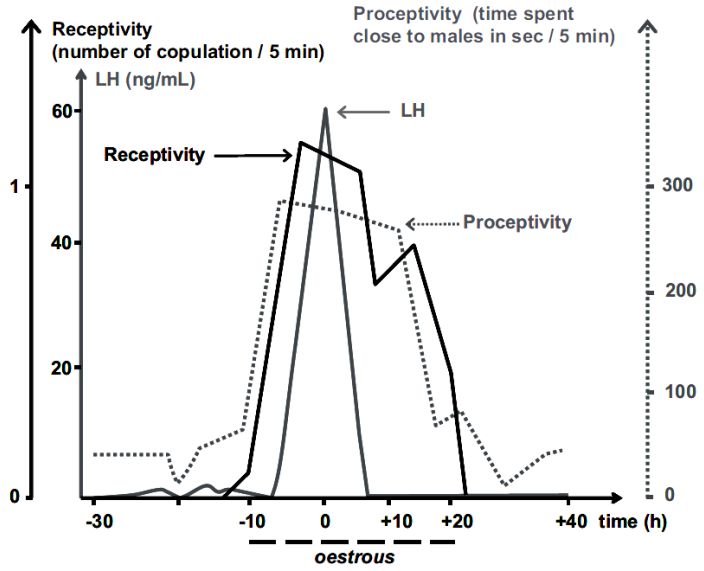


Figure 2.3 Evolution of sexual behavior during estrous cycle in Japanese dwarf goat Source: Okada et al. (1996)

The duration of estrous behavior is about 36 h but varies from 24 h to 48 h depending on age, individuals and breeds, season and the presence of a male. Angora goats and Mossi goats are known to have a short estrus lasting only 22 h and 20 h, respectively (Shelton, 1978). Creole goats exhibit 27 h of estrous behavior and

French Alpine goats are reported to experience a 31-h estrus (Baril et al., 1993). In Boer goats, the mean duration of estrous period is about 37 h (Greyling, 2000) and it is of about 58 h in Matou goats in Central China (Moaeen-ud- Din et al., 2008).

The interval from the beginning of estrus to the LH surge varies with breeds and individuals: 14.5 h in Alpine goat, 14–22 h in the Mossi goat in Burkina Faso and as short as 8 h in Boer goat (Greyling, 2000). The exact timing of ovulation relative to the onset of estrus is variable ranging from 9 h to 37 h, and is reported generally as occurring towards the end of standing estrus.

Continuous presence of a male and service during the estrous period may reduce the duration of estrus although it did not affect ovulation times or ovulation rates in Nubian dairy goats (Romano and Fernandez Abella, 1997).

In goats, the plasma progesterone (P4) concentration, measured during various physiologic stages, is one of the most important parameters of the reproductive status of a doe. P4 concentrations are used to monitor the luteal function, estrous cycle, and seasonality of reproduction, given that they reflect the development and regression of the corpus luteum. (De Castro et al., 1999). Moreover, P4 concentrations can be used to predict ovulation and detect estrus (Błaszczyk et al., 2004) as well as to diagnose follicular cysts (Medan et al., 2005). The parameter can also be helpful in a diagnosis of gestation status and parturition date estimations. Because the information on plasma P4 concentration in goats is so valuable, a commercially available measuring kit and a simple procedure are highly desirable (Singer et al., 2004). According to the majority of reports published to date, P4 analysis in goats has been carried out mainly by radioimmunoassay (RIA). For obvious reasons, this procedure must be carried out with special safety procedures in laboratories authorized to work with radioactive materials (Błaszczyk et al., 2004). Hence, research has been undertaken to seek new nonisotopic methods of P4 concentration measurement in animals, such as enzyme immunosorbent assay (EIA) (Singer et al., 2004) or fluorescent antibody test (FAT) (Takahashi et al., 2002). The time-resolved fluorescent antibody test (TR-FAT) is a method that combines highly purified antigens and monoclonal antibodies in a sandwich-type assay, with the long fluorescence decay time of lanthanide chelates, such as europium, samarium, and terbium, used as labels, and a special time-resolving fluorometer for nanosecond measurements. This system has advantages over RIA,

such as being free from radiologic decay and meeting relevant safety requirements. A direct TR-FAT system was evaluated for measuring P4 concentrations in Sika deer, Iberian red deer, and cattle (Elliot et al., 1995).

4. Application of assisted reproductive technology in reproductive management

The application of assisted reproduction technologies (ART) enables the rate of genetic progress to be increased (Nicholas, 1996). The ART techniques include artificial insemination, estrus synchronization, estrous induction, synchronization of parturition, superovulation, in vitro fertilization, in vivo and in vitro embryo production, embryo collection, embryo transfer, embryo cryopreservation, embryo splitting, cloning, production of transgenic animals, and preimplantation genetic diagnosis. ART allows animals of high genetic merit to produce more offspring than would be possible by natural breeding. Moreover, in combination with hormonal synchronization of estrus and ovulation, some of these techniques allow the production of offspring and milk in times of the year that are not the natural breeding period of seasonally reproductive species such as the goat (Corteel et al., 1988; Chemineau and Cognie, 1991).

Artificial insemination is the most widely used ART and the one that has made the most significant contribution to genetic improvement worldwide (Evans and Maxwell, 1987; Chemineau and Cognie, 1991; Leboeuf et al., 2000). Combined with an appropriate system for sire evaluation (progeny testing), AI offers a relative simple and low cost method for dissemination of valuable genes. The use of frozen semen facilitates international exchange of genetic material, allows the use of semen in both the reproductive and non-reproductive seasons, and extends the effective reproductive life of a valuable male beyond its own life. AI and heat synchronization are key technologies for managing production systems, allowing the concentration of mating and parturition, and production of meat and milk during specific times of the year for strategic marketing and other purposes. Multiple ovulation and embryo transfer (MOET) is often referred as the ART that is “to the female, what AI is to the male”, i.e. a method of producing more offspring from a genetic valuable female than would be possible by natural breeding. While the statement is theoretically correct, MOET has not yet become a widespread tool for genetic improvement for a variety of reasons

that will be discussed later in this review including its costs, technical demands, and variable and unpredictable efficiency (Baril et al., 1993; Cognie, 1999; Cognie et al., 2003).

Many practitioners consider MOET to be the most frustrating of all ART, since the results can vary from complete failure to total success without any variation in the standard operating procedure. The main factors contributing to the unpredictability of this technique are the variability of the superovulatory response, the poor fertilization associated with high ovulatory responses, and early regression of corpora lutea (Cognie, 1999; Cognie et al., 2003). These unpredictable results, combined with high costs and the use of surgical procedures for collecting and transferring embryos, have prevented large-scale use of MOET in goat improved programs. An average of six to eight transferable embryos per donor can be produced in a successful goat MOET program (Baril et al., 1993; Cognie, 1999; Cognie et al., 2003). These results, however, depend on many factors (including breed, age and nutrition) that contribute to the high variability. It is common for the number of transferable embryos to range from 0 to 30 per donor with 25–50% of the donors failing to produce any transferable embryos due to fertilization failure and early regression of corpora lutea. Variation in superovulatory response is believed to reflect the follicular population present at the initiation of gonadotropin treatment (Gonzalez-Bulnes et al., 2003), which is not controlled by standard superovulatory protocols. Several strategies have been suggested for increasing the number of small recruitable ovarian follicles at the time of FSH treatment, while avoiding the presence of large (dominant) follicles. Some of these strategies include the use of GnRH agonist/antagonists and the administration of FSH shortly after an induced estrus/ovulation. Pre-treatment with a Buserelin implant (PepTech Animal Health, NSW, Australia) one week prior to superovulatory treatment did not improve the response of superovulated oocyte and embryo donors (Baldassarre and Karatzas, 2004). It is possible that GnRH pre-treatment should be administered for more than 1 week to deplete the pituitary of gonadotropins and allow the ovary to build-up a large number of small follicles. Pre-treatment with Antarelix (GnRH antagonist) for 10 days prior to superovulation resulted in an increased number of small follicles at the time of FSH administration and an increased number of ovulations (Cognie et al., 2003). However, this improvement in superovulatory

response did not yield a larger number of transferable embryos because of poor fertilization (>30%). A so-called “day 0 protocol” has been proposed recently to avoid the deleterious effects of large dominant follicles and improve results from superovulation (Menchaca et al., 2002). This protocol is based on initiating FSH administration immediately after ovulation and resulted in a 30% increase in the number of CL following superovulation, but only a small number of does were treated. However, improvements in terms of the number and quality of embryos recovered have not been reported.

Principles of inducing superovulation in sheep are the same as in cattle. A follicle stimulating gonadotropin is administered either near the end of the luteal phase of the cycle (days 11-13) or around 1 or 2 days before the end of the synchronizing treatments (Jablonka-Shariff et al., 1993; Stenbak et al., 2001, Grazul-Bilska et al., 1996). A high degree of ovulatory response is observed in sheep during superovulatory treatment which hampers the process of fertilization. This fertilization failure appears to be due to faulty transport of spermatozoa through the cervix whether bred naturally or inseminated artificially. This problem can be overcome by direct deposition of semen into the uterus. An enormous amount of literature concerning superovulation in sheep has been produced and from its analysis it is evident that an accurate control of ovulation has never been achieved. Embryo yield after superovulation is dependent upon many factors that can be grouped as follows (Loi et al., 1998):

1. Factors inherently variable and difficult to modify (breed, season, management). It is easy to understand that very little improvement can be expected from factors like breed and consequently flock management techniques as well as nutrition. Reproductive biologists made a major effort in the past to fit suitable superovulatory protocols into a large number of domestic breeds under a broad environmental range (Gordon, 1997).

2. Factors susceptible on improvement (gonadotropin, knowledge of ovarian physiology). The two most widely used gonadotropin preparations for superovulation are pregnant mare serum gonadotropin (PMSG) and pituitary follicle stimulating hormone (FSH-P). Pregnant mare serum gonadotropin is administered as a single subcutaneous or intramuscular injection given 1 day prior to the last synchronization

treatment. FSH-P is given at 12h intervals in decreasing doses for about 3 days on days 12-16 of the estrous cycle. Prostaglandin F_{2a} is administered i.m. at the time of the fifth FSH injection (Senn and Richardson, 1992). Exogenous gonadotropin interplay with somatic and germinal compartments of the follicle leads to greater than normal ovulation rates. Additional negative effects can occur during early embryonic development as a result of unbalanced hormonal profiles. Several strategies have been suggested for optimizing the yield of transferable embryos from superovulated donors including the administration of anti-PMSG antibodies, pituitary follicle stimulating hormone-FSH instead of PMSG, association of these two gonadotropins, single versus multiple injections, or inclusion of GnRH or growth hormone in the treatments (Bindon and Piper, 1986; Ryan et al., 1991; Meinecke-Tillman, 1993; Walker et al., 1986). However, the well-known side-effects of the superovulatory treatment such as unovulated follicles, low fertilization and recovery rates, were still not fully solved (Loi et al., 1998). It seems that progress in the effectiveness of superovulation will be associated with development and availability of systems for controlling follicular recruitment and selection. A detailed understanding of the processes involved in growth and differentiation of ovulatory follicles has been achieved in cattle and has led to the development of strategies for the control of the follicular wave (Bo et al., 1995). For sheep, several successful superovulatory protocols have been reported (Gordon, 1997).

Once a suitable superovulatory protocol is established, the next step is to verify responsiveness of the same donor to repeated treatments. Multiple superovulations can be induced in sheep at a 1 year interval without a significant reduction in ovarian response (Loi at al., 1998). Whether immunological responses induced by gonadotropins used for superovulation can reduce the ovarian response still remains an open question. However, side-effects of repeated treatment with gonadotropins are not the major factors limiting multiple superovulation in sheep. The major problems related to repeated superovulation and frequent laparoscopic procedures of oocyte or embryo collections are adhesions caused by protrusions of the endometrium at the puncture site in laparoscopic recovery. The occurrence of adhesions may reduce the number of flushing obtainable from one donor (Nellenshulte and Nieman, 1992).

Stenbak et al. (2001) reported, administration of FSH increases the number of developing follicles, and affects oocyte health and cleavage rate. To determine the optimal level of FSH treatment, studies were conducted during the normal breeding season and seasonal anestrus. In Experiment 1, ewes were implanted with Syncro-Mate-B (SMB; norgestomet) for 14 days during the breeding season. Beginning on Day 12 or 13 after SMB implantation, ewes were treated with saline (control; n=10), or treated with FSH for two days (2D; n=9) or three days (3D; n=10). In Experiment 2, conducted during seasonal anestrus, ewes were implanted with SMB for 14 days (n=23) or were not implanted (n=26). The SMB-implanted and nonimplanted ewes were assigned to one of three treatments as in Experiment 1: control (n=l3), 2D (n=21) or 3D (n=l5)

Table 2.1 Number of ≤ 3 mm and > 3 mm follicles in control and FSH-treated ewes during breeding season

		Number of follicles/ewe		
Treatment	Number of ewe	≤ 3 mm	> 3 mm	Total
Control	10	3.3±0.8	4.9±0.7[a]	8.2±1.0 [a]
2D FSH	9	2.0±1.0	14.2±1.6 [b]	16.2±2.1[b]
3D FSH	10	1.3±0.6	20.1±1.9 [c]	21.4±2.0 [c]

[a,b,c] means ± SEM differ within a column, P<0.01

Source: Stenbak et al. (2001)

Table 2.2 Number of oocytes recovered from ≤ 3 mm and > 3 mm follicles in control and FSH-treated ewes during the breeding season

		Number of oocytes/ewe		
Treatment	Number of ewe	≤ 3 mm	> 3 mm	Total
Control	10	2.8±0.6 [a]	3.7±0.7[a]	8.2±1.0 [a]
2D FSH	9	1.1±0.6 [b]	9.4±1.5 [b]	10.5±1.7[b]
3D FSH	10	0.7±0.4 [b]	20.1±1.9 [c]	14.4±2.0 [c]

[a,b,c] means ± SEM differ within a column, P<0.02

Source: Stenbak et al. (2001)

In Experiments 1 and 2, ewes were laparotomized to count the number of follicles 3 mm and >3 mm and to retrieve oocytes. Healthy oocytes from each treatment were used for IVF. In Experiment 3, ewes (n=6) were implanted twice with SMB for 14 days during seasonal anestrus. Ewes were injected with FSH for 2 days, and the oocytes were collected and fertilized as in Experiments 1 and 2. In Experiment 1, FSH-treatment increased ($P< 0.05$) the number of follicles >3 mm, the number of oocytes retrieved from follicles < 3 mm and >3 mm, the proportion of healthy oocytes, and the number of oocytes used for IVF. Oocytes from control and 2D ewes had greater ($P<0.01$) cleavage rates than 3D ewes (68% and 71% vs. 42%). In Experiment 2, implanted and nonimplanted ewes had similar ($P>0.05$) numbers of follicles, total oocytes, and healthy oocytes; therefore, data were combined. The FSH treatment increased ($P<0.01$) the number of follicles >3 mm, and the number of oocytes recovered from follicles >3 mm. The recovery rate of oocytes and the percentage of healthy oocytes were similar for control and FSH-treated ewes. The cleavage rate in Experiment 2 ranged from 4 to 16%. In Experiment 3, the cleavage rate for ewes treated twice with SMB was 27% which tended to be greater ($P< 0.07$) than for the 2D ewes that received one SMB implant in Experiment 2. These data indicate that FSH increased the number of developing follicles and the number of healthy oocytes retrieved from ewes during the breeding season and seasonal anestrus. However, cleavage rates during seasonal anestrus were lower than during the normal breeding season in both FSH-treated and control ewes. Treatment of ewes for 2 days with FSH resulted in a greater cleavage rate than treatment of ewes for 3 days.

Gonzalez-Bulnes et al. (2003) study evaluates the response of Murciano-Granadina goats to superovulatory FSH treatments, in terms of number of corpora lutea (CL) and transferable embryos, as well as the variability between replicates and the possible effects of follicular status on superovulatory yields. A total of 169 goats were allocated to nine different groups, and treated with 45 mg fluorogestone acetate (FGA) sponges for 16 days plus a single dose of 100 μg i.m., cloprostenol on Day 14. The superovulatory treatment in all groups consisted of eight doses of 1.25 ml of Ovagen^{TM}, twice daily from 60 h before to 24 h after the removal of the progestagen treatment. In the animals from the last three groups (50 females), all follicles ≥2 mm were evaluated by transrectal ultrasonography at the time of the first FSH injection.

The response to the FSH treatment, in all the goats, was 14.3±0.5 corpora lutea, 11.3 ±0.5 recovered embryos (RE) and 6.8±0.4 viable embryos (VE) per goat.

Table 2.3 Superovulatory yields obtained in different groups of Murciano-Granadina does treated with a commercial preparation (Ovagen^{TM}) and the same protocol

Group (n)	Corpora lutea	Recovered embryos	Recovery rate (%)	Viable embryos	Viability rate (%)
1 (22)	16.8±1.1	14.4±1.2	83.1±5.2	9.5±1.1	69.5±5.5
2 (20)	15.0±1.1	13.7±1.4	88.9±5.5	10.1±1.3	70.5±4.1
3 (25)	15.1±1.5	12.0±1.6	78.6±4.9	6.6±1.3	60.7±6.2
4 (22)	11.0±1.3	9.3±1.2	85.1±4.5	6.5±1.1	67.9±6.6
5 (18)	12.6±1.4	10.2±1.6	77.2±6.2	5.9±1.3	64.4±8.6
6 (12)	10.6±1.6	6.7±1.1	67.7±7.3	2.5±0.9	32.5±11.1
7 (16)	15.7±1.5	9.8±1.4	67.7±7.5	4.8±1.1	48.4±8.9
8 (19)	13.7±1.2	10.6±1.2	75.7±6.7	6.4±1.3	56.7±6.2
9 (15)	17.1±1.9	14.3±2.5	76.9±5.6	6.5±1.1	53.1±7.6
Significance (P)	<0.01	<0.05	ns	<0.01	<0.05

Source: Gonzalez-Bulnes et al. (2003)

Superovulatory yields varied widely between replicates, with significant differences in the number of corpora lutea ($P<0.01$), recovered embryos ($P<0.05$) and viable embryos ($P<0.01$). This variability in response to the superovulatory protocol is related with follicular status of the donor at the beginning of the treatment. The number of corpora lutea was positively correlated with the total number of follicles with a diameter of 2–6mm ($P<0.05$; $r = 0.826$). However, the number of recovered and viable embryos were related to the more limited category of follicles of 4–6 mm in size (6.2±0.5), which could indicate that oocytes from smaller follicles are not fully mature. The results indicate that ultrasonography can be used as a practical criteria for selection of donor goats, which could avoid the treatment of poor-responding females, and provide a basis for the study of suitable treatments to make ovarian follicular populations uniform.

5. Application of compensatory growth in reproductive management

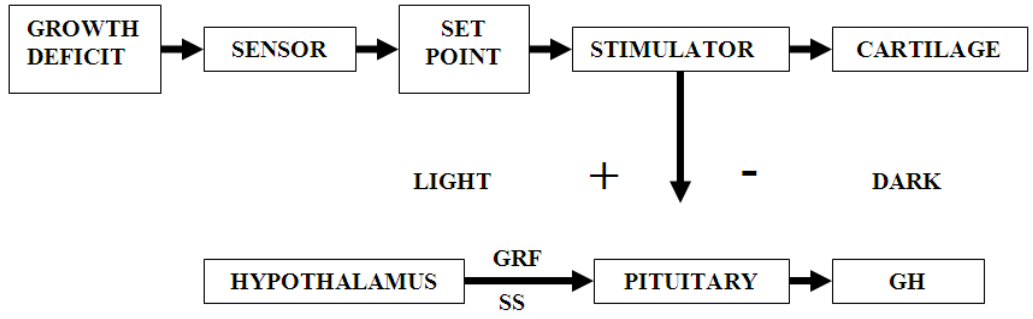
5.1 Definition of compensatory growth

Compensatory growth is referred to as the rapid weight gain that usually follows a period of reduced nutrient intake of animals, when it is placed back on a high quality diet. The most frequently used working definitions of ‘‘compensatory growth’’ describe it as a growth acceleration seen following the return of favorable conditions after a period of growth depression. Compensatory growth may follow a period of reduced growth resulting from food restriction or some other unfavorable environmental condition (Jobling, 1994; Ali et al., 2003; Nicieza and Alvarez, 2009). The term may be applied to cover increases in body mass or linear dimensions (accelerated growth in length), the latter involving a compensatory increase in skeletal growth (Jobling, 1994; Ali et al., 2003; Nicieza and Alvarez, 2009). Compensatory growth is often observed to bring about some recovery in body mass, but the degree of recovery seems dependent upon the duration and severity of growth depression (Skalski et al., 2005; Mitchell, 2007; Martinez-Ramirez et al., 2009).

The phenomenon of compensatory growth has long been recognized as having the potential to have profound effects on the rate of growth and body composition of most animals. Wilson and Osbourn (1960) reported that one of the first references on the subject was in 1908 where beef steers, which had been under nourished subsequently, recovered and reached normal mature weight and height. Some years later, Osborne and Mendel (1915) described how rats that had been restricted in growth exhibited greater rates of gain once the restriction was removed. Later, Bohman (1955) termed this faster rate of growth relative to age compensatory growth. An animal whose growth has been slowed by nutritional deprivation may exhibit an enhanced rate of growth when realimented. If this exceeds the maximal rate of gain when adequate nutrition has been provided, the animal is said to have undergone compensatory or catch-up growth (McMurtry et al., 1988). Some workers (Yu and Robinson, 1992) feel that catch-up growth is a more precise term because the word compensatory suggests excessive growth of a body part in compensation for the loss of part of its function. Hence, depending on the author and their preference, these terms are used interchangeably.

5.2 The control of compensatory growth

The mechanisms governing compensatory growth have been studied by a number of workers (Wilson and Osbourn, 1960; Winick and Nobel, 1966; Mosier, 1986; Pitts, 1986). Two theories have been proposed to explain how compensatory growth is regulated. First, compensatory growth mechanisms may involve a set-point or reference for body size appropriate for age and that the control resides in the central nervous system (Wilson and Osbourn, 1960; Mosier, 1986). Figure 2.4 shows a hypothetical sequence of events from the sensing of a growth deficit to the stimulation of compensatory growth. The system producing increased growth hormone (GH) is related to compensatory growth control but is not directly responsible for growth acceleration. The link between the compensatory growth control and GH release is regulated by photoperiod. Thus, after a period of undernutrition, the body tries to attain a size that is appropriate for age in the shortest possible time (Zubair, 1994). According to Mosier (1986), the mechanism for sensing a deficit in body size and for stimulating compensatory growth acceleration remains unknown (Doyle and Lesson, 2008).



GH = GROWTH HORMONE
GRF = GROWTH HORMONE RELEASING FACTOR
SS = SOMATOSTATIN

Figure 2.4 Control of compensatory growth
Source: Doyle and Lesson (2008)

The second theory relates to so called “peripheral control” which suggests that tissues, per se, control body size through cell number or by the total content of DNA (Zubair, 1994). As suggested by Pitts (1986), the number of DNA units is usually the principal determinant of nature size. In studies with adult rats, Pitts (1986) found that nutritional deprivation reduced the size but not the number of DNA units. Because the number of DNA units remained unchanged, it was felt that after nutritional stress, a certain memory mechanism took over to realiment the animal back to its appropriate size for age. If nutritional stress was imposed at too young an age, then the number of DNA units were changed, meaning that realimentation was not as successful, since the memory mechanism was unable to function properly. Winick and Nobel (1966), also working with rats, reported that a reduction in cell numbers seemed to result in permanent stunting, whereas a reduction in cell size resulted in the recovery of normal stature after refeeding.

5.3 Factors influencing compensatory growth

The pattern of compensatoty growth is influenced by the age and maturity of the animal, the serverity of prior undernutrition, and duration of undernutrition, as well as sex of the animal and the type of realimentation diet used.

5.3.1 The severity and duration of undernutrition

During a period of undernutrition animals may be fed at above or below maintenance energy requirements. Usually the level of restriction imposed is calculated to meet the maintenance energy requirement (Zubair, 1994). Plavnik and Hurwitz (1991) restricted broiler chickens to about 40 kcal ME/bird/day, or approximately 35% of the normal ad libitum intake for 2 weeks (7-21 days of age). In spite of this severe feed restriction, broilers gained approximately 4g/day and so the maintenance energy need was likely overestimated. Upon refeeding, however, growth of the restricted birds exceeded controls and at 7-8 weeks of age the birds had almost completely compensated for the previous loss in body weight. Contrary to these results, other researchers (Robinson et al., 1992) were unable to demonstrate complete recovery of broilers subjected to similar levels of feed restriction.

In a later trial, Plavnik and Hurwitz (1991) found that a mild feed restriction of broilers at 7 d of age (allowing for 60 to 75% of normal growth) could

offer an economic advantage over a continuous ad libitum feeding program. Four different feed restriction treatments were used to support 22, 15, 6 or 0 g/day of weight gain over an 8-day period (7-14 days of age). The results demonstrated that broilers restricted to 60 or 75% of their normal growth rate showed complete body weight recovery by 56 days of age. In addition, feed conversion efficiency, both overall and during the period after feed restriction, was superior in all restricted treatments compared to that of the control group. Therefore, the severity of the restriction, as well as its duration, plays an important role in the realimentation response.

Wilson and Osbourn (1960) reported that the more severe the restriction, the greater the initial rate of gain immediately after realimentation. As suggested by Jones and Farrell (1992), it may, therefore, be advantageous to split up the period of restriction into several discrete periods interspersed with ad-lib feeding. Jones and Farrell (1992) showed no real advantage to a discontinuous system of feed restriction, although they did suggest that those birds were less nervous and flighty compared to those 2-3 days into a long continuous restriction period.

Wilson and Osbourn (1960) point out in their paper that there may be a fundamental difference in response to realimentation of: (a) animals restricted enough to cause weight loss during the period of undernutrition, (b) animals restricted so that they maintain constant weight during the period of undernutrition, and (c) animals mildly restricted that make small weight gains during the period of undernutrition. Ryan et al. (1993) restricted Hereford steers that were 9-10 months old for a period of 89 days. During this time period, the steers lost on average 16.4% or 41 kg of their initial body weight. Upon realimentation, using a high quality diet, the restricted steers were found to compensate completely.

In contrast, other workers have demonstrated either no growth compensation or only partial compensation (Horton and Holmes, 1978; Tudor and O'Rourke, 1980; Wanyoike and Holmes, 1981). A significant difference in these later trials compared to that of Ryan et al. (1993), is that the cattle either maintained weight or gained weight slowly during the period of restriction. Ryan et al. (1993) demonstrated that steers exhibited compensatory growth for the 11 months between the start of realimentation and the end of the experiment. Many other researchers

have been unable to encourage cattle to compensate for such a long period with the response usually diminishing after 12 weeks. This lack of response may be due to the severity of the restriction and/or the quality of diet used during realimentation (Ryan et al., 1993)

Kyriazakis et al. (1991) conducted trials on weanling pigs using feeds with low (L), medium (M) and high (H) levels of protein but with similar digestible energy content. Groups of pigs, ranging in weight from 6 to 13 kg, were offered either the L (16% CP) or M (27% CP) diet, in order to create two groups with differing body composition. The L diet was formulated to be inadequate in CP to support potential growth, while the M diet was a mixture of equal parts of the L and H diet (40% CP). The pigs on L were expected to have more fat (F-fat pigs) while those on M (T-lean pigs) were expected to have the desired level of fatness. From 13 kg to 30kg live weight the F and L pigs were then divided into 2 groups and fed either the M or H ration. All feeds were offered ad libitum.

The NRC (1988) requirements for swine state that pigs from 5-10 kg should have 20% CP as opposed to the 16% CP fed in this trial. The restricted pigs gained 293 g/day as opposed to 449 g/day for the non-restricted pigs, and took 11 days longer to reach the same weight. Upon realimentation at 12 kg, the F pigs grew 1.18 times faster, had a lower daily feed intake and converted feed more efficiently than did the T pigs. The body composition of the restricted pigs over the period 12 to 30 kg showed a substantial compensatory gain of protein and water, with little or no lipid gain. The restriction imposed in this trial would not be termed severe, because the pigs still gained approximately 65% compared to the non-restricted pigs.

Prince et al. (1983) restricted pigs to 70% or 85% of ad libitum intake for either 2 or 4 weeks. Among the restricted pigs, those restricted to 85% for 4 weeks performed the best. Those restricted to 70% of ad libitum intake for 4 weeks were unable to fully compensate, suggesting that the restriction was either too severe and/or too prolonged. Upon realimentation the pigs restricted to 70% of ad libitum for only 2 weeks showed average daily gains and feed to gain ratios similar to those of controls and the 85% restricted group. Other trial (Owen et al., 1971) have shown that complete compensation was not fully achieved, likely because the duration of undernutrition was longer than that used by Prince et al. (1983).

Pond and Mersmann (1990) restricted the intake of weanling pigs such that they lost weight over a 21 days period. Two groups of pigs were offered a diet containing 80% alfafa meal (high fiber) on an ad libitum basis, or limit-fed a control diet to elicit a comparable weight loss. Because other work (Pond et al., 1980) has shown that protein restriction may have little effect on response to realimentation, this trial restricted energy intake (by dilution with high fiber alfafa meal) to see if a compensatory response could be obtained.

Weanling pigs lost weight at 139 g/day and 178 g/day for the high fiber (ad libitum) and restricted control diets respectively. This loss continued over a 21 days period after which the control diet was gradually reinstated before reaching ad libitum levels. There was no evidence of overt compensatory growth. However, the liver, kidneys and back fat depth from 21 to 126 days did exhibit additional compensatory growth. It would appear that the level of restriction used in this study was far too severe, inducing a weight loss that the pigs could not recover from. As stated by Mersmann et al. (1987), the magnitude of increase in growth rate following feed restriction may well be affected by the change in physiological status imposed by the weight loss during restriction.

Within the three species discussed to date, it can be seen that a wide range in the severity of feed restriction has been used and these techniques produce variable response as compensatory growth. In poultry, the limits seem to be more narrowly defined, because the days to market are quite low which reduces the amount of time they have to "catch up" from previous interruptions in growth. Feed restriction of not more than 7 and 5 days for male and female broilers respectively, starting at 6 days of age, appears to allow for a complete recovery of body weight in broiler chickens (McMurty et al., 1988).

In swine, a longer period of restriction can be employed lasting from 2-4 weeks in duration (Prince et al., 1983). Many studies have shown that complete compensation is possible providing the restriction is not too severe. Contrary to the situation with broilers, finishing pigs have more time in which to exhibit a compensatory response, although days to market is still economically very important to producers. Beef steers appear to be able to recover from a wider range of feed

restriction programs, again related to the fact that they have a much longer time in which to attain market weight.

5.3.2 The stage of development (relative to maturity) of the animal

Wilson and Osburn (1960) state that undernutrition in the earlier stage of growth is more detrimental to an animal than is restriction at the later stage. Consequently, the age at which an animal is subjected to undernutrition may be as important as the severity of undernutrition. With broilers (depending on the sex of the bird) it is generally recommended that feed restriction start at approximately 6 days of age which usually allows for full recovery of body weight (McMurty et al., 1988; Zubair, 1994). Other workers (Plavnik and Hurwitz, 1991), have shown that feed restriction at any age between 3 to 11 days post hatch in male broilers seems to permit complete body weight recovery by 8 weeks of age. However, Fontana et al., (1992) showed that broilers restricted to 40 kcal ME per bird per day from 4-11 days of age, had significantly lower mean body weight than did non restricted control at 49 days of age. Female broilers have been found to respond better if feed restriction is initiated before day 6 post hatch (McMurtry et al., 1988). Washburn and Bondari (1978) initiated feed restriction after 3 weeks of age and found little evidence of compensatory growth likely because insufficient time was allowed for recovery. Similar results were found by Arafa et al., (1983) who restricted broilers in the final stage of production (5-8 weeks of age).

The age and weight ranges at which feed restriction may start with beef steers or heifers are not as well defined as they are with poultry. Most research involves feed restriction starting at round 240-270 kg corresponding to an age of 7-10 months. It would seem that the initial age or weight is not as critical as it is with poultry likely due to the large difference in the relative weight of the two species and the greater range of market weight. Thus, contrary to work with poultry, most work with cattle offers little or no explanation as to why a particular weight or age was used. Ryan et al. (1993), in a trial comparing compensatory growth in sheep and cattle, assessed the two species to be a similar proportion of their mature body size before starting a period of feed restriction.

In studies with pigs, the body weight at which feed restriction is usually implemented is around 15-25 kg (Wahlstrom and Libal, 1983; Prince et al., 1983).

Stamataris et al. (1985) restricted pigs to 300 grams of feed per day over the weight range of 6 to 12 kg live weight. The pigs were then fed ad libitum and were found to exhibit compensatory growth. However, the restricted pigs took 31.7 days to reach 12 kg while those fed ad libitum took 12.6 days. Upon realimentation, the restricted pigs took 5.5 days less to reach 24 kg (from 12 kg) than did those fed ad libitum. It was concluded that although there was compensatory growth, the time lost in growth (during restriction) could not be regained. This suggests that the restriction was imposed at too early an age causing a deficit from which the pigs could not recover. Unfortunately, all these pigs were slaughtered at 24 kg, so it was not known if the restricted pigs could have attained normal market weight for age.

5.3.3 Genotype and sex

Male and female may respond differently to compensatory growth. For example, male broilers have been shown to have a greater ability to exhibit compensatory growth than do females (McMurty et al., 1988; Plavnik and Hurwitz, 1991). This is likely due to the higher innate rate of growth of male broilers and their lower deposition of body fat. Similarly, Plavnik and Hurwitz (1991) demonstrated that male, but not female, broilers were able to exhibit complete compensatory growth when subjected to similar conditions. However, Kyriazakis et al. (1991) found no significant difference in growth rate between either male or female pigs upon realimentation after feeding a low protein diet.

The relative rate at which an animal matures may also affect the degree of recovery after a period of nutritional stress (Wilson and Osbourn, 1960). Generally, faster growing (early maturing) breeds are not likely to compensate as quickly as are slower growing breeds that are usually late maturing. Cherry et al. (1978) and Plavnik and Hurwitz (1991) compared fast and slow growing broiler strains and found that the fast growing strains exhibited little compensatory growth.

In work with pigs, De Greef et al. (1992) found that two different strains of pigs responded similarly to realimentation. In this trial, the two strains of pigs had different ratios of fat to lean deposition rates during restriction and realimentation. However, at 105 kg live weight the body composition for the two strains was similar. The partitioning of energy and other nutrients into protein and lipid tissues changed with live weight and was different for the two strains of pigs, emphasizing the

importance of designing feeding strategies for different genotypes (De Greef et al., 1992). In contrast to the work of De Greef et al. (1992), Hogberg and Zimmerman (1978) found that a lean strain of pig exhibited little growth compensation possibly because the protein restriction was too severe. However, as De Greef et al. (1992) point out, the two strains of pigs used by Hogberg and Zimmerman (1978) differed considerably more than did the ones used in their studies.

Moran and Holmes (1978) suggest that the relative compensating performance of fast versus slow maturing beef breeds would likely depend on the severity of any grazing undernutrition. However Denham (1977) found little difference in the growth compensating ability of Hereford, Angus or Charolais x Hereford steers after being subjected to mild grazing undernutrition. Coleman et al. (1993) found that feeding strategy was important depending on whether the steer was early or late maturing. Young steers or those previously feed restricted tended to accumulate fat more rapidly than larger steers when animals were fed feedlot-type diets. This was thought to be an advantage in late-maturing types; however, moderate growth through approximately 75% of slaughter weight was recommended for early-maturing strains.

5.3.4 Feed intake during realimentation

The amount of feed consumed during realimentation may have an effect on compensatory growth (Ryan et al., 1993). However, results with poultry, cattle and swine have shown varying results with respect to the amount of feed consumed during realimentation. In work with male broilers, Zubair (1994) found that after undergoing nutritional stress by consuming a diluted diet, broilers initially consumed less feed upon realimentation (day 21-35). From day 35 to day 49, previously restricted broilers consumed similar amounts of feed, as did controls, suggesting that increased growth was due, in some way, to better nutrient utilization. Similar results were found by McMurtry et al. (1988) who reported that significantly less feed was needed per unit of weight gain.

Ryan et al. (1993) found that during realimentation, steers that were previously restricted had greater feed intake than non-restricted control animals for approximately 140 days. For the last two-thirds of a 330-day period, the extra growth of the realimentation cattle could be explained entirely on the basis of higher feed

intake. Thus, Ryan et al. (1993) postulated greater feed intake as the main mechanism responsible for long term compensatory growth, supporting the conclusions of Graham and Searle (1975). However, other workers (Thomson et al., 1982; Coleman and Evans, 1993; Wright and Russel, 1991) have found that a period of feed restriction has resulted in a decrease in the total amount of feed required to reach a given weight. It is important to remember that the severity of restriction and the duration of the restriction and post-restriction period may account for some of the variability in these results. In addition, the method by which the restriction is imposed (i.e. protein restriction, energy restriction, diet dilution, etc.) can also influence feed intake during realimentation.

Wahlstrom and Libal (1983) and Pond and Mersmann (1990) found no evidence of increased feed intake in previously restricted pigs fed ad libitum during realimentation. Similar results were reported by De Greef et al. (1992), who found that pigs fed low protein diets had reduced feed intakes during the restriction period, which carried over into the realimentation phase. The pigs did demonstrate (incomplete) compensatory growth, which was accompanied by improved feed efficiency (De Greef et al., 1992). Increases in feed intake and daily gain after a period of feed restriction have been reported by other workers (Owen et al., 1971; Donker et al., 1986). Bikker et al. (1994) demonstrated that feed intake levels were similar for restricted and non-restricted gilts during realimentation. However, compensatory gain and feed efficiency improved with increased feeding level in the realimentation period, stressing the importance of the dietary conditions during realimentation.

5.3.5 Conditions of realimentation

Factors such as the length of time allowed for refeeding and the composition of the realimentation diet may influence compensatory growth. In studies with broilers, compensatory growth has been found to be more consistent when the growth period was extended to 8 weeks or beyond (Plavnik and Hurwitz, 1991). However, numerous other studies (McMurtry et al., 1988; Jones and Farrel, 1992) have shown that full compensatory growth can be achieved within shorter times enabling broilers to reach market weight at earlier ages. This is important from a commercial point of view since broilers are marketed at a wide range of ages and

body weights depending on the market need. As discussed previously, other factors such as severity and duration of restriction may also influence the length of the refeeding period.

With the beef steers, the length of the refeeding period can be much more variable because the restriction may be started over a wider range of initial weights and ages. Rompala et al. (1985) found that steers realimented after a 70 days period of live weight constancy exhibited compensatory growth between 200-300 kg live weight, after which they exhibited normal growth patterns to the completion of the trial. However, Ryan et al. (1993) found that steers exhibited compensatory growth over a much wider weight range (350-600 kg) spanning a time period of approximately 11 months.

In studies with swine, Prince et al. (1983) showed compensatory growth for the total test period with the length of feeding averaging 80 days in one experiment. Kyriazakis et al. (1991) showed that restricted pigs gained weight 1.47 times faster than did control pigs in the first week after realimentation. During the second week however they grew only 1.05 times faster, with little compensation after this time.

5.3.6 Composition of realimentation diet

The composition of the diet eaten during realimentation has a significant effect on the ability of an animal to demonstrate compensatory growth (Yu and Robinson, 1992). Most studies involving feed restriction in early life have reported improvement in feed efficiency, particularly during the period of refeeding (Zubaire, 1994). Consequently, the quality of the diet used during realimentation can greatly influence both the magnitude and the efficiency of the subsequent growth. For example, Plavnik and Hurwitz (1991) showed that based on model prediction, the requirements for most of the essential amino acids were higher for broilers during the first 2 weeks of refeeding. Jones and Farrell (1992) found that during the supplementation phase (28-49 d) birds fed a lysine supplemented diet grew faster than did non-restricted control birds. They also found that diets supplemented with either lysine or methionine reduced the weight of the abdominal fat pad, producing a leaner carcass. This data supports the work of Gous (1977) who found that the ability of the chicken to absorb some amino acids may be increased as a result of prior feed

restriction. Other research (Fontana et al., 1992) has shown that protein might be a limiting nutrient during the recovery after a period of restriction.

Ryan et al. (1993) postulated that the lack of persistence of compensatory growth in other prior studies (Horton and Holmes, 1978; Wanyoike and Holmes, 1981) was likely due to the level of restriction and the quality of the diet during realimentation. In their experiment, Ryan et al. (1993) restricted steers for 89 days starting at 250 kg, after which they were realimented on a high quality diet given ad libitum. The realimentation diet provided between 10.9 and 11.7 MJ of ME/kg dry matter (depending on the level of intake) and contained 16.2% crude protein on a dry matter basis. This was fed until the steers reached approximately 600 kg. When these steers were subjected to feed restriction that induced weight loss, the steers compensated completely when realimented on these quality feeds. The restricted cattle had greater feed intakes than did controls for about 140 days (day 100-240 post restriction) offering support to the results of Graham and Searle (1975), who reported that greater feed intake may be the main mechanism responsible for long-term compensatory growth.

Hays et al. (1995) restricted steers for a period of 66 days starting at around 270 kg live weight after which they were realimented for 98 days on diets containing 9, 12 or 15% CP. A differential growth response to dietary protein was limited to the initial 14 days of realimentation, likely because cattle deposit greater quantities of protein during the initial phase of realimentation (Wright and Russell, 1991; Hayden et al., 1993). However, as Hays et al. (1995) suggests, the responsiveness to dietary protein may have been more evident if the steers had been subjected to a more severe restriction that resulted in a loss of body weight and the depletion of some protein stores.

Kyriazakis et al. (1991) found that pigs fed a diet low in protein, when realimentated with a diet of sufficiently high protein content, showed a substantial increase in growth rate. Pigs fed a diet free choice but low in protein, were found to have less protein and a lipid excess compared to those fed a diet of adequate protein.

It seems as though changes in body composition during realimentation are influenced by prior condition during restriction. If nutrient restriction is severe

enough to reduce body protein reserves, then during realimentation there is compensatory deposition of protein. On the other hand, with a more mild restriction, care must be taken to ensure that compensatory growth is not causing excessive fat deposition. It is important to remember that animals realiment on high protein diets will dissipate more heat. This concept is supported by Ferrel (1988) who found that the heat loss associated with maintenance requirement may increase in pigs offered diets high in amino acids. If the environmental temperature is too high, then feed intake will not be maximized. It was thought that the feed intake of the pigs in this particular experiment may have been limited by the ambient temperature (22 ^{o}C).

Wahlstom and Libal (1983) realimented previously feed restricted pigs with diets containing 12, 14 or 16% CP. In one trial they found that pigs fed a 12% CP diet from 25 to 52 kg had the highest average daily gain when realimented on a 16% CP diet from 52 to 79 kg. They also found that complete compensation was evident only when pigs were fed at least a 14% CP diet through to 100 kg. It was suggested that there may be a relationship of body weight at each growth period and subsequent compensatory performance. For example, the reduction in overall performance of feeding a 14% CP diet increased as the initial weight of the pigs decreased. However, this is not in agreement with the results of Shields and Mahan (1980) who found that pigs initially averaging 22.3 kg completely compensated for early reduce performance when fed a diet containing only 14.5% CP.

5.4 Stair-step feeding regimen

Recently, researchers have developed a nutrition regimen to a so called “stair-step feeding regimen” that is a combination of alternating dietary energy restriction and realimentation phases (Ford and Park, 2001; Park, 2005). The basic concept of this model is to exploit the biological nature of both dietary energy restriction and the compensatory growth phenomenon in concert with one or more hormone dependent allometric phases of body composition development (i.e., prepuberty, puberty, and late gestation). Energy restriction (i.e., providing all known essential nutrients but reducing caloric intake) has a profound influence on the biology and health of animals including the retardation of aging and the reduction of cancer incidence and other late-life diseases (Hursting et al., 2003). Through modulation of endocrine and

enzymatic status, energy restriction shifts the physiological focus to energy-conserving activities, mainly maintenance and repair functions, and decreases certain energy-wasteful metabolic pathways (e.g., substrate cycles) that are not essential for growth. Realimentation (refeeding) after energy restriction induces compensatory growth, which is characterized by an accelerated anabolism, a reduced maintenance requirement, an activated endocrine status, and an altered tissue composition (Wilson and Osbourn 1960; Ashworth and Millward, 1986). Compensatory growth enhances the efficiency of general body development and induces hyperplasia and hypertrophy of tissues and organs, including the mammary gland (Park, 2002). Hence, when using the stair-step compensatory nutrition model, mammary development is minimized during the energy restriction phase and maximized during the realimentation or compensatory growth phase. There are various stair-step feeding regimens (one, two, or three-step models) for dairy and beef heifers, gilts, female rats and other animals (Park, 2005).

5.4.1 One stair-step feeding regimen

Kim and park (2004) who developed a one stair-step feeding model or compensatory nutrition regimen (CNR), which is designed to stimulate mammary growth by exploiting the biological characteristics of the energy restriction and compensatory growth phenomenon (Figure 2.5). In the trial feeding study, they examined the effect of compensatory growth induced only once during late gestation upon mammary development and subsequent lactation potential over 2 lactation cycles. Female rats were mated and randomly assigned to either the control or the CNR group. Control rats were offered the control diet throughout the experiment. CNR rats were subjected to a 40% energy restriction during the first 10 d of gestation followed by free access to the control diet for the remainder of the experiment. Dams on the CNR produced 14% more milk than control dams ($P = 0.12$).

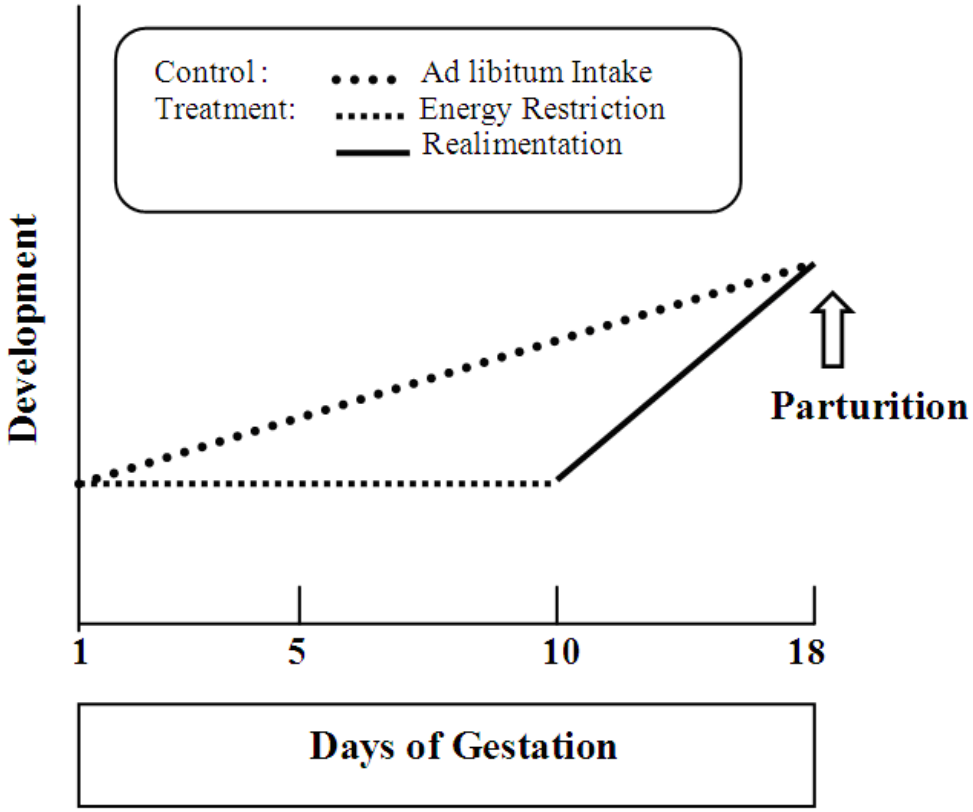


Figure 2.5 One stair-step feeding model in rats
Source: Kim and Park (2004)

Mammary cell proliferation rates were ~46% ($P<0.05$) and 27% ($P = 0.07$) higher in the CNR group than in the control during late gestation and early lactation of the first lactation cycle, respectively. Caspase-3 enzyme activity was decreased 15% ($P<0.05$) and 22% ($P = 0.11$) in mammary tissues from the CNR group compared with that from the controls during the first and second lactation cycles, respectively. These results indicate that compensatory growth induced only once during late gestation increases mammary cell proliferation and differentiation and decreases regression of mammary cells throughout consecutive lactation cycles.

Table 2.4 In situ identification of mammary cell proliferation during late gestation (day 18) and early lactation (day 3) of the first lactation cycle of rats on control or CNR.[1,2]

Items	N	Control	CNR
Late gestation	2	7.19 ± 0.30	10.48 ± 0.69* (46%)
Early lactation	4	2.11 ± 0.18	2.67 ± 0.18 (27%)

[1] Values are means ± SEM. * Different from the control, P<0.05.

[2] The CNR group was fed an energy-restricted diet for the first 10 d of gestation

Source: Kim and Park (2004)

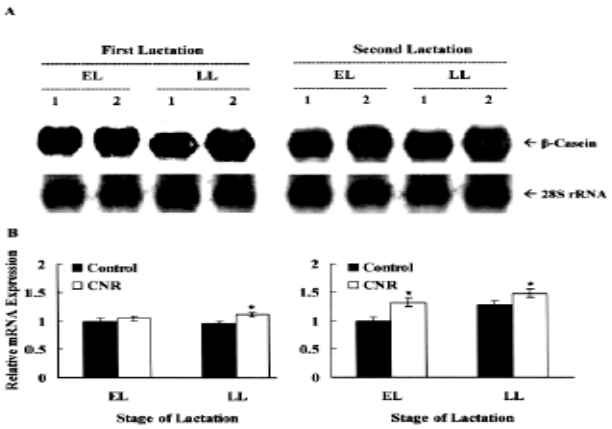


Figure 2.6 Northern blot analysis of the β-casein gene in mammary tissues collected during the first and second lactation cycles from female rats on a CNR during gestation. The data shown are arbitrary densitometric unit means with standard errors represented by vertical bars (n = 4). *Different from the control (P < 0.05)

Source: Kim and Park (2004)

Amal et al. (2008) reported the effect of diet restriction and re-feeding on some reproductive and metabolic response in Egyptian native goats. Ten native multiparous non-pregnant goats were equally divided according to their body weight into light (<15 kg) and heavy (>15 kg) groups. Goats were subjected to a 50% diet restriction for 35 days followed by re-feeding for another 35 days. Estrus was

synchronized using 60 mg medroxyprogesterone acetate intra-vaginal sponges for 10 days starting on day 4-post re-feeding. Blood samples were collected twice a week with each endorectal ultrasound examination and body weight was recorded every week. Progesterone, insulin like growth factor-1, leptin and nitric oxide concentrations as well as total proteins, albumin, urea, total cholesterol and triglycerides levels were analyzed. In both groups, goats lost their weight during diet restriction and regained it with re-feeding. Ultrasonography revealed that feed restriction persisted corpora lutae in 80% of goats in both groups. One goat in each group (20%) showed signs of estrus and ovulated near the end of the diet restriction period. During the period of re-feeding, all animals in the heavy group and 80% of the light one responded to synchronization and ovulated. During the first estrus after synchronization, heavy group goats showed estrus earlier than the light one. Two out of five (40%) goats had double ovulation and two out of three goats with single ovulation were conceived after mating. All the ovulated light group goats had a single ovulation and one of them conceived after mating. During the 2nd estrus after sponge removal, all of the three remnant goats of the heavy group had double ovulation and all conceived after mating, but in the light group, three out of the four had a single ovulation, one did not ovulate and only one conceived after mating.

Table 2.5 Effect of food restriction and re-feeding on follicular development and ovulation

	Light group			Heavy group		
periods	0-15	16-50	51-85	0-15	16-50	51-85
SF	4.00±0.63	4.33±0.44^{a}	3.21±0.34	4.00±1.23	2.11±0.46^{b}	2.83±0.28
MF	1.40±0.25	1.11±0.20^{a}	2.04±0.27	1.50±0.50	3.11±0.51^{b}	2.17±0.24
LF	0.00±0.00^{A}	0.13±0.07^{A}	0.35±0.10^{B}	0.25±0.15^{A}	0.18±0.13^{A}	0.74±0.19^{B}
TF	5.25±0.48	5.56±0.32	5.54±0.30	5.75±0.75	5.39±0.26	5.59±0.29
DF/cm	0.40±0.03	0.41±0.02	0.46±0.03	0.46±0.06	0.45±0.01	0.49±0.02
Ov.R	1.20±0.20	0.80±0.09^{a}	1.00±0.12	1.40±0.41	1.20±0.11b	1.40±10

0-15 = acclimation period 16-50 = restriction period 51-85 = re-feeding period. SF = small folliclesnumber, MF = medium follicles number, LF = large follicles number, TF = total follicles number, DF = dominant follicle diameter, Ov.R= ovulation rate. Means ± SEM with different superscript within period (a,b,c) and within group (A,B,C) are significantly at $P<0.05$.

Source: Amal et al. (2008)

Table 2.6 Effect of food restriction and re-feeding on reproductive performance

Treatment periods	Light group (n=5)	Heavy group (n=5)
During food restriction		
Estrus activities and ovulation	20% (1/5)	20% (1/5)
Persistent corpora lutea	80% (4/5)	80% (4/5)
1st Estrus after synchronization		
Response to synchronization	80% (4/5)	100% (5/5)
Time to estrus	>72 h	<72h
Double ovulation	00% (0/4)	40% (2/5)
Single ovulation	100% (4/4)	60% (3/5)
Conception after mating	25% (1/4)	40% (2/5)
2nd Estrus after synchronization		
Double ovulation	00%	100% (3/3)
Single ovulation	66.6% (2/3)*	00%
Conception after mating	50% (1/2)	100% (3/3)

*One (33.3%) did not showed estrus or ovulate until the end of the experiment

Source: Amal et al. (2008)

5.4.2 Multi stair-step feeding regimen

Ford and Park (2001) conducted trials on heifers in prepubertal, pubertal and gestation periods using a multi stair-step feeding regimen, to examine the interactive influence of a compensatory nutrition regimen and lasalocid supplementation on dairy heifer growth performance and to document the extent to which compensatory growth sustains lactation potential over the first two lactation cycles. Twelve Holstein heifers, weighing an average of 160 kg (about 6 months of age) were randomly assigned to treatments arranged in a 2 x 2 factorial design. Treatment variables were two dietary regimens (control and stair-step compensatory nutrition) and two levels of lasalocid (0 and 200 mg/d). The control heifers were fed a diet containing 12% crude protein (CP) and 2.35 Mcal of metabolizable energy (ME) per kilogram of dry matter. The stair-step compensatory nutrition heifers were subjected to a phased nutrition regimen and reared according to an alternating 3-2-4-3-4-2-months schedule (Figure 2.7). The first stair-step (prepubertal phase) consisted of energy restriction [17% CP and 2.35 Mcal/kg of ME] for 3 months followed by

realimentation (12% CP and 3.05 Mcal/kg of ME) for 2 months. The second step (puberty and breeding) consisted of energy restriction for 4 mo followed by realimentation for 3 months. The third step (gestation period) was energy restriction for 4 mo concluding with realimentation for 2 months. Dry matter intake of heifers during the restriction phase was limited to 70% of the control intake. Heifers were given ad libitum access to a high energy density diet during realimentation to allow compensatory development.

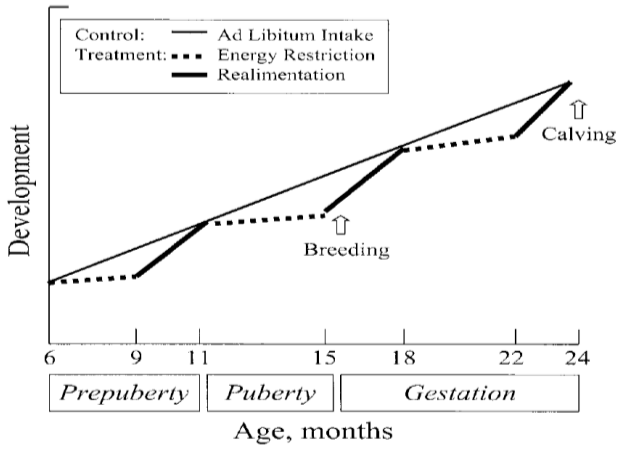


Figure 2.7 A stair-step compensatory nutrition regimen for dairy heifers
Source: Ford and Park (2001)

Stair-step heifers supplemented with lasalocid had the highest efficiency of growth (body weight gain/dry matter intake), suggesting synergistic metabolism of lasalocid with compensatory growth action. Compensatory growth induced during the last trimester enhanced metabolic status by increasing circulating insulin and decreasing triglyceride levels. Heifers on the stair-step regimen had a significant increase in milk yield during the first (21%) and second (15%) lactation cycles. These results indicate that compensatory growth induced during an allometric growth phase improves mammary development and energy and protein metabolic status of dairy heifers.

Table 2.7 Treatment effects by growth phase on dairy heifer growth response

	Nutrition regimen				
Lasalocid, mg/d	Control 0	Control 200	Stair-step 0	Stair-step 200	SE[1]
Initial BW, kg	165.2	158.3	162.1	156.5	7.4
Prepuberty (6–11 mo of age)					
Restricted (3 mo)					
Daily gain, kg/d	0.77[b]	0.73[b]	0.58[a]	0.62[a]	0.04
Growth efficiency, %[2]	8.8	8.0	8.9	9.3	0.8
BW, kg	239.0	228.4	221.7	218.3	9.8
Realimented (2 mo)					
Daily gain, kg/d	0.82 [a]	0.84 [a]	0.91[ab]	0.97[b]	0.05
Growth efficiency, %[2]	8.0 [a]	8.8 [a]	10.3[ab]	12.7[b]	0.7
BW, kg	282.7	277.5	272.3	272.0	12.2
Puberty/Breeding (11–18 mo of age)					
Restricted (4 mo)					
Daily gain, kg/d	0.83	0.85	0.77	0.72	0.05
Growth efficiency, %[2]	7.3	8.1	8.2	7.9	1.0
BW, kg	376.5	371.8	358.1	352.6	13.8
Realimented (3 mo)					
Daily gain, kg/d	0.85 [a]	0.87 [a]	1.13b	1.44 [a]	0.12
Growth efficiency, %[2]	7.1 [a]	7.5 [a]	10.8b	16.0 [a]	1.3
BW, kg	453.7	447.5	460.7	483.2	12.5
Gestation (18–24 mo of age)					
Restricted (4 mo)					
Daily gain, kg/d	0.75	0.81	0.65	0.70	0.09
Growth efficiency, %[2]	6.0	6.2	6.5	6.9	0.9
BW, kg	540.2	544.5	538.6	568.4	15.4
Realimented (2 mo)					
Daily gain, kg/d	0.67 [a]	0.73 [a]	1.60[b]	1.80[b]	0.25
Growth efficiency, %[2]	4.8 [a]	5.7 [a]	13.7[b]	18.0[c]	2.6
BW, kg	585.7 [a]	590.0 [a]	641.2[ab]	681.5[b]	23.6
Overall					
Daily gain, kg/d	0.78 [a]	0.81 [a]	0.89[ab]	1.01[b]	0.06
Dry matter intake, kg/d	11.4 [a]	11.1 [a]	9.4[ab]	8.3[a]	0.6
Growth efficiency, %[2]	7.0 [a]	7.4 [a]	9.4[ab]	12.2[c]	1.2

[a,b,c] Means within a row with different superscripts differ (P<0.05). [1] n = 3.
[2] Growth efficiency (gross) = gain 100/DMI.

Source: Ford and Park (2001)

6. The effects of nutrition on reproduction

The effects of nutrition on reproduction are well known and widely reported. They occur not only in the ruminant species (Lucy, 2003) but in monogastric species as well (Hazeleger et al., 2005). Nutritional condition has a strong influence on the activity of the hypothalamo–pituitary–gonadal axis in mammals (Ohkura et al., 2004). In females of small ruminant species, nutritional supplementation stimulates development of the small follicle population (Rondian et al., 2005), growth rate and size of the ovulatory follicle (Webb et al., 2003), ovulation rate (Rondian et al., 2005), and litter size (Downing and Scaramuzzi, 1991).

Blood metabolites such as glucose, non-esterified fatty acids (NEFA) and blood urea nitrogen (BUN) are thought to be among the signals for nutritional status. It is noticeable that, changing feeding level, changes in blood metabolites were in close agreement with other studies in underfed ruminants. During energy deficiency due to fasting or low feed intake, plasma glucose decreases whereas the concentration of NEFA in blood increases as a result of mobilization of body fat (Dzakuma et al., 2004).

6.1 Effect of nutrition on endocrine system

The primary target area for sensing and reacting to nutritional status is the hypothalamus (Moss et al., 1985). The body is regulated by two basic systems, nervous and endocrine. The endocrine or hormonal system, in general, is specifically concerned with the control of metabolic functions, rates of chemical reactions in cells, transport through cell membranes, and other functions such as growth and secretion. All of these are key components of the total lactation complex. Hormones are chemical components comprised of steroids, peptides, proteins, and glycoprotein secreted into body fluids at one site with their actions on target tissues and organs at adjacent or other sites within the body. The tissue or organ response to the hormone is influenced by the number of receptors present on the cell membrane or within the cell and by the amount of hormone that is present. The amount of hormone presented will be under the influence of blood flow and concentration. Nutrition or perhaps more specifically certain food nutrients can influence the hormonal status of

the animal at several levels. Inadequate intake of nutrients or inadequate body reserves, needed to meet production requirements, after kidding, results in suppressed reproductive performance in small ruminant (Delgadillo et al., 2007).

Potential sites of action of nutrition on ovarian function include systemic effects at: (i) the hypothalamic level via gonadotrophin releasing hormone (GnRH) synthesis and release; (ii) the anterior pituitary through control of synthesis and release of follicle stimulating hormone (FSH), luteinizing hormone (LH) and growth hormone (GH); and (iii) at the ovarian level through regulation of follicle growth and steroid synthesis (Scaramuzzi et al., 2006)

Many studies in both sheep (Moenter et al., 1991; Skinner et al., 1997) and goat (De Castro et al., 1999) have established that LH is released episodically from the anterior pituitary in response to pulsatile release of GnRH from the hypothalamus. Therefore, the absence of a LH and FSH surge could be mediated at either the hypothalamus or the anterior pituitary. During spontaneous luteolysis, as progesterone concentrations decline, LH pulse frequency increases (Bergfeld et al., 1996) in response to increased pulses of GnRH (Gazal et al., 1998). This increase in LH pulse frequency stimulates follicular androgen production (Hansel and Convey, 1983) and hence increased estradiol secretion from the dominant follicle. The exact mechanism whereby increasing estradiol concentrations stimulate a gonadotropin surge has not been fully established, but it is believed to act on specific neuronal pathways impinging on GnRH neurons within the hypothalamus, leading to an increase in the secretion of GnRH (Caraty et al., 1995). Some evidence suggests that the pituitary sensitivity to GnRH pulses is decreased during under-nutrition. Tatman et al. (1990) found that the pituitary content of LH was lower in thin ewes while Kile et al. (1991) noted that under-nutrition suppressed pituitary synthesis of LH as the concentration of mRNA for both ά and β subunits of LH were less in nutritionally restricted ovariectomised ewes. However, pulsatile administration of GnRH was capable of restoring LH synthesis and secretion.

Similarly, cows fed restricted diets released more LH in response to exogenous GnRH than cows fed moderate or high diets (Rasby et al., 1991) and had increased concentrations of GnRH in the stalk median eminence of the hypothalamus (Rasby et al., 1992). This suggested that the greater sequestration of

LH in the anterior pituitary gland and decreased LH secretion in nutritionally restricted animals is due to reduced GnRH release. Therefore, it appears that the nutritionally-induced suppression of LH may be at least in part modulated by factors affecting the GnRH pulse generator and the pituitary response to GnRH, but the mechanism responsible remain to be elucidated.

Murphy et al. (1991) determined the effect of different levels of dietary intake on the pattern of follicular growth and luteal function during the estrus cycle. Their study involved the use of beef heifers fed 0.7, 1.1 and 1.8 % of body weight as dry matter per day for 10 weeks to study the effects of dietary intake. During an estrous cycle, commencing approximately 5 weeks after diet allocation, the maximum diameter and persistence of the dominant follicle was decreased in the restricted heifers though these heifers continued to ovulate. Similar observations have been found in subsequent studies using heifers. Under-nutrition is associated with elevated growth hormone, reduced IGF-1, an uncoupling of the link between growth hormone and insulin-like growth factor-I (IGF-I) and failure of the dominant ovarian follicle to produce enough estradiol to generate the preovulatory LH surge. Protracted intervals to first estrus are also associated with delays in the recovery of leptin concentrations after calving (Kadokawa et al., 2000) and low concentrations of leptin have been observed in cows with abnormal post-partum reproductive cycles.

6.2 Effect of energy status on fertility

Energy status is generally considered to be the major nutritional factor that influences reproductive processes, with prolonged low energy intake impairing fertility. One way of viewing the relationship between nutrition and reproduction is through energy balance. When the animals' net nutrient requirement is more than the net nutrient intake the animals will use their energy stores (glycogen, triglycerides and protein) to meet the deficit. When an animal is in this state, it is in "negative energy balance". Similarly, when the net nutrient requirement is less than the net nutrient intake, the animal will store the excess nutrients (as glycogen and triglycerides) and/or disperse the excess nutrients as metabolic heat (Lozana et al., 2003). When an animal is in this state it is in "positive energy balance". These metabolic states and

the accompanying alterations in appetite and nutrient partitioning within the body are regulated by a series of complex interactions among the blood concentrations of metabolic hormones and various whole-body nutrient fluxes. Many of the metabolic hormones and nutrients that help to maintain whole-body nutrient homeostasis also affect the reproductive system. Consequently, there are well-defined associations between metabolic state and reproduction (Table 2.8).

The effects of negative energy balance on reproduction are primarily at the hypothalamo-pituitary level of reproductive control and are characterized by hypoglycaemia, hypoinsulinaemia, suppressed plasma IGF-I and elevated plasma GH, changes that are associated with the inhibition of GnRH pulsatility, anovulation and anoestrus in the female. There is little evidence to suggest that negative energy balance has any direct ovarian effects in the ewe that are independent of its effects on the hypothalamo-pituitary axis (Martin et al., 2004).

In ruminant, negative energy balance (NEB) causes a linear decrease in the maximum diameter of successive dominant follicle, eventually resulting in anoestrus. It is well known that cows over conditioned at calving will exhibit decreased appetite and develop more severe NEB than cows of moderate conditioning (Garnsworthy and Topps, 1982). As a result, over conditioned cows undergo increased mobilization of body fat and accumulate more triglycerols in the liver (Rukkwamsuk et al., 1999) that are associated with a longer interval to first ovulation and reduced fertility (Rukkwamsuk et al., 1999). Alterations in concentrations of growth hormone, insulin, IGF-I, glucose, and non-esterified fatty acids (NEFA) in blood are indicative of energy availability and may provide short or long term signals that mediate the effects of nutrition on LH secretion.

Dufour (1975) reported that the effects of undernutrition (energy, protein) on growing heifer resulted in increased age at puberty, subnormal conception rates, and underdeveloped udders whereas overfeeding resulted in weak estrus symptoms, reduced conception rates, high embryonic mortality, decreased mammary gland development, and decreased milk production (Gardner et al., 1977).

Table 2.8 Some known associations between energy balance and reproduction

Metabolic state	Metabolic consequences	Effects on reproduction
Negative energy balance	– Weight loss – Fat stores depleted – Muscle wasting – Hypoinsulinemia – Hypoglycaemia – Elevated βOH butyrates and NEFA – Elevated GH – Low Leptin – Reduced metabolic heat – Suppressed IGF system – Elevated urea	– Inhibition of GnRH secretion by the hypothalamus – Absence of LH pulses – Low FSH concentrations – Inhibition of folliculogenesis – Low estradiol – High negative feedback sensitivity – Anovulation – Anestrus – Delayed puberty
Energy balance	– Weight maintained – Fat stores maintained – Normal insulin – Normoglycaemia – Low NEFA and βOH butyrate – Normal GH – Normal Leptin – Normal IGF system – Normal urea	– Normal GnRH secretion by the hypothalamus – Normal LH pulsatility – Normal FSH concentrations – Normal folliculogenesis – Normal estradiol and inhibin – Normal negative feedback – Ovulation – Estrus – Ovulation rate below natural maximum
Positive energy balance	– Long-term weight gain – Fat stores increased – Hyperinsulinemia – Hyperglycaemia – Low NEFA and βOH butyrate – Low GH – Elevated leptin – Increased metabolic heat – Stimulated IGF system – Urea normal but can be high if dietary nitrogen is high	– Normal GnRH secretion by the hypothalamus – Normal LH pulsatility – Increased FSH concentrations – Enhanced folliculogenesis – Reduced estradiol – Reduced negative feedback – Ovulation – estrus – Maximum natural ovulation rate – Advanced puberty

Source: Scaramuzzi et al. (2006)

Inadequate amount of energy delays sexual maturity in heifers. It is also reported that if energy deficient rations are fed to heifers that have begun to have normal estrus cycles, they may stop cycling (McDonald et al., 1987).

Fasanya et al. (1992) reported that the effects of undernutrition on growing Savanna Brown goats resulted in increased age at puberty. First estrus is generally considered to represent the onset of puberty in does can precede the first behavioural

estrus. It is well-known that inadequate nutrition during the growing period retard growth and delays puberty in the young doe. It is generally considered that does may be mated when they reached 60% of their adult body weight this weight can be attained at varying ages according to diet composition.

Positive energy balance leads to increased leptin and insulin concentrations in the blood and increased glucose uptake; these changes appear to affect the ovary directly and are associated with increased folliculogenesis and increased ovulation rate in sheep. Positive energy balance is also associated with alterations in the hepatic metabolism of steroids that can lead to disturbances in negative feedback between the ovary and the hypothalamo-pituitary system and theoretically, to increased folliculogenesis (Parr et al., 1993). There is little evidence to suggest that positive energy balance has a specific stimulatory action on the hypothalamo-pituitary axis. It is worth noting that because of the strong negative feedback interrelationship between the hypothalamo-pituitary axis and the ovary, the task of identifying the anatomical sites in the reproductive axis that are influenced by nutrition is proving to be exceedingly difficult (Kiyma el al., 2004).

Positive energy balance, if it persists, will inevitably increase body weight. However, the stimulatory effect of nutrition on folliculogenesis can occur before there is any detectable increase in body weight. The careful descriptive analysis of the effects of nutrition on body weight has led to a classification of nutritional effects on ovulation rate. The “acute” effect is seen in the absence of a detectable change in body weight, the “dynamic” effect is associated with increasing body weight and the “static” effect is associated with elevated body weight per se (Scaramuzzi et al., 2006). Many of the hormonal systems that respond to nutrition also affect the ovary and it is from among these that several research teams around the world are seeking to unravel the mechanisms that link nutrition and the follicle. Strong contenders among many for the “link” between nutrition and the follicle are the glucose-insulin system, IGF system and leptin system.

The nutrient requirements for folliculogenesis are not known but they are unlikely to be significant in terms of whole body energy utilization. However, the nutrient requirement for other reproductive events such as fetal growth, lactation and pubertal growth are all very high and significant in the context of whole body energy

utilisztion. In these later states the effect of nutrition on reproduction is a question of nutrient supply, particularly energy. In these reproductive states, failure to meet the nutrient demand will compromise reproduction. The mechanisms of nutritional effects on folliculogenesis are probably not effects of quantitative nutrient supply per se; it is much more likely that they are specific nutrient signalling effects that link reproduction with favourable environmental conditions for reproduction. For spermatogenesis and folliculogenesis, nutrition acts as a metabolic signalling mechanism (Van Suan et al., 2008).

6.3 Effect of protein on fertility

Animals require protein as a source of essential amino acids and as a nitrogen source for rumen microflora. In ruminant, fat or thin, need protein supplementation to consume and utilize low quality forage with any degree of effectiveness. The protein requirement of an animal is dependent on its physiological status and level of production. Ruminants are also capable of reducing protein loss by recycling urea, a product of protein metabolism that is normally excreted. Thus, some urea can be recycled to the rumen when the diet is low in nitrogen. It is also important to ensure that the diet contains the correct level of protein during the joining period. If there is too much protein in the diet the rumen bacteria are unable to convert it into microbial protein. Feeding more dietary protein has been negatively associated with dairy cow fertility. Excess ammonia is conjugated to urea and then excreted. Thus, high urea levels are consistent with excess protein intake, possibly with concomitant energy shortage, and are likely to be associated with high levels of ammonia circulation. This results in a high level of ammonia in the rumen, which is absorbed across the rumen wall into the blood stream, where it is carried to the liver and converted into urea. Excess urea in the blood or blood urea nitrogen (BUN) can be toxic to sperm, eggs and embryos (Van Suan et al., 2008).

Fahey et al. (1998) reported that the effects of urea on embryo quality are likely to be due to alterations in the oviduct environment or deleterious changes in the follicle, rather than changes in the uterine environment. Depending upon protein quality and composition, serum concentrations of progesterone may be lowered, the uterine environment altered, and fertility decreased (Butler, 1998). Diets high in crude

protein (17% to 19%) are typically fed during early lactation to both stimulate and support milk production, however, high protein diets have been associated with reduced reproductive performance (Butler, 1998; Westwood et al., 1998). Uterine pH was also affected in heifers fed excess rumen degradable protein (RDP) and was associated with reduced fertility (Butler, 1998). Feeding diets high in crude protein (CP) increased plasma urea concentrations which may interfere with the normal inductive actions of progesterone on the environment of the uterus and thereby cause suboptimal conditions for support of embryo development (Butler, 2000).

Over-feeding of protein in early lactation can exacerbate body condition loss, whilst under-feeding of protein invariably affects feed intake as well as the efficiencies of feed digestion and conversion into milk. It remains that the rumen is the key driver of feed intake and efficient feed utilization, and both can impact on overall cow performance. It has been suggested that excess rumen degradable protein (RDP) may exacerbate NEB and its negative effect on fertility (Butler, 1998). Westwood et al. (2000) showed in their research that feeding more RDP deteriorated expression of estrus at first ovulation, had a lower first service conception rate and a longer calving to conception interval. Garcia-Bojalil et al. (1998) observed signs of a reduced fertility with feeding excess RDP which could be eliminated by the inclusion in the diet of calcium salts of long-chain fatty acids. They also showed a negative effect of RDP on plasma progesterone, which could be restored by the inclusion of fat, resulting in an increased pregnancy rate with fat supplementation.

The detrimental effect of ammonia on cleavage rates and blastocyst formation was confirmed by Sinclair et al. (2000), who demonstrated a reduction of the proportion of oocytes that developed after fertilization. According to Jorritsma et al. (2003), ammonia is most likely to play a role before ovulation, whereas the effects of urea, that has been shown to lower the pH in the uterine fluid, are exerted during cleavage and blastocyst formation of the fertilized embryo. The cause of this reduction in pH is not clear. It has been suggested that ureagenesis removes bicarbonate (Zhu et al., 2000) and reduces pH, at least in blood. Infusing urea in the blood lowered the uterine pH which was explained by an effect on carbonic anhydrase (Rhoads et al., 2004). This would suggest that excess RDP is more detrimental to

fertility than excess rumen undegradable protein. Feeding excess protein costs money and adds to environmental pollution.

7. Summary

The research study were focus and investigate of principle application of assisted reproductive technology (ART) such as induce multiple follicular development and ovulation with FSH and hCG (FSH decreasing dose, 2 or 3 days protocols) and compensatory growth application (using stair-step feeding regimen) on reproductive management can be an effective protocol in goats for Thai-native goat production expecting that these appropriate technologies and management regimens could be used to enhance the efficiency of goat production.