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Histological Cyclic Endometrial Changes in Dairy Cows: An Overview

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Abstract

Dairy farms try to reach the highest reproductive efficiency of the herd to obtain economic benefits; however, there are several factors that negatively affect cow´s reproduction. Problems affecting reproductive health of the cow provoke the absence of lactation that normally follows parturition. One of the main functions of uterus is to harbor the fertilized oocyte providing optimum conditions for the embryo development. Histologically, uterus is formed by three layers: perimetrium, myometrium, and endometrium; endometrium is the organ mucosa that varies as hormonal profile changes during estrous cycle. Endometrium at follicular stage of the cycle is proliferative under the influence of estradiol, whereas at luteal stage is secretory under the influence of progesterone. At proliferative stage endometrium thickness increases because of cellular mitosis; at secretory stage endometrium reaches its maximum thickness and glands produce histotrophe. Inflammatory cells may be present in the endometrium throughout estrous cycle. Early diagnosis of uterine pathologies helps to establish therapeutic or control measures to minimize economic losses.

Keywords: Estrous cycle; Uterine glands; Proliferative, Secretory stages

Introduction

Reproductive problems have a negative impact on the productive efficiency of dairy farms [1,2]. The most common method of diagnosis to determine uterine diseases is rectal palpation; however, this method is imprecise compared to histomorphological analysis of endometrial tissue. Histomorphological analysis is an effective technique to determine the real condition of the uterus; it allows identifying the cyclic status of the cow as well as the type and degree of the different uterine diseases. For this, it is important to know the normal uterine anatomy and histology in the different stages of estrous cycle.

Anatomy and histology of uterus

Uterus is a muscular hollow organ developed from Muller ducts that plays several reproductive functions; inside it the embryo and fetus develop and mature; it nurtures the pre-implanted embryo and provides the optimum environment for its development; during delivery, uterine contractility helps to expulse both the product and placenta, effect mediated by prostaglandins produced in the endometrium; in addition, prostaglandins (PGF2α) are involved in the lysis of corpus luteum. On the other hand, uterus favors sperm transport toward the oviduct where capacitation takes place before fertilization occurs [3-6].

Uterus is constituted by the cervix, body, and two horns; it continues cranially to the oviducts, and caudally to the vagina. In some areas of the endometrium there are from 70 to 120 elevated structures called caruncles, arranged in four longitudinal lines [3-6].

Histologically, uterus is formed by perimetrium, myometrium, and endometrium; perimetrium is located in the external uterus surface, it is a serosa layer, prolongation of the peritoneum, and a thin layer of connective tissue. Myometrium is formed by smooth muscle fibers arranged in an internal, circular, and thick layer, and an external, longitudinal and less thick layer; these two are separated by a vascular layer. Endometrium, the organ mucosa, varies constantly by hormonal changes from each stage of estrous cycle, and pregnancy. The luminal epithelium is columnar simple or cubic simple with some ciliated portions. Under the luminal epithelium is located the stroma that is formed by connective tissue containing the uterine glands; stroma includes a densely organized zone of fibroblasts called stratum compactum extending into a more loosely organized zone in the deeper endometrium (stratum spongiosum), blood vessels, and immune cells [6-8]. Uterine glands are tubular, simple and ramified; they produce the histotrophic secretion [6-10], and are distributed throughout the whole endometrium, except the

caruncles [8,11].

Histological characteristics of endometrium vary as a function of each stage of the estrous cycle; these variations depend mainly on the level of both estrogens and progesterone. Estrogens provoke mucosa proliferation during the follicular stage, and the synthesis of receptors to progesterone; in this way estrogens prepare the uterus for the secretory (luteal) stage dominated by progesterone. These cyclic uterine modifications create an adequate environment for embryo implantation and a successful pregnancy [6,12,13].

Histological cyclic endometrial changes

Dairy cows are polyestrous, exhibiting frequent periodic estrous cycles per year. Estrous cycle is 21 days long (range 18-24 days), and it is divided in two stages on the basis of the dominant structures on the ovary:

(i) follicular (proestrus and estrus) that is the period from the regression of corpus luteum (CL) until ovulation occurs, and

(ii) luteal (metestrus and diestrus) that is the period from ovulation until CL regression [14].

Endometrium during follicular stage is in proliferative status under the influence of estradiol, whereas during luteal stage is in secretory status under the influence of progesterone [15]. Changes in the endometrial morphology along estrous cycle are more evident in the glandular epithelium and stroma than in the luminal epithelium [16,17].

Endometrium at proliferative stage coincides with follicle growing and secretion of estrogens; it is characterized by a progressive increase in the endometrium thickness due to an increase in the number of cells [6,15]. At the beginning of this proliferative stage endometrium is thin, stroma is loose, and low-simple columnar glands are scarce and straight, lumen is narrow. Later on, vascularization increases, stromal, luminal, and glandular cells display mitosis; number of both stromal and glandular cells increases and edema is present. At the end of this stage, stroma becomes dense, glands are bigger in number, elongated, and sinuous, epithelium looks higher, pseudo stratified and the lumen is empty [6-18].

Secretory stage is the period when corpus luteum is functional and progesterone is secreted; endometrium reaches its maximum thickness, blood vessels enlarger remarkably, and glands display secretory capacity [6,15]. Before ovulation, blood vessels continue enlarging, and glands become progressively tortuous. In this stage, glands are abundant, tortuous, and shortened; lumen is wide, full of secretion, and ready to produce histotrophe [6,12,13]. Glandular epithelium is columnar simple, although some parts are columnar stratified, and contains a great amount of secretion vacuoles [6,12,18].

Luteolysis ends secretory stage, as progesterone concentration decreases estradiol takes control of a new cycle of cellular proliferation [6].

Presence of inflammatory cells in the endometrium is still a controversial issue; a variable number of inflammatory cells are located in the stratum compactum, beneath the luminal epithelium, they represent a defense against infections. Neutrophils are frequently seen during proestrus, estrus, and metestrus; in the diestrus they are either rarely seen or absent [11,17,19]. Eosinophils may be present in the whole layers of endometrium; in general, they are located in the stratum compactum [11], and their number does not change throughout estrous cycle [11,19]. However, Döcke [15] described a strong presence of eosinophils during estrus. Mastocytes are located in the stratum compactum forming clusters of 5 to 10 cells, regardless of the stage of estrous cycle; they may be also located in the myometrium and perimetrium [20,21]. Lymphocytes may be present throughout estrous cycle; however this is controversial [11,17,19]. Some isolated lymphocytes can be seen in the stratum compactum as well as some lymphocytic foci [11,17,19,20,22]. It has been proposed that such lymphocytes foci do not match with endometrial physiology but they are remnants of previous infections [17,23]. A progressive increase in the total number of natural killer (NK) cells during the luteal stage usually occurs [24]. Some plasmatic cells are present in both follicular and luteal stages [11,19]; macrophages are mainly located in the compactum and spongiosum strata, their density varies as estrous cycle progresses [11,25]; an increase in their number during diestrus has been reported [17]. Infiltration of endometrium by inflammatory cells may vary by cow age; that is, plasmatic cells, mastocytes, and lymphoid follicles increases as cows become older [11].

Conclusion

It is necessary to develop effective and convenient tools to diagnose uterine disorders in order to establish an appropriate therapeutic management. A detailed histomorphological examination in the different stages of estrous cycle allows obtaining a more accurate diagnosis of endometrial diseases; thus, an integral assessment of reproductive problems in the cow may improve its fertility.

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