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Ovarian function in ruminants

B. Berisha, D. Schams *

Department of Physiology, Technical University Munich-Weihenstephan, Weihenstephaner Berg 3, D-85354 Freising, Germany

Abstract

The purpose of this overview is to highlight important steps of ovarian regulation during follicle development, ovulation and the life span of corpus luteum (CL) in ruminants. The ovarian cycle is central to reproductive function. It is characterized by repeating patterns of cellular proliferation, differentiation and transformation that encompass follicular development and ovulation as well as the formation, function and regression of the CL. In the first part, the importance and regulation of final follicle growth and especially of angiogenesis and blood flow during folliculogenesis, dominant follicle development and CL formation are described. Our results underline the importance of growth factors especially of insulin-like growth factor (IGF), vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF) for development and completion of a dense network of capillaries (angiogenesis) during follicle growth and CL formation. In the second part, the regulation of CL function by endocrine/paracrine and autocrine acting regulators is discussed. There is evidence that besides the main endocrine hormones luteinizing hormone (LH) and growth hormone (GH) local regulators as growth factors, peptides, steroids and prostaglandins are important modulators of luteal function. During early CL development until midluteal stage oxytocin (OT), prostaglandins and progesterone (P) itself stimulate luteal cell proliferation and function supported by the luteotropic action of a number of growth factors. The still high mRNA expression, protein concentration and localization of VEGF, FGF and IGF family members in the cytoplasm of luteal cells during midluteal stage suggest that they play pivotal role in the maintenance (survival) of this endocrine tissue. The major function of the CL is to secrete P. Progesterone itself regulates the length of the estrous cycle via influencing the timing of the luteolytic PGF2α signal from the endometrium. At the end of a nonfertile cycle, the regression of CL commences, steroidogenic capacity is lost (functional luteolysis), cell death is initiated, and tissue involution as well as resorption occurs within a few days (structural luteolysis). The cascade of mediators during luteolysis is very complex and still awaits elucidation. Evidence is given for participation of blood flow, inflammatory cytokines,

* Corresponding author. Tel.: +49 8161 71 3508; fax: +49 8161 71 4204.
E-mail addresses: physio@wzw.tum.de, schams@wzw.tum.de (D. Schams).

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vasoactive peptides (angiotensin II and endothelin-1), and decrease of the classical luteotropic mediators.

Keywords: Ovary; Growth factors; Hormones; Follicle; Corpus luteum; Ruminants; Ovarian function

1. Introduction

The aim of this overview is to discuss recent findings being important for final maturation of antral follicles, formation and function of the corpus luteum (CL) and luteal regression.

2. Final follicle development and corpus luteum formation

Ovarian follicular growth and development in ruminants is characterized by two or three consecutive follicular waves per estrous cycle [1,2]. Each wave involves the recruitment of a cohort of follicles and the selection of a dominant follicle, which continues to grow and mature to the preovulatory stage while others in the wave undergo atresia. A complex regulatory system must exist to determine which follicles are selected. Although it is well established that the ovarian function is regulated primarily by the pituitary gonadotropins follicle-stimulating hormone (FSH), luteinizing hormone (LH) and their receptors (FSHR and LHR), it is also evident that locally produced factors, such as steroid hormones, peptides and growth factors have essential modulatory roles in follicular development (recruitment, selection and dominance) and ovulation [2].

Formation of the CL is initiated by series of morphologic and biochemical changes in cells of the theca interna (TI) and granulosa cells (GC) of the preovulatory follicle. These changes, termed luteinization, occur after the preovulatory LH surge.The CL is a heterogeneous tissue consisting of endothelial cells (EC), steroidogenic large luteal cells (LC) and small LC as well as fibroblasts, smooth muscle cells and immune cells [3]. In a complex tissue, the various cell types must interact to ensure normal growth and development. Tissue growth (follicle or CL) depends upon growth of new blood vessels (angiogenesis) and establishment of a functional blood supply. Blood flow decreased shortly after ovulation but increased afterwards gradually in parallel with the increase in CL volume and plasma progesterone (P) concentration from days 2–5 with angiogenesis [4]. This increase reflects normal CL development and underlines the importance of angiogenesis. In the mature CL nearly every parenchymal cell is in contact with one or more capillaries [5]. The CL is one of the few adult tissues that exhibits regular periods of growth (angiogenesis), function and luteolysis (CL regression).

2.1. Ovarian angiogenesis

Angiogenesis is the preferred term for processes leading to the generation of new blood vessels through sprouting from already existing ones. This process includes degradation