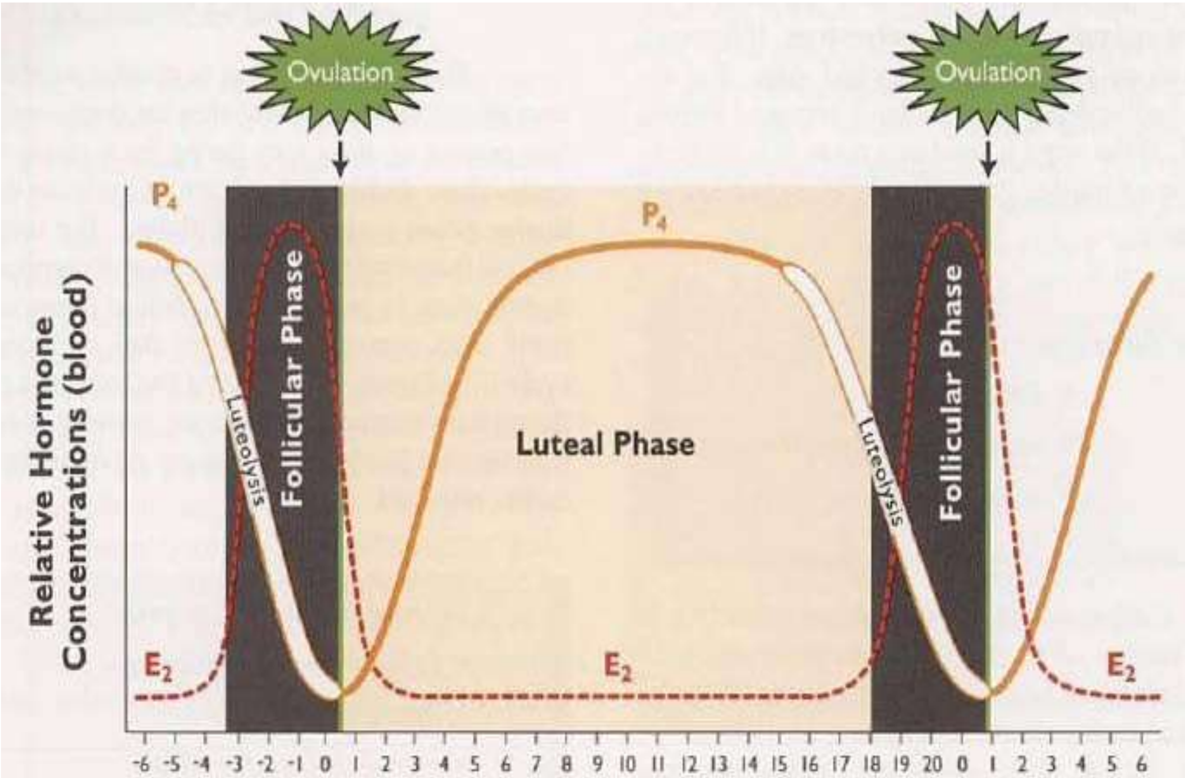
The follicular phase of estrous cycle

-The estrous cycle can be divided into two distinct phases that are named after the dominant structure present on the ovary during each phase of the cycle. These divisions of the estrous cycle are the **follicular phase** and the **luteal phase** see Figure (1)**.** The follicular phase is the period from the regression of corpora lutea to ovulation. In general, the follicular phase is relatively short, encompassing about 20% of the estrous cycle. During the follicular phase, the primary ovarian structures are growing dominant follicles that produce the primary reproductive hormone, estradiol.

-The luteal phase is the period from ovulation until corpora lutea regression. The luteal phase is much longer than the follicular phase and, in most mammals, occupies about 80% of the estrous cycle. During this phase, the dominant ovarian structures are the corpora lutea (CL) and the primary reproductive hormone is progesterone.

Figure (1). Phases of the Estrous Cycle



- The follicular phase of the estrous cycle consists of proestrus and estrus. During the follicular phase four significant events take place. They are: 1) gonadotropin release from the anterior lobe of the pituitary; 2) follicular preparation for ovulation; 3) sexual receptivity and 4) ovulation.

1- Gonadotropin Release is controlled by Ovarian Estrogen and Hypothalamic GnRH.

-The secretion of GnRH in the female is controlled by two separate areas in the hypothalamus. First is called **the tonic center** is responsible for basal secretion of GnRH. The neurons in this center release small pulses of GnRH over a substantial period of time (days to weeks), While the second known as the **surge center** (also called the "**preovulatory center**") is responsible for the preovulatory release of GnRH that stimulates a surge of LH, causing ovulation.

- Elevated GnRH is essential for initiating the follicular phase of the estrous cycle. The tonic center releases small amplitude episodes (pulses) of GnRH that stimulate release of FSH and LH from the anterior lobe of the pituitary, causing growth and development of ovarian follicles. However, when estradiol levels are high, as they would be during the mid-to late follicular phase (See Figure 2). The preovulatory center responds dramatically by releasing large quantities of GnRH. This stimulation in response to rising concentrations of estradiol is referred to as positive feedback The surge center is responsible for release of large quantities of GnRH, thus causing a surge of LH that causes ovulation.

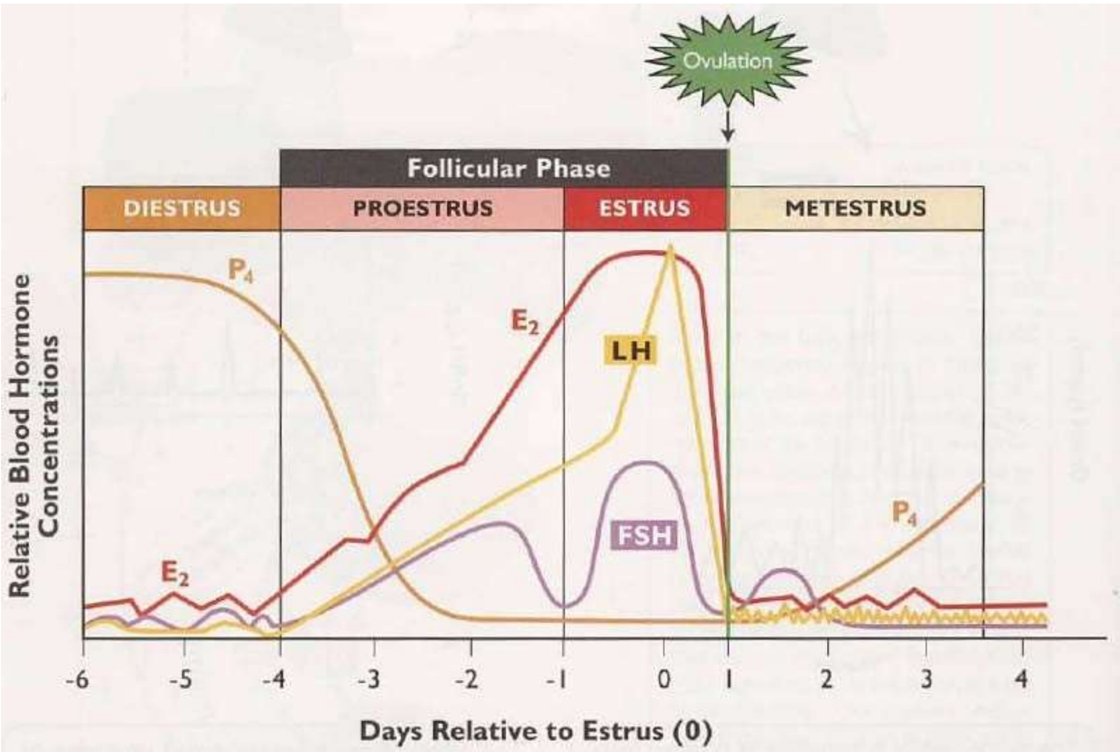


Figure (2). Hormonal Changes during the Follicular Phase

2- Follicular Dynamics is controlled by FSH and LB and Involves Both Growth and Death of These Follicles

- The dynamics of antral follicles involve four processes. These processes are **recruitment, selection, dominance and atresia.**

Figure (3). Follicular Recruitment, Selection and Dominance

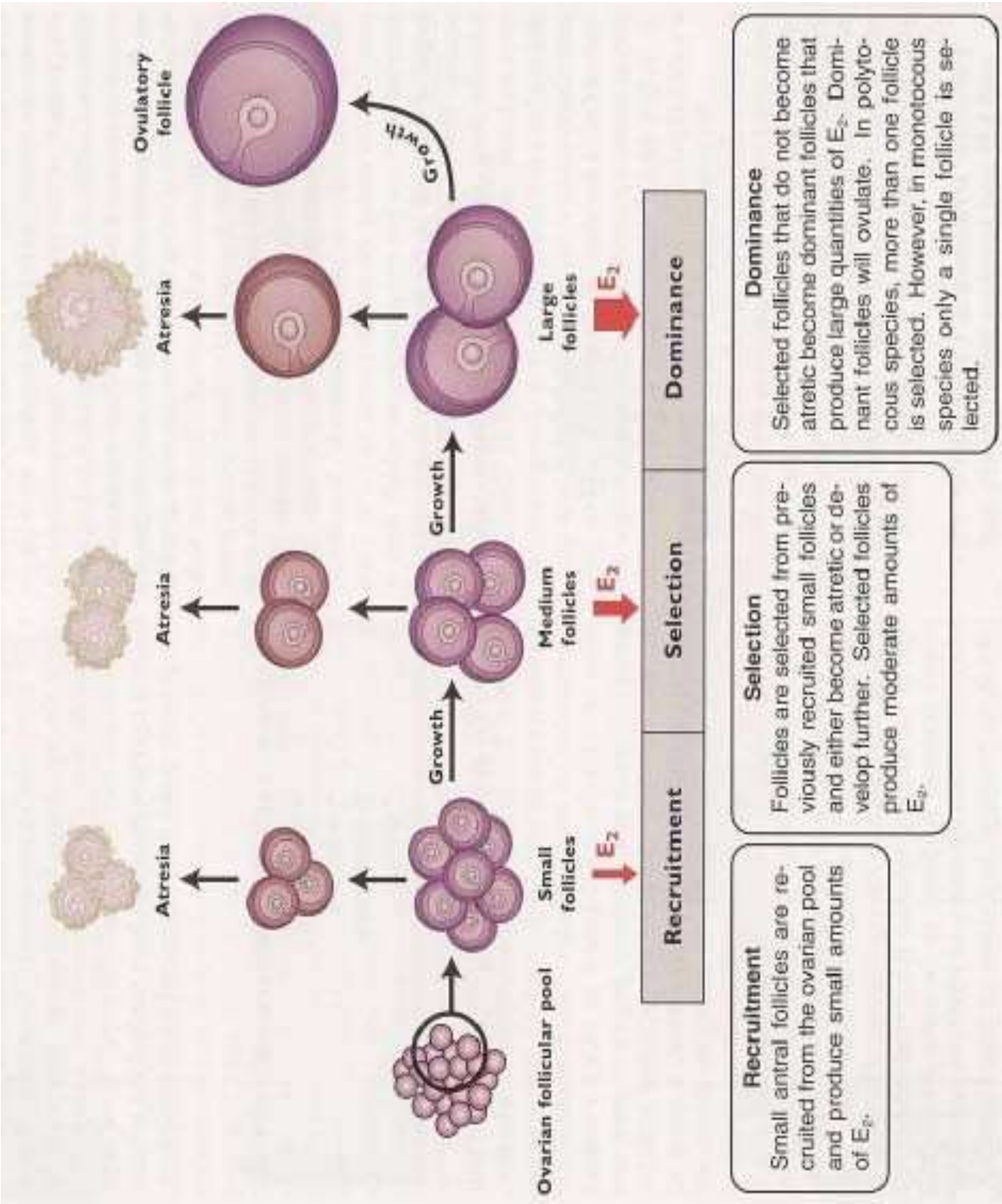
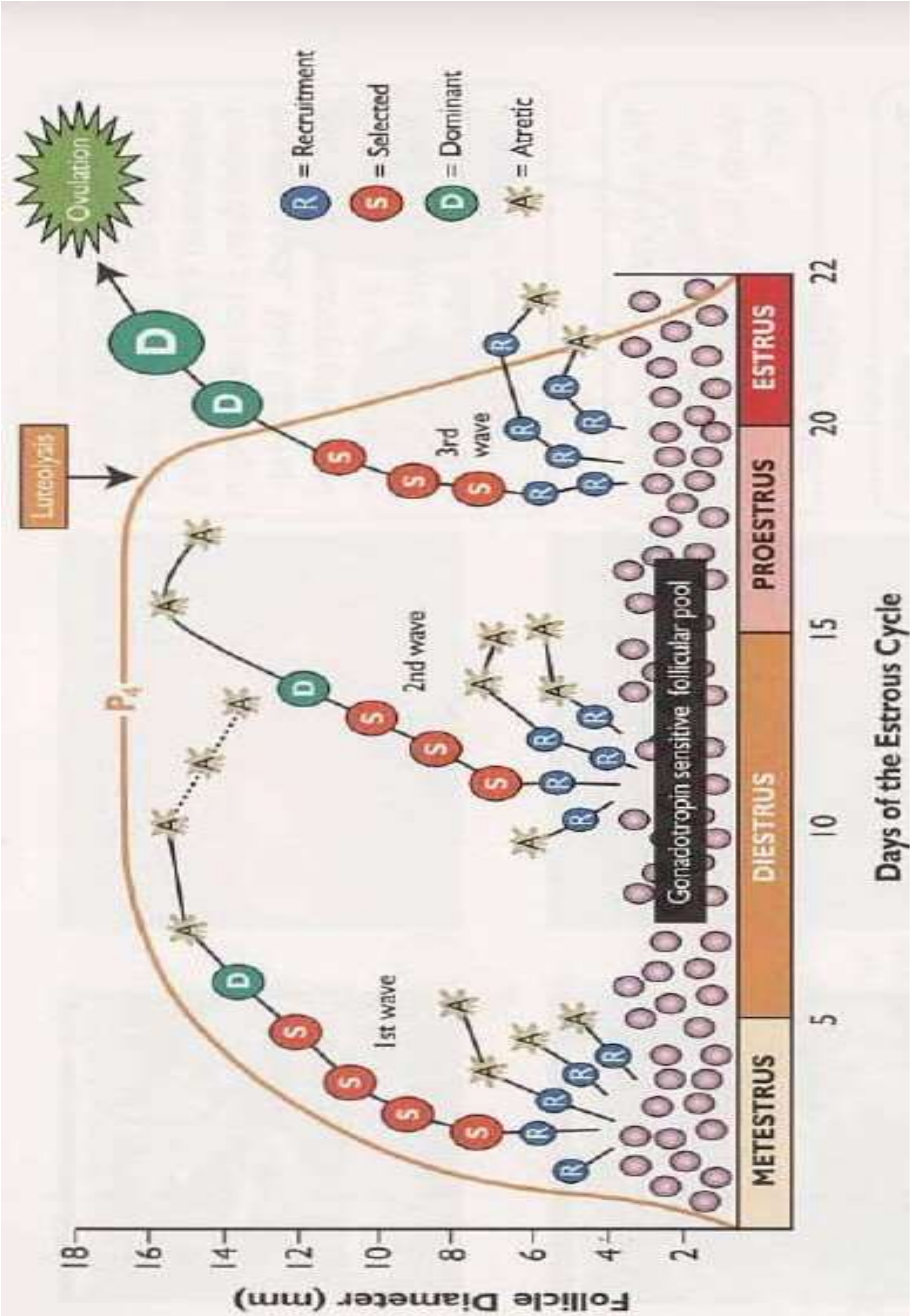


Figure (4). Several Follicular Waves Occur During One Cycle



- During metestrus (days 3 to 5 in cattle), a group of follicles is recruited. However, these follicles are not exposed to the appropriate endocrine conditions for continued development and undergo atresia within the ovary. During diestrus, a second follicular wave occurs, but these follicles also undergo atresia. Note that the first two follicular waves begin and terminate during times in the cycle when progesterone is increasing or is at its highest level (See Figure 4). Neither complete follicular development nor ovulation can occur under progesterone dominance.

- However, the dominant follicle of each wave will ovulate if luteolysis occurs. During progesterone dominance, GnRH is released in low quantities only and thus FSH and LH are low. It should be emphasized that even though follicles in the first two follicular waves become atretic they still produce some estradiol.

- In fact, midcycle estradiol increases and declines with each follicular wave but blood concentrations are low. After luteolysis (corpus luteum regression), a third wave of follicles develops. One or more of these follicles will develop into the dominant and the preovulatory follicle.

- It must be emphasized that the endocrine condition for final follicular development will exist only after luteolysis and subsequent decline in progesterone that removes the negative feedback on the hypothalamus. Also it is important to recognize that the number of follicular waves within a given cycle varies among and within species.

3- Sexual receptivity (Practical)

Recruitment= high FSH +low LH +no inhibin +no estradiol

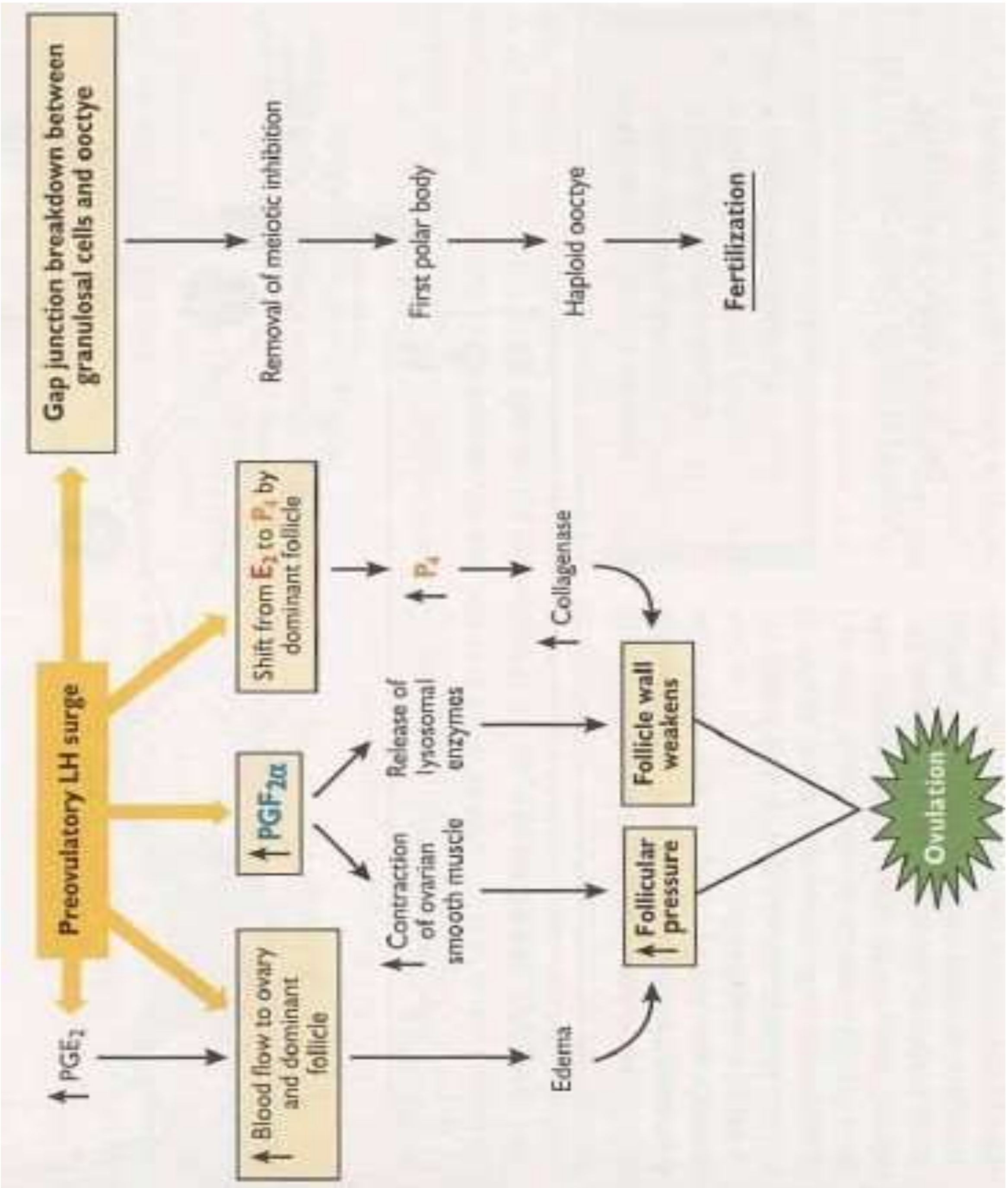
Selection = low FSH +moderate LH + low inhibin

Dominance = low FSH + high LH + high inhibin

Atresia = degeneration of follicles

4- <u>Ovulation:</u> Ovulation is a complicated process that involves purposeful destruction of follicular tissue. The main events of the ovulatory cascade resulting from the LH surge are shown in Figure (5).

Figure (5). Ovarian Events Caused by the Preovulatory LH Surge



- Hyperemia (local elevated blood flow) is believed to be controlled at the tissue level by histamine and prostaglandin E2 (PGE_2). In addition, there is elevated local blood flow to dominant follicles. Accompanying this local hyperemia, the theca interna becomes edematous because of increased vascular permeability brought about by histamine.

- Following the LH surge, the cells of the theca interna begin to produce progesterone instead of testosterone. At first, this transition involves only a small quantity of progesterone that is produced locally (at the follicular level). This local elevation of progesterone is essential for ovulation because progesterone stimulates synthesis of an enzyme called **collagenase** by the theca intema cells. Collagenase causes the breakdown of collagen, a major component of connective tissue. Thus, follicular enlargement is closely coordinated with the enzymatic degradation of the tunica albuginea. As these two processes advance, the apex of the follicle, called the **stigma** begins to push outward and weaken.

- After the LH surge, both prostaglandin $F_{2\alpha}$ and prostaglandin E_2 are synthesized and released locally by the ovary. Prostaglandin $F_{2\alpha}$ causes contractions of the myoid (smooth muscle) components of the ovary. Thus, intermittent contractions may increase pressure locally and force the stigma to protrude even more dramatically from the surface of the ovary. Prostaglandin $F_{2\alpha}$ also causes **lysosomes** within the granulosal cells to rupture, releasing their enzymes. These lysosomal enzymes cause further connective tissue deterioration at the apex of the follicle.

- The role of prostaglandin E_2 is to help the follicle remodel itself into a corpus luteum after ovulation. The follicle receives its direction for this reorganization from prostaglandin E_2. Prostaglandin E_2 is believed to activate a substrate called plasminogen. Plasminogen is converted to plasmin by plasminogen activator. Plasmin is the active enzyme that participates in tissue remodeling.

Figure (6). The Pathway for Induced Ovulation