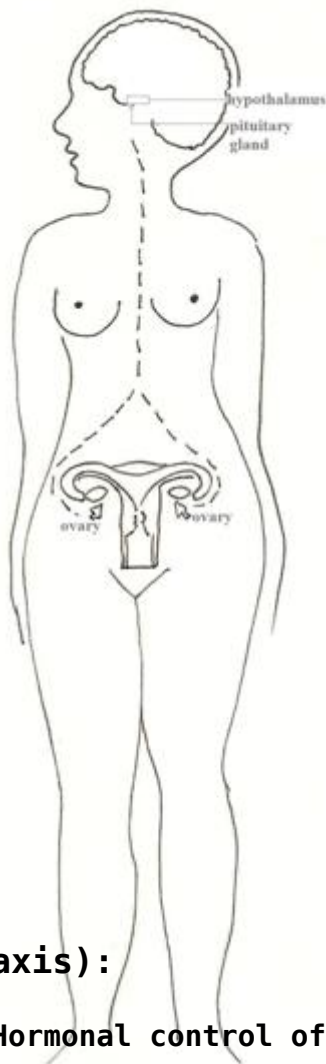


The HPO Axis



THE HPO AXIS (Hypothalamic-Pituitary-Ovarian axis):

Hormonal control of the menstrual cycle/ Feedback Mechanism:

The events of the menstrual cycle are controlled by an interplay of **five** hormones secreted by **three** organs and known as the hypothalamic-pituitary-ovarian-axis, (HPO axis). (Fig. 6-6).

The three organs are:

- (i) the **Hypothalamus** at the base of the brain which secretes gonadotropic releasing hormone (**GnRH**),
- (ii) the **Pituitary gland**, a tiny gland just below the hypothalamus which secretes follicle stimulating hormone (**FSH**) and luteinizing hormone (**LH**),
- (iii) the **Ovaries** which secretes the steroid hormones **oestrogen** and **progesterone**.

The interplay of hormones in the **HPO axis** is regulated by a **feedback mechanism**.

<< **Fig. 6-6; The HPO Axis:** The three organs of the H-P-O axis are the **hypothalamus** at the base of the brain, the **pituitary gland** just below it and the **ovaries**, one on each side of the pelvis. (Diagram courtesy of Mary Kane)

Feedback Mechanism – role of the hypothalamus and pituitary gland, (Fig. 6-7):

The gonadotropin hormones FSH and LH are secreted by the pituitary gland. FSH is necessary for the development of the immature ovum, (i.e. the primordial follicle in the ovary), and LH triggers ovulation. The secretion of FSH and LH from the pituitary gland is under the control of gonadotropin releasing hormone (GnRH) from the hypothalamus, and the hypothalamus in turn is controlled by the levels of the ovarian steroid hormones oestrogen and progesterone in the blood by means a **feedback mechanism**. The hypothalamus may also be affected by external factors **e.g. stress**. (see **topic** 'Factors that interfere with the interpretation of mucus' under the 'Cervical Mucus' heading).

Regulation of Hormones (Feedback Mechanism)

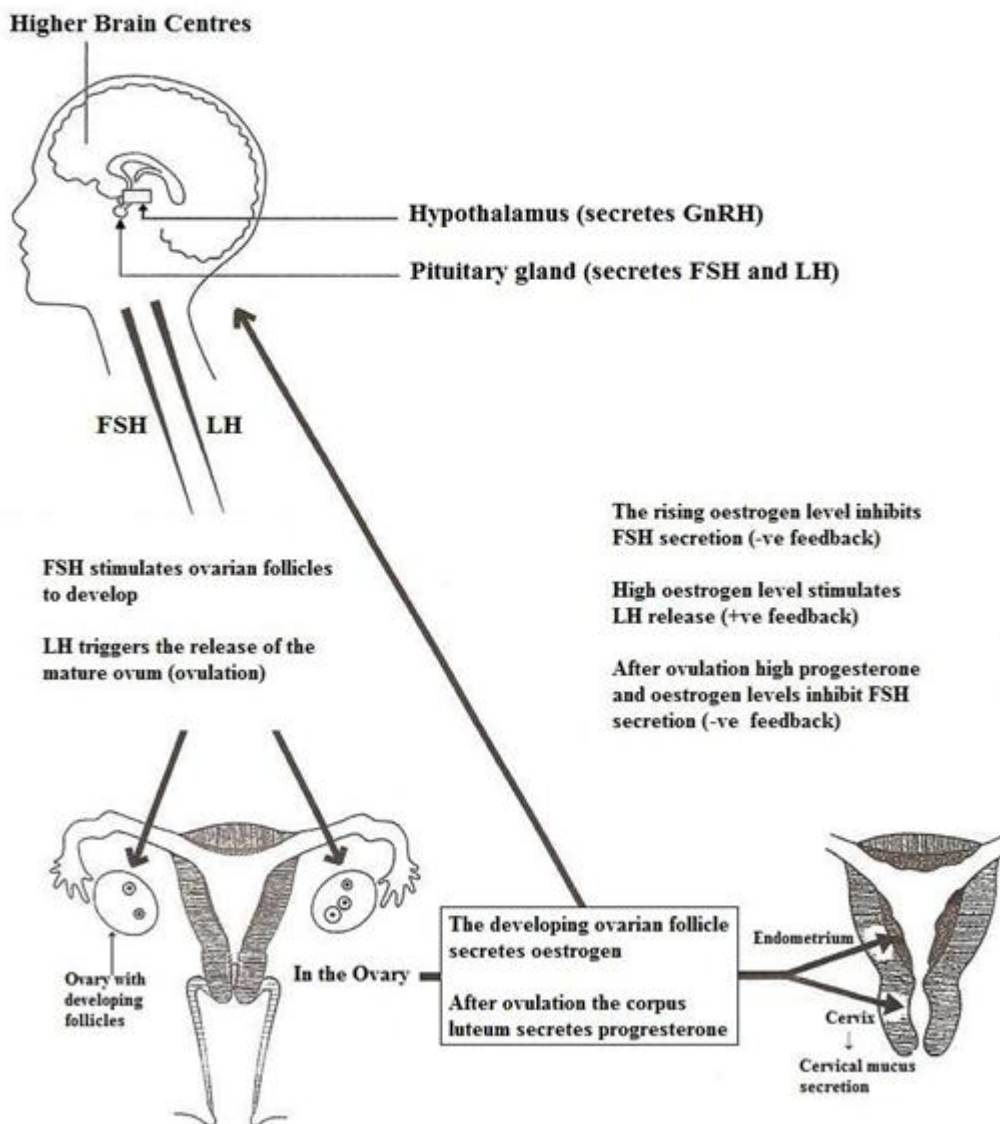


Fig 6-7; The hypothalamic-pituitary-ovarian axis (HPO axis) and feedback

mechanism: As oestrogen and progesterone levels are low at the beginning of the cycle this allows follicle stimulating hormone (FSH) to be released from the pituitary gland under the stimulation of Gonadotropin Releasing Hormone (GnRH) from the hypothalamus. FSH stimulates a number of ovarian follicles to develop. The growing follicles in the ovary secrete oestrogen which causes proliferation of the endometrium (proliferative phase of the endometrium), and secretion of cervical mucus. The rising oestrogen from the developing follicles suppresses FSH secretion in order to inhibit development of any new follicles, (negative feedback mechanism). By day 7 of an average 28 day cycle one of the developing follicles becomes dominant (Graafian follicle), and the others regress. The high oestrogen from the dominant follicle stimulates the secretion of luteinizing hormone (LH surge) from the pituitary (positive feedback) which triggers ovulation. After ovulation the ruptured follicle becomes the corpus luteum which secretes progesterone and oestrogen. Progesterone stimulates further development of the endometrium to prepare for possible pregnancy, (secretory phase of the endometrium), and stimulates the glands in the cervical crypts to secrete gestogenic G mucus which occludes the cervical canal. The high progesterone and oestrogen levels in the luteal phase suppress FSH secretion (negative feedback). If pregnancy does not occur the corpus luteum regresses 14 days after ovulation and the drop in progesterone causes sloughing of the endometrium (*menstruation*). The low oestrogen and progesterone at the beginning of the cycle allows the suppression of FSH to be lifted and a new cycle begins. (*Diagram courtesy of Fergal Mulcahy*) (See **Diagram** on Changes in different organs during the menstrual cycle, **Page 9** in <http://Pictures & Diagrams>)

THE FEEDBACK MECHANISM – WHAT IS HAPPENING IN THE OVARY (Fig. 6-7)

BEFORE OVULATION (follicular phase):

At the end of the menstrual cycle just before menstruation begins, oestrogen and progesterone are both at a low level allowing FSH secretion from the pituitary to rise. FSH stimulates some follicles (immature ova) in the ovary to develop and they secrete oestrogen. The rising oestrogen level from the developing follicles then suppresses FSH secretion by negative feedback mechanism on the pituitary gland in order to inhibit the development of more follicles. By day 7 of an average 28 day cycle one follicle becomes dominant and continues to grow and is called the Graafian follicle. When oestrogen reaches a high level it stimulates the release of LH, (LH surge), by a positive feedback mechanism on the pituitary gland and LH triggers ovulation.

AFTER OVULATION (luteal phase):

After ovulation, (luteal phase), the granulosa cells in the wall of the ruptured follicle in the ovary become the corpus luteum. During the **luteal phase** of the cycle, the corpus luteum secretes progesterone and oestrogen which suppress the secretion of FSH by a negative feedback mechanism on the pituitary so that no further ovulation can occur in that cycle, (Fig. 6-7). Progesterone, which maintains the endometrium, is at its highest level seven days after ovulation. If fertilisation has not occurred the corpus luteum then starts to regress causing the progesterone level to fall. The drop in progesterone to a critical low level has two effects; (a) the endometrium is no longer maintained and is shed as menstruation about 14 days after ovulation, (b) the suppression of FSH secretion is lifted and a new cycle

begins.