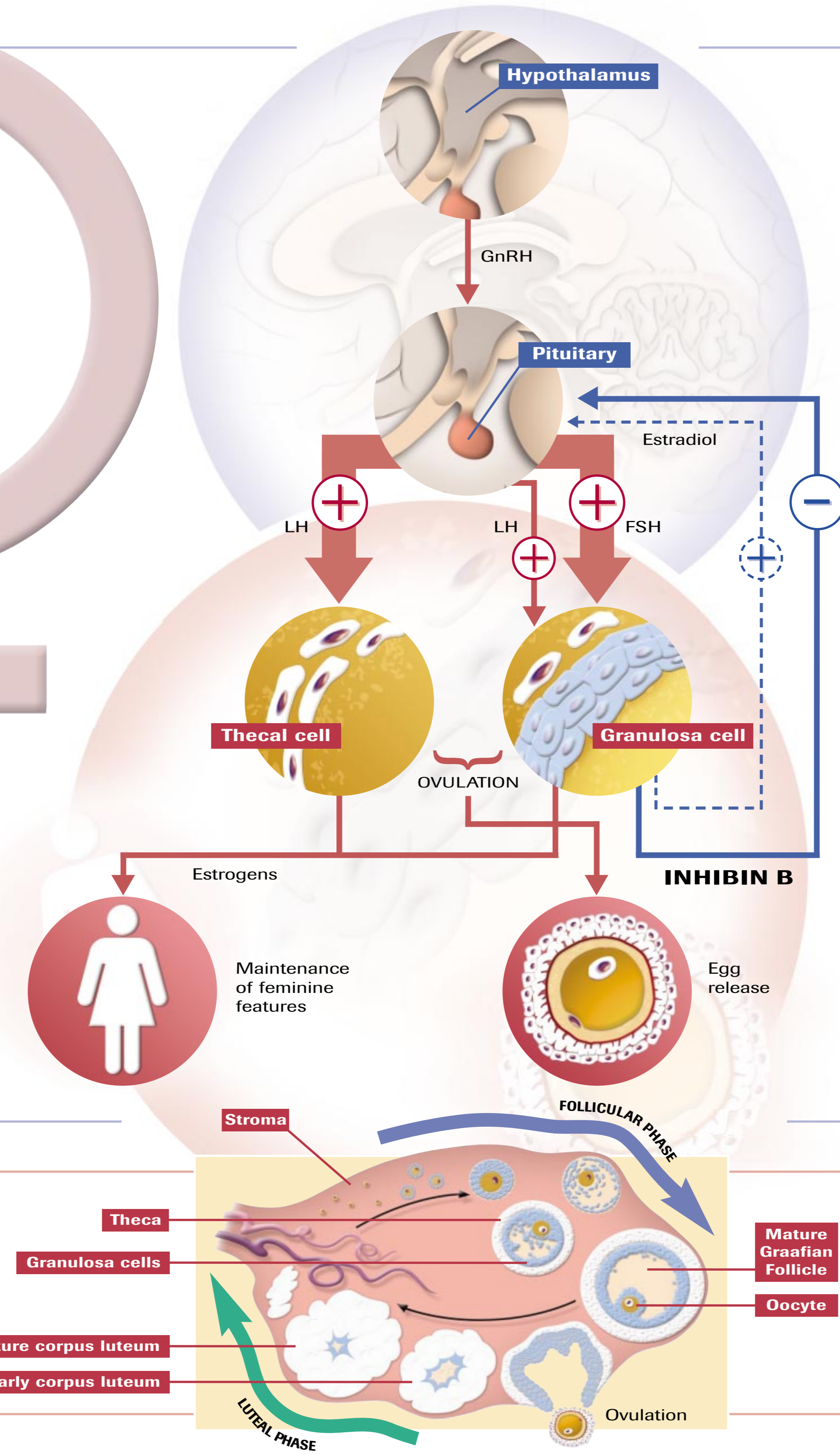
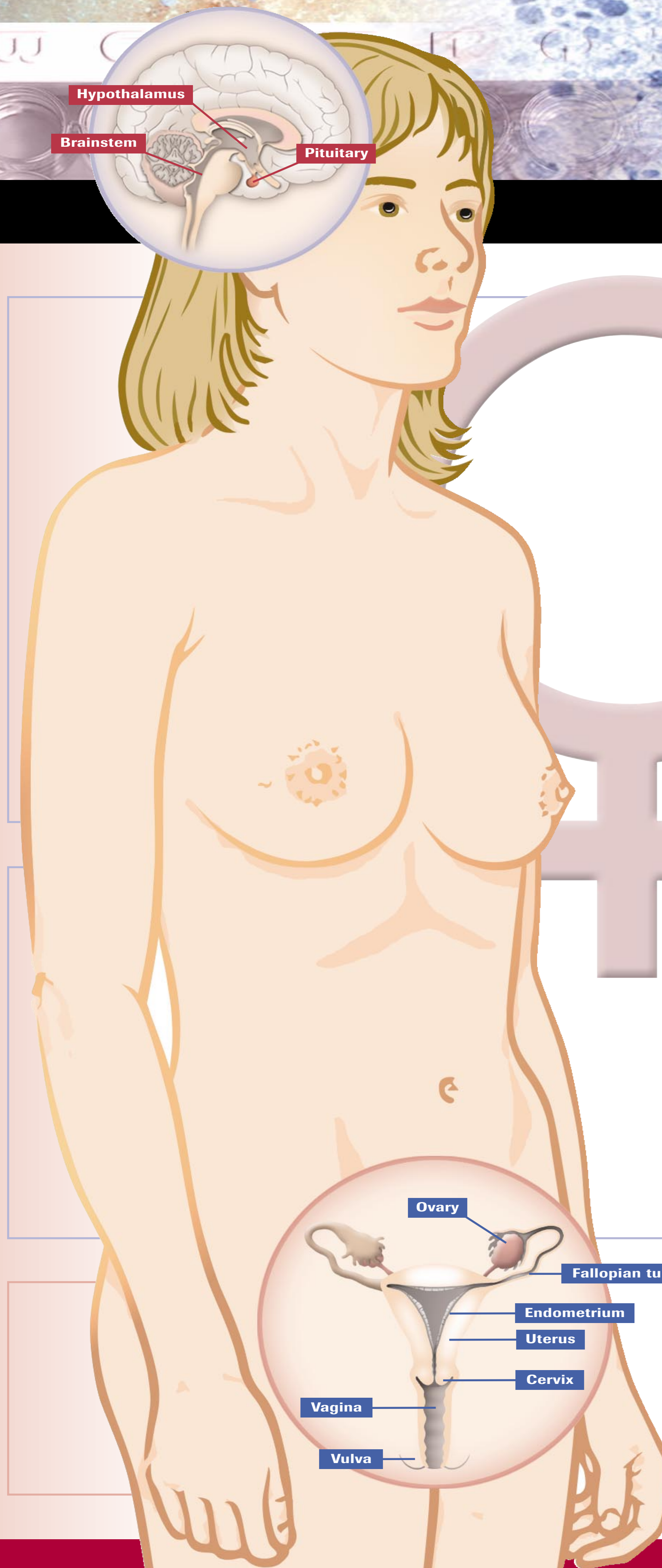


Inhibin & Female Fertility

INFERTILITY MAY BE DEFINED AS FAILURE TO CONCEIVE AFTER ONE YEAR OF UNPROTECTED SEXUAL INTERCOURSE



INFERTILITY *A female problem, a male problem or both?*

Female Infertility – Of the problems facing couples having difficulty conceiving, up to 30% are due to female problems, 30% male and 20% are due to combined male-female factors. When diagnostic tests fail to reveal the cause of infertility, this is referred to as unexplained infertility and occurs in 20% of infertile couples. Correct diagnosis is therefore the key to effective fertility therapy and both partners should have their fertility status assessed **before** commencing fertility treatments.

Female factor infertility or sub-fertility can encompass many different conditions and may be a multi-factorial problem for an individual comprising one or more of the following:

- Congenital absence of eggs (oocytes)
- Intrauterine adhesions, fibroids or polyps
- Hormone (endocrine) abnormalities
- Premature menopause
- Endometriosis
- Reproductive tract infections
- Immunological abnormalities
- Tubal blockage or damage
- Polycystic Ovaries (PCO)
- Low Ovarian reserve
- Uterine abnormalities

In addition to routine physical examination, hormone profiles at different times in the menstrual cycle, pelvic ultrasound and details of patient history with regard to growth and development, stress, infection and sexual history contribute to the assessment of a woman's fertility status. Family history may be highly relevant as premature menopause, endometriosis and PCOS are all conditions with a strong genetic association.

Amenorrhea is the complete absence or abnormal suppression of ovulation and therefore menstruation; sporadic menstruation/ovulation is termed **oligomenorrhea**. Such conditions may arise for many reasons of which the commonest are polycystic ovarian syndrome (PCOS), hypothalamic (induced by excessive weight loss or exercise) or hyperprolactinaemic (caused by stress or microadenoma of the pituitary).

Polycystic ovaries are characterised by enlarged ovaries containing multiple small cysts caused by unbalanced hormone levels that perpetuate incomplete follicular development. Ovulation is irregular and sporadic and the incidence of miscarriage is increased.

Many therapies and procedures can be used to improve fertility. Corrective surgery can be used for structural abnormalities such as blocked or damaged fallopian tubes, endometriosis or fibroids and polyps. Hormonal treatment may improve fertility in the clinical management of patients with absent or irregular ovulation. A wide range of *in vitro fertilization* techniques can overcome inoperable tubal damage or severe male factor infertility.

HORMONES *The regulators of ovulation*

Hormones are chemical messengers that are secreted at one site and have their effect at another. They play a crucial role in reproduction and in the control of **gametogenesis**, - the production and release of **oocytes or eggs** in the female and **sperm** in males. The **hypothalamus** and **pituitary** glands in the brain regulate the actions of the ovaries by a complex set of feedback loops. The hypothalamus secretes a substance, **gonadotrophin-releasing hormone (GnRH)** in regular pulses, which stimulates the **anterior pituitary** to release **follicle-stimulating hormone (FSH)** and **lutetinsing hormone (LH)**.

The increased levels of FSH result in the recruitment of a cohort of antral follicles from which a 'dominant' follicle will be selected. The granulosa cells of this "dominant follicle" produce **Inhibin B**, which suppresses FSH production by the pituitary, and estradiol which both suppresses FSH and has a positive feedback effect on LH, allowing a surge that prompts the follicle to release the egg. The **corpus luteum** develops from the post-ovulatory follicle, and produces progesterone which changes the nature of the endometrium or uterine lining thickened by estradiol. These changes are essential for normal implantation of the fertilized egg to occur. In the absence of fertilisation and implantation progesterone production ceases, and the corpus luteum degenerates. It is the rapid fall in the amount of progesterone that results in expulsion of the uterine lining during menstruation. In the presence of fertilisation and implantation, progesterone production by the corpus luteum is maintained by hCG secreted by the foeto-placental unit and acts to prevent spontaneous abortion.

Measurement of the concentration of hormones in the circulation can provide vital information concerning reproductive function. Women undergoing clinical investigations for fertility problems should therefore expect to have **Inhibin B** levels measured in their serum together with **FSH, LH, progesterone** and **estradiol**.

THE OVARY

Each ovary comprises supporting tissue or **stroma**, containing blood vessels and nerves and encapsulated by a layer of germinal epithelium. The fluid-filled structures responsible for **ovulation**, the **follicles**, are embedded in the stroma and develop at the periphery of the ovary. Each follicle bears an outer, **thecal**, layer of cells and an inner, **granulosa** cell layer that surrounds, nurtures and protects the maturing egg or **oocyte**. The fully matured, **Graafian**, follicle ruptures to release the oocyte into the fimbriae of the **fallopian tube** where fertilization may take place before the fertilised **embryo** continues its journey to the uterus where implantation (to produce a pregnancy) or expulsion (with the arrival of menstruation) occurs. The ruptured follicle becomes a **corpus luteum** which secretes progesterone

A female foetus of 22 weeks gestation bears 7 million immature oocytes (primordial follicles). This number drops to 2 million by the time of birth and 500,000 by menarche (puberty). During the years of maximum fertility, follicular loss occurs at a relatively stable rate of 1000 each month by a process of atresia until the age of 35. After this, the rate of loss accelerates until the ovaries are depleted at the menopause.



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