HPG in the adult

GEP Reproductive Medicine

January 2013

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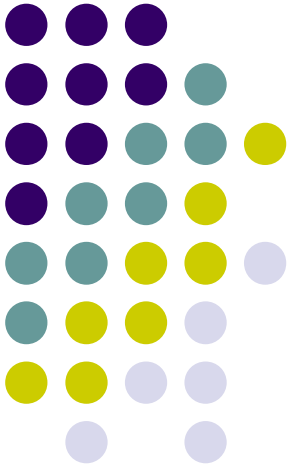
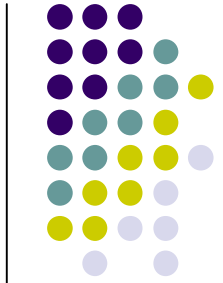
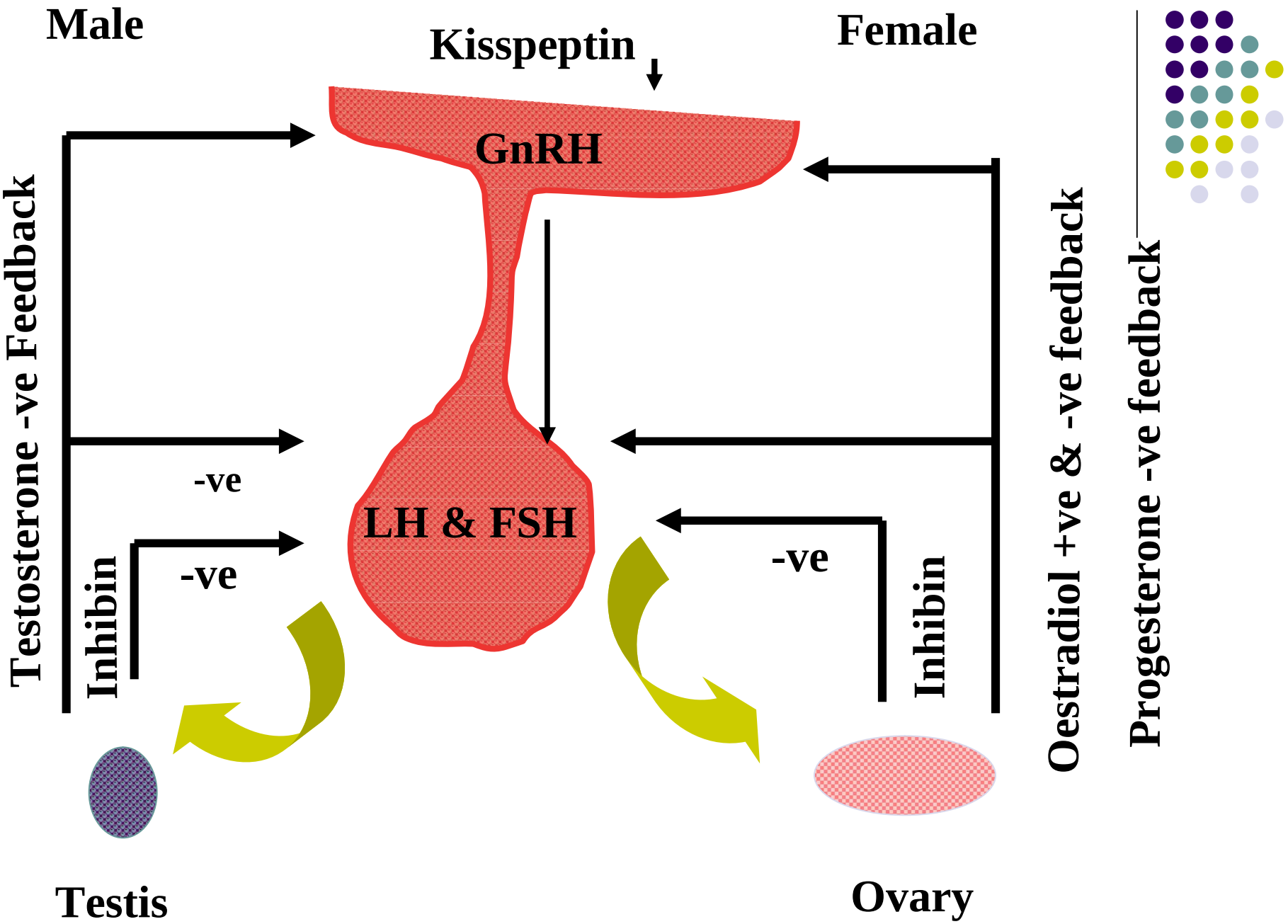
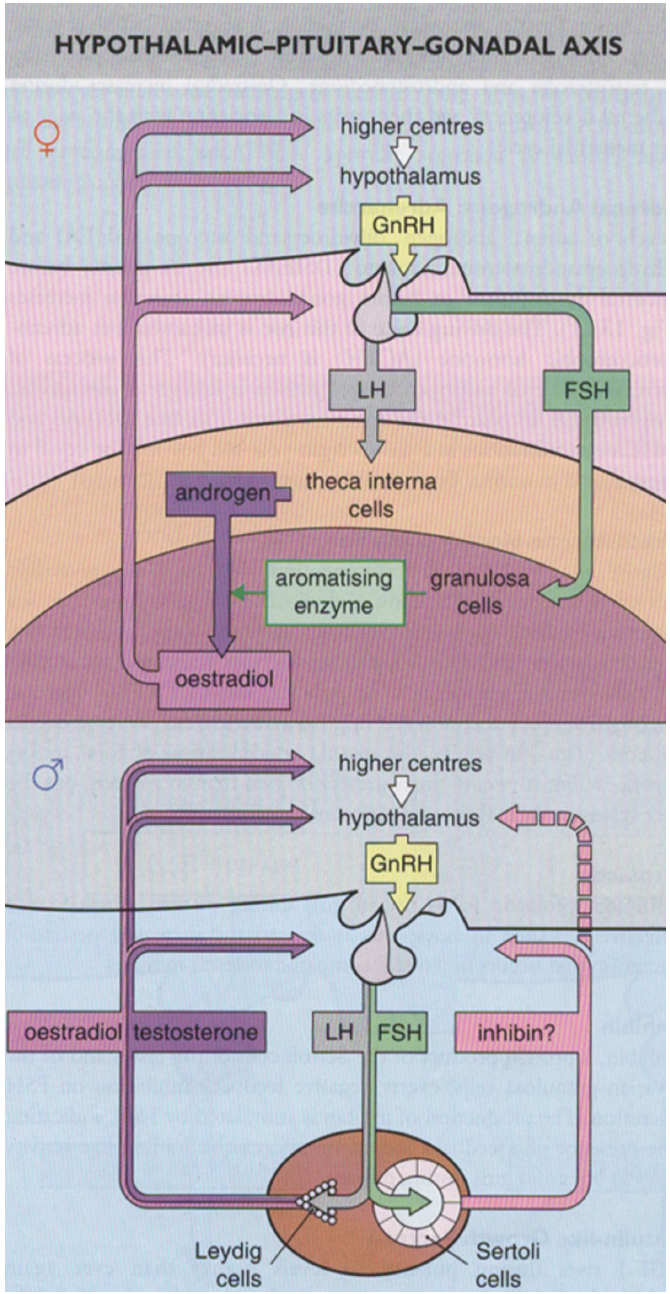


Learning Objectives

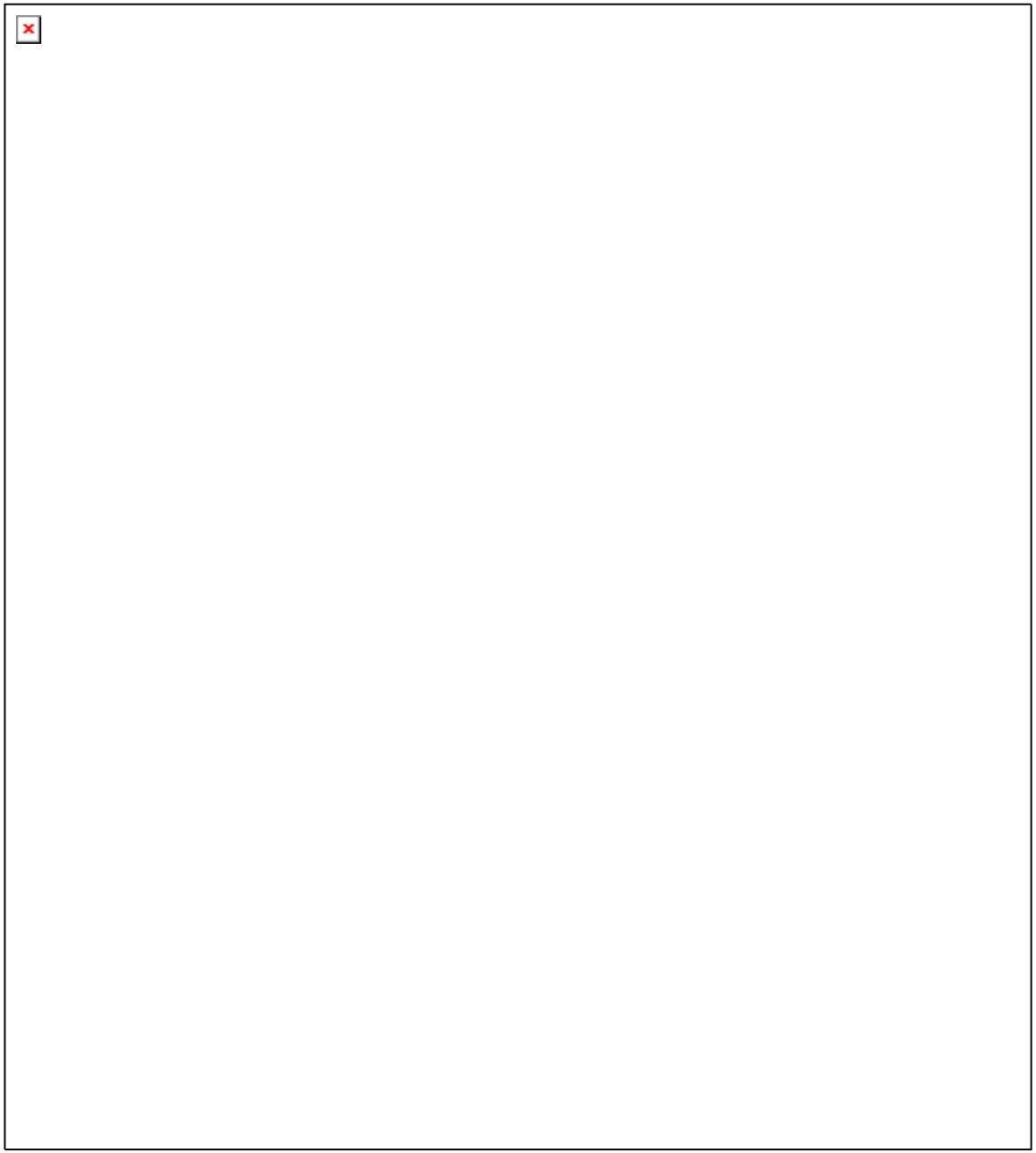


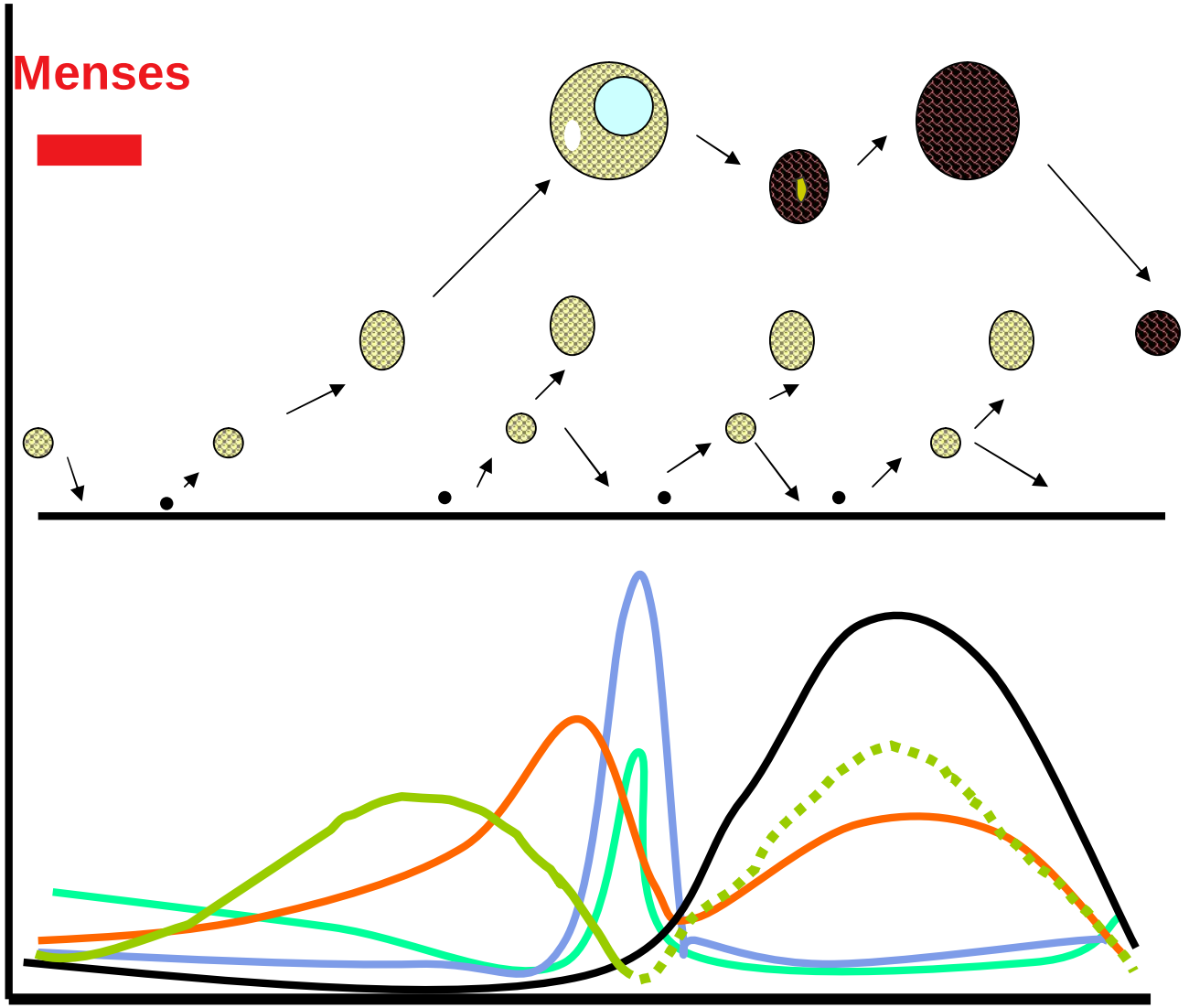
- To understand the control of HPG in the adult male and female
- To understand control of prolactin secretion
- To understand aging and the HPG
- To be aware of disorders of the HPG


Male
Kisspeptin
Female
GnRH
Testosterone -ve Feedback
-ve
Inhibin
-ve
LH & FSH
-ve
Inhibin
Oestradiol +ve & -ve feedback
Progesterone -ve feedback
Testis
Ovary


HYPOTHALAMIC–PITUITARY–GONADAL AXIS
♀
higher centres
hypothalamus
GnRH
LH
FSH
androgen
theca interna cells
aromatising enzyme
granulosa cells
oestradiol
♂
higher centres
hypothalamus
GnRH
oestradiol
testosterone
LH
FSH
inhibin?
Leydig cells
Sertoli cells

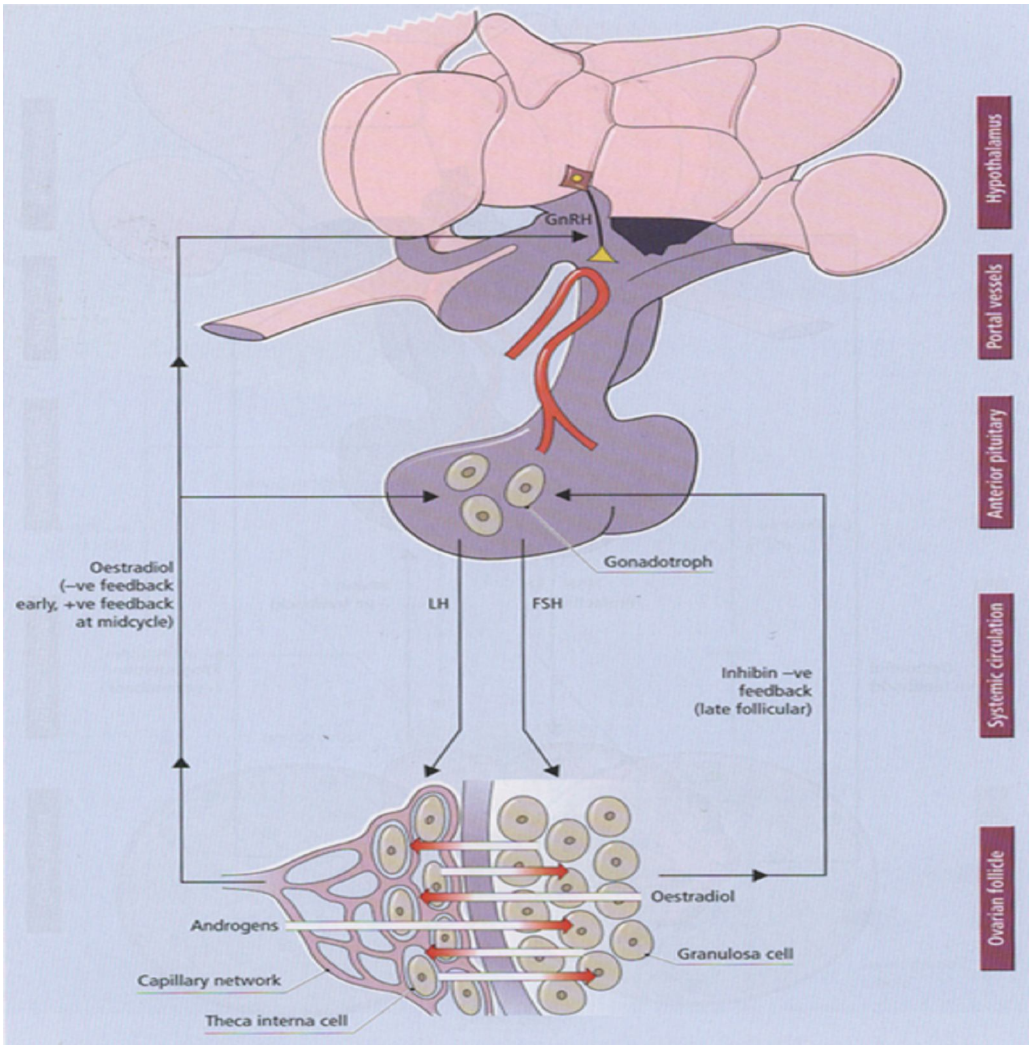
Male HPG



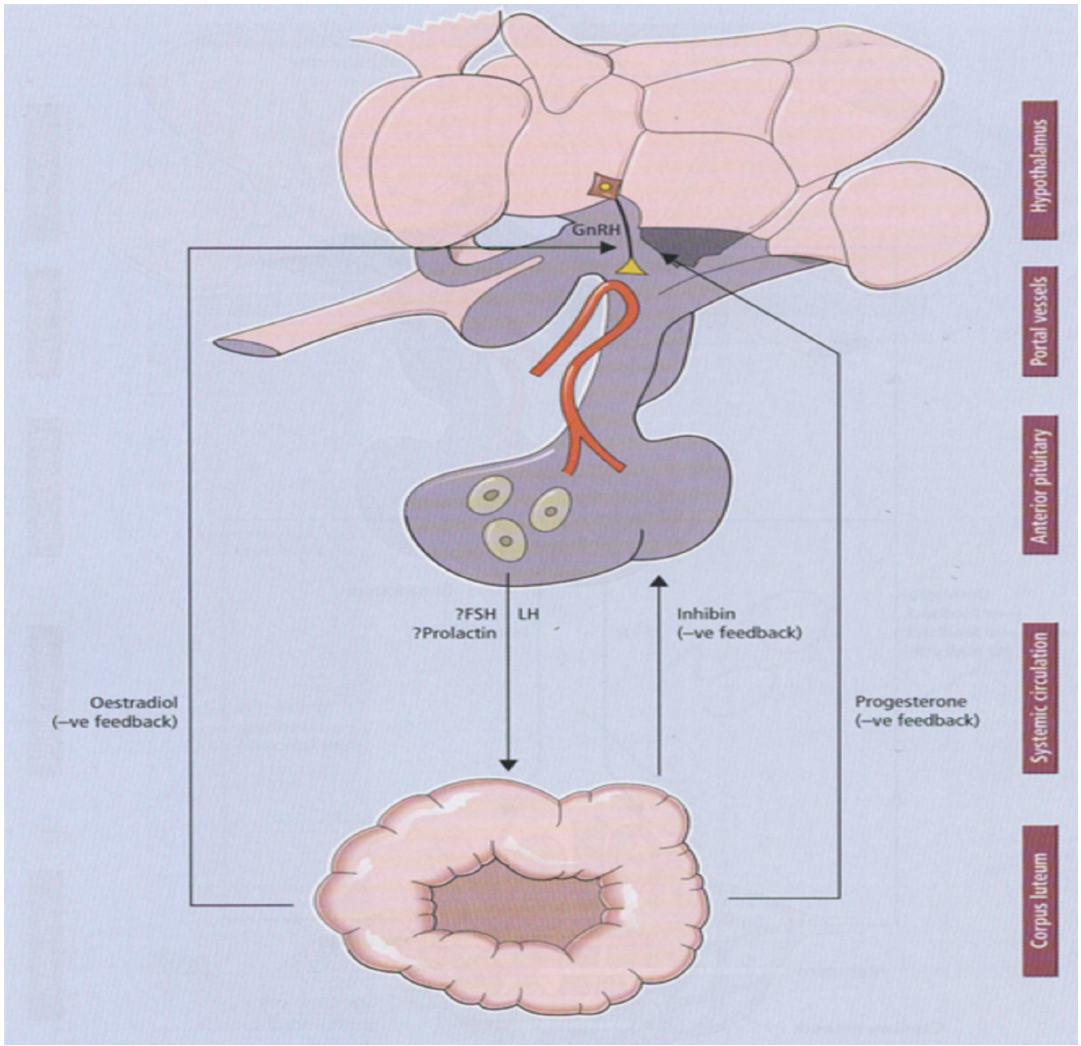


The Normal Menstrual Cycle

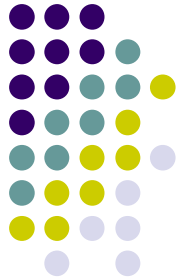
Feedback mechanisms in the follicular phase



Feedback mechanisms in the luteal phase

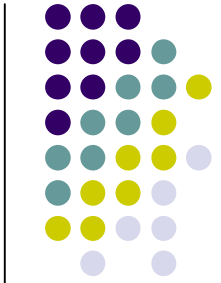


Control of prolactin secretion



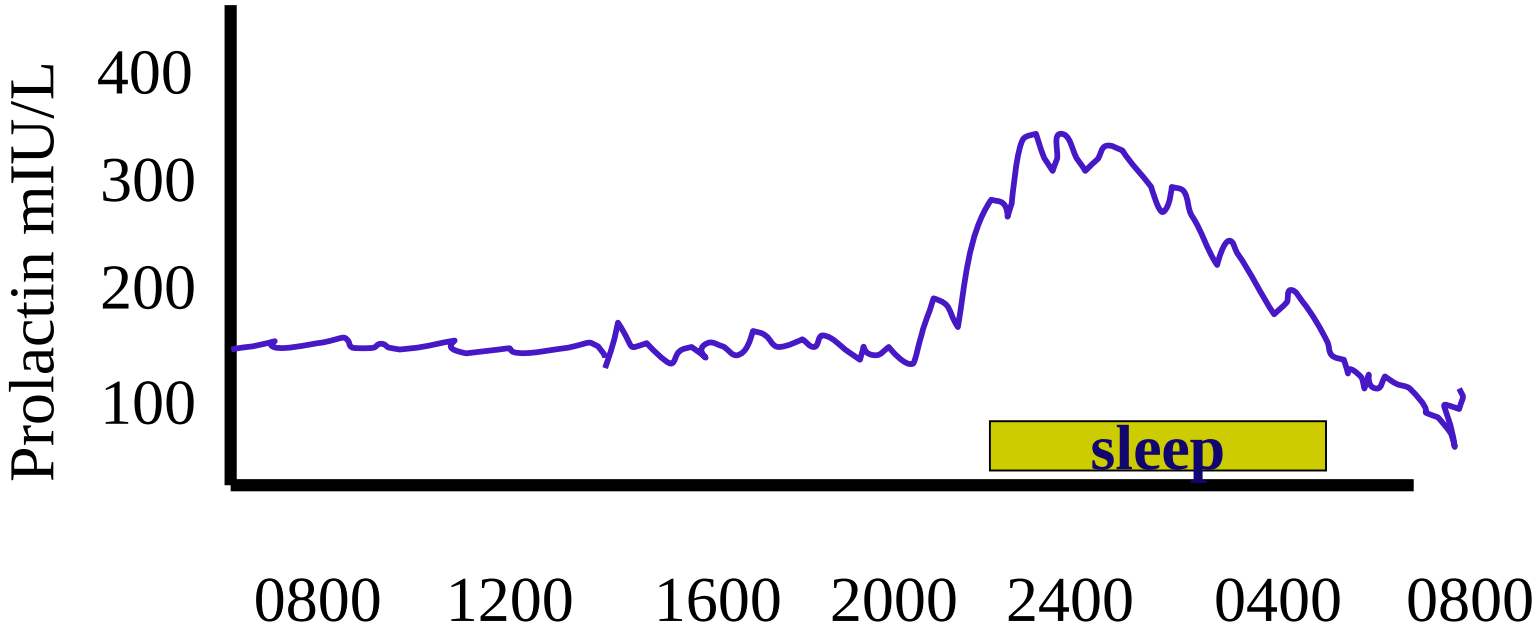
- Diurnal variation – secretion during sleep
- Negative feedback mechanism
- Dopamine produced by the tubero-infundibular (TIDA) neurons of the hypothalamus.
- Prolactin accelerates dopamine turnover in the TIDA
- Increased dopamine in the portal vessels inhibits prolactin secretion
- Hyperprolactinaemia can be caused by failure of dopamine secretion eg drugs inhibiting dopamine

Prolactin control cont'd



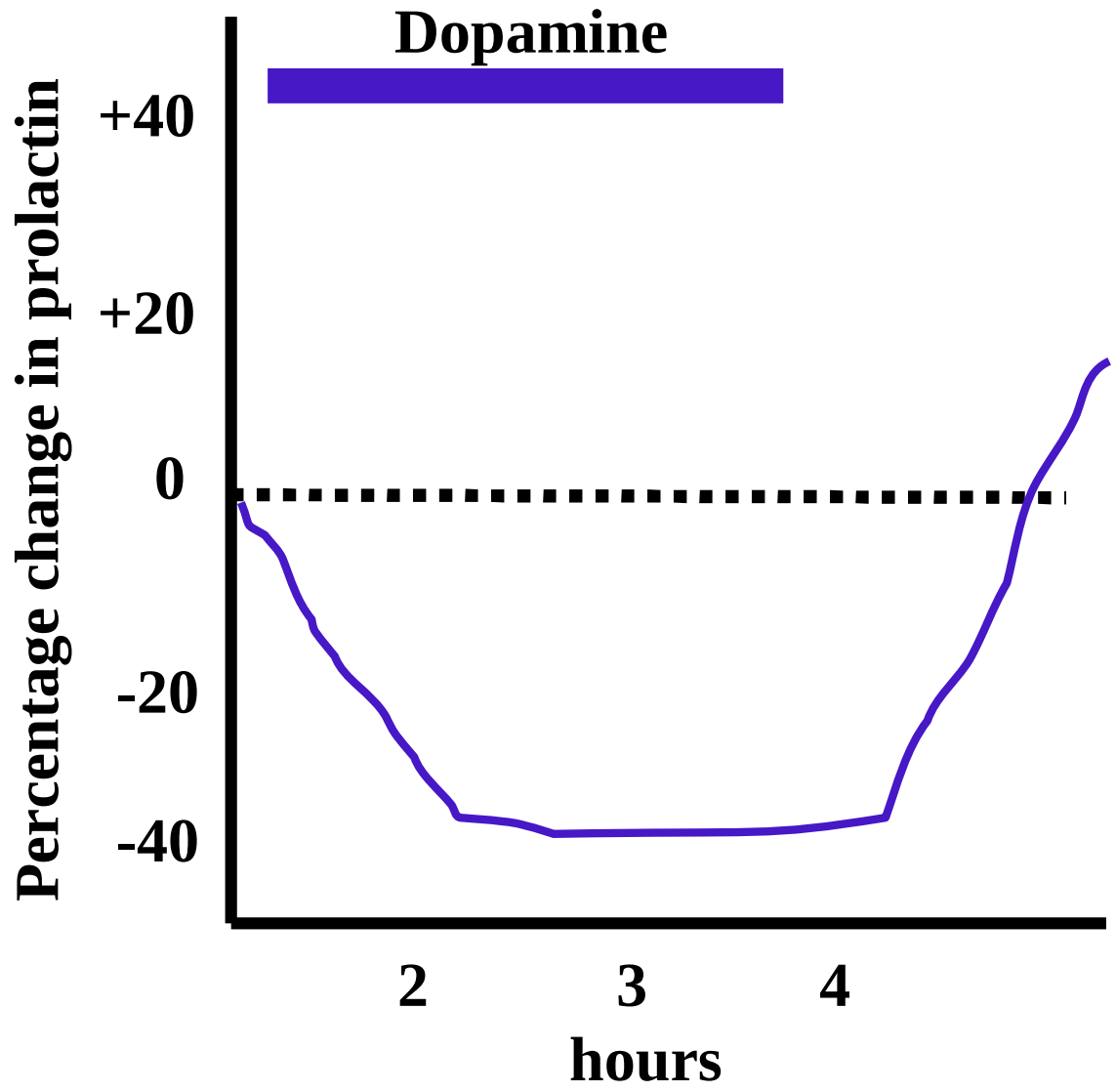
- Thyrotrophin releasing hormone (TRH); at pharmacological doses TRH stimulates prolactin release eg CPT. ? Physiologic.
- Vasoactive intestinal peptide (VIP) stimulate prolactin during lactation
- Drugs interfering in dopamine turnover eg many antidepressants, bromocriptine, L-DOPA
- Oestrogens sensitise the pituitary to release prolactin
- Profound stress increases circulating prolactin eg anaesthesia, epileptic fit, terminal disease

Diurnal rhythm of prolactin secretion

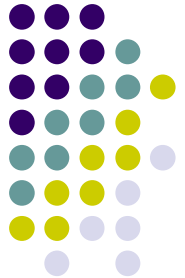


Secretion is episodic and of highest during sleep (similar to GH pattern). Increases 60-90 minutes after onset of sleep and Secretion occurs during REM. Increase achieved by increasing pulse amplitude

Effect of infusion of dopamine on circulating prolactin



HPG and aging in the female



- A female develops stock of primary follicles in during fetal life, the number is finite
- Their development to preantral follicles (ready to enter a menstrual cycle) is independent of the hormonal environment
- Primary follicles therefore develop and undergo atresia throughout life.
- The stock of primary follicles becomes exhausted usually in middle life – the menopause

Follicular development

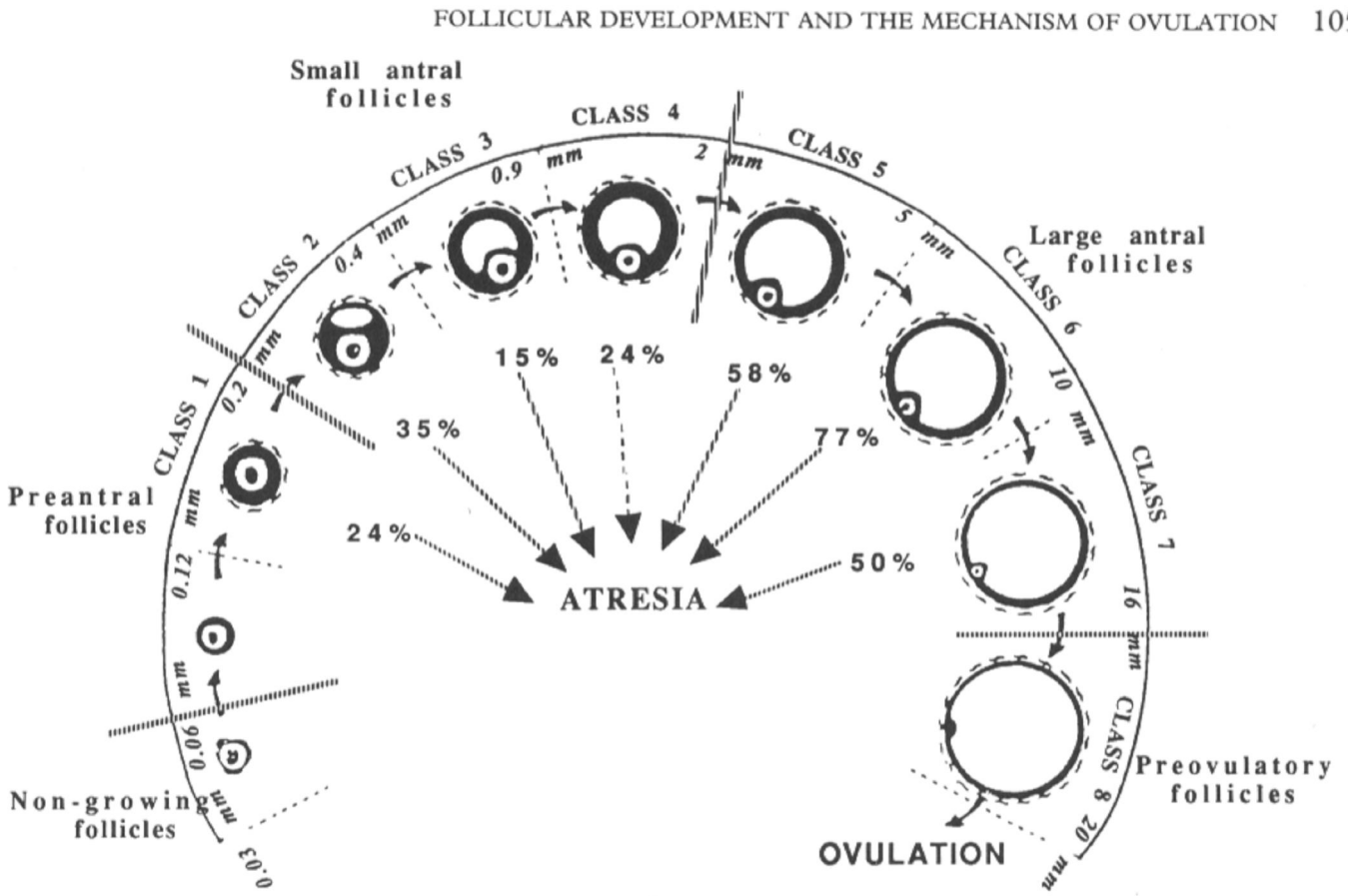
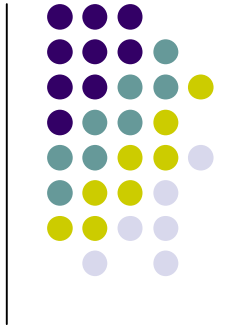


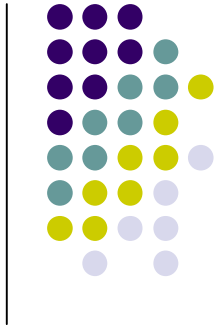
Fig. 6.2 Classification of follicles in the human ovary. (Modified with permission from Gougeon 1986.)

The menopause



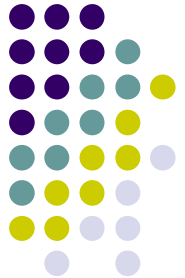
- Median age for menopause 50 years
- Without follicles oestrogens and inhibins decrease.
- Lack of negative control increases LH and FSH
- Loss of two control mechanisms for FSH results in its rise being earlier and higher than LH
- Gonadotrophins rise to values >100 IU/L for some years then fall but remain elevated above premenopausal values throughout remaining life
- Lack of oestrogen is associated with unpleasant symptoms (hot flushes, dry changes, vaginal dryness)
- It may also result in osteoporosis and increasing risk of cardiovascular disease.
- Many women use hormone replacement therapy

Aging in the male



- Testosterone production and spermatogenesis continue throughout post pubertal male life
- Testosterone production peaks during third decade then declines gradually throughout remaining life but RARELY decreases below the normal range
- The myth of the ‘Andropause’
- Increasing life span is resulting in low values in some individuals in extreme old age.
- Generally testosterone values below the normal reference interval require investigation

Disorders of the HPG



- Hypothalamus and pituitary
  - Congenital – genetic disorders such as Turners and Kleinfelters syndromes, also Kallmans's syndrome (lack of GnRH) and rare disorders resulting in abnormal gonadotrophin receptors
  - Adenomas of the pituitary – prolactinomas (50%), Non secretory (20%) and gonadotrophinomas (very rare)
  - Disorders of the ovaries – polycystic ovarian syndrome, premature ovarian failure, ovarian tumours
  - Disorders of the testis- failure of spermatogenesis, testicular tumours