"Figure 54-10" I can't find it in the booklet but figure 38.5 page 38 represents the same thing

In the same way that the male reproductive system (represented by the Testes) is made of two types of cells "leydig and sertoli cells", Female ovaries develop in its follicle two types of cells; theca and granulosa cells.

Notice that there is a crosstalk between the cells of the two reproductive systems.

Theca cells:

* They are affected by LH.
* They produce only androgens
* The final result is androstenedione and testosterone.
* Androstenedione crosses into the granulosa cells.

Granulosa cells:

* They are affected by both gonadotropins LH and FSH.
* LH produces progesterone but progesterone is **not** converted into androstenedione because granulosa cells lack the enzyme needed for this step.
* Androstenedione from theca cells is converted into estrone and testosterone (both are **enzymes)**
* Both enzymes (estrone and testosterone) produce estradiol

This figure illustrates the production of hormones in the follicle of theca cells and granulosa cells and shows that they function together at the same time; they don't function separately.

**Figure 38.1 page 19 in the booklet**

The same hierarchy:

Brain centers 🡪 Hypothalamus 🡪 anterior pituitary 🡪 ovaries

Hypothalamus secretes gonadotropin releasing hormone "GnRH" and prolactin.

Prolactin inhibits the activity of the ovaries during lactation but this only occurs in 50% of the cases.

50 % of women cannot get pregnant for at least 6 to 9 months after their previous delivery. (obviously the other 50% can). Why? Prolactin inhibits the activity of the ovaries during lactation.

Gonadotropin hormones LH and FSH affect the ovaries to produce two hormones estrogens and progesterone

Estrogen is the feminine hormone.

Progesterone is the pregnancy hormone. Pregnancy doesn't continue if there is a deficiency in the progesterone hormone or if it is absent.

Both LH and FSH regulate the production of androgen and estrogens. LH regulates the secretion of progesterone from corpus luteum.

Inhibin suppresses the secretion of FSH. Activin (an inhibin binding protein) increases the secretion of FSH. Follistatin (an activin binding protein) reduces the secretion of FSH.

Notice there is a big difference between suppression and reduction.

This figure illustrates the hierarchy of the control of the female hormones from the brain centers till the ovaries.

* Note: The next two slides are not present in the booklet

**1# Ovaries also produce peptide hormones: Inhibins , which inhibit FSH secretion, and Activins which activate it**

The inhibins are produced by granulosa cells of the follicle as well as other tissues including pituitary, brain, adrenal glands, kidney, the bone marrow, corpus luteum and placenta.

The biological action of the inhibins is primarily confined to the reproductive system in spite of the fact they are present in other tissues.

The activins are produced in the same tissues as inhibins , but they stimulate rather than inhibit the FSH release from the pituitary cells.

**2# The Hypothalamic pituitary axis regulates the menstrual cycle**

Reminder: GnRH stimulates the release of both FSH and LH.

If we block GnRH; the FSH and LH will be reduced or inhibited totally.

Neurons from other brain regions regulate the secretion of GnRH by the Hypothalamus – this confirms the ascending and descending hierarchy of the regulation of the female reproductive hormones by the ovaries-.

Neurotransmitters such as epinephrine and norepinephrine stimulate the secretion of GnRH. whereas dopamine and serotonin inhibit the secretion of GnRH.

This explains the connection between the hypothalamus, the brain centers and anterior pituitary.

**Refer to the Female productive system page 30 in the booklet**

Ovaries are similar to the testes; they produce hormones ( estrogens "feminine hormone" and progesterone " pregnancy hormone" ) and ovum.

Estrogens are mainly responsible during puberty for the development of accessory sex organs (Fallopian tubes, vagina , uterus and mammary glands), as well as the appearance and maintenance of the secondary sex characteristics.

**Figure 28-18 page 40**

Two cycles occur in the female reproductive system; ovarian cycle and uterine/endometrial cycle. These occur every 28 days from puberty till menopause. They don't stop unelss there's pregnancy or disease.

* Ovarian cycle is represented by the changes that occur in the ovaries.
* Uterine cycle is represented by the changes that occur in the uterus.
* Ovarian cycle dominates the uterine cycle

**Figure 28-13a page 36**

Additional notes on the figure:

* 5 million ova have been degenerated at birth.
* Each month one of the two ovaries ovulates (they usually take turns) but sometimes
* both of them ovulate
* one ovary ovulates two ova
* one ovary ovulates one ovum which might split to give identical twins
* From fetal life, the follicles are produced and stored in the ovaries
* down syndrome in babies is due to :
* Pregnancy at the age of 45 and above
* Medications
* Smoking
* Etc.

In the last few years the US army studied more than 1500 medications. Their expiry dates range from one year to 10 years. They noticed that the efficiency didn't decrease more than 5% if the storage conditions were kept normal.

In the same way, if the storage conditions of the follicles are normal, there will be no problems in the pregnancy and the infant will be normal.

* Through reproductive life 90-95% of all follicles are primordial follicles (non growing)
* In fetal life and childhood some primordial follicles develop all the way to the antral stage however all these follicles undergo atresia.

**Back to Figure 28-18 page 40**

Ovarian cycle represent changes in the ovaries

3 phases take place:

* Follicular phase: in which the follicles develop
* Ovulation phase: in which the dominant follicle rupture and ovulate
* Luteal phase: in which the corpus luteum is formed

**Figure 28-19 page 41**

The level of hormones during ovarian cycle:

* At the beginning of menstruation, all hormones are low (the highest is FSH)
* Estrogen then LH starts to increase
* Estrogen produces positive feedback on the increase secretion of LH.
* Usually estrogen inhibits LH (the only positive feedback between them is during the menstrual cycle)
* It's also said that progesterone levels increase so as to strengthen the action of estrogen or something similar to the permissive action
* Activin also increases at this stage ( before ovulation) which causes an increase in the secretion of FSH (but not too much as seen in the figure)
* LH causes the ovulation
* *What is the action of the estrogen?* To increase LH secretion

Estrogen increases the sensitivity of gonadotroph cells to GnRH, it also modulates the neuronal activity and induces the GnRH search (High increase)

* *What causes the transformation of estrogen from negative feedback to positive feedback at this stage? And Why ?*

Normal levels of estrogen exhibit negative feedback, yet when the levels of estrogen increase above that level they produce a positive feedback.

And Because of the following reasons:

* The receptors of the GnRH on the somatotrophs are increased immediately.
* The release of gonadotrophs hormones (LH) to affect ovulation
* Therefore exogenous estrogen injection (by the time of ovulation) causes premature ovulation. ( LH immediately increases and causes ovulation)
* Ovulation at day 14
* After ovulation, the follicle left in the ovaries is called corpus luteum
* Progesterone is produced by corpus luteum for the pregnancy to continue and little bit of estrogen
* It's duration 28 days

**Figure 19-15 (not found in the booklet )**

At the beginning of the cycle, many follicles are activated (2 or 3 days before the previous menstrual cycle is finished) depending on many factors those include genetic factors, the environment etc.

The follicle activation is genetic (even if there are no hormones). If there is a deficiency in the hormones, then the activated follicles don't develop any further.

At day 7, one follicle becomes dominant and continues to grow; the rest degenerate.

Most probably the dominant follicle (because of the high blood supply) becomes highly sensitive to the FSH.

The dominant follicle produces estrogen which inhibits FSH. No matter how low the FSH concentration becomes it will not degenerate, the others however will since they need more FSH than the dominant follicle.

In the degenerating cells, the concentration of Dihydrotesterone is found to be high; so they attributed the degeneration of these cells to high concentration of DHT.

