Parathyroid hormone

Four small parathyroid glands lie on the thyroid gland. They secrete PTH whose main function is to increase plasma Ca concentrations.

The stimulus for PTH release is a decrease in plasma Ca monitored by a cell membrane Ca-sensing receptor (CaSR). PTH acts on bone, kidney and intestine to increase plasma Ca++. Increased plasma Ca acts as negative feedback and shuts off PTH secretion.

- **Parathyroid hormone:** increases plasma Ca concentration by stimulating its release/reabsorption from bone, kidney, and intestine.
  - Mobilizes calcium from bone-
  - Enhances renal reabsorption-
  - Indirectly increases intestinal absorption-

Calcitriol – vitamin D3

The body makes calcitriol or vit D that has been obtained through diet or made in the skin by the action of sunlight. Taking sunlight is so important, people who can not get enough should consider taking vitamin supplements.

Vit D3 is modified in two steps: first in liver then in kidneys to make vit D3.

It is primary hormone responsible for enhancing Ca uptake from small intestine. In addition it facilitates renal reabsorption of Ca and helps mobilize Ca out of bone.

The production of calcitriol is regulated at the kidney by PTH.
Decreased plasma Ca increases PTH secretion which stimulated calcitriol synthesis.
Intestinal and renal absorption of Ca raises blood Ca, turning off PTH in a negative feedback loop that decrease calcitriol synthesis.
Prolaction also stimulates calcitriol synthesis which ensures maximal absorption of Ca from diet when metabolic demands for calcium are high.

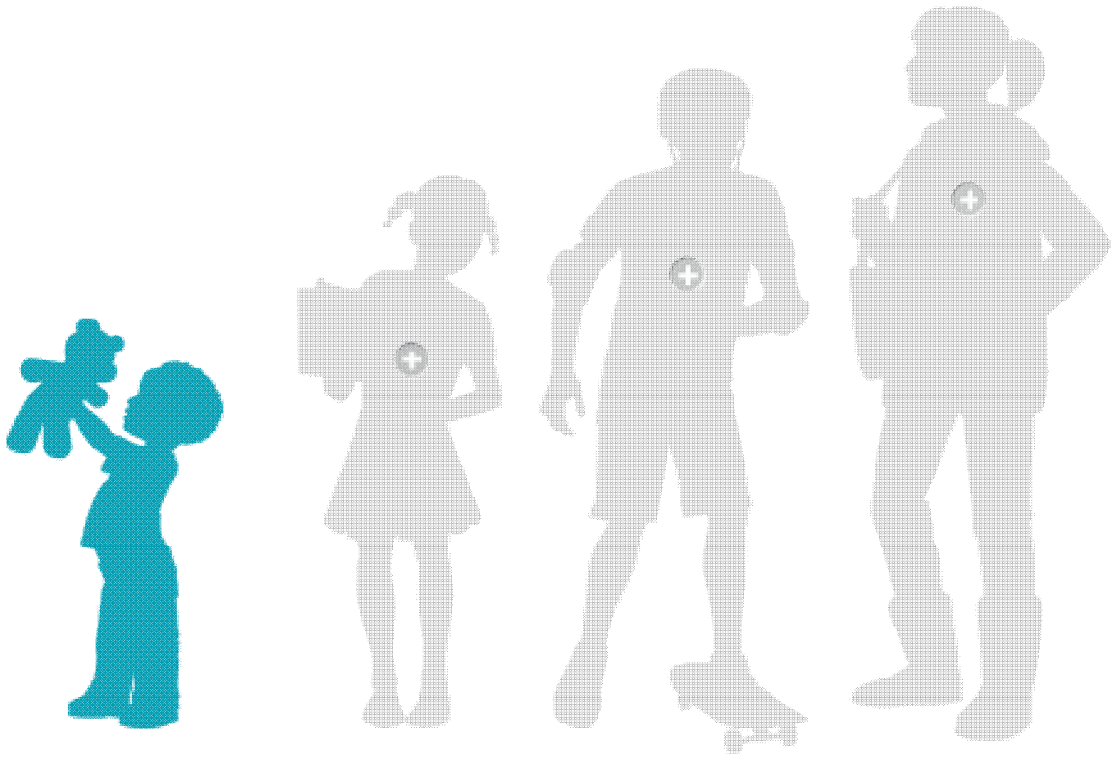
Calcitonin- targets osteoclasts and reduces bone resorption, thus dropping blood Ca^{2+}

It is a peptide produced by C cells of thyroid gland. Its actions are opposite to those of PTH. It is released when plasma Ca increases. It decreases bone resorption and increases renal calcium excretion.

Osteoporosis

- One of the best known pathologies is osteoporosis, a metabolic disorders in which bone reabsorption exceeds bone deposition. The result is fragile, weakened bones. It is most common in women after menopause when estrogen falls. Older men also develops. To avoid osteoporosis, young women need to maintain dietary calcium intake and perform weight-bearing exercises, such as running or aerobics, which increase bone density. Loss of bone may begin at age 30, most women suffer from low bone mass (osteopenia) before they are aware of the problem.

GROWTH HORMONE



Normal Growth

- Growth hormone and other hormones -
- An adequate diet –
- Absence of stress –

  Genetics –

They are anabolic for protein and promote protein synthesis which is essential for bone and tissue growth.
They also stimulate cartilage growth.
They increases plasma fatty acids by promoting fat breakdown.
They also increase glucose concentration by hepatic glucose output.

Acromegaly

Once bone growth stops in late adolescence, GH can not increase height. GH and IGFs can continue to act on cartilage and soft tissues. Adults with excess secretion of GH develops acromegaly characterized by lengthening of the jaw, coarsening of facial features, growth of hands and feet.

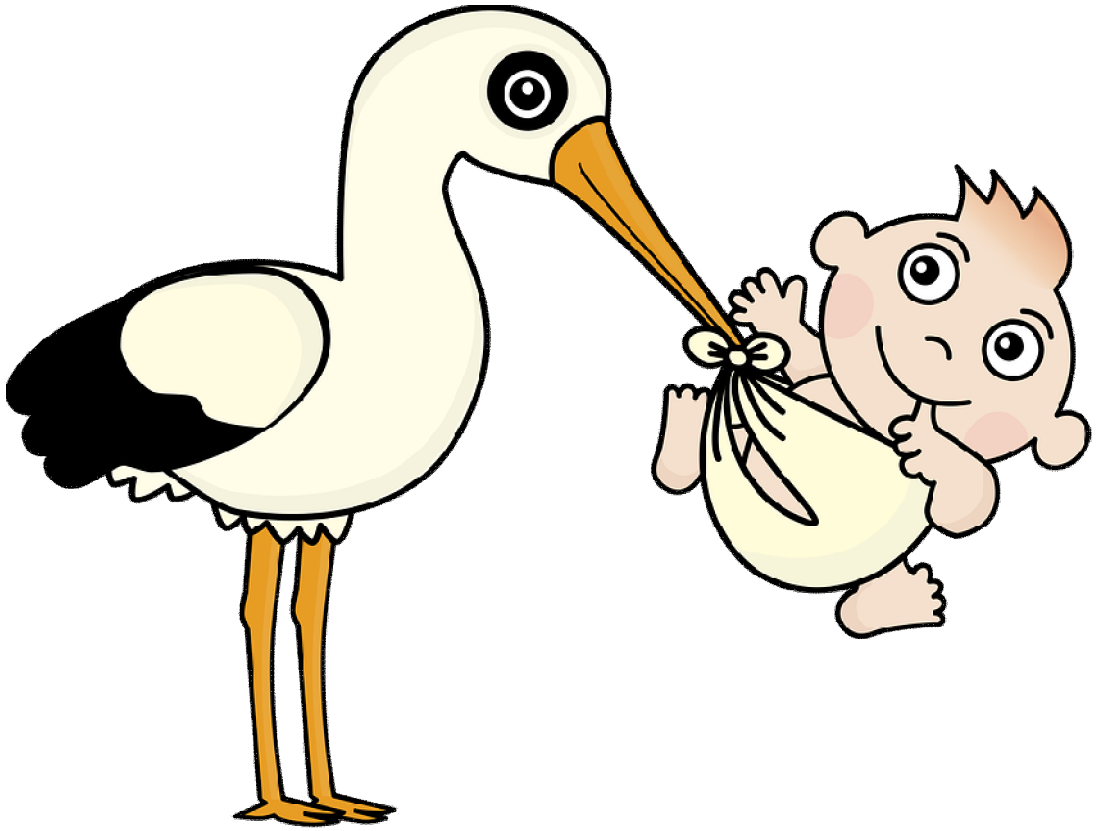
Growth Hormone

- Severe GH deficiency leads to **dwarfism**
- Oversecretion of GH in children leads to **giantism**
- Oversecretion of GH in adults leads to **acromegaly**

Tissue and Bone Growth

- Growth is determined by increase in **soft tissue** (weight) and **bone length** (height)
- Tissue growth requires hormones and paracrines
  - GH and IGFs
  - Thyroid hormone
  - Insulin
- Bone growth requires hormones, protein adequate dietary calcium

HORMONAL CONTROL OF REPRODUCTION



Functions:

•Producing gametes (gametogenesis)

- Sperms (spermatozoa) in male
- Eggs (ova) in females

- Secreting sex hormones
- Testosterone in male
- Estrogen and progesterone in female

Synthesis Pathways of Steroid Hormones

- Steroid hormones contain cholesterol, are structurally similar and share production pathways with other steroid hormones
- Ovary
  - Progesterone
  - Estrogen
- Testis
  - Testosterone

General pattern of hormonal control of reproduction

FSH and LH act on gonads:

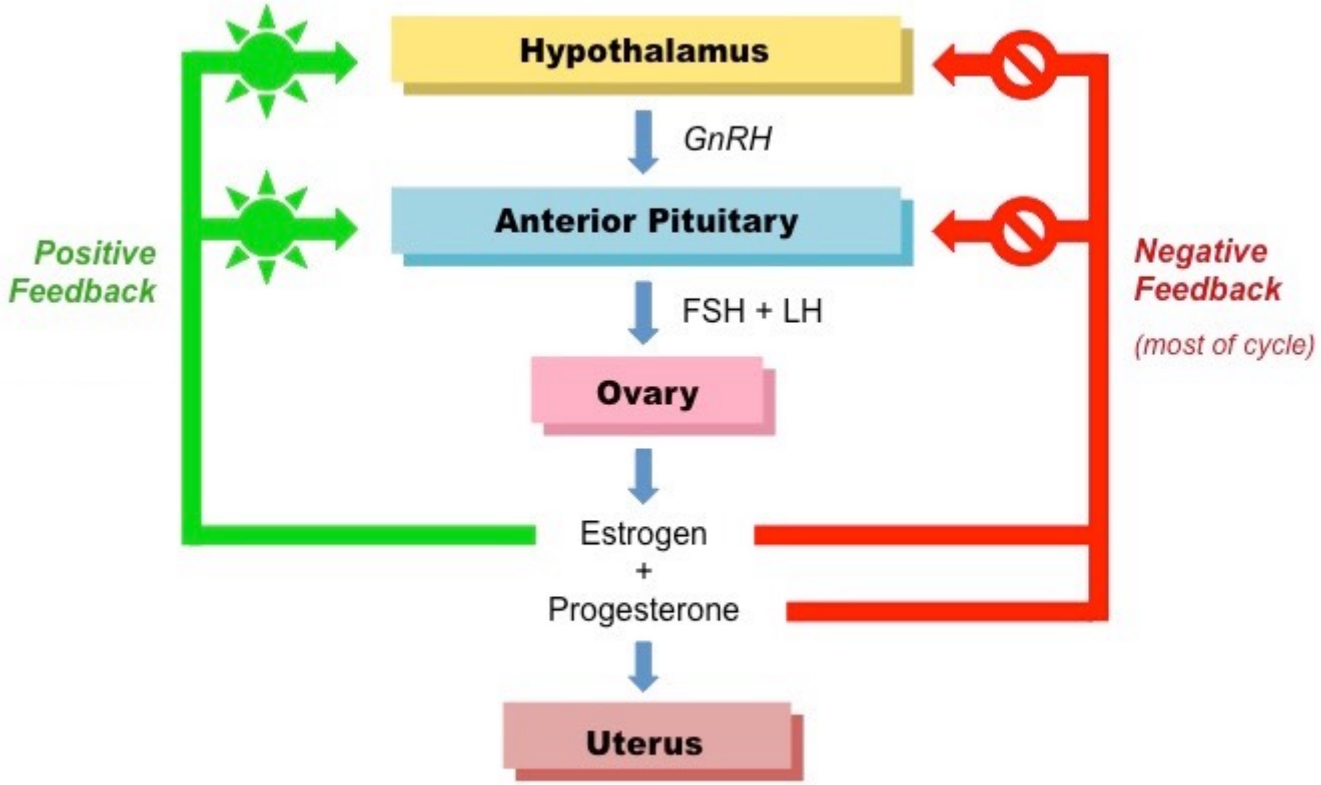
- FSH, along with sex hormones, is required to initiate and maintain gametogenesis.

- LH acts on endocrine cells, stimulating production of sex hormones.

General pattern of hormonal control of reproduction

- Long-loop: hormone production by gonads alters
  - GnRH
  - FSH
  - LH
- Short-loop: feedback from pituitary alters
  - GnRH

When circulating levels of gonadal steroid are low, pituitary secretes FSH and LH. As steroid secretion increases, negative feedback usually inhibits gonadotropin release



However, in an unusual twist, higher concentration of estrogen can exert either positive and negative feedback.

GnRH pulse generator coordinates pulsatile secretion

small pulses every 1-3 hours

If it would be secreted steadily high levels of GnRH would cause down regulation of GnRH receptors, so make pituitary unable to respond.

FSH targets **Sertoli** cells and stimulates synthesis of paracrine molecules needed for spermatogonia, mitosis and spermatogenesis.

The primary target of LH is the **interstitial Leydig cells** which produce **testosterone**.

Ovarian and uterine cycle are under primary control of various hormones:

During follicular phase, **estrogen** is the dominant hormone. Ovulation is triggered by surges in LH and FSH. In the luteal phase, **progesterone** is dominant, although estrogen is still present. **AMH** (Anti-müllerian hormone) acts as a brake to keep too many follicles from developing at one time.

Some primordial follicles develop slowly into **primary follicles**. The oocyte enlarges and **granulosa cells** begin to divide but remain in a single layer.

As the growing follicle enlarge, a layer of cells known as **theca** develops outside the basal lamina. At this point the follicle are known as **preantral or secondary follicles.**

As the secondary follicles enlarge, granulosa cells begin to secrete fluid that collects in a central cavity in the follicle known as **antrum**. Antral fluid contains hormones and enzymes needed for ovulation. At this point the follicle becomes a **tertiary follicle.**

The Menstrual Cycle: Ovarian & Uterine Cycle

Females produce gametes in monthly cycles (24-35 days). **The menstrual cycle** can be described by following changes that occur in follicles of the ovary, the **ovarian cycle** or by following chances in the endometrial lining of the uterus , the **uterine cycle.**

The Menstrual Cycle: Ovarian & Uterine Cycle

Follicular phase is the first part, is a period of follicular growth in ovary.

Once one or more follicles, have ripened, the ovary releases oocyte during **ovulation**.

In **luteal phase**, ruptured follicle is tranformed into a **corpus luteum**, named for its yellow pigment and lipid deposits. It secretes hormones that continue the preparations for pregnancy. If a pregnancy does not occur, the corpus luteum ceases to function after about two weeks, the ovarian cycle begins again.

The Menstrual Cycle: Ovarian & Uterine Cycle

Uterine cycle of endometrial lining

Menses is the beginning of the follicular phase in the ovary corresponds to menstrual bleeding from the uterus.

In the latter part, **proliferative phase**, endometrium adds a new layer of cells in the anticipation of pregnancy.

After ovulation, hormones from corpus luteum convert thickened endometrium into a secretory structure. This means that luteal phase of the ovarian cycle corresponds to the **secretory phase** of the uterine cycle. If no pregnancy occurs, the superficial layers of the secretory endometrium are lost during menstruation as the uterine cycle begins again.

The Menstrual Cycle: Ovarian & Uterine Cycle

- High levels of estrogen
  - LH surge and FSH spike
    - Egg release
- High levels of inhibin
  - Inhibits production of FSH
    - Decrease new follicle development
- Low levels of progesterone
  - Positive feedback
    - GnRH and LH

The first day of menstuation is day 1 of a cycle. Just before the beginning of each cycle, gonadotropin release from pituitary increases. Under the influence of FSH, a group of tertiary follicles begins to mature. As follicles grow, their granulosa cells (under the influence of FSH) and their thecal cells (under the influence of LH) starts to produce steroid hormones. Granulasa cells begin to secrete AMH. This AMH (**anti-müllerian** hormone) decreases follicle sensitivity to FSH which prevents recruitment of additional follicles once one group has started developing.

As the follicular phase nears its end, ovarian estrogen secretion peaks. By this point, only one follicle is still developing. As the follicular phase ends, granulosa cells of the dominant follicle begin to secrete **inhibin** and **progesterone** in addition to **estrogen**.

Estrogen, which had exerted a negative feedback effect on GnRH earlier in the follicular phase, changes to **positive feedback,** leading to a preovulatory GnRH surge.

After ovulation, follicular thecal and granulosa cells transform into luteal cells of the **corpus luteum**. This process, known as **luteinization**, involves biochemical and morphological changes. The newly formed luteal cells accumulate lipid droplets and glycogen granules in their cytoplasm and begin to secrete hormones. As the luteal phase progresses, the corpus luteum produces steadily increasing amounts of **progesterone, estrogen and inhibin.**

Corpus luteum has an intrinsic life span of 12 days. If pregnancy does not occur , it undergoes apoptosis. As the cells degenerate, progesterone and estrogen production decrease.
This fall removes the negative feedback signal to the pituitary and hypothalamus, so secretion of FSH and LH increases.
When the corpus luteum degenerates and hormone production decreases, blood vessels contract. Without oxygen and nutrients, surface cells die. About 2 days after corpus luteum ceases to function, endometrium begins slough, menstruation begins. It continues for 3-7 days, well into the follicular phase of the next ovulatory cycle.

If the egg released from the ruptured follicle, meets with a sperm, **fertilization** occurs. Fertilized egg becomes a **zygote**, it begins mitosis as it slowly moves through the uterus and settles there for gestation period. Under the influence of progesterone, smooth muscle of the tube relaxes. When it reaches uterus, it is called a **blastocyst**.

Human Chorionic Gonadotropin

Under the influence of hCG, corpus luteum keeps producing progesterone to keep the endometrium intact.
By the 7th week, corpus luteum degenerates. hCG production peaks at three months then diminishes.

Human Chorionic Gonadotropin
Human Placental Lactogen
•Contribute to lactation
•Alters mother's glucose and fatty acid metabolism to support fetal growth
Estrogen
Progesterone
They are produced continuously (first by corpus luteum then by placenta)
With high circulating levels, feedback suppression prevents another set of follicles from beginning development
Estrogen contributes to the development of milk-secreting ducts of breasts
Progesteron helps suppress uterine contractions

Parturition: The birth process

Pregnancy ends with labor and delivery.
As labor begins, the fetus is normally head down in the uterus.
Uterine contractions push the head against the softened cervix, streching and dilating it.
Once the cervix is fully dilated and streched, the uterine contractions push the fetus out.

Cervical strech triggers uterine contraction that moves from top, pushing the fetusIt starts a + feedback cycle. The contractions are reinforced by secretion of oxytocin from posterior pituitary with continued strech reinforcing oxytocin secretion. PG are produced reinforce uterine contractions.

Lactation: Milk Secretion

Milk production is stimulated by prolactin from anterior pituitary. It is controlled by **prolactin inhibiting hormone (PIH).**

During later stages of pregnancy, PIH falls, and prolactin increases.

Suckling, the mechanical stimulus of the infant, inhibits PIH.

Oxytocin is also required to initiate smooth muscle contraction.