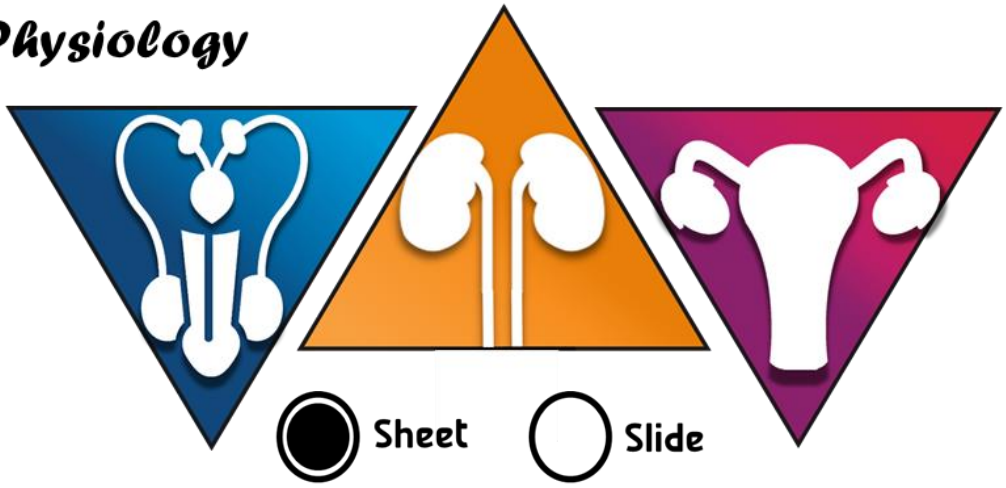
Urogenital system

Physiology



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Male reproductive system

Primary sex organs of the male reproductive system are 2 testes which have 2 main functions: -

1. Hormone production, not only male hormones but also, they produce estrogens
2. Spermatogenesis (productions of sperms)
   ** usually we concentrate on the endocrine function of the reproductive system:

Endocrine function of the testes

Endocrine function resides in two cells:
Leydig cells and Sertoli cells.
These 2 cells work together as one functional unit, none of which can function alone.

Leydig cells

- Leydig cells are required for the production of testosterone.
- Leydig cell produce testosterone under the effect of **LH**, so LH acts on Leydig cells, increasing the production of androgens (testosterone).
- testosterone produced passes into the circulation but some pass to the Sertoli cells which bind to androgens binding proteins and under the effect of **aromatase** enzyme testosterone will be converted into **estradiol**.
- LH and FSH produce factors such as: Steroidogenic factor $_1$ (SF1) and cAMP response elements binding protein (CREB).
  These factors are important for spermatogenesis and production of androgens (testosterone), through: -
  1) Producing enzymes for the production of testosterone from the Leydig cells
  2) LH stimulates the synthesis of other proteins including **estriol carrier protein** and **estriol activating protein**.

  Note: LH and its substitute Human chorionic gonadotropin (HCG) are therapeutic to treat azoospermia (no sperm), oligospermia (little amount of sperm), there is a rare syndrome called Sertoli cells only syndrome (no Leydig cells/or more commonly Leydig cells don't function or inactivated), treating this syndrome isn't effective.

  - Leydig cells produce 95% of the testosterone and the other 5% is produced by other tissues (Adipose tissue, brain, muscles, skin and adrenal cortex).

  Although testosterone is the main secreted product, testes also secrete: -

- Pregnenolone

- Progesterone
- 17-hydroxyprogesterone
- Dihydrotestosterone
- Androsterone
- Androstenedione – serves as precursor for extraglandular estrogen formation.

Note: all these androgens are weak except dihydrotestosterone and testosterone.

Sertoli cells

- Sertoli cells produce hormones and glycoprotein hormones

1. Estradiol,
2. Activins,
3. Inhibins
4. Follistatins

These hormones regulate the release of LH and FSH from anterior pituitary as following:

- Generally, Testosterone, Estradiol, Inhibin inhibits secretion of males' LH & FSH.
- Inhibins directly inhibit the secretion of FSH, but NOT LH. (I think in females)
- Follistatins inhibit the secretion of FSH.
- Activins stimulate the secretion of FSH.

During the development of sperms, the sperms will be attached to Sertoli cells about 8 sperms attach one Sertoli cells, when the development ends the sperms will lose the attach to the cells and will be released into the lumen in a process called (**spermeation**).

So, you can notice that Sertoli cells are Critical for germ cell (sperms) development, as indicated by their close contact (attachment to sperm cells), Sperms during development are attached to Sertoli cells, about 6-12 per 1 Sertoli cell.

Other functions of Sertoli cells:

- Sertoli cells produce growth factors essential for spermatogenesis and the survival of sperms.
- phagocytose damaged germ cells and also residual bodies (excess cytoplasm resulting from the transformation of spermatids to spermatozoa)
- provide structural support and nutrition for germ cells.
- synthesize large amounts of transferrin; an iron transport protein important for sperm development.
- secrete fluids and assist in spermeation; (which is the final detachment of spermatozoa from Sertoli cells into the lumen of seminiferous tubules).

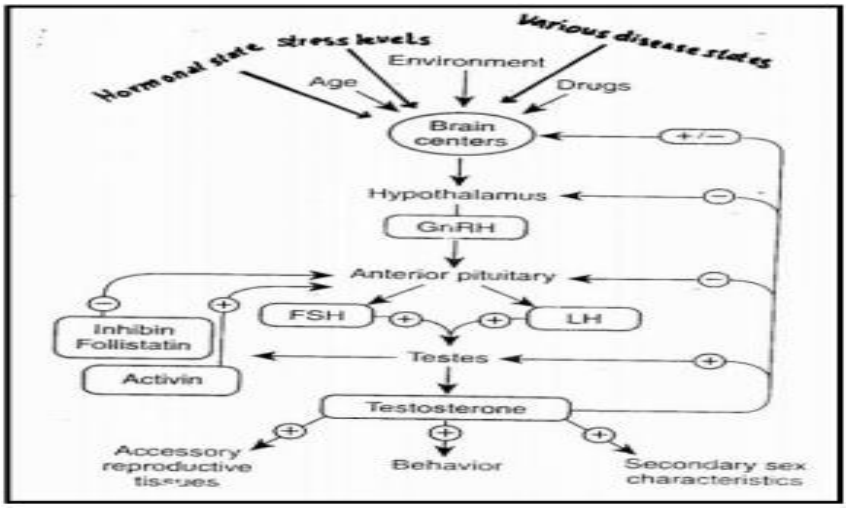
Spermeation involves Plasminogen activator which converts plasminogen to plasmin; a proteolytic enzyme that assists in the release of mature sperms into the lumen (spermeation)
note: plasmin here is different from that in blood.

Testosterone Regulation:
Look at the diagram below

- Brain centers respond to several factors including:
  Hormonal state, Age, Drugs, Stress, disease, Environment, and Genetic.
- These centers stimulate the hypothalamus to produce Gonadotropin-Releasing hormone (GnRH).
- GnRH stimulates the anterior pituitary to release gonadotropins (LH & FSH).
- LH & FSH act on Leydig & Sertoli cells in the testes in order to produce testosterone.
  note: either the two hormones act or one of them alone which is sufficient.
- Testosterone affects the Behavior, Accessory reproductive tissues & Secondary sex characteristics.

- Testosterone and other testes hormones sends –ve feedback to levels of
  1. Brain centers, 2. Hypothalamus, 3. Ant. Pituitary, 4. testes.
  therefore reducing the secretion of
  1. factors from brain centers, 2. GnRH, 3. LH, 4. FSH.

Note: Difference between males and females is one chromosome and 2 endocrine glands (ovaries and testes).



Puberty

At puberty testosterone responsible for development of secondary male organs: -
1. epididymis
2. vas deferens

3. seminal vesicles
4. prostate gland
5. penis
6. appearance of secondary sex characteristics.

Spermatogenesis

- Spermatogenesis duration ranges from 70-75 days,
- Occurs in all seminiferous tubules in successive cycles, cycles are initiated at a regular interval every 2-3 weeks and new cycle begins before the previous one is completed.
- hormones can alter the number of sperms but can't change the duration of each step.
- 3 Steps of spermatogenesis: -
  1) **Mitosis:** Production of primary spermatocytes, same number of chromosomes (46), the duration of this step is 25 days.
  2) **Meiosis:** Production of spermatids, with half the number of chromosomes (23).
  3) **Spermiogenesis:** maturation of sperms.
- meiosis is a very delicate and rapid process, it's so sensitive to external agents that alter cell division, such as chemical carcinogens, chemotherapeutic agents, certain drugs, environmental agents, irradiation; even extreme temperature can affect the number of dividing cells or cause chromosomal abnormalities.
- these three steps are regular, ordered (ordered under the effect of hormones and other factors) and sequential, resulting in the production of mature sperms.
- These steps eventually result in mature sperms.
- Approximately, 200 million produced daily by the two testes.

Note: Injury/infection of the testes may produce antibodies against the sperms, those antibodies may be in one of 3 cases:
1. High levels of antibodies against the sperms results in infertility
2. low or moderate ab levels then infertility may not occur
3. In bad situations, both the male and the Female have antibodies against sperms, here in this case 100% infertility will occur. (both male and female produce ab against sperms)

Sperms
In the epididymis

- Sperms that are removed immediately from the testes are immotile, and they need time in the epididymis to mature from hours to 1 day (this is called maturation of sperms in the epididymis)

Functions of epididymis: -

1. Progressive increase in the forward motility of sperms (they become motile).
2. Sperms will gain the ability to fertilize (when they become motile they will be able to reach the ovum and fertilization occur).
3. Maturation of acrosome (we'll talk about it).
4. Molecular reorganization of plasma membrane as lipids or proteins:
In terms of lipids - stabilization of membrane.
proteins - shedding and acquisition of new proteins.
5. Ability to bind pellucida zone.
Extra Note: Pellucida zone is a glycoprotein layer surrounding the plasma membrane of mammalian oocytes.
6. Acquisition of receptors for the proteins in pellucida zone.
7. Decrease cytoplasmic and cell volume.

- Sperms gain the **fertility power** in the epididymis. If sperms were removed from the head of the epididymis they will become infertile (cannot fertilize the ovum).
  - If sperms were removed from the body of epididymis, 50% of them will be able to fertilize the ovum.
  - if we removed sperms from the tail of epididymis, all the sperms (100%) will be able to fertilize the ovum.

- During the maturation in the epididymis, sperms gain a protein called **catsperm** this is localized in the tail of the sperm. This protein is mostly for calcium ion channel (for the influx of calcium) so by that sperms gain motility and power of fertilization the ovum, so removing the sperms immediately from the testes without passing through the epididymis means the catsperm protein won't be present in the tail of sperms.

- After maturation, sperms have to be stored, some of them will be stored in the epididymis, majority remain in the vas and ampulla of vas. The sperm can remain in the testes for about 1 month, but in the female sperms can only stay fertile for 1-2 days usually 2.

  Note: sperm motility and movement are essential for in vivo fertilization not in vitro; because in vitro fertilization sperms are microinjected into the ovum and fertilization occur.

In female repro system (capacitation)

- The sperm gain more motility and more ability to fertilize the ova through passing the uterus and fallopian tubes, this is called **capacitation.**

- Capacitation involve 2 components as said in the previous point: increasing the motility of sperms and facilitating their tendency for the acrosome reaction. However, the role of capacitation appears to be faciliatory rather than obligatory, this is proven because fertilization occurs in vitro just fine.
- Further maturation of the sperm involves facilitating their preparation for the acrosome reaction
- They say there is no chemotaxis between sperms and ova, however there are olfactory receptors in sperms that respond to odorant- like chemicals produced by the ova in order to attract sperms.
- Remember that there are huge number of sperms which move in every direction, from 50-100 reach the fertilization site, and there are glycoproteins on the membrane of the ova, these glycoproteins choose which sperm will penetrate the ova (specific sperm).
  ex. From the doctor: a mule sperm can't fertilize a female horse ovum because the ova glycoproteins won't bind to the mule sperm receptors.

Hormones and factors that affect spermatogenesis

- LH: no testosterone without LH.
- FSH: is essential for Sertoli cells to do their functions.
- Testosterone: it is essential for meiosis, meiosis doesn't occur without testosterone.
  note: males require normal levels of testosterone for spermatogenesis (this normal level varies from one male to another), extra testosterone will not increase spermatogenesis however it will help show secondary male characteristics and it might cause homosexuality.
- Estradiol: is also essential for spermatogenesis.
- Thyroid hormones: in thyroid cancer infertility occurs, other similar diseases that raise body temp also affect spermatogenesis.
  ex, mumps, typhoid, Tb.
  - Complete starvation also affects spermatogenesis.
- Growth hormone: for the activation of spermatogonia cells.
- Actually, almost all other hormones are important for normal spermatogenesis to occur.

Testosterone level

Testosterone level From fetal life all the way till death, it doesn't reach zero level.

- high level during Fetal life:

  -This high level of testosterone is not a result of LH secreted from the fetal pituitary, instead it results from the HCG that is secreted from placenta. Fetal pituitary isn't mature yet.

-The highest level of testosterone is between week 8 and 18 because of the **active steroidogenesis** which is obligatory for the differentiation of male genitalia, again this is because of HCG no LH. Also small amounts of HCG hormone produced by testes, pituitary gland and other non-placental tissues .
this also gives male secondary characteristic.
- In the last three months of pregnancy, under the effect of testosterone and insulin like hormones testes descend from the abdomen down to the scrotum, sometimes they don't descend this is called cryptorchidism. No problem if the testes remain in the abdomen for 1 year because usually in the first 1-3 months after birth testes descend by their own.
- Cryptorchidism usually has low incidence in full term babies (3%).
- More common in premature babies (30%)

- low level during Childhood:
  Therefore, before puberty boys and girls have the same BMI, skeletal mass, fat.
- Testosterone level increases in Puberty:
  Here in this age, differences between males and females occur. Men have 150% more lean and skeletal mass (twice number of muscle cells and 1.2 times the muscle mass than that of women), also, women have 200% more fat than men.
- It Remains high during adulthood.
- The level of testosterone decreases a little bit after age 67, but still that individual can have children (sperms are fertile), however other changes occur such as changes in semen content.

Best Of Luck ^^