Spermatogenesis

Figure 31.2

The hypothalamic hormones stimulate the anterior pituitary hormones, the hypothalamus regulate the production of anterior pituitary hormones by 2 ways:
* The long portal passage (way) and * The short portal passage (way)
(The posterior pituitary hormones came from the hypothalamus released down the posterior pituitary gland.)

Table 75-1

These are the cell types of the anterior pituitary gland:

- Somatotrophs produce growth hormone.
- Corticotrophs secrete Adrenocorticotropic hormone (ACTH)
- Gonadotrophs secrete 2 hormones FSH, LH
- Lactotrophs secrete prolactin
- Thyrotrophs secrete TSH

Table 75-2

The hormones of the anterior pituitary are stimulated or inhibited by the hormones of hypothalamus : Thyrotropin-releasing hormone (TRH) , Gonadotropin-releasing hormone (GnRH) , Corticotropin-releasing hormone (CRH), Growth hormone releasing hormone, growth hormone inhibitory hormone and prolactin inhibiting hormone. The hormones concern us are gonadotrophs hormones FSH and LH.
In this group of cells there are 3 types: - some types produce just LH - another group produce just FSH - the third group produce both LH and FSH. (But, usually, the cell produce mainly LH and FSH in normal cases and in abnormal cases and this is applied to the somatotrophs and lactotrophs). GnRH receptors are present on all these cell types.

Figure 53-3

Two cells produce the male hormones: Leydig cells and Sertoli cells.
Leydig cells affected by LH produce the testosterone which passes into sertoli cells.
Sertoli cells affected by FSH have the following functions and even more:

1) Production of ABP (androgen binding protein), these proteins bind testosterone...
2) Production of Aromatase enzyme in order to synthesize estradiol from testosterone.
3) Production of growth factors and other products.
Sertoli cells along with the LH affecting leydig cells to produce factors steroidogenic factor SF-1 and cyclic (CAMP) response element binding protein. These factors activate enzymes that control the production of testosterone. In addition LH stimulates other proteins such as steroid carrier protein and steroid activating proteins; they play a role in the metabolism of cholesterol- the precursor of steroid hormones testosterone and estradiol. All these are essential for the production of the male hormones.

4) Production of Inhibin (more than 2 types)

Sertoli cell only syndrome : infertile male (can't produce sperms.)

These two cells function as one unite (don't function separately) to produce the male hormones as well as estradiol which is essential for the regulation of gonadotropin hormone and it is also essential for spermatogenesis.

The leydig cells of the testis produce 95% of the circulating testosterone. Although testosterone is the major secretory product , the testis also secretes pregnenolone , progesterone , hydroxyprogesterone, androstenedione (is of major importance because it serves as a precursor for extraglandular estrogen formation), androsterone and DHT.

Leydig cells receptors can bind prolactin and hCG from the placenta, so the leydig cells bind 3 hormones :1. LH 2. prolactin 3.hCG

*Prolactin synergizes with LH to produce normal amount of Testosterone; but in pathological conditions like hypo- prolactinemia and hyper-prolactinemia → testosterone level decreases → no normal spermatogenesis→ infertility in male.

Figure 37.1

This is the regulation of reproduction in male:
Brain centres under the effect of hormonal state ,Age, Environment, Drugs , stress level and various disease states affect the hypothalamus to produce **GnRH** which affect the anterior pituitary to produce FSH and LH , FSH and LH induce testis to produce testosterone.

Testosterone, Activin, Inhibin, follistatin as well as estradiol regulate the production and release of FSH and LH from the gonadotroph cells. In general testosterone, estradiol and inhibin reduce the secretion of LH and FSH (feedback control), Activin activates the FSH secretion, follistatin inhibits the FSH secretion, inhibin act directly on the anterior pituitatry and inhibit the secretion of FSH but <u>not</u> LH.
Testosterone is responsible for the development of secondary sex organs, behavior and accessory and secondary sex characteristics.
Testosterone and Estradiol exert feedback control on all levels from brain centers to the testis.

Figure 36.2

GnRH in the preprogonadotropin releasing hormone connected with signal peptide and GnRH associated peptide (GAP). The neuron transport both GnRH and GAP down into the portal circulation. GAP may inhibit prolactin secretion.

Figure 52.14

The structure of FSH, LH formed of alpha (non specific) and beta (specific) subunits is similar to TSH, hCG.

Figure 10.1

The most important difference between males and females are two:
1. One single chromosome (Y in male, X in female) this is called genetic sex.
2. One single pair of endocrine gland (testes in male, ovary in female) this is called gonadal sex.

The differentiation into male or female (the sex determination) is genetically determined, but the development (formation) of genital organs is hormonally determined (depends on the presence of functional testis).
Testis or ovaries have 2 functions:
1- production of hormones or
2- production of sperms or ovums

The primary sex organ in the male is the testis which produces the sperms as well as the male hormones the most important of which is the testosterone, it also produces DHD. At puberty testosterone is responsible for the development of secodary sex organs and the appearance and maintenance of secondary sex characteristics.

The Dr showed a figure of the secondary sex organs of the male just to show you the glands which secrete the seminal plasma: bulbourethral, prostate and seminal vesicles. It shows the epididymis, vas deferens and the ampula of vas deferens. It shows also the location of the prostate gland. Any enlargement of the prostate gland will affect the urination. The enlargement of the prostate gland either benign or malignant can affect the urethra. one type of the enlargement is because of the concentration of the DHD and even in the malignant the testosterone itself has a role, we don't know exactly.
* Stages of spermatogensis:
Spermatogenesis occurs in all seminiferous tubules starting from primordial germ cells till the mature sperms.
Three phases :
- mitosis: production of cells have the same number of chromosomes (primary spermatocytes).
- meiosis: production of cells have half number of chromosomes (spermatids).
- spermiogenesis: changing in the metabolism, function, motility, fertility and morphology.
All these are delicate processes, ordered, regular and sequential. Therefore these processes are sensitive to external agents that alter cell division such as chemical carcinogens, chemotherapeutic agents , certain drugs, environmental toxins, irradiation and extreme temperature and factors that can reduce the number of replicating germ cells or cause chromosomal abnormalities in the individual germ cells.

The duration of spermatogenesis 70 days +/− 5 (65-75 days). New cycle every 16 days. Hormones can't affect(alter/ shorten/lengthen) the duration but hormones can affect the number of spermatozoa produced.
The testis is exposed to injuries or infections and sometimes it's affected after vasectomy. Antibodies are produced against the sperms. If the concentration of these antibodies is low or moderate then it can't produce any harm but if the concentration

is high it will affect the fertility. Sometimes, by accident, there are AB against the sperms in both the man and the women, this will affect the fertility despite their level.

Figure 36.4

This is a summary of the functions of sertoli cells:
1) Sertoli cells are critical to germ cell development as indicated by their close contact. As many as 6 to 12 spermatids be may attached to a Sertoli cell.
2) sertoli cells phagocytose residual bodies (excess cytoplasm resulting from the transformation of spermatids to spermatozoa) and damaged germ cells.
3) provide structural support and nutrition for germ cells.
4) secrete fluids
5) assist in **spermiation** (the final detachment of mature spermatozoa from the Sertoli cell into the lumen) .
6) Spermiation may involve plasminogen activator which converts plasminogen to plasmin, a proteolytic enzyme that assists in the release of the mature sperm into the lumen.
7) Sertoli cells also synthesize large amounts of transferrin, an iron-transport protein important for sperm development
8) Sertoli cells also produce glycoprotein hormones --inhibin, activin and follistatin- that regulate the secretion of FSH

- After production sperms need maturation to gain motility which occurs in the epididymis (10-24 hrs) , in some people the maturation process may prolong for 10 days this depends on individual differences and this is not only a matter of wasting time, but it is a matter of spending time and affection by some hormones and chemicals in the epididymis.
- After maturation they are stored in the epididymis , the vas deferens and the ampulla of vas , the amount stored in each depends on the marital status.
- In singles the sperm storage happen mainly in the vas deferens, but among married people the sperms are stored in the epydidmes.

Figure 10.16

This is the epididymis. If the sperms removed from the tail are totally motile and fertile , in the body 50% of the sperms are fertile and motile and the others are not , in the head they are neither motile nor fertile.
They say, in the epididymis to gain more motility there is activation of a unique protein called **CatSper protein,** which is localized in the principle piece of the sperm tail, this protein appears to be calcium ion channel that turn cAMP generalized calcium entrance.

The daily production of sperms is 200 millions/day, sperms can survive in male reproductive system for many weeks but in female reproductive system for about 2 days. They can't gain the capability to fertilize the ovum unless they are in the female reproductive system, this process is called the **capacitation** which is a falicitatory "most probably not obligatory because even if we remove the sperms from the testis, they can fertilize the ovum!!". It’s an irreversible process which last for about 1 hour,

in this one hour, if the sperm reach the ovum, it can fertilize it otherwise after one hour if they can't gain the capacitation, they can't fertilize the ovum in this one hour. Motility and capacitation seem to be essential in vivo but not in vitro.

We have indicated all the hormones involved in Spermatogenesis except:
- **Growth hormone** is essential for spermatogenesis.
- **Thyroid hormone** is also important, as in thyroid cancer the person becomes infertile (the sperms can't fertilize the ovum).

Other factor also important:
- Diet (Nutrition), complete starvation can affect the spermatogenesis.
- Diseases: the diseases which raise the body temperature such as Mumps and typhous disease affect the spermatogenesis, especially if the occur in the childhood they may cause infertility.

- Testosterone is essential (in normal concentration) for the spermatogenesis specifically in the meiosis.
- In the last 3 months of pregnancy the testosterone and the insulin like hormone **"IGF-1"** from leydig cells promote the descending of the testes from their place in the abdominal cavity into the scrotum.
- Some people may develop **Cryptorchidism** which refers to the absence of one or both testes from the scrotum (remain in the abdominal cavity). It is the most common birth defect regarding male genitalia about 3% of full-term and 30% of premature infant boys are born with at least one **undescended testis.** It means there is no sufficient amount of testosterone to call the descending of the testis into the scrotum.
- The presence of the testes in the scrotum is essential for normal spermatogenesis because the optimum temperature for the spermatogenesis is about 2-3 degrees below the body temperature.

- 2 systems are needed to keep the testes at the right (cooler) temperature :
    1. The arrangement of the blood vessels of the testes, similar to the *counter current exchanger* in the kidney, warm arterial blood reaches the testes and cooler venous blood leaves it **"pampiniform plexus".**
    2. Cremasteric muscle responds to the change in temperature when it is high the muscle relaxes, and when the temperature is low the muscle contracts and becomes near the body. This contraction relaxation helps to keep the testes temperature in the right range about 35 degree.

- Figure 44-5 shows the level of testosterone from fetal life to death. Between the 8^{th} week and the 18^{th} the testosterone level is high, during fetal life testosterone secretion and synthesis (by the leydig cells) is controlled by placental hormones, mainly human chorionic gonadotropin hormone **(HCG)** not LH from the pituitary**. HCG** stimulate the fetal testes to secrete testosterone… shortly before and shortly after birth, testosterone secretion and synthesise isn't controlled by that placental hormones because there is decrease then eventually NO (HCG) so the testosterone level decreases.
  HCG is also secreted in the pituitary gland, testis and other non-placental tissues.

- You can notice that during the life (from fetal life till death) there's no any stage that has zero testosterone level at all**.**

- From 25 years to 70 years the testosterone level is almost constant, this means that the age doesn't affect the fertility of males and the decreasing of fertility with age is related to some diseases that affect the old males such as diabetes and some neurologic disorders not the sexual drive.
- At age of 70 testosterone decrease a little bit in the testosterone level, this is called "climacteric", similar to the menopause in females.
- Before puberty there is almost no difference between boys and girls because testosterone level is very low, they both have same mean body mass, skeletal mass and body fat. However, after puberty men have 150% of the average woman's lean and skeletal body mass, and women have 200% of the body fat of men. Men have twice number of muscle cells that women have and 1.5 times muscle mass.

*Extra note may help you to understand how the 2 systems keep the tetes at the right temperature :

1. **The cremaster[13] muscle**—strips of the internal abdominal oblique muscle that enmesh the spermatic cord. When it is cold, the cremaster contracts and draws the testes closer to the body to keep them warm. When it is warm, the cremaster relaxes and the testes are suspended farther from the body.
2. **The pampiniform[12] plexus**—an extensive network of veins from the testis that surround the testicular artery in the spermatic cord. As they pass through the inguinal canal, these veins converge to form the testicular vein. Without the pampiniform plexus, warm arterial blood would heat the testis and inhibit spermatogenesis. The pampiniform plexus, however, prevents this by acting as a *countercurrent heat exchanger.* The relatively cool blood (about 35°C) ascending through the plexus absorbs heat from the warmer blood descending through the testicular artery. By the time the arterial blood reaches the testis, it is 1.5° to 2.5°C cooler than the core body temperature.