

# Testosterone

- Several tissues besides the testes, including adipose, brain, muscle, skin and adrenal cortex produce testosterone, that's why we can never have a zero level of testosterone.
- Testosterone may be synthesised de novo or produced by the conversion of other precursors.

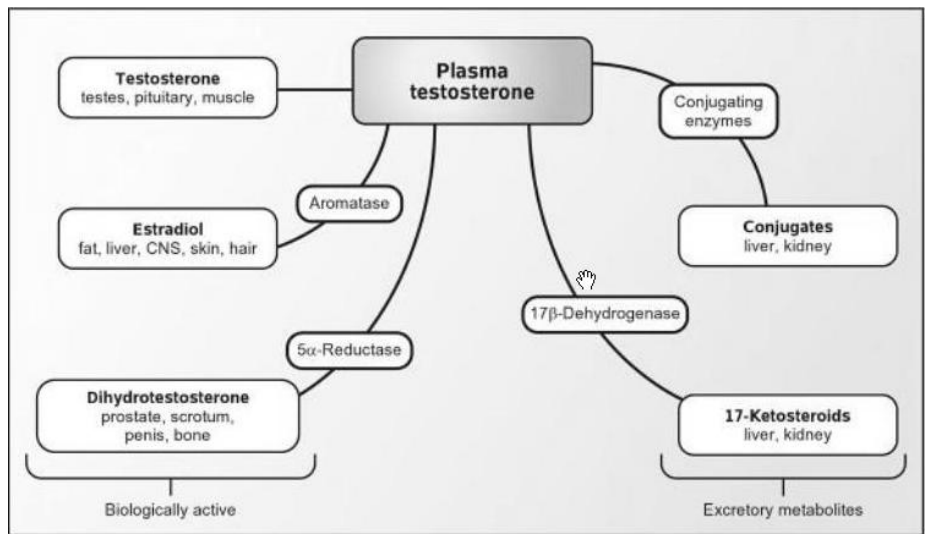


Figure 36.11 Conversion of testosterone to different products in extratesticular sites.

- Testosterone is considered a prohormone. It produces active and inactive metabolites.
- It functions in testes, pituitary and muscles as testosterone.
- In fat, liver, CNS, skin and hair it is converted into Estradiol under the effect of the aromatase enzyme.
- Dihydrotestosterone (DHT) is produced under the effect of 5 alpha reductase, and is found in the prostate, scrotum, penis and bones.
- Conjugating enzymes in the liver and kidney produce conjugates.
- 17-ketosteroids which are inactive metabolites are excreted in the liver and kidneys.
- Because DHT produces hyperplasia of prostatic epithelial cells, drugs that inhibit 5 alpha reductase are currently used to reduce prostatic hypertrophy. This is called **chemical castration** (reduction of conversion of testosterone to DHT)
- The biological activity of DHT is 30-50 times stronger than testosterone
- Another indirect way to reduce the levels of DHT is by continuous administration of GnRH or any hCG analogue. When there is continuous administration of GnRH, receptors of gonadotropic cells (cells of the anterior pituitary) stop responding and LH and FSH are not produced, consequently testosterone is not produced by Leydig cells. This is called **GnRH desensitization**.

(Desensitization is like when people who live next to unclean areas with bad smells get used to the bad smell, however passers by still smell it and find it annoying.)

## Slide with a drawing about testosterone effects (figure 44.6)

- We know that testosterone has many functions as testosterone or as DHT or as estrogen, such as:
  - Intrauterine differentiation.
  - Imprint male pattern of gonadotropins.
  - Sex drive and behaviour.
  - Estradiol.

- Larynx: production of male voice.
  - Upper body fat.
  - Muscle mass.
  - RBCs.
  - Cholesterol derivatives (LDL,)
  - Sperm production: testosterone affects sperm production on two levels. 1) It is essential for meiosis. 2) Remodelling of sperms.
- Remember, there is no zero level of testosterone.
- The conversion of testosterone to DHT in males and to Estradiol in females is needed for good health and well being, and it helps decrease the chances of having osteoporosis.
- The Dr mentioned the following points and said they were important:
    - Unlike most species which mate only to produce offspring, human sexual activity and procreation are not tightly linked.
    - Superimposed on the base of reproductive mechanisms dictated by hormones are numerous psychological and society factors.
    - No correlation has been found between circulating testosterone levels and sexual drive, frequency of intercourse or sexual fantasies.
    - Similarly there is no correlation between testosterone levels and impotence or homosexuality. Impotent and homosexual patients may have normal testosterone levels.
    - Homosexuality is either habitual or genetic.
    - Castration of an adult causes regression of the reproductive tract. Results in a slow decline but not a complete elimination in sexual interest and activity but this interest is psychological. (the Dr read this then said he doesn't believe it is right since eventually there is no sexual activity.)
    - A male without testosterone (or without testes) is completely sterile.
    - Humans need normal levels of testosterone, there is no need for them to be above normal levels, it makes no difference. Above normal levels may produce unwanted side effects.
- The growth and secretory activity of sebaceous glands on the face, upper back and chest are stimulated by androgens primarily DHT and inhibited by estrogen.
- Increased sensitivity of target cells to androgenic action especially during puberty is the cause of Acne vulgaris in both males and females. It appears more in females. The most successful drug for this is Roaccutane which is a form of vitamin A, it is only recommended in severe cases of acne.

# Sperms

## Slide with a picture of a sperm

- This is a mature sperm; it consists of a head, a midpiece and a tail.
- The head contains the nucleus which contains the chromosomes (22+y) or (22+x).
- The top part of the head is the acrosome. The acrosome contains enzymes that are activated when the sperms are in contact with the ovum. These enzymes lyse the tissues around the ovum. The midpiece contains mitochondria for energy and the tail is for movement.

## Slide about acrosome

- These are the enzymes which are present in the acrosome. They are released when the sperms are activated in the medium (in contact with the ovum, not necessarily the inner zone.). This is the final part of the capacitation process (activation of acrosome).
- The most important enzyme is the hyaluronidase enzyme. This enzyme is also present in semen. Hyaluronidase is not produced by accessory glands, it comes from the acrosome.
- Acrosin, neuraminidase, phospholipase and esterases are enzymes that are released only when the sperms are activated.

# Puberty

- Puberty occurs at an age between 8-13 in females and 9-14 in males, sometimes earlier sometimes later. This depends on many factors.
- At the beginning of puberty, sperms appear in the early morning urine. This is called Spermathe (the first appearance of sperms).
- There are three main factors that decide the **time of beginning of puberty**:
  1. Genetic Factors
  2. Nutritional Factors
  3. Environmental factors.
- In some cases, **puberty is delayed** (after 15 years old). This could be caused by
  - Normal variance: familial (males in the family have delayed puberty) or racial.
  - Coincidental serious illness (example: mumps during early childhood)
  - Psychological stress.
  - Hypogonadism.
  - Hyperprolactinemia : Leydig cells have receptors that bind LH, prolactin and hCG. Prolactin and LH usually function synergistically to maintain normal levels of testosterone. In hyperprolactinemia, prolactin occupies almost all receptors on Leydig cells and no receptors are left to bind LH therefore the production of testosterone is reduced and puberty is delayed.

- Before puberty males and females have the same lean body mass. However, men have 150% of the average women lean and skeletal body mass.
- Women have 200% of the body fat of men. Men have twice the number of muscle cells that women have and 1.5 times the muscle mass. This is because of male and female hormones.

# **Impotency and Infertility**

➤ **Impotent:** the inability of an adult male to have an erection. He is sterile in this case.

➤ **Sterile (infertile):** The inability to fertilize the ovum. This does not imply impotence. The patient could be sterile but not impotent.

➤ Causes of impotence:

- Psychological disturbances: the most common cause of impotence.
- Drugs like cocaine.
- Autonomic neuropathies including diabetes (especially severe stages).
- Hyperprolactinemia
- Hypogonadism
- Some heart diseases especially after heart surgery, most commonly due to the drugs used and not the surgery itself.

➤ **Slides about Viagra:**

- *Mechanism of Action:* Nitric Oxide from vascular epithelial cells and from parasympathetic axons activates guanylyl cyclase to produce cGMP from GTP which causes in a series of reactions vasodilatation and erection. This is the normal process of erection. cGMP is inactivated by phosphodiesterase enzyme after sometime, we need to prolong its action. Viagra (sildenafil) inactivates phosphodiesterase to prolong the action of cGMP.
- The doctor said that most of the users (>75%) are young people below the age of 30, and this is very bad.
- The importance of Viagra comes from the fact that it is not an aphrodisiac drug; when a patient takes Viagra, erection does not occur immediately, it may not occur at all unless the person is stimulated.
- *Precautions and contraindications:*
  - Patients with renal diseases, liver diseases, heart diseases asthma ...etc have to be careful when using Viagra.
  - Some patients with heart diseases take organic nitrates or nitric oxide. When these patients take Viagra, drug interactions occur, which may in some cases cause death. Nowadays, patients who need to take Viagra are given an alternative drug for their heart problem for a week while using Viagra then they go back to taking their regular prescribed drug.
  - Viagra (Sildenafil) should not be taken with antihypertensive drugs, especially ACE inhibitors. When a patient takes Viagra with ACE inhibitors, none of the drugs function (neither Viagra nor ACE inhibitors.).

# Semen

## Slide with table 25-4

- Sperms compose 10% of semen; The remaining 90% of semen is composed of secretions from accessory glands → bulbourethral, seminal vesicles and prostate gland.
  - Secretions from seminal vesicles = 60%
  - Secretions from prostate = 30%
  - Very little from the bulbourethral.
- Substances in semen include chemicals, hormones, enzymes, buffers, acids, vitamins ...etc.
- Remember that hyaluronidase is present in semen but is not produced by accessory glands, it is produced by the acrosome.
- The secretions of accessory glands are essential for the normal survival of sperms and fertility.
- When semen is ejaculated into the female reproductive system, it coagulates immediately to minimize the expulsion of semen from the vagina. After about 5 minutes, semen liquefies again so that the sperms would be free to reach the fertilization site. Coagulation occurs due to the action of proteins similar to the ones present in blood. Liquefaction occurs due to enzymes inside semen.
- Liquefaction has to be about within 15-30 minutes maximally, otherwise will be non-motile and won't fertilize.
- To establish the causes of reproductive dysfunction, physical examination, medical history, semen analysis, hormone determination, hormone stimulation tests and genetic analysis are performed

## Semen analysis

There is one step in the evaluation of fertility, which is semen analysis. Semen is analysed from specimens that are collected after 3-5 days of sexual abstinence.

**1. Semen volume:** the broad range is from (1-7)ml, but the normal range is from (3-4)ml. let's say that 80% of males ejaculate (3-4)ml per sexual intercourse.

**2. Sperm count:** it is from (20 million-120 million)/ml, but normally 100 million sperms/ml. so how many sperms are ejaculated in one sexual intercourse? it is from (300 million-400million). Dr said in section 2 that below 10 million he is absolutely infertile.

**3. Motility:** the percentage of motile sperms is from (60-70)%. There is no way for all sperms to be motile, they will never be above 80%.

**4. Morphology (the normal shape):** it is similar to the motility ranging from (60-70)%. Here the dr showed a picture of morphologically different sperms which are all abnormal except the typical one that you know.

**5. Liquefaction:** It must occur within 5 minutes and it has to be complete within 15 or maximally 30 minutes, otherwise no fertilization will occur. Recall that it is necessary so that sperms become free

and go to the site of fertilization.

## 6. Fructose concentration: for nourishment

- **Oligospermia** is low sperm count while **aspermia** is no sperms at all

Slide with a picture showing female ovaries and uterus (figure 16-16)

-Note the fertilization site in the oviduct.

-The time (mins) after ejaculation and the percentage of sperms in different sites. (all from the slide)

- Sperms have to reach the fertilization site maximally after **one hour** of ejaculation, otherwise no fertilization will occur.
- The percentage of ejaculated sperms that reach the fertilization site is 0.001.

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There is a lot of variation in indicating the number of sperms reaching the fertilization site. Some books say its 100-150, some books say thousands, but the dr doesn't think they're in hundreds, they must be in thousands.