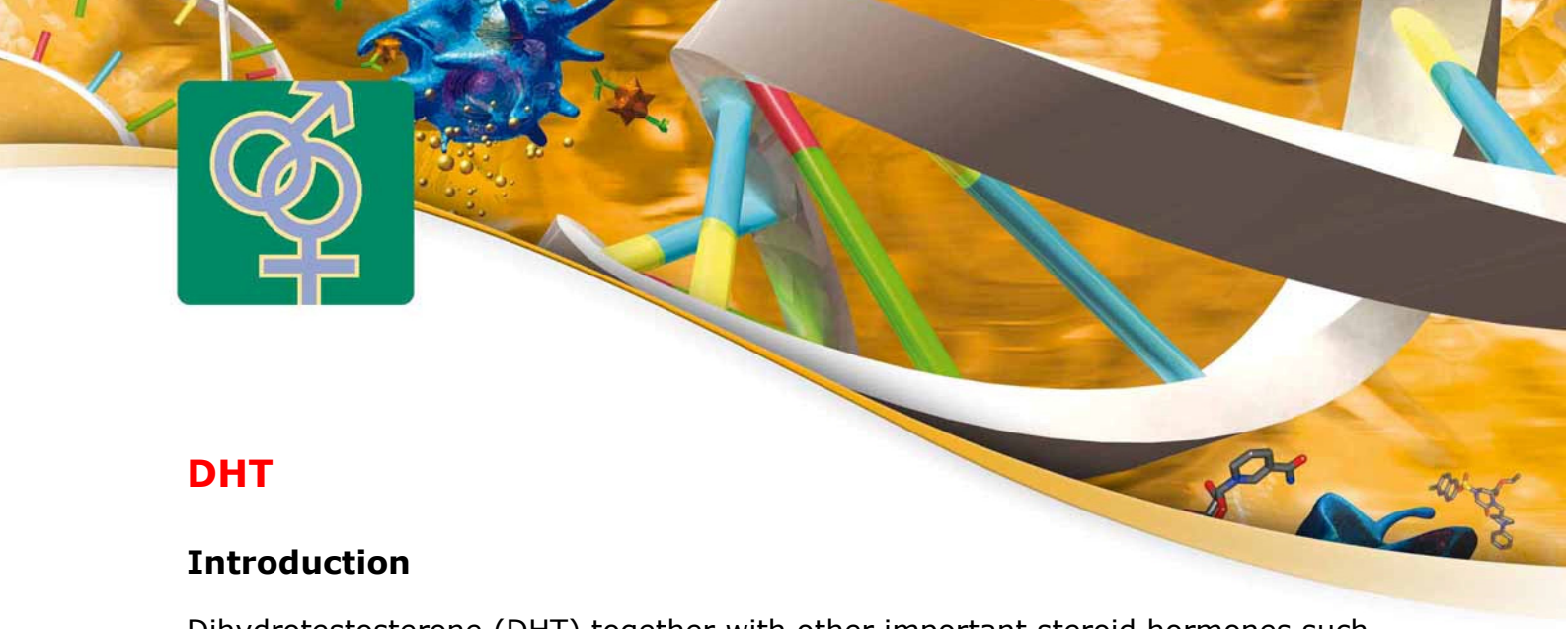
Reproductive

DHT

Analyte Information

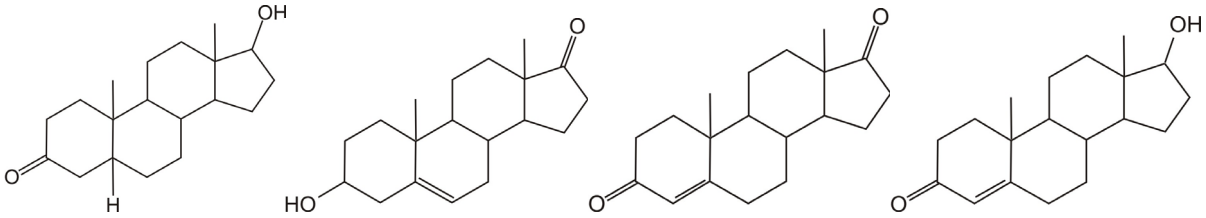


DHT

Introduction

Dihydrotestosterone (DHT) together with other important steroid hormones such as testosterone, androstenedione (ASD) and dehydroepiandrosterone (DHEA) belongs to the group of androgens. Androgens are a group of C_{19} steroids that stimulate or control the development and maintenance of male characteristics. This includes the activity of the male sex organs and development of secondary sex characteristics. Androgens are also precursors of all estrogens, the female sex hormones.
The chemical name of DHT is 17β-hydroxy-5α-androstan-3-one. Its summary formula is $C_{19}H_{30}O_2$ and its molecular weight (Mr) is 290.4 Da. The structural formulas of DHT and related androgens are shown below (Fig.1):

Fig.1: Structural formulas of the most important androgens



Dihydrotestosterone **DHEA** **Androstenedione** **Testosterone**

There are more than 30 other names for DHT. Some of them are presented here for illustration: 17-Hydroxy-androstan-3-one; 4,5 Dihydrotestosterone; 5-a-Androstalone; Anaboleen; Anabolex; Drolban; Stanorone, and so on.

Biosynthesis

DHT is an androgenic metabolite of testosterone and the most potent naturally occurring androgen. DHT is generated by a 5α reduction of testosterone; about 6 – 8 % of testosterone is converted to DHT[1,2].
Androgens such as testosterone are synthesized de novo, i.e., from cholesterol (Fig.2) in the endocrine glands. DHT is then formed from testosterone (Fig.3) primarily in the prostate gland, genital skin, hair follicles, adrenal glands and testes by the enzyme 5α-reductase (5-ARD). This enzyme is responsible for reduction of the α-4,5 double-bond. The concentration of 5α-reductase is highest in peripheral tissues (genital skin and hair follicles). 5α-reductase is localized intracellularly in association with the nuclear membrane.

Fig.2: Steroidogenesis

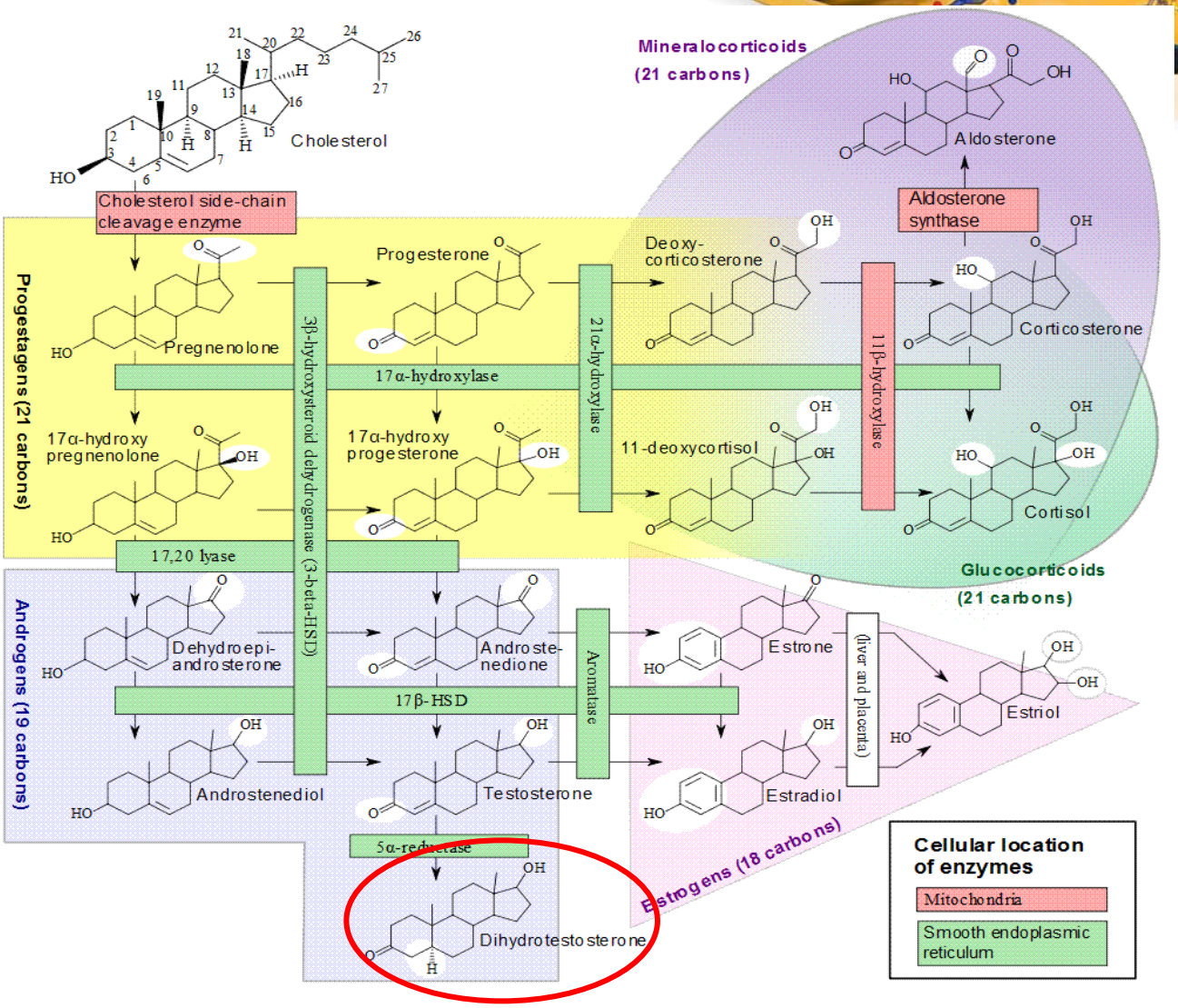
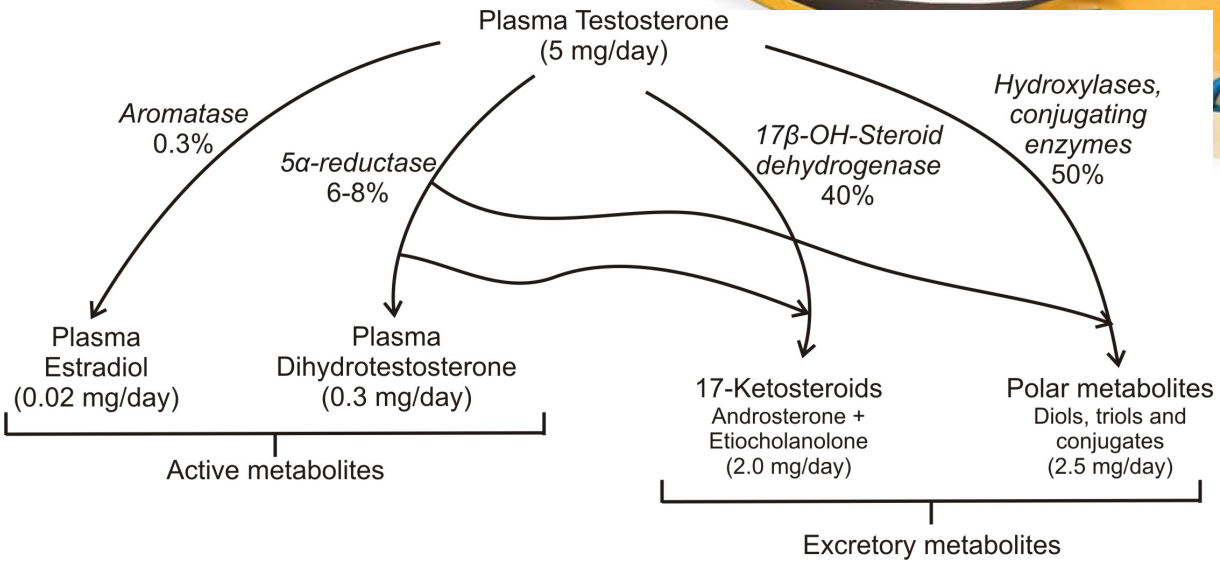
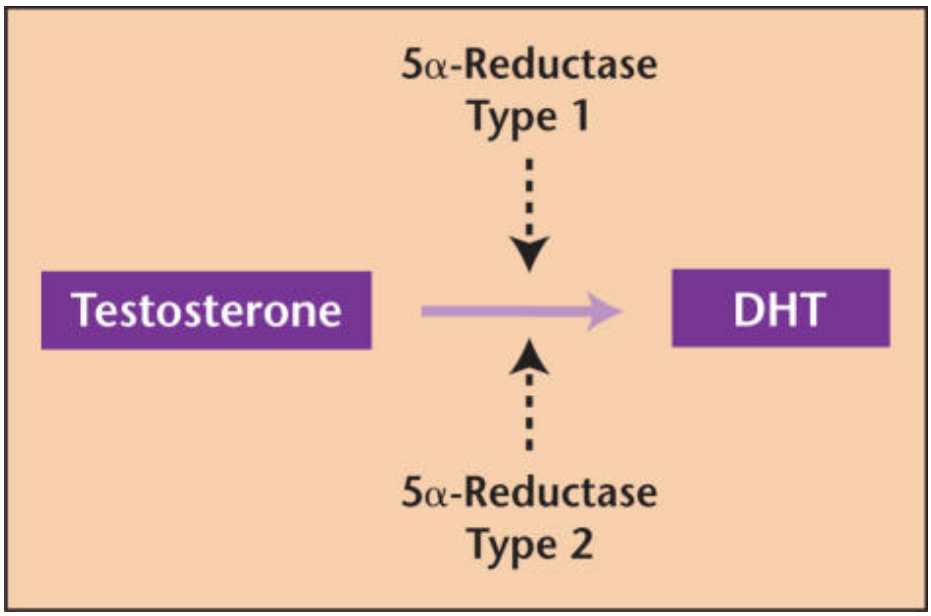


Fig.3:Testosterone conversion



Two isoenzymes of 5α-reductase (Fig.4) have been discovered. Type 1 is present in the most tissues in the body where the enzyme is expressed, and it is the dominant form in sebaceous glands. Type 2 is the dominant form in genital tissues, including the prostate[3].
This reaction is irreversible. Only a small proportion of DHT produced in target tissues is excreted into peripheral circulation, where it is primarily bound to sex-hormone binding globulin (SHBG)[4] or albumin. 2 – 3 % of DHT may circulate in free form.

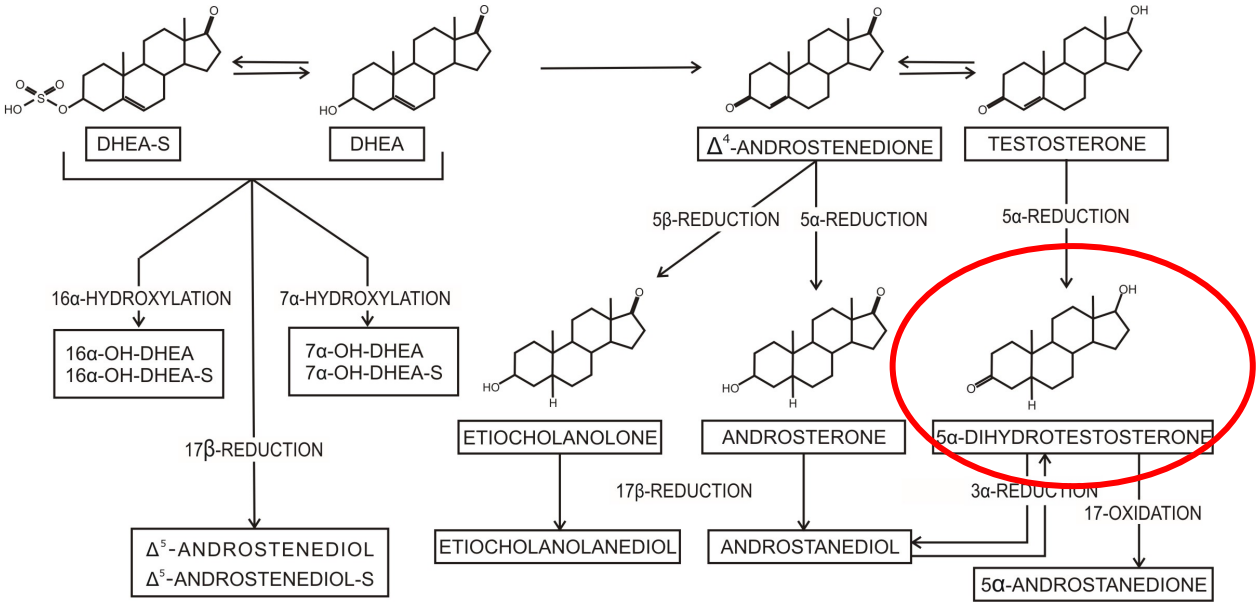
Fig.4: Conversion of testosterone to DHT



Metabolism

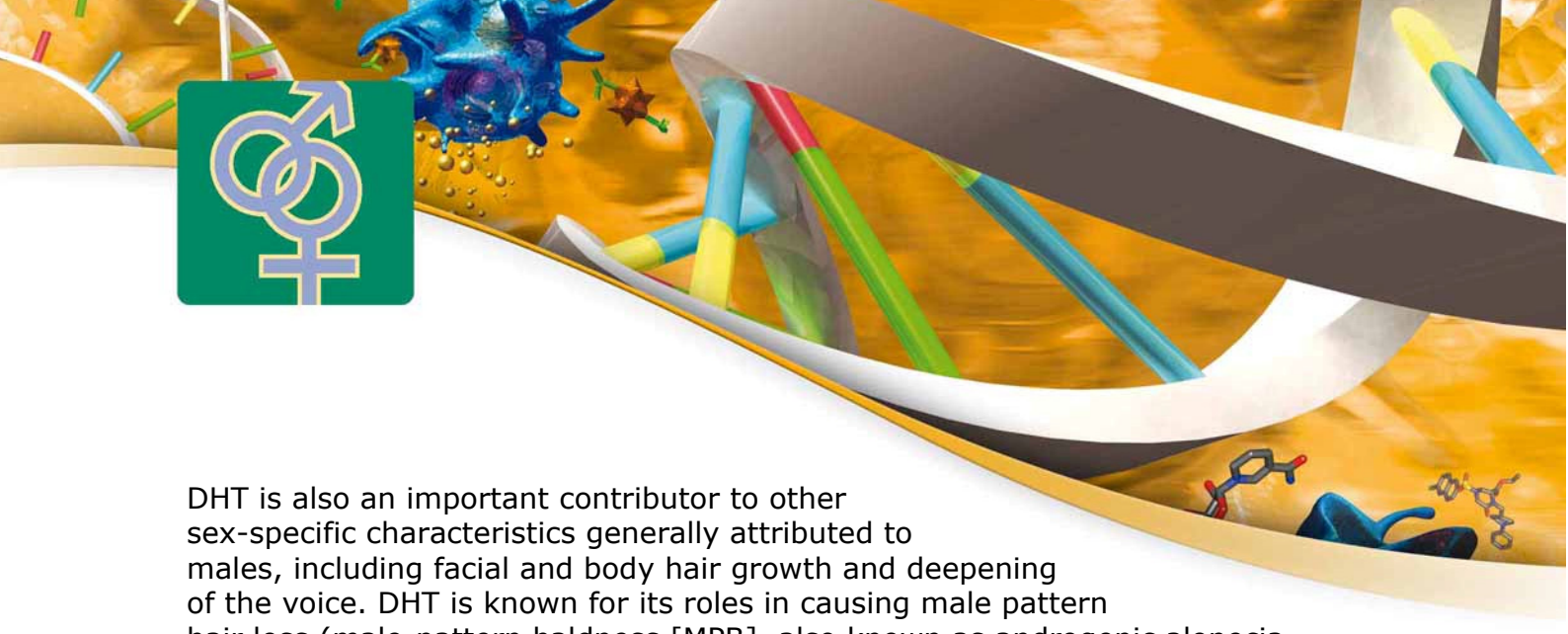
DHT is metabolized to 3α-androstanediol and 3α-androstanediol glucuronide (Fig.5) – the final product of peripheral androgen metabolism. These metabolites have been used as markers of DHT production in peripheral tissues. Serum concentrations of 3α-androstanediol glucuronide or 3α-androstanediol reflect the production of DHT in peripheral tissues[2]. These metabolites are excreted in urine.

Fig.5: Androgen metabolism



Physiological Function

The target cells for DHT are cells of the prostate gland, seminal vesicles, external genitals and genital skin. DHT binds directly to the androgen receptor (AR) and the complex DHT-AR interacts with specific DNA sequences and regulates gene transcription[5] in above mentioned cells.
DHT has a higher affinity for androgen receptors (AR) than does testosterone. Because of this, DHT is three times more potent than testosterone.
In fetal life, DHT is responsible for the development of the external male genitalia and prostate while testosterone causes virilization of the Wolffian ducts. In order for normal male sexual development to occur, the conversion of testosterone to DHT is very important. A microphallus (less than 2.5 cm fully stretched) at birth can be caused by a lack of DHT or testosterone, or defective androgen receptors.

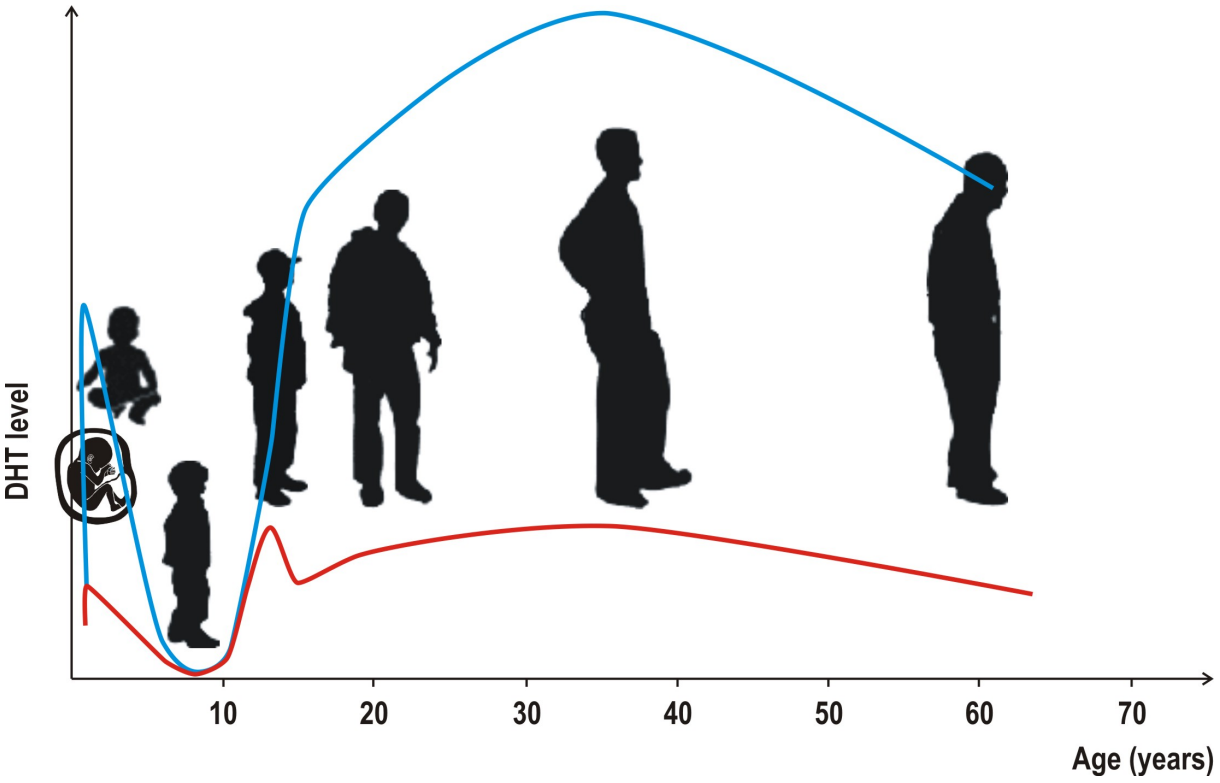


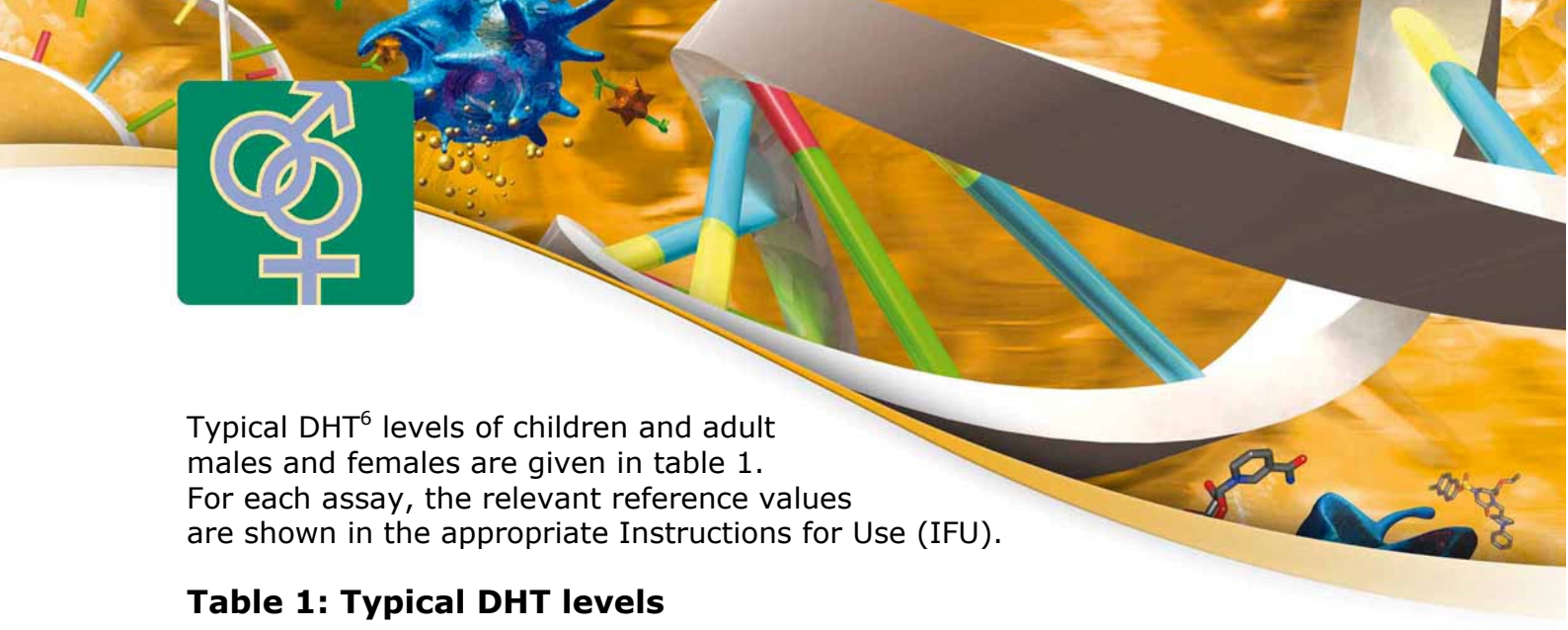
DHT is also an important contributor to other sex-specific characteristics generally attributed to males, including facial and body hair growth and deepening of the voice. DHT is known for its roles in causing male pattern hair loss (male-pattern baldness [MPB], also known as androgenic alopecia [AGA]) and prostate problems. DHT is also necessary to mitigate estrogen effects in men. Unlike other androgens such as testosterone, DHT cannot be converted by the enzyme aromatase to estradiol, and therefore acts as a pure androgen. DHT has no known role in female development.

Levels

Serum levels of DHT decrease rapidly in males in the first weeks after birth. They then increase, reaching a level of 120 – 850 pg/mL in the 2nd month, and then gradually decrease to 30 pg/mL by the 7th month. In females, DHT decreases to prepubertal levels during the first month[1]. The production of DHT increases during puberty.
The mean DHT production rate is 0.3 mg/day in men and 0.056 mg/day in women.
Serum concentrations of DHT are closely related to those of testosterone, but are lower. There is a decrease in the ratio of DHT to testosterone throughout pregnancy.
Serum DHT levels reflect the synthesis of androgens in the peripheral tissues (essentially the target tissues) depending on the level of circulating androgens and cellular 5α-reductase.

Fig.6: Changes of DHT levels during the life cycle



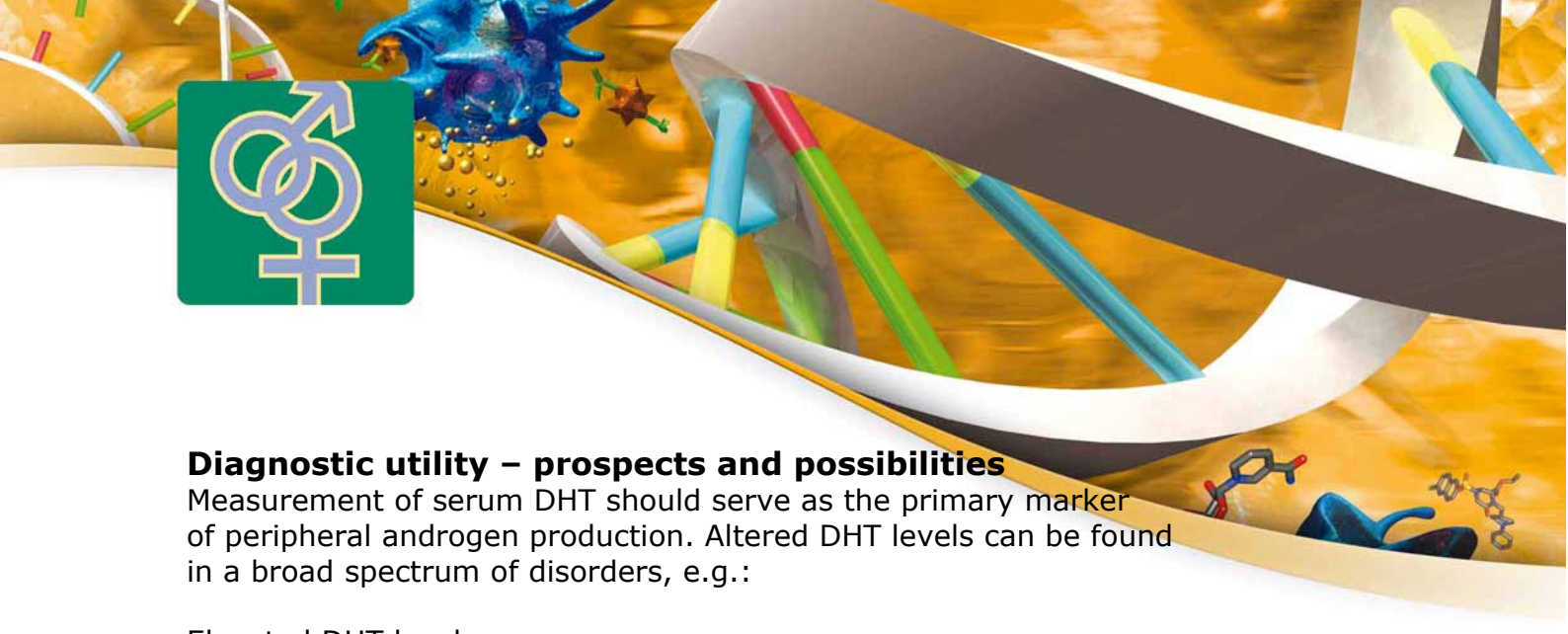


Typical DHT[6] levels of children and adult males and females are given in table 1.
For each assay, the relevant reference values are shown in the appropriate Instructions for Use (IFU).

Table 1: Typical DHT levels

Specimen (serum)	**Reference interval** (pg /mL)
Cord blood:	20 - 80
Premature	
male:	100 - 530
female:	20 - 130
Newborn	
male:	50 - 600
female:	< 20 - 150
Prepubertal children (1 – 10 year):	< 30
Puberty Tanner stage:	
Stage I	
male, female:	< 30
Stage II	
male:	30 - 170
female:	50 - 120
Stage III	
male:	80 - 330
female:	70 - 190
Stage IV	
male:	220 - 520
female:	40 - 130
Stage V	
male:	240 - 650
female:	30 - 180
Adult	
male:	300 - 850
female:	40 - 220

Equation for the conversion of units: 1 pg/mLx3.44 = pmol/L



Diagnostic utility – prospects and possibilities

Measurement of serum DHT should serve as the primary marker of peripheral androgen production. Altered DHT levels can be found in a broad spectrum of disorders, e.g.:

Elevated DHT levels

- hirsutism
- male pattern baldness
- benign prostatic hyperplasia
- prostate cancer

Decreased DHT levels

- 5α-reductase deficiency (autosomal-recesive genetic deficiency of 5α-reductase, called male pseudohermaphroditism or pseudovaginal perineoscrotal hypospadias)
- hypogonadism
- Klinefelter's syndrome (a condition in which males have an extra X sex chromosome resulting in small testicles and reduced fertility)

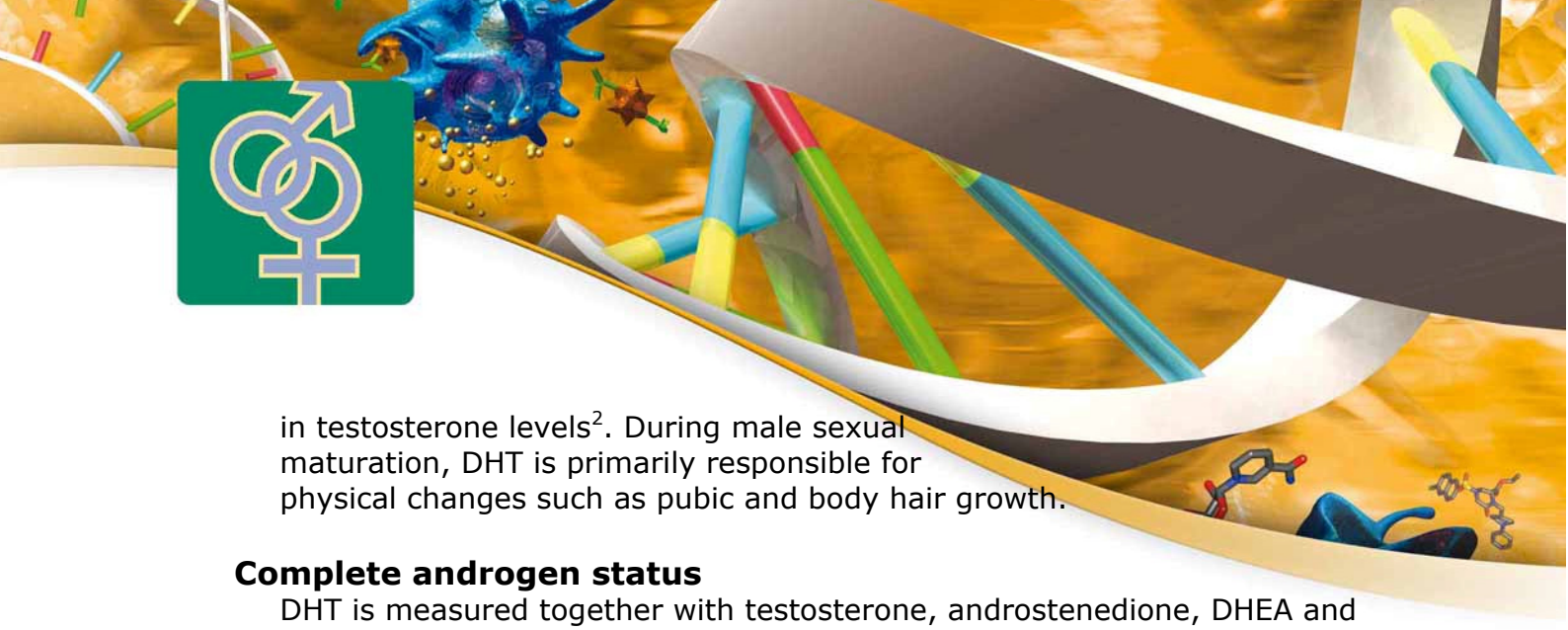
Diagnostic utility – Practical applications

Monitoring of patients receiving 5α-reductase inhibitor therapy

These inhibitors can be used for treatment of benign prostatic hyperplasia, and are effective in treating hirsutism and male-pattern baldness (androgenic alopecia – AGA). They diminish the conversion of testosterone to DHT.

Evaluating patients with possible 5α-reductase deficiency

This autosomal-recessive genetic deficiency of the enzyme 5α-reductase, sometimes called male pseudohermaphroditism or pseudovaginal perineoscrotal hypospadias, leads to inadequate differentiation of DHT-dependent peripheral tissues. Male infants with this disorder have ambiguous genitalia and are often raised as females, although significant virilization may occur later in life, presumably due to the natural increase



in testosterone levels[2]. During male sexual maturation, DHT is primarily responsible for physical changes such as pubic and body hair growth.

Complete androgen status

DHT is measured together with testosterone, androstenedione, DHEA and DHEA-S.

Distinguishing between androgenic and estrogenic effects of testosterone

DHT is largely derived from peripheral tissue conversion of testosterone catalyzed by a steroid 5α-reductase enzyme. As DHT cannot be converted by the enzyme aromatase to estradiol, it is frequently used in research settings to distinguish between these effects of testosterone caused by binding to androgen receptors (AR) and those caused by testosterone conversion to estradiol and subsequent binding to estrogen receptors.

DHT is also known to participate in the development of some cases of acne.

References

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