Androgens are steroid hormones that are secreted primarily by the testis, and testosterone is the principal androgen secreted. Its primary function is to regulate the differentiation and secretory function of male sex accessory organs. Androgens also possess protein anabolic activity that is manifested in skeletal muscle, bone, and kidneys. As a class, androgens are reasonably safe drugs, having limited and relatively predictable side effects.

CHEMISTRY AND BIOSYNTHESIS

The basic structure of all steroid hormones is similar (see Chapter 60, Fig. 60.4). The addition of a hydrogen atom at position 5 and an angular methyl group at positions 18 and 19 establishes the basic chemical framework for androgenic activity.

CHARACTERIZATION OF PLASMA ANDROGENS

In males, testosterone is the principal circulating androgen, and the testes are the principal source. Although the adrenals are capable of androgen synthesis, less than 10% of the circulating androgens in men are produced in the adrenals. Testosterone is synthesized by Leydig cells of the testes at the rate of about 8 mg/24 hours, providing a plasma concentration of 0.5 to 0.6 μg/dL. In females, the ovaries contribute approximately one-third of the total androgens synthesized, while the adrenals contribute the rest.

Androstenedione, dehydroepiandrosterone (DHEA), and dehydroepiandrosterone sulfate (DHEA-S) are other mildly androgenic compounds of secondary importance in males and females. The gonads and the adrenal cortex are capable of secreting androstenedione...
and DHEA, while DHEA-S is secreted primarily by the adrenal.

Concentrations of plasma testosterone and other androgens vary throughout the day in both sexes; whether such variation is simply random or fits a repeatable diurnal pattern is a matter of debate. Compared with the diurnal variation seen with cortisol, plasma testosterone concentrations are reasonably constant. Plasma androgen concentrations also vary greatly in women through the menstrual cycle, with peak levels seen in the luteal phase.

**SEX HORMONE–BINDING PROTEINS**

Circulating testosterone is reversibly bound to two major plasma proteins, albumin and gamma globulin. Binding to albumin is a relatively nonspecific low-affinity and high-capacity association. In contrast, binding to the specific γ-globulin fraction, called sex hormone–binding globulin (SHBG), is a high-affinity steroid-specific interaction. Under physiological conditions, 98% of testosterone is protein bound, 40% to albumin and 58% to SHBG. Thus, 2% or less of circulating testosterone is unbound or free. Free testosterone reflects the amount that is biologically active and available for interaction with peripheral target cells.

SHBG levels are known to be influenced by a variety of clinical conditions. In females, the high estrogen levels of pregnancy or the use of oral contraceptives result in increased SHBG concentrations. In males, elevated levels of SHBG are seen most commonly in individuals with liver cirrhosis or during normal aging. Elevated SHBG levels are also seen in hyperthyroidism and hypogonadism. All of these conditions are associated with elevated estrogen levels, which result in increased hepatic SHBG synthesis. SHBG levels are suppressed by androgen replacement or chronic glucocorticoid therapy. Elevations of SHBG do not necessarily result in a fall in free testosterone levels. When assessing the androgenic status of an individual, whether male or female, it is necessary to measure both total and free testosterone plasma levels.

Plasma testosterone levels also exhibit age-associated changes. The levels of the hormone are very low throughout childhood and until early adolescence, when increasing testicular steroidogenesis precedes the onset of puberty in boys. Levels peak in the early 20s, and beginning at about age 30, testicular production of testosterone begins to decline. Urinary 17-ketosteroid excretion declines slowly as a result of a concomitant decrease in the metabolic clearance rate of testosterone. Therefore, there is a relatively constant serum testosterone concentration that often does not decline significantly until after age 70. After the fifth decade, free testosterone levels do decrease as a result of increased SHBG levels. In females, testosterone levels also decline with age; however, at menopause the decline in female hormones is so much greater that many postmenopausal women have higher androgen to estrogen ratios, resulting frequently in significant hirsutism.

**STEROIDOGENESIS**

The main steroidogenic components of the testis are the interstitial cells of Leydig found between the seminiferous tubules. The principal secretory product of Leydig cells, testosterone, is not stored to any significant degree within these cells. Biochemical studies of Leydig cell steroidogenic function have shown that testosterone synthesis begins with acetate derived either from glucose or products of lipid metabolism. Acetate is converted to cholesterol through numerous reactions in or on the smooth endoplasmic reticulum. Cholesterol, once formed, is stored in lipid droplets in an esterified form. The cholesterol required for steroidogenesis is transferred into the mitochondria, where the side chain is cleaved by enzymes on the inner membranes to form pregnenolone. This reaction is the rate-limiting step in testosterone biosynthesis and is the step stimulated by luteinizing hormone (LH). Pregnenolone is then returned to the cytoplasm, where it serves as the principal precursor of testosterone.

Testosterone synthesis from pregnenolone can occur along two distinct metabolic pathways (Fig. 63.1). The names given to these two routes of metabolism refer to the position in the steroid molecule where an unsaturated bond is maintained. Thus, in the delta-4 pathway an unsaturated position is between C4 and C5 of ring A, whereas in the delta-5 pathway, the unsaturated position is between C5 and C6 of ring B. In the human tests, the delta-5 pathway is the predominant (but not exclusive) one used for the biosynthesis of testosterone.

Sertoli cells, in the seminiferous tubule wall, are known to be important in spermatogenesis, in part through their synthesis of an androgen-binding protein (ABP). ABP, when secreted into the lumen of the seminiferous tubules, selectively binds testosterone of Leydig cell origin and serves as a hormone reservoir and transport protein for the androgen.

**REGULATION OF PLASMA TESTOSTERONE**

The regulation of plasma testosterone is accomplished through a dynamic feedback interaction among the hypothalamus, pituitary, and testis (Fig. 63.2). The hypothalamus synthesizes and releases gonadotropin releasing hormone (GnRH) into the hypothalamic–hypophyseal portal system. Pulsatile release of GnRH stimulates the release of the pituitary gonadotropins LH and follicle-stimulating hormone (FSH). LH and FSH then reach the
FIGURE 63.1
Synthetic pathways of testosterone. 1. Andrenostenedione pathway (delta-4).
2. Dehydroepiandrosterone pathway (delta-5).
Androgens, Antiandrogens, and Anabolic Steroids

The testes, where they regulate testosterone synthesis and spermatogenesis, respectively. The resultant increases in serum testosterone levels exert a negative feedback at both the hypothalamic and the pituitary levels.

The hypothalamus releases GnRH in a pulsatile manner. The pulse frequency is sex specific, with males exhibiting a 120-minute frequency and females exhibiting a 60- to 90-minute frequency. The pulsating levels of GnRH from the pituitary modulate LH and FSH release. Androgens and estrogens can modulate gonadotropin release at both the hypothalamus and pituitary levels.

MECHANISM OF ACTION

Given the wide spectrum of androgen actions, it is reasonable to expect the intracellular processes mediating these diverse effects to vary among target tissues. The currently accepted hypothesis of androgen action in male sex accessory organs is depicted in Fig. 63.4. Testosterone diffuses from the blood across the plasma membrane of the sex accessory organ cell, where it is rapidly metabolized to DHT and androstanediol. In many sex accessory organs, DHT, rather than testosterone, is the primary intracellular androgen and is more potent than testosterone. Once formed, DHT preferentially binds to a receptor protein in the nucleus. This DHT–receptor complex is subsequently activated and binds to proteins on the nuclear matrix. Following this interaction, RNA synthesis results in enhanced protein synthesis and cellular metabolism. If sufficient androgen stimulation occurs, DNA synthesis and cellular division begin.

Non-sex accessory tissues also are targets for the protein anabolic actions of androgens. These tissues possess lower levels of endogenous hormone, minimal 5α-reductase activity, and lower concentrations of specific androgen receptors. The protein anabolic actions are probably mediated by an interaction with the androgen receptor.

PHARMACOLOGICAL ACTIONS

Androgens produce both virilizing and protein anabolic actions (Table 63.1). The virilizing actions of testosterone include irreversible effects that occur during embryogenesis, that is, those that induce differentiation of the central nervous system and male reproductive tracts, and the excitatory actions at puberty that are
responsible for secondary sexual development. In addition to the effects on male reproductive function, androgens influence a number of other systems, many of which are associated with masculinity. These actions include the growth of male-pattern facial, pubic, and body hair, the lower vocal pitch resulting from a thickening and lengthening of the vocal cords, and a significant (30%) increase in the rate of long bone growth. Androgens also terminate long bone growth by inducing closure of the epiphyses. The degree of virilization and timing of puberty also affect peak bone density and risk of osteoporosis in males.

The protein anabolic actions of androgens on bone and skeletal muscle are responsible for the larger stature of males than females. Androgens induce some degree of anabolism in other tissues, including bone marrow, liver, kidney, and heart. They also have several other actions, not necessarily associated with maleness, such as lymphoid tissue regression during puberty.

**TABLE 63.1 Pharmacological Actions of Androgens**

<table>
<thead>
<tr>
<th>Virilizing effects</th>
<th>Gonadotropin regulation</th>
<th>Spermatogenesis</th>
<th>Sexual dysfunction</th>
<th>Sexual restoration and development</th>
<th>Protein anabolic effects</th>
<th>Increased bone density</th>
<th>Increased muscle mass</th>
<th>Increased red blood cell mass</th>
</tr>
</thead>
</table>

**CLINICAL USES**

The primary therapeutic use of androgens is as replacement therapy in testicular deficiency (Table 63.2), a condition in which induction and maintenance of male secondary sex characteristics are desired. Although re-
placement therapy is the primary use of androgen administra-
tion, these hormones also are used and abused for their protein anabolic effects.

**Hypogonadism**

Testicular failure may occur before puberty and present as delayed puberty and the eunuchoid phenotype, or after puberty, with the development of infertility, impotence, or decreased libido in otherwise fully virilized males. The source of hypogonadism can be testicular, as occurs in *primary hypogonadism*, or it may result from abnormalities of the hypothalamic–pituitary axis, as in *secondary hypogonadism*.

**Prepuberal Hypogonadism**

Prepuberal hypogonadism is often unsuspected until a delay in male sexual development is noticed at the time of puberty. The eunuchoid phenotype is caused by absent or deficient androgenic induction of the undifferentiated embryonic bipotential tissue into fully developed male sex accessory organs. Causes of this condition include deficient testicular steroidogenesis (both congenital and acquired), target organ androgen insensitivity syndromes (receptor defects, 5α-reductase deficiency), deficient pituitary LH and FSH secretion, or deficient hypothalamic GnRH production. Androgen replacement therapy is effective only when the end organs are sensitive to androgens, so certain forms of pseudohermaphroditism are unresponsive to androgen replacement.

The compounds most effective in bringing about masculinization are the long-acting enanthate, cypionate, or propionate esters of testosterone; these preparations require intramuscular injection. Recently effective cutaneous forms of androgens have become available and may be equally effective. Owing to inconsistent drug absorption, oral androgen preparations do not result in full sexual development in prepuberal hypogonadotropic males.

**Postpuberal Hypogonadism**

Postpuberal hypogonadism is also classified as either primary hypogonadism or secondary hypogonadism. Primary hypogonadism occurs after puberty as the result of surgical castration or testicular destruction (e.g., through orchitis, radiation) and is associated with elevated levels of LH and FSH. Secondary hypogonadism is usually associated with hypopituitarism from destruction or infiltration of the hypothalamus or pituitary by infarction, tumoral replacement, or surgical removal.
Thus, these individuals have inappropriately low LH and FSH levels that do not respond to GnRH stimulation. Androgen replacement in these individuals usually restores secondary male sexual characteristics, such as libido and potency.

**Aging and Impotence**

Aging in men is associated with decreased testicular function that results in reduced testicular steroidogenesis, decreased free plasma testosterone levels, decreased 17-ketosteroid excretion, and increased gonadotropin levels. Decreased testicular function has been implicated as a cause of reduced libido, muscle mass, muscle strength, and bone density in elderly men. However, these observations are so variable that a causal relationship between lowered androgen levels has not been firmly established. **Androgen replacement in elderly men has not been demonstrated to be beneficial unless there is true androgen deficiency.** In addition, it is wise to avoid the indiscriminate use of androgens in this age group because of the high incidence of prostate neoplasms (benign and malignant). Androgen administration in replacement doses has proved to be moderately successful in increasing libido and sexual performance in men who have true testicular failure.

**Anemia**

Androgens stimulate erythrocytosis and are effective in the treatment of certain anemias that are secondary to endocrine hypofunction or myeloid hypoplasia. In high dosages, these compounds in the past were used in the treatment of several forms of anemia. However recombinant erythropoietin has replaced the androgens as a more effective treatment of most forms of anemia.

**Therapeutic Use of Androgens in Women**

Because of the antagonistic action of androgens in many estrogen-sensitive tissues, it would seem logical that androgens might be effective therapeutic agents in clinical situations of estrogen excess or in the presence of estrogen-dependent neoplasms. However, the virilizing side effects of these compounds have limited their clinical use. Selective protein anabolic forms of androgens have been used in certain clinical situations.

**Endometriosis**

*Endometriosis* is abnormal growth of endometrial tissue in the peritoneal cavity. Women with this disorder have dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility. Danazol (*Danocrine*) is a 2,3-isoxazol derivative of 17β-ethyltestosterone (ethisterone) that has weak virilizing and protein anabolic properties. It is effective in endometriosis through its negative feedback inhibition of LH and FSH release, which in turn results in decreased ovarian steroidogenesis and regression of endometriomas. Because of the virilizing side effects of danazol, causing acne and hirsutism, its use in endometriosis has been largely supplanted by the use of GnRH analogues. Danazol is also approved for use in fibrocystic breast disease and hereditary angioneurotic edema.

**Female Hypogonadism**

Female hypogonadism, especially prepuberal, may be an indication for androgen therapy. Androgens are necessary for normal pubic hair induction and long bone growth in both sexes. In prepuberal females with hypopituitarism in whom all other hormonal deficiencies (estrogen, progesterone, thyroid, adrenal, and growth hormone) have been corrected, normal sexual development and long bone growth are not complete without androgen hormone replacement. Estrogen administration during adolescence is necessary for the development of the breast, the gynecoid pelvis, and other female characteristics. However, maximal long bone growth and development of axillary and pubic hair will not occur without small amounts of androgen replacement. The use of methyltestosterone (*Android*) and diethylstilbestrol in combination has been demonstrated to be very effective in inducing complete secondary sexual development in these females. Finally, low doses of androgens have been used to facilitate impaired libido in postmenopausal women when combined with estrogen replacement therapy.

**Use of Androgens as Protein Anabolic Agents**

**Anabolic** activities of testosterone, such as increases in amino acid incorporation into protein and in RNA polymerase activity, have been demonstrated in skeletal muscle. Apart from the direct anabolic effects in specific tissue, androgens antagonize the protein catabolic action of glucocorticoids. The androgen compounds with the greatest ratio of protein anabolic effects to virilizing effects are the 19-nortestosterone derivatives. Compounds that are used clinically (Table 63.3) include nandrolone phenpropionate (*Durabolin*), nandrolone decanoate.
(Deca-Durabolin), methandrostenolone (Dianabol), oxymetholone (Anadrol, Adroyd), stanozolol (Winstrol), and oxandrolone (Anavar).

The protein anabolic compounds are most commonly used to stimulate appetite and muscle mass in persons with advanced malignancy or other conditions characterized by advanced malnutrition. These compounds are also often abused by athletes who are trying to build muscle mass. Athletes often take multiple compounds at the same time (stacking) or sequentially to try to maximize their anabolic effects. This type of use is not based on scientific data but rather on hyperbole often spread by individuals with no medical or scientific background. Athletes who use these compounds in this way are unaware of the potential adverse effects or do not care.

ADVERSE EFFECTS

As a class, the androgens are relatively safe and non-toxic. However, in inappropriate doses or for inappropriate reasons, their use can result in significant toxicity.

Toxicity in Men

The administration of androgens to sexually mature hypogonadal men is associated with few untoward effects. However, prepuberal or hypogonadal males never exposed to testosterone show enhanced sensitivity to administered androgens, and many do not like the effects. Testosterone administration can cause irritability, agitation, or aggressive behavior. Androgen administration to normal males inhibits the release of the pituitary gonadotropins FSH, LH, and as a consequence, endogenous testicular production of testosterone is reduced. Spermatogenesis is also reduced, and if administration is continued, azoospermia and infertility may result. Peripheral aromatization of androgens to estrogens can cause gynecomastia. Cessation of exogenous androgen treatment in normal males usually results in restoration of normal sperm levels over a 6-month period. Finally, androgen replacement therapy in elderly men should be monitored closely. Men at this age are at risk for developing prostatic neoplasms (benign and malignant), and use of androgens in this setting is contraindicated because of the likelihood of stimulating growth of these tumors.

Toxicity in Women

Although masculinization is a desired action of androgens in the treatment of men with testicular deficiencies, these effects can be quite distressing to women. The degree of virilization in women will vary with the dosage, duration of therapy, and particular androgen preparation used. In women receiving high doses of androgen for any reason, facial hair growth may progress to total body hair growth, baldness may develop, breasts may shrink, and the voice may deepen. In addition, clitoral hypertrophy, uterine atrophy, and menstrual irregularities may develop. Although some of the symptoms are reversible and disappear upon cessation of therapy, several effects—baldness, growth of facial hair, clitoral enlargement, and deepening of the voice—are commonly irreversible. Steroids taken by women during pregnancy may cause pseudohermaphroditism in the genetically female fetus and may even cause its death.

Toxicity in Either Sex

Androgen administration to male or female adults, especially at high dosages, results in erythrocytosis and polycythemia, fluid retention, and it may produce or exacerbate edema. This can be serious when associated with congestive heart failure, cirrhosis of the liver, or nephrotic syndrome. Since androgens stimulate the activity of sebaceous glands, oily skin and acne are found in some individuals who are receiving androgen therapy. A change in cholesterol levels can result from androgen therapy, such as decreased levels of high-density lipoprotein cholesterol and increased levels of low-density lipoprotein cholesterol. This change in the distribution of cholesterol may contribute to increased risk of atherosclerosis and coronary artery disease, especially in athletes who are exposed for long periods to high levels of anabolic steroids.

Oral androgen preparations that have the 17-methyl substitution on the steroid molecule are associated with the development of liver disorders, including hyperbilirubinemia, and elevated liver function tests. As many as 80% of individuals who take these compounds have been shown to develop liver problems. Although these changes are usually reversed if steroid treatment is discontinued, use of the oral preparations is also associated with the development of benign liver tumors and a rare liver disorder involving the development of blood-filled sacs (peliosis hepatis). Finally, worsening of sleep apnea and precipitation of superior sagittal sinus thrombosis—seizures, facial palsy, hemiplegia, stupor, and coma—have been associated with androgen therapy.

ANTIANDROGENS

By definition, antiandrogens are substances that prevent or depress the action of male hormones in their target organs. Potential sites of action include gonadotropin suppression, inhibition of androgen synthesis, and androgen receptor blockade. Compounds that affect each of these sites are available. Potential clinical uses of antiandrogens include suppression of androgen excess and treatment of androgen-dependent tumors.
Extreme clinical examples of androgen excess include central precocious puberty, the adrenogenital syndromes, and androgen-secreting adrenal, ovarian, or testicular tumors. Less severe problems include idiopathic hirsutism, premenstrual syndrome, and severe cystic acne.

**Inhibitors of Androgen Biosynthesis**

Ketoconazole (Nizoral) is a broad-spectrum antifungal agent (see Chapter 52) that in very high doses inhibits several steps in the biosynthesis of both adrenal and gonadal steroids. While the normal antifungal dose is 200 mg/day, testosterone biosynthesis in both the adrenal and testis is completely abolished by doses of 800 to 1,600 mg/day. This drug is used most commonly for large virilizing adrenal tumors that cannot be surgically removed.

**Androgen Receptor Antagonists**

Spironolactone (Aldactone) is a compound originally developed as a mineralocorticoid antagonist and is used as a diuretic and antihypertensive agent (see Chapter 21). However, at high doses spironolactone binds to the androgen receptor. In clinical practice it is a weak androgen antagonist used to treat hirsutism in women by blocking testosterone binding to androgen receptors in hair follicles. Use of spironolactone in women for the treatment of hirsutism or male pattern baldness can result in elevated serum potassium levels; these levels should be checked within 1 month of starting the medication.

Flutamide (Eulexin) is a nonsteroidal androgen receptor antagonist that inhibits androgen binding to its nuclear receptor. It is effective in inducing prostatic regression and is approved for the treatment of prostatic carcinoma. For maximum clinical effectiveness it has to be used in combination with a GnRH antagonist (e.g., leuprolide acetate) that inhibits androgen production. Flutamide may eventually be used for the treatment of hirsutism and male pattern baldness in women if a topical preparation is developed.

Cyproterone acetate is a progestational antiandrogen that blocks androgen receptor binding and suppresses androgen-sensitive tissues. It is available in a topical form in Europe for the treatment of hirsutism.

**5α-Reductase Inhibitors**

Finasteride (Proscar) is a 5α-reductase inhibitor that blocks the conversion of testosterone to DHT in target tissues. Since DHT is the major intracellular androgen in the prostate, finasteride is effective in suppressing DHT stimulation of prostatic growth and secretory function without markedly affecting libido. It is approved for the treatment of benign prostatic hyperplasia. Although there is usually some regression in the size of the prostate gland following administration of finasteride, clinical response may take 6 to 12 months. If the obstructive symptoms are severe, there is often not enough time to allow this compound to work. The principal adverse effects of finasteride are impotence, decreased libido, and decreased volume of ejaculate. The compound is generally well tolerated in men.

**Gonadotropin-Releasing Hormone Analogues**

GnRH analogues (see Chapter 59) can induce chemical castration by suppressing the pulsatile release of LH and FSH, hence inhibiting testicular steroidogenesis. Administration of these compounds reduces circulating testosterone levels. These compounds are inhaled, injected subcutaneously, or implanted subcutaneously. They are used in males in the treatment of precocious puberty and carcinoma of the prostate.

**PREPARATIONS**

Androgens come in oral, injectable, implantable, and topical preparations. Because of the toxicity of the oral preparations and the inconvenience of the injectable forms, the transdermal gels have been a major clinical advance for treatment of hypogonadal males.

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**Study Questions**

1. The serum level of testosterone in males from adolescence through the fifth decade of life is a primarily a consequence of
   (A) A relatively constant level of testicular testosterone production
   (B) A significant decline in testosterone production
   (C) A decline in the metabolic clearance rate of testosterone
   (D) An increase in the metabolic clearance rate of testosterone
   (E) A sharp drop in urinary 17-ketosteroid levels

2. Which of the following is mostly likely to be found in a male who lacks functional 5α-reductase?
3. The formation of what as a principal precursor of testosterone is considered the biosynthetic rate-limiting step?
   (A) Pregnenolone
   (B) Cholesterol
   (C) Androstenediol
   (D) Estrogen
   (E) Progesterone

4. Normal skeletal muscle cells
   (A) Typically lack androgen receptors and thus are not affected by high concentrations of testosterone
   (B) Respond more readily to dihydrotestosterone than to testosterone
   (C) Have higher levels of 5α-reductase than do prostatic tissue cells
   (D) Use the androgen receptor to enhance protein anabolic activity
   (E) Produce testosterone in response to FSH stimuli

5. Upon examination, a 68-year-old married man was found to have a greatly enlarged prostate. Which one of the following drugs is most likely to suppress prostatic growth without affecting libido?
   (A) Spironolactone
   (B) Finasteride
   (C) Ketoconazole
   (D) Flutamide
   (E) Stanozolol

ANSWERS
1. C. In adolescent males, testicular testosterone production dramatically rises from prepuberal levels and then declines into adulthood. However, with advancing adulthood there is a drop in the metabolic clearance rate of testosterone, increasing the length of time that testosterone remains in the serum. Evidence of a relatively constant level of serum testosterone is seen in the relative constant levels of urinary 17-ketosteroids, a metabolite of testosterone, from the second to the fifth decade of life.

2. D. The enzyme 5α-reductase catalyzes the formation of dihydrotestosterone from testosterone. In normal accessory sex gland tissues, such as the prostate, most of the direct androgen effect is due to dihydrotestosterone rather than testosterone. Thus when 5α-reductase is lacking, serum levels of testosterone may be normal or even slightly elevated with a hypotrophied prostate gland.

SUPPLEMENTAL READING


Ron Diggs is a 15-year-old white cross-country runner who comes to your office requesting help in gaining muscle strength and endurance. He is a good athlete who would like to get a college scholarship and thinks that if he can increase his muscle strength, he will get better and win a scholarship. He knows of some other athletes who are using anabolic steroids and requests your help. What would you do?

**Answer:** The use and abuse of anabolic steroids by athletes and body builders of either sex to increase strength and muscle mass is widespread. Surveys indicate that in the United States 6% of high school athletes, 20% of college athletes, and more than 50% of professional athletes in certain sports use or abuse anabolic steroids at some time. Use of these compounds does result in increased muscle mass, strength, and endurance. However, much of this benefit is now thought to be due as much to enhanced training effort as it is to the protein anabolic effects of the androgens. Individuals who take these compounds typically use 100 to 200 times the normal dose and will cycle or stack multiple anabolic compounds together in an effort to enhance the biological effect.

Common endocrine side effects of these compounds include virilization in women, suppression of endogenous gonadotropins, hypogonadism (amenorrhea in women, impotency in men), and severe psychological disturbances (depression, mania, steroid rage). Other physiological side effects are hepatotoxicity, suppression of high-density lipoprotein cholesterol, increased cardiovascular risk, insulin resistance, and decreased thyroid hormone production. It would be malpractice and unlawful to consider such treatment for this person. However, it is important to educate him about the risk–benefit ratio and reason for not using them.