

Ethical and Medical Considerations of Androgen Deprivation Treatment of Sex Offenders

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Context: Blood testosterone codetermines the threshold for erotosexual imagery and sexual activity. Androgen deprivation may therefore have a place in the treatment of unacceptable sexual behavior. Although androgen deprivation can be effective for sex offenders, their basic human rights must be respected; otherwise such treatment constitutes a violation of their physical integrity and is ethically unacceptable. As experience in treating prostate cancers demonstrates, androgen deprivation may have serious side effects. Endocrinologists are qualified to advise on and monitor androgen deprivation, but they are placed in an atypical position because the indication for such treatment is not dictated by endocrine disease.

Objective: The aim of this study was to provide an ethical framework for advising on androgen deprivation treatment of sex offenders and dealing with side effects.

Evidence Acquisition and Synthesis: A literature search was conducted in PubMed, Psycinfo, and references from the multiple systematic reviews and meta-analyses published on this topic. An attempt has been made to provide an appreciation of the ethical aspects of androgen deprivation in sex offenders, the efficacy of treatment, the potential risks of treatment, therapeutic options, and recommendations for monitoring treatment.

Conclusions: Provided that the human rights of sex offenders are respected and informed consent is given, androgen deprivation within a comprehensive framework of psychotherapeutic treatment can make a meaningful contribution to the prevention of recidivism by enabling better control of sexual impulses. Knowledge of side effects and their treatment has been mostly gleaned from experience with prostate cancer patients, and this should be made available to sex offenders undergoing androgen deprivation. (*J Clin Endocrinol Metab* 96: 3628–3637, 2011)

Over the past 20–30 yr, a biological substrate of human sexuality and its pathologies, traditionally the domain of psychiatry, has emerged (1, 2). The extent of biological determinants is still not well understood, but behaviors once regarded with moral opprobrium as acts of choice may in fact be related to the neurobiology of brain function with an implication of biological determinism. Sexual compulsion may be associated with neuropathologies for which psychological treatment together with pharmacotherapy can be provided (3, 4). This paper focuses on the role that androgen reduction can play in sexual behavior disorders that violate the rights of others.

Sexual arousal is dependent on neural (sensory and cognitive), hormonal, and genetic factors and, in the human case, the complex influences of culture and sociosexual context (1, 5). People who are compulsively responsive to and dependent on abnormal sexual stimuli for arousal and orgasm for a duration of at least 6 months are defined as paraphiliac (6) in Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (Text Revision) 2000 (7). Paraphilias occur predominantly in men but also in women (8). Extreme paraphilias (such as pedophilia or lust murder) may bring individuals into conflict with others in society and the law. Although such behavior is

intolerable, it should be noted that perpetrators are suffering from a pathological condition and (forensic) medicine may play a part in their treatment, potentially including pharmacological interventions.

In men, androgens are fundamental to normal sexual behavior (9) and are primarily directed at sexual interest or desire (5, 10, 11). In all people, including persons with a paraphilia, testosterone codetermines the threshold at which erotosexual imagery and sexual activity occurs. Reducing the biological activity of androgens raises this threshold, particularly for those paraphilias characterized by intense and frequent sexual desire and arousal. Sexual behavior with overtones of compulsivity may not respond so well to androgen reduction and is better treated with selective serotonin reuptake inhibitors (4, 12).

Despite methodological shortcomings, there is evidence that treatment lowers sexual recidivism significantly (13–15), although a person's basic inclinations are not changed (16). Interventions are mostly designed to increase voluntary control over sexual arousal, reduce sex drive, or teach self-management and relapse prevention skills to individuals who are motivated to avoid acting upon their sexual impulses and thus contribute to the prevention of recidivism (13, 15, 17, 18).

Endocrine intervention to reduce androgen action may be deemed effective by a forensic mental health professional, but endocrinologists who become involved in the decision-making process in this context are placed in an atypical position because such an indication is not dictated by endocrine disease. This review is primarily intended to address the information needs of endocrinologists who find themselves in this situation. It does not examine in great detail the potential for ethical and legal complications, although this is also obviously a serious point of consideration.

Ethical Aspects

The ethical approach to the medical treatment of sex offenders is contentious and complex. The field of ethics is not an objective reality that can be divorced from values, attitudes, feelings, or (religious) beliefs that all exert a decisive influence, preventing full agreement, or even consensus. An additional complicating factor is that many sex offenders also suffer from serious co-psycho pathology (19).

There can be no question that society is entitled to punish those who violate the rights of others or that it has a duty to protect its citizens by curtailing the freedom of the violators. For decades, the penal approach to sex offenders has focused almost entirely on issues of punishment and

risk assessment and management for the purpose of community protection and retributive justice (20), with limited success in reducing recidivism (21).

Because the only options for preventing repeat offending are ongoing incarceration or behavior modification, effective treatment is an obvious goal. Androgen reduction unquestionably reduces sexual interest (libido) and performance (10). It also reduces reoffending (16). Past involuntary castration of sex offenders (16), although morally reprehensible and not always targeted at high-risk cases (22, 23), resulted in recidivism rates of less than 5% invariably being reported over long follow-up periods, compared with expected rates of 50% or more (1, 16, 24), although some reports are more conservative (25).

Studies of the use of antiandrogenic drugs report similar efficacy (24, 26–28), and a comprehensive meta-analysis of sex offender treatment has found that both surgical and hormonal interventions reduce recidivism much more than any other treatment approach, particularly when used alongside psychological treatment (14). Although hormonal intervention is sometimes referred to as “chemical castration,” this is something of a misnomer; it also evokes the clearly unethical involuntary castrations of earlier times and can influence the discourse on ethics. The more neutral “androgen deprivation treatment” (ADT), widely used in the scientific literature on the treatment of prostate carcinomas, may be preferable when discussing androgen reduction.

Some experts are cautiously optimistic that sex offenders can be successfully treated (13, 16, 21), and ADT has the important advantage that it is reversible. However, this gives rise to questions regarding the basis of medical involvement. It can be argued that medical input in these cases not only straddles the boundary between treatment and punishment, but also may shift the doctor's focus from the best interests of the patient to one of public safety while carrying with it a sense of symbolic retribution (29). Evidently, providing hormonal treatment from such an approach poses ethical questions of informed consent and truly free choice.

Certainly, pharmacotherapy should be voluntary because mandatory treatment is not only ethically questionable, but also carries a high risk of noncompliance (not taking the medication or procuring testosterone from the black market). However, the correctional system is ultimately an environment of legal coercion and retribution; some may argue that pharmacological treatment cannot be offered on a genuinely voluntary and consensual basis in this context because it forces the sex offender to choose to consent to the lesser evil, and that it is unethical to place anyone in this position, also in view of the considerable risk of side effects. However, this position can also lead to

therapeutic nihilism because it would be equally unethical not to offer treatment with proven efficacy.

A more complete interpretation of the Hippocratic injunction to do no harm can be found in the Hippocratic Corpus in Epidemics: “The physician must have two special objects in view with regard to disease, namely, to do good or to do no harm” (30).

From the perspective of the offender, the good may be freedom from obsessive sexual thoughts or a dominating sex drive, enabling participation in treatment programs (29). The fact that there are side effects to a treatment need not, in itself, necessarily be an absolute contraindication. There are many situations where a degree of harm is inflicted on patients to achieve a net benefit, like certain forms of surgery or cancer treatment. There is an intrinsic moral difference between intentionally inflicting harm and prescribing treatment that carries a risk of causing harm but has an expected net beneficial outcome.

Some professionals working with sex offenders have adopted a policy of treatment primarily directed at rehabilitation that embraces human rights as a core value. They recognize that a sex offender is also a human being in need of support, and that help should be given on the basis of general fundamental principles and values of medical ethics, such as compassion, respect for the individual, and a nonjudgmental attitude. This ensures autonomy in making informed voluntary decisions, nonmaleficence in avoiding harm to the offender, beneficence in ensuring that the welfare of the individual is the primary goal of treatment, and justice in that the offender is treated fairly, equitably, and in accordance with his or her rights (20, 31). The extension of human rights and related protections to sex offenders need not infringe on the public’s right to safety (32), and the objective of humane treatment must be carefully balanced against that (33).

With the more humane approach to sex offenders has also come greater understanding that the person behind the label is an individual with sexual deviance and (dynamic) offender characteristics that may be amenable to treatment (13, 15, 16). Recent treatment approaches that have found acceptance are the “good lives model” and the “risk-need-responsivity” model (34, 35), often combined with pharmacological treatment (14–16) depending on the psychological disposition of the offender.

A special category of sex offenders is made up of juveniles experiencing paraphiliac impulses with the emergence of hormonal puberty (36, 37). Here, the ethics of ADT are compounded by potential interference with the developmental course of puberty and the legality of informed consent. Experts agree that any use of ADT in this circumstance should be judicious and exceptional (36, 38, 39). With regard to side effects, a parallel may be drawn

with juvenile transsexuals whose hormonal puberty is halted for 2–4 yr and who, receiving cross-sex hormones later in puberty, show a near-normal catch-up of pubertal development (40).

Another special category is formed by people with intellectual disabilities. Their sexual behavior may be socially inappropriate to an extent that sometimes, although not always, amounts to sexual offending (41). In these situations as well, the rights of the individual must be carefully balanced against the rights of society before a decision is taken to provide ADT.

In the context of a rehabilitative approach to sex offenders, it is ethical to offer hormonal treatment to achieve a reduction of androgen action and potentially improve control of sexual impulses and desires that can help prevent recidivism. The physician’s aims are directed at the offender as a person in need of help and not primarily at the interests of the correctional system, which are legitimate but are not the physician’s main professional responsibility. In view of the multitudinous actions of androgens, side effects of hormonal interventions are probable and should not be underestimated. In this regard, the endocrinologist may play an advisory role so as to prevent or minimize undesired effects (for review, see Refs. 42 and 43). Obviously, considerations of whether ADT treatment is truly helpful (16), along with its long-term potential deleterious effects (42, 43), will weigh heavily in judging its ethical acceptability.

Patients have not traditionally been included in the decision-making process of medical practice and ethics, but increasing patient autonomy has become part of modern medicine, and there is no good reason not to present the ethical dilemma to candidates for ADT and openly discuss it with them. If we genuinely believe in patient autonomy, we must be prepared to concede that there is indeed little freedom of choice when long-term detention is the only alternative to androgen deprivation. A truly informed decision cannot be made unless this insight is fully shared with the offender. It goes without saying that psychiatric comorbidity may interfere with the capacity to give informed consent and with the legality of any consent that is given (42, 44).

Increasingly, sex offenders and others driven by unacceptable paraphilias may wish to explore the possibilities of ADT as a means of improving control of their impulses before they come into conflict with the law (45). It will be clear that any indication for ADT should also involve an expert mental health professional.

Aspects of Androgen Deprivation

Guidelines for the role of pharmacological agents in the treatment and management of paraphilia have been de-

veloped in conjunction with specific psychosocial and psychotherapeutic interventions (16). Double-blind, placebo-controlled studies of antiandrogens are virtually absent because of the practical difficulties of carrying them out.

The traditional approach to pharmacological treatment of sex offenders has been much like that of prostate cancer, where the aim is to reduce the biological action of androgens to an absolute minimum (46–48). A question is whether this is in fact necessary for the actual purpose of the treatment, which is a better control of sexual impulses (49, 50). It should be noted that sexual offenders often have a compulsive element to their aberrant behavior, not related to the action of testosterone.

The blood level of testosterone critical for normal male sexual function varies somewhat among individuals, although studies of a clinical nature indicate that on average it approximates the lower limit of the eugonadal reference range for young men (51–54). In an experimental study to determine dose/response relationships in young men, graded doses of testosterone had no differential effects on sexual function, visual-spatial cognition, and mood (55). A reduction of serum testosterone below the lower limit of reference values is necessary to achieve success in reducing recidivism, but it may not be necessary to reduce this to the extent of prostate cancer treatment.

Whether retaining some level of androgen action might have benefits in preventing or slowing the cumulative detrimental side effects of ADT is addressed in *Side Effects of Androgen Deprivation Treatment*. Ideally, the period of ADT should be as brief as possible (22). Paraphilia is, however, a chronic condition; for severe cases, a minimum ADT duration of 3 to 5 yr is necessary, and for mild cases, at least 2 yr (16). This span of time is sufficient for serious side effects to occur, although these are reversible when testosterone levels return to normal again. With recurrence of paraphiliac sexual fantasies, treatment should be reinstated (16). Because sex offenders are on average 20–30 yr younger than men with prostate cancer, they are less likely to be suffering comorbidities, although these must be tended to if present.

Pharmacological Reduction of Androgen Action

Three main classes of antiandrogens have been used for this purpose. For a review of the properties of these drugs, each with a specific pharmacological action, see Ref. 12.

Cyproterone acetate (CPA)

CPA has a dual action; it inhibits LH secretion due to its progestational properties, but it is also a weak partial

agonist and a competitive inhibitor of intracellular androgen receptors (56). It is associated with gynecomastia in 20% of men (56). Other reported possible adverse effects include liver dysfunction and adrenal suppression, particularly in the case of (female) adolescents (57), although not confirmed in a large-scale study (58). CPA is available in both oral and im injection formulations, although not in the United States.

In a brief (3-month) double-blind placebo-controlled study of 19 men with paraphiliac disorders, CPA significantly reduced sexual arousal, fantasy, and most importantly, self-reported sexual activity (59). Summaries of the efficacy of this medication in the treatment of sex offenders have been published (59, 60). In a review of seven studies involving 96 sex offenders treated with CPA and followed for up to 4.5 yr (average follow-up time was 3 yr), six studies reported a recidivism rate of 0%, and the seventh study reported a recidivism rate of 16.7% (61).

Medroxyprogesterone acetate (MPA)

Like CPA, MPA also has the important action of inhibiting LH secretion. In a review of eight studies of 452 male sex offenders treated with MPA and followed from 1 to 13 yr, recidivism rates (defined in a variety of ways across the studies) ranged from 1% to as high as 17% (62). In a double-blind, placebo-controlled study of 11 pedophiles who completed a 3-month treatment trial, the five men treated with MPA reported fewer sexual fantasies. However, no difference in other factors such as frequency of orgasm or quality of erection was found between groups (63).

GnRH agonists

A third means of decreasing circulating testosterone is the use of GnRH agonists. The best studied in sex offender research are leuprolide (64) and triptorelin (65), reviewed in Refs. 12, 48, and 66. One study involved nonblinded treatment of 30 men with paraphilias (25 of whom were pedophiles) using triptorelin. All men reported complete elimination of deviant fantasies and deviant sexual activities. This effect persisted for all 25 men who continued treatment for over 1 yr. During the study, five men stopped treatment for a variety of reasons (including in two cases the wish to have children). Of the three who stopped due to “side effects,” all were switched to CPA, but two subsequently reoffended (67). Usually studies comprise small groups of men (47).

Side Effects of ADT

Upon administration of drugs like MPA, CPA, and GnRH agonists, a profound decline in sex steroid levels follows,

TABLE 1. Estimated risks for selected side effects of ADT in men

Side effects	ADT duration	% Change or hazard ratio (Ref.)
Bone mineral density and fracture risk		
Bone mineral density	6 months	–3.5% (79, 80)
	12 months	–5.3% (79, 80)
	12 months	–3.3% (73)
	12 months	–4.9% and –6.8% (65)
Any fracture ^a	5 yr	1.45 (95% CI, 1.36–1.56) (74, 80)
Fracture resulting in hospitalization ^a	5 yr	1.66 (95% CI, 1.47–1.87) (74, 80)
Glucose and lipid metabolism		
Weight and body mass index	6 months	+0.8% (92, 95)
	11 months	+2.4% (91)
Fat body mass	3 months	+8.4% (91)
	11 months	+9.4% (72, 80)
Lean body mass	3 months	–2.8% (72)
	11 months	–2.7% (72, 80)
Muscle area	11 months	–3.2% (72, 80)
Total cholesterol level	6 months	+6.1% (92)
	11 months	+9.0% (89–91)
High-density lipoprotein cholesterol level	11 months	–11.3% (89–91)
Low-density lipoprotein cholesterol level	11 months	+7.3% (89–91)
Triglyceride level	6 months	+8.2% (92)
	11 months	+27% (89–91)
Fasting insulin level	3 months	+64% (90, 94)
Incident diabetes	4.6 yr	1.44 (95% CI, 1.34–1.55) (91, 94)
Cardiovascular disease/mortality		
Incident coronary heart disease	4.6 yr	1.16 (95% CI, 1.10–1.21) (93)
Incident myocardial infarction	4.6 yr	1.11 (95% CI, 1.01–1.21) (93)
Incident sudden cardiac death	4.6 yr	1.16 (95% CI, 1.05–1.27) (93)
Mood disturbances		
Depression (or other affective disorder)	4.3 yr	1.08 (95% CI, 1.02–1.15) (105)
Constitutional symptoms (e.g. fatigue, malaise, anorexia, abnormal weight gain, debility)	4.3 yr	1.17 (95% CI, 1.13–1.22) (105)

Data were extracted from studies on men treated for prostate cancer with androgen deprivation. Therefore, extrapolation to treatment of sex offenders has limited value. Adapted from E. J. Giltay and L. J. Gooren: Potential side effects of androgen deprivation treatment in sex offenders. *J Am Acad Psychiatry Law* 37:53–58, 2009 (43), with permission. © American Academy of Psychiatry and the Law.

^a Observed among those receiving nine or more doses of GnRH agonist in the first 12 months after diagnosis of prostate cancer.

not only of serum testosterone but also of estradiol, predominantly the product of peripheral aromatization of androgens, and a complete suppression of testosterone will also result in low serum estradiol. Yet estrogens are important in the male (68, 69). They have favorable effects on skeletal growth and bone maturation (69), brain function (70), and cardiovascular physiology (71). Estimated risks of ADT are presented in Table 1. Suggestions for monitoring are presented in Table 2.

Bone mineral density and fracture risk

Commencement of ADT treatment in adult men with advanced prostate cancer produces rapid bone loss of a magnitude comparable to the depletion of skeletal integrity in women after surgical ovariectomy or early menopause. Within 1 yr the density of lumbar spine bone decreases by about 5–10% (72–74), with further bone loss thereafter. Also lean body mass decreases upon ADT (by about 5%), which may increase the risk of falls adding to the risk of fractures. Sex steroid deficiency resulting from

treatment for prostate cancer will lead to microarchitectural decay, probably more closely linked to lack of testosterone than estradiol (75). Correlations between serum testosterone, estradiol, and SHBG have been demonstrated (76, 77), suggesting that beneficial effects on bone might result from less than complete suppression of testosterone.

A comparison of men with prostate cancer found that those who underwent ADT had a significant overall increased fracture risk of 23% [summary relative risk, 1.23; 95% confidence interval (95% CI), 1.10–1.38] compared with those who did not (78–80).

A recent study argues in favor of bone mineral density measurement and the use of alendronate in cases of osteoporosis before commencing ADT (81). Bisphosphonate treatments in men with hormone-sensitive prostate cancers slow bone resorption by their inhibitory effects on osteoclast activity effectively preventing bone loss associated with ADT, underscoring the importance of treating early to avoid this (82, 83).

TABLE 2. Recommended clinical assessment of men before the start of ADT and during follow-up

Risk assessment before the initiation of ADT
History taking: prior fractures, prior cardiovascular events, family history of osteoporosis and cardiovascular disease, alcohol consumption, and smoking habits
Rule out and/or treat affective disorders
Advise lifestyle modification, including weight-bearing exercise, healthy dietary pattern, and abstinence from smoking and excessive alcohol use
Physical examination: especially weight, height, waist circumference and blood pressure
Complete laboratory screening, with fasting glucose (to detect incident diabetes), lipid profiles, hemoglobin and hematocrit level
DEXA
Clinical assessment after the initiation of ADT
History taking and physical examination (at least every 6 months): especially check for signs and symptoms of weight gain, hypertension, hot flashes, depression, emotional disturbances, and other constitutional symptoms
Laboratory examination: fasting glucose, lipid profile, hemoglobin, and hematocrit level
DEXA (every 1 or 2 yr)

Adapted from E. J. Giltay and L. J. Gooren: Potential side effects of androgen deprivation treatment in sex offenders. *J Am Acad Psychiatry Law* 37:53–58, 2009 (43), with permission. © American Academy of Psychiatry and the Law. DEXA, Dual-energy x-ray absorptiometry.

Estrogens are probably more significant than androgens in maintaining bone mineral density (69, 84). Consequently, treatment that preserves the biological action of estrogens, such as bicalutamide (85), may be preferable in principle, although this will produce substantial gynecostasia due to unopposed estrogen action. However, there is no experience with drugs like bicalutamide in the treatment of sex offenders.

Selective estrogen receptor modulators with intrinsic estrogen activity (tamoxifen, toremifene) may be helpful (86). Denosumab is a fully human monoclonal IgG (2) antibody that binds to the receptor activator of nuclear factor- κ B ligand (RANKL) and inhibits bone resorption due to RANKL-mediated osteoclastogenesis. In Europe, sc denosumab is indicated for cancer treatment-induced bone loss in men and in postmenopausal women with breast cancer (87, 88).

Metabolic effects: glucose and lipid metabolism

The risks of developing atherosclerosis from ADT have been reviewed (89–92), particularly in the advisory of the American Heart Association (93). Men undergoing ADT for prostate cancer show that within 3 months significant metabolic changes have occurred (43% increase in fat mass and 26% increase in insulin levels) (94, 95). More recently, visceral fat accumulation was more closely linked to testosterone than to estradiol, with insulin resistance as

a secondary effect (96). ADT for prostate cancer generally takes place in elderly men, whereas the age range of sex offenders may be lower. In a 10-wk study of healthy lean men (23.2 ± 0.5 yr), suppression of testosterone by a GnRH analog was associated with a marked decrease in measures of whole body protein anabolism, decreased strength, decreased fat oxidation, and increased adiposity (97). Epidemiological prospective studies have examined the association between low testosterone levels in men and the subsequent development of diabetes type 2 over 7–10 yr. The odds of future diabetes were 1.58 for a decrease of 1 SD in free testosterone (4 ng/dl) (98). Low levels of testosterone are associated with the development of metabolic syndrome and diabetes in men. After 11 yr of follow-up, 147 of 702 men had developed metabolic syndrome, and 57 had diabetes. Men with total testosterone, calculated free testosterone, and SHBG levels in the lower fourth had a many times greater risk of developing metabolic syndrome and diabetes after adjustment for age (99). Another recent report came to a similar conclusion (100). The degree of suppression of serum testosterone may be an element in the development of metabolic syndrome and diabetes mellitus, and a nontotal suppression of testosterone may slow the occurrence of side effects of ADT.

As already pointed out in regard to bone mass, adding a selective estrogen receptor modulator like toremifene may help to reduce the negative effects of ADT treatment on serum lipids (101).

Statins lower blood low-density lipoprotein levels and reduce the risk of cardiovascular events serving as primary prevention. This has not only been found in patients with cardiac disease, but also in diabetics, in whom the first major cardiovascular events were reduced by 37% (102). Diet and physical activity may also be helpful in counteracting the effects of ADT (103).

Fertility

ADT leads to suppression of spermatogenesis. After hormonal regimens of male contraception, spermatogenesis recovers within 24 months of termination (104). Sperm cryostorage might also be offered.

Mood

Mood disturbance and depression are often associated with low androgen levels (105). Men receiving ADT may also experience decreases in cognitive function and self-esteem, as well as libido and sexual function (106, 107). For review, see Ref. 108. Aging and comorbid conditions may be codeterminants (109).

In the case of sex offenders receiving ADT, emotional disturbances, fatigue, memory difficulties, asthenia, lack

of drive and listlessness have been reported. The risk may be relatively small (56, 67) but should not be ignored. The effects of a depot of leuprolide acetate on mood have been tested in a double-blind, placebo-controlled trial in healthy men. Although testosterone levels were markedly suppressed, there were only slight increases in depressive symptoms on the group level, although a subgroup of men (10–15%) displayed clinically relevant increases (as assessed by the Beck Depression Inventory) (110). It is plausible that negative effects on mood induced by long-term hypogonadism are much more prevalent among sex offenders than in the selected group of healthy young men only treated for 4 wk. Presumably, mood disorders and depression will be diagnosed by the attending health professional, but it is pertinent to associate mood disorders with ADT.

Other complications

Hot flushes (and night sweats) occur, with varying intensity, in the majority (up to 80%) of men receiving ADT, which may reduce quality of life (67, 110, 111). Hemoglobin levels decline by about 10% (112, 113), usually not affecting health unless cardiac or pulmonary functions are marginal. ADT reduces sebaceous gland activity, which may lead to a dry skin and brittle nails (114). Itching and skin tears can be alleviated by topical application of moisturizing creams. Sexual hair growth decreases upon ADT (*i.e.* feminization) (67).

Potential other side effects encountered are migraine, leg (muscle) cramps, phlebitis, vertigo, elevation of blood pressure, gastrointestinal complaints, gall bladder stones, thromboembolic complications (deep vein thrombosis), tender breasts and, especially with the use of CPA, gynecomastia (115, 116).

Conclusion

ADT raises the threshold at which erotosexual imagery and sexual activity occur, and it may have a place in the treatment of unacceptable sexual behavior. ADT reduces recidivism when offered to sex offenders within a comprehensive context of psychotherapeutic treatment. It enables better control of sexual impulses. But unless it is provided on a voluntary basis, with respect for the basic human rights of the sex offender, ADT is a violation of physical integrity and is unethical. Sex offenders have the right to refuse ADT. As evident from the treatment of prostate cancers, ADT may have serious side effects that should be prevented or treated to ensure that they do not outweigh the positive aspects (43, 117, 118). At the very least, men about to undergo ADT should receive reliable

information and counseling on its effects and be carefully monitored for any complications of treatment, including the effects already mentioned as well as fatigue, sexual dysfunction, hot flushes, and anemia. In the treatment of androgen-sensitive prostate cancer, intermittent androgen deprivation has been experimented with as a way of limiting side effects (119). It would be worthwhile to study whether this approach might work in sex offenders. Selective androgen receptor modulators are a class of androgen receptor ligands that bind to androgen receptors and display tissue-selective activation of androgenic signaling. If a compound could be developed that retains its anabolic effects on bone and muscle but selectively does not exert androgen effects on libido (the brain) (120), this would be an important step forward.

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References

1. Bancroft J 2009 Human sexuality and its problems. 3rd ed. New York: Churchill Livingstone
2. Pfau JG 2009 Pathways of sexual desire. *J Sex Med* 6:1506–1533
3. Berlin FS 2008 Basic science and neurobiological research: potential relevance to sexual compulsivity. *Psychiatr Clin North Am* 31:623–642
4. Codispoti VL 2008 Pharmacology of sexually compulsive behavior. *Psychiatr Clin North Am* 31:671–679
5. Schober JM, Pfaff D 2007 The neurophysiology of sexual arousal. *Best Pract Res Clin Endocrinol Metab* 21:445–461
6. Laws DR, O'Donohue WT 2008 Sexual deviance. Theory, assessment, and treatment. New York: Guilford Press
7. 2000 Diagnostic and statistical manual of mental disorders (DSM-IV-TR). 4th ed. Washington DC: American Psychiatric Association
8. Fazel S, Sjöstedt G, Grann M, Långström N 2010 Sexual offending in women and psychiatric disorder: a national case-control study. *Arch Sex Behav* 39:161–167
9. Buvat J, Maggi M, Gooren L, Guay AT, Kaufman J, Morgentaler A, Schulman C, Tan HM, Torres LO, Yassin A, Zitzmann M 2010 Endocrine aspects of male sexual dysfunctions. *J Sex Med* 7:1627–1656
10. Bancroft J 2005 The endocrinology of sexual arousal. *J Endocrinol* 186:411–427
11. Jordan K, Fromberger P, Stolpman G, Muller JL 2 August 2011 The role of testosterone in sexuality and paraphilia-A neurobiological approach. Part I: Testosterone and sexuality. *J Sex Med* 10.1111/j.1743-6109.2011.02394.x

12. **Guay DR** 2009 Drug treatment of paraphilic and nonparaphilic sexual disorders. *Clin Ther* 31:1–31
13. **Fedoroff JP** 2009 The paraphilias. In: Gelder MG, ed. *New Oxford textbook of psychiatry*. 2nd ed. Oxford, UK: Oxford University Press; 832–842
14. **Schmucker M, Lösel F** 2008 Does sexual offender treatment work? A systematic review of outcome evaluations. *Psicothema* 20:10–19
15. **Hanson RK, Bourgon G, Helmus L, Hodgson S** 2009 The principles of effective correctional treatment also apply to sexual offenders. A meta-analysis. *Crim Justice Behav* 36:865–891
16. **Thibaut F, De La Barra F, Gordon H, Cosyns P, Bradford JM** 2010 The World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of paraphilias. *World J Biol Psychiatry* 11:604–655
17. **Ward T, Gannon TA** 2006 Rehabilitation, etiology, and self-regulation: the comprehensive good lives model of treatment for sexual offenders. *Aggress Violent Behav* 11:77–94
18. **Stinson JD, Sales BD, Becker JV** 2008 Sex offending. Causal theories to inform research, prevention, and treatment. American Psychological Association. Washington DC: SAGE Publications
19. **Saleh FM, Malin HM, Grudzinskas Jr AJ, Vitacco MJ** 2010 Paraphilias with co-morbid psychopathy: the clinical and legal significance to sex offender assessments. *Behav Sci Law* 28:211–223
20. **Ward T, Birgden A** 2007 Human rights and correctional clinical practice. *Aggress Violent Behav* 12:628–643
21. **Marshall WL, Marshall LE, Serran GE, O'Brien MD** 2011 Rehabilitating sexual offenders. A strength-based approach. Washington DC: American Psychological Association
22. **Gijs L, Gooren, L** 1996 Hormonal and psychopharmacological interventions in the treatment of paraphilias: an update. *J Sex Res* 33:273–290
23. **Krueger RB, Wexler R, Kaplan M, Saleh F** 2009 Orchiectomy. In: Saleh FM, Bradford JM, Grudzinskas AJ, Brodsky DJ, eds. *Sex offenders*. New York: Oxford University Press; 171–188
24. **Losel F, Schmucker M** 2005 The effectiveness of treatment for sexual offenders: a comprehensive meta-analysis. *J Exp Criminol* 1:1–29
25. **Jordan K, Fromberger P, Stolpman G, Müller JL** 28 July 2011 The role of testosterone in sexuality and paraphilia—A neurobiological approach. Part II: Testosterone and paraphilia. *J Sex Med* 10.1111/j.1743-6109.2011.02393.x
26. **Prentky RA** 1997 Arousal reduction in sexual offenders: a review of antiandrogen interventions. *Sex Abuse* 9:335–347
27. **Maletzky BM, Tolan A, McFarland B** 2006 The Oregon Depo-Provera program: a five-year follow-up. *Sex Abuse* 18:303–316
28. **Grubin D** 2008 Medical models and interventions in sexual deviance. In: Laws DR, O'Donohue WT, eds. *Sexual deviance: theory, assessment, and treatment*. 2nd ed. New York: Guilford Press; 594–610
29. **Grubin D, Beech A** 2010 Chemical castration for sex offenders. *BMJ* 340:c74
30. **Smith CM** 2005 Origin and uses of primum non nocere—above all, do no harm! *J Clin Pharmacol* 45:371–377
31. **Birgden A, Perlin ML** 2009 “Where the home in the valley meets the damp dirty prison”: A human rights perspective on therapeutic jurisprudence and the role of forensic psychologists in correctional settings. *Aggress Violent Behav* 14:256–263
32. **Ward T, Gannon TA, Birgden A** 2007 Human rights and the treatment of sex offenders. *Sex Abuse* 19:195–216
33. **Saleh FM, Grudzinskas Jr AJ, Malin HM, Dwyer RG** 2010 The management of sex offenders: perspectives for psychiatry. *Harv Rev Psychiatry* 18:359–368
34. **Mann RE, Hanson RK, Thornton D** 2010 Assessing risk for sexual recidivism: some proposals on the nature of psychologically meaningful risk factors. *Sex Abuse* 22:191–217
35. **Andrews DA, Bonta J** 2010 *The psychology of criminal conduct*. 5th ed. New Providence, NJ: LexisNexis Matthew Bender
36. **Bradford JM, Federoff P** 2008 Pharmacological treatment of the juvenile sex offender. In: Barbaree HE, Marshall WL, eds. *The juvenile sex offender*. New York: Guilford Press; 358–395
37. **Seto MC, Lalumière ML** 2010 What is so special about male adolescent sexual offending? A review and test of explanations through meta-analysis. *Psychol Bull* 136:526–575
38. **Sawyer AM, Borduin CM** 25 July 2011 Effects of multisystemic therapy through midlife: a 21.9-year follow-up to a randomized clinical trial with serious and violent juvenile offenders. *J Consult Clin Psychol* 10.1037/a0024862
39. **Dwyer RG, Letourneau EJ** 2011 Juveniles who sexually offend: recommending a treatment program and level of care. *Child Adolesc Psychiatr Clin N Am* 20:413–429
40. **Delemarre-van de Waal HA, Cohen-Kettenis PT** 2006 Clinical management of gender identity disorder in adolescents: a protocol on psychological and paediatric endocrinology aspects. *Eur J Endocrinol* 155:S131–S137
41. **Sajith SG, Morgan C, Clarke D** 2008 Pharmacological management of inappropriate sexual behaviours: a review of its evidence, rationale and scope in relation to men with intellectual disabilities. *J Intellect Disabil Res* 52:1078–1090
42. **Birgden A, Cuccolo H** 2011 The treatment of sex offenders: evidence, ethics, and human rights. *Sex Abuse* 23:295–313
43. **Giltay EJ, Gooren LJ** 2009 Potential side effects of androgen deprivation treatment in sex offenders. *J Am Acad Psychiatry Law* 37:53–58
44. **Harrison K, Rainey B** 2011 Morality and legality in the use of anti-androgenic pharmacotherapy with sex offenders. In: Boer D, et al., eds. *International perspectives on the assessment and treatment of sexual offenders theory, practice and research*. Chichester, UK: Wiley-Blackwell; 627–654
45. **Jones N, Pelissier B, Klein-Saffran J** 2006 Predicting sex offender treatment entry among individuals convicted of sexual offense crimes. *Sex Abuse* 18:83–98
46. **Perachino M, Cavalli V, Bravi F** 2010 Testosterone levels in patients with metastatic prostate cancer treated with luteinizing hormone-releasing hormone therapy: prognostic significance? *BJU Int* 105:648–651
47. **Schober JM, Kuhn PJ, Kovacs PG, Earle JH, Byrne PM, Fries RA** 2005 Leuprolide acetate suppresses pedophilic urges and arousability. *Arch Sex Behav* 34:691–705
48. **Schober JM, Byrne PM, Kuhn PJ** 2006 Leuprolide acetate is a familiar drug that may modify sex-offender behaviour: the urologist's role. *BJU Int* 97:684–686
49. **Briken P, Kafka MP** 2007 Pharmacological treatments for paraphilic patients and sexual offenders. *Curr Opin Psychiatry* 20:609–613
50. **Krueger RB, Kaplan MS** 2002 Behavioral and psychopharmacological treatment of the paraphilic and hypersexual disorders. *J Psychiatr Pract* 8:21–32
51. **Gooren LJ** 1987 Androgen levels and sex functions in testosterone-treated hypogonadal men. *Arch Sex Behav* 16:463–473
52. **Kelleher S, Conway AJ, Handelsman DJ** 2004 Blood testosterone threshold for androgen deficiency symptoms. *J Clin Endocrinol Metab* 89:3813–3817
53. **Zitzmann M, Faber S, Nieschlag E** 2006 Association of specific symptoms and metabolic risks with serum testosterone in older men. *J Clin Endocrinol Metab* 91:4335–4343
54. **Bagatell CJ, Heiman JR, Rivier JE, Bremner WJ** 1994 Effects of endogenous testosterone and estradiol on sexual behavior in normal young men. *J Clin Endocrinol Metab* 78:711–716
55. **Bhasin S, Woodhouse L, Casaburi R, Singh AB, Bhasin D, Berman N, Chen X, Yarasheski KE, Magliano L, Dzekov C, Dzekov J, Bross R, Phillips J, Sinha-Hikim I, Shen R, Storer TW** 2001 Testosterone dose-response relationships in healthy young men. *Am J Physiol Endocrinol Metab* 281:E1172–E1181
56. **Neumann F, Kalmus J** 1991 Cyproterone acetate in the treatment of sexual disorders: pharmacological base and clinical experience. *Exp Clin Endocrinol* 98:71–80

57. Cremoncini C, Vignati E, Libroia A 1976 Treatment of hirsutism and acne in women with two combinations of cyproterone acetate and ethinylestradiol. *Acta Eur Fertil* 7:299–314
58. Heinemann LA, Will-Shahab L, van Kesteren P, Gooren LJ 1997 Safety of cyproterone acetate: report of active surveillance. *Pharmacoepidemiol Drug Saf* 6:169–178
59. Bradford JM, Pawlak A 1993 Double-blind placebo crossover study of cyproterone acetate in the treatment of the paraphilias. *Arch Sex Behav* 22:383–402
60. Bradford JM 2000 The treatment of sexual deviation taking a pharmacological approach. *J Sex Res* 37:248–257
61. Appelt M, Floru L 1974 [The effect on sexuality of cyproterone acetate]. *Int Pharmacopsychiatry* 9:61–76
62. Grossman LS, Martis B, Fichtner CG 1999 Are sex offenders treatable? A research overview. *Psychiatr Serv* 50:349–361
63. Hucker S, Langevin R, Bain J 1988 A double-blind trial of sex drive lowering medication in pedophiles. *Ann Sex Res* 1:227–242
64. Krueger RB, Kaplan MS 2001 Depot-leuprolide acetate for treatment of paraphilias: a report of twelve cases. *Arch Sex Behav* 30:409–422
65. Rösler A, Witzum E 2000 Pharmacotherapy of paraphilias in the next millennium. *Behav Sci Law* 18:43–56
66. Briken P, Hill A, Berner W 2003 Pharmacotherapy of paraphilias with long-acting agonists of luteinizing hormone-releasing hormone: a systematic review. *J Clin Psychiatry* 64:890–897
67. Rösler A, Witzum E 1998 Treatment of men with paraphilia with a long-acting analogue of gonadotropin-releasing hormone. *N Engl J Med* 338:416–422
68. Rochira V, Granata AR, Madeo B, Zirilli L, Rossi G, Carani C 2005 Estrogens in males: what have we learned in the last 10 years? *Asian J Androl* 7:3–20
69. Khosla S 2010 Update on estrogens and the skeleton. *J Clin Endocrinol Metab* 95:3569–3577
70. Dumitriu D, Rapp PR, McEwen BS, Morrison JH 2010 Estrogen and the aging brain: an elixir for the weary cortical network. *Ann NY Acad Sci* 1204:104–112
71. Luczak ED, Leinwand LA 2009 Sex-based cardiac physiology. *Annu Rev Physiol* 71:1–18
72. Smith MR 2002 Osteoporosis during androgen deprivation therapy for prostate cancer. *Urology* 60:79–85; discussion 86
73. Greenspan SL, Coates P, Sereika SM, Nelson JB, Trump DL, Resnick NM 2005 Bone loss after initiation of androgen deprivation therapy in patients with prostate cancer. *J Clin Endocrinol Metab* 90:6410–6417
74. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS 2005 Risk of fracture after androgen deprivation for prostate cancer. *N Engl J Med* 352:154–164
75. Hamilton EJ, Ghasem-Zadeh A, Gianatti E, Lim-Joon D, Bolton D, Zebaze R, Seeman E, Zajac JD, Grossmann M 2010 Structural decay of bone microarchitecture in men with prostate cancer treated with androgen deprivation therapy. *J Clin Endocrinol Metab* 95:E456–E463
76. Araujo AB, Travison TG, Leder BZ, McKinlay JB 2008 Correlations between serum testosterone, estradiol, and sex hormone-binding globulin and bone mineral density in a diverse sample of men. *J Clin Endocrinol Metab* 93:2135–2141
77. Rucker D, Ezzat S, Diamandi A, Khosravi J, Hanley DA 2004 IGF-I and testosterone levels as predictors of bone mineral density in healthy, community-dwelling men. *Clin Endocrinol (Oxf)* 60:491–499
78. Taylor LG, Canfield SE, Du XL 2009 Review of major adverse effects of androgen-deprivation therapy in men with prostate cancer. *Cancer* 115:2388–2399
79. Alibhai SM, Duong-Hua M, Cheung AM, Sutradhar R, Warde P, Fleshner NE, Paszat L 2010 Fracture types and risk factors in men with prostate cancer on androgen deprivation therapy: a matched cohort study of 19,079 men. *J Urol* 184:918–923
80. Saylor PJ, Kaufman DS, Michaelson MD, Lee RJ, Smith MR 2010 Application of a fracture risk algorithm to men treated with androgen deprivation therapy for prostate cancer. *J Urol* 183:2200–2205
81. Ito K, Elkin EB, Girotra M, Morris MJ 2010 Cost-effectiveness of fracture prevention in men who receive androgen deprivation therapy for localized prostate cancer. *Ann Intern Med* 152:621–629
82. Saad F, Abrahamsson PA, Miller K 2009 Preserving bone health in patients with hormone-sensitive prostate cancer: the role of bisphosphonates. *BJU Int* 104:1573–1579
83. Campbell SC, Bhoopalam N, Moritz TE, Pandya M, Iyer P, Vanveldhuizen P, Ellis NK, Thottapurathu L, Garewal H, Warren SR, Friedman N, Reda DJ 2010 The use of zoledronic acid in men receiving androgen deprivation therapy for prostate cancer with severe osteopenia or osteoporosis. *Urology* 75:1138–1143
84. Vandenberg L, Ohlsson C 2010 Sex steroid metabolism in the regulation of bone health in men. *J Steroid Biochem Mol Biol* 121:582–588
85. Wadhwa VK, Weston R, Parr NJ 2011 Bicalutamide monotherapy preserves bone mineral density, muscle strength and has significant health-related quality of life benefits for osteoporotic men with prostate cancer. *BJU Int* 107:1923–1929
86. Smith MR, Morton RA, Barnette KG, Sieber PR, Malkowicz SB, Rodriguez D, Hancock ML, Steiner MS 2010 Toremifene to reduce fracture risk in men receiving androgen deprivation therapy for prostate cancer. *J Urol* 184:1316–1321
87. Smith MR, Egerdie B, Hernández Toriz N, Feldman R, Tammela TL, Saad F, Heracek J, Szwedowski M, Ke C, Kupic A, Leder BZ, Goessl C 2009 Denosumab in men receiving androgen-deprivation therapy for prostate cancer. *N Engl J Med* 361:745–755
88. Muir VJ, Scott LJ 2010 Denosumab: in cancer treatment-induced bone loss. *BioDrugs* 24:379–386
89. Shahani S, Braga-Basaria M, Basaria S 2008 Androgen deprivation therapy in prostate cancer and metabolic risk for atherosclerosis. *J Clin Endocrinol Metab* 93:2042–2049
90. Basaria S 2008 Androgen deprivation therapy, insulin resistance, and cardiovascular mortality: an inconvenient truth. *J Androl* 29:534–539
91. Haseen F, Murray LJ, Cardwell CR, O'Sullivan JM, Cantwell MM 2010 The effect of androgen deprivation therapy on body composition in men with prostate cancer: systematic review and meta-analysis. *J Cancer Surviv* 4:128–139
92. Nishiyama T, Ishizaki F, Anraku T, Shimura H, Takahashi K 2005 The influence of androgen deprivation therapy on metabolism in patients with prostate cancer. *J Clin Endocrinol Metab* 90:657–660
93. Levine GN, D'Amico AV, Berger P, Clark PE, Eckel RH, Keating NL, Milani RV, Sagalowsky AI, Smith MR, Zakai N 2010 Androgen-deprivation therapy in prostate cancer and cardiovascular risk: a science advisory from the American Heart Association, American Cancer Society, and American Urological Association: endorsed by the American Society for Radiation Oncology. *CA Cancer J Clin* 60:194–201
94. Smith MR, Lee H, Nathan DM 2006 Insulin sensitivity during combined androgen blockade for prostate cancer. *J Clin Endocrinol Metab* 91:1305–1308
95. Galvão DA, Spry NA, Taaffe DR, Newton RU, Stanley J, Shannon T, Rowling C, Prince R 2008 Changes in muscle, fat and bone mass after 36 weeks of maximal androgen blockade for prostate cancer. *BJU Int* 102:44–47
96. Hamilton EJ, Gianatti E, Strauss BJ, Wentworth J, Lim-Joon D, Bolton D, Zajac JD, Grossmann M 2011 Increase in visceral and subcutaneous abdominal fat in men with prostate cancer treated with androgen deprivation therapy. *Clin Endocrinol (Oxf)* 74:377–383
97. Mauras N, Hayes V, Welch S, Rini A, Helgeson K, Dokler M, Veldhuis JD, Urban RJ 1998 Testosterone deficiency in young men: marked alterations in whole body protein kinetics, strength, and adiposity. *J Clin Endocrinol Metab* 83:1886–1892

98. **Stellato RK, Feldman HA, Hamdy O, Horton ES, McKinlay JB** 2000 Testosterone, sex hormone-binding globulin, and the development of type 2 diabetes in middle-aged men: prospective results from the Massachusetts Male Aging Study. *Diabetes Care* 23:490–494
99. **Laaksonen DE, Niskanen L, Punnonen K, Nyysönen K, Tuomainen TP, Valkonen VP, Salonen R, Salonen JT** 2004 Testosterone and sex hormone-binding globulin predict the metabolic syndrome and diabetes in middle-aged men. *Diabetes Care* 27:1036–1041
100. **Li C, Ford ES, Li B, Giles WH, Liu S** 2010 Association of testosterone and sex hormone-binding globulin with metabolic syndrome and insulin resistance in men. *Diabetes Care* 33:1618–1624
101. **Smith MR, Malkowicz SB, Chu F, Forrest J, Sieber P, Barnette KG, Rodriguez D, Steiner MS** 2008 Toremifene improves lipid profiles in men receiving androgen-deprivation therapy for prostate cancer: interim analysis of a multicenter phase III study. *J Clin Oncol* 26:1824–1829
102. **Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, Thomason MJ, Mackness MI, Charlton-Mennys V, Fuller JH** 2004 Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 364:685–696
103. **Haseen F, Murray LJ, O'Neill RE, O'Sullivan JM, Cantwell MM** 2010 A randomised controlled trial to evaluate the efficacy of a 6 month dietary and physical activity intervention for prostate cancer patients receiving androgen deprivation therapy. *Trials* 11:86
104. **Liu PY, Swerdloff RS, Christenson PD, Handelsman DJ, Wang C** 2006 Rate, extent, and modifiers of spermatogenic recovery after hormonal male contraception: an integrated analysis. *Lancet* 367:1412–1420
105. **Seidman SN** 2006 Normative hypogonadism and depression: Does 'andropause' exist? *Int J Impot Res* 18:415–422
106. **Cherrier MM, Aubin S, Higano CS** 2009 Cognitive and mood changes in men undergoing intermittent combined androgen blockade for non-metastatic prostate cancer. *Psychooncology* 18:237–247
107. **Mottet N, Prayer-Galetti T, Hammerer P, Kattan MW, Tunn U** 2006 Optimizing outcomes and quality of life in the hormonal treatment of prostate cancer. *BJU Int* 98:20–27
108. **Elliott S, Latini DM, Walker LM, Wassersug R, Robinson JW** 2010 Androgen deprivation therapy for prostate cancer: recommendations to improve patient and partner quality of life. *J Sex Med* 7:2996–3010
109. **Shahinian VB, Kuo YF, Freeman JL, Goodwin JS** 2006 Risk of the "androgen deprivation syndrome" in men receiving androgen deprivation for prostate cancer. *Arch Intern Med* 166:465–471
110. **Schmidt PJ, Berlin KL, Danaceau MA, Neeren A, Haq NA, Roca CA, Rubinow DR** 2004 The effects of pharmacologically induced hypogonadism on mood in healthy men. *Arch Gen Psychiatry* 61:997–1004
111. **Sharifi N, Gulley JL, Dahut WL** 2005 Androgen deprivation therapy for prostate cancer. *JAMA* 294:238–244
112. **Timilshina N, Hussain S, Breunis H, Alibhai SM** 16 October 2010 Predictors of hemoglobin decline in non-metastatic prostate cancer patients on androgen deprivation therapy: a matched cohort study. *Support Care Cancer* 10.1007/s00520-010-1023-6
113. **Choo R, Chander S, Danjoux C, Morton G, Pearce A, Deboer G, Szumacher E, Loblaw A, Cheung P, Woo T** 2005 How are hemoglobin levels affected by androgen deprivation in non-metastatic prostate cancer patients? *Can J Urol* 12:2547–2552
114. **Giltay EJ, Gooren LJ** 2000 Effects of sex steroid deprivation/administration on hair growth and skin sebum production in transsexual males and females. *J Clin Endocrinol Metab* 85:2913–2921
115. **Meyer 3rd WJ, Cole C, Emory E** 1992 Depo provera treatment for sex offending behavior: an evaluation of outcome. *Bull Am Acad Psychiatry Law* 20:249–259
116. **Bradford JM** 2001 The neurobiology, neuropharmacology, and pharmacological treatment of the paraphilias and compulsive sexual behaviour. *Can J Psychiatry* 46:26–34
117. **Berlin FS** 2009 Risk/benefit ratio of androgen deprivation treatment for sex offenders. *J Am Acad Psychiatry Law* 37:59–62
118. **Grossmann M, Zajac JD** 2011 Androgen deprivation therapy in men with prostate cancer: how should the side effects be monitored and treated? *Clin Endocrinol (Oxf)* 74:289–293
119. **Shore ND, Crawford ED** 2010 Intermittent androgen deprivation therapy: redefining the standard of care? *Rev Urol* 12:1–11
120. **Bhasin S, Jasuja R** 2009 Selective androgen receptor modulators as function promoting therapies. *Curr Opin Clin Nutr Metab Care* 12:232–240