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Persistent Sexual, Emotional, and Cognitive Impairment Post-Finasteride: A Survey of Men Reporting Symptoms

Christine Anne Ganzer, PhD[1], Alan Roy Jacobs, MD[1], and Farin Iqbal[1]

Abstract

Finasteride is a synthetic 5-α reductase inhibitor, which prevents the conversion of testosterone to dihydrotestosterone and has been used for more than 20 years in the treatment of male pattern hair loss. Randomized, controlled trials have associated finasteride with both reversible and persistent adverse effects. In this pilot study, we sought to characterize sexual and nonsexual adverse effects that men reported experiencing at least 3 months after stopping the medication. Based on previous research on persistent side effects of finasteride, we constructed an Internet survey targeting six domains: physical symptoms, sexual libido, ejaculatory disorders, disorders of the penis and testes, cognitive symptoms, and psychological symptoms and was e-mailed to patients who reported experiencing symptoms of side effects of finasteride. Responses from 131 generally healthy men (mean age, 24 years) who had taken finasteride for male pattern hair loss was included in the analysis. The most notable finding was that adverse effects persisted in each of the domains, indicating the possible presence of a "post-finasteride syndrome."

Keywords

andrology, erectile dysfunction, behavioral research, sexual health, cognitive performance

Introduction

Androgenic alopecia, also referred to as male pattern hair loss (MPHL), is the most common cause of hair loss and affects up to 70% of men and 40% of women at some point in their lives (McElwee & Shapiro, 2012). Although the overall etiology is not fully understood, it is known that genetics and environment both have a role—that male hormones are involved in triggering follicular changes in genetically susceptible men.

Testosterone is synthesized in testicular Leydig cells in response to pituitary-derived luteinizing hormone. Once in circulation, testosterone uptake occurs in several target tissues, enters cells, and is converted by the enzyme 5-α reductase into its more active form, dihydrotestosterone (DHT). The androgenic properties of DHT are much more potent than testosterone; it is responsible for many important functions including sexual differentiation in the womb and male secondary sexual characteristics.

Research has reported that hair follicles convert testosterone into DHT and men who are thought to be genetically sensitive experience MPHL (Lam, 2013).The dermal papilla is central to the hair follicle and responsible for cell differentiation and the growth of new follicles. It is also in direct contact with capillaries supplying nutrient-rich blood essential for hair growth. Men have a large number of androgen receptors in the skin, which are responsible for male hair patterns on the body and on the face, and DHT has been reported to undermine the absorption of essential nutrients needed for hair growth (Larsen, 2012). Normal hair growth involves phases of resting and growing. However, without proper nutrition the hair follicle's stages of resting are drawn out, causing its progressive shrinking. Affected hair follicles become more sensitive to DHT, causing miniaturization, in which hair becomes lighter and finer and enters the vellus stage. Vellus hair is normally found on the arms and is barely visible.

There are relatively few treatments available for MPHL, which for some men can be quite psychologically distressing, particularly if it is excessive or occurs early in life. The most commonly prescribed medication for MPHL is finasteride (Propecia®), a synthetic 5-α reductase inhibitor. Biochemically there are three 5 α-reductase isotype enzymes, and it is established that they are all

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present in various structures of the brain (Aumuller et al., 1996; Azzouni, Godoy, Li, & Mohler, 2011; Eicheler, Dreher, Hoffmann, Happle, & Aumuller, 1995). Finasteride mechanism of action blocks the conversion of testosterone to DHT and has been used for more than 20 years in the treatment of MPHL. A considerable number of men have reported intolerable adverse effects after initiating finasteride therapy and continue to experience these effects after stopping the medication (Irwig, 2012b). These peripheral or secondary effects have undesirable consequences that are collectively becoming known as post-finasteride syndrome (PFS; Post Finasteride Syndrome Foundation, 2012).

Many clinicians are unaware of the scope of the persistent physical and psychological adverse effects of finasteride. Symptoms range from minor to severe. Physical effects can include chronic fatigue, gynecomastia (the development of breasts), muscle atrophy, thinning skin, and penile and scrotal shrinkage. Sexual changes include decreased libido, intermittent erectile dysfunction, and impotence. Cognitive effects include a difficulty in maintaining attention and an overarching "brain fog." Psychological effects can include emotional sensitivity, depressed affect, and excessive anxiety leading to functional decline.

There is a limited amount of research into the long-term effects of finasteride. Much of the work being done is focused on individual symptoms—in particular sexual dysfunction. In a systematic review researchers evaluated 12 randomized clinical control trials that focused on the efficacy and safety of finasteride therapy (Mella, Perret, Manzotti, Catalano, & Guyatt, 2010). Results of the review concluded that moderate evidence exists that the daily use of finasteride slows MPHL by improving hair count; however, there may be an associated increase in the risk for sexual dysfunction. In a recent study, researchers sought to characterize the type and duration of persistent sexual adverse effects associated with the use of finasteride for MPHL. The researchers conducted standardized interviews (N = 71) in a group of otherwise healthy men (age 21-46 years) who reported new symptoms that endured for at least 3 months after stopping the medication (Irwig & Kolukula, 2011). The mean duration of finasteride use in this sample was 28 months; 94% reported low libido; 92%, erectile dysfunction, 92%, decreased arousal; and 69%, difficulty achieving orgasm. The authors concluded that physicians who treat MPHL with finasteride should forewarn their patients of the potential risks of persistent sexual adverse effects associated with finasteride use.

In another study investigators prospectively followed otherwise healthy men younger than 40 years (N = 54) who reported persistent sexual adverse effects associated with finasteride; they sought to determine whether the adverse effects resolved or endured over time (Irwig, 2012b). The men were assessed at 3 months after stopping the medication and again after 9 to 16 months. The primary outcome measured was sexual function—libido, arousal, erectile function, ability to reach orgasm, and orgasm satisfaction—via the Arizona Sexual Experience Scale. The scale has a reported sensitivity and specificity of 82% and 90%, respectively, to identify sexual dysfunction (McGahuey et al., 2000). At the time of reassessment, 96% of subjects reported continued sexual adverse effects and 89% met the Arizona Sexual Experience Scale criteria for sexual dysfunction. The study concluded that most men who had developed persistent sexual side effects continued to have symptoms for many months and even years, despite discontinuation of the drug (Irwig, 2012b).

Several studies have explored the effects of finasteride on male fertility (Hotaling, 2013; Ricci et al., 2012; Samplaski, Lo, Grober, & Jarvi, 2013). Researchers concluded that in some men even low-dose finasteride can reduce sperm counts (Samplaski et al., 2013).

Irwig (2012a) reported significantly higher rates of depressed affect and suicidal ideation among former users of finasteride for MPHL (75%) than in controls (10%; $p < .0001$). Additionally, moderate to severe depressive symptoms were present in 64% of the finasteride group and in 0% of the controls; 44% of the former finasteride users experienced suicidal thoughts, as did only 3% of the controls ($p < .0001$; Irwig, 2012a). It is thought that neurosteroids and neuroactive steroids play a significant role in neuroprotection, augment memory, and have anxiolytic and antidepressant properties (Dubrovsky, 2006). Production of neurosteroids occurs in the central nervous system from adrenal and gonadal steroids (Reddy, 2010). The synthesis of these endogenous regulators requires the presence of 5-α reductase, and finasteride has been shown to inhibit its biosynthesis (Dusková, Hill, Hanus, Matousková, & Stárka, 2009). Depression has also been associated with the dysregulation of neurosteroids and androgen deficiency (Rizvi et al., 2010; Traish, Hassani, Guay, Zitzmann, & Hansen, 2011).

There are a limited number of studies that have explored the effects of testosterone on brain activity. However, the role of testosterone in brain organization and sexual development is established as well as its importance as a cognitive modulator in the brain either by being converted to DHT and binding to androgen receptors or being transformed into estrogen by aromatase enzymes (Beauchet, 2006; Hampson, 1995; Janowsky, 2006). Androgen and aromatase receptors are found in areas of the brain such as the hippocampus and amygdala and are involved in both learning and memory (Janowsky, 2006). Finasteride acts to inhibit the conversion of testosterone to DHT thereby changing its circulating levels or

bioavailibity (Kaufman et al., 1998). Variations in testosterone levels have been associated with changes in cognitive performance with mixed results (Holland, Bandelow, & Hogervorst, 2011; Janowsky, 2006). In a population-based sample, researchers evaluated cognitive performance and testosterone levels among 1,276 women and 1,107 men. In this study, there was a positive association between cognitive performance and higher levels of free testosterone in both men and women (Thilers, MacDonald, & Herlitz, 2006). It remains unclear as to the role of finasteride and the development of cognitive changes that are reported after stopping the medication and further investigation may be warranted.

Aims

To our knowledge no studies have sought to characterize clinically the global syndrome that some men experience after initiating and stopping finasteride therapy for MPHL. The researchers therefore set out in this pilot study to explore the extent to which generally healthy men with a recent history of taking finasteride for MPHL experience persistent physical, psychological, and cognitive effects after stopping the medication.

Method

Design

A web-based survey was constructed after conducting an extensive literature search of MEDLINE (restricted to the years 1995-2013) using the key words *finasteride, sexual dysfunction, 5-α reductase, male pattern hair loss, Propecia*, and *side effects*. Self-reported symptoms were also incorporated from more than 100 patients in one of the authors' private practices. Questions on demographic characteristics (e.g., age, race and ethnicity, and general health) were included, as were questions on dose and duration of finasteride use and whether the participant was currently taking the drug. Questions were asked about symptom onset after starting and stopping therapy. Symptom onset was characterized as beginning immediately after initiating finasteride, 3 to 6 months or 6 to 12 months into the therapy, or never while taking finasteride. Physical symptoms included were gynecomastia, fatigue, muscular atrophy, and skin-related changes as were several questions pertaining to sexual libido, ejaculatory disorders, and changes to the penis and testes (specifically, penile and testicular shrinkage). Sexual adverse effects included on the survey were loss of morning erections, intermittent erectile dysfunction, and impotence. To assess cognitive side effects questions pertaining to cognitive impairment and psychological sequelae, including insomnia and suicidal ideation were included. The survey asked about the type of medical care men sought out for symptoms and about satisfaction with clinical assessment and treatments offered. The investigators were interested in whether subjects were hopeful that they would recover from their symptoms and asked them to qualitatively tell us anything else that they thought was important to their experience of taking finasteride for MPHL.

Participants

Subjects were recruited from two sources. First, an e-mail link to the online questionnaire was sent to 100 patients who had sought medical treatment at the office of one of the authors for persistent adverse effects (lasting 3 months or longer) related to the use of finasteride to treat MPHL. Second, the link was posted on Propeciahelp.com, an online forum for exchange of information about unresolved adverse effects of finasteride. The institutional review board of the City University New York, Hunter College, approved the study. Inclusion criteria for participation were the following: subjects were male, age 18 years or older, had taken finasteride for MPHL, and had experienced persistent adverse effects after taking the medication for at least 3 months. Exclusion criteria were a history of baseline sexual dysfunction or psychiatric condition. Subjects were provided a written consent form after accessing a link informing them that by completing the questionnaire they consented to participate. To minimize nonresponse bias a reminder was sent out 4 weeks after sending out the initial survey.

Results

A total of 149 surveys were retrieved with 18 excluded because they were less than 70% complete. The overall response rate was 88% (n = 131). Survey data were entered and statistical analysis was performed using SPSS software (IBM, Armonk, NY). Descriptive statistics were used to delineate the men's sociodemographic and health-related characteristics. Our analysis included 131 surveys. A significant proportion (n = 105, 80%) of the sample were collected from patients that were evaluated for persistent side effects after taking finasteride for more than 3 months and were seen as private patients in one of the authors' clinical practice. Participants were men, ages 21 to 62 years (mean, 24 years; SD = 8.7). See Table 1 for sample demographics.

Most participants (n = 124, 95%) had stopped taking the medication at the time of their participation. See Table 2 for data on duration of finasteride use and time since stopping the therapy. Overall, 93% (n = 121) of the sample reported that they had taken the 1-mg dose of finasteride; 84% (n = 108) reported that they had no symptoms while taking the medication but that symptom onset

Table 1. Subject Demographics (*N* = 131).

	n (%)
Mean age in years (range)	24 (21-62)
Race and ethnicity	
White	92 (70)
Latino	16 (12)
Asian	8 (6)
Other	15 (12)

Table 2. Duration of Finasteride Use and Discontinuation (*N* = 131).

	Duration of finasteride use, *n* (%)	Time since stopping finasteride, *n* (%)
≥3 months	31 (24)	17 (13)
4-7 months	15 (11)	11 (8)
8-12 months	13 (10)	22 (17)
>12 months	72 (55)	81 (62)

began (*n* = 89, 68%) immediately after discontinuing the medication. Study questions asked if they had taken the medication on more than one occasion and whether they experienced symptoms intermittently while they were off the medication and identified that 52% (*n* = 68) experienced symptoms. More than half of men reported that symptoms came on gradually over time while on the medication (*n* = 72, 55%).

Symptoms were divided into six categories: physical, sexual, ejaculatory, penile and testicular, cognitive, and psychological. As reported in Table 3, men reported physical symptoms that included fatigue, changes in musculature and skin texture and tone, and enlarged breasts. A greater proportion reported sexual dysfunction, including changes in libido, loss of morning erections, erectile dysfunction, and anhedonia in sex. Shrinkage of the penis and scrotum were reported, as well as changes in sensation. Behavioral and psychiatric symptoms were reported, as well, including memory and attentional disturbances, increased anxiety, and depressed mood. A significant number of respondents reported that they had been suicidal and felt a loss of hope. As to medical care sought out once symptoms appeared, participants said that they initially saw either an urologist (*n* = 50, 38%) or a primary care or internal medicine provider (*n* = 81, 62%). Many said their physician was unaware of the possible relationship between finasteride and their presenting symptoms. Respondents described that their physicians generally attributed physical symptoms as being psychological in nature and encouraged them to seek out psychiatric consultation (*n* = 53, 69%). Overall, men reported that they were frustrated and dissatisfied with the medical care that they received and their physicians' lack of awareness and recognition of their symptoms as being valid (*n* = 121, 93%).

Discussion

Research describing the global clinical impact of finasteride on men's physical, cognitive, and psychological health is limited; many studies target only individual symptoms. The aim of this pilot study were to describe the overall types and characteristics of symptoms that men experienced after initiating and stopping finasteride therapy for MPHL and to describe whether the constellation of symptoms might constitute a "post-finasteride syndrome."

Men reported several physical side effects that they believed were associated with finasteride use. Approximately 70% reported gynecomastia, or the enlargement of breast tissue. Previous research supports that finasteride at higher levels has effects on breast tissue (Kaufman et al., 1998). The U.S. Food and Drug Administration reported the observation of gynecomastia in 214 men who had taken finasteride (5 mg, as Proscar) from 1992 to 1995 for the treatment of benign prostatic hypertrophy (Green, Wysowski, & Fourcroy, 1996) It is postulated that 5-α reductase inhibitors may, through the inhibition of DHT synthesis, alter the metabolism of testosterone in the direction of estradiol and change the ratio of estrogen to androgen, leading to gynecomastia (Traish et al., 2011). More than two-thirds of our respondents reported increased lethargy, feelings of listlessness, and lack of motivation. Several studies refer to symptoms of lethargy in men who have taken finasteride for either benign prostatic hypertrophy or MPHL, although whether the lethargy is related to the use of finasteride or to a preexisting psychological condition remains unclear (Irwig & Kolukula, 2011; Traish et al., 2011).

A majority of our participants reported changes to the skin, especially dry skin. Androgen receptors in the skin convert testosterone via 5-α reductase to DHT, which is known to stimulate sebum production (Lai, Chang, Lai, Chen, & Chang, 2012; Seo et al., 2014). The investigators hypothesized that as finasteride blocks the conversion of testosterone to DHT, it may also block the production of sebum and result in dry skin.

Persistent sexual side effects were prevalent in this study. A large majority of our respondents reported an overall decrease in sexual drive, intermittent erectile dysfunction, or a loss of spontaneous morning erections—or all three—and many reported physical and sensory changes to the penis and scrotum included penile and scrotal shrinkage and diminished semen volume and force. These findings are consistent with several studies that have investigated sexual adverse effects in this population (Canguven & Burnett, 2008; Canguven & Talib, 2013; Irwig, 2012b, 2014; Irwig & Kolukula, 2011;

Table 3. Specific Types of Symptoms Experienced (*N* = 131).

Symptom Category	*n* (%)
Physical	
Gynecomastia	91 (70)
Lethargy and fatigue	90 (69)
Muscle atrophy, weakness	73 (56)
Muscle twitching	61 (47)
Decreased oil and sebum production	53 (41)
Dry thinning skin	89 (68)
Changes in metabolism; increased fat deposition	70 (54)
Reduced HDL cholesterol, raised fasting glucose and triglycerides	18 (14)
Sexual libido	
Decreased sex drive	121 (93)
Complete loss of sex drive	82 (63)
Intermittent erectile dysfunction	108 (83)
Complete impotence	52 (40)
Loss of morning and spontaneous erections	116 (89)
Failure to achieve orgasm on most occasions	52 (40)
Sexual anhedonia, loss of pleasurable orgasm	91 (70)
Disorders of penis and testes	
Diminished semen volume and force	107 (82)
Penile shrinkage, sensory changes	103 (79)
Scrotal shrinkage and numbness	64 (51)
Peyronie's disease	26 (20)
Cognitive disorders	
Severe memory/recall impairment	71 (56)
Slowed thought processes	93 (74)
Impaired problem solving	87 (69)
Mental cloudiness or brain fog	95 (75)
Confusion	69 (55)
Attentional difficulties	93 (74)
Repeating questions during a conversation	66 (52)
Psychological disorders	
Elevated anxiety	96 (74)
Depressed affect	95 (73)
Emotional sensitivity	72 (55)
Anhedonia	95 (73)
Sleep disturbance/Insomnia	75 (58)
Suicidal ideation	82 (63)

Note. HDL = high-density lipoprotein. Four participants did not respond to the survey questions concerning disorders of the penis and testes and cognitive disorders.
Source. The Post-Finasteride Syndrome Foundation, http://www.pfs-foundation.org/.

Mysore, 2012). In a recent review, Irwig (2014) discussed the results of several studies that explored the relationship between finasteride use and persistent side effects. Results found men that experienced adverse effects of finasteride were younger men with symptoms that include erectile dysfunction, low libido, and lack of orgasms, depression, and decreased alcohol consumption (Irwig, 2014).

Roughly three quarters of our survey respondents reported that they experienced an inability to think clearly due to a slowing of their thought processes, mental cloudiness or brain fog, and attentional difficulties. More than half reported chronic insomnia associated with taking finasteride. Several studies suggest that neurosteroids and neuroactive steroids—in particular pregnenolone, dehydroepiandrosterone, and allopregnanolone—may be involved in the modulation of memory processes and sleep (Rupprecht, 1997; Rupprecht & Holsboer, 1999). It is established that the presence of 5-α reductase is necessary in the biosynthesis of these important compounds. Research supports that all three of the 5-α reductase isoenzymes are present in a various brain structures (Aumuller et al., 1996; Eicheler et al., 1995). Finasteride reduces the plasma and cerebrospinal fluid (CSF) levels of these neurosteroids and this factor may contribute to lower brain levels of these compounds and subsequent cognitive and sleep disturbances in this population.

Nearly three quarters of our respondents reported increased anxiety, depressed mood, and emotional flatness. Several studies have suggested a possible link between mood disturbances and finasteride use for MPHL. In a case report researchers reported that patients experienced what was characterized as a "substance-induced mood disorder" after initiating, stopping, and reintroducing finasteride (Traish et al., 2011). The investigators that examined neuroactive steroid levels of plasma and CSF in a subset of patients also reported excessive anxiety and depressed mood after discontinuation of finasteride (Melcangi et al., 2013). These researchers reported that in comparison with normal healthy controls lower levels of neurosteroids in both serum and CSF were identified in patients that presented with a complex pattern of neuropsychiatric symptoms after finasteride therapy.

Of particular concern was suicidality in our population. Targeted questions asked men if they experienced suicidal ideations once they discontinued finasteride therapy. In our sample, 63% (*n* = 82) acknowledged that they had experienced negative thoughts and felt that they could not continue living with the extreme side effects on a daily basis.

Limitations

Study subjects were recruited from patients who had sought treatment for symptoms that they were experiencing and therefore selection bias and recall bias may affect the results. Subjects were also recruited from the Propeciahelp.com, a website that hosts a forum for finasteride sufferers, and this similarly may have allowed bias

to enter the sample. Furthermore, the results of this pilot study may not be generalizable, due to the self-report nature of the survey. Another limitation of this study is that the percentages of specific side effects cannot be calculated due to lack of a control group. This study did not explore external major life events (e.g., births, deaths, divorce) as contributing factors to suicidal ideations and should be incorporated in future studies. The investigators performed routine laboratory studies on all clinically evaluated participants; however, analysis of this data was not included in the present article. Future research will incorporate valid and reliable biochemical measures to serve as the likely mechanism of each of the reported adverse effects.

Implications for Research and Clinical Practice

Overwhelmingly, respondents in our study reported adverse effects during and after taking finasteride for MPHL—affects that often persisted despite stopping the medication. These findings suggest that the aggregate of physical, cognitive, and psychological symptoms and resultant functional impairments may be a definable syndrome, but further research is needed in this population to confirm whether these persistent adverse effects indeed constitute a post-finasteride syndrome. Another important unanswered question is how minimal an exposure can trigger the syndrome. Based on this unknown prescribers should caution patients prior to initiation of finasteride therapy for MPHL on the potential for adverse effects of unknown duration.

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References

Aumuller, G., Eicheler, W., Renneberg, H., Adermann, K., Vilja, P., & Forssmann, W. G. (1996). Immunocytochemical evidence for differential subcellular localization of 5-alpha-reductase isoenzymes in human tissues. *Acta Anatomica (Basel)*, *156*, 241-252.

Azzouni, F., Godoy, A., Li, Y., & Mohler, J. (2012). The 5-alpha-reductase isozyme family: A review of basic biology and their role in human diseases. *Advances in Urology*, *2012*, 530121. doi:10.1155/2012/530121

Beauchet, O. (2006). Testosterone and cognitive function: Current clinical evidence of a relationship. *European Journal of Endocrinology*, *155*, 773-781. doi:10.1530/eje.1.02306

Canguven, O., & Burnett, A. L. (2008). The effect of 5-α-reductase inhibitors on erectile function. *Journal of Andrology*, *29*, 514-523.

Canguven, O., & Talib, R. A. (2013). Persistent sexual side effects of finasteride: Could they be permanent? *Journal of Sexual Medicine*, *10*, 1441. doi:10.1111/jsm.12089

Dubrovsky, B. (2006). Neurosteroids, neuroactive steroids, and symptoms of affective disorders. *Pharmacology, Biochemistry, and Behavior*, *84*, 644-655.

Dusková, M., Hill, M., Hanus, M., Matousková, M., & Stárka, L. (2009). Finasteride treatment and neuroactive steroid formation. *Prague Medical Report*, *110*, 222-230.

Eicheler, W., Dreher, M., Hoffmann, R., Happle, R., & Aumuller, G. (1995). Immunohistochemical evidence for differential distribution of 5-α-reductase isoenzymes in human skin. *British Journal of Dermatology*, *133*, 371-376.

Green, L., Wysowski, D. K., & Fourcroy, J. L. (1996). Gynecomastia and breast cancer during finasteride therapy. *New England Journal of Medicine*, *335*, 823. doi:10.1056/nejm199609123351116

Hampson, E. (1995). Spatial cognition in humans: Possible modulation by androgens and estrogens. *Journal of Psychiatry and Neuroscience*, *20*, 397-404.

Holland, J., Bandelow, S., & Hogervorst, E. (2011). Testosterone levels and cognition in elderly men: A review. *Maturitas*, *69*, 322-337.

Hotaling, J. M. (2013). Finasteride and male infertility: A case for prospective collaborative research databases? *Fertility and Sterility*, *100*, 1528-1529. doi:10.1016/j.fertnstert.2013.08.023

Irwig, M. S. (2012a). Depressive symptoms and suicidal thoughts among former users of finasteride with persistent sexual side effects. *Journal of Clinical Psychiatry*, *73*, 1220-1223. doi:10.4088/JCP.12m07887

Irwig, M. S. (2012b). Persistent sexual side effects of finasteride: Could they be permanent? *Journal of Sexual Medicine*, *9*, 2927-2932. doi:10.1111/j.1743-6109.2012.02846.x

Irwig, M. S. (2014). Persistent sexual and nonsexual adverse effects of finasteride in younger men. *Sexual Medicine Reviews*, *2*, 24-35.

Irwig, M. S., & Kolukula, S. (2011). Persistent sexual side effects of finasteride for male pattern hair loss. *Journal of Sexual Medicine*, *8*, 1747-1753. doi:10.1111/j.1743-6109.2011.02255.x

Janowsky, J. S. (2006). Thinking with your gonads: Testosterone and cognition. *Trends in Cognitive Sciences*, *10*(2), 77-82. doi:10.1016/j.tics.2005.12.010

Kaufman, K. D., Olsen, E. A., Whiting, D., Savin, R., DeVillez, R., Bergfeld, W., . . .Gormley, G. J. (1998). Finasteride in the treatment of men with androgenetic alopecia. Finasteride

Male Pattern Hair Loss Study Group. *Journal of the American Academy of Dermatology*, *39*(4 Pt. 1), 578-589.

Lai, J.-J., Chang, P., Lai, K.-P., Chen, L., & Chang, C. (2012). The role of androgen and androgen receptor in skin-related disorders. *Archives of Dermatological Research*, *304*, 499-510.

Lam, S. M. (2013). Hair restoration. In M. A. Shiffman & A. Di Guiseppe (Eds.), *Cosmetic surgery* (pp. 517-538). New York, Ny: Springer.

Larsen, L. (2012). Men's changing beauty habits: Male grooming. *South African Pharmaceutical and Cosmetic Review*, *39*(11), 19-20.

McElwee, K. J., & Shapiro, J. S. (2012). Promising therapies for treating and/or preventing androgenic alopecia. *Skin Therapy Letter*, *17*(6), 1-4.

McGahuey, C. A., Gelenberg, A. J., Laukes, C. A., Moreno, F. A., Delgado, P. L., McKnight, K. M., & Manber, R. (2000). The Arizona Sexual Experience Scale (ASEX): Reliability and validity. *Journal of Sex & Marital Therapy*, *26*, 25-40.

Melcangi, R. C., Caruso, D., Abbiati, F., Giatti, S., Calabrese, D., Piazza, F., & Cavaletti, G. (2013). Neuroactive steroid levels are modified in cerebrospinal fluid and plasma of post-finasteride patients showing persistent sexual side effects and anxious/depressive symptomatology. *Journal of Sexual Medicine*, *10*, 2598-2603. doi:10.1111/jsm.12269

Mella, J. M., Perret, M. C., Manzotti, M., Catalano, H. N., & Guyatt, G. (2010). Efficacy and safety of finasteride therapy for androgenetic alopecia: A systematic review. *Archives of Dermatology*, *146*, 1141-1150. doi:10.1001/archdermatol.2010.256

Mysore, V. (2012). Finasteride and sexual side effects. *Indian Dermatology Online Journal*, *3*, 62-65. doi:10.4103/2229-5178.93496

Post Finasteride Syndrome Foundation. (2012). *Post-finasteride syndrome*. Retrieved from http://www.pfsfoun-dation.org/post-finasteride-syndrome-overview/

Reddy, D. S. (2010). Neurosteroids: Endogenous role in the human brain and therapeutic potentials. *Progress in Brain Research*, *186*, 113-137.

Ricci, G., Martinelli, M., Luppi, S., Lo Bello, L., De Santis, M., Skerk, K., & Zito, G. (2012). Finasteride and fertility: Case report and review of the literature. *Journal of Drugs in Dermatology*, *11*, 1511-1513.

Rizvi, S. J., Kennedy, S. H., Ravindran, L. N., Giacobbe, P., Eisfeld, B. S., Mancini, D., & McIntyre, R. S. (2010). The relationship between testosterone and sexual function in depressed and healthy men. *Journal of Sexual Medicine*, *7*(2 Pt. 1), 816-825.

Rupprecht, R. (1997). The neuropsychopharmacological potential of neuroactive steroids. *Journal of Psychiatric Research*, *31*, 297-314.

Rupprecht, R., & Holsboer, F. (1999). Neuropsychopharmacological properties of neuroactive steroids. *Steroids*, *64*(1), 83-91.

Samplaski, M. K., Lo, K., Grober, E., & Jarvi, K. (2013). Finasteride use in the male infertility population: Effects on semen and hormone parameters. *Fertility and Sterility*, *100*, 1542-1546. doi:10.1016/j.fertnstert.2013.07.2000

Seo, Y. J., Li, Z. J., Choi, D. K., Sohn, K. C., Kim, H. R., Lee, Y., . . .Lee, J. H. (2014). Regional difference in sebum production by androgen susceptibility in human facial skin. *Experimental Dermatology*, *23*, 70-72.

Thilers, P. P., MacDonald, S. W. S., & Herlitz, A. (2006). The association between endogenous free testosterone and cognitive performance: A population-based study in 35 to 90 year-oldmen and women. *Psychoneuroendocrinology*, *31*, 565-576. doi:10.1016/j.psyneuen.2005.12.005

Traish, A. M., Hassani, J., Guay, A. T., Zitzmann, M., & Hansen, M. L. (2011). Adverse side effects of 5-α reductase inhibitors therapy: Persistent diminished libido and erectile dysfunction and depression in a subset of patients. *Journal of Sexual Medicine*, *8*, 872-884. doi:10.1111/j.1743-6109.2010.02157.x