Common urologic diseases in older men and their treatment: how they impact fertility

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As men age, medical and surgical diseases involving the genitourinary tract become more common. The conditions themselves, if not their treatments, can negatively impact the fertility potential of an affected man. Many older men maintain the desire to father children, so it is critical to understand the disturbed anatomy and physiology involved to properly counsel that individual. Should this or that treatment regimen be employed? Should sperm banking be undertaken before institution of a permanently ablative/suppressive therapy? What are the long-term consequences of one therapy over another vis-à-vis sperm production, sperm quality, and/or sperm transport? In this context, some of the more common genitourinary afflictions of the older male and the treatment options that are available will be discussed. (Fertil Steril® 2017;107:305–11. ©2016 by American Society for Reproductive Medicine.)

Key Words: Advanced paternal age, ejaculatory dysfunction, infertility

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The effects of aging are compounded by the additional medical comorbidities one develops over time. In turn, these conditions and their treatments, medical and surgical, can contribute to male infertility. Infertility affects 60–80 million couples worldwide. Male factor infertility underlies more than 40% of these cases. Paternal age at time of conception has been steadily increasing over the past several decades (1). Presently almost 25% of men fathering children are >35 years old compared with 1970 when it was <15%. This trend to delay fatherhood is likely related to many diverse socioeconomic and cultural factors. Natural fertility attainment depends on multiple interrelated physiologic and psychological necessities, including, but not limited to, libido, erection, orgasm, ejaculation, and spermatogenesis. Alterations in any of these factors may reduce or eliminate conception success. We will focus on a variety of common urologic conditions and their treatments that are seen frequently in the aging male population and discuss their direct and indirect effects on male fertility potential.

INCREASED MALE AGE AS AN OVERALL FACTOR

As reviewed by Di Sante et al. (2), ejaculatory dysfunction (EjD)—a decreased amount of seminal fluid or anejaculation—increases in frequency from 3% of men aged 50 to 54 years to 35% of men aged 70 to 78 years (3). Laumann et al. (4), as part of the findings of the Global Study of Sexual Attitudes and Behaviors International Survey, reported that the inability to reach orgasm (anorgasmia) steadily increases with age as well. With the referent population of men aged 40 to 49 years, the odds ratio for anorgasmia increased steadily in northern European men to 1.5 at 50–59 years, 1.9 at 60–69 years, and 4.9 at 70–80 years. The odds ratios for southern European men were found to be 3.4, 7.7, and 7.7, respectively, for the same age groups and a referent cohort of 40- to 49-year-old men. Perceived ejaculate volume reduction and decreased force of ejaculation also increase progressively, and they are at least three times more common in men aged 60 to 70 years than in men <40 years old (5).

Finally, as the European Male Ageing Study (6) and the National, Social Life, Health and Aging Project (7) have clearly shown, it is most likely comorbidities and a decline in overall physical health that are the proximate reasons for decreases in total sexual performance. Failure of any component of the male sexual act when pregnancy is the goal is obviously limiting, if not partially then completely. Specific organ-based urologic conditions in older men that impact fertility will be discussed herein, mainly of the prostate and bladder.

Penis

Erectile dysfunction may distressingly emerge at any stage of adult life.

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However, studies show a high direct correlation with increasing age (8) and the extent of coexistent cardiovascular disease (9). Obviously, if the male partner is unable to vaginally penetrate adequately, the ejaculate may not be delivered appropriately during intercourse, and achieving a natural pregnancy will be difficult. Either correcting the erectile dysfunction or using masturbated ejaculate as the sperm source for intrauterine insemination or in vitro fertilization would be two courses of action the couple may consider.

One of the most common forms of initial therapy for psychogenic or vasculogenic erectile dysfunction is use of an oral phosphodiesterase type 5 (PDE5) inhibitor, either acutely or chronically. The four most often prescribed are sildenafil, tadalafil, vardenafil, and avanafil. These compounds do not appear to have negative effects on in vivo spermatogenesis or sperm concentration, its surrogate, although studies of in vitro incubation with spermatozoa have suggested there may be a negative impact on sperm motility in the form of a decline in ATP and mitochondrial function (10). Several recent studies have allayed concerns by demonstrating improved sperm parameters in vivo in fertile and infertile men: vardenafil enhanced sperm motility after acute administration in infertile men (11); tadalafil increased semen volume and sperm motility after 12 weeks of treatment in fertile men (12); and tadalafil and sildenafil showed no uptick in the premature acrosome reaction rate of spermatozoa (13). All in all, the use of oral PDE5 inhibitors appears to be safe in men with erectile dysfunction who desire fertility (Table 1).

Prostate: Benign

Benign prostatic hyperplasia (BPH), the nonmalignant growth of the prostate, is a commonly observed condition of the aging male. Both BPH and lower urinary tract symptoms (LUTS) have a prevalence rate of 50% in men 50 years of age, which rises to 80% as men move into their 70s (14). Many studies have demonstrated a statistically significant relationship between LUTS and either decreased ejaculatory volume or anejaculation in up to 68% of men (15). As Rosen et al. (16) have also shown in their large, multinational survey with over 12,000 responses from men aged 50 to 80 years, sexual dysfunction was related not only to age but also the severity of LUTS, with 41% of mild LUTS sufferers reporting EjD, and 76% in those with severe LUTS doing so. The mechanism of association is unclear, although 10% of men with severe LUTS received an undefined medical treatment and this may have had a negative additive effect as well. Absent medical or surgical treatment, BPH and

TABLE 1

Common urologic medications: fertility effects.

		Fertility effect		
Drug	**Use**	**Adverse**	**Beneficial**	**None**
PDE5 inhibitors Sildenafil Tadalafil Vardenafil Avanafil	Erectile dysfunction	–	Possible improvement in semen volume and sperm motility	–
Alpha blockers Silodosin Tamsulosin Doxazosin Alfuzosin Terazosin	BPH	Failure of emission Silodosin Tamsulosin	–	Doxazosin Alfuzosin Terazosin
5ARIs Finasteride Dutasteride	BPH	Finasteride, dutasteride (decreased sperm count, postfinasteride syndrome)	–	–
Nonsteroidal antiandrogens Flutamide Bicalutamide Nilutamide	Prostate cancer	–	–	As monotherapy Flutamide Bicalutamide Nilutamide
GnRH agonists Leuprolide (e.g.) GnRH antagonists Ganirelix (e.g.)	Prostate cancer	Suppression of spermatogenesis, libido, ejaculatory/erectile function (via hypogonadotropic hypogonadism)	–	–
Systemic chemotherapy Docetaxel Gem-Cis (e.g.)	Prostate cancer Bladder cancer	Suppression of spermatogenesis	–	–
Intravesical therapy BCG Mitomycin	Bladder cancer	Decreased semen parameters	–	–
Testosterone	Age-related hypogonadism	Decreased semen parameters, azoospermia	–	–

Note: 5ARIs = 5α-reductase inhibitors; BCG = Bacille Calmette-Guérin; BPH = benign prostatic hyperplasia; Gem-Cis = gemcitabine/cisplatin; GnRH = gonadotropin-releasing hormone; PDE5 = phosphodiesterase type 5.

Avellino. Urologic disease: impact on fertility. Fertil Steril 2016.

the pathology it creates leading to LUTS apparently also affect the ejaculatory process, perhaps through external compression of the ejaculatory ducts as they course through the prostate to their termination on the verumontanum, although no data exist to support this hypothesis.

Medical therapy of BPH: alpha blockers. Alfuzosin, doxazosin, tamsulosin, terazosin, and silodosin are the five main medications used to treat symptomatic urinary complaints that are thought to be secondary to BPH. While causing relaxation of the smooth muscle components of the prostatic stroma (the beneficial effect), α-receptor antagonists can reduce and even completely inhibit emission (the detrimental effect).

As reviewed by Phillips et al. (17), the complete ejaculatory sequence has two neurologically independent but interrelated components. The ejaculatory reflex center is located within spinal segments T12–L2 and is activated by genital tactile stimulation afferents via the dorsal and pudendal nerves (S2–4) coupled with augmentative cerebral input. Emission is the first in the temporal sequence of events and involves contraction of the vasa deferentia, the seminal vesicles, the prostate, and the bladder neck with deposition of the seminal fluid into the posterior urethra. Emission is mediated via the sympathetic outflow and the short adrenergics embedded as the second neurons in the adventitia of the structures mentioned. The second phase of the ejaculatory event involves contraction of the bulbospongiosus muscle and forceful expulsion of the seminal fluid in an antegrade direction via somatic efferents (S2–4). Therefore, it is easy to imagine how α-blockers as a class can interfere with the efficiency of emission by potentially inhibiting the sympathetic stimulation of the vasa, seminal vesicles, bladder neck, and prostate. That is why a lowered semen volume or no ejaculate at all, although there is the sensation of orgasm, can result from use of certain α-blockers. This negative consequence is additive to the effect that LUTS has as a baseline on emission/ejaculation and the ultimate deposition of the seminal fluid during coitus.

Thought to be more "prostate specific," tamsulosin and silodosin are two α_{1A}-selective antagonists. They may have less effect on the peripheral vasculature and the consequent lowering of blood pressure, but they have more sexual side effects than the nonselective α-blockers alfuzosin, doxazosin, and terazosin (18–20). As Gacci et al. (18) demonstrated in their comprehensive systematic review and meta-analysis, the odds ratio of a particular α-blocker inducing ejaculatory dysfunction as compared with placebo was 8.58 for tamsulosin and 32.5 for silodosin while doxazosin and terazosin were similar to placebo. Rosen et al. (19) addressed alfuzosin specifically and found no difference in ejaculatory dysfunction rates as compared with placebo. The results of a multicenter, double-blind study of >50-year-old men with BPH supported these findings relative to silodosin and tamsulosin, reporting reduced or absent ejaculation in 14% of patients receiving silodosin and 2% of those taking tamsulosin (21). Although the effect is reversible upon discontinuation of silodosin, Kobayashi et al. (22) found an even more profound inhibitory effect with 8 mg daily of silodosin, with all 15 male volunteers describing complete failure of emission. When ejaculation and fertility are important issues for the men with BPH and LUTS, consideration must be given to the choice of α-blocker to use to minimize failure of emission and maximize reproductive potential.

Medical therapy of BPH: 5α-reductase inhibitors (5ARIs). Finasteride and dutasteride are frequently used medications for the treatment of BPH. Finasteride is also used at lower doses in the care paradigm of androgenic alopecia. Both inhibit 5α-reductase, an enzyme that converts testosterone to dihydrotestosterone, the primary and more potent androgen in the prostate and in hair follicles. In the treatment of BPH, finasteride doses at 5 mg daily can reduce prostate size up to 30% (23).

Because of the mechanism of action and the known importance of androgens in spermatogenesis, there has been concern regarding use of 5ARI compounds in patients desiring fertility. Studies have shown that finasteride at 5 mg daily and dutasteride at 0.5 mg daily have a reversible negative effect on semen parameters, particularly total sperm count (sperm concentration multiplied by semen volume) and motility but not morphology, at 26 weeks of treatment but not at 52 weeks or 24 weeks after discontinuation (24). In their case report of men taking a 1-mg finasteride dose for androgenic alopecia, Chiba et al. (25) suggested that perhaps the suppressive effect is more pronounced when baseline sperm production is impaired and that discontinuation of finasteride should be considered. Samplaski et al. (26) echoed these recommendations, noting that most men in their cohort who were taking a 1-mg dose to treat hair loss saw improvement in sperm counts (up to 11-fold) upon cessation of finasteride: "finasteride should be discontinued in subfertile men with oligospermia, and used with caution in men who desire fertility" (26). Liu et al. (27) noted that eliminating finasteride use may improve low sperm counts sufficiently to expand the therapeutic options for couples desiring fertility.

In addition to the direct effect of finasteride on semen parameters, more men are reporting symptoms now being categorized as a "post-finasteride syndrome," including physical (erectile dysfunction, loss of penile sensitivity, decreased force of ejaculation), cognitive (lack of mental concentration), and psychological symptoms (sexual anhedonia), which persist beyond cessation of the medication (28, 29). These symptoms may arise, as well as any spermatogenic decrease, from finasteride's recently described inhibition of 5-AR type 3 found in the brain, frontal cortex, skin, testis, and several other organs (30).

Finally, Gacci et al. (18) reported that 5ARIs may also lead to ejaculatory dysfunction, which may be worsened with a combination of 5ARIs and α-blockers, a commonly used BPH treatment regimen. All these factors combined, especially in view of the emerging evidence of a post-finasteride syndrome, require that men with BPH who potentially desire fertility must be counseled appropriately. If it is clinically appropriate, 5ARIs may be stopped until such time as fertility is realized.

Surgical therapy of BPH. When a patient is intolerant of or his symptoms are refractory to medical therapy of BPH, surgical management may relieve urinary outflow symptoms. Multiple approaches are available, including monopolar and bipolar transurethral resection of prostate (TURP), laser outlet

procedures using holmium and GreenLight to ablate or enucleate tissue, or minimally invasive methods such as transurethral microwave therapy and needle ablation. The anticipated consequences of opening the bladder neck or resecting and cauterizing the ejaculatory ducts as they travel from their origins at the base of the prostate to their terminations at the verumontanum are either retrograde ejaculation or occlusion of the ejaculatory ducts with reduced or absent emission, respectively. Accordingly, the rates of retrograde ejaculation/anejaculation after traditional TURP have been cited upward of 70% (31).

In an elegant systematic review of the literature in an effort to determine rates of ejaculatory impairment after the many alternative treatment techniques employed for BPH, Marra et al. (32) found that there were only a very limited number of publications with well-described definitions and results. However, they concluded that standard TURP (no difference between monopolar and bipolar) and recent laser ablative/resection techniques have similar rates of postoperative EjD whereas transurethral incision of the prostate (21% incidence), transurethral needle ablation (almost no retrograde ejaculation or anejaculation), transurethral microwave thermotherapy (21% incidence), and prostatic lift procedures (no change postoperatively) have much less, if any. In response to this unwanted outcome for some men, Alloussi et al. (33) modified the basic monopolar TURP technique to intentionally spare tissue proximal to the verumontanum for up to 1 cm while the lateral lobes and bladder neck were resected in standard fashion. With preservation of this apical tissue, 90% of men retained ejaculatory function.

As this series of studies demonstrates, men of advanced paternal age with BPH may indeed want to father children, so the postoperative issues need to be addressed preoperatively. The selection of the specific surgical therapy employed may or may not be modified to address concerns of future fatherhood.

Prostate: Malignant

Prostate cancer (PCa) is the most common cancer in men, and many treatment modalities and schema exist for treatment, depending on the histology, stage, and other patient variables such as age. There are no data demonstrating a direct link between PCa as a disease and male reproductive impairment. However, almost all therapies for PCa markedly impair fertility potential, whether surgical, via radiotherapeutic, or hormonal in nature.

Surgical therapy of PCa. Open or minimally invasive (laparoscopic or robot-assisted) radical prostatectomy as a surgical treatment of PCa involves complete removal of the prostate, seminal vesicles, and vasal ampullae and necessarily results in aspermia (absence of ejaculate), abolishing any possibility of a "natural" pregnancy. As reported in their cross-sectional study of 495 PCa patients who were candidates for radical prostatectomy, Salonia et al. (34) found that 20% of men "expressed a wish for preoperative sperm banking." Men who wanted to bank sperm had a mean age of 62.2 years. Therefore, before such extirpative surgical therapy, the question should be asked of all men whether sperm cryopreservation is a desire that they would like to act on. In the absence of this, future operative sperm retrieval coupled with advanced reproductive techniques would be the only option.

Radiation therapy for PCa. Radiotherapy as a treatment for PCa comes in two general approaches, external and interstitial (brachytherapy). Negative effects on fertility may occur via radiation-induced harm to sperm production/quality or by precipitating EjD (most importantly anejaculation). External beam radiotherapy to the prostate bed will invariably have varying amounts of internal scatter in the direction of the testes, depending on whether the beam is more focused as with newer techniques and whether the testes are shielded (35). Irradiation in excess of 15 cGy results in a slight spermatogenic decline; escalating the absorbed doses between 35 cGy and 50 cGy leads to reversible oligospermia. When in the upper ranges of $>$120 cGy, much greater and long-lasting (even permanent) damage to the seminiferous epithelium occurs with consequent azoospermia (36). So, although it is difficult to estimate before therapy the scatter dose to the testes, oligospermia and even azoospermia would not be unexpected, and a return to pretherapy values may take many, many months. Although the recommendation is empirical, couples are advised to wait 1 year after radiation to begin anew trying to conceive.

Brachytherapy has a much less injurious impact on spermatogenesis as the testes are sufficiently distant and thus do not absorb much of the radiation from the implanted seeds. Mydlo and Lebed (37) reported on four young men with normal semen parameters subsequent to brachytherapy, and three out of four succeeded in fathering a child. Grocela et al. (38) discussed three patients who fathered unintended pregnancies after brachytherapy; they hypothesized that it is the distance of the testes from the apex of the prostate that determines whether sufficient radiation will be absorbed by the seminiferous epithelium to produce a mild oligospermic effect or no effect at all. The semen parameters in their patients were essentially normal.

However, Singh et al. (39) reported on five men after prostate brachytherapy who had statistically significantly lower semen volumes, total sperm counts, and percentage of motility as well as increased sperm DNA fragmentation. Their cautionary conclusion was that "infertility may well be a long-term adverse effect of brachytherapy." They further advised, based on the half-life of ^{125}I, that patients delay conception for at least 1 year from treatment because of the risk of infertility or possible malformation of offspring and that they consider pretreatment sperm cryopreservation. The latter recommendation may be quite valuable for those men who have even the slightest inkling that they may want to father children after therapy is completed, based on the rates of postbrachytherapy anejaculation that occur as years pass.

Although spermatogenesis may recover from scatter radiation to the testes, the seminal vesicles and intraprostatic ejaculatory ducts may become more and more "dysfunctional" or "scarred" as a natural consequence of the radiation, as documented by Sullivan et al. (40). These investigators provided a time line of developing anejaculation after external beam radiotherapy and prostate brachytherapy. The

proportion of men reporting lack of emission (no antegrade or retrograde ejaculate) at 1 year, 3 years, and 5 years after completion of therapy was 16%, 69%, and 89%, respectively, with little difference between external beam and brachytherapy. Even though higher doses of radiation led to a higher chance of EjD, it would certainly be wise to counsel all men of this particular possibility. Sperm cryopreservation should be a consideration for them *before* beginning radiation treatment of either type.

Hormone ablation therapy for PCa. Prostatic cancer cells are, in general, androgen dependent. Treatment for locally advanced (often in conjunction with radiotherapy) or metastatic disease involves elimination or suppression of testosterone production by the testes. In addition, certain agents block the effect of androgens. Flutamide, bicalutamide, and nilutamide are nonsteroidal antiandrogens that thwart androgenic action at the cellular level. As reviewed by Mahler et al. (41), patients on these agents alone have preserved sexual function and potency, but they are seldom used as monotherapy. Usually they are employed as a prelude to complete androgen blockage with gonadotropin-releasing hormone agonists or antagonists.

Patients who require androgen deprivation therapy often develop erectile dysfunction and infertility as a direct result of total hypothalamic-pituitary-gonadal axis suppression leading to castrate levels of testosterone. The depletion of intratesticular testosterone (a requirement for spermatogenesis) results in azoospermia. In addition, Ng et al. (42) reviewed their experience with maximal androgen-deprivation therapy (flutamide and leuprolide) and concluded that "libido, sexual activity, and perceptions of masculinity deteriorate" profoundly during this combination therapy. Therefore, a man placed on maximal androgen blockage will have fertility affected in every way possible: decreased/absent libido, decreased/absent erectile capability, decreased/absent spermatogenesis, and decreased/absent ejaculatory capability. Fertility preservation should be discussed and offered before the initiation of treatment.

When PCa has become androgen independent, chemotherapy with agents such as docetaxel may be employed. In a study of men with other types of cancer, Chatziderellis et al. (43) found statistically significant decreases in inhibin B and simultaneous increases in serum follicle-stimulating hormone (FSH) in patients after completion of taxane-based therapy, reflecting severely impaired spermatogenesis. Their patients may not recover sperm production, and the same may hold true for PCa patients treated with taxanes.

Bladder: Malignant

Bladder cancer, which primarily affects older individuals—almost 90% being over 55 years of age—is the ninth most frequently diagnosed cancer worldwide (44). The sexual side effects of bladder cancer, even in non-muscle-invasive disease, should not be overlooked because decreased sexual drive can result from the cancer and/or the intravesical treatments (45).

Intravesical therapy. For non-muscle-invasive bladder cancer, the treatment options include primary endoscopic surgery and often secondary intravesical therapy, which can reduce the risk of recurrence and progression of disease. Intravesical regimens often require weekly instillations in 6-week regimens, repeated for several cycles. Bacille Calmette-Guérin (BCG) is one of the staples of this management scheme as it incites an immunologic reaction within the exposed bladder mucosa.

Garg et al. (46) studied 17 young men with noninvasive bladder cancer and detected a statistically significant decrease in total sperm concentration in 12 of 17, with 5 men dropping to oligospermic levels. Seven patients also had declines in motility. Raviv et al. (47) prospectively studied young men who underwent transurethral resection of bladder tumor (TURBT) with follow-up intravesical instillation of mitomycin or BCG; at 3 months of follow-up observation, they found a statistically significant decline in sperm count and altered sperm quality parameters, including motility and morphology, in half the patients treated with BCG but found little effect from the use of mitomycin. All patients had normal volume semen except for one patient who had undergone multiple TURBTs, and there were no alterations in circulating hormone levels.

Although both were small studies with no long-term follow-up evaluations to determine whether any negative changes were permanent, each group of investigators recommends offering pretreatment semen cryopreservation to men interested in future fertility. Other genitourinary effects of BCG instillation that have been cited, which may indirectly influence fertility, include prostate abscess, epididymo-orchitis, symptomatic granulomatous prostatitis, penile edema, and meatal ulcers.

Surgical therapy. If the transitional cell carcinoma is muscle-invasive or otherwise high risk, a patient may be a candidate for curative cystoprostatectomy. Standard surgery involves removal of the bladder, prostate, seminal vesicles, and vasal ampullae, resulting in aspermia. Neoadjuvant chemotherapy in the form of gemcitabine/cisplatin or methotrexate/vinblastine/doxorubicin/cisplatin also is often applied with consequent acute and potentially long-term negative effects on spermatogenesis (48). Thus, before initiation of neoadjuvant chemotherapy and/or operative management, fertility preservation should be discussed with and offered to the patient while keeping in mind the not mutually exclusive goals of cancer control and paternity.

In an attempt to obviate the consequent effects on erectile and ejaculatory function of standard cystoprostatectomy, Salem (49) described a modified surgical approach. A nerve-sparing radical cystectomy with preservation of the vas deferens, seminal vesicles, whole prostate, and neurovascular bundles was performed in seven patients who had a single site of cancer on the lateral bladder wall. Postoperatively all 7 patients had normal erectile function and were able to have intercourse. Six individuals were shown to have antegrade ejaculation. There was no evidence of recurrence with a mean follow up-time of 20 months. In a further modification, Salem (50) reported removal of the bladder, prostate, and seminal vesicles with anastomosis of the vas deferens to the bulbous urethra in four men with resultant antegrade ejaculation in two and procreation in one. These techniques have not gained widespread popularity, and even if attempted

do not guarantee postoperative fertility. Again, the strong recommendation is that future fertility be a part of the pretherapy discussion with men of any age.

Reproductive Ductal System: Occlusion

Polypropylene mesh, often used in modern-day inguinal hernia repair, incites a tremendous scar-tissue reaction to solidify the floor of the canal. As Zendejas et al. (51) reported in their population study in Olmstead County, Minnesota, the incidence (per 100,000 person years) of inguinal hernia repair in men increased with age from 194 men aged 30 to 648 men aged 70, with bilateral repairs becoming more common in the latter years of the study. Vasal obstruction at this level is a possible negative consequence when patency for fertility is desired. Shin et al. (52) reported on 14 cases, submitted from eight institutions, of obstructive azoospermia due to inguinal vasal blockage (trapped or obliterated vasa) following hernia repair. A history of inguinal hernia repair is thus important in the fertility evaluation of the older men as it may shed light on why an individual is azoospermic. The same would be true for vasectomies: the National Survey of Family Growth documented a 6% prevalence of azoospermia in 2002 (53). Finally, epididymitis from either a sexually transmitted disease or an ascending uropathogen infection also can result in obstructive azoospermia (54).

Testis: Spermatogenesis

A significant and increasing threat to spermatogenesis in older men is the use of suppressive exogenous testosterone. As reviewed by Handelsman et al. (55), starting at age <40 years serum testosterone levels in men decline with age by 0.5% annually. In a comprehensive panel opinion of the International Society for Sexual Medicine authored by Dean et al. (56), a review of testosterone deficiency in adult men has shown approximately 2% to 12% of men aged 40 to 70 years experience symptomatic hypogonadism. Exogenous testosterone in the form of topical or injectable delivery systems is being prescribed to the older men in ever increasing numbers in almost all countries surveyed (57). The sale of testosterone more than doubled between 2006 and 2015.

Exogenous testosterone reduces or eliminates pituitary secretion of luteinizing hormone and FSH leading to a cessation of intratesticular testosterone production by the Leydig cells, a necessity for spermatogenesis. This results in oligospermia or azoospermia within 3 to 4 months of initiation. Although recovery of spermatogenesis can occur, some patients may remain azoospermic, depending on their prior fertility status. Khera et al. (58) reviewed the current state of adult-onset hypogonadism and summarized several studies that demonstrated that recovery of spermatogenesis to full pretreatment levels only occurs in about 50% of men at an average of approximately 6 months. It should never be assumed that testosterone supplementation has only a temporary, completely reversible effect on sperm production and thus on fertility. It is critically important to assess the patient's desire for future paternity before recommending testosterone usage and to ask about it specifically in older men undergoing fertility evaluation.

CONCLUSION

A multitude of disease processes affect the aged genitourinary system, ranging from voiding abnormalities to malignancy may have, as a direct consequence or as collateral injury from applied treatment, significant effects on the fertility potential of the afflicted male. Desires, or lack thereof, for future paternity should never be assumed by the evaluating and treating clinicians, and all older male patients should at least be queried about whether they consider fertility a long-term consideration. If so, then education about potential limiting factors, including the condition itself and any therapies that might be offered, should be a part of the strategic discussion. For instance, avoiding certain medications for symptomatic BPH such as silodosin in favor of others that do not impair seminal fluid ejaculation would be worthy of dialogue. Whether active surveillance, radical surgery, or radiation therapy should be chosen for PCa is a question whose answer may well be informed by any potential hopes the patient and his partner have for biological paternity. A simple, easily asked query initiated by the provider could have incredible import and consequences, so it should not be viewed as irrelevant to the conversation.

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