

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® 2016; ■: ■–■. ©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 vol-

ume 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.

Drug	Use	Adverse	Fertility effect	
			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.)	Prostate cancer	Suppression of spermatogenesis, libido, ejaculatory/erectile function (via hypogonadotropic hypogonadism)	–	–
GnRH antagonists Ganirelix (e.g.)	Prostate cancer	Suppression of spermatogenesis	–	–
Systemic chemotherapy Docetaxel Gem-Cis (e.g.)	Prostate cancer Bladder cancer	–	–	–
Intravesical therapy BCG Mitomycin	Bladder cancer	Decreased semen parameters	–	–
Testosterone	Age-related hypogonadism	Decreased semen parameters, azoospermia	–	–

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

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