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GERIATRIC UROLOGY

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Urology is undergoing rapid changes with the introduction of new technology and laboratory discoveries. These changes will exert a considerable influence in the way urologic diseases are managed in the future. Not only will they dramatically shift our diagnostic and management paradigms, they will also dictate future thinking and the directions of new research. Finding answers to several key urologic questions, especially as they pertain to the geriatric patient, has never been more important, given the aging of our population and its increased longevity. The chapter on geriatric urology in *New Frontiers in Geriatrics Research*, the project publication which this supplement updates, analyzed existing knowledge regarding various important urologic conditions that particularly affect older adults and identified several key research areas and questions pertaining to each of these urologic conditions that merited further investigation. [1] In this update of that chapter we have assessed the progress made since the literature review for *New Frontiers* was completed. We have sought to determine the extent and manner in which the Key Questions in geriatric urology identified in *New Frontiers* have been addressed by ongoing research. We determined that although some questions have been directly addressed in the interim, there are several areas where results are still forthcoming or progress needs to be encouraged. We have also identified several new topics where research efforts could be directed (see the section New Horizons in Geriatric Urology, at the end of the chapter). In discussing the research results that pertain to each Key Question identified in *New Frontiers,* we also point out contradictions and further questions that have resulted from these investigations.

The three Key Questions in urology identified in *New Frontiers* are listed below. Although these questions define the general theme for analysis of all the data identified in the literature, several nuances to these questions need to be addressed in the context of the individual disease processes and our population of interest. We have attempted to clarify these nuances in this chapter.

> *Urol KQ1*: **Research is needed to better define the pathophysiology and natural history of the most common genitourinary disorders affecting older adults. These include but are not limited to urinary incontinence, urinary tract infection, prostate diseases, urologic malignancies, sexual dysfunction, stone disease, and renal failure and transplantation.**

> *Urol KQ2*: **Research is needed to develop and validate predictive models to identify appropriate candidates for early surgical or other more active therapies for urologic disorders versus appropriate candidates for an initial trial of more conservative treatment options.**

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> *Urol KQ3*: **Research is needed to analyze the longitudinal outcomes of various urologic therapies, including potential risks, benefits, and costs.**

METHODS

An exhaustive and systematic literature search was performed to identify all published articles pertaining to six specific subject areas in urology. The PubMed database of the National Library of Medicine was used for all searches. The major MeSH headings used as search terms were *general urology, prostatic diseases, kidney disease, sex disorders, urinary incontinence,* and *urinary tract infections*. These MeSH headings were combined with the following MeSH terms to restrict the search to articles directly related to geriatrics: *age, geriatric assessment, aged, 80 and over, frail elderly, longevity,* and *geriatrics*. Limit specifications for the searches included age 65 years and older, English language, human, and year of publication 2000–2006. Larger search results were broken down by category of publication into clinical trial, meta-analysis, randomized controlled trial, and review articles. The numbers of articles identified by the search were general urology 44, prostatic diseases 109, kidney disease 7346, sex disorders 7940, urinary incontinence 1265, and urinary tract infections 408. An additional search of the National Library of Medicine database using search terms *65 or older, aged,* and *geriatric* among English-language articles in core clinical journals yielded 91 articles for the years 2000–2005. Additional searches to identify publications that may address the specific questions raised in *New Frontiers* were also conducted. For example, for agenda item Urol 25, the search terms included *urinary calculi, minimally invasive surgery, geriatrics,* and *elderly*. For Urol 13, the search terms were *benign prostatic hyperplasia, elderly, phytotherapy*, and *medical therapy*. Again, limits applied were publication years 2000–2005, English language, human, and age 65 years and older. These additional searches yielded well over 2500 articles. We also searched for articles on the general subject matter without the keyword *elderly* or *geriatrics* in order to capture all data on the subject. If these articles included results obtained in elderly patients even though the entire target population was not limited to those aged 65 years or older, we included them in our literature review.

All the articles identified through the various search strategies were reviewed, and those that contained data clearly relevant to the area of interest were selected by one of the authors (BRK). The article abstracts were reviewed in the context of the research agenda set forth in *New Frontiers*. Those articles that addressed the urology Key Questions and any of the proposed areas of investigation were reviewed in their entirety, and their results were summarized. Our updated understanding of the available state of evidence forms the basis for the modifications of and additions to the research agenda from *New Frontiers*.

PROGRESS IN GERIATRIC UROLOGY

URINARY INCONTINENCE

Background and Epidemiology

See *New Frontiers,* pp. 270–271.

Types of Urinary Incontinence

See *New Frontiers,* pp. 271–272.

Diagnostic Evaluation

See *New Frontiers,* pp. 272–273.

Treatment

See *New Frontiers,* pp. 273–276.

Needed Research in Urinary Incontinence

> **Urol 1 (Level B)**: **Studies are needed on the pathophysiology of nocturia, which occurs in a wide variety of conditions, including heart failure, renal failure, vascular insufficiency, sleep disorders, prostate enlargement, and polyuria of various causes.**

New Research Addressing This Question: Nocturia is one of the main complaints of most patients with benign prostatic hyperplasia (BPH). Population-based cohort studies conducted in Japanese men suggest that even in men with normal-sized prostates and no other symptoms of BPH, nocturia more than one time per night is prevalent in men aged 55 years or older and nocturia more than two times per night is prevalent in men aged 75 years or older. [2] The presence of nocturia is directly correlated with the age of the patient. It appears to be related to reduced nocturnal bladder capacity, since diurnal urine volume variation actually decreases with age. [3] Nocturnal urinary volume is also known to increase with age, and this in combination with decreased capacity could precipitate the nocturia. Of further importance, nocturia is a significant risk factor for falls among older adults. Reducing fluid intake before bedtime may be one good strategy to decrease nocturia. Other interventions to increase bladder capacity may include the administration of anticholinergics, though such medications may have central nervous system side effects that are not very desirable in this population. Some of the newer anticholinergic medications cross the blood-brain barrier to a lesser extent, mitigating some of this toxicity.

Worsening of lower urinary tract symptoms with increasing age appears to be present in both sexes. [4] Men aged 70 years or older have an International Prostate Symptom Score (IPSS) score of 7 (mild symptoms), and women have a score of 5.6 (even milder symptoms). Most of the increase in the scores in older age groups is related to increased complaints of weak stream and nocturia in men and of nocturia and urgency in women.

Modification of This Question in Light of New Research: These data further emphasize the need for studies in older persons to ascertain the pathophysiology of nocturia.

> **Urol 2 (Level B)**: **Studies are needed to establish the validity of new and existing survey instruments to assess the types and degrees of urinary incontinence in older adults.**

New Research Addressing This Question: Studies have used various survey instruments to assess the degree and impact of incontinence in older adults. Some of the tools that have been used include the Protection, Amount, Frequency, Adjustment, Body Image assessment tool, the Incontinence Impact Questionnaire, and the Urogenital Distress Inventory (UDI). [5] The Epidemiology of Prolapse and Incontinence Questionnaire attempts to

identify symptoms related to overall pelvic floor dysfunction. [6] Bradley et al used a modified version of the Pelvic Floor Distress Inventory similar to the UDI to assess prevalence of incontinence in a cohort of older women participating in the Women's Health Study. They found both stress and urge urinary incontinence to be prevalent in almost 50% of the cohort with a mean age of 68 years. They identified lifestyle factors, such as daily exercise and coffee drinking, that are associated with higher likelihood of incontinence. [7]

A variety of questionnaires are available to assess the degree of urge incontinence and have been comparatively validated in a small cohort of older women with a mean age of 66 years. In comparing the Overactive Bladder Questionnaire, the Patient Perception of Bladder Condition, Urgency Questionnaire, and Primary OAB Symptom Questionnaire, Matza et al found that all were equally consistent in measuring symptom severity and better than micturition diaries. [8] Hence, these instruments could be potentially useful in evaluating elderly patients with incontinence. One must be cautious about extrapolating to an older population the accuracy of incontinence assessment questionnaires validated in a younger cohort. Prior studies suggest that as few as 4% of octogenarians who report stress urinary incontinence on a questionnaire will actually have stress incontinence demonstrable on urodynamic evaluation. [9] This further underscores the need to develop age-specific disease assessment tools for use in older persons.

One strategy employed to assess quality of life (QOL) in these patients has been to couple validated instruments (eg, the Medical Outcomes Study Short Form 36-item health survey, or SF-36) that assess QOL with indigenous short surveys that in the elderly patient assess degree of incontinence. In one such study, Ko et al determined that incontinence had significant negative impact on the global QOL as determined by the SF-36 in persons aged 65 years or older. Interestingly, the gender-based prevalence of incontinence in this population was not very different (20.9% in men, 27.5% in women). [10] The Incontinence Quality of Life (I-QOL) is an instrument specifically developed to assess the impact of incontinence on QOL. Validation studies on this instrument have included elderly patients; 46% of patients in one study of 605 respondents were in the age group 65 years or older. The impact of incontinence on QOL does not appear to vary by age. Comparison of scores obtained using I-QOL appear to correlate well with scores obtained on more generic instruments, such as the SF-36 or the SF-12, but the I-QOL is more sensitive in identifying degree of bother from the incontinence. [11] In a validation study of the I-QOL instrument conducted in 288 patients with incontinence participating in a clinical trial, 32% were aged 60 years or older. Although the data were not analyzed after age stratification, the instrument appeared to have across the board a high internal consistency and cross-sectional validity. [12] Total scores on the I-QOL instrument do appear to be higher (better) among older patients (aged 60 years or older), an effect ascribed to the adaptability of older patients to their disease. [13] This has been observed in earlier studies using more standardized instruments such as the SF-36. This finding further emphasizes the need to specifically validate such instruments in an older cohort of patients in order to determine "ceiling and floor effects." If baseline scores are already high among the older persons, there may not be much room for improvement, hence precluding identification of QOL differences by intervention. Other measures that have been used to assess outcome following incontinence surgery include the Stress, Emptying, Anatomy, Protection, and Instability score. [14]

Modification of This Question in Light of New Research: Although these results suggest that several instruments can be used adequately in an elderly population of patients, the use of targeted analysis with QOL instruments in an elderly cohort would ensure that results are valid in this population.

> *Urol 3 (Level B)*: **Systematic prospective cohort or case-control studies are needed to determine whether urodynamic and imaging techniques are associated with better outcomes in urinary incontinence in older patients.**

New Research Addressing This Question: Retrospective analysis of older patients with incontinence suggests that other than cognitive status and medications, measured bladder capacity and ability to voluntarily suppress voiding are important predictors of urge urinary incontinence. [15] These data offer additional targets for intervention in future studies. Randomized trials comparing several treatment options for incontinence in older women have used various urodynamic measures of response. However, there appears to be a disconnect between measured urodynamic response and clinical response, such as avoidance of accidents, which suggests that more comprehensive measures of bladder function beyond routine urodynamics may be required to provide a more complete picture of the disease. [16] Newer evaluation techniques, such as ambulatory urodynamics, have been incorporated into randomized clinical trials evaluating pharmacologic agents for treating urge incontinence. [17] Although the studies include older patients, none of them have specifically assessed the benefit of these investigations in a cohort of older patients. Lack of data in this regard is underscored by the fact that there is great observed variability in the frequency, type, and appropriateness of the urodynamic evaluation used by various physicians. [18] Studies analyzing the benefits of urodynamic evaluation in large cohorts of patients suggest that reliance on clinical symptoms alone will risk underdiagnosis of overactive bladder. In one study of 4500 women with overactive bladder, 1641 or 36.5% had urodynamic findings of overactive bladder. Only 27.5% of the 1641 women actually had symptoms representing bladder overactivity. [19]

Modification of This Question in Light of New Research: Urodynamic assessment may provide a more objective measure of baseline function from which relative change can be judged. It is assumed that the same normal expected baseline applies to patients of all ages. Directed determination of urodynamic parameters in an older cohort can help determine if the current approach is valid and define normal bounds for common urodynamic measurements in the older adult. This will also help better assess outcomes of therapy in this age group.

> *Urol 4 (Level A)*: **Depending on the results of studies of the impact of urodynamic and imaging techniques on outcomes (Urol 3), the effect of particular urodynamic or imaging studies on the accuracy of diagnosis and outcomes of treatment should be assessed in randomized controlled trials.**

New Research Addressing This Question: Almost all of the recent clinical trials assessing various therapeutic interventions for incontinence incorporate some objective measure of outcome assessment. Several of them use QOL and other questionnaires to assess outcome, and others use urodynamic measurements at baseline and after the intervention

to assess improvement. Combinations of the two methods have also been used. There are no large studies focused on older patients (aged 65 years or older) that specifically address the validity of the various methods of outcome assessment. This is particularly true for the objective measures, such as urodynamics and radiographic evaluation. Such a comparative evaluation would allow us to define a reference standard that can be used in all studies and allow easier comparison of data across studies.

Evaluation of the benefit of routine urodynamics before initiation of therapy has been conducted in a prospective manner in women 50 to 74 years of age. Ultimate outcomes were no different in those patients who underwent pre-intervention urodynamics and in those who underwent urodynamics only following intervention. A change in diagnosis and therapy based on urodynamics was required in 26% of patients in this trial, but this did not affect final outcome. This led the authors to suggest that routine urodynamics may not be necessary, at least before initiation of first-line therapy. [20] It is unclear if these findings will apply generally to an older population, but they do provide food for thought. The accuracy of specific subjective and objective criteria to diagnose stress urinary incontinence has been evaluated in a large study of 950 women of all ages. Using urodynamic demonstration of stress incontinence as a standard, the authors were able to identify a small subset of patients who met predetermined criteria for incontinence that correlated highly with the urodynamic results. [21]

Modification of This Question in Light of New Research: Previously identified clinical diagnostic criteria have to be validated in an older cohort of patients to determine if the criteria can facilitate selection of patients who would require urodynamic evaluation.

> ### Urol 5 (Level A): Further randomized controlled trials are needed to test the efficacy and safety of both new and established anticholinergic drugs for the management of urinary incontinence in older adults.

New Research Addressing This Question: Several of the newer agents for overactive bladder have been used safely in treating older adults. In a randomized, double blind, placebo-controlled trial, tolterodine was found to be safe and more effective than placebo in treating symptoms of overactive bladder. In this study the mean age of patients was 75 years, and a dosage of 2 mg twice a day was used. [22] Other agents, such as calcium channel blockers, have been evaluated for the treatment of urge incontinence in older patients in randomized trials and found not to be very effective. [23] Several new anticholinergic agents have demonstrated efficacy in treating detrusor overactivity. Most of them have a more benign side-effect profile than oxybutynin, which previously was the most commonly used agent. One of the main concerns with using oxybutynin is the risk of cognitive impairment in the older patient, since the drug is able to cross the blood-brain barrier. Many of the newer agents have a decreased risk of this side effect. This has been demonstrated for darifenacin in a randomized placebo-controlled trial in patients aged 65 years or older. [24] Another newer anticholinergic agent, solifenacin, has also been shown to be well tolerated in older adults. Higher plasma concentrations and areas under the curve, indicating duration of exposure, were achieved in older persons treated with solifenacin for 14 days. [25]

Modification of This Question in Light of New Research: Further specific trials targeted at the geriatric age group are required to thoroughly evaluate the effects of these agents in this population of patients.

> *Urol 6 (Level A)*: **Randomized controlled trials with large numbers of subjects will be required to determine whether acupuncture or other complementary therapies have a significant beneficial effect in treating urge or mixed urinary incontinence in older patients.**

New Research Addressing This Question: Analysis of prospective trial data indicates that behavioral therapy may be more effective than pharmacotherapy or placebo in treating older women with irritative symptoms, such as nocturia. [26] Initiating behavioral modification therapy before the occurrence of incontinence can significantly reduce the subsequent development of incontinence. This effect lasted up to a year after stopping the intervention in postmenopausal women who participated in a randomized controlled trial in which the control group received no intervention. [27] From a systematic review of four randomized trials and four before-and-after studies in the published literature, Teunissen et al reported that behavioral therapy alone or in combination with drug therapy appeared to be as effective if not better than drug therapy alone in treating incontinence. Behavioral modification appeared to consistently reduce urinary accidents in a substantial number of women aged 55 years or older, but the benefit of drug therapy was not consistent. [28] There have been no randomized controlled trials to examine the benefit of acupuncture in treating incontinence. Single-arm phase II studies in women aged 66 to 82 years suggest that such treatment can result in durable symptomatic improvement. [29] Randomized placebo-controlled trials of acupuncture for the treatment of overactive bladder have been performed with good results in younger women. [30] It remains to be seen if similar results can be achieved in older patients. Similarly, randomized trials of intravesical injection of botulinum toxin have included older patients and demonstrate promising results. However, in this study complications such as urinary retention, constipation, and dry mouth occurred in 4 patients, 3 of whom were aged 65 years or older. This suggests that complications of botulinum injection may be more common in the older patient. [31]

Modification of This Question in Light of New Research: The applicability of various conservative therapies and their relative toxicities need to be further assessed prospectively before it will be clear whether such approaches are safely applicable to older patients.

> *Urol 7 (Level A)*: **The bladder neck suspension and sling procedures have been proven effective in older women studied an average of 17 months after surgery. Prospective cohort studies with longer-term follow-up periods are needed to determine whether these procedures have sustained longevity.**

New Research Addressing This Question: Prospectively obtained objective and subjective assessment data following transvaginal urethral suspensions suggest that similar long-term outcomes (at up to 22 months) can be obtained regardless of age, even in octogenarians. [32] This substantiates prior retrospective data that suggest equivalent results following pubovaginal sling surgery in women above and below 70 years of age. [33] Needle suspension procedures using either the Raz or the Stamey technique generally do not appear to be effective in older women, as demonstrated by prior studies. [34,35] Large studies of tension-free vaginal tape for the treatment of incontinence in elderly women suggest that long-term outcomes are better for those with stress incontinence but that in women with mixed (stress plus urge) incontinence the cure rate declines to 60% at 4 years

and further to 30% at 8 years. The mean age of the patients in this study was 67 years for those with mixed incontinence and 61 years for those with stress incontinence. [36] Anterior vaginal wall repair for treatment of cystocele along with a urethral sling has been reported to be successful in a majority of elderly patients at a mean follow-up of 15 months; 80% had a minimum follow-up of 6 months or more. All patients demonstrated improvement in stress urinary incontinence, but younger patients were more likely to report improvement of urge incontinence. [37] Retrospective data indicate that surgery for pelvic organ prolapse can also be safely performed in octogenarians; satisfaction was expressed by as many as 80% of patients. [38] Randomized controlled studies comparing periurethral bulking agents to the pubovaginal sling in older women demonstrate that although the morbidity of the bulking agent injection is lower, the sling is more effective in the long term. [39]

Modification of This Question in Light of New Research: This question can be dropped from the research agenda.

> *Urol 8 (Level B)*: **Prospective cohort studies are needed to explore the factors that identify which elderly patients will do better with early surgical intervention than with more conservative treatment options.**

New Research Addressing This Question: Several retrospective and prospective analyses have attempted to identify factors that will predict a favorable outcome following conservative therapy for urinary incontinence. Several anatomic parameters, such as body mass index, prior pelvic surgery, and other factors, emerge as predictors, but age is not consistently among these factors. [40]

Modification of This Question in Light of New Research: More focused prospective studies in the older age group are required to compare conservative and surgical therapy and identify the best candidates for each approach. The fact that many patients progress from conservative to surgical therapy will make these studies difficult to design and will challenge adequate accrual.

> *Urol 9 (Level A)*: **Performing randomized controlled trials to extend the studies of factors that identify appropriate candidates for early surgery for incontinence could lead to the development and validation of predictive models useful for guiding treatment decisions for various types of urinary incontinence in older patients (see also the Key Questions, at the beginning of the chapter).**

New Research Addressing This Question: Prior studies have identified several factors that can predict the success of various interventions, such as pelvic floor exercises for the treatment of incontinence. Severity of symptoms at baseline, urodynamic criteria such as leak-point pressure, and pharmacologic history can all determine the likelihood of response to pelvic floor exercises. [41] Other predictors that are particularly relevant to stress urinary incontinence being treated with behavioral therapy include literacy level and prior surgery. Interestingly, the baseline urodynamic parameters, race, age, medical history, and obstetric history do not seem to consistently predict outcomes of behavioral therapy. [42] The diagnosis of urge incontinence may be facilitated by utilizing a model that includes both symptoms and demographic data, such as age and gender. [43] The presence of urgency and urge incontinence at baseline bodes ill for older men (60 to 89 years) in particular, as

they have a higher relative risk of 10-year mortality even after controlling for comorbidity and lifestyle factors. [44] The increased risk of mortality can probably be attributed to secondary events such as falls and injuries that could stem from the voiding problems. This emphasizes the need to identify and treat urge incontinence in older patients to limit the risk of secondary adverse events that can occur as a result of the urgency and urge incontinence. This can be facilitated by the use of predictive models in this population.

Modification of This Question in Light of New Research: Future studies could focus on practice patterns and barriers to implementation of existing models or diagnostic criteria to treat voiding dysfunction and predict outcomes in the geriatric age group.

URINARY TRACT INFECTIONS

See *New Frontiers,* pp. 278–280.

> *Urol 10 (Level B)*: **Additional research is needed to clarify the operational definitions of urinary tract infection and of asymptomatic bacteriuria.**

New Research Addressing This Question: Previous studies indicate that 24% of noninstitutionalized older adults, who constitute about 95% of the geriatric age group, will develop a urinary tract infection (UTI) during a 2-year observation period. [45] Most research, however, is focused on the 5% who are institutionalized. Approximately 50% of women and 30% of men in the institutionalized geriatric population have asymptomatic bacteriuria that does not typically require treatment, though several antibiotic-based therapeutic intervention studies nevertheless include such patients. Though pyuria often accompanies a positive urine culture in this setting, less than 10% of febrile institutionalized elderly persons without an indwelling catheter and with asymptomatic bacteriuria will benefit from a treatment of their presumed UTI. [46] Diagnosis of UTI in this population relies on symptoms, signs, and clinical judgment, rendering it hard to interpret the efficacy of many therapies. Misinterpretation of nonspecific signs and symptoms may lead to the false diagnosis of a UTI in many of these individuals with asymptomatic bacteriuria. [47]

Modification of This Question in Light of New Research: Additional work is needed to clarify the criteria for defining a UTI in older patients. Provider education is also necessary in order to prevent overtreatment and emergence of resistant strains of bacteria.

> *Urol 11 (Level B)*: **The natural history and potential risks of urinary tract infection or asymptomatic bacteriuria and forms of preventive therapy warrant further study (see the Key Questions, at the beginning of the chapter).**

New Research Addressing This Question: Several studies have attempted to evaluate various preventive nonantibiotic therapies to manage UTI and bacteriuria. Dessole et al randomized postmenopausal women to placebo versus estriol vaginal suppositories and determined that women in the treatment group had significantly lower rates of significant bacteriuria (14% versus 45%, $P < .001$). The average age of participants was 58 years (treated) and 56 years (control). Improvements were also observed in colposcopic examinations and urethral pressure profiles. [48] The use of oral nitrofurantoin macrocrystals appears to be much more effective in preventing UTI than the use of vaginal estriol pessaries. In a randomized comparison of the two treatment approaches, Raz et al discov-

ered that UTI rates as well as the rates of bacteriuria were significantly lower in those treated with nitrofurantoin; 90% of patients in the estriol group and 84% of patients in the nitrofurantoin group were 60 years of age. [49] The prevention of UTI following surgery does not appear to be facilitated by the use of a suprapubic tube rather than a urethral catheter, and often patients may need to be recatheterized per urethra after developing a complication following removal of the suprapubic catheter. This limits the use of this approach. [50] Data from the Heart and Estrogen/Progestin Replacement Study (HERS) suggests that oral hormone replacement does not impact the risk of UTI in postmenopausal women. Higher UTI frequencies were observed in women in the hormone therapy arm than in those receiving placebo, though the difference was not statistically significant. [51] Hence, it does appear that urinary antiseptic therapy with mild agents such as nitrofurantoin may be as effective as, if not better than, topical or systemic hormonal therapy for prevention of UTI.

Modification of This Question in Light of New Research: Future research should focus on the prophylactic role of agents such as cranberry juice and changes in local hygiene in preventing UTI through prospective trials in the geriatric age group. A combined approach adding antibacterials to prevention may yield better results.

> ***Urol 12 (Level A)*: Research on new antibiotic agents for the treatment of urinary tract infection should include randomized controlled trials specifically designed to assess the safety and efficacy of these drugs in geriatric patient populations.**

New Research Addressing This Question: Antibiotic use is very prevalent among older adults residing in nursing homes. This contributes to increased risk of resistance, costs, side effects, and drug interactions. The prevalence of antibiotic use is estimated to be between 8% and 17%. [52–56] Trials to test algorithm-based approaches to govern the use of antibiotics in geriatric residents of long-term-care facilities are under way, and once completed, they will enable the establishment of standard protocols to manage this common problem in this population. [56] Vogel et al randomized 183 women aged 65 years or older to receive either a short (3-day) course of ciprofloxacin or a 7-day course of ciprofloxacin. These researchers discovered that bacterial eradication rates were no different between the groups, at 98% and 93%, respectively. [57] Treatment-related side effects were much lower in those receiving the shorter course of antibiotics. This suggests that in older women with uncomplicated UTI, a 3-day course of oral ciprofloxacin is adequate and less toxic. In a randomized comparison, oral ciprofloxacin was found to be more effective in eradicating both the clinical symptoms of UTI and bacteriuria when compared with trimethoprim/sulfamethoxazole in women aged 65 years or older. [58] Fewer adverse effects were also observed in women receiving ciprofloxacin. These findings contradict those from previous studies which suggest that short-term antibiotic therapy is inadequate for the older adult, with 75% of patients having positive urine cultures at 6 months post-treatment when a 3-day course is used. [59] A systematic review of 13 trials evaluating different durations of antibiotic therapy for uncomplicated symptomatic UTI in elderly women indicated that single-dose therapy is less effective than a short (3- to 7-day) course of therapy but is better accepted by patients. There appears to be no significant difference in efficacy between a short (above) or long (7- to 14-day) course of therapy. [60] Hence, it appears that for

uncomplicated UTI in older women, a short 3-day course of oral ciprofloxacin may be the optimal treatment.

Funguria is relatively prevalent among older persons since many of them are residents of long-term-care facilities and have indwelling catheters. The presence of other comorbid illness, such as diabetes mellitus, can also contribute to the development of funguria. [61] *Candida albicans* is most commonly involved (52% of cases), and *C. glabrata* is the second most common (16%). Removal of the catheter can result in resolution of the funguria in many cases, and up to 75% of cases resolve with no treatment. Amphotericin bladder irrigation can eradicate funguria in 54% of cases, whereas oral fluconazole is effective in 45% of cases. In a randomized study, patients with an average age of 70 years took oral fluconazole or placebo for the treatment of asymptomatic or minimally symptomatic candidal UTI. A 14-day course of oral fluconazole eradicated the UTI in 50% of patients, but eradication occurred in 29% of the placebo group. [62] Still, most patients with asymptomatic funguria may require no treatment other than removal of the catheter. Those needing treatment can be managed with oral fluconazole, and amphotericin B bladder irrigation is reserved for the recalcitrant cases.

Modification of This Question in Light of New Research: This question can be dropped from the research agenda.

PROSTATE DISEASES

Benign Prostatic Hyperplasia

See *New Frontiers,* pp. 280–282.

Prostate Cancer

See *New Frontiers,* pp. 282–284.

Needed Research in Prostate Disease

> *Urol 13 (Level A)*: **Randomized controlled trials in elderly men are needed to compare phytotherapies with placebo or with established medical therapies for benign prostatic hyperplasia.**

New Research Addressing This Question: Although there are very few well-conducted randomized trials of phytotherapy versus medical therapy for BPH, the available evidence is controversial. Gross et al determined that conversion from phytotherapy to α-blockers such as tamsulosin is well tolerated and more effective in providing symptom relief. [63] An international study randomizing patients to saw palmetto or tamsulosin revealed equivalent improvements with both therapies up to 1 year of follow-up. [64] Comparison of α-blockers and other natural agents such as eviprostat also do not demonstrate any objective or subjective benefit of using the herbal agents. [65] A meta-analysis of 11 randomized trials and 2 single-arm studies published before 2000 suggested that saw palmetto may yield symptomatic as well as uroflow improvements significantly greater than placebo alone. [66] However, at least one recent randomized prospective study comparing saw palmetto with placebo revealed that there were no significant differences in symptomatic improvement or urinary flow rates between the treatment and placebo groups. [67] Systematic analysis of the randomized studies using *Pygeum africanum*, another common

phytotherapy for BPH, also revealed that this agent may result in slight improvement in symptoms of BPH. [68] However, none of the studies have compared the agent with standard medical therapy for BPH, and most studies are small, with short follow-up. Hence, it is hard to make definitive conclusions regarding its efficacy. Botanically derived 5-α-reductase inhibitors have also been compared with placebo and pharmacologic 5-α-reductase inhibitors, demonstrating equivalent effects in terms of symptom improvement. Agents such as β-sitosterols and Cernilton (rye grass pollen extract) also appear to be effective in providing symptomatic relief in men with BPH while being well tolerated. However, the available randomized studies are poorly conducted, and long-term data are lacking. [69,70]

Modification of This Question in Light of New Research: Future studies should focus on the benefits of phytotherapy in older men with BPH and their specific toxicities in this population, given older men's higher likelihood of having limited mobility and cognitive impairment as well as other comorbidities. The effect and extent of interaction of various phytotherapeutic agents with conventional medications is also essential to discern, given that many older men are taking multiple medications.

> *Urol 14 (Level A)*: **Randomized trials in elderly men are needed to compare minimally invasive surgical therapies for benign prostatic hyperplasia with the gold-standard procedure, transurethral resection of the prostate.**

New Research Addressing This Question: Several minimally invasive alternatives to transurethral resection of the prostate (TURP) have emerged. TURP was long considered the gold-standard surgical therapy for BPH. In the two randomized comparisons of TURP with transurethral needle ablation of the prostate (TUNA), both symptomatic improvement and urine flow rates were found to be better among patients undergoing TURP, but the differences were not substantial. Improvements achieved following TUNA appeared to last 5 years, though the number of patients followed up to that time point was low in at least one of the studies. Both these studies enrolled men with a mean age over 65 years. [71,72] A meta-analysis of 13 published studies of TUNA concluded that TUNA is a reasonable alternative to TURP or medical therapy for men with severely symptomatic BPH, and that perhaps it is more cost-effective. The analysis also suggested that it might be a good choice for men who do not want medical therapy or TURP or who are poor surgical candidates. [73] In a similar manner, a systematic review of six randomized clinical studies involving 540 men compared TURP with microwave therapy in men with symptomatic BPH. Results suggested that transurethral microwave therapy (TUMT) is a reasonable short-term alternative with acceptable side effects, but improvements in both symptom score and uroflow rate were substantially better with TURP. However, almost all of these studies had inadequate reporting of methods and varied widely in enrollment criteria. Side effects were fewer in the microwave therapy group. [74] The attractiveness of both the minimally invasive methods is that they can be performed as an outpatient procedure in the office. Men who fail either of these therapies can usually be salvaged with TURP. Randomized comparisons of gold-standard surgical therapy for BPH, ie, TURP, with newer methods of transurethral resection, such as laser vaporization and holmium laser enucleation (HOLEP), have been performed. In men with larger prostates (> 40 g), the three approaches appear to be equally effective in terms of objective and subjective symp-

tom relief at 6 months and 1 year. [75] Both HOLEP and laser vaporization tend to have lower perioperative morbidity and blood loss. Other studies confirm the similarity in outcomes. HOLEP appears to result in more irritative voiding symptoms but has shorter hospital stay and catheterization time. Duration of surgery may be longer with a HOLEP. [76] The average age of men in these trials was 65 years. Overall, minimally invasive therapies may be particularly attractive for older men with multiple comorbidities since they can be performed as an outpatient procedure under local anesthesia, and complications are minimal.

Modification of This Question in Light of New Research: This question can be dropped from the research agenda.

> ***Urol 15 (Level A)***: **Randomized controlled trials are needed to compare outcomes of early transurethral resection of the prostate with outcomes of initial medical therapy followed by subsequent transurethral resection of the prostate when clinically necessary.**

New Research Addressing This Question: There are no studies comparing initial TURP with medical therapy followed by TURP. It would probably be very difficult to pursue such studies at this time, given data indicating that medical therapy is effective in many men with BPH. Data do suggest that patients initially treated with α-blockers are more likely to progress to TURP than those treated with 5-α-reductase inhibitors. [77] Retrospective analysis of the effect of medical therapy on surgical treatment of BPH suggests that men are on average 5 years older with larger glands when undergoing surgery for BPH. The advent of medical therapy has decreased the use of TURP by 17% over the past decade, but open surgery for BPH is more often required now than it was 10 years ago (19% versus 29%). [78]

Modification of This Question in Light of New Research: It is increasingly important to define strict criteria for monitoring the efficacy of medical therapy and to establish guidelines for switching to surgical alternatives, particularly in older men where some deliberation may be required before embarking on surgical interventions. A large proportion of these men are already old when starting medical therapy, and by the time surgical therapy becomes necessary, their comorbidities and general functional status may also have changed, thereby restricting therapeutic alternatives.

> ***Urol 16 (Level B)***: **Prospective cohort studies and decision-analysis models are needed to identify the characteristics that predispose an older patient with benign prostatic hyperplasia to benefit from early transurethral resection of the prostate (see the Key Questions, at the beginning of the chapter).**

New Research Addressing This Question: Cost-effectiveness models suggest that cost equivalence with medical therapy may be reached by some of the minimally invasive therapies, such as TUNA, within 3 to 5 years. Naslund et al determined that TUNA is cost-equivalent to medical management combined with α-blockers and 5-α-reductase inhibitors after about 2.5 years of therapy. [79] Cost comparisons of TUMT with TURP suggest that total costs during a 3-year follow-up period are lower for TUMT than for TURP, though the risk of retreatment is higher with TUMT. The main explanation for the difference is the outpatient delivery of TUMT, which significantly reduces costs over those with

inpatient TURP. [80] Cost-utility analysis using Markov models suggests that risk-averse patients are likely to choose medical management and that non–risk-averse patients will choose TUMT. Neither type of patient will choose TURP. [81]

Modification of This Question in Light of New Research: These data are probably applicable to men in the geriatric age group, but additional functional and cognitive concerns have to be taken into consideration while evaluating these cost-utility data. It would be reasonable to assume that to a large extent the available cost-utility data will hold true, albeit with some modifications, in older men. Hence, this question can be dropped from the research agenda.

> *Urol 17 (Level B)*: **Because screening for prostate cancer is so widespread, it may be very difficult to design a randomized controlled trial comparing prostate-specific antigen screening with rectal examination alone, using risks, benefits, and costs as outcome measures. Therefore, the decision as to when to stop routine screening for prostate cancer in elderly men may depend on prospective cohort studies.**

New Research Addressing This Question: PSA levels clearly increase with increasing noncancerous prostate volume. Since prostate volume increases with age, there is an indirect link between PSA and age. [82] Hence, it is hard to interpret elevated PSA values in older men. There are currently no data to indicate a survival benefit to screening for prostate cancer. Ongoing studies in Europe—European Randomized Study of Screening for Prostate Cancer (ERSPC)]—and the United States—Prostate, Lung, Colorectal and Ovarian Screening Trial (PLCO)—are expected to provide data that clarifies this issue in the next few years. However, the proportion of older men is limited in both of these studies. Currently there appears to be an age-related decline in routine PSA testing and screening for prostate cancer, with lower rates being observed in the older age group. However, the rate of persistent PSA testing is small but not insignificant. Observational cross-sectional studies indicate a 3% to 5% rate of PSA testing in men aged 75 years or older. [83,84] The rate of PSA-based screening and the use of different types of therapy also vary by region, with rates of screening in men aged 75 years or older being much higher in Florida. [85]

Modification of This Question in Light of New Research: Further cohort studies are needed establish and ratify an age to stop screening for prostate cancer (as is done for cervical cancer) and develop a uniform and systematic approach to evaluation and treatment of prostate cancer in older men.

> *Urol 18 (Level A)*: **Because there is so much uncertainty regarding the best treatment plan for localized or locally metastatic prostate cancer, it is justified and indeed necessary to design randomized clinical trials in large populations of elderly men, with subgroup analyses, to examine the effects of clinical characteristics on treatment decisions.**

New Research Addressing This Question: A well-controlled clinical study with 10-year follow-up suggests a long-term benefit with regard to disease progression and survival in men who undergo radical prostatectomy for prostate cancer in comparison with watchful

waiting. [86,87] All the patients enrolled in this study were men aged 75 years or younger with a mean age of 64 years ($\pm$ 5.1) in each of the two groups. The survival and delayed progression benefits were not restricted by age. The majority of these men had clinically detectable cancers, and very few were identified by routine screening. This raises concerns regarding the applicability of these data in the current context of screening-detected prostate cancer, which is the more likely scenario at the present time. However, the results cannot be generalized to men aged 75 years or older.

Modification of This Question in Light of New Research: Randomized clinical trials of therapeutic alternatives are very hard to conduct in prostate cancer. This will be especially true for older men, in whom risk-stratified therapy is being utilized increasingly, with watchful waiting being the main recourse in those with low-risk disease. Furthermore, the clinical criteria (PSA, Gleason grade, disease stage) that are currently used to risk stratify younger patients are equally applicable to older patients. Hence, this question can be dropped from the research agenda.

OTHER GENITOURINARY MALIGNANCIES

See *New Frontiers,* pp. 285–286.

> *Urol 19 (Level A)*: **Randomized clinical trials are needed to determine the overall safety and long-term efficacy of less invasive therapy for bladder and renal malignances in older adults, comparing these with the standard procedures (radical cystectomy and radical nephrectomy).**

New Research Addressing This Question: Several observational uncontrolled cohort studies report that radical cystectomy and radical nephrectomy can be performed in elderly patients with outcomes comparable to those observed in younger patients. There does appear to be an increase in complication and mortality rates following radical cystectomy in older adults, but in well-selected individuals these differences are not significant. [88,89] In larger population-based studies, age does appear to be an independent predictor of negative outcomes following radical cystectomy. [90] Although several studies have suggested that a bladder-sparing approach to treat muscle-invasive bladder cancer is as effective as cystectomy, these studies have not been randomized, nor have they specifically enrolled older patients. The same is true for the evaluation of minimally invasive therapies, such as cryoablation and radiofrequency ablation, for kidney tumors. All of these are now recognized as viable therapeutic alternatives in older patients. Surveillance of small renal masses is also considered acceptable in patients with small exophytic masses ($<$ 3 cm) that are easily accessible percutaneously and do not involve the collecting system.

Modification of This Question in Light of New Research: Future studies should concentrate on the evaluation of bladder-sparing therapy for the treatment of bladder cancer and minimally invasive therapy for the management of renal masses in older patients. The prospective evaluation of surveillance with delayed treatment as a management option in biopsy-proven renal cancer, particularly in older individuals, is also important.

> *Urol 20 (Level A)*: **Predictive outcomes models to identify who would most benefit from the various forms of therapy for bladder and renal malignances need to be developed and validated (see the Key Questions, at the beginning of the chapter).**

New Research Addressing This Question: There are predictive algorithms that can help identify patients who are more likely to respond to surgical and nonsurgical therapy for renal cancer. [91,92] Because age is not used as a predictive variable in these models, they have not been specifically validated in cohorts of different age groups. Similar predictive nomograms to predict outcomes from therapy for bladder cancer are under development, but none are currently available.

Modification of This Question in Light of New Research: Further research in this area is required to develop and validate predictive algorithms for cancer-specific outcomes for bladder and kidney cancers in older patients.

SEXUAL DYSFUNCTION

Male Sexual Dysfunction

See *New Frontiers,* pp. 286–287.

Female Sexual Dysfunction

See *New Frontiers,* p. 287.

Influence of Comorbid Disease

See *New Frontiers,* pp. 287–288.

Treatment of Sexual Dysfunction

See *New Frontiers,* p. 288.

Needed Research in Sexual Dysfunction

> *Urol 21 (Level B)*: **Most of the studies that examine the relationship between sexual dysfunction and comorbid conditions are small retrospective reviews or case series, and they typically do not focus on elderly subjects. Larger, well-designed prospective cohort studies will be necessary to confirm these associations in older adult populations (see the Key Questions, at the beginning of the chapter).**

New Research Addressing This Question: Several population-based studies suggest that erectile dysfunction (ED) is very prevalent in older men. [93,94] More recent data estimates that 77% of men aged 75 years or older may have some form of ED. [93] Secondary analysis of data from the Prostate Cancer Prevention Trial indicates that at least 47% of men aged 55 years or older report some form of erectile dysfunction. [94] In this study, the development of new-onset ED was reported by 65% of men at 7 years of follow-up and was a significant predictor of cardiovascular disease. The presence of ED has also been linked to a 75% higher risk of peripheral vascular disease. [95] In the study by Blumentals et al, which was a retrospective analysis of over 12,000 men with and without ED, the odds of developing peripheral vascular disease and its association with ED was found to increase with increasing age. [95] In men with diabetes mellitus, the presence of ED may even be the most effective predictor of asymptomatic coronary artery disease. [96] The presence of chronic stable liver disease does not appear to increase the risk of ED. [97] The presence of

ED as documented on self-reported questionnaires such as the International Index of Erectile Function is prevalent in 71% of men with diabetes and 67% of men with hypertension.[98] Even the presence of mere dyslipidemia and depression can increase the prevalence of ED.[99,100] Lower urinary tract dysfunction has been linked to the presence of ED in men of various ages.[101,102] It is reasonable to assume that this would be true for older men, though specific data are not available.

Modification of This Question in Light of New Research: There are now excellent epidemiologic data linking ED to various comorbidities. Although these data do not focus on populations of elderly men, it would be reasonable to assume that the results would hold true across age groups. This question can be dropped from the research agenda.

> *Urol 22 (Level B)*: **Time series (before-and-after) studies may be sufficient to assess the effect of sildenafil on sexual function of women aged 65 to 74, 75 to 84, and 86 years and older.**

New Research Addressing This Question: Sildenafil citrate has been found to be effective in treating female sexual arousal disorder, a form of female sexual dysfunction. In one prospective randomized trial, postmenopausal women up to age 71 years were enrolled, but the data were not analyzed by age strata and hence do not allow us to assess the efficacy of this approach specifically in older women.[103] These positive results have not been consistent.[104,105]

Modification of This Question in Light of New Research: More detailed studies focused on elderly postmenopausal women are necessary in order to determine if therapy with a phosphodiesterase 5 (PDE 5) inhibitor such as sildenafil would be of benefit in women who complain of sexual dysfunction.

> *Urol 23 (Level B)*: **Time series (before-and-after) studies may be sufficient to assess the effect of sildenafil on sexual function of men aged 65 to 74, 75 to 84, and 86 years and older.**

New Research Addressing This Question: PDE 5 inhibitors appear to work equally well in older men (aged 60 years or older), but the rate of improvement may be faster in younger men.[106] The proportion of men 65 years or older who report improvement of ED with sildenafil therapy is similar to that for men who are a decade younger but considerably lower than that for men in their 20s.[107] An analysis of combined data from five large, randomized, placebo-controlled studies of sildenafil indicates that this agent is equally safe and efficacious in men aged 65 years or older and in younger men.[108] Tadalafil, another long-acting PDE 5 inhibitor, has been evaluated in men aged 65 years or older and found to be safe and efficacious.[109]

Modification of This Question in Light of New Research: This question can be dropped from the research agenda.

> *Urol 24 (Level B)*: **Prospective clinical series are needed to examine the use of intracavernosal injections, vacuum erection devices, and penile prostheses by men who are nonresponsive to sildenafil or are ineligible to use it.**

New Research Addressing This Question: In assessing preferences for the treatment of ED, researchers find that older men seem to prefer injection therapy over oral medications.

Dropout rates following oral therapy are as high as 78%, whereas those for injection therapy and vacuum erection devices are much lower, at 48% and 29%, respectively. [110] This has to be borne in mind when counseling older men regarding therapy for ED. In older men considering intracorporeal injections, the combination of prostaglandin E_1 (PGE_1), phentolamine, and papaverine appears to be more effective than PGE_1 alone. [111] Intracorporeal injection with PGE_1 such as alprostadil can improve erectile function in men who have failed PDE 5 inhibitors such as sildenafil. [112] This study included men up to 80 years of age, but it is not clear if equivalent response rates were obtained in men of all ages. However, intracorporeal injection therapy appears to work better than intraurethral PGE pellets. [113] This suggests that intracorporeal injections are a better first-line salvage therapy in men who fail oral agents such as PDE 5 inhibitors. It would be reasonable to assume that this would hold true for both older and younger men until further verification is available.

Sequential therapy is a very attractive concept for managing ED, given the variety of treatment options and the graded invasiveness of the actual therapeutic alternatives. It ranges from oral agents to surgical intervention. At least one prospective study of sequential treatment consisting of oral agents, followed by vacuum erection device, followed by intracorporeal injections, and ending with implantation of penile prosthesis suggests that short-term complete symptomatic improvement is achievable in 91% of patients. Forty-five percent of the men in this study were over the age of 60 and had diabetes mellitus. The results, however, were not analyzed by age strata, again making it difficult to estimate the benefit of such a program in elderly men. [114]

Modification of This Question in Light of New Research: Even though many of the studies described were not restricted to older men, it would be reasonable to assume that the results would hold true in older men. However, there are unique concerns regarding the applicability of various types of therapy in older men who may have some degree of cognitive impairment, dexterity issues, or partner issues. The feasibility of using these second-line therapies for ED and the barriers to adherence need to be investigated in order to determine the best second-line alternatives for older men.

STONE DISEASE

See *New Frontiers,* pp. 289–290.

> *Urol 25 (Level B)*: **Cohort studies are needed to evaluate the safety and clinical efficacy of minimally invasive surgical techniques in older adults with stone disease.**

New Research Addressing This Question: Studies suggest a peak in incidence of urinary calculi between the ages of 40 and 60 years. More recent studies suggest a later peak in incidence at 60 to 70 years, with stone rates declining dramatically thereafter. [115–117] The composition of the stones also tends to vary by age. Calcium oxalate stones predominate during the years of peak stone incidence, but uric acid stones are more frequent in the older age group. [118] Other stones such as cystine may be found more often with increasing age. Age-related changes in stone composition follow similar patterns in men and women. The incidence of struvite stones appears to be high at the extremes of age. [118] These findings have been corroborated by other studies in the geriatric population. [119] Higher excretion of urinary calcium may also be prevalent in older adults, contributing to stone

formation, though stone recurrence rates are no higher than for younger adults. [119] Interestingly, increased oral calcium intake does not appear to increase the risk of stone formation in postmenopausal women. The presence of hypertension and low magnesium intake do contribute to a higher stone risk in postmenopausal women. [120]

These data have significant implications for stone management and prevention in the older adult. One potential explanation for the higher incidence of uric acid stones is the greater prevalence of metabolic syndrome with insulin resistance and acidic urine pH in older adults, with almost 40% of people aged 60 years or older demonstrating these features. [121,122] Better control of metabolic syndrome in the older adult, along with control of infection and decreasing placement of indwelling catheters, may help decrease stone formation. Recurrent bladder stone formation has been linked to catheter encrustation by biofilm formed by organisms such as *Proteus mirabilis*, which tends to occur quite rapidly after replacement of long-term indwelling catheters. [123] Decreased use of catheters or their frequent replacement with prompt attention to symptoms suggestive of bladder stones may help mitigate this problem. Estrogen replacement may decrease urinary calcium excretion and calcium oxalate saturation. [124] Studies suggest that the lower stone rates observed in women in general may be due to lower urinary excretion of calcium, oxalate, and dissociated uric acid or to higher levels of citrate. Estrogen replacement in postmenopausal women restores the urinary milieu to premenopausal levels, thereby decreasing stone risk. [124]

Modification of This Question in Light of New Research: In terms of specific therapeutic approaches to the management of stone disease, there were no reports identified through our literature search that examined these issues in geriatric patients or any analysis that described the results in an age-stratified manner with sample sizes large enough to make the results generally applicable. Studies addressing these issues in the geriatric population are recommended.

RENAL TRANSPLANTATION

The Older Adult as Donor

See *New Frontiers,* pp 290–291.

The Older Adult as Recipient

See *New Frontiers,* pp. 291–292.

Needed Research in Renal Transplantation

> *Urol 26 (Level B)*: **The role of renal transplantation in older adults has grown recently, with the expansion of both donor and recipient age limits and other clinical criteria. Research is needed to clarify the unique needs of geriatric transplant patients, particularly with regard to immunosuppression and clinical outcomes. The effect of age of the kidney donor, age of the recipient, methods and degrees of immunosuppression, and the presence of concomitant disease need to be evaluated in prospective cohort studies.**

New Research Addressing This Question: With increasing requirement for donor kidneys, there is a strong push in the transplant community to expand the donor pool by utilizing cadaveric kidneys from older donors. Large-scale database analysis does suggest that kidneys from older donors have lower graft survival and greater delay in normalization of renal function post-transplant. [125] A prolonged cold ischemia time may be one of the factors responsible for the less satisfactory function observed in these donor kidneys. However, it should be pointed out that in the context of kidney donors, all individuals aged 55 to 60 years are typically included in the older age group. In some large European series, about 14% of all donors are classified as older (60 years or older). [126] The proportion of recipients in the United States who were older (aged 64 years or older) was approximately 9% in 2000. [127] Older donor age is an independent predictor of delayed graft function, chronic allograft nephropathy, and creatinine level at 1 year. There is some indication that cardiovascular morbidity and subsequent mortality are also increased in recipients of kidneys from older donors. [126] Several centers are advocating the concept of "old for old," with kidneys from older donors being placed in older recipients. The Eurotransplant Senior Programme that was launched in January 1999 in order to increase the acquisition of kidneys from older (65 years or older) donors and transplant them into older (65 years or older) recipients. This program outlines strict criteria for the acceptance of older kidneys for transplantation. Several innovative approaches are being tested under this program. [128] The use of dual kidney transplantation if the donor glomerular filtration rate (GFR) is below 50 to 70 mL/min is increasing in popularity; several small cohort studies demonstrate graft survival and function equivalent to that of single kidney transplants with high GFR into elderly recipients. [129] Some cohort studies even suggest that the best dialysis-free outcomes and lowest rejection rates are present in older recipients and donor grafts from older patients, respectively. [130,131] If the Eurotransplant Senior Program criteria are followed and the donors and recipients are well matched, early evidence suggests that outcome in terms of graft survival may be identical to that achieved in transplants that were matched for human leukocyte antigens (HLA). [128] Graft survival rates of 86% have been observed in the participants of the program (age matched but not necessarily HLA matched), in comparison with 79% in control groups (HLA matched and age matched). [132] Three-year graft survival was 64% for "old for old" transplants versus 67% for HLA-matched transplants into older recipients. These rates were further enhanced to 80% or better if initial graft function was good. It is interesting to note that the presence of comorbidities in the recipients or interventions to correct these (eg, coronary artery bypass grafting for coronary artery disease) does not seem to affect outcomes.

There is also evidence to suggest that using less atherogenic and less nephrotoxic immunosuppressive regimens can yield graft survival rates comparable to those achieved in younger patients who are transplanted with kidneys from younger donors. [133] The recognition of the importance of initial graft function as a predictor of subsequent graft survival, particularly in elderly recipients of kidneys from older donors, has led to the investigation of various strategies to delay the use of strong immunosuppressive agents, such as tacrolimus and cyclosporine. [134] Decreasing or delaying the use of calcineurin inhibitors appears to enhance the survival of old-for-old transplants. These strategies largely appear to be successful. [135,136] The less vigorous baseline immune response status of older patients may also be beneficial in this regard, with decreased risk of acute rejection (as low as 6% in some series) along with the need to use less exogenous immunosuppression. [127]

Despite the encouraging results from kidney transplantation using older donors and recipients, there are several concerns. The concerns lie more on the merit of pursuing transplants in older recipients rather than the use of kidneys from older donors per se. Recipient age continues to be an independent predictor of graft survival; however, the absolute effect of age on 5-year graft survival, though statistically significant, is small at 2.1%. [137] The larger concern may the fact that older recipients are more prone to develop chronic allograft nephropathy, which still limits enthusiasm for pursuing transplantation in older recipients.

Modification of This Question in Light of New Research: Most of these data are based on cohort studies, and even though truly randomized prospective trials may be difficult to accrue patients to, further investigation is clearly needed to establish criteria and standards to guide transplantation in the elderly age group.

NEW HORIZONS IN GERIATRIC UROLOGY

ANDROPAUSE

Studies suggest that serum total testosterone levels as well as free testosterone levels decline with age in most men aged 40 to 69 years. There are corresponding increases observed in sex hormone–binding globulin levels. It is estimated that the prevalence of true symptomatic androgen deficiency is 6% to 12%. [138] That would mean a total of 2.4 million men with androgen deficiency, or 480,000 new cases per year. Treatment of such androgen deficiency usually relies on androgen supplementation that carries some concern regarding the risk for either promoting or initiating the growth of unsuspected prostate cancer in these men. Supplementation with dihydrotestosterone gel appears to be acceptable, as it can increase muscle strength and does not appear to affect prostate volume or prostate-specific antigen levels. [139] This is an area of great clinical interest that needs additional research.

> *Urol 27 (Level A)*: **The benefit of androgen supplementation in the aging male needs to be determined. The appropriate agents that can be used for androgen supplementation, dose, duration of therapy, and necessary monitoring for concomitant diseases such as benign prostatic hyperplasia and prostate cancer need to be better examined in randomized clinical trials.**

> *Urol 28 (Level B)*: **Observational studies will be required to determine the impact of androgen supplementation on the risk of subsequent development of prostate cancer or symptomatic benign prostatic hyperplasia.**

> *Urol 29 (Levels B, A)*: **Observational case-control cohort studies will be required to assess the risk and prevalence of osteoporosis in aging men with low sex steroid hormone levels. This could lead to further randomized trials of agents to treat such osteoporosis if it is present.**

ASSESSMENT OF LIFE EXPECTANCY

A reasonably accurate assessment of remaining life expectancy on an individual patient basis is required before initiating therapy for many men or women with various urologic conditions and particularly for issues such as prostate cancer screening. Prostate cancer treatment decisions also often hinge on the likelihood of 10-year life expectancy. Current studies suggest that clinicians can underestimate life expectancy an average of 33% of the time and overestimate it 3.9% of the time. [140] This indicates that certain therapeutic and preventive interventions may be denied to elderly patients on the basis of incorrect estimates of life expectancy. In another study conducted in Canada, physicians were asked to review 18 different patient scenarios and predict life expectancy. Eighty-two percent of the responses correctly estimated life expectancy as being greater than or less than 10 years. However, 67% of responses were accurate within 3 years of actual and only 31% were within 1 year of actual lifespan, evaluated on the basis of Markov modeling. [141] The average error in predicted life expectancy ranged between 2.4 and 5.2 years. Hence, it could be very useful for most medical decision making but particularly for urology to develop tools to assist in more accurate estimation of remaining life expectancy.

> *Urol 30 (Level B)*: **Observational cohort studies to test the accuracy of tools to measure life expectancy in several real-life situations would be useful for more informed therapeutic and other management decisions in treating the older adult.**

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