MEN’S HEALTH GUIDELINES

SEXUAL FUNCTION:
Primary
1. Maximize sexual function, fertility, and quality of life in men with spina bifida

Secondary
1. Evaluate and characterize penile and genital sensation
2. Evaluate and characterize erectile function
3. Evaluate and characterize orgasmic and ejaculatory function
4. Maximize desired fertility potential of men with spina bifida
5. Determine the sexual activity and interest in males with spina bifida
6. Assess the impact of fertility on the QoL in male adults with spina bifida
7. Ensure sexual education and safe practices

Tertiary
1. Evaluate therapies for decreased sensation and erectile/orgasmic/ejaculatory dysfunction
2. Evaluate therapies for decreased fertility

Cumulative clinical questions based on age:
Newborn
Clinical questions:
1. Are testicles descended?

Guidelines:
1. Cryptorchidism is more prevalent in spina bifida. Examine position of testicles. If undescended, spontaneous descent often occurs in first six months of life. (14-16)

Toddler (1-3 years)
Clinical questions:
1. Are testicles descended?

Guidelines:
1. Cryptorchidism is more prevalent in spina bifida. Examine position of testicles. Secondary ascent can occur. If not in scrotum and unable to bring both into the scrotum, then refer to urologist for evaluation and possible surgical management. (14-16)

Pre-School (3-5 years)
Clinical questions:
1. Are testicles descended?
Guidelines:
1. Cryptorchidism is more prevalent in spina bifida. Examine position of testicles. Secondary ascent can occur. If not in scrotum and unable to bring both into the scrotum, then refer to urologist for evaluation and possible surgical management. (14-16)

School age (5-12 years)
Clinical questions:
1. Are testicles descended?

Guidelines:
1. Cryptorchidism is more prevalent in spina bifida. Examine position of testicles. Secondary ascent can occur. If not in scrotum and unable to bring both into the scrotum, then refer to urologist for evaluation and possible surgical management. (14-16)

Teenaged (13-18 years)
Clinical questions:
1. Are testicles descended, symmetrical and normal size for pubertal stage of development?
2. What is the prevalence of decreased penile/genital sensation in adolescents with SB?
3. How to best assess penile sensation?
4. What is the prevalence and nature of erectile dysfunction in adolescents with SB?
5. How to best inquire and assess about erectile function in this age group?
6. What is the prevalence and nature of orgasmic and ejaculatory dysfunction in adolescents with SB?
7. How to best inquire about sexual function including nocturnal emissions, non-genital stimulation, masturbation, oral sex, and intercourse?
8. What is the understanding of normal sexual function as well as SB-related alterations in adolescents with SB?
9. At what age should such education begin?
10. Are adolescent males with SB aware of contraceptive techniques, specifically the availability of latex condoms? Are they as effective as latex-containing condoms? Are there alternative methods of barrier contraception for this population?

Guidelines:
1. Cryptorchidism is more prevalent in spina bifida. Examine position of testicles. Secondary ascent can occur. If not in scrotum and unable to bring both into the scrotum or if asymmetric or seem small of stage of pubertal development, then refer to urologist for evaluation and possible surgical management. (14-16)
2. Limited data exists to answer clinical questions 2-10.
a. Open ended conservations should be initiated with adolescents with SB about their knowledge of normal sexual function when the provider deems the patient developmentally ready, or when there is evidence of sexual curiosity/experimentation on history and physical.

b. Patients should be educated that sexual function may be altered by sequelae of SB.

c. Information about safe sexual practices, including the use of barrier contraceptive methods (latex allergy), should be provided when the provider deems the patient developmentally appropriate, or when the patient inquires.

d. Penile and scrotal sensation should be evaluated with physical exam.

e. In the absence of a validated instrument for the measure of erectile function, IIEF or SHIM. (1,2) may be administered.

f. In the absence of validated instruments for the measure of orgasmic and ejaculatory function, patients should be asked whether they have any concerns and presence or absence of ejaculation/orgasm noted in the medical record.

**Adult (> 18 years)**

**Clinical questions:**

1. Are testes intra-scrotal, symmetrical, and normal adult-sized?
2. What is prevalence of hypogonadism in men with SB? If so, are there endocrinologic considerations?
3. What is the prevalence of decreased penile/genital sensation?
4. How to best assess penile sensation?
5. What is the prevalence and nature of erectile dysfunction in men with SB?
6. How to best inquire and assess erectile function?
7. What is the prevalence and nature of orgasmic and ejaculatory dysfunction in men with SB?
8. What is the understanding of normal sexual function as well as SB-related alterations in sexual function in men with SB?
9. How to best inquire about sexual function including nocturnal emissions, non-genital stimulation, masturbation, oral sex, and intercourse?
10. How much does sexual function influence the QoL in adult man with spina bifida?
11. What is the frequency of sexual activity in males with spina bifida?
12. At what age/developmental level should sexual function and infertility evaluation be offered?
13. Are men with SB aware of contraceptive techniques, specifically the availability of latex condoms? Are they as effective as latex-containing condoms? Are there alternative methods of barrier contraception for this population
14. What are paternity outcomes in men with SB?
15. What is the optimal approach to men with SB desiring an infertility evaluation?
16. How much does fertility influence the QoL in the adult male spina bifida population?
17. Are there special considerations for the implementation of artificial reproductive techniques (ART) in men affected with SB?

Guidelines:
1. Cryptorchidism is more prevalent in spina bifida. If testicular exam is abnormal, then refer to urologist. Scrotal/testicular ultrasound may be indicated. (14-16)
2. Limited data exist to support questions 2-17.
   a. Open ended conservations should be initiated with adolescents with SB about their knowledge of normal sexual function when the provider deems the patient developmentally ready, or when there is evidence of sexual curiosity/experimentation on history and physical.
   b. Patients should be educated that sexual function may be altered by sequelae of SB.
   c. Information about safe sexual practices, including the use of barrier contraceptive methods (latex allergy), should be provided when the provider deems the patient developmentally appropriate, or when the patient inquires.
   d. Penile and scrotal sensation should be evaluated with physical exam.
   e. In the absence of a validated instrument for the measure of erectile function, IIEF or SHIM. (1,2) may be administered.
   f. In the absence of validated instruments for the measure of orgasmic and ejaculatory function, patients should be asked whether they have any concerns and presence or absence of ejaculation/orgasm noted in the medical record.
   g. Patients should be educated about the risk of heritability of the condition for offspring and female partners offered additional supplementation with folic acid to reduce risk(4 mg of folic acid daily one month before pregnancy and during early pregnancy).

RESEARCH GAPS
• No validated questionnaires for erectile, ejaculatory, and orgasmic dysfunction in SB individuals. Also none validated for adolescents.
  o IIEF for erectile dysfunction – all related to activity in past month
  o Ejaculatory dysfunction – related to prior normal function
  o Orgasmic dysfunction – no good definition of orgasm
• Limited availability concerning sexual interest in male adolescence and adults with spina bifida
• There are no large studies detailing the incidence of erectile, ejaculatory, and orgasmic dysfunction in adolescents and men with SB.
• There are only a handful of studies assessing treatment of erectile dysfunction in men with SB.
• There is no standardized examination for penile sensation.
• There are only scant data on incidence of decreased penile sensation in men with SB.
• There are only four small studies of a nerve transfer operation to improve penile sensation in men with SB.
• There is only scant data on incidence of cryptorchidism in newborns and older children with SB?
• There is only one study on the incidence of testicular hypotrophy in adolescents and men with SB?
• There is only scant data on management of decreased fertility in men with SB.
• Mechanisms/tools to assess the developmental readiness to discuss sexual function and interest
• Lack of information concerning the usage and safety of latex condoms in males with spina bifida
REFERENCES/RESEARCH

ERECTILE FUNCTION

Physiology
Parasympathetic neural event – sacral spinal cord
Psychogenic erections require intact T11-L2 nerve roots

Assessment
IIEF = International Index of Erectile Function
1. Self-administered questionnaire
   a. Assesses function/activity OVER THE LAST FOUR WEEKS
   b. 15 questions
      i. Scored 0-5
      ii. 7 Categories
         1. Ejaculation -1 item
         2. Orgasm – 1 item
         3. Erectile function – 6 items
            a. Max of 30 points; Erectile dysfunction – score <14
         4. Sexual desire – 2 items
         5. Intercourse satisfaction – 3 items
         6. Overall satisfaction – 2 items.
      iii. Very focused on intercourse, not masturbation or oral sex
   a. 40% had had intercourse in past month – correlated with age
      i. 16 (25%) had normal erections (IIEF = 26-30)
      ii. 3 had mild ED (22-25), 4 mild to moderate ED (17-21) and 5 severe ED (6-10) [moderate = 11-16]
   b. ED is mostly associated with inability to maintain erections
   c. ED related to sacral nerve root involvement
   d. ED related to not living with parents

Principal origin of ED is difficulty maintaining erections

SHIM – abridged version (5 item) of IIEF (IIEF-5) – confidence to get & keep erection, hard enough for penetration, maintain after penetration, difficulty maintaining erection, satisfaction with intercourse

Physiologic measures (from Arrington – Questionnaires)
Nocturnal penile tumescence (NPT)
Intracavernosal injection of prostaglandin (+ other) – transdermal?
Penile branchial pressures indices
Doppler studies
Sacral evoked potentials

Rigiscan


Rigiscan - Normal in 2/15 – more than 4 erections of 15 min or longer (1 sacral;1 L5)
   No erection 6/15
   Brief erections in 7/15
   # erections stat sig correlated with sensory level.

Stimulated erections – 11/15


Self-report questionnaire

IIEF5 with Sharrard classification of lower extremity function in 26 SB men

<table>
<thead>
<tr>
<th></th>
<th>Sensate</th>
<th>Not Sensate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychogenic erections</td>
<td>85%</td>
<td></td>
</tr>
<tr>
<td>Rigidity w/ tactile stim</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>Ejaculation</td>
<td>88%</td>
<td></td>
</tr>
<tr>
<td>Orgasm</td>
<td>65%</td>
<td></td>
</tr>
<tr>
<td>ED</td>
<td>42%</td>
<td></td>
</tr>
</tbody>
</table>

ED could be predicted to some degree by Sharrard classification and touch sensation

(5) Lee et al The effect of spinal cord level on sexual function in the SB population. J Ped Urol. 11: 142, 2015 (page 15)

Used SHIM and IIEF

10/17 had severe ED
6/17 mild ED
1/17 mild ED
Correlated with lesion level

(6) Bong & Rovner. Sexual Health in adult men with spina bifida. The Scientific World J 7: 1466-69, 2007 - Difficulty in maintaining erection is major component.
PENILE SENSATION

Sensation involves more than light touch
Other senses are involved in sexual stimulation and may be compromised in NTD
  - Proprioception, olfaction, vision, auditory

Physiology
  - Sensation mediated through S2-4 to pudendal nerve to dorsal penile nerve
  - Necessary for reflex erections and vibratory ejaculation

Assessment
  - Physiology
    - Fine touch – A-beta myelinated fibers
    - Pain/thermal sensation – myelinated and unmyelinated C fibers – erotic
  - Assessment
    - Tactile – filaments to test tactile sensation and pain sensation
    - Thermal – feeling of warmth and pain
    - Tested on glans, midshaft, and foreskin, if present

(3) Sandler
  - Assessment
    - Genital sensation – light touch and pinprick
    - Anal wink
    - Bulbocavernosus reflex
    - Voluntary anal squeeze

TOMAX Procedure papers
  - Tested sensitivity on right and left halves of the shaft and glans + 3 areas on groin
    1. Touch – point and blunt sensation
    2. Temperature – 37°C and 4°C
    3. Quantitative fine touch – monofilament
    4. Bulbocavernosus reflex with EMG

Findings
  - Self-administered questionnaire – ED associated with tactile sensation – see Erectile Fx

Male genital sensation – normal | 7% | 53% | 53%
---|---|---|---
Male sexual activity | 30% | 14% | 14%
Female genital sensation – normal | 56% | 87% | 4%
Female sexual activity | More | Less | Less

**Treatment**

TOMAX procedure – re-routing ilioinguinal nerve (L1) to pudendal nerve (S2-4)
Must have sensation in ipsilateral groin

Dutch group

30 patients – unilateral procedures

*(10) Neurol Urodyn 34: 343-48, 2015*
30 patients – some bilateral (risk of losing reflex erections)

43 patients – 21 had spina bifida
3 bilateral

Seattle group

(L5/S1)
ORGASM

No unifying description
Very few tools to assess
Courtois F et al. Assessing and conceptualizing orgasm after a SCI. BJUI 108: 1624-33, 2010

See Questionnaires

Only questionnaire on orgasm – developed for men with SCI
They suggest that ejaculation and climax is an autonomic dysreflexia event with rapid suppression of tachycardia, incr. systolic BP, etc. by supraspinal inhibitory pathways in able-bodied individuals

Cardiovascular: 4 items 3
Respiratory 1 item 2
Muscular 8 items 6
Autonomic 9 items 5
Autonomic dysreflexia 11 items 4

Self-report questionnaire
IIEF5 with Sharrard classification of lower extremity function in 26 SB men
Orgasm 65%

WSFQ (Watts Sexual Function Questionnaire) – Lassman
Both sexes
During the past week... - 17 items
Desire 6 items
Arousal 4 items
Orgasm 4 items
Satisfaction 3 items

3/15 described good sexual feelings at time of ejaculation

Females
Joyner – orgasm
Empty bladder – painful contraction
Full bladder – incontinence
Vibrators – difficult to get into position to use and many contain latex
EJACULATION

See information on Orgasm

Assessment

MSHQ EjD Short Form


1. In past month,
   a. How often have been able to ejaculate
   b. Strength or force of ejac (relative to past ejac)
   c. Volume (relative to past ejac)
   d. Bother

Findings

(6) Bong & Rovner. Sexual Health in adult men with spina bifida. The Scientific World J 7: 1466-69, 2007 - from 4 articles

Up to 75% of SB men experience ejaculation
Tends to be dripping
May not be associated with sensation of orgasm

11/15 ejaculated – mostly dribbling (9 had erections; 2 did not)
4 had ejaculate in urine

Self-report questionnaire
IIEF5 with Sharrard classification of lower extremity function in 26 SB men
Ejaculation 88%
FERTILITY/CRYPTORCHIDISM

10 men with SB – electroejaculation – azoospermia – biopsy – Sertoli only
Normal testosterone production in 90%

10/15 had small (<12 cc) testes

Men with SCI have decreased Leydig cell population
Disrupted thalamic-pituitary-gonadal axis leads to decreased T levels.

Cryptorchidism in SB

75 males with MMC – 14.8% had cryptorchidism
Associated with lesion level of L2-3 or higher and absent cremasteric reflex

Review of literature and experimental model of transecting SC in neonatal rats
Two other studies + Hutson – 15/85 (18%)
International Myelodysplasia Project 81/345 (23%)
Lesion level-dependent - 19% of low lesions: 36% of high lumbar lesions


Available information from the literature:
1. Questionnaires are not created for individuals with disabilities
   a. International Index of Erectile Function (IIEF) for men
   b. Sexual Health Inventory for Men (SHIM)
   c. WSFQ, Watts Sexual Function Questionnaire
      i. WSFQ is a 17-item, self-reported instrument assessing the 4 domain scores of sexual experience, including desire (6 items), arousal (4 items), orgasm (4 items) and satisfaction (3 items) with gender specific versions for arousal and orgasm
d. SF-36
   i. General health related QOL was measured using the validated SF-36, a 36-item questionnaire that assesses health in the 8 domains of physical function, limitations due to physical problems, limitations because of emotional problems (role emotional), social function, mental health, energy, pain (role physical) and general health perception

2. Mental development and maturity does not match their age
      i. Performance of all 3 groups of children with SB was below that of the control group, which also reflects the lower socioeconomic status of the children with SB.
      i. The scores of the children with spina bifida only (without hydrocephalus) were closest to normal, but still below average. Those with spontaneously arrested hydrocephalus were in the backward range of abilities, and those with shunt-treated hydrocephalus had scores which generally were incompatible with normal levels of intelligence and attainment
      ii. Abnormal visuo-perceptual functioning closely correlated with defects in intelligence. The results of the school-attainment tests paralleled the distribution of intelligence but many of the children were found to be functioning below expectation for both age and measured intelligence

3. Level of sexual experience and education is lower in comparison to non-affected individual. Especially there is a lack of information concerning how they should address sexuality in their situation.
      i. 17 females and eight males aged 16-35 years
      ii. One subject answered correctly on all questions related to body anatomy, and seven answered correctly on all questions related to body part functions
      iii. Young adults with SB who live in Israel exhibit a relatively low level of sexual experience.
      i. Although sex education had been provided to almost all patients, fewer than a quarter received information specific to people with SB
ii. 52% were satisfied with their present sex life. Incontinence and lack of self-confidence were important obstacles

iii. Relationships and sexuality are important for young adults with SB. Hydrocephalus (HC) patients are less active and perceive more problems than HC-patients. Counseling in relationships and sexuality should be part of the regular care for this group.


   i. The aim of this paper was to examine sexual knowledge, concerns and needs of youth with spina bifida
   ii. 14 participants (13-28 years old) with SB
   iii. Youth with SB reported difficulties in finding answers to questions regarding their sexuality, romantic relationships and fertility


   i. Forty-nine percent of subjects indicated that the sexual education they received at puberty was useful; however, 32% lacked knowledge about their sexual functioning with regard to their disability

e. **Sexual and reproductive health in young people with spina bifida.** Sawyer SM, Roberts KV. Dev Med Child Neurol. 1999 Oct;41(10):671-5

   i. Most young people were satisfied with the amount of general sex education they had received. However, 95% stated they had inadequate knowledge about sexual and reproductive health relating to spina bifida and 59% of parents considered they had inadequate knowledge


   i. We found that only 40% of men with spina bifida engage in sexual activity, although their mean age was 29 years. These were the older men and those who no longer lived with their parents. The initiation of sexual activity is thus delayed compared with the general population, 14 the principal reason being continued living in the parental home.


   i. The majority of the patients learned about sexual reproduction from school classes with 48 (84%) having achieved a twelfth grade education or higher
   ii. A total of 41 patients (72%) accurately described the basic concepts of reproductive physiology

4. **Frequency of sexual activity.** Sexuality is not tied to continence and mobility but rather to level of lesion. They have interest in sexuality but it does not seem to affect their quality of life.
   i. Men had learned sex education from friends/media (41.6%) and women had learned it from parents (37.5%) or at school (33.7%)
   ii. Lesion level did not affect the ability to form relationships in patients of either gender
   iii. Education level was the same across all patients with no difference when male/female groups were compared by lesion level
   iv. Predictors indicated that patients with the highest chance of finding a partner and engaging in sexual activity were those with the lowest lesion level

   i. 17 females and eight males aged 16-35 years, three of the participants had a partner (12%) and seven (28%) indicated that they had had intimate sexual relationships

   i. 25% had a partner, 70% desired sexual contact, 47% had had sexual contact, and 22% had had sexual intercourse during the last year. Only 52% were satisfied with their present sex life

   i. A significant degree of sexual intimacy was reported, with 60% reporting an intimate relationship, and 25% (10 females, three males) reporting sexual intercourse. Thirty-seven percent of females had experienced unwanted sexual attention, and 30% reported unwanted sexual touching

   i. Of the 76 patients 18 (24%), including 9 women and 9 men, achieved sexual intercourse at least once in the last 2 months. There was no difference regarding gender distribution and mean age ± SD in sexually active vs not sexually active patients (25.8 ± 4.2 vs 24 ± 4.5 years, p = 0.13)
   ii. All levels (thoracic to sacral) of myelomeningocele were seen in the 2 groups with significant higher lesions of neurological impairment in not sexually active than in sexually active patients
iii. No difference was seen in relation to ambulatory status and urinary incontinence
iv. 24% of adult patients with spina bifida were sexually active. Sexual activity was not related to gender, level of urinary incontinence or extent of physical disability but it was more likely in patients with more caudal levels of neurological impairment

   i. The response rate was 72.7%. Of the 40 men who replied, 16 (40%) had had sexual intercourse at least once during the previous month. These were the older men (age 31.9 ± 5.7 years versus 27.7 ± 5.5 years, P = 0.027).
   ii. Young adult men with spina bifida and myelomeningocele begin sexual activity late. Moreover, 75% have erectile dysfunction that is related to difficulty in maintaining erections

5. Satisfaction with sexuality. Difficult to evaluate without control group. No literature found on desire of fertility and how much interest there is in fertility.
      i. 25% had a partner, 70% desired sexual contact, 47% had had sexual contact, and 22% had had sexual intercourse during the last year. Only 52% were satisfied with their present sex life
      i. Fifty-one percent of subjects regarded their sexual life as a failure or dysfunctional. However, 45% reported being satisfied with their sexual life
      i. Intercourse satisfaction and overall satisfaction were better in patients with impaired urethral relaxation and who were living outside the parental home
      i. Sexual function seems not to affect health related QOL in these patients
      ii. Sexual activity was not related to gender, level of urinary incontinence or extent of physical disability but it was more likely in patients with more caudal levels of neurological impairment
   i. The level of the neurological lesion was not predictive of erectile or ejaculatory function but it appears that reproductive potential is favored by lower and less severe lesions

6. **Latex sensitivity/ allergy and latex barrier products.** There are alternative products but no studies in their applicability in spina bifida.
      i. The purpose of the study was to evaluate whether atopy was a risk factor for latex sensitization in a specific population such as the young male soldiers of the Italian Army
      ii. One thousand five hundred male subjects (1000 subjects who were atopic and 500 subjects who were nonatopic)
      iii. The protocol included a questionnaire (symptoms of atopy, use of latex gloves and condoms and possible reactions previous surgical procedures), a clinical examination, a skin-prick test to latex and common allergens to evaluate atopy, and in part a latex challenge.
      iv. Among the 1000 subjects who were atopic, 2.8% had evidence for sensitization to latex compared with 1.2% in the 500 subjects in the nonatopic group
      v. The risk of latex sensitization was 19 times higher for subjects with a history of reactions to latex exposure and had a twofold increase for each surgical procedure and for each skin test positivity for inhalant allergens
   b. **Condoms are not a risk factor for sensitization to latex.** Chen FC, Büscher U, Niggemann B. Contraception. 2002 Dec;66(6):439-41.
      i. The study was conducted to assess the prevalence of sensitization to latex in a group of women with a high risk for atopy and to determine whether the use of condoms is a relevant risk factor
      ii. Our results indicate that prior use of condoms does not appear to be a specific risk factor for sensitization to latex in post-partum women at high-risk for atopy
      i. This study was an open label acceptability study that compared three lubricated condom products during vaginal intercourse: a natural rubber latex condom, a polyurethane condom, and a new non-latex (styrene ethylene butylene styrene, SEBS) condom
      ii. Fifty-four couples who were using condoms for birth control were enrolled in this three-way crossover study. Each couple tested three condoms of each type in a randomized sequence
      iii. Couples reported condom performance after each use and rated condom acceptability after use of three condoms of each type
iv. All three condom types had low clinical breakage and slippage rates (\(\leq 3.3\%\)) although the polyurethane condom did not perform as well in other measures of performance including unrolling, discomfort, stretching, bunching, and sliding along the penis during intercourse.

v. A statistically higher proportion of couples preferred both the natural rubber latex condom and the new non-latex condom above the polyurethane condom for ease of unrolling, and the natural rubber latex condom above the other condom types for perceived safety.


   i. Although the nonlatex condoms were associated with higher rates of clinical breakage than their latex comparison condoms, the new condoms still provide an acceptable alternative for those with allergies.


      i. In 1994, the London International Group introduced the first male polyurethane condom in the US.

      ii. The 360 couples who participated in the masked crossover study were randomized to use 3 polyurethane condoms and 3 latex condoms. After each use, couples recorded condom breaks, condom slips, and other aspects of performance.

      iii. The clinical breakage rates of the polyurethane and latex condoms were 7.2% and 1.1%, respectively.

      iv. The complete slippage rates of the polyurethane and latex condoms were 3.6% and 0.6%, respectively.

      v. Most male users found the polyurethane condom to be more sensitive than the latex condom.

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### Prostate Health

**NOTE: These guidelines only apply to adults with SB (>18 yo)**

**Primary outcome:**

Address urologic cancer specific screening criteria for adults

**Secondary**

- Optimal use of PSA testing
- Considerations for advanced screening in the adult male SB population
- Treatment considerations for adults with PCA and SB

**Clinical Questions:**

- How should men w SB be screened for PCA?
• What additional testing could be offered to patients to appropriately screen for PCA (genomic testing, MRI) and when are these appropriate?
• Are there specific recommendations for antibiotic prophylaxis for TRUS biopsy in a man with chronic bacteruria?
• Are PSA “norms” established in the ISC population?

Guidelines
• Men with <10-15 y life expectancy, those <55 and >69 should not be offered PSA testing.
• For those with neuropathic bladder and chronic bacteruria with at least 10-15 years life expectancy by the ages 55-69, the value of PSA alone as a screening tool is low.
• Providers should monitor PSA dynamics, consider advanced testing with MRI-based techniques and genomic testing and engage in a conversation with the patient regarding the risks of diagnostic biopsy and treatment of prostate cancer prior to checking PSA.
• If a biopsy is recommended, consideration should be made to use of MRI-guidance, transperineal technique, and the patients should be pre-treated with culture-specific antibiotics prior to biopsy.
• Research need: investigate use of higher sensitivity/specificity screening in men with neurogenic bladder, including genomic testing, serum markers, and MRI-based imaging and biopsy.
• Before determining whether a biopsy should be performed based on elevated PSA in a patient with congenital neuropathic bladder on ISC, one should consider waiting for fPSA normalization and tPSA nadir; typically about 12 weeks.
• Pre-treatment bowel, urinary and sexual function should be adequately assessed to guide counseling.
• In the setting of a patient with spina bifida, additional testing (eg cystourethroscopy to evaluate the external sphincter or urodynamics to evaluate bladder storage function) may be required.

Research gaps
• The question of PSA cut-off for biopsy has not been clearly elucidated
• Incidence of screening in men with SB is unknown
• No studies investigating outcomes after treatment for prostate cancer in men with spina bifida.

Incidence of screening in men with SB is unknown. Among patients with SCI, evidence suggests that men are likely under screened and subsequently tend to be diagnosed at more advanced stages of cancer than unaffected men, with nearly 64% of spinal cord injured men in one study demonstrating locally advanced (T3) or metastatic disease at the time of diagnosis (Scott PA, Perkash I, Mjode D. et al. Prostate cancer diagnosed in spinal cord injured patients is more commonly advanced stage than in able-bodied patients. Urology 2004; 63(3): 509-12). This suggests that there may be opportunity to better screen individuals so that diagnosis and treatment can be made at a timepoint where the disease may be curable.
Prostate cancer screening in the United States has evolved over the past 5 years, stimulated by a report by the US PSTF recommendation in 2012 against the use of routine PSA testing for prostate cancer surveillance (Moyer VA. US Preventative Services Task Force. Screening for prostate cancer: US Preventative Services Task Force recommendation statement. Ann Int Med. 2012; 157(2): 120-134). The American Urological Association responded to this recommendation with new guidelines for PCA screening, suggesting that PSA testing should not be offered to men under 40 or over 70, men with less than an 10-15 life expectancy of any age, and should only selectively be offered to men between 40-54 (those with a family history or African American). They recommended routine testing for men ages 55-69 with biannual PSA testing and DRE (Carter HB, Albertson PC, Barry MJ, et al. Early detection of prostate cancer: AUA guideline. J Urol. 2013; 190(2):419-26.) The basis of this dramatic decrease in utilization of PSA screening was twofold: 1) a recognition of the potential harm to the patient in PCA screening, and 2) a recognition that many cancers that are detected are not clinically significant, and therefore attempts should be made to minimize detection of low-risk PCA in all men. Known harms of PCA screening include the cost of testing and the morbidity associated with TRUS biopsy. It is estimated that approximately 4% of TRUS biopsies result in hospitalization within 30 days, the majority of these due to sepsis and other infectious sequelae (Loeb S van den Heuvel S, Zhu Z et al. Infectious complications and hospital admissions after prostate biopsy in a European randomized trial. Eur Urol 2012; 61: 1110.) Detection of clinically insignificant cancers has been noted to present three substantial risks: 1) the psychologic burden of diagnosis, 2) the actual cost of overtreatment, and 3) subjecting patients unnecessarily to the side effects of treatment, which include erectile dysfunction, urinary obstruction, urinary incontinence, bladder and bowel dysfunction, and higher risk for secondary cancers of the bladder and rectum (with radiation).

Over the past 5-10 years, the urological community has begun to investigate the role of adjunct radiological or genomic testing to help improve the performance of screening and to stratify those who are diagnosed with cancer into risk strata to better drive therapeutic treatments. Multiparametric MRI of the prostate has demonstrated diagnostic accuracy (44-87%), sensitivity (58-96%) and sensitivity (23-87%) superior to PSA, PSA kinetics and ultrasound-alone (Futterer JJ, Briganti A, De Visschere P, et al. Can clinically significant prostate cancer be detected with multiparametric Magnetic resonance imaging? A systematic review of the literature. Eur Urol 2015, 68; 1045-1053). Interobserver variability in grading lesions found on MRI has limited clinical application of MRI-based techniques on a large scale, but continued refinements in the Prostate Imaging-Reporting and Data System (PI-RADS) scoring system and technological improvements in the imaging hardware and software will no doubt overcome many of these challenges in the near term.

Concurrent with decreased surveillance, the urological community has increasingly adopted active surveillance as a treatment modality for men with low risk prostate cancers as well as more vigorously sought more sophisticated noninvasive testing to discriminate biologically inert cancers from more aggressive cancers. In addition to
improving performance of diagnosis, MRI based imaging has shown promise in discriminating tumor severity. Genomic testing has also demonstrated promise in categorizing tumor risk profile, so that patients can be better stratified into active surveillance, monotherapy, or multimodal therapy, thus decreasing untoward treatment side effects on patients with biologically insignificant disease. These tests can be of particular use in men with high baseline PSA who have already undergone an initial negative ultrasound guided biopsy.

Men with SB may be at increased risk for overtesting, higher risk for morbidity due to testing, and higher risk for side effects of treatment for prostate cancer for many reasons. Men with SB may have chronic bacteruria and prostatic inflammation from intermittent catheterization and/or incomplete bladder emptying. In addition, frequent use of antibiotics for urinary infections and chronic constipation may alter fecal flora and increase risk or the virulence of sepsis after TRUS biopsy. Community based rates of ESBL e coli have increased substantially over the past decade in many US communities, largely attributed to widespread use of fluoroquinolones. While not proven, fluoroquinolone-resistant e coli is likely higher among men with neurogenic bladder, for whom urinary tract infections and fluoroquinolone use are common. ESBL e coli is the pathogen most commonly associated with sepsis following TRUS biopsy (ref). Many routinely culture and treat urinary infections prior to TRUS biopsy, although there remains little proof that this reduces risk of post-TRUS sepsis (Lindert KA, Kabalin JN, Terris MK. Bacteremia and bacteruria after transrectal ultrasound guided prostate biopsy. J Urol 2000; 164: 76-80 Bruyere F, d’Arcier BF, Boutin J-M et al Is urine culture routinely necessary before prostate biopsy? Prostate Can and Prostatic dis 2010; 13: 260-262;). The actual risk of sepsis after TRUS biopsy in men who are chronically bacteruric is not known with or without antibiotic treatment prior to biopsy. Among a general population of patients undergoing transurethral resection of the prostate, subclinical bacteremia has been shown to occur in nearly one-quarter of patients after surgery, and that treatment with antibiotics within the two week period prior to surgery substantially reduced risk of bacteremia (4.3-fold reduction). Curiously, the bacteria identified and treated prior to surgery was often discordant with the bacterial isolated in the blood intraop (Mohee AR, Gascoyne-Binzi D, West R et al, Bacteremia during transurethral resection of the prostate: what are the risk factors and is it more common than we think? PLOS ONE DOI:10.1371/journal.pone.0157864 July 8, 2016).

The question of PSA cut-off for biopsy has not been clearly elucidated by the AUA, since the studies used to inform the guidelines used various cut offs. One study suggested that approximately 80% of PSA screening values between 2.5-4 ng/mL were not associated with a cancer diagnosis in a general population of European men (Schroder FH, Hugosson J, Roobol MJ et al. Screening and prostate cancer mortality in a randomized European study. NEMJ 2009; 360:1320.) “Normal” PSA values have never been established for men using CIC. A handful of small, single institution have looked at PSA values for patients with SCI, many of whom were using CIC or indwelling tubes to manage their bladders, and did not note a difference bt age-matched controls regardless of bladder management technique (Pramudji CK, Mutchnik SM DeConcini D et al. Prostate cancer screening with prostate specific antigen in spinal cord injured men. J
One single center study confirmed no difference in PSA scores in men with SCI as compared with age-matched unaffected controls, but did notice a nearly 2-fold increase in PSA among those men who were performing ISC, suggesting that ISC may be the factor that drives elevated PSA (Torricelli FCM, Lucon M, Vicentini F et al. PSA levels in men with spinal cord injury and under intermittent catheterization. Neurourol and Urodynamics 2011; 30: 1522-1524.) One study suggested that free and total PSA in men with chronic prostate inflammation (which occurs more commonly in the chronically bacteruric patient performing CIC) did not differ from those with prostate cancer, suggesting that PSA testing alone is insufficient to screen these men for biopsy (Stancik I, Luftengger W, Klimpfinger M et al Effect of NIH-IV prostatitis on free and free-to-total PSA. Eur Urol 2004; 46; 760-764). Others have failed to show a relationship between PSA and prostate inflammation (Nickel JC, Downey J, Young I et al. Asymptomatic inflammation and/or infection w serum prostate specific antigen. J Urol 2003; 169: 589. Nadler RB, Humphrey PA, Smith DS, et al. Effect of inflammation and benign prostatic hyperplasia on elevated serum prostate antigen levels. J Urol 1995; 154: 407). A single study considered total PSA values after a febrile UTI in men over time. They noted that median total PSA did not nadir until at least 6 months following febrile UTI, although free PSA levels nadired within one month following febrile UTI (Zackrisson B, Ulleryd P, Aus G et al. Evolution of free, complexed, and total serum prostate-specific antigen and their ratios during 1 year follow up of men with febrile urinary tract infection. Urology 2003; 62(2): 278-81). The tPSA resolved to near baseline by 3 months.

TREATMENT CONSIDERATIONS

Not surprisingly, there are no studies investigating outcomes after treatment for prostate cancer in men with spina bifida. A single study considered outcomes of men with SCI who underwent extirpative surgery in the setting of clinically organ-confined disease. Only 14 patients were evaluated in this study and long-term outcomes were not reported. None the less, over ½ of the patients experienced complications from surgery and LOS was substantially elevated in this cohort with a mean LOS following prostatectomy of 15 days (Gammon SR, Berni KC, Virgo KS et al. Surgical treatment for prostate cancer in patient with prior spinal cord injury. Ann Surg Onc 2005; 12(8): 674-78).

Given this, it would seem reasonable that a determination about method of treatment for prostate cancer should follow best practice for treatment of prostate cancer. According to the AUA guidelines, it is recommended that “a patient with clinically localized prostate cancer should be informed about the commonly accepted initial interventions including, at a minimum, active surveillance, radiotherapy (external beam or interstitial), and radical prostatectomy. A discussion of the estimates for benefits and harms of each intervention should be offered to the patient.” This guideline also states “Patient preferences and health conditions related to urinary, sexual and bowel function should be considered in decision making.” (Thompson I, Thrasher JB, Aus G, et al. Guideline for the management of clinically localized prostate cancer. AUA guidelines 2007)