

Urology

Workgroup Members: David B. Joseph, MD, FACS, FAAP (Chair); Sharon Baillie, RN, CNC, MN; Michelle A. Baum, MD; Dominic C. Frimberger, MD; Rose Khavari, MD; Rosalia Misseri, MD, FAAP; Stacey T. Tanaka, MD, MS; Hadley Wood, MD; Elizabeth B. Yerkes, MD

Introduction

The goals of urologic management and care of individuals with Spina Bifida focus on maintaining normal renal function during all ages, transitioning through stages of urinary continence, and achieving independence with personal care as aging continues through adulthood. Significant advancements in other specialties, particularly neurosurgery, have prolonged life and unmasked the importance of maintaining normal renal function and a healthy bladder. Over 90% of children at birth have a normal upper urinary tract (kidney and ureter). Historically, we know that if left unattended, 50% of those children will suffer upper urinary tract damage due to lower urinary tract (bladder and urethra) hostility.¹

During the first several years of life, the urologic focus on a child's health is based on maintaining normal kidney function at a time when the kidneys are most susceptible to kidney damage. As the child begins to approach school age, greater interest is directed toward gaining urinary continence. As a teenager, there is structured transition of care. Each of these urologic management milestones builds upon the last, potentially affecting their status in a positive or negative fashion.

Institutions create protocols based on their program's philosophy and available resources. Two general philosophies prevail: a proactive approach that attempts to identify children at risk for upper urinary tract deterioration and treat them before a problem occurs; and a reactive approach that follows a child closely and begins management at the first sign of any adverse change.²⁻⁴

Advocates of a proactive approach favor early identification of "at risk" children by assessing bladder function and managing hostile bladder parameters. This is done in an attempt to prevent adverse upper urinary tract changes and preserve normal renal function, thus limiting exposure to possible irreversible upper tract deterioration.

Institutions favoring a reactive approach rely on close evaluation of the upper urinary tract, renal function, and documentation of urinary infections. It is felt that adverse upper urinary tract changes can be detected early with minimally invasive assessment using ultrasonography. Renal function is typically assessed and followed with a serum creatinine. Adverse changes are assumed to be reversed with medical, pharmacologic, and operative management. Treating children reactively "as needed" allows for precise selective management limiting the stress and potential side effects of invasive procedures, medications, catheterization, and surgery.

The importance for maintaining normal renal function within this guideline cannot be overstated. It is also appreciated that while creatinine is a good screening tool of renal function, it is limited in the non-ambulatory child and adult with Spina Bifida with low muscle mass and thus provides a false sense of normality.⁵ Renal function may be more accurately measured with serum cystatin C or with a nuclear medicine glomerular filtration rate test (GFR).⁶ Currently, the best measure of renal function in children and adults with Spina Bifida is unknown and will require

ongoing investigation.

This guideline merges aspects of proactive and reactive philosophies based on a best practice methodology. The Centers for Disease Control and Prevention (CDC) are undertaking a prospective management protocol for newborns through age five developed by a team of pediatric specialists.⁷ It is anticipated that the outcome will positively impact the urologic care of children as well as the kidney health for individuals with Spina Bifida across the lifespan. Providing a strong foundation for pediatric care directly impacts the lifetime goals related to continence, self-management, and renal health. It is appreciated that urologic care is a dynamic, ever changing process.

Outcomes

Primary

1. Maintain normal renal function throughout the lifespan.
2. Achieve urinary continence as early as socially acceptable.
3. Maximize urologic independence.

Secondary

1. Eliminate hostile bladder dynamics through medical management.
2. Reduce or eliminate operative reconstruction of the bladder.
3. Maximize renal outcome while minimizing expense of studies, keeping watch over the timing and frequency of studies such as urodynamic testing, upper tract imaging, and lab studies.
4. Reduce impact of urinary tract infections (UTIs) and antibiotic overuse.
5. Establish a care program that allows for urologic independence, such as through clean intermittent self-catheterization (self-CIC).

Tertiary

1. Determine the best measure of renal function.
2. Minimize occurrence of urolithiasis.
3. Determine whether surgical interventions are effective in the long-term.

0-11 months

Clinical Questions

1. How do you define a symptomatic urinary tract infection and what is its long-term sequela?
2. Can diagnostic studies of the lower urinary tract (urodynamic) or upper urinary tract (ultrasonography) predict and prevent an adverse change in kidney function?
3. What is proactive management?
4. Is proactive management better than reactive to maintain normal upper tract?

Guidelines

1. Obtain the following baseline studies within three months of birth:
 - Renal/bladder ultrasound and repeat in six months
 - Urodynamic testing
 - Serum creatinine³ (clinical consensus)
2. Initiate CIC and antimuscarinic therapy for the treatment of mixed incontinence when indicated based on the above results.³ (clinical consensus)
3. Consider the presence of a UTI when there is a fever (100.4 F / 38.0 C). In neonates less than one month of age with failure to thrive and dehydration.

Define a UTI by:

4. a positive UA, and
5. a positive urine culture (UC) on a catheterized specimen, and
6. fever (100.4 F / 38.0 C).

Define a positive Urine Analysis (+ UA) as:

7. >trace nitrite or leukocyte esterase on dip UA, and
8. >10 white blood cells/high power field (WBCs/hpf), uncentrifuged specimen, or
9. >5 WBCs/hpf, centrifuged specimen.

Define a positive UC (+UC) as:

10. >50,000 colony forming units/milliliter (CFUs/mL) (sterile specimen obtained by catheter or suprapubic catheter aspirate).
11. >100,000 CFUs/mL in a clean voided specimen.⁸

1-2 years 11 months

Clinical Questions

1. How can providers account for neurologic bladder changes due to growth and/or tethering?
2. What diagnostic tools are reliable to assess renal function?
3. Are upper tract changes reversible once they occur?
4. How should symptomatic UTIs be defined? What is the sequela of symptomatic UTIs? What is the optimal upper and lower urinary tract surveillance?
5. Does the use of proactive CIC and antimuscarinic medication help to maintain a normal upper tract?

Guidelines

1. Obtain renal/bladder ultrasound every six months when the child is under the age of two. After that, obtain an ultrasound yearly if the child is stable, without UTIs or imaging changes. (clinical consensus)
2. Obtain a renal/bladder ultrasound, as needed if the child has recurring symptomatic UTIs or if urodynamic testing identifies bladder hostility. (clinical consensus)
3. Obtain urodynamic testing yearly through age three. Repeat as needed if the following are noted:^{1,2,7} (clinical consensus)
 - bladder hostility
 - upper urinary tract changes
 - recurrent symptomatic UTIs
4. Obtain a serum creatinine test if there is a change in the upper urinary tract. (clinical consensus)
5. Assess suspected UTIs with a urine specimen obtained by sterile catheterization technique. Repeat a positive bag urine specimen with a catheterized specimen. (clinical consensus)

Define a UTI by:

- a positive UA, and
- a positive urine culture (UC) on a catheterized specimen, and
- fever (100.4 F / 38.0 C).

Define a positive Urine Analysis (+ UA) as:

- >trace nitrite or leukocyte esterase on dip UA, and
- >10 white blood cells/high power field (WBCs/hpf), uncentrifuged specimen, or
- >5 WBCs/hpf, centrifuged specimen.

Define a positive UC (+UC) as:

- >50,000 colony forming units/milliliter (CFUs/mL) (sterile specimen obtained by catheter or suprapubic aspirate).
- >100,000 CFUs/mL in a clean voided specimen. ⁸

6. Initiate CIC and antimuscarinic therapy for the treatment of mixed incontinence when indicated by upper urinary tract changes, recurrent symptomatic UTIs, or bladder hostility noted on urodynamic testing.²⁻⁴ (clinical consensus)

3-5 years 11 months

Clinical Questions

1. How can providers account for neurologic bladder changes due to growth and/or tethering?
2. What diagnostic tools are reliable to assess renal function?
3. Are upper tract changes reversible once they occur?
4. How should symptomatic UTIs be defined? What is the sequela of symptomatic UTIs? What is the optimal upper and lower urinary tract surveillance?
5. Does the use of proactive CIC and antimuscarinic medication help to maintain a normal upper tract?
6. Are the caregivers compliant with CIC? Who is performing CIC – the caregivers and/or the child?

Guidelines

1. Obtain a renal/bladder ultrasound yearly, if the child is stable. (clinical consensus)
2. Obtain a renal/bladder ultrasound as needed, if the child has recurrent symptomatic UTIs or if urodynamic testing identifies bladder hostility. (clinical consensus)
3. Obtain urodynamic testing only if the following are present: (clinical consensus)
 - upper tract changes
 - recurring UTIs
 - interest in beginning a urinary continence program
4. If the child is on CIC, begin to involve the child in the process of self-catheterization. ⁹ (clinical consensus) (Self-Management and Independence Guidelines)
5. Obtain a serum creatinine test if there is a change in imaging of the upper urinary tract. (clinical consensus)
6. Obtain serum chemistries (includes serum creatinine) at age 5. Assess suspected UTIs with a catheterized urine specimen. Repeat a positive bag urine specimen with a catheterized specimen. (clinical consensus)

Define a UTI by:

- a positive UA, and
- a positive urine culture (UC) on a catheterized specimen, and
- leakage between CIC, and
- onset of pelvic or back pain, and
- fever (100.4 F / 38.0 C).

Define a positive UA (+ UA) as:

- >trace nitrite or leukocyte esterase on dip UA, and
- >10 white blood cells/high power field (WBCs/hpf), uncentrifuged specimen, or
- >5 WBCs/hpf, centrifuged specimen.

Define a positive UC (+UC) as:

- >50,000 colony forming units/milliliter (CFUs/mL) (sterile specimen obtained by catheter or suprapubic aspirate).
 - >100,000 CFUs/mL in a clean voided specimen.⁸
7. Initiate CIC and antimuscarinic therapy when indicated by upper urinary tract changes, recurring symptomatic UTIs, or bladder hostility noted on urodynamic testing.²⁻⁴ (clinical consensus)
 8. Introduce urinary continence and discuss interest in beginning the program and options at each visit.⁹⁻¹⁰ (clinical consensus) (Self-Management and Independence Guidelines)
 9. Introduce bowel management and discuss interest and options at each visit. (clinical consensus) (Bowel Function and Care Guidelines)

6-12 years 11 months

Clinical Questions

1. What is the best way to measure renal function in the child that is non-ambulatory?
2. What social, environmental, and economic limitations or hurdles are encountered when working to achieve urinary continence?
3. What is worse: stool or urinary incontinence?
4. How we define urologic continence? Is the definition of continence congruent with the perspective of the patient, family, and physician?

Guidelines

1. Obtain a renal/bladder ultrasound yearly, if the child is stable. (clinical consensus)
2. Obtain a renal/bladder ultrasound as needed if the child has recurrent symptomatic UTIs or if urodynamic testing identifies bladder hostility. (clinical consensus)
3. Obtain urodynamic testing when initiating a urinary continence program, if the following are present: (clinical consensus)
 - upper urinary tract changes such as hydronephrosis or renal scarring
 - recurring symptomatic UTIs
 - changes in urinary continence status
4. Obtain a serum creatinine test yearly. If the child has low muscle mass, consider an alternative measure of renal function.⁵ (clinical consensus)
5. Obtain serum chemistries yearly on any child who has had urinary reconstruction.
6. Obtain a serum B12 level test every year beginning two years after urinary reconstruction.¹¹⁻¹³ (clinical consensus)
7. Discuss a urinary continence program and interest in beginning the program and options at each visit.⁹⁻¹⁰ (clinical consensus) (Self-Management and Independence Guidelines)
8. Discuss a bowel management program and the interest and options at each visit. (clinical consensus) (Bowel Function and Care Guidelines)

13-17 years 11 months

Clinical Questions

1. How is continence affected by a shift in responsibility to self-care?
2. How is a normal upper urinary tract affected by a shift in responsibility to self-care?
3. What is optimal surveillance of the upper and lower urinary tract?
4. If reconstructive continent bladder surgery was undertaken, would you do it again?
5. If no reconstructive surgery was undertaken do you wish it had been?

Guidelines

1. Obtain a renal/bladder ultrasound yearly, if the child is stable. (clinical consensus)
2. Obtain a renal/bladder ultrasound as needed, if the child has recurring symptomatic UTIs or if urodynamic testing identifies bladder hostility. (clinical consensus)
3. Obtain a serum creatinine test yearly. If the child has low muscle mass, consider an alternative measure of renal function.⁵ (clinical consensus)
4. Obtain serum chemistries including B12 yearly on any child who has had urinary reconstruction.¹¹⁻¹³ (clinical consensus)
5. Transition urologic care to self-management, if doing so is developmentally appropriate for the child.¹⁴⁻¹⁵ (clinical consensus) (Self-Management and Independence Guidelines)
6. Transition bowel program to self-management, if doing so is developmentally appropriate for the child. (clinical consensus) (Bowel Function and Care Guidelines)

18+ years

Clinical Questions

1. What is optimal surveillance of the upper and lower urinary tract? What cancer screening is needed?
2. How do we define UTI in the adult and when do we treat?
3. How do we minimize sequelae of secondary incontinence in adulthood?

Guidelines

1. Obtain a renal/bladder ultrasound yearly. (clinical consensus)
2. Obtain a renal/bladder ultrasound, as needed if the adult has recurring symptomatic UTIs or if urodynamic testing identifies bladder hostility. (clinical consensus)
3. Obtain a serum creatinine test yearly. If the adult has low muscle mass, consider an alternative measure of renal function.⁵ (clinical consensus) (Self-Management and Independence Guidelines)
4. Obtain serum chemistries including B12 on anyone who has had urinary reconstruction.¹¹⁻¹³ (clinical consensus)
5. Undertake cystoscopy and appropriate upper tract imaging in adults who have had a bladder augmentation when the following are present:¹⁶⁻¹⁸ (clinical consensus)
 - clinically-noted change in upper or lower urinary tract status
 - gross hematuria
 - recurrent symptomatic UTIs
 - increasing incontinence
 - pelvic pain
 - the adult has had a renal transplant with the presence of BK/polyomavirus
6. Evaluate patterns of continence/incontinence and address issues collaboratively with the individual and family. Include assessment of amount (volume) of incontinence as the amount in adults may be more bothersome than frequency.¹⁹
7. Continue to support self-management and independent living. (Self-Management and Independence Guidelines)

Research Gaps

Proactive treatment: The foundation of management is based on the ability to predict individuals at risk for kidney deterioration and then influence management prior to an adverse event.

1. What is the ability of urodynamic testing to identify individuals at risk?

2. Does early medical (e.g. intermittent catheterization) and pharmacologic (antimuscarinic) management based on urodynamic testing prevent upper tract deterioration?

Renal Function: Renal function is assessed through serum studies and imaging. However, it is not known what the best assessment is in the population with Spina Bifida.

1. How is creatinine influenced by height, weight and mobility status of a patient with Spina Bifida?
2. Is cystatin C a more accurate indicator of renal function in the population with Spina Bifida?
3. What degree of renal dysfunction has occurred by the time changes are noted on imaging (i.e., renal scarring in ultrasonography or DMSA)?
4. Are changes on imaging reversible?
5. Is yearly serum and upper tract testing necessary?

Urinary Infections: Chronic bacteriuria is suspected to have less of an impact on adverse health and renal deterioration than symptomatic UTIs.

1. What is the definition of a symptomatic UTI?
2. Does the definition of symptomatic UTI change with aging?
3. Do symptomatic UTIs in children under the age of five have greater morbidity?

Continenence: Continenence of the bowel and bladder plays an important role in socialization. The following only relates to urinary continence. Continenence from a medical perspective is absolute (i.e. dry or wet).

1. Does the medical definition of absolute continence translate into a patient's and their family's quality of life?
2. Is the perception of continence from the perspective of the medical care provider and patient and family congruent?
3. Does achieving "some" degree of continence become beneficial?
4. Is there a threshold of "social" continence that is critical?
5. Is the cost (e.g. change in patient and family lifestyle, need for increased supervision, risk of intermittent catheterization, risk of medicines, and both short- and long-term surgical risk) worth the benefit?
6. What are the long-term challenges of patients who have undergone surgical intervention?
7. Would patients who have chosen surgery as a management option, make the same decision if they had the opportunity?

References

1. Bauer, S. B., & Joseph, D. B. (1990). Management of the obstructed urinary tract associated with neurogenic bladder dysfunction. *The Urologic clinics of North America*, 17(2), 395-406.
2. Bauer, S. B., Hallett, M., Khoshbin, S., Lebowitz, R. L., Winston, K. R., Gibson, S., ... & Retik, A. B. (1984). Predictive value of urodynamic evaluation in newborns with myelodysplasia. *Jama*, 252(5), 650-652.
3. Edelstein, R. A., Stuart, B., Kelly, M. D., Darbey, M. M., Peters, C. A., Atala, A., ... & Retik, A. B. (1995). Long-term urological response of neonates with myelodysplasia treated proactively with intermittent catheterization and anticholinergic therapy. *The Journal of urology*, 154(4), 1500-1504.

4. Hopps, C. V., & Kropp, K. A. (2003). Preservation of renal function in children with myelomeningocele managed with basic newborn evaluation and close followup. *The Journal of urology*, 169(1), 305-308.
5. Quan, A., Adams, R., Ekmark, E., & Baum, M. (1997). Serum creatinine is a poor marker of glomerular filtration rate in patients with spina bifida. *Developmental Medicine & Child Neurology*, 39(12), 808-810.
6. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. (2009). KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney international. Supplement*, (113), S1.
7. Routh, J. C., Cheng, E. Y., Austin, J. C., Baum, M. A., Gargollo, P. C., Grady, R. W., ... & Paramsothy, P. (2016). Design and methodological considerations of the centers for disease control and prevention urologic and renal protocol for the newborn and young child with spina bifida. *The Journal of urology*, 196(6), 1728-1734.
8. Madden-Fuentes, R. J., McNamara, E. R., Lloyd, J. C., Wiener, J. S., Routh, J. C., Seed, P. C., & Ross, S. S. (2013). Variation in definitions of urinary tract infections in spina bifida patients: a systematic review. *Pediatrics*, peds-2013.
9. Edwards, M., Borzyskowski, M., Cox, A., & Badcock, J. (2004). Neuropathic bladder and intermittent catheterization: social and psychological impact on children and adolescents. *Developmental medicine and child neurology*, 46(3), 168-177.
10. Moore, C., Kogan, B. A., & Parekh, A. (2004). Impact of urinary incontinence on self-concept in children with spina bifida. *The Journal of urology*, 171(4), 1659-1662.
11. Ganesan, T., Khadra, M. H., Wallis, J., & Neal, D. E. (2002). Vitamin B12 malabsorption following bladder reconstruction or diversion with bowel segments. *ANZ journal of surgery*, 72(7), 479-482.
12. Steiner, M. S., Morton, R. A., & Marshall, F. F. (1993). Vitamin B12 deficiency in patients with ileocolic neobladders. *The Journal of urology*, 149(2), 255-257.
13. Fujisawa, M., Gotoh, A., Nakamura, I., Hara, I. S. A. O., Okada, H., Yamanaka, N., ... & Kamidono, S. (2000). Long-term assessment of serum vitamin B12 concentrations in patients with various types of orthotopic intestinal neobladder. *Urology*, 56(2), 236-240.
14. Mahmood, D., Dicianno, B., & Bellin, M. (2011). Self-management, preventable conditions and assessment of care among young adults with myelomeningocele. *Child: Care, health and development*, 37(6), 861-865.
15. Lindehall, B., Möller, A., Hjälmsås, K., Lindehall, B., Möller, A., Hjälmsås, K., ... & Abrahamsson, K. (2008). Psychosocial factors in teenagers and young adults with myelomeningocele and clean intermittent catheterization. *Scandinavian journal of urology and nephrology*, 42(6), 539-544.
16. Husmann, D. A. (2016). Long-term complications following bladder augmentations in patients with spina bifida: bladder calculi, perforation of the augmented bladder and upper tract deterioration. *Translational andrology and urology*, 5(1), 3.
17. Higuchi, T. T., Granberg, C. F., Fox, J. A., & Husmann, D. A. (2010). Augmentation cystoplasty and risk of neoplasia: fact, fiction and controversy. *The Journal of urology*, 184(6), 2492-2497.
18. Mbeutcha, A., Lucca, I., Mathieu, R., Lotan, Y., & Shariat, S. F. (2016). Current status of urinary biomarkers for detection and surveillance of bladder cancer. *Urologic Clinics*, 43(1), 47-62.
19. Szymanski, K. M., Misseri, R., Whittam, B., Kaefer, M., Rink, R. C., & Cain, M. P. (2016). Quantity, not frequency, predicts bother with urinary incontinence and its

impact on quality of life in adults with spina bifida. *The Journal of urology*, 195(4), 1263-1269.

Additional Reading

1. Abrahamsson, K et al. Estimation of Renal Function in Children and Adolescents with Spinal Dysraphism, *J of Urology*, 179:2407-2409, 2008
2. Almodhen F, Capolicchio JP, Jednak R, El Sherbiny M. Postpubertal urodynamic and upper urinary tract changes in children with conservatively treated myelomeningocele. *J Urol* 2007; 178:1479–82
3. Armour BS, Ouyang L, Thibadeau J, Grosse SD, Campbell VA, Joseph D. Hospitalization for urinary tract infections and the quality of preventive health care received by people with Spina Bifida. *Disabil Health J*. 2009 Jul;2(3):145-52. doi: 10.1016/j.dhjo.2009.02.001.
4. Ausili E; Focarelli B; Tabacco F; Murolo D; Sigismondi M; Gasbarrini A; Rendeli C.: The role of the retrograde colonic enema in children with Spina Bifida: is it inferior to the antegrade continence enema? *Pediatric Surgery International*. 26(5):529-33, 2010 May.
5. Austin JC, Elliott S, Cooper CS. Patients with Spina Bifida and bladder cancer: atypical presentation, advanced stage and poor survival. *The Journal of urology* 2007; 178(3 Pt 1): 798-801.
6. Bauer Spina Bifida, Austin PF, Rawashdeh YF, de Jong TP, Franco I, Siggard C, Jorgensen TM; International Children's Continence Society: International Children's Continence Society's recommendations for initial diagnostic evaluation and follow-up in congenital neuropathic bladder and bowel dysfunction in children. *NeurourolUrodyn*. 2012 Jun;31(5):610-4. doi: 10.1002/nau.22247. Epub 2012 Apr 24.
7. Broderick KM, Munoz O, Herndon CD, Joseph DB, Kitchens DM. Utility of urodynamics in the management of asymptomatic tethered cord in children *World J Urol*. 2015 Aug;33(8):1139-42.
8. Buffart LM, Nan Den Berg-Emons R, Van Meeteren JV, et al. Lifestyle, participation, and health related quality of life in adolescents and young adults with myelomeningocele. *Dev Med Child Neurol* 2009; 89: E 133.
9. Cardenas DD, Topolski TD, White CJ, et al. sexual functioning in adolescents and young adults with Spina Bifida. *Arch Phys Med Rehabil* 2008; 89: 31-5.
10. Carr MC. Urological results after fetal MM repair in pre-MOMs trial patients at CHOP. *Fetal Diagnostic Therapy* 37: 211-218, 2015.
11. Carrasco A and Vemulakonda VM. Managing adult urinary incontinence from the congenitally incompetent bladder outlet. *Curr Opinion Urol* 2016; 26(4): 351-356.
12. Choi EK, Im YJ, Han SW: Bowel Management and Quality of Life in Children With Spina Bifida in South Korea.. *GastroenterolNurs*. 2015 Nov 10.
13. Clayton Db, Tanaka ST, Trusler L etal. Long term urological impact of fetal myelomeningocele closure. *J Urol* 186: 1581-1585, 2011
14. Couloures KG, Anderson M, Machiorlatti M, Marsenic O, Opas L. Discontinuation of Antimicrobial Prophylaxis (AP) in Children With Spina Bifida: A Case Series Analysis. *Nephrourol Mon*. 2016 Jul 25;8(5):e38484. eCollection 2016 Sep
15. deKort LM, Bower WF, Swithbank LV, Marschall-Kehrel D, de Jong TP, Bauer Spina Bifida:The management of adolescents with neurogenic urinary tract and bowel dysfunction. *NeurourolUrodyn*. 2012 Sep;31(7):1170-4. doi: 10.1002/nau.22206. Epub 2012 Mar 27.

16. DeLair SM, Eandi J, White MJ, Nguyen T, Stone AR, Kurzrock EA. Renal cortical deterioration in children with spinal dysraphism: analysis of risk factors. *J Spinal Cord Med.* 2007;30Suppl 1:S30-4.
17. Dicianno BE, Kurowski BG, Young JM et al. Rehabilitation and medical management of the adult with Spina Bifida. *Am J Phys Med Rehabil* 2008; 87(12): 1027-50.
18. Dicianno BE, Wilson R. Hospitalizations of adults with Spina Bifida and congenital spinal cord anomalies. *Arch Phys Med Rehabil.* 2010 Apr;91(4):529-35. doi: 10.1016/j.apmr.2009.11.023.
19. Dik P, Klijjn AJ, vanGool JD, et al. Early start to therapy preserves kidney function in Spina Bifida patients. *EurUrol* 49:908-913, 2006
20. Fagerskiold, A. M; Mattsson, G. Glad: Disabled children and adolescents may be outsiders in the community *International Nursing Review.* Vol.57(4), 2010, pp. 470-477.
21. Filler G, Gharib M, Casier S, Lödige P, Ehrich JH, Dave S. Prevention of chronic kidney disease in Spina Bifida. *IntUrolNephrol.* 2012 Jun;44(3):817-27. doi: 10.1007/s11255-010-9894-5. Epub 2011 Jan 13.
22. Fischer N, Church P, Lyons J, McPherson AC: A qualitative exploration of the experiences of children with Spina Bifida and their parents around incontinence and social participation. *Child Care Health Dev.* 2015 Nov;41(6):954-62. doi: 10.1111/cch.12257.
23. Fox, J et al. Cystatin C as a marker of early renal insufficiency in children with congenital neuropathic bladder, *J of Urology*, 191:1602-1607, 2014
24. Freeman KA, Smith K, Adams E, Mizokawa S, Neville-Jan A: Is continence status associated with quality of life in young children with Spina Bifida? *West Coast Spina Bifida Consortium.JPediatrRehabil Med.* 2013 Jan 1;6(4):215-23. doi: 10.3233/PRM-140263.
25. Galloway NT, Mekras JA, Helms M, Webster GD. An objective score to predict upper tract deterioration in myelodysplasia. *The Journal of urology* 1991; 145(3): 535-7.
26. Gatti C, Del rossi C, Ferrari A et al. Predictors of successful sexual partnering of adults with Spina Bifida. *J Urol* 2009 182: 1911-1996
27. Hamid R, Greenwell TJ, Nethercliffe JM, Freeman A, Venn SN, Woodhouse CR. Routine surveillance cystoscopy for patients with augmentation and substitution cystoplasty for benign urological conditions: is it necessary? *BJU international* 2009; 104(3): 392-5.
28. Hensle TW, Bingham J, Lam J, Shabsigh A. Preventing reservoir calculi after augmentation cystoplasty and continent urinary diversion: the influence of an irrigation protocol. *BJU international* 2004; 93(4): 585-7.
29. Higuchi T, Shimizu M, Owaki A, et al. A possible mechanism of intravesical BCG therapy for human bladder carcinoma: involvement of innate effector cells for the inhibition of tumor growth. *Cancer immunology, immunotherapy: CII* 2009; 58(8): 1245-55.
30. Hunt GM, Oakeshott P. Outcome in people with open Spina Bifida at age 35: prospective community based cohort study. *BMJ* 2003; 326: 1365-6
31. Husmann DA, Fox JA, Higuchi T. Malignancy following bladder augmentation: Recommendations for long-term follow-up and cancer screening. *AUA Update Series* 2011; 30(Lesson 24): 222-7.
32. Husmann DA, Rathbun SR. Long-term follow up of enteric bladder augmentations: the risk for malignancy. *Journal of pediatric urology* 2008; 4(5): 381-5; discussion 6.
33. Husmann DA, Spence HM. Current status of tumor of the bowel following ureterosigmoidostomy: a review. *The Journal of urology* 1990; 144(3): 607-10.

34. Joseph DB: Practice Point commentary-Untethering of the spinal cord in children with myelomeningocele:, Nature Clinical Practice Urology in press for publication Nat Clin Pract Urol 49:472-3 2007
35. Kaefer M, Pabby A, Kelly M, et al. Improved bladder function after prophylactic treatment of the high risk neurogenic bladder in newborns with MM. J Urol 162: 1068-71, 1999
36. Kari JA, Safdar O, Jamjoom R, Anshasi W. Renal involvement in children with Spina Bifida. Saudi J Kidney Dis Transpl. 2009 Jan;20(1):102-5.
37. Kaye IY, Payan M, Vemulakonda VM. Association between clean intermittent catheterization and urinary tract infection in infants and toddlers with Spina Bifida J Pediatr Urol. 2016 Oct;12(5):284.e1-284.e6. doi: 10.1016/j.jpuro.2016.02.010. Epub 2016
38. Kessler TM, Lackner J, Kiss G, et al. Early proactive mgmt. improves upper urinary tract function and reduces the need for surgery in patient with myelomeningocele. NeurourolUrodyn 25:758-762 2006
39. Kiddoo D, Sawatzky B, Bascu CD, Dharamsi N, Afshar K, Moore KN. Randomized Crossover Trial of Single Use Hydrophilic Coated vs Multiple Use Polyvinylchloride Catheters for Intermittent Catheterization to Determine Incidence of Urinary Infection. J Urol. 2015 Jul;194(1):174-9. doi: 10.1016/j.juro.2014.12.096.
40. Klose, A. G., Sackett, C. K., Mesrobian, H. G.: Management of children with myelodysplasia: urological alternatives. J Urol, 144: 1446, 1990
41. Kokorowski PJ, Routh JC, Borer JG, Estrada CR, Bauer Spina Bifida, Nelson CP. Screening for malignancy after augmentation cystoplasty in children with Spina Bifida: a decision analysis. The Journal of urology 2011; 186(4): 1437-43.
42. Kurzrock EA, Polse S. Renal deterioration in myelodysplastic children: urodynamic evaluation and clinical correlates. J Urol 159:1657-61, 1998
43. Lee NG, Gomez P, Uberol V et al. In Utero closure of myelomeningocele does not improve lower urinary tract function J Urol 188:? 1567-1571, 2012
44. Lemelle JL, Guillemin F, Aubert D, Guys JM, Lottmann H, Lortat-Jacob S, Moscovici J, Mouriquand P, Ruffion A, Schmitt M: A multicentre study of the management of disorders of defecation in patients with Spina Bifida..NeurogastroenterolMotil. 2006 Feb;18(2):123-8
45. Lemelle JL, Guillemin F, Aubert D, Guys JM, Lottmann H, Lortat-Jacob S, Mouriquand P, Ruffion A, Moscovici J, Schmitt M:Quality of life and continence in patients with Spina Bifida. Qual Life Res. 2006 Nov;15(9):1481-92.
46. Lloyd JC, Nseyo U, Madden-Fuentes RJ et al. Reviewing definitions of urinary incontinence in the contemporary Spina Bifida literature: a call for clarity. J PedUrol 2013; 9: 567-574.
47. Luther, Brenda Lou: Food and physical activity Choices to prevent overweight in children with Spina bifida Dissertation Abstracts International: Section B: The Sciences and Engineering. Vol.71(6-B),2010, pp. 3597. AN: 2010-99240-196
48. Ma Y, Li B, Wang L, Han X. The predictive factors of hydronephrosis in patients with Spina Bifida: reports from China. Int Urol Nephrol. 2013 Jun;45(3):687-93. doi: 10.1007/s11255-013-0409-z. Epub 2013 Mar 13.
49. Malm-Buatsi E, Aston CE, Ryan J, Tao Y, Palmer BW, Kropp BP, Klein J, Wisniewski AB, Frimberger D.J: Mental health and parenting characteristics of caregivers of children with Spina Bifida. Pediatr Urol. 2015 Apr;11(2):65.e1-7. doi: 0.1016/j.jpuro.2014.09.009.
50. McGuire EJ, Woodside JR, Borden TA, Weiss RM. Prognostic value of urodynamic testing in myelodysplastic patients. The Journal of urology 1981; 126(2): 205-9.

51. McLorie GA, Perez-Marero R, Csima A, Churchill BM. Determinants of hydronephrosis and renal injury in patients with myelomeningocele. *The Journal of urology* 1988; 140(5 Pt 2): 1289-92.
52. Miklaszewska M, Korohoda P, Zachwieja K, Wolnicki M, Mizerska-Wasiak M, Drożdż D, Pietrzyk JA. Can We Further Improve the Quality of Nephro-Urological Care in Children with Myelomeningocele? *Int J Environ Res Public Health*. 2016 Sep 1;13(9)
53. Mirkin K, Casey JT, Mukherjee S, Kielb SJ. Risk of bladder cancer in patients with Spina Bifida: case reports and review of the literature. *Journal of pediatric rehabilitation medicine* 2013; 6(3): 155-62.
54. Morgan C et al. Correlation between cystatin C and renal scan determined GFR in children with Spina Bifida, *Pediatric Nephrol*, 23L329-332, 2008
55. Mutlu H1, Ekinci Z. Urinary tract infection prophylaxis in children with neurogenic bladder with cranberry capsules: randomized controlled trial. *Pediatr* 2012;2012:317280. doi: 10.5402/2012/317280.
56. Nanigian DK, Nguyen T, Tanaka ST, Cambio A, DiGrande A, Kurzrock EA: Development and validation of the fecal incontinence and constipation quality of life measure in children with Spina Bifida. *J Urol*. 2008 Oct;180(4 Suppl):1770-3; discussion 1773. doi: 10.1016/j.juro.2008.03.103.
57. Olandoski KP, Koch V, Trigo-Rocha FE. Renal function in children with congenital neurogenic bladder. *Clinics (Sao Paulo)*. 2011;66(2):189-95.
58. Olesen JD, Kiddoo DA, Metcalfe PD: The association between urinary continence and quality of life in paediatric patients with Spina Bifida and tethered cord. *Paediatr Child Health*. 2013 Aug;18(7):e32-8.
59. Ozel SK, Dokumcu Z, Akyildiz C, Avanoğlu A, Ulman I. Factors affecting renal scar development in children with Spina Bifida. *Urol Int*. 2007;79(2):133-6.
60. Rickwood AM, Hodgson J, Lonton AP and Thomas DG: Medical and surgical complications in adolescent and young adult patients with Spina Bifida. *Health Trends* 1984; 16: 91-95.
61. Rickwood AMK. Neuropathic bladder in childhood. In Mundy AR, Stephenson TP, Wein AJ eds. *Urodynamics: Principles, Practice and Application*. Edinburgh: Churchill Livingstone, 1994: 403–22
62. Robertson WG, Woodhouse CR. Metabolic factors in the causation of urinary tract stones in patients with enterocystoplasties. *Urological research* 2006; 34(4): 231-8.
63. Satar N, Bauer Spina Bifida, Shefner J, Kelly MD, Darbey MM. The effects of delayed diagnosis and treatment in patients with an occult spinal dysraphism. *J Urol*. 1995 Aug;154(2 Pt 2):754-8.
64. Schwartz G and Work, D, Measurement and Estimation of GFR in children and adolescents. *CJASN*, 2009, 4(1832-43)
65. Seki N, Akazawa K, Senoh K, et al. An analysis of risk factors for upper urinary tract deterioration in patients with myelodysplasia. *BJU international* 1999; 84(6): 679-82.
66. Sharma, A et al. Diagnostic accuracy of Cystatin C based eGFR equations at different GFR levels in children, *CJASN*, 6:1599-1608, 2011
67. Shiroyanagi Y, Suzuki M, Matsuno D, Yamazaki Y. The significance of 99mtechnetium dimercapto-succinic acid renal scan in children with Spina Bifida during long-term follow up. *J Urol*. 2009 May;181(5):2262-6; discussion 2266. doi: 10.1016/j.juro.2009.01.057. Hatlen T,
68. Sidi AA, Dykstra DD, Gonzalez R. The value of urodynamic testing in the management of neonates with myelodysplasia: a prospective study. *The Journal of urology* 1986; 135(1): 90-3.

69. Snodgrass W, Villaneuva C, Gargollo P. New hydronephrosis and/or vesicoureteral reflux after bladder outlet surgery without augmentation in 75 children with neurogenic bladder. *J PedUrol* 2014; 10: 90-910.
70. Snow DC, Yerkes EB, Cheng EY: Update on Urological Management of Spina Bifida from Prenatal Diagnosis to Adulthood *JUROL* 194:288-296 2015
71. Song K, Shurtleff D, Duguay S. Contributory factors to postoperative spinal fusion complications for children with myelomeningocele. *Spine (Phila Pa 1976)*. 2010 Jun 1;35(13):1294-9
72. Szymanski KM, Misseri R, Whittam B, et al. Quantity, not frequency, predicts bother with urinary incontinence and its impact on quality of life in adults with Spina Bifida. *J Urol* 2015; 195: 1263-1269.
73. Szymanski KM, Misseri R, Whittam B, et al. Mortality after bladder augmentation in children with Spina Bifida. *The Journal of urology* 2015; 193(2): 643-8.
74. Szymanski KM, Rink RC, Whittam B et al. Long-term outcomes of the Kropp and Salle urethral lengthening bladder neck reconstruction procedures. *J PedUrol* 2016; 12(6): 403.
75. Tarcan T, OnoIf, Ilker Y et al. The timing of primary neurosurgical repair significantly affects NGB prognosis in children with myelomeningocele. *JUrol* 176: 1161-1165, 2006
76. Teichman JM, Scherz HC, Kim KO, etal. An alternative approach to myelodysplasia management : aggressive observation and prompt intervention. *J Urol* 152: 807-811, 1994
77. Veenboer PW, Hobbelink MG2, Ruud Bosch JL1, Dik P, van Asbeck FW, Beek FJ, de Kort LM Diagnostic accuracy of Tc-99m DMSA scintigraphy and renal ultrasonography for detecting renal scarring and relative function in patients with spinal dysraphism. *NeurourolUrodyn*. 2015 Aug;34(6):513-8. doi: 10.1002/nau.22608. Epub 2014 Apr 7.
78. Verhoef M, Lurvink M, Barf HA, Post MW, van Asbeck FW, Gooskens RH, PrevoAJ: High prevalence of incontinence among young adults with Spina Bifida: description, prediction and problem perception..*Spinal Cord*. 2005 Jun;43(6):331-40.
79. Wang QW, Wen JG, Song DK, et al. Is it possible to use urodynamic variables to predict upper urinary tract dilatation in children with neurogenic bladder-sphincter dysfunction? *BJU international* 2006; 98(6): 1295-300.
80. Werhagen L, Gabrielsson H, Westgren N, Borg K. Medical complication in adults with Spina Bifida. *Clin Neurol Neurosurg*. 2013 Aug;115(8):1226-9. doi: 10.1016/j.clineuro.2012.11.014.
81. Wide P, Glad Mattsson G, Mattsson S. Renal preservation in children with neurogenic bladder-sphincter dysfunction followed in a national program. *J Pediatr Urol*. 2012 Apr;8(2):187-93. doi: 10.1016/j.jpuro.2011.02.003. Epub 2011 Mar 15
82. Wilson R, Lewis SA, Dicianno BE. Targeted preventive care may be needed for adults with congenital spine anomalies *PM R*. 2011 Aug;3(8):730-8. doi: 10.1016/j.pmrj.2011.05.021.
83. Woo j, Palazzi K, Dwek J, etal. Early CIC may not prevent DMSA renal scan abnormalities in children with spinal dysraphism. *J Ped Urol* 10: 274-277, 2014
84. Wu HY, Baskin LS, Kogan BA. Neurogenic bladder dysfunction due to MM: neonatal versus childhood treatment. *J Urol* 157: 2295-7, 1997
85. Yang CC, Clowers DE. Screening cystoscopy in chronically catheterized spinal cord injury patients. *Spinal cord* 1999; 37(3): 204-7.
86. Zappitelli, M et al. Derivation and validation of cystatin C based prediction equations for GFR in children. *AJKD*, 2006, 48(2):221-230

87. Zegers B, Uiterwaal C, Kimpen J, van Gool J, de Jong T, Winkler-Seinstra P, Houterman S, Verpoorten C, de Jong-de Vos van Steenwijk C. Antibiotic prophylaxis for urinary tract infections in children with Spina Bifida on intermittent catheterization. *Urol.* 2011 Dec;186(6):2365-70.
88. Zegers BS, Winkler-Seinstra PL, Uiterwaal CS, de Jong TV, Kimpen JL, de Jong-de Vos van Steenwijk CC. Urinary tract infections in children with Spina Bifida: an inventory of 41 European centers. *FormatPediater Nephrol.* 2009 Apr;24(4):783-8. doi: 10.1007/s00467-008-1067-8. Epub 2008 Dec 9.