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Considerations for Urological Care and Pregnancy

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to (1) develop a treatment strategy for a pregnant female with asymptomatic bacteriuria or risks for complicated urinary tract infection. This includes understanding the risks and risk factors of pyelonephritis and selection of appropriate antibiotic during pregnancy; (2) manage and counsel a pregnant patient with chronic or new lower urinary tract conditions or pelvic floor dysfunction, specifically, management of overactive bladder, interstitial cystitis/bladder pain syndrome, and stress incontinence; and (3) discuss the importance of multidisciplinary care of the pregnant patient with placenta accreta spectrum and malignancy.

This AUA Update aligns with the American Board of Urology Module on Neurogenic Bladder, Voiding Dysfunction, Female Urology, BPH, and Urethral Stricture. Additional information on this topic can be found in the AUA Core Curriculum section on Female Pelvic Medicine.

Charles H. Schlaepfer, MD,[1] Annah J. Vollstedt, MD,[1] and Elizabeth B. Takacs, MD[1]

[1]Department of Urology, University of Iowa, Iowa City, Iowa

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KEY WORDS: pregnancy, pyelonephritis, delivery method, medication safety, urinary incontinence

INTRODUCTION

Caring for pregnant patients involves a multidisciplinary team of specialists at every stage during and after pregnancy. Pregnancy poses unique physiological and social scenarios for providers involved in patient care, including their urological care. In this Update, we summarize the important considerations for urologists when taking care of patients during and following pregnancy. We address urological problems that arise during pregnancy. In addition, we discuss how pregnancy and delivery may affect the care of chronic urological conditions.

HYDRONEPHROSIS

Though not always the case, hydronephrosis during pregnancy can be a normal finding in many patients. **The increasing size of the gravid uterus compressing neighboring structures is the primary cause of physiological hydronephrosis of pregnancy, though changes in levels of estrogen, progesterone, and prostaglandin-like agents may also impact hydronephrosis.**[1] Generally, physiological hydronephrosis in pregnancy is mild to moderate in severity, worse on the right than left, and often has no outward symptoms or clinical consequences.

Secondary to some form of obstruction, pathological hydronephrosis may also occur during pregnancy. Ureteral stones affect 1 in 2,000 pregnancies[2] and may present with microscopic or gross hematuria, flank pain, and irritative voiding symptoms. Patients requiring intervention can be managed with ureteral stent placement, percutaneous nephrostomy tube placement, or ureteroscopy.[3] Experienced clinicians can use US rather than fluoroscopy to more safely perform ureteroscopy during pregnancy.[4] **Clinicians should be aware extracorporeal shock wave lithotripsy is contraindicated during pregnancy, and the recommended time between exchange for stents and percutaneous nephrostomy tube (PCN) is shorter, generally every 4-6 weeks.**[5] Pathological ureteral obstruction without stones also may be managed with stent or PCN.

Hydronephrosis noted on US may be due to prior, persistent, or new vesicoureteral reflux. For patients with hydronephrosis prior to pregnancy or history of recurrent febrile urinary tract infection (UTI), workup of possible reflux could be considered with voiding cystourethrogram pre- or postpartum. It is important to recognize and identify reflux nephropathy as this may lead to increased rates of maternal complications (eg, UTI, hypertension, proteinuria, edema, renal insufficiency, nephrolithiasis, and hematuria). Notably, if bilateral renal scarring is present, patients are at elevated risk for preeclampsia.[6]

UTIs AND BACTERIURIA

In the pregnant population, asymptomatic bacteriuria and UTIs pose multiple unique risks. Asymptomatic bacteriuria and UTIs are common in the pregnant population with UTI prevalence rates estimated ranging from 1.9% to 9.5%.[7] **A Cochrane review of antibiotic treatment of asymptomatic bacteriuria found that treatment reduced the risk of pyelonephritis (RR 0.24, CI 0.13-0.41), reduced the risk of preterm birth <37 weeks (RR 0.34, CI 0.13-0.88), and reduced the risk of birthweight less than 2,500 g (RR 0.64, CI 0.45-0.93).**[8] Similar meta-analyses have found no specific antibiotics to be superior to others[9] but have demonstrated there may be improved efficacy for short 4- to 7-day courses of antibiotics relative to single-dose regimens.[10] Table 1 contains more information on antibiotic safety. The United States Preventive Services Task Force recommends screening for and treatment of asymptomatic bacteriuria in pregnancy due to a moderate decrease in perinatal complications with only minimal risk of harm from antibiotics.[11]

Additional risk factors for complicated UTI in pregnancy include diabetes melilites, history of recurrent UTI, polycystic kidneys or other renal abnormalities, and sickle cell disease.[12] **While patients without risk factors should at least be screened in the first trimester or first prenatal visit if establishing care later in pregnancy, patients with risk factors for UTIs or development of complicated UTIs may require additional screening and lower threshold for placing on longer-term prophylactic antibiotics.**

Acute pyelonephritis may result from untreated asymptomatic bacteriuria and UTIs. Pyelonephritis poses risks to both the mother and the fetus. Untreated bacteriuria during pregnancy leads to a 30% increased risk of developing pyelonephritis.[8] For patients who do progress to pyelonephritis, a patient-centered discussion should take place regarding prophylactic antibiotics and other techniques for preventing UTIs for the duration of pregnancy following acute illness and treatment.

URINARY RETENTION

Though less common than bothersome overactive bladder symptoms, urinary retention also occurs in pregnancy and poses unique risks and management considerations.

Antenatal urinary retention (AUR) is not common but does occur in around 1 in 1,000 pregnancies. Though AUR is caused by pelvic floor dysfunction (PFD), some studies have identified incarcerated uterus, retroverted uterus, or cervical pregnancy as risk factors. However, most pregnant patients who develop AUR do not have specific antepartum risk factors.[13] For severe cases requiring intervention, some case reports have demonstrated most patients who require initial catheterization are able to return to voiding on their own following bladder rest. However, approximately 1 in 4 may require longer-term clean intermittent catheterization (CIC).[13] The most common time period for

ABBREVIATIONS: angiomyolipoma (AML), antenatal urinary retention (AUR), clean intermittent catheterization (CIC), cesarean section (C-section), onabotulinum toxin (onabotA), placenta accreta spectrum (PAS), percutaneous nephrostomy tube (PCN), pelvic floor dysfunction (PFD), pelvic organ prolapse (POP), postpartum urinary retention (PUR), sacral neuromodulation (SNM), urethral diverticulum (UD), urinary tract infection (UTI)

Table 1. Medication Safety in Pregnancy

Class	Drug	FDA pregnancy guidelines
Anticholinergic	Oxybutynin	Inadequate human data available; no known risk of fetal harm based on animal data
	Tolterodine	No human data available; no risk of teratogenicity based on animal data at 9-12× MRHD
	Solifenacin	No human data available; no known risk of fetal harm based on animal data at up to 1.8× MRHD, though possible risk of decreased fetal weight based on animal data at 3.6× MRHD
	Darifenacin	No human data available; no known risk of fetal harm based on animal data at up to 10× MRHD
	Trospium	No human data available; no known risk of teratogenicity based on animal data at 10× MRHD
Beta-3 agonist	Mirabegron	No human data available; no known risk of fetal harm based on animal data at 6× MRHD
Alpha agonist	Tamsulosin	No human data available; no known risk of fetal harm based on animal data at 50× recommended human dose
	Terazosin	No human data available; no known risk of teratogenicity based on animal data up to 280× MRHD
	Prazosin	Risk of fetal harm not expected based on limited human data; no known risk of fetal harm based on animal data at up to 225× greater than MRHD
Antibiotic	Penicillin	May use during pregnancy; no known risk of fetal harm based on human data
	Cephalosporins	May use during pregnancy; low risk of teratogenicity based on conflicting human data; no risk of fetal harm based on animal data
	Doxycycline	Avoid use during pregnancy; possible risk of spontaneous abortion, fetal permanent bone/teeth discoloration, enamel hypoplasia based on human data, possible risk of embryo/fetal toxicity based on animal data
	Trimethoprim/ sulfamethoxazole	Possible risk of spontaneous abortion in first trimester, possible risk of congenital neural tube and cardiovascular defects based on conflicting human data, risk of kernicterus in third term based on human data
	Ciprofloxacin	No known risk of teratogenicity based on human and animal studies; possible risk of spontaneous abortion based on conflicting human data; possible risk of bone/ cartilage damage based on animal data
	Nitrofurantoin	Contraindicated at 38-42 wk, otherwise may use during pregnancy; possible risk of teratogenicity and hemolytic anemia based on conflicting human data; dose-dependent risk of teratogenicity based on animal data at 50-68× recommended human dose
	Fosfomycin	May be used during pregnancy; risk of fetal harm not expected based on limited human data; no known risk of teratogenicity based on human data at 1.4-9× recommended human dose

Abbreviations: FDA, Food and Drug Administration; MRHD, maximum recommended human dose.
Data gathered from Epocrates Data Repository on Pregnancy Medical Safety (www.epocrates.com) and FDA drug labels for individual drugs or classes (https://labels.fda.gov/proprietaryname.cfm).

the development of retention is between the end of the first and beginning of the second trimester. Postpartum urinary retention (PUR) is a common condition in the immediate time following delivery. Studies have identified that instrument delivery, epidural, episiotomy, and nulliparity are associated with development of PUR.[14] However, prolonged PUR, greater than 3 days following delivery, is rare, and there is minimal evidence to quantify the risks associated with lifelong urinary issues.[15]

Catheterization is the mainstay for treatment of acute retention while the cause can be elucidated and longer-term treatment established. During pregnancy, catheterization, either intermittent or indwelling, does increase the risk of bacteriuria and associated pregnancy complications. Though there have previously been concerns for neonatal complications, selective alpha blocker tamsulosin has been demonstrated to be safe during pregnancy.[16] Providers should work up retention during or after pregnancy as they would for the nonpregnant population. Clinicians should counsel patients on increased risk of UTI with unmanaged retention or incomplete emptying, as well as with catheter-based treatment. CIC is preferred over indwelling catheter, but the increasing size of the gravid uterus can present significant functional challenges to performing CIC.

HEMATURIA

The prevalence of asymptomatic microscopic hematuria in pregnancy is approximately 3%.[17] The approach to asymptomatic microscopic hematuria in the pregnant patient is similar to that taken for the nonpregnant patient. Urinalysis with microscopy is required to confirm the presence of microscopic hematuria and to exclude infection. Patients found to have 1+ protein on urinalysis should have further assessment with a 24-hour urine collection. If there is greater than 1 g per 24 hours of total protein excreted, patients should have evaluation with nephrology for possible renal parenchymal disease.[18] In the first trimester, parenchymal disease may be due to acute tubular necrosis secondary to hyperemesis or a septic abortion. In the second and third trimesters, alterations in renal function can be caused by thrombotic microangiopathy (ie, hemolytic uremic syndrome, preeclampsia), renal cortical necrosis, or acute fatty liver of pregnancy. Further urological workup is discussed in the malignancy section of this Update. Table 2 contains a summary of causes of hematuria.

NEUROMODULATION

Neuromodulation, both sacral and tibial, is commonly performed in women of childbearing age. However, pregnancy is considered an absolute contraindication for the use of neuromodulation because of both the fluoroscopy needed for the placement of sacral neuromodulation (SNM) as well as the unknown potential side effects of active treatment on the developing fetus. **Medtronic, Axonics, and Cogentix advise caution during pregnancy, leading to a general recommendation of stopping stimulation for the duration of pregnancy.**[19-21] The International Urogynecological Association also recommends turning off the device when planning pregnancy and during pregnancy.[22] For patients with existing neuromodulation, device deactivation may increase the risk of urinary retention, and may worsen bothersome urinary symptoms.

There are no prospective data involving humans within the urology literature to validate device deactivation. In an animal trial, the effects of electrical stimulation of the S3 sacral nerve vs sham treatment on 20 pregnant rats and fetuses found no difference in the pregnant rats or the fetuses in the active vs control group.[23] There have been a handful of retrospective reviews regarding SNM for the treatment of pelvic floor disorders during pregnancy. One retrospective study examined the beneficial effect of implantable SNM on urinary symptoms in pregnancy, effects of SNM on childbirth and labor duration, and the impact of SNM on delivery mode. No lead displacement during or after pregnancy and no congenital abnormalities were observed in any of the subjects.[24] Clinicians should be aware of theoretical effects that gestation and labor may have on the implanted system. Increase in abdominal girth and mass effect and pushing during delivery may interfere with device function.

As more SNM and potentially implantable percutaneous tibial nerve stimulation is performed on patients of childbearing age, more safety data are needed to confidently support the continued use of neuromodulation during pregnancy.

Table 2. Etiology for Hematuria (Gross and Microscopic) in Pregnant and Nonpregnant Females

	Pregnant or not pregnant	Pregnancy specific
Renal	Acute pyelonephritis	ATN due to hyperemesis, septic abortion Thrombotic microangiopathy (ie, preeclampsia) Renal cortical necrosis Acute fatty liver of pregnancy
Ureteral	Stones	
Bladder	Bladder cancer Endometriosis Urinary tract infection	Placenta percreta

Abbreviations: ATN, acute tubular necrosis.

BLADDER CHEMODENERVATION

Another common treatment option for patients with overactive bladder symptoms and of childbearing age is bladder chemodenervation. Onabotulinum toxin (onabotA) may pose unique risks with pregnancy. **Allergan, the manufacturer of Botox, states that based on animal studies, Botox may cause fetal harm.** Animal studies demonstrated fetal body weight reduction and diminished skeletal ossification with 2 onabotA doses at >8 U/kg during pregnancy.[25] However, this dose far exceeds the human dose equivalent for intradetrusor injection. There have been minimal studies examining the safety of intradetrusor onabotA injection during pregnancy. Some have argued that onabotA for the treatment of chronic migraine is safe. One study analyzed the Allergan safety database for pregnancies with maternal onabotA exposure and identified 232 pregnancies with exposure and tracked outcomes. Of those patients, 96% of fetal exposures occurred before or during the first trimester and 83% received <200 U. Out of 137 pregnancies in prospective trials, 79% resolved in live births and 21% in fetal loss, which is comparable to the background rate in the United States. Congenital defects were present in 2.7% of live births, which is also comparable to the background rate. Most of these treatments were for movement, cosmesis, and pain disorders. Only 5 patients in the cohort were undergoing urological treatment.[26] Further research is needed to fully quantify the risk associated with intradetrusor onabotA therapy.

CONSIDERATIONS FOR CHRONIC PELVIC PAIN AND THE IMPACT OF PREGNANCY

Though bladder pain syndrome or interstitial cystitis is more likely to present in female patients, little is known about the effect of pregnancy on symptoms. Recently, a large retrospective population-based study analyzed outcomes of 793 pregnant women who were found to have chronic interstitial cystitis. This cohort was found to have an increased risk of adverse pregnancy-related outcomes including pregnancy-induced hypertension, preeclampsia, preterm delivery, preterm premature rupture of membranes, chorioamnionitis, delivery via cesarean section (C-section), maternal infection, and deep venous thromboembolism.[27] This risk is possibly due to increased rates of hypertension and preeclampsia because of increases in vascular endothelial growth factor, which has been shown to have increased expression in bladder biopsies from patients with interstitial cystitis.[27]

MODE OF DELIVERY IN PATIENTS WITH PFD

Vaginal delivery is often reported as a primary risk factor of PFD, but there is significant debate and contradictory evidence that elective C-sections can be protective against PFD. A 2020 meta-analysis including 11 studies of 1,726 primiparous patients showed no difference in short-term pelvic floor muscle strength after childbirth between primiparous patients who underwent C-section or vaginal delivery, as assessed through vaginal manometry. They did find reduced pelvic floor muscle strength in those who underwent an episiotomy or instrumented vaginal delivery compared against those who underwent C-section, but this was based on very low–quality studies.[28]

In a review article endorsed by the European Board & College of Obstetrics and Gynaecology, the authors recommend extreme caution when counseling patients regarding prelabor C-section to protect from PFD given the lack of available evidence to support it.[29] Others have been critical of this recommendation, citing that in patients with increased risk factors for birth trauma and PFD (older maternal age, obesity, and higher birthweight), the risks of vaginal delivery vs prelabor C-section should be discussed.[30]

As with many aspects of urological care in pregnancy, a patient-centered and individualized approach is critical. **UR-CHOICE is a useful counseling tool for clinicians to quantify the risk of future PFD based on several major risk factors, including urinary incontinence before pregnancy, ethnicity, age at birth of first child, body mass index, family history of PFD, baby's weight, and maternal height (Figure 1).**[31] Ultimately, a decision should be made with the obstetrician, urologist, and patient deciding how best to proceed.

PREGNANCY AND DELIVERY AFTER PELVIC FLOOR SURGERY

With increasing maternal age clinicians may encounter patients who will become pregnant after surgical treatment for stress urinary incontinence or pelvic organ prolapse (POP). The American Urogynecologic Society has published guidelines regarding pregnancy after anti-incontinence surgery and prolapse repair.[32]

There are limited data regarding the probability of recurrent POP after subsequent pregnancy and delivery in those who have undergone a POP surgery, namely a hysteropexy with or without mesh. After sacral hysteropexy or transvaginal mesh placement, theoretical risks include failure of vaginal and uterine physiological changes that are needed to accommodate a developing fetus and vaginal delivery.[32] Among patients who have become pregnant after sacral hysteropexy with mesh,

A

Outcomes	Route of Delivery	Any	Bothersome	Treatment	Bothersome or Treatment	Average Risk of Bothersome or Treatment
Pelvic Organ Prolapse	Vaginal	10%	3%	1%	4%	9%
	C-Section	3%	1%	<0.5%	1%	3%
Urinary Incontinence	Vaginal	30%	14%	2%	15%	20%
	C-Section	20%	10%	1%	10%	15%
Fecal Incontinence	Vaginal	14%	3%	1%*	2%	3%
	C-Section	10%	1%	2%*	2%	3%
Any Pelvic Floor Disorder	Vaginal	40%	18%	4%	20%	27%
	C-Section	26%	10%	2%	12%	18%
Two or More Pelvic Floor Disorders	Vaginal	13%	2%	<0.5%	2%	4%
	C-Section	6%	1%	<0.5%	1%	2%

B

Outcomes	Route of Delivery	Any	Bothersome	Treatment	Bothersome or Treatment	Average Risk of Bothersome or Treatment
Pelvic Organ Prolapse	Vaginal	29%	>10%	3%	20%	9%
	C-Section	12%	5%	<0.5%	5%	3%
Urinary Incontinence	Vaginal	68%	33%	7%	>30%	20%
	C-Section	55%	25%	3%	27%	15%
Fecal Incontinence	Vaginal	14%	3%	1%*	4%	3%
	C-Section	10%	1%	2%*	4%	3%
Any Pelvic Floor Disorder	Vaginal	72%	>40%	10%	48%	27%
	C-Section	57%	28%	6%	33%	18%
Two or More Pelvic Floor Disorders	Vaginal	32%	>10%	<0.5%	>10%	4%
	C-Section	17%	5%	<0.5%	6%	2%

Figure 1. Example of the UR-CHOICE, an online calculator for models that predict pelvic floor disorders 20 years after delivery. The patient is a 28-year-old primigravid woman who weighs 150 pounds, whose height is 5 feet, 4 inches, whose estimated infant weight is 7 pounds, 2 ounces with a head circumference of 35 cm, and who has no history of urinary incontinence before or during pregnancy. A, The average-risk patient has no family history of pelvic organ prolapse or urinary or fecal incontinence. B, The high-risk patient has a positive family history of pelvic organ prolapse and urinary incontinence as well as urinary incontinence during her pregnancy. C-section indicates cesarean section. Reprinted from Jelovsek et al, *Am J Obstet Gynecol*. 2018;218(2):222.e1-222.e19 with permission from Elsevier.

there are isolated reports of pain which has been attributed to tension of the mesh in the third trimester. Theoretically, a mesh-augmented repair may cause a certain degree of rigidity that may make vaginal delivery challenging. However, because of the limited data, no recommendations are made concerning the mode of delivery after POP surgery.

PREGNANCY WITH A HISTORY OF BLADDER AUGMENTATION/URINARY DIVERSION

There are several issues for clinicians to consider for pregnant patients with prior bladder reconstruction. Depending on the reconstruction, clinicians must recognize the effect of an expanding uterus on the vascular pedicle of the prior reconstruction, the inherent risk of bacteriuria in patients with bowel augmentations or in those who performed CIC, and that C-section may be necessary in most or all patients. **Clinicians should also counsel patients of childbearing age with any form of bowel augmentation of the urinary tract that there is a 57% false-positive rate for urine pregnancy tests.**[33] This is likely due to mucus contamination, but the exact mechanism is unknown. Pregnancy should always be confirmed with a serum human chorionic gonadotropin in patients with a history of an enterocystoplasty.

Fortunately, to date, there have been no reports of the gravid uterus compromising the augmentation's pedicle, leading to devascularization of the augmentation.[34] In a retrospective study of 18 pregnancies in 11 women who previously underwent lower urinary tract reconstruction, patients had a very high rate of complications during pregnancy and at the time of C-section. New or worsening hydronephrosis was the most common complication, occurring in 87%, of which almost half of cases were managed with a PCN so as to avoid risk of stent failure to mucus plugging. PCN may also be favored in this group due to the challenging nature of the altered anatomy. Two-thirds of patients developed UTIs and one-third developed urinary incontinence. Forty percent of cases experienced an intraoperative complication at the time of C-section, most commonly a cystotomy.[35]

Some argue that an extensive pelvic surgery such as that with a bladder augmentation may prevent development of the flaccid, distensible pelvic tissues that are necessary for progression to spontaneous vaginal delivery.[34] This theory is an argument for why patients who have had extensive bladder repair should consider prelabor C-section.

There is no consensus regarding the proper mode of delivery after major lower urinary tract reconstruction. In fact, American Urogynecologic Society guidelines state that "in women with congenital anomalies with a history of complex reconstructive surgery with or without artificial urinary sphincter, risks of surgical complications at the time of C-section may outweigh the benefits."[32] This statement is made based on 1 case series of 13 women with a history of a neural tube defect or bladder exstrophy who were status-post bladder augmentation and artificial urethral sphincter. In this series, 11 of the 13 patients had spontaneous vaginal deliveries and 2 underwent C-section. Only 1 of the 13 patients had postpartum urinary incontinence, and this was transient.[36]

If C-section is performed, it is imperative to protect the augmentation or continent stoma and the vascular pedicle.[34] **C-section would ideally involve a reconstructive urologist who is familiar with the patient and the patient's reconstruction.**

Placenta accreta spectrum (PAS) is a disorder of abnormal attachment of the placenta that can have significant impact on pregnancy, delivery, and neighboring urological structures. The spectrum is defined by the absence of the decidua basalis layer resulting in the placental chorionic villi invading into and sometimes beyond the myometrium. The specific form of PAS is determined by the depth of invasion: (from least to most invasive) placenta accreta occurs when the placenta villi are attached directly to the surface of the myometrium, placenta increta occurs if the villi invade into the myometrium, and placenta percreta is when the placenta villi invade through the uterine serosa and into surrounding structures including bladder, ureters, bowel, and vessels.[37] In 2002, an estimated 1 in 533 pregnancies was complicated by PAS.[38] The incidence of PAS is rising and widely attributed to the increase in C-section rate. Other risk factors for PAS include the presence of placenta previa, prior uterine surgery (uterine curettage, myomectomy, hysteroscopic surgery, prior endometrial ablation, uterine embolization), and pelvic radiation.[38]

PAS will often be identified on prenatal routine US; however, sensitivity and specificity are variable and are influenced by ultrasonographic quality, ultrasonographer skill, and clinical experience.[38] MRI is also useful in the assessment of PAS; however, it is not recommended for routine screening. Indications for MRI include when US findings are inconclusive, posterior located previas, or for suspected percreta.

For patients with concern for percreta on routine US or in the assessment of hematuria in a pregnant patient, urologists should be involved. Patients present with hematuria in 31% of cases of percreta involving the bladder.[39] **For all patients with PAS, multidisciplinary care is necessary to determine the optimal time of delivery (often 34-36 weeks). This is generally accomplished with C-section and concurrent hysterectomy.**[38] **At the time of C-section, it is common for urology to assist with either intentional or unintended cystotomy or ureteral injuries.** There is no definitive consensus on the placement of prophylactic stents. Though many surgeons and institutions commonly use stents for ureteral identification intraoperatively, the benign and malignant gynecologic surgery literature has not demonstrated a decrease in the incidence of ureteral injury, though studies have shown it helpful for the detection of injuries.[38]

BLADDER MALIGNANCY

Urological malignancies are extremely rare during pregnancy, and may present with symptoms such as hematuria, urinary urgency, high blood pressure, and back pain that could otherwise be attributed to pregnancy. In a review of the International Network on Cancer, Infertility and Pregnancy, of the 18 cases of bladder cancer reviewed, 66% presented with hematuria and 22% were an incidental finding on imaging disease.[40] For pregnant patients presenting with hematuria, US, MRI, and cystoscopy are all safe diagnostic modalities. Cystoscopy is imperative for assessment of painless hematuria in the absence of identified source such as infection.[40] Differential diagnosis of a bladder mass in pregnancy includes urothelial carcinoma, squamous cell carcinoma, adenocarcinoma, PAS, endometriosis,

rhabdomyosarcoma, nephrogenic adenoma, or other even more rare malignant and benign conditions.

When a pregnant patient is diagnosed with bladder cancer, treatment is dependent on the stage of disease and gestation of the fetus. Gestational age not only determines the ideal time of initial management but further management post resection.[40] Ideally surgical intervention would occur in the second trimester. It is ideal to avoid the first trimester due the risks of birth defects and spontaneous abortion, and avoid third trimester with the risk of preterm labor or significant changes in anatomy due to the gravid uterus compressing the bladder.

Once the patient is fully staged, a multidisciplinary team and the patient determine the treatment plan. In the International Network on Cancer, Infertility and Pregnancy review, 72% of bladder cancers were urothelial cell carcinoma, with 50% being noninvasive pTa disease.[40] Maggen et al proposed a treatment algorithm for bladder cancer (Figure 2).[40] Patients with pTa disease should undergo regular surveillance at 3-month intervals; this strict follow-up is critical for patients with intermediate or high-risk but <T2 disease. In this patient cohort, adjuvant intravesical therapies should be delayed until after delivery. Bacillus Calmette-Guérin, due to its live nature, is contraindicated during pregnancy,[40] and mitomycin has been shown to cross the placental barrier with known toxicity in animals.[41] For patients with nonmetastatic muscle-invasive disease, treatment becomes more complex. It is critical to weigh the maternal needs and neonatal risks while respecting patients' autonomy.[40] The patient should be counseled on the risks and benefits from a multidisciplinary team, and consideration should be given to neoadjuvant chemotherapy during pregnancy and delayed radical cystectomy 3-4 weeks postpartum.[40]

PERIURETHRAL MASSES

Though uncommon during pregnancy, urethral diverticulum (UD) and Skene's gland cysts or abscess can occur. Presentation during pregnancy mimics those in nonpregnant women. With Skene's gland abnormalities, patients may sense or palpate an increasing bulge alongside the urethra. In the absence of Skene's gland abscess, management should be conservative during pregnancy. If surgical intervention is indicated, either marsupialization or with excision of the gland can be performed.

Diagnosing UD can be challenging. Symptoms are often more subtle than Skene's gland issues and may include nonlocalizing pelvic pain, dyspareunia, or urethral discharge or urinary dribbling, and dysuria. US can sometimes visualize UD, but MRI will provide a more comprehensive assessment of the lesion. During pregnancy conservative management such as analgesia, antibiotics, and fine needle aspiration is recommended, but definitive management of UD would be transvaginal excision.[42] Marsupialization can also be considered as a temporizing measure prior to definitive repair. Historically, the risk of rupture of the UD or obstruction of labor with vaginal delivery in a patient with UD has been raised, but this is more a concern with large, proximal UD because of compression by the descent of the neonate against the pubic symphysis.[43]

RENAL MASSES

Renal neoplasms including renal cell carcinoma and angiomyolipoma (AML) are uncommon in pregnancy but do occur. Only half of reported cases of renal masses during pregnancy presented with pain or hematuria, and only 1 out of 4 had the classic triad of flank pain, hematuria, and a palpable mass.[44]

Indications for treatment of AMLs include suspicion for malignancy, size and growth rate concerning for rupture, or spontaneous hemorrhage. **In the pregnant patient, renal AMLs are riskier given that the physiological changes of pregnancy are inherent risk factors for AML growth, progression of aneurysms, and rupture. Pregnancy specifically plays a role as a risk for rapid growth and higher risk of rupture of AMLs, up to 75% in some studies,[45] and the highest risk around 26-28 weeks.** Multiple physiological changes of pregnancy including the hormonal effect on smooth muscle cells and increased blood volume and renal perfusion can lead to tumor growth, more unstable aneurysms, and rupture.[46] Other peripartum physiological changes including abdominal pressure rise during uterine contraction as well as labile blood pressures during delivery can also contribute to heightened risk of rupture.[47]

Up-front prophylactic treatment with selective arterial embolization for high-risk patients desiring pregnancy is recommended,[47] and for those with lower risk AMLs close surveillance around pregnancy is indicated. In the pregnant population, embolization is often contraindicated. If intervention is required, laparoscopic nephrectomy is the better choice[48] and during the second trimester poses the lowest anesthesia risks.[49] In the pregnant population, tumors less than 4 cm should be managed conservatively with semiannual US to assess growth. However, patients seeking to become pregnant with tumors greater than 4 cm symptomatic or bilateral lesions should be considered for prophylactic selective arterial embolization.[47]

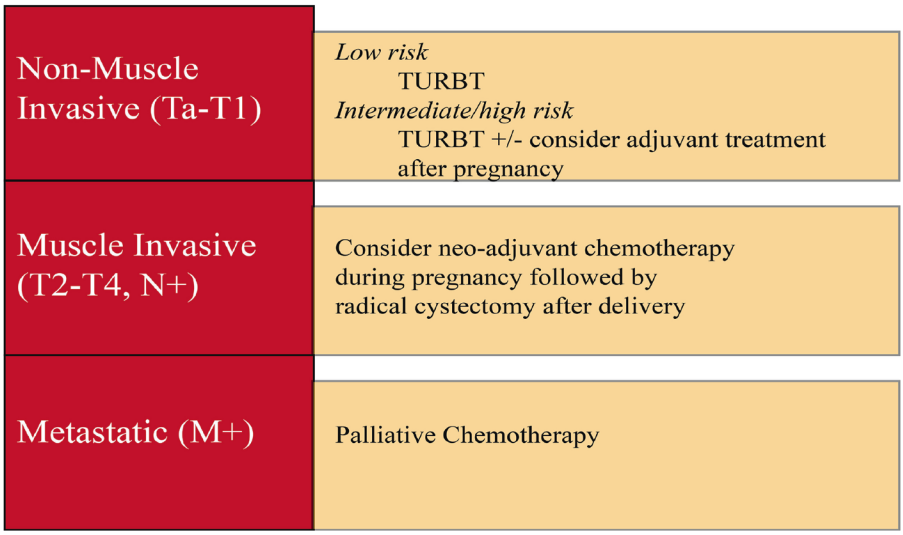

Figure 2. Bladder cancer treatment considerations: proposed treatment considerations for pregnant patients diagnosed with urothelial carcinoma by Maggen et al.[40] TURBT indicates transurethral resection of bladder tumor. Reprinted from Maggen et al, *Urology*. 2021;151:118-128 with permission from Elsevier.[40]

DID YOU KNOW?

- Pregnancy can have physiological hydronephrosis, but further testing and treatment may be necessary in the setting of ureteral obstruction or bladder outlet obstruction.
- Providers should treat pregnant patients with asymptomatic bacteriuria and should have a low threshold for prophylactic antibiotics in those at high risk of UTI.
- Sacral neuromodulation and chemodenervation of the bladder are not recommended during pregnancy, which can significantly impact patient quality of life.
- Patients with reconstructed anatomy or placenta accreta spectrum have special needs and should be managed with a multidisciplinary team involving a urologist and obstetrician.
- Urological malignancy is rare in pregnancy, but urologists should be aware of special considerations in timing to diagnose and treat urological malignancies for pregnant patients.

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Study Questions Volume 42 Lesson 29

1. A 30-year-old female returned with an implanted sacral nerve stimulator placed 1 year ago, which is working well to control her overactive bladder symptoms. She is now 12 weeks pregnant and is concerned about the effect of the device on the pregnancy, but is concerned about possible return of symptoms. What should you advise the patient?
   a. Reassurance. The device has been shown in clinical trials to have a low likelihood of negative impact on the pregnancy
   b. Addition of anticholinergic medications due to decreased efficacy of SNM in pregnant patients
   c. Turn the device off and complete a bladder diary
   d. Turn the device off with intradetrusor Botox injections

2. A 26-year-old female with a history of urinary urgency managed with pelvic floor physical therapy and urge suppression presents to your office. She is now 16 weeks pregnant and concerned about the effect of a vaginal delivery on her symptoms. Which is the most accurate statement to counsel the patient?
   a. Unequivocally, prelabor C-section has been shown to prevent pelvic floor dysfunction
   b. UR-CHOICE is a useful counseling tool for clinicians to quantify the risk of future PFD based on several major risk factors
   c. C-section should always be performed in patients with increased risk factors for birth trauma and pelvic floor dysfunction (older maternal age, obesity, and higher birthweight)
   d. If the patient has a history of a prior mid urethral sling, vaginal delivery is not considered safe

3. A 34-year-old female presents with an incidentally found 5-cm AML in the lower pole of her right kidney discovered on a CT scan for severe abdominal pain that has since resolved. She is seeking to become pregnant, and she and her partner have been working with an infertility specialist who has suggested they should proceed with testicular sperm extraction and in vitro fertilization due to male infertility factors. What is the best recommendation for her?
   a. Encourage patient to proceed with infertility treatments, and no further follow-up is needed
   b. Serial US surveillance every 3 months during pregnancy
   c. Delay first round of in vitro fertilization and undergo interventional radiology selective arterial embolization
   d. Robotic partial nephrectomy in second trimester of pregnancy if there is greater than 2 cm of growth of the AML on monthly US

4. A 26-year-old female presents at 30 weeks' gestation for gross hematuria to your office. Her obstetrician obtained a pelvic MRI that demonstrated likely placental invasion into the dome of the bladder. Which of the following is the most accurate statement regarding the patient's delivery?
   a. In patients with PAS, C-section should not be performed until the patient begins labor
   b. If MRI does not indicate invasion of the trigone, urological assistance is generally not required at time of C-section
   c. At time of C-section, concurrent hysterectomy is likely to be performed as well as possible partial cystectomy
   d. Referral should be made to interventional radiology for embolization of placental tissue where it invades the bladder

5. A 29-year-old female presents at 10 weeks' gestation with gross hematuria. Urinalysis and culture are negative for infectious source. Magnetic resonance urogram is performed that demonstrates enhancing mass concerning for malignancy in the anterior bladder wall without concern for invasion. Which of the following is the appropriate counseling?
   a. Diagnostic transurethral resection of bladder tumor should be performed as soon as a bladder mass is identified regardless of gestational age of the fetus
   b. In a patient with high-risk but <T2 disease, intravesical therapy should be delayed until the end of pregnancy
   c. Diagnostic transurethral resection of bladder tumor should be delayed until the second trimester to minimize anesthesia risks to the fetus
   d. Systemic neoadjuvant chemotherapy is preferred over intravesical bacillus Calmette-Guérin during pregnancy