Urologic Considerations in Pregnancy

Editors:

H. Henry Lai, MD

Authors:

Gina M. Badalato, MD; Ojas Shah, MD

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1. Section Summary

This unit will help the reader understand urologic issues pertaining to pregnancy, including lower urinary tract symptoms and associated physiology, the management of urinary tract infections and asymptomatic bacteriuria, the evaluation of hydronephrosis, and the assessment and treatment pathways for nephrolithiasis/renal colic. Peri- and post-partum considerations will also be reviewed, such as iatrogenic injury to the urinary tract during caesarean section, considerations for delivery in patients with a history of urologic congenital anomalies, and genitourinary tract fistula assessment.

2. Introduction

Pregnancy is a unique physiologic state, which may incite, exacerbate, or complicate new or preexisting urologic conditions. This review will focus on specific urologic issues that may present during pregnancy or complicate pregnancy, which may differ from treatment algorithms in the non-pregnant state. Specific topics will include a discussion of lower urinary tract symptoms, urinary tract infections/asymptomatic bacteriuria, hydronephrosis, and urolithiasis/renal colic. Unique considerations pertaining to delivery and complications associated with various forms of delivery will also be described.

3. Lower Urinary Tract Symptoms

The physiologic changes associated with pregnancy can cause new storage and voiding symptoms; these changes include hormonal effects on bladder and pelvic floor musculature, anatomic and structural shifts related to the gravid uterus, and alterations in intracellular and extracellular fluid equilibrium. Specifically, rising estrogen levels stimulate detrusor hypertrophy, while progesterone will perpetuate bladder hypotonia and increased bladder capacity. In combination with this, extravesical compression of the gravid uterus on the bladder can reduce capacity. Urine volume may be increased by heightened glomerular filtration and sodium excretion, reabsorption of

edema/extracellular fluid, and polydipsia. [1]

These physiologic alterations can translate clinically into symptoms that range from urinary frequency, nocturia, urinary hesitancy, retention, and incontinence, with urinary frequency (40 to 81% by the third trimester) and nocturia (23 to 79%) being the most common complaints.[2,3] During the postpartum period, the risk of urinary retention can range from 1.7 to 17.9%. Risk factors for postpartum urinary retention include epidural anesthesia, long duration of labor, episiotomy, high birth weight, caesarean section, elevated body mass index, instrument assisted delivery, and nulliparity. [3,4,5,6] Typically incomplete bladder emptying in this setting can be managed with clean intermittent catheterization and rarely results in long-term consequences.[7]

Stress urinary incontinence (SUI) is the most common form of urinary incontinence during pregnancy with a prevalence of 41% and increases with gestational age. The etiology is related to increased strain on the pelvic diaphragm and the relaxing effect of progesterone on bladder and urethral musculature. [2,8] Risk factors for the development of SUI during pregnancy include obesity, pre-existing SUI, gestational diabetes, advanced age, and constipation.[9] First line treatment of SUI during pregnancy is Kegels exercises, with multiple studies demonstrating better efficacy in the setting of a dedicated pelvic floor physical therapy program.[10,11,12] Although behavioral changes are the mainstay of treatment during pregnancy, an incontinence pessary may also be used for temporary treatment.[12] Overall, urinary incontinence during pregnancy increases the risk of future and persistent incontinence and associated decreased quality of life measures in the postpartum period.[13,14]

4. Asymptomatic Bacteriuria and Symptomatic Urinary Tract Infections

Asymptomatic bacteriuria (ASB) or symptomatic urinary tract infections (UTI) may occur during pregnancy, with overall rates of ASB being 2-10% and lower UTI/ cystitis 1-2%.[15]

UTIs in pregnancy should be treated; they are associated with preterm birth, low birth weight, and pre-eclampsia. In selecting the appropriate antimicrobial agent, consideration should be given to bacterial sensitivity as well as minimizing fetal toxicity. Duration of treatment for cystitis and pyelonephritis are similar to the general population, but antibiotics differ based on fetal safety profiles. The aminopenicillins and cephalosporins are considered safe and generally effective during pregnancy. In patients with a penicillin allergy, nitrofurantoin is a commonly used alternative.[16] Although nitrofurantoin is believed to be safe in pregnancy, there is some evidence it may be associated with cleft lip/ palate when given in the first trimester; additionally, it should be avoided near term due to risk of hemolytic anemia in fetuses with G6PD deficiency.[3] Nitrofurantoin may be used for bacterial cystitis, however it has poor tissue penetration thus should not be used to treat pyelonephritis.

Antibiotics to be avoided in pregnancy include the following: 1) fluoroquinolones because of risk of fetal cartilage defects, 2) sulfonamides at term due to the risk of hyperbilirubinemia, 3) trimethoprim to

due increased risk of congenital abnormalities including neural tube defects, 4) prolonged aminoglycosides due to renal toxicity and ototoxicity, and 5) tetracyclines due to bone defects and discoloration of deciduous teeth. [3,16] (see **Table 1**)

Table 1. Common Antibiotics and Pregnancy Considerations

	FDA Category*	Toxicity	Notes
Penicillins	B	Low risk, commonly used	
Cephalosporins	B	Low risk, commonly used	Limited data on ceftazidime and cefepime
Monobactams	B	Low risk, limited data	
Clindamycin	B	Low risk, commonly used	
Macrolides	B	Low risk	Azithromycin has fewer gastrointestinal side effects than erythromycin
Nitrofurantoin	B	Conflicting risk, commonly used	ACOG recommends it if no alternatives available in trimester 1, and as first line in trimesters 2 and 3; use for lower urinary tract UTIs only; not for pyelonephritis; avoid

			use for glucose-6-phosphate dehydrogenase deficiency
Fosfomycin	B	Low risk, limited data	Use for lower UTIs
Vancomycin	Vancomycin	Limited data	
Daptomycin	B	Very limited data	
Gentamicin	C	Conflicting risk, commonly used	Risk of nephrotoxicity and ototoxocity; useful for pyelonephritis
Carbapenems	C—imipenem, B—meropenem	Very limited data	
Sulfonamides	C	High risk, avoid if possible	
Linezolid	C	Very limited data	
Fluoroquinolones	C	Conflicting risk, avoid	Risk of teratogenicity

Tetracyclines	D	High risk, avoid	Risk of tooth and bone discoloration

* FDA categories defined as B (animal studies failed to demonstrate risk to the fetus and there are no adequate, well controlled studies in pregnant women), C (animal studies have shown teratogenic/lethal effects in the fetus but no controlled studies in pregnant women) and D (demonstrated human fetal risks in adverse reaction data but potential benefits may warrant use). In 2015 the FDA started to phase out risk categories but they are still commonly seen in labeling.[8,15]

Patients with pyelonephritis or three or more culture-confirmed UTIs during pregnancy are considered to have recurrent UTIs, and suppression antibiotics for the duration of pregnancy, either with low dose amoxicillin, cephalexin or nitrofurantoin daily, should be considered.[3,16]

The American College of Obstetricians and Gynecologists (ACOG) recommends all pregnant women be screened for ASB with a urine culture at their initial visit. If ASB screening is positive, pregnant patients should be treated for their ASB, and then screened periodically for recurrent ASB. Although pyelonephritis develops in 1 to 4% of all pregnancy women, it increases to 15 to 45% in those with untreated bacteriuria. [16,17,18,19] Most cases of pyelonephritis occur in the third trimester, when hydronephrosis and stasis in the urinary tract is most evident.[16] The increased likelihood that bacteriuria may progress to acute pyelonephritis during pregnancy increases the morbidity of bacteriuria in this group, making it a select population where ASB is treated. [20,21]

5. Hydronephrosis

Hydronephrosis is estimated to occur in 43 to 100% of pregnant women; it is often physiologic with an increasing prevalence correlating with advancing gestational age.[22] This phenomenon is thought to be related to expanding renal vascular and interstitial volume, hormonal changes (such as the effect of progesterone on reducing ureteral peristalsis), and mechanical compression of the distal ureters by the gravid uterus. Hydronephrosis is more often noted on the right side possibly from the dextrorotation of the gravid uterus and the angular trajectory of the right ureter as it traverses the pelvic brim. Pregnant patients with hydronephrosis can have a variety of presentations including pyelonephritis or flank pain similar to renal colic, although often they are asymptomatic. [3] Physiological right-sided hydronephrosis is common during pregnancy, while left-sided hydronephrosis associated with renal colic is more likely to be caused by an obstructing ureteral stone.

6. Urolithiasis

6.1 Presentation and Metabolic Phenomenology

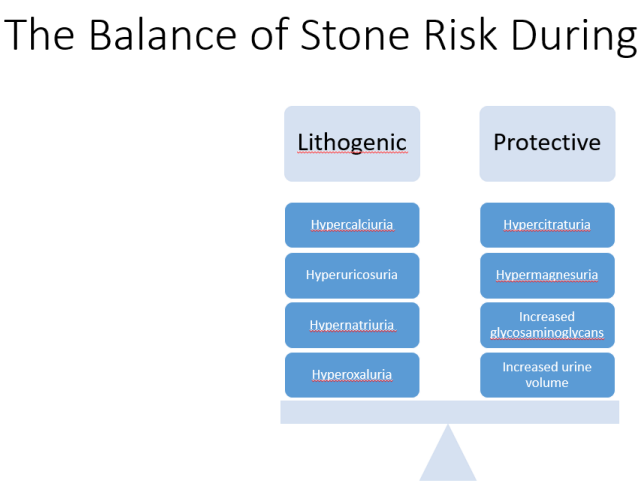

Figure 1. Stone Risk during pregnancy

Renal colic is the most common non-obstetric cause of hospitalization during pregnancy.[3] Large epidemiologic studies are lacking, but the incidence of symptomatic stones during pregnancy is estimated to be 1 in 200 to 1 in 1500 pregnancies.[23]

Several metabolic changes occur during pregnancy that result in roughly an equal stone diathesis as compared to the general population, but a change in the predominant stone composition from calcium oxalate to calcium phosphate, which forms in alkaline pH.[24] Increasing renal blood flow and glomerular filtration rate will increase urinary sodium, calcium, and uric acid, which collectively are lithogenic risk factors. These changes are offset by increased urine volume and urinary stone inhibitors such as citrate, magnesium and glycosaminoglycans[3] (**Figure 1**).

Stone disease/renal colic during pregnancy has been associated with adverse gestational events such as preeclampsia, premature rupture of membranes, and premature onset of labor. However, there has been no statistically significant correlation of compromised birth outcomes (e.g. perinatal mortality or low birth weight) in patients with nephrolithiasis.[25,26,27]

6.2 Imaging Modalities

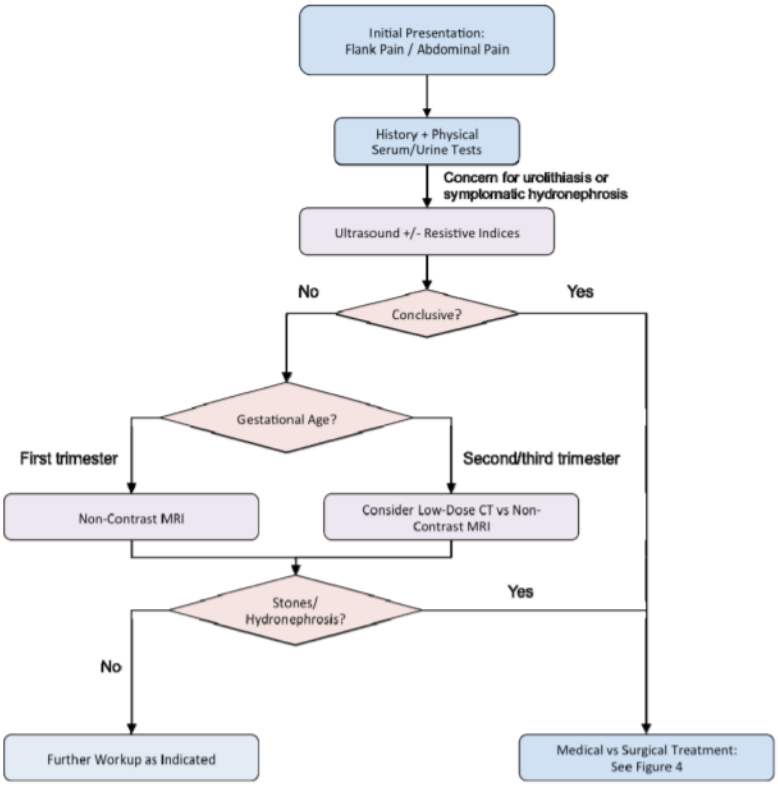

Figure 3. Algorithm for initial management and imaging of renal colic in pregnancy

Figure 2

Ultrasound is the modality of choice to evaluate pregnant patients with suspected renal stones, as it is readily available and involves no radiation exposure. Nevertheless, although ultrasound can

establish the presence of hydronephrosis, it cannot reliably distinguish between physiologic hydronephrosis and calculus obstruction of the ureter. Adjunctive techniques have been utilized to help increase the diagnostic yield of ultrasound, including 1) transvaginal ultrasound to assess for a distal ureteral stone, 2) evaluation of ureteral jets on the symptomatic side, and 3) calculating the absolute and relative resistive indices for each kidney. [3,28]

If ultrasound is non-diagnostic, MRI is a second-line imaging option that also has no associated radiation exposure and can be helpful in evaluating for the presence of ureteral stones. In particular, T2- weighted sequences without IV contrast can suggest a ureteral filling defect with surrounding high signal urine. Additional observations such as ureteral dilation above or below the pelvic brim ("double kink sign") and perinephric/ periureteral fluid can also point to an obstructing stone.[3,29]

Non-contrast CT remains the gold standard for the diagnosis of nephrolithiasis in non-pregnant patients, although it has traditionally been avoided due to concerns about radiation on the developing fetus. According to a 2004 ACOG policy statement, exposure to less than 50 mGy "has not been associated with an increase in fetal anomalies or pregnancy loss."[30] Low dose CT exposures ranges from 2 to 14 mGy, well below the aforementioned threshold, and can be a viable imaging option after joint discussion with the patient and the obstetrics team.[3,31]

In general sonography is the first-line imaging modality to evaluate a pregnant patient with renal colic. If ultrasound is inconclusive, further imaging can be performed that takes into account gestational age. **Figure 2** features an algorithm for diagnostic imaging: second-line imaging for patients in their first trimester includes non-contrast MRI and those in their second and third trimesters have the option of either MRI or low dose CT scan.[32]

6.3 Management

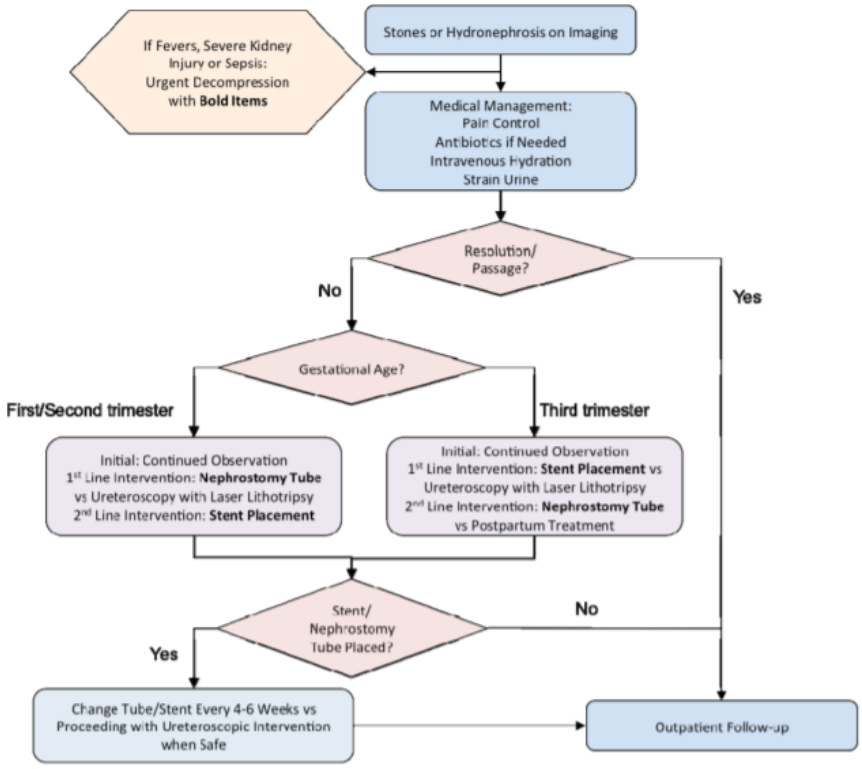

Figure 4. Algorithm for treatment of symptomatic stones and hydronephrosis in pregnancy

Figure 3

In a non-toxic pregnant patient, management pathways should take into account stone size and location (if known) as well as gestational age. **Figure 3** highlights treatment options progressing from conservative management toward surgical intervention. Notably, stone passage during pregnancy is very common, with an estimated 66-84% of patients not requiring surgical intervention.[3,33,34] As with non-pregnant counterparts, the initial management of renal colic in this population involves medical therapy, with consideration of the fetal safety profiles of traditionally used agents. As per the 2016 AUA guidelines, pregnant patients with ureteral stones and well-controlled symptoms should be offered observation as first-line therapy. The care of these patients, inclusive of conservative pharmacologic management, should be coordinated with the obstetrical team.[35,36] Pain control with acetaminophen or opiates is the basis for medical management, with non-steroidal anti-inflammatory drugs and aspirin discouraged given increased risk for bleeding as well as spontaneous abortion and cardiac malformations/ductal closure. A large percentage of pregnant women with symptomatic stones also harbor infection, and treatment of associated UTIs according to culture sensitivity and antimicrobial safety profile remains important. Medical expulsive therapy with alpha blockers (FDA fetal risk category B) and calcium channel blockers (category C) cannot be routinely recommended due to respective unknown and adverse safety profiles, although some retrospective data has suggested tamsulosin is safe during pregnancy. [35,36] Conservative therapy should also include hydration, anti-emetics, and routine straining of urine to document stone passage; in conjunction with these measures, fetal monitoring and, as mentioned previously, close collaboration with obstetrician

colleagues is paramount.

For those pregnant patients who fail conservative management for their ureteral stones, the AUA guidelines specify that clinicians may offer ureteroscopy as a standard intervention. Ureteral stenting and nephrostomy tube placement represent alternative options, that may require frequent stent or tube exchanges.[35,36] Of note, shock wave lithotripsy is contraindicated in pregnancy as the shock waves may cause fetal injury and demise. Ureteral stent placement can be performed with minimal fluoroscopy or under ultrasound guidance. Once the stent is in place, stent exchanges are recommended to occur every 4-6 weeks due the high risk of early incrustation (see lithogenic factors in **Figure 1**) and a higher incidence of bacterial growth. The need for frequent stent changes and anesthesia in conjunction with the potential for stent-associated lower urinary tract symptoms and pain make this an unfavorable first-line therapy in the first and second trimesters (<22 weeks). Nephrostomy tube placement is a viable temporizing measure, although these tubes still require frequent exchange and are more commonly employed earlier in pregnancy. Ureteroscopy with laser lithotripsy is generally accepted as a safe and effective option for the definitive management of ureteral stones which may be performed under regional anesthesia. Given all of these considerations, **Figure 3** outlines considerations for the surgical management of stone disease.

7. Labor Considerations

7.1 Intraoperative Considerations

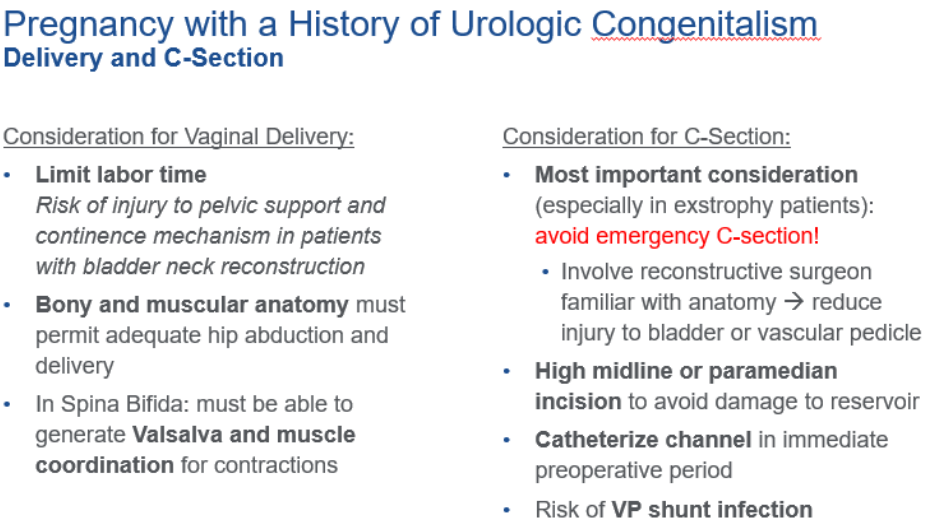

Figure 4. Moran G. Transitional Urology: Defining the Challenge for Patients and Providers. Columbia Urology Grand Rounds Conference. NY, NY, 8/5/2021. Permission to use this slide obtained.

Over the past twenty years, the rates of caesarean delivery have increased significantly, representing 32.2% of all births in North America in 2014.[37] Bladder injury during caesarean delivery is considered

rare and ranges in incidence from 0.08-0.94%.[38] Risk factors for bladder injury in this setting include bladder adhesions, failed vacuum attempt prior to caesarean delivery, size of uterine incision extension, emergent delivery with fetal distress, concurrent uterine rupture, and caesarean section (C-section) performed during stage 2 of labor. [8,39] Ureteral injury is also a rare complication of C-section with rates ranging from 0.03 to 0.10%. The recognition of upper tract injury may not be at the time of delivery, with forms of ureteral compromise ranging from ligation, transection/ resection, laceration, and crush/ ischemic events. [8]

Management strategies for peri-partum bladder and ureteral injury vary. Traditional management of an inadvertent cystotomy at the time of section consists of a two-layer water-tight closure with absorbable suture material in combination with prolonged catheterization, although the exact approach may vary based on the extent and location of the injury. Patients with a bladder injury predominantly at the trigone should have cystoscopy performed after primary repair to re-assess the area and evaluate for concomitant ureteral injury. The first step in the diagnosis of a ureteral injury involves cystoscopy to assess for the presence of clear ureteral efflux, with retrograde ureteropyelography representing the gold standard to evaluate ureteral integrity. [8] The site of ureteral injury during C-section may range from the mid to distal ureter, with options and considerations for repair outlined in other sections of the core curriculum.[40]

Regarding patients who had prior bladder augmentation, there is no clear consensus as to whether delivery should be done via a vaginal or caesarean approach. Women in this subset who have had extensive bladder neck repair, particularly in the setting of potentially prolonged labor, should consider a caesarean approach to minimize risk of injury to pelvic support and continence mechanisms. [41] If a caesarean delivery is performed, an understanding of the anatomy of the reconstruction and the segment utilized is paramount to avoid compromise to the bladder or vascular pedicle at the time of delivery; a reconstructive surgeon should be involved and available in these cases. [8] Other considerations in patients with a history of urologic congenital anomalies are represented in **Figure 4**.[42,43,44,45,46]

7.2 Long-Term Complications

7.2.1 Pelvic Organ Prolapse

Vaginal delivery is a risk factor for pelvic organ prolapse. According to a large scale study of participants in the Women's Health Initiative, a single child birth increased the odds of prolapse in all vaginal compartments, and each subsequent delivery up to five births increased the risk of prolapse by 10 to 20%. [47] Instrument or forceps delivery has also been more strongly correlated with prolapse as compared to routine vaginal delivery.[8,9] Algorithms for the evaluation and management of prolapse are outlined separately in the core curriculum. [48]

7.2.2 Urinary Fistulas

Although the topic of urinary fistulas is covered in separate sections of the core curriculum,[49] several key points pertaining to pregnancy merit specific reference in this unit. First, although gynecologic

surgery is the most common cause of urogenital fistula in the United States, obstructed labor represents the most common cause of fistulas world-wide, largely due to lack of access to obstetric care in developing countries. During obstructed labor, pressure from the fetal vertex can cause pressure necrosis of the surrounding vaginal tissues and allow for eventual fistula formation. Other reported risk factors for obstetric fistula formation in developing countries include poor nutrition, sexual abuse, and female genital mutilation. [8,50]

It is important to recognize that upper tract imaging, in the form of CT urography, excretory urography, or retrograde pyelography, should be performed for all cases of vesicovaginal fistula; this imaging is done to assess for concomitant ureteral injury including ureterovaginal fistula. According to some estimates, 12% of postoperative vesicovaginal fistulas are associated with ureteral injury, although newer data may support a lower incidence. [8,50,51]

8. Conclusion

Pregnancy is a unique physiologic state that introduces additional important considerations when evaluating both lower and upper urinary tract issues. Understanding issues during pregnancy, delivery, and postpartum are all under the urologist's purview and are critical to optimizing treatment strategies.

Presentations

Urologic Considerations in Pregnancy Presentation 1

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