URINARY TRACT INFECTION DURING PREGNANCY
Urinary tract infections and asymptomatic bacteriuria in pregnancy
Urinary tract infections (UTIs) are common in pregnant women.

UTI is defined either as a lower tract (acute cystitis) or upper tract (acute pyelonephritis) infection.
Epidemiology

- The incidence of bacteriuria in pregnant women is approximately the same as that in nonpregnant women.
- Recurrent bacteriuria is more common during pregnancy.
- The incidence of pyelonephritis is higher than in the general population, likely as a result of physiologic changes in the urinary tract during pregnancy.
- Asymptomatic bacteriuria occurs in 2 to 7 percent of pregnant women. It typically occurs during early pregnancy, with only approximately a quarter of cases identified in the second and third trimesters.
- Factors that have been associated with a higher risk of bacteriuria include a history of prior urinary tract infection, pre-existing diabetes mellitus, increased parity, and low socioeconomic status.
Acute cystitis occurs in approximately 1 to 2 percent of pregnant women,

incidence of acute pyelonephritis during pregnancy is 0.5 to 2 percent

Most cases of pyelonephritis occur during the second and third trimesters.
Pregnancy outcomes

- **Untreated bacteriuria** has been associated with an increased risk of **preterm birth, low birth weight, and perinatal mortality** in most but not all studies.

- **No correlation** has been clearly established between **acute cystitis** of pregnancy and increased risk of low birth weight, preterm delivery, or pyelonephritis, perhaps because pregnant women with symptomatic lower UTI usually receive treatment.

- **Pyelonephritis**, however, has been associated with **adverse pregnancy outcomes**.
**PATHOGENESIS**

- The organisms that cause bacteriuria and urinary tract infections (UTI) in pregnant women are of the same species and have similar virulence factors as in nonpregnant women.
- The mechanism of entry of bacteria into the urinary tract is likely to be the same for both groups.
- The smooth muscle relaxation and subsequent ureteral dilatation that accompany pregnancy are thought to facilitate the ascent of bacteria from the bladder to the kidney, resulting in the greater propensity for bacteriuria to progress to pyelonephritis during pregnancy.
- Pressure on the bladder and ureters from the enlarging uterus.
- The immunosuppression of pregnancy (mucosal interleukin-6 levels and serum antibody responses to *Escherichia coli* antigens appear to be lower in pregnant women).
**MICROBIOLOGY**

- *E. coli* is the predominant (70 percent)
- *Klebsiella* and *Enterobacter* (3 percent each)
- *Proteus* (2 percent)
- gram-positive organisms, including group B *Streptococcus* (10 percent).
ASYMPTOMATIC BACTERIURIA

- **Screening** is performed at **12 to 16 weeks gestation** (or the first prenatal visit, if that occurs later) with a urine culture.

- **Rescreening** among those who did not have bacteriuria on the initial test is generally **not performed in low-risk women**.

- It is **reasonable** to rescreen women at high risk for infection (e.g., history of UTI or presence of urinary tract anomalies, diabetes mellitus, hemoglobin S, or preterm labor),

- however the optimal target populations for this is uncertain.

- There is minimal evidence informing the benefits and harms of repeat screening following an initial negative culture.
Specimen collection

- Although the optimal method for collecting voided urine is uncertain, instructing women to **spread their labia and collect a midstream urine** (without requiring a clean-catch) seems most reasonable.

- Routine **catheterization** to screen for bacteriuria is **not warranted** due to the risk of introducing infection.

- In order to minimize contamination of the voided specimen, it is often recommended that the patient collect a **clean-catch** (after local cleansing of the urethral meatus and surrounding mucosa) **midstream** (collection of the second portion of the voided urine after discarding the initial stream) specimen. However, it is not clear that these measures reduce contamination.

- Findings from this and other studies suggest that collection of a **clean-catch** voided urine specimen is of **little value**.
Diagnostic criteria

- For asymptomatic women, bacteriuria is formally defined as two consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts of $\geq 10^5$ colony-forming units (cfu)/mL or a single catheterized urine specimen with one bacterial species isolated in a quantitative count of $\geq 10^2$ cfu/mL.

- In clinical practice, however, only one voided urine specimen is typically obtained, and diagnosis (and treatment initiation) is made in women with $\geq 10^5$ cfu/mL without obtaining a confirmatory repeat culture.

- If bacteria that are not typical uropathogens (such as lactobacillus) are isolated, treatment should be reserved for patients in whom the organism grows as a single isolate on consecutive cultures.
Management

- Management of asymptomatic bacteriuria in pregnant women includes *antibiotic therapy* tailored to culture results.
- *Follow-up cultures* to confirm sterilization of the urine.
Rationale for treatment

- Asymptomatic bacteriuria during pregnancy increases the risk of pyelonephritis.
- And has been associated with adverse pregnancy outcomes, such as preterm birth and low birth weight infants.
- Antimicrobial treatment reduces the risk of subsequent development of pyelonephritis and is associated with improved pregnancy outcomes.
Antimicrobial treatment

- Asymptomatic bacteriuria is treated with an antibiotic tailored to the susceptibility pattern of the isolated organism, which is generally available at the time of diagnosis.
- beta-lactams
- nitrofurantoin
- fosfomycin

The choice of antimicrobial agent should also take into account safety during pregnancy (including the particular stage of pregnancy).

The optimal duration of antibiotics for asymptomatic bacteruria is uncertain.

Short courses of antibiotics are preferred to minimize the antimicrobial exposure to the fetus.
## Antibiotics for asymptomatic bacteriuria and cystitis in pregnancy

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin</td>
<td>100 mg orally every 12 hours</td>
<td>Five to seven days</td>
<td>Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected. Avoid use during the first trimester and at term if other options are available.</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg orally every 8 hours or 875 mg orally every 12 hours</td>
<td>Five to seven days</td>
<td>Resistance may limit its utility among gram-negative pathogens.</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>500 mg orally every 8 hours or 875 mg orally every 12 hours</td>
<td>Five to seven days</td>
<td>Resistance may limit its utility among gram-negative pathogens.</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>250 to 500 mg orally every 6 hours</td>
<td>Five to seven days</td>
<td>Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected. Avoid during the first trimester and at term.</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>100 mg orally every 12 hours</td>
<td>Five to seven days</td>
<td>Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected. Avoid during the first trimester and at term.</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>3 g orally as single dose</td>
<td>Three days</td>
<td>Does not achieve therapeutic levels in the kidneys so should not be used if pyelonephritis is suspected. Avoid during the first trimester and at term.</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>800/160 mg (one double strength tablet) every 12 hours</td>
<td>Three days</td>
<td>Avoid during the first trimester and at term.</td>
</tr>
</tbody>
</table>
Follow-up

- Up to 30 percent of women fail to clear asymptomatic bacteriuria following a short course of therapy.
- Repeat culture is generally recommended as a test of cure, a week after completion of therapy for asymptomatic bacteriuria.
- If repeat culture has no growth, there is no indication for further testing for bacteriuria in the absence of symptoms suggestive of urinary tract infection.
We generally **repeat antibiotic treatment** tailored to antimicrobial susceptibility testing if the repeat culture yielded the same species as the first culture,

we give either the **same antimicrobial** as administered the first time for a longer course (eg, seven days, if a three-day regimen was used previously) **or** a different antimicrobial for a typical duration

However, **we do not continue testing** for asymptomatic bacteriuria following this second treatment course.

There are **insufficient data to support the use of suppressive or prophylactic antibiotics** for persistent or recurrent asymptomatic bacteriuria, **and we do not do this**.
The typical symptoms of acute cystitis in the pregnant woman are the same as in nonpregnant women and include:

- the sudden onset of dysuria and urinary urgency and frequency
- Hematuria and pyuria are also frequently seen on urinalysis
- Systemic symptoms, such as fevers and chills, are absent in simple cystitis
- The presence of fever and chills, flank pain, and costovertebral angle tenderness should raise suspicion for pyelonephritis
Diagnosis

- A urinalysis and urine culture
- Specimen collection is the same as for asymptomatic bacteriuria.
- It is reasonable to use a quantitative count $\geq 10^3$ cfu/mL in a symptomatic pregnant woman as an indicator of symptomatic UTI.
- If bacteria that are not typical uropathogens (such as lactobacillus) are isolated, the diagnosis of cystitis is typically made only if they are isolated in high bacterial counts ($\geq 10^5$ cfu/mL).
Differential diagnosis

- vaginitis or urethritis.
- Similarly, urinary frequency and urgency may be symptoms of normal pregnancy in the absence of urinary tract infection.
- However, true bacteriuria is typically not present in these settings and thus distinguishes acute cystitis.
testing for sexually transmitted infections (such as chlamydia and gonorrhea)

- If not already performed is warranted for pregnant women with dysuria without bacteriuria
- or women who have persistent dysuria despite successful treatment of bacteriuria
Management of acute cystitis

- **empiric antibiotic therapy** that is subsequently tailored to culture results
- **follow-up cultures** to confirm sterilization of the urine
- For those women with **persistent or recurrent bacteriuria**, **prophylactic or suppressive antibiotics** may be warranted in addition to retreatment.
Antimicrobial treatment

- beta-lactams
- Nitrofurantoin
- fosfomycin

The choice of an antimicrobial agent should also take into account any prior microbiological data and drug safety during pregnancy. For empiric therapy...
we typically choose between cefpodoxime, amoxicillin-clavulanate, and fosfomycin, given their safety in pregnancy and the somewhat broader spectrum of activity compared with other agents (such as amoxicillin or cephalaxin).

Nitrofurantoin: during the second or third trimester or if the others cannot be used for some reason (eg, drug allergy)

We treat acute cystitis with a three to seven day course of antibiotics as long as there are no symptoms suggestive of pyelonephritis

Single-dose therapy is generally limited to fosfomycin.
Follow-up

- A follow-up culture should be obtained as a test of cure.
- We typically perform this a week after completion of therapy.
- As above, if the patient is asymptomatic but has bacteriuria on test of cure, the optimal management is uncertain.
Management of recurrent cystitis

- In women who have three or more episodes of recurrent cystitis during pregnancy, antimicrobial prophylaxis for the duration of pregnancy is a reasonable strategy to prevent additional episodes.

- Prophylaxis can be postcoital if the cystitis is thought to be sexually related (which it commonly is) or continuous.

- In the setting of other conditions that potentially increase the risk of urinary complications during episodes of cystitis (e.g., diabetes or sickle cell trait), prophylaxis following the first episode of cystitis during pregnancy is also reasonable.
The choice of antimicrobial used for prophylaxis should be based on the susceptibility profile of the pathogens causing the cystitis.

- **daily or postcoital prophylaxis with low-dose** nitrofurantoin (50 to 100 mg orally postcoitally or at bedtime)

- or **cephalexin** (250 to 500 mg orally postcoitally or at bedtime) can be used.
ACUTE PYELONEPHRITIS

- Clinical manifestations: The typical symptoms of acute pyelonephritis in the pregnant woman are the same as in nonpregnant women.
  - Fever (≥38°C or 100.4°F)
  - Flank pain
  - Nausea, vomiting
  - And/or costovertebral angle tenderness
  - Symptoms of cystitis (e.g., dysuria) are not always present.
  - Pyuria is a typical finding.

- Most cases of pyelonephritis occur during the second and third trimesters.
Diagnosis

- For pregnant women who present with such symptoms, we check a urinalysis and urine culture.
- **Pyuria** is present in the majority of women with pyelonephritis, and its absence should prompt consideration of an alternative diagnosis or complete obstruction.
- However, absence of pyuria does not rule out UTI if symptoms and urine culture are consistent with the diagnosis.
- Blood cultures in those with signs of sepsis or serious underlying medical conditions such as diabetes.
- Other tests, such as a serum lactate level, can also be useful in women with suspected sepsis to inform the severity of disease.
Imaging

- Imaging is not routinely used to diagnose pyelonephritis.
- However, in patients with pyelonephritis who are severely ill or who also have symptoms of renal colic or history of renal stones, diabetes, history of prior urologic surgery, immunosuppression, repeated episodes of pyelonephritis, or urosepsis, imaging of the kidneys can be helpful to evaluate for complications.
- In pregnant women, renal ultrasound is the preferred imaging modality in order to avoid contrast or radiation exposure.
Differential diagnosis

- Nephrolithiasis
- Intraamniotic infection,
- Placental abruption
- other infections (eg, influenza, pneumonia, appendicitis)
Management of acute pyelonephritis

- hospital admission for parenteral Antibiotic therapy
- Once afebrile for 48 hours, pregnant patients can be switched to oral therapy guided by culture susceptibility results
- and discharged to complete 10 to 14 days of treatment
- Following the treatment course, suppressive antibiotics are typically used for the remainder of the pregnancy to prevent recurrence
### Parenteral regimens for empiric treatment of pyelonephritis in pregnancy

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose, Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate pyelonephritis</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>1 g every 24 hours</td>
</tr>
<tr>
<td>Cefepime</td>
<td>1 g every 12 hours</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>1 g every 8 hours</td>
</tr>
<tr>
<td>Amoxicillin*</td>
<td>1.2 g every 6 hours</td>
</tr>
<tr>
<td>Penicillin PLUS</td>
<td>1.5 mg/kg every 8 hours</td>
</tr>
<tr>
<td>Gentamicin*</td>
<td></td>
</tr>
<tr>
<td>Severe pyelonephritis with an impaired immune system and/or incomplete urinary drainage</td>
<td></td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>3.375 g every 6 hours</td>
</tr>
<tr>
<td>Meropenem</td>
<td>1 g every 8 hours</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>1 g every 24 hours</td>
</tr>
<tr>
<td>Doripenem</td>
<td>500 mg every 8 hours</td>
</tr>
</tbody>
</table>

Doses are for patients with normal renal function.

If methicillin-resistant S. aureus (MRSA) is known or suspected, see treatment regimens outlined separately in topics addressing MRSA management.
If symptoms and fever persist beyond the first 24 to 48 hours of treatment

- a repeat urine culture
- renal ultrasound should be performed to rule out persistent infection and urinary tract pathology
For women who do not use antimicrobial prophylaxis for the duration of pregnancy following an episode of pyelonephritis we generally check monthly urine cultures to evaluate for recurrent bacteriuria and treat as indicated because of the risk of recurrent pyelonephritis.
Obstetric management

- Pyelonephritis is **not itself an indication for delivery**
- If induction of labor or cesarean delivery for standard obstetrical indications is planned in a patient on treatment for pyelonephritis, **we favor waiting until the patient is afebrile**, as long as delaying the delivery is relatively safe for the mother and fetus.
- Tocolysis is typically not administered after 34 weeks gestation. If a woman with pyelonephritis prior to that gestational age experiences preterm labor, administration of tocolysis and steroids is reasonable to attempt to prolong the pregnancy.
- If the patient is **septic**, tocolysis is generally avoided.
- Pregnant women with pyelonephritis are at **increased risk of pulmonary edema and acute respiratory distress syndrome (ARDS)**, which may be exacerbated by administration of tocolysis with or without corticosteroids.
Preventing recurrence

- Recurrent pyelonephritis during pregnancy occurs in 6 to 8 percent of women.
- After an initial episode of pyelonephritis, low-dose antimicrobial preventive therapy with an agent to which the original organism is susceptible for the remainder of the pregnancy is a reasonable strategy.
- If preventive therapy is utilized, reasonable options include **nitrofurantoin** (50 to 100 mg orally at bedtime) or **cephalexin** (250 to 500 mg orally at bedtime).
- Breakthrough bacteriuria can occur during preventive therapy, so we usually perform at least one later culture, such as at the start of the third trimester, to ensure preventive therapy is working.
thank you