

# Alaska Urinary Tract Infection Treatment Toolkit



## ***Urinary Tract Infection Treatment Guidelines***

These clinical guidelines are intended to aid in the selection of antimicrobial therapy for patients residing in Alaska who present with a urinary tract infection. Treatment guidelines available for the following Alaska care setting:

- ❖ Inpatient Adult UTI Clinical Pathway
- ❖ Outpatient Adult UTI Clinical Pathway
- ❖ Long term care Adult UTI Clinical Pathway
- ❖ Pediatric UTI Clinical Pathway

These guidelines will help Alaska physicians and pharmacists ensure patients receive the right antibiotic at the right time and only when necessary.

## **Clinical Pearls for Providers**

***May 2019 - Urinary Uncertainty: Demystifying Culture Collection in Urinary Tract Infections***

***October 2019 - Urinary Tract Infections: Treatment and De-escalation***

***December 2019 - Antibiotic duration in uncomplicated cystitis and outpatient pyelonephritis***

Clinical pearls available for download on the A2SC website at [alaskahha.org/antimicrobial-stewardship-collaborative](http://alaskahha.org/antimicrobial-stewardship-collaborative).

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## ***About Alaska Antimicrobial Stewardship Collaborative***

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The Alaska Antimicrobial Stewardship Collaborative (A2SC) is an active partnership of hospitals and other health care stakeholders dedicated to developing innovative strategies to ensure appropriate antibiotic use. A2SC's goal is a simple one: all patients in Alaska will receive the right antibiotic at the right time and only when necessary.

The emergence of antibiotic-resistant bacteria caused by the misuse and overuse of antibiotics is pushing the healthcare industry to re-evaluate how medicine is practiced. Together we will accelerate positive changes to achieve this critical goal.



# Alaska Antimicrobial Stewardship Collaborative (A2SC)

## Adult INPATIENT Urinary Tract Infection Treatment Guideline (Last Updated 10-2018)

Category	Asymptomatic Bacteriuria	Acute Cystitis	Acute Pyelonephritis	Complicated UTI / Catheter-Associated UTI (CAUTI)
Symptoms and/or Risk Factors	Isolation of a specific quantity of bacteria in an appropriately collected urine specimen ( $\geq 10^5$ cfu/mL or from catheter; $\geq 10^2$ cfu/mL) from an individual <b>WITHOUT</b> signs or symptoms of infection.	<b>General symptoms:</b> Acute onset dysuria, frequency or urgency	<b>Upper UTI</b> is frequently associated with general symptoms <b>PLUS back/flank pain, fever &amp; chills.</b>	<b>Complicated UTI:</b> Infection in males or in the presence of an anatomic/functional abnormality (e.g. enlarged prostate, calculi, obstruction, catheter or stent, neurogenic bladder, neutropenia).
		Consider deviation from the below recommendations (or consult to ID provider) if any of the following risk factors for multidrug resistant organisms are present: antibiotic exposure within 90 days, presence of urinary invasive device(s), history of UTI with multi-drug resistant organism.		
Culture & Susceptibility (C&S) Investigation	Routine C&S is <b>NOT indicated</b> in asymptomatic patients <i>unless</i> screening in pregnancy or prior to urologic procedure with compromise of the urothelial mucosa.	If patient requires inpatient admission for acute cystitis, acute pyelonephritis, or complicated/catheter associated cystitis, <b>urine C&amp;S are critical</b> in order to optimize therapy.  Urine cultures should be collected from a midstream void prior to antibiotics or a freshly placed urinary catheter.		
Recommended Treatment and Duration	Treatment is <b>NOT</b> recommended for patients who fail to meet the below criteria (e.g. pregnancy or those undergoing urologic procedures).  <u>Pregnant women: (select one option)</u> <ul style="list-style-type: none"> <li><b>Nitrofurantoin</b> 100mg PO BID x 5d</li> </ul> <i>** Note: contraindicated at 38-42 weeks gestation</i>  <ul style="list-style-type: none"> <li><b>Cephalexin</b> 500mg PO BID x 5d</li> </ul> <u>Urologic procedure:</u> Direct treatment based on pre-procedure screening C&S.	<u>First Line: (select one option)</u> <ul style="list-style-type: none"> <li><b>Nitrofurantoin</b> 100mg PO BID x 5d</li> <li><b>Cephalexin</b> 500mg PO BID x 7d</li> </ul> <b>Fluoroquinolone FDA Safety Alert:</b> <i>Disabling &amp; potentially permanent adverse effects outweigh benefit in cystitis. Only use when no other alternatives exist.</i>  <u>Second Line:</u> <ul style="list-style-type: none"> <li><b>Ciprofloxacin</b> 250mg PO BID x 3d</li> </ul> <i>**Note: If at risk for STIs w/ symptoms of urethritis, consider screening for chlamydia.</i>	<u>First Line:</u> <ul style="list-style-type: none"> <li><b>Ceftriaxone</b> 1g IV Q24H</li> </ul> <u>Second Line:</u> <ul style="list-style-type: none"> <li><b>Ciprofloxacin</b> 400mg IV Q12H</li> <li><b>Levofloxacin</b> 750mg IV Q24H</li> </ul> <i>Above recommendations are for empiric antimicrobial therapy, tailor maintenance therapy to C&amp;S report.</i>  <b>Duration:</b> <ul style="list-style-type: none"> <li>Duration may vary based upon final antibiotic selection.</li> <li>Shorter courses (<b>7 days</b>) are reasonable, if symptoms promptly resolve.</li> <li>Longer courses (<b>10-14 days</b>) if delayed response, regardless if catheterized or not.</li> <li>If female and <math>\leq 65</math> years of age, a <b>3-day</b> regimen <u>may be considered</u> for CAUTI with catheter removal.</li> </ul>	

- Scope of this guideline is limited to immunocompetent adults >18 y/o without history of renal transplant.
- **Nitrofurantoin** is contraindicated for CrCl < 30mL/min and in pregnancy at term (38-42wks).
- Statewide *E. coli* susceptibility to **TMP/SMX** is <80% and should be avoided as empiric therapy, but may be considered if confirmed by C&S for complicated UTI or pyelonephritis (2 week duration).
- If patient reports penicillin allergy, inquire about onset and severity of symptoms, as well as prior beta-lactam exposure and update patient medical record. Severe or life-threatening allergic reactions may include: anaphylaxis, angioedema, urticaria, Stevens-Johnson Syndrome (SJS), etc.
- Patients with recurrent UTIs should have empiric therapy selected based upon prior C&S results.
- Chronic antibiotic prophylaxis for most patients with risk factors for recurrent, complicated UTI is NOT typically recommended. Risk of resistance outweighs the slight reduction in infection rate.

**Note: This guideline is intended to aid in the selection of antimicrobial therapy in adult INPATIENTS residing in Alaska who are diagnosed with a urinary tract infection. It is not intended to replace the clinical judgment of the prescribing provider or to be used for those residing outside the State of Alaska.**

Executive Summary: International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: **CID 2011;52(5):561-564**. Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults: **CID 2010; 50:625-663**. IDSA Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults. **CID 2005; 40:643-54**. 2015 Updated Beers Criteria.

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# Alaska Antimicrobial Stewardship Collaborative (A2SC)

## Adult OUTPATIENT Urinary Tract Infection Treatment Guideline (Last Updated 10-2018)

Category	Asymptomatic Bacteriuria	Acute Cystitis	Acute Pyelonephritis	Complicated UTI / Catheter-Associated UTI (CAUTI)
<b>Symptoms and/or Risk Factors</b>	Isolation of a specific quantity of bacteria in an appropriately collected urine specimen ( $\geq 10^5$ cfu/mL or from catheter; $\geq 10^2$ cfu/mL) from an individual <b>WITHOUT</b> signs or symptoms of infection.	<b>General symptoms:</b> Acute onset dysuria, frequency or urgency  <b>Risk factors for resistance:</b> <ul style="list-style-type: none"> <li>• Antibiotic exposure within 90d</li> <li>• Hospitalization within 90d</li> <li>• Presence of invasive device(s)</li> </ul>	<b>Upper UTI</b> is frequently associated with general symptoms <b>PLUS back/flank pain, fever &amp; chills.</b>	<b>Complicated UTI:</b> Infection in males or in the presence of an anatomic/functional abnormality (e.g. enlarged prostate, calculi, obstruction, catheter or stent, neurogenic bladder, neutropenia).
<b>Culture &amp; Susceptibility (C&amp;S) Investigation</b>	Routine C&S is <b>NOT</b> indicated in asymptomatic patients <u>unless</u> screening in pregnancy or prior to urologic procedure with compromise of the urothelial mucosa.	Routine C&S is <b>NOT</b> indicated <u>unless</u> risk factor(s) for resistance exist; consider if prescribing 2 <sup>nd</sup> line therapy	<b>Urine C&amp;S are critical</b> in order to optimize therapy. Urine cultures should be collected from a midstream void prior to antibiotics or a freshly placed urinary catheter.	
<b>Recommended Treatment and Duration</b>	Treatment is <b>NOT</b> recommended for patients who do not meet the below criteria (e.g. pregnancy or those undergoing urologic procedures).  <u>Pregnant women: (select one option)</u> <ul style="list-style-type: none"> <li>• <b>Nitrofurantoin</b> 100mg PO BID x 5d <i>** Note: contraindicated at 38-42 weeks gestation</i></li> <li>• <b>Cephalexin</b> 500mg PO BID x 5d</li> </ul> <u>Urologic procedure:</u> Direct treatment based on pre-procedure screening C&S.	<u>First Line: (select one option)</u> <ul style="list-style-type: none"> <li>• <b>Nitrofurantoin</b> 100mg PO BID x 5d</li> <li>• <b>Cephalexin</b> 500mg PO BID x 7d</li> </ul> <b>Fluoroquinolone FDA Safety Alert:</b> <i>Disabling &amp; potentially permanent adverse effects outweigh benefit in cystitis. Only use when no other alternatives exist.</i>  <u>Second Line:</u> <ul style="list-style-type: none"> <li>• <b>Ciprofloxacin</b> 250mg PO BID x 3d</li> </ul> <i>**Note: If STI risk w/ symptoms of urethritis, consider treatment for chlamydia.</i>	<u>First Line:</u> <ul style="list-style-type: none"> <li>• <b>Ceftriaxone</b> 1g IM/IV x 1 dose</li> </ul> If severe or life-threatening beta-lactam allergy consider <b>Gentamicin</b> 5mg/kg IM/IV x 1 dose  <u>Followed by:</u> <u>First line:</u> <ul style="list-style-type: none"> <li>• <b>Cephalexin</b> 1g PO TID x 10-14d</li> </ul> <u>Second line:</u> <ul style="list-style-type: none"> <li>• <b>Ciprofloxacin</b> 500mg PO BID x 7d</li> </ul> <i>Tailor maintenance therapy to C&amp;S report.</i>	Base empiric treatment on prior culture data. If stable vitals & afebrile, provide definitive therapy when new C&S result.  <b>Duration:</b> <ul style="list-style-type: none"> <li>• Shorter courses (<b>7 days</b>) are reasonable, if symptoms promptly resolve.</li> <li>• Longer courses (<b>10-14 days</b>) if delayed response, regardless if catheterized or not.</li> <li>• <i>If female and <math>\leq 65</math> years of age, a 3-day regimen <u>may be considered</u> for CAUTI with catheter removal.</i> </li></ul>

- Scope of this guideline is limited to adults >18 y/o without signs of severe physiologic disturbance. This guideline should not be used for patients who are immunocompromised or kidney transplant recipients.
- **Nitrofurantoin** is 1<sup>st</sup> line for most patients without symptoms of pyelonephritis. Contraindicated for CrCl < 30mL/min and in pregnancy at term (38-42wks).
- Statewide *E. coli* susceptibility to **TMP/SMX** is <80% and should be avoided as empiric therapy, but may be considered if confirmed by C&S for complicated UTI or pyelonephritis (2 week duration).
- For ESBL (Extended Spectrum Beta-lactamase) producing organisms, treat according to reported susceptibility with **nitrofurantoin, TMP/SMX or ciprofloxacin**. If resistant to all tested antibiotics or multiple allergies, consult Infectious Diseases for potential alternatives. ESBL pyelonephritis may require inpatient admission and/or IV antibiotics.
- If patient reports penicillin allergy inquire about onset and severity of symptoms, as well as prior beta-lactam exposure and update patient medical record. *Severe or life-threatening allergic reactions may include: anaphylaxis, angioedema, urticaria, Stevens-Johnson Syndrome (SJS), etc.*
- Antibiotic prophylaxis for most patients with risk factors for recurrent, complicated UTI is NOT typically recommended. Risk of resistance outweighs the slight reduction in infection rate.

**Note: This guideline is intended to aid in the selection of antimicrobial therapy in adult OUTPATIENTS residing in Alaska who present with a urinary tract infection. It is not intended to replace the clinical judgment of the prescribing provider or to be used for those residing outside the State of Alaska.**

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# Alaska Antimicrobial Stewardship Collaborative

## Adult LONG TERM CARE Urinary Tract Infection Treatment Guidelines (Last Updated 10-2018)

**INDICATION FOR URINALYSIS IN NON-CATHETERIZED RESIDENTS – FOLLOW THE LOEB/MCGEER CRITERIA:** Acute dysuria alone **OR** Fever > 100 F **AND** 1 of the following → New or worsening: urgency, frequency, suprapubic pain, gross hematuria, costovertebral tenderness, urinary incontinence (*Note: urinalysis is NOT indicated in non-catheterized patients for work up of worsening mental status changes without other symptoms of UTI*)

**INDICATION FOR URINALYSIS IN CATHETERIZED RESIDENTS:** New onset suprapubic pain or costovertebral tenderness, swelling/tenderness of the testes, epididymis or prostate, or purulent discharge from around the catheter; **OR** Fever > 100 F, rigors, acute change in mental status, new-onset hypotension, with **NO** alternate diagnosis or site of infection

Category	Asymptomatic Bacteriuria	Acute Cystitis	Acute Pyelonephritis	Complicated UTI/ Catheter-Associated UTI (CAUTI)
<b>Symptoms and/or Risk Factors</b>	Presence of bacteria in urine ( $\geq 10^5$ cfu/mL or from catheter; $\geq 10^2$ cfu/mL) from an individual <b>WITHOUT</b> signs or symptoms of infection.	<b>General symptoms:</b> Acute onset dysuria, frequency or urgency	<b>Upper UTI</b> is frequently associated with general symptoms <b>PLUS back/flank pain, fever &amp; chills.</b>	<b>Complicated UTI:</b> Infection in males or in the presence of an anatomic/functional abnormality (e.g. enlarged prostate, calculi, obstruction, catheter or stent, neurogenic bladder, neutropenia).
<b>Culture &amp; Susceptibility (C&amp;S) Investigation</b>	Routine C&S is <b>NOT indicated</b> in asymptomatic patients <i>unless</i> screening in pregnancy or prior to urologic procedure with compromise of urothelial mucosa.	<b>Urine C&amp;S are critical</b> in order to optimize therapy. Urine cultures should be collected from a midstream void prior to antibiotics or a freshly placed urinary catheter.		
<b>Recommended Treatment and Duration</b>	<p>Treatment is <b>NOT</b> recommended for patients who do not meet the below criteria (e.g. pregnancy or those undergoing urologic procedures)</p> <p><u>Pregnant women: (select one option)</u></p> <ul style="list-style-type: none"> <li><b>Nitrofurantoin</b> 100mg PO BID x 5d</li> <li><b>Cephalexin</b> 500mg PO BID x 7 days</li> </ul> <p><b>** Note: contraindicated at 38-42 weeks gestation</b></p> <p><b>Cephalexin</b> 500mg PO BID x 5d</p> <p><u>Urologic procedure:</u> Direct treatment based on pre-procedure screening C&amp;S.</p> <p><b>**Note: when NOT giving antibiotics, close monitoring is recommended</b></p>	<p><u>First Line: (select one option)</u></p> <ul style="list-style-type: none"> <li><b>Nitrofurantoin</b> 100mg PO BID x 5d</li> <li><b>Cephalexin</b> 500mg PO BID x 7 days</li> </ul> <p><b>Fluoroquinolone FDA Safety Alert:</b> <i>Disabling &amp; potentially permanent adverse effects outweigh benefit in cystitis. Only use when no other alternatives exist.</i></p> <p><u>Second Line:</u></p> <ul style="list-style-type: none"> <li><b>Ciprofloxacin</b> 250mg PO BID x 3 days</li> </ul> <p><b>**Note: If STD risk w/ symptoms of urethritis, consider treatment for chlamydia.</b></p>	<p><u>First Line:</u></p> <ul style="list-style-type: none"> <li><b>Ceftriaxone</b> 1g IM/IV x 1 dose</li> </ul> <p>If severe or life-threatening beta-lactam allergy consider <b>Gentamicin</b> 5mg/kg IM/IV x 1 dose</p> <p><u>Followed by:</u> <u>First line:</u></p> <ul style="list-style-type: none"> <li><b>Cephalexin</b> 1g PO TID x 14 days</li> </ul> <p><u>Second line:</u></p> <ul style="list-style-type: none"> <li><b>Ciprofloxacin</b> 500mg PO BID x 7d</li> </ul> <p><i>Tailor maintenance therapy to C&amp;S report.</i></p>	<p>Base empiric treatment on prior culture data. <b>If stable vitals &amp; afebrile</b>, provide definitive therapy when new C&amp;S result.</p> <p><b>Duration:</b></p> <ul style="list-style-type: none"> <li>Shorter courses (<b>7 days</b>) are reasonable, if symptoms promptly resolve.</li> <li>Longer courses (<b>10-14 days</b>) if delayed response, regardless if catheterized or not.</li> <li>If female and <math>\leq 65</math> years of age, a <b>3-day</b> regimen <i>may be considered</i> for CAUTI with catheter removal.</li> </ul>

- Scope of this guideline is limited to adults >18 y/o without signs of severe physiologic disturbance. This guideline should not be used for patients who are immunocompromised or kidney transplant recipients.
- **Nitrofurantoin** is 1<sup>st</sup> line for most patients **without** symptoms of pyelonephritis. Contraindicated for CrCl < 30mL/min and in pregnancy at term (38-42wks).
- Statewide *E. coli* susceptibility to TMP/SMX is <80% **and should be avoided as empiric therapy** but may be considered if confirmed by C&S for complicated UTI or pyelonephritis (2 week duration).
- Risk factors for resistance: Antibiotic exposure within 90 days, hospitalization within 90 days, presence of invasive device(s)
- For ESBL (Extended Spectrum Beta-lactamase) producing organism, treat according to reported susceptibility with **nitrofurantoin, TMP/SMX or ciprofloxacin**. If resistant to all tested antibiotics or multiple allergies, *consult Infectious Diseases* for potential alternatives. ESBL pyelonephritis may require inpatient admission and/or IV antibiotics.
- If patient reports penicillin allergy inquire about onset and severity of symptoms as well as prior beta-lactam exposure and update patient medical record. *Severe or life-threatening allergic reactions may include: anaphylaxis, angioedema, urticaria, Stevens-Johnson Syndrome (SJS), etc.*
- Antibiotic prophylaxis for most patients with risk factors for recurrent, complicated UTI is NOT typically recommended. Risk of resistance outweighs the slight reduction in infection rate.

**Note: This guideline is intended to aid in the selection of antimicrobial therapy in adult LONG TERM CARE residents in Alaska who present with a urinary tract infection. It is not intended to replace the clinical judgment of the prescribing provider or to be used for those residing outside the State of Alaska.**

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## Pediatric FEBRILE Urinary Tract Infection Treatment Guideline (2-24 months)

Symptoms	Diagnostic Criteria for Acute Pyelonephritis <sup>1</sup>	Risk Factors <sup>1</sup>				
<ul style="list-style-type: none"> <li>Fever</li> <li>Poor feeding</li> <li>Vomiting</li> <li>Irritability</li> <li>Strong-smelling urine</li> </ul>	<u>Urinalysis results that suggest infection</u> <ul style="list-style-type: none"> <li>Positive nitrite <u>OR</u></li> <li>Leukocyte esterase <u>OR</u></li> <li>Pyuria <u>AND</u></li> <li>&gt;50,000 CFUs per mL of a uropathogen cultured from a urine specimen obtained through catheterization or SPA</li> </ul>	<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <u>Girls</u>                      Age &lt;12 months                      Temp ≥39 C                      Fever ≥2 days                 </td> <td style="width: 50%; vertical-align: top;"> <u>Boys</u>                      Temp ≥39 C                      Fever ≥24 hours                      Uncircumcised                 </td> </tr> <tr> <td colspan="2" style="text-align: center;">Absence of another source of infection</td> </tr> </table>	<u>Girls</u> Age <12 months Temp ≥39 C Fever ≥2 days	<u>Boys</u> Temp ≥39 C Fever ≥24 hours Uncircumcised	Absence of another source of infection	
<u>Girls</u> Age <12 months Temp ≥39 C Fever ≥2 days	<u>Boys</u> Temp ≥39 C Fever ≥24 hours Uncircumcised					
Absence of another source of infection						
Test	Treat	Imaging <sup>1</sup>				
Obtain urine culture <u>PRIOR</u> to starting antibiotics	Adjust therapy based on sensitivity testing	<ul style="list-style-type: none"> <li>Renal/bladder ultrasound for 1st febrile UTI</li> <li>VCUG for 2nd febrile UTI or if abnormalities seen on renal/bladder ultrasound</li> </ul>				

### Antibiotic Selection<sup>1</sup>

	Ambulatory Empiric Treatment	Inpatient Empiric Treatment	Duration of Therapy
<b>Preferred Treatment<sup>1</sup></b>	<b>Cephalexin</b> 50mg/kg/day PO divided TID or QID (max 4gm/day)	<b>Ceftriaxone</b> 50mg/kg IV Q24H (max 2gm/day)	7-10 days
<b>Beta-lactam allergic<sup>1</sup></b>	<b>Sulfamethoxazole/trimethoprim</b> 4-5mg/kg PO BID (trimethoprim component for dosing; max 160mg trimethoprim/dose)	<b>Gentamicin</b> 5mg/kg/day IV	

1.Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128(3):595-610.

## Pediatric Urinary Tract Infection Treatment Guideline (>24 months)

Symptoms <sup>2</sup>	Risk Factors <sup>2</sup>	Test/Treat		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <u>Preverbal</u> <ul style="list-style-type: none"> <li>Fever</li> <li>Abdominal/flank pain</li> <li>Vomiting</li> <li>Poor feeding</li> <li>Lethargy</li> <li>Malodorous urine</li> </ul> </td> <td style="width: 50%; vertical-align: top;"> <u>Verbal</u> <ul style="list-style-type: none"> <li>Frequency</li> <li>Dysuria</li> <li>Hesitancy</li> <li>Urgency</li> <li>Abdominal/flank pain</li> </ul> </td> </tr> </table>	<u>Preverbal</u> <ul style="list-style-type: none"> <li>Fever</li> <li>Abdominal/flank pain</li> <li>Vomiting</li> <li>Poor feeding</li> <li>Lethargy</li> <li>Malodorous urine</li> </ul>	<u>Verbal</u> <ul style="list-style-type: none"> <li>Frequency</li> <li>Dysuria</li> <li>Hesitancy</li> <li>Urgency</li> <li>Abdominal/flank pain</li> </ul>	Prior history of UTI <ul style="list-style-type: none"> <li>Review prior organism/susceptibilities for guidance on empiric therapy selection if recurrent UTI</li> </ul> Fever ≥ 2 days or prolonged ≥ 5 days	Obtain urine culture <u>PRIOR</u> to starting antibiotics  Adjust therapy based on sensitivity testing
<u>Preverbal</u> <ul style="list-style-type: none"> <li>Fever</li> <li>Abdominal/flank pain</li> <li>Vomiting</li> <li>Poor feeding</li> <li>Lethargy</li> <li>Malodorous urine</li> </ul>	<u>Verbal</u> <ul style="list-style-type: none"> <li>Frequency</li> <li>Dysuria</li> <li>Hesitancy</li> <li>Urgency</li> <li>Abdominal/flank pain</li> </ul>			

### Antibiotic Selection<sup>2</sup>

	Ambulatory Empiric Treatment	Inpatient Empiric Treatment	Duration of Therapy
<b>Preferred Treatment<sup>2</sup></b>	<b>Cephalexin</b> 50mg/kg/day PO divided TID or QID (max 4gm/day)	<b>Ceftriaxone</b> 50mg/kg IV Q24H (max 2gm/day)	7-10 days
<b>Beta-lactam allergic<sup>2</sup></b>	<b>Sulfamethoxazole/trimethoprim</b> 4-5mg/kg PO BID (trimethoprim component for dosing; max 160mg trimethoprim/dose)	<b>Gentamicin</b> 5mg/kg/day IV	

*Adopted Nov. 2018 - Approved 2018*

2.Shaw K, et al. Pathway for the Evaluation and Treatment of Children with Febrile UTI. Children's Hospital of Philadelphia. <https://www.chop.edu/clinical-pathway/urinary-tract-infection-uti-febrile-clinical-pathway>. Accessed Oct 2018.



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## Urinary Uncertainty: Demystifying Culture Collection in Urinary Tract Infections (UTI)



Obtaining urine culture from patients with various forms of UTI can represent an important step in providing definitive therapy. In others, cultures may not be indicated and, in fact, may lead to inappropriate treatment. Knowing which clinical syndromes require urine culture and how to navigate typical urinalysis (UA) and urine culture order variations will assist the clinician in providing superior care to patients.

### **General Guidelines for Appropriate Urine Culturing:**

When obtaining urine cultures it is important to collect culture specimens in a manner that minimizes the potential for culture contamination. Additionally, urine cultures should be obtained prior to the administration of antibiotics in order to maximize the diagnostic yield of the culture.<sup>1-3</sup>

Urine cultures in non-catheterized patients should be collected from a clean-catch, midstream void.<sup>1,2</sup> When urine cultures are indicated in a catheterized patient and the catheter has been in place for longer than 2 weeks, the catheter should be changed prior to obtaining the culture with the collected specimen coming from the freshly placed catheter. If the catheter can be discontinued at the time the culture is indicated then the specimen should be obtained via a clean-catch, midstream void.<sup>3</sup>

### **Asymptomatic Bacteriuria (ASB):**

The Infectious Diseases Society of America (IDSA) defines ASB as “isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen obtained from a person without symptoms or signs referable to urinary infection”.<sup>1</sup> The only two patient populations which have shown benefit from antimicrobial management of ASB are pregnant patients and those scheduled to undergo urologic procedures that will compromise the urogenital mucosa. In patients with the above two indications routine screening is appropriate with the use of a **urine culture**. When screening for ASB the UA with reflex culture should NOT be used given that screening for pyuria has a low sensitivity for the identification of bacteriuria. Use of the UA with reflex culture order may result in cultures not being performed due to a lack of pyuria and, therefore, lack of identification of bacteriuric patients. If the patient does not have one of the above listed indications for screening and treatment then no routine screening or culturing of the urine is recommended.<sup>1</sup>

### **Acute Cystitis and Pyelonephritis:**

Acute bacterial cystitis implies the patient is acutely experiencing urinary symptoms; however, is another condition which may not always require obtaining urine culture to guide management.<sup>2</sup> In the outpatient care setting, in women without risk factors for resistant pathogens (i.e. antibiotic exposure/hospitalization in the previous 90 days or previous infection/colonization with multidrug resistant bacteria) empiric management can be initiated using agents with adequate local bacterial susceptibility rates. In outpatient complicated cystitis (i.e. infection in males, those with urogenital structural abnormalities, or recurrence), inpatient acute cystitis (complicated or uncomplicated), or acute pyelonephritis appropriate obtainment of urine cultures and antimicrobial sensitivities is critical to the management of antimicrobial therapy. In these cases providers should consider utilization of an

order for **UA with urine culture**. The UA with reflex culture if indicated is NOT recommended in this scenario as a culture is likely indicated due to the presence of symptoms regardless of UA findings.<sup>2</sup> In the cases where the patient is unable to provide information regarding symptoms and cystitis or pyelonephritis is possible (i.e. fever or sepsis of unknown origin), it may be reasonable to utilize the UA with reflex culture if indicated order.

### **Catheter Associated UTI:**

Patients with urinary catheters are at a higher risk for the development of UTI. Urinalysis and/or urine cultures should ONLY be collected in catheterized patients when symptom(s) are present. Conversely, it is important to NOT perform urinalysis and/or urine cultures when the only symptoms present are malodorous urine, cloudy appearance, or change in color.<sup>3</sup> In most cases, if the catheter is functioning properly and the patient does NOT have urinary symptoms (i.e. urgency, suprapubic tenderness, or back/flank pain, or fever), then UA and culture will only identify ASB/pyuria related to catheter colonization. This is typically clinically insignificant and should not be empirically treated with antibiotics. When high suspicion of catheter associated urinary tract infection exists due to the presence of symptoms a **UA with urine culture** should be utilized. Similar to non-catheterized patients, in catheterized patients with fever or sepsis of unknown origin it is reasonable to utilize the UA with reflex culture if indicated order.

For more information on the diagnosis, testing, and treatment of urinary tract infections please refer to the Alaska Antimicrobial Stewardship Collaborative's statewide UTI guidelines for inpatients, outpatients, and those residing in long term care facilities (attached).

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## Urinary Tract Infections: Treatment and De-escalation



The previous article “Urinary Uncertainty: Demystifying Culture Collection in Urinary Tract Infections (UTI)” discussed the antimicrobial stewardship principles of diagnostic testing for UTIs. As a follow-up in the series focusing on UTIs, this article will discuss antimicrobial stewardship principles of treatment and de-escalation which include a follow-up assessment of the continued need for antibiotic therapy, recommendations for antibiotic therapy choices, balancing treatment efficacy and severity of illness, and using the results of cultures and diagnostic tests to de-escalate to the lowest risk, most effective regimen for the patient.<sup>1</sup>

### Asymptomatic Bacteriuria (ASB):

Updated practice guidelines from 2019 define ASB as the “presence of 1 or more species of bacteria growing in the urine at specified quantitative counts ( $\geq 10^5$  CFU/mL), irrespective of the presence of pyuria, in the absence of signs or symptoms attributable to urinary tract infection (UTI).” It is a common finding particularly in elderly persons in long term care facilities, where it can occur in up to 50% of residents, and persons with long term indwelling catheters (100%).<sup>2</sup>

ASB guidelines direct that ASB should NOT be screened for and should NOT be treated in the majority of patients. The two exceptions for which screening and treatment for ASB are indicated are 1) pregnant women and 2) patients undergoing endoscopic urologic procedures associated with mucosal trauma.<sup>2</sup> It is recommended that pregnant women receive 4-7 days of antibiotic treatment, using the shortest effective course depending on the antibiotic selected (see A2SC guidelines for guidance on possible agents).<sup>2</sup> Patients undergoing urologic procedures should receive a short course (1 or 2 doses) initiated 30-60 minutes prior to the procedure. Selection of an antibiotic in this case would be directed therapy based on pre- procedure screening urine culture and susceptibility results.<sup>2</sup>

Inappropriate treatment of ASB with antibiotics has been a significant driver of antibiotic resistance in addition to placing patients at risk for adverse events such as *Clostridioides difficile* infection and adverse drug effects.<sup>2</sup> When presented with results from a urinalysis and urine culture, the clinician must take into context the original indication for performing the test. If no localizing symptoms referable to the urinary tract were present, presence of bacteria in urine culture would not indicate infection but asymptomatic bacteriuria and should be labeled as such rather than as infection. Bacteriuria and delirium are commonly found together in older adults and causal relationships can be erroneously made. Delirium, falls or confusion by themselves, without localizing genitourinary symptoms, are not symptoms associated with UTIs. Mental status changes and ASB is not an indication for antibiotic treatment. However, if patients have signs and/or symptoms of systemic infection antibiotic therapy would be warranted.<sup>2</sup>



### **Acute Cystitis and Pyelonephritis**

Urine cultures are not typically required in the outpatient care setting for uncomplicated acute cystitis in women without risk factors for resistant pathogens. In those cases, empiric treatment options recommended by the A2SC guidelines include nitrofurantoin (100mg twice daily for 5 days) or cephalexin (500mg twice daily for 7 days).<sup>3</sup> Bactrim, endorsed by the IDSA for uncomplicated cystitis, is generally not recommended as an empiric choice in the State of Alaska at this time due to *E coli* resistance rates exceeding 20%<sup>4</sup>; however, this would be an appropriate choice if susceptibilities to Bactrim were known or local susceptibilities varied from those outlined by the State of Alaska antibiogram. The cost and availability for fosfomycin somewhat limit its use, but it is also endorsed by IDSA guidelines and remains an option for cystitis when available. Fluoroquinolones are effective in 3 day regimens but are not preferred for uncomplicated cystitis and should only be used if the first line options are not appropriate. Fluoroquinolones have a high propensity for collateral damage (selection of drug resistant organisms) and their adverse effects limit their use in uncomplicated cystitis.<sup>3</sup>

For those patients with acute pyelonephritis, ideally cultures should have been obtained prior to the initiation of antibiotic therapy. Empiric treatment can begin with an extended spectrum cephalosporin (such as ceftriaxone 1gm), a fluoroquinolone (if resistance rates of *E coli* do not exceed 10%), or a consolidated 24-h dose of an aminoglycoside. Other options including extended-spectrum penicillins or carbapenems may be selected depending on local resistance data. Once cultures and susceptibilities are available, therapy should be reviewed and de-escalated to the most effective, narrowest spectrum, safest regimen taking into consideration patient specific factors (allergies, drug interactions/contraindications, compliance etc). Recommended regimens (based on known susceptibilities) include fluoroquinolones (ciprofloxacin 7 days, levofloxacin 5 days), TMP/SMX (10-14 days) and cephalosporins (10-14 days) and switch from IV to PO therapy if this has not already been initiated.<sup>3</sup> Of note, nitrofurantoin and fosfomycin are not indicated for pyelonephritis or perinephric abscesses and are inappropriate choices as step down therapy for pyelonephritis.

### **Complicated UTI**

Complicated UTI encompasses a variety of syndromes including catheter-associated UTI (CAUTI), UTI in males, UTI in the presence of urologic abnormalities and UTI during pregnancy. In addition to antibiotic therapy, source control measures may need to be undertaken. Empiric therapy should be based on prior culture data if available, how ill the patient appears and whether the symptoms are more suggestive of a lower urinary tract infection (cystitis) versus an upper urinary tract infection (pyelonephritis). Definitive therapy will be dependent on culture and susceptibility results. Shorter courses of therapy (7 days) are reasonable if symptoms promptly resolve and longer courses (10-14 days) if there is a delayed response to therapy. Oral cephalosporins, fluoroquinolone and TMP/SMX can all be used as options for oral step down therapy, factoring in the time on IV therapy when determining total duration. If bacteremia is present, the selection of an agent with high oral bioavailability such as fluoroquinolones and TMP/SMX may be preferred.<sup>5,6</sup>

For more information on the diagnosis, testing, and treatment of urinary tract infections, please refer to the Alaska Antimicrobial Stewardship Collaborative's statewide UTI guidelines.

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## Antibiotic duration in uncomplicated cystitis and outpatient pyelonephritis



There is growing evidence supporting shorter durations of antibiotic therapy in uncomplicated cystitis and pyelonephritis to minimize, antibiotic resistance, adverse events and infection recurrence.

Data from the early 2000's were incorporated in the 2011 Infectious Disease Society of America (IDSA) guidelines that highlighted >90% cure rates with nitrofurantoin x 5 days, fluoroquinolones x 3 days, and beta-lactams x 3-5 days in females with uncomplicated cystitis. In pyelonephritis, these guidelines also identified fluoroquinolones x 5-7 days being effective compared

traditional 14 day antibiotic courses that were associated with greater rates of resistance, *Clostridioides difficile* (*C diff*) infections, and increased risk for serious adverse events.<sup>1</sup> Newer data has since confirmed these recommendations in pyelonephritis and provided further insight into appropriate antibiotic durations in unique situations not previously addressed, including women with diabetes and men with uncomplicated cystitis.

Regarding pyelonephritis, two major studies, published since the 2011 guidelines, have identified shorter durations (5-7 days) of fluoroquinolones as non-inferior to longer durations (10-14 days) in non-elderly women. One prospective, multi-site randomized, double blind, non-inferiority trial compared oral ciprofloxacin 500 mg twice daily for 7 versus 14 days in women with community acquired, acute pyelonephritis. The majority of urinary isolates revealed *Escherichia coli* (*E. coli*) and 27% of participants with positive blood cultures and 17% initially receiving intravenous doses of ciprofloxacin. Results from this study found clinical cure in 97% of patients treated for 7 days versus 96% treated for 14 days (-0.9% difference, 90% CI -6.5 to 4.8, p=0.004) and long term cure rates were equal for both study groups (-0.3% difference, 90% CI -7.4 to 7.2, p= 0.015).<sup>2</sup> The other study tested non-inferiority of fluoroquinolones in acute, community acquired pyelonephritis with 5 days versus 10 days of oral levofloxacin 500 mg daily or ofloxacin 200 mg twice daily. This study was prospective, multi-site, randomized, open-label and included 68 female patients with confirmed pyelonephritis, 97.7% with urinary isolates of *E coli* and 3.4% with positive blood cultures. This study found similar cure rates at day 10 and day 30 between both groups (93% versus 97.7% at day 10, p=1.00; and 100% for both groups at day 30, p=1.00).<sup>3</sup> Results from these two trials are consistent with past literature, including key trials, that also enrolled male participants, finding shorter antibiotic courses non-inferior to longer courses in complicated urinary tract infections and pyelonephritis.<sup>4, 5</sup>

Furthermore, unique populations have been studied and found to benefit from shorter antibiotic durations in uncomplicated cystitis. One large, retrospective study conducted at Baylor Medical School in 2017, identified a trend for longer antibiotic durations in women with cystitis and comorbid diabetes that ironically correlated to an increased risk for early cystitis recurrence when treatment durations were greater than 5 days compared to 5 days or less (OR 2.17, 95% CI 1.07-4.41).<sup>6</sup> Similarly, a recent study found 7 day antibiotic courses sufficient in men with uncomplicated cystitis and found more than double infection recurrence rates with longer antibiotic durations (> 7days) in a subgroup of patients with fewer complications (i.e. no anatomical abnormalities, catheterization, or immunosuppression; OR 2.62, 95% CI 1.04-6.61).<sup>7</sup> This observational study has prompted a randomized, controlled trial comparing 7 versus 14 day antibiotic therapy for urinary tract infections in men that is currently

underway<sup>8</sup> and is consistent with other previous trials finding antibiotic durations longer than 7 days do not provide a protective benefit in infection reoccurrence rates<sup>7</sup> and fluoroquinolone durations of 5 days being as effective as 10 days.<sup>10</sup> It has been suggested that the longer durations may alter normal urogenital flora thus predisposing patients to unnecessary treatment failure as observed in these trials.

Shorter antibiotic durations have been incorporated into the A2SC's Alaska specific Urinary Tract Infection Treatment Guidelines published in November of 2018. These recommended durations reflect the latest literature that supports shorter durations of therapy to prevent collateral damage and treatment failure (Table 1) in conjunction with antibiotic susceptibility specific to Alaska.

*Table 1: Antibiotic durations for urinary tract infections*

<b>Cystitis</b>	
Nitrofurantoin	5 days
or Cephalexin	7 days
or Ciprofloxacin (second line)	3 days
<b>Pyelonephritis</b>	
Ceftriaxone and	1 dose
Cephalexin	10-14 days
or Ciprofloxacin (second line)	7 days

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