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POST-ACUTE AND LONG-TERM CARE KNOWLEDGE NETWORK FOR OLDER ADULTS AND WORKFORCE

Molecular Diagnostics in UTI

Margaret Fitzpatrick, MD, MS
Associate Professor of Medicine, Infectious Diseases

Background

UTIs are among the most common causes of bacterial infections in LTCF residents

Key issues

- Presence of microorganisms identified at appropriate counts on quantitative urine culture (bacteriuria) is important ***but not sufficient*** to diagnose UTI
- ***Many*** patients in LTCF will have bacteriuria, regardless of presence of UTI
- Conventional urine culture:
  - 50-80% sensitive in patients with acute, uncomplicated UTI
  - Selects for mainly aerobic, fast-growing bacteria

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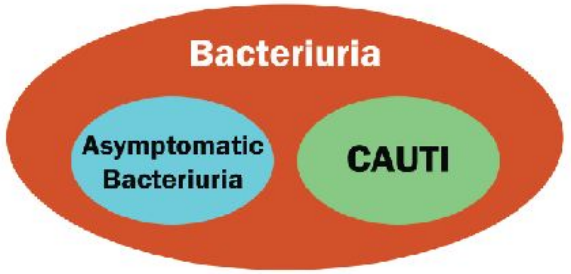
4 Things You Should Know About Urine Cultures

1. Bacteria in the urine does not necessarily mean a catheter-associated urinary tract infection (CAUTI) is present.

Bacteriuria is the term used to describe a positive urine culture, the presence of bacteria in the urine. This could point to either asymptomatic bacteriuria or to CAUTI. People can have bacteria in the urine that do not cause symptoms or harm; asymptomatic bacteriuria is not a urinary tract infection.



2. Chronically catheterized residents have bacteriuria 99% of the time.

Inappropriate triggers for urine cultures include—

- Urine color
- Urine smell
- Urine sediment
- Cloudy urine
- White blood cells in the urine
- Positive dipstick

3. Urine culturing can actually harm residents who have no CAUTI symptoms.

If a urinary catheter is present...
...urine may become cloudy and odorous and have sediments,
...and providers might incorrectly assume infection and obtain a urine culture,
...which can lead to incorrect diagnoses and inappropriate treatment and antibiotic use,
...as well as more resistant organisms, *Clostridium difficile*, increased cost, and further complications.

4. Urine cultures should only be ordered if one or more CAUTI symptoms are present.

The presence of cloudy, odorous urine with sediments does not alone indicate a CAUTI. CAUTI signs and symptoms are the following:

- Fever (even if the resident has another possible cause for the fever such as pneumonia)*
- Rigors
- New confusion or functional decline (with NO alternative diagnosis AND leukocytosis)
- New suprapubic pain or costovertebral angle pain or tenderness
- New, very low blood pressure (with no alternate noninfectious cause)
- Acute pain, swelling or tenderness of testes, epididymis, or prostate
- Pus around the catheter

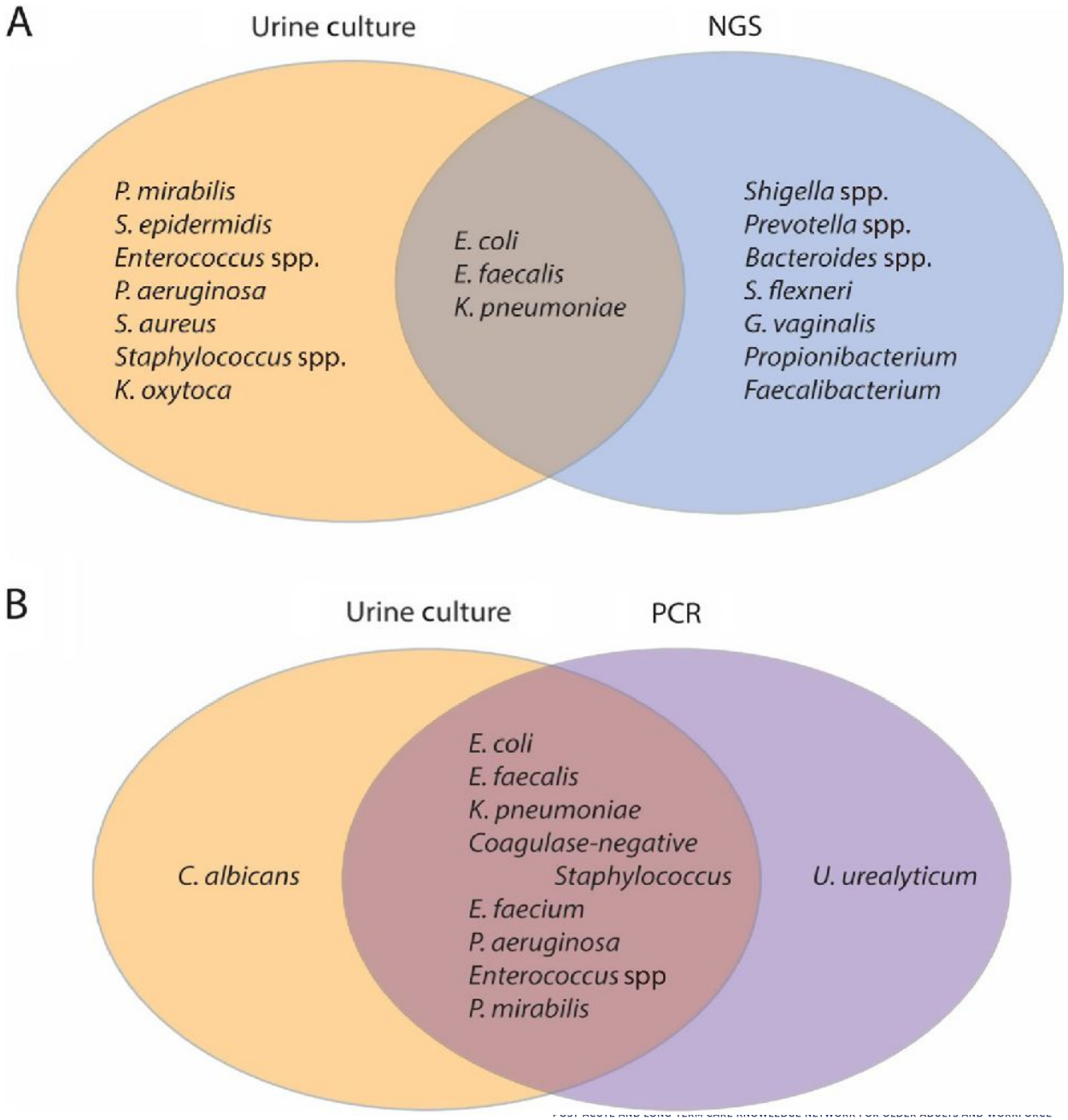
* See CDC's January 2016 "Urinary Tract Infection (UTI) Event for Long-term Care Facilities," listed below.

Evidence For Molecular Tests to Identify Urine Microorganisms

Culture-independent techniques rely on various ways to detect microorganisms in urine, most commonly via DNA

Highlights

1. **Next generation sequencing (NGS)** vs culture
   - 78% of culture-negative urine samples were positive by NGS
   - 82% of culture-positive urine samples were positive by NGS
   - Species diversity greater
2. **PCR** vs culture
   - In half of studies, PCR was positive more often than culture



McGinn et al. *Eur Uro Op Sci* 2022;44: 113-124

Limitations and Caveats to Molecular Tests for UTI

1. **Poor specificity**
   - *Of asymptomatic healthy controls, 95% had positive molecular tests vs 23% who had positive urine cultures*
   - Detects commensal and colonizing microorganisms that are not pathogenic
   - Molecular tests cannot distinguish alive pathogens from dead or quiescent microbes
2. **Lack of standardization, quality control**
   - Variable results from different protocols, platforms, and labs
     - No FDA or CLSI validation
   - Data quality issues
   - No standardized algorithms to predict causative microorganisms
3. **Lack of clinical data**
   - No studies on what threshold of bacteria present in molecular tests correlates best with infection or which bacteria are likely to be associated with UTI and need treatment
   - Less information about antibiotic susceptibility
     - 'Pooled' predicted antibiotic susceptibility results misleading
   - Extremely limited data on clinical outcomes

Questions/ Discussion

RESULTS: PATHOGENIC DNA DETECTED

ORGANISM(S) TESTED - DETECTED: (See last page for Organism(s) Tested - Not Detected)

- *Escherichia coli* ≥100,000 cells/mL
- *Citrobacter freundii* 50,000-99,999 cells/mL
- *Morganella morganii* <10,000 cells/mL
- *Ureaplasma urealyticum* <10,000 cells/mL

LEGEND S = Pooled Susceptibility Detected R = Pooled Resistance Detected RGD = Resistance Gene(s) Detected	Tetracycline	Sulfamethoxazole / Trimethoprim	Nitrofurantoin	Gentamicin	Meropenem	Amoxicillin / Clavulanate	Ampicillin	Piperacillin / Tazobactam	Ampicillin / Sulbactam	Cefazolin	Ciprofloxacin	Levofloxacin	Fosfomycin	Vancomycin	Cefaclor	Ceftriaxone	Cefepime	Ceftazidime	Cefoxitin
1 Formulations	PO	PO/IV	PO	IM/IV	IV	PO	PO/IV	IV	IV	IV	PO/IV	PO/IV	PO	IV	PO	IM/IV	IV	IV	IV
2 Pooled Antibiotic Susceptibility Testing (P-AST™)	S	S	S	S	S	S	S	S	S	S	R	R	R	R	R	R	R	R	R
3 Resistance Gene(s) Detected						RGD	RGD	RGD	RGD	RGD					RGD	RGD	RGD	RGD	RGD
Pooled MIC Results (µg/mL)	2	2/38	32	4	2	8/4	16	16/4	8/4	8									

Organism(s) Tested - Detected: ✓ = Check marks are supportive data and are NOT patient specific.

4																			
Escherichia coli	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓
Citrobacter freundii	✓	✓	✓	✓	✓						✓	✓	✓		✓	✓	✓	✓	
Morganella morganii	✓	✓		✓	✓			✓	✓		✓	✓				✓	✓	✓	✓
Ureaplasma urealyticum	✓											✓							