

# Emerging human uropathogens, including *Aerococcus urinae* and Coagulase-Negative Staphylococci are more frequently detected by Guidance® UTI than standard urine culture, in female patients symptomatic of urinary tract infection

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## Introduction: SUC Misses Emerging Organisms

Introduction: The standard urine culture (SUC) has been the gold standard test for the diagnosis of urinary tract infection (UTI). Its limited culture conditions are bias for the identification of classical *E. coli* and monomicrobial UTI infections. Recently, other bacterial species, including other Gram-negative and Gram-positive bacteria, have increasingly been acknowledged for their role in UTI. Furthermore, recent research in this field has demonstrated that not all UTIs are monomicrobial and that polymicrobial infections are common. Novel advanced methods, such as multiplex polymerase chain reaction (M-PCR) can provide clinically relevant microbiological data missed by SUC.

*Aerococcus urinae* is a Gram-positive bacterium that has been isolated from urine from UTI, urgency urinary incontinence, and overactive bladder. It has been known to cause bacteremia and endocarditis, generally preceded by UTI and UTI symptoms.

Coagulase-Negative Staphylococci (CoNS) is a group of Gram-positive cocci. Nosocomial isolates of CoNS are often found in polymicrobial cultures. Among them, *S. saprophyticus* is the second most frequent causative microorganism of uncomplicated lower UTI in young, sexually active women. The organisms are increasingly being studied as they can become pathogenic in certain conditions.

Both *A. urinae* and CoNS are found in catheter samples and Mid stream collected samples (Table 1)

**Objective:** This study was conducted to compare Guidance® UTI, a M-PCR-based test that includes Pooled Antibiotic Susceptibility Testing (P-AST) with SUC for the detection of *A. urinae* and CoNS in female symptomatic UTI patients.

Table 1: Catheter vs Midstream Collected Samples

N = 1,884	Catheter n = 942	Voided-matched n = 942	
Age, mean(SD), range 15-122	68.3 ± 15.5	68.5 ± 16.5	
Age, n(%)			
<65	301 (32.0)	301 (32.0)	
65-75	341 (36.0)	341 (36.0)	
Office Type, n (%)			
OB/Gyn	4 (0.4)	4 (0.4)	
Urology/Uroynecology	838 (89.6)	838 (89.6)	
Type of tests order, n (%)			
Single Cystitis	398 (42.3)	398 (42.3)	
Recurrent UTI	544 (57.7)	544 (57.7)	

N = 1,884 females	Catheter n = 942 n (%)	Voided-matched n = 942 n (%)	p value
Coagulase Negative Staphylococci	17 (1.8)	11 (1.2)	0.25
<i>Aerococcus urinae</i>	58 (6.2)	71 (7.5)	0.24

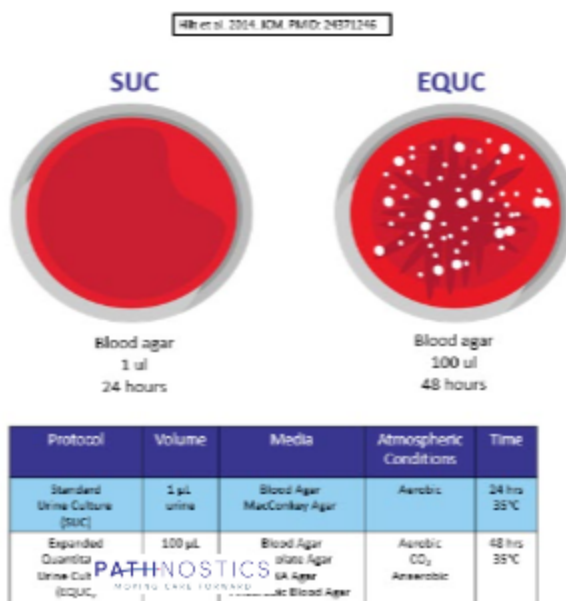


Fig 2: Determining pathogenic nature of CoNS in blood culture



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Table 2: Patient demographics and clinical information

Demographical and clinical characteristics (N = 1,360)	
Age, mean (SD)	73.3 (8.7)
Method of urine collection	
Voided, n (%)	1281 (94.2%)
Catheterized, n (%)	75 (5.5%)
UTI Symptoms, n (%)	
Dysuria	459 (33.8%)
Urine cloudy or strong smell	242 (17.8%)
Pain/Pelvic discomfort	465 (34.2%)
Fever	36 (2.7%)
LUTS	973 (71.5%)
Urinary incontinence	532 (39.1%)
Gross hematuria	295 (21.7%)
Antibiotic Usage in the Last 3 Weeks, n (%)	226 (16.9%)
Positive Urine Analysis or Dipsticks Results, n (%)	1123 (82.6%)

## Methods and Results

**Methods:** Female patients from a prospective study, recruited by 75 physicians from 37 urology offices in seven states between July 26, 2018 and February 27, 2019, were included in the analysis (Western IRB 20181661). Guidance® UTI and SUC were performed on their urine samples. Detections at  $> 10^5$  CFUs in SUC or  $> 10^5$  bacteria/mL in Guidance® UTI were defined as positive for *A. urinae* and CoNS (*S. epidermidis*, *S. haemolyticus*, *S. lugdunensis*, and *S. saprophyticus*).

**Results:** A total of 1,360 female patients, with the average age of 73.3 years, were included in this analysis. All patients enrolled in the study presented with UTI symptoms. Most of the urine samples (94.2%) were voided mid-stream urine (Table 2).

*A. urinae* and CoNS were detected in 159 and 15 ( $p < 0.0001$ ) and 55 and 17 ( $p < 0.0001$ ) patients by PCR and SUC, respectively (Table 3).

There were 144 patients detected with *A. urinae* by PCR, but missed by SUC (Table 2). Among the 144 patients, 70.8% were polymicrobial (*A. urinae* was detected with  $> 1$  other bacteria). SUC reported normal urogenital microflora in 38 of the 144 patients (26.4%) and no bacteria detected in 57 (39.6%) patients (Table 4).

PCR identified 40 patients with CoNS that were missed by SUC (Table 3), with 67.5% being polymicrobial (Table 4). Thirty percent (30%) of these patients were reported as normal urogenital microflora by SUC (Table 4).

Table 3: Detection of *A. urinae* and CoNS by PCR and SUC

N = 1,360	Detected by SUC # of patients (%)	Detected in by PCR # of patients (%)	Detected by PCR, but not by SUC # of patients (%)	p value
<i>Aerococcus urinae</i>	15 (1.1%)	159 (11.7%)	144 (10.7%)	<0.0001
Coagulase-Negative Staphylococci	17 (1.2%)	55 (4.0%)	40 (2.9%)	<0.0001

Table 4: Results of the patient samples detected by PCR, but missed by SUC

	<i>Aerococcus urinae</i> (N = 144) # of patients (%)	Coagulase-Negative Staphylococci (N = 40) # of patients (%)
<b>PCR Results</b>		
Monomicrobial	42 (29.2%)	13 (32.5%)
Polymicrobial	102 (70.8%)	27 (67.5%)
<b>SUC Results</b>		
No bacteria detected	57 (39.6%)	22 (55.0%)
Normal urogenital microflora	38 (26.4%)	15 (30.0%)
Other bacteria detected	87 (60.4%)	16 (40.0%)
Monomicrobial	70 (48.6%)	16 (40.0%)
Polymicrobial	17 (11.8%)	2 (5.0%)

## Conclusions

M-PCR/P-AST-based Guidance® UTI is more powerful than SUC in detecting emerging uropathogens, *A. urinae*, and CoNS in female symptomatic UTI patients. This may be due to the limited ability of SUC to detect emerging organisms and polymicrobial infections.

## References

- Hilt EE, McKinley K, Pearce MM, Rosenfeld AB, Zilliox MJ, Mueller ER, Brubaker L, Gai X, Wolfe AJ, Schreckenberger PC. Urine is not sterile: use of enhanced urine culture techniques to detect resident bacterial flora in the adult female bladder. J Clin Microbiol. 2018;56(1):1-7.
- Michels R, Last K, Becker SL, Papan C (2021) Update on Coagulase-Negative Staphylococci—What the Clinician Should Know. Microorg 9:830. <https://doi.org/10.3390/microorganisms9040830>