Challenge M233-1

November 2023

Urine: *Staphylococcus epidermidis*

HISTORY

A simulated midstream urine sample collected from a 90 year old symptomatic male was sent to category A laboratories.

Participants were expected to isolate *Staphylococcus epidermidis* and report colony count and susceptibility results.

MAIN EDUCATIONAL POINTS from M233-1

1. The significance of an organism isolated in urine is dependent on the quantity and the type of organism recovered.
2. Diagnosis of a urinary tract infection can be made with significant urinary tract symptoms and bacteriuria.

CMPT QA/QC/STATISTICS

All simulated urine samples are produced at CMPT according to CMPT internal protocols. The sample contained a pure culture of *Staphylococcus epidermidis*.

The samples are assessed for homogeneity and stability using in-house quality control methods and random selection of samples before and during production, and post sample delivery. The number of random samples selected is 15% of the total production batch.

The challenge sample lot was confirmed to be homogeneous and stable for 16 days.

Organism identification was confirmed by a reference laboratory.

All challenge components have in-house assigned values based on the most clinically appropriate result; the most clinically appropriate result is determined by expert committee evaluation. No further statistical analysis is performed on the results beyond that described under "Suitability for grading."

SURVEY RESULTS

Reference laboratories

Colony count: 12/12 (100%) labs reported colony counts ≥10 - ≥100 x 10^6 cfu/L,

Identification: 12/12 (100%) labs reported *Staphylococcus epidermidis*/coagulase-negative *Staphylococcus*, 1 did not report

Susceptibility: 10/12 (83%) labs reported oxacillin R, 1 did not report, 1 reported "contact microbiologist before performing/reporting AST (CMAST)"; 10/12 (83%) labs reported vancomycin S, 1 lab did not report, 1 reported CMAST; 11/12 (92%) labs reported SXT S, 1 reported CMAST; 8/12 (67%) labs reported Nitrofurantoin R, 3 did not report, 1 reported CMAST.

One lab indicated it does not normally process this type of sample.

Participants

Colony count: 49/49 (100%) processing and reporting labs reported colony counts between ≥10 - ≥100 x 10^6 cfu/L (Table 1).

Identification: 46/49 (100%) labs reported *Staphylococcus epidermidis*/coagulase-negative Staphylococcus, 2 participants reported s. epidermidis, unlikely pathogen/probable contaminant; 1 lab reported probable contaminant. (Table 2)

Susceptibility: 38/46 (83%) labs that reported identification reported oxacillin R, 6 did not report, 2 reported "contact microbiologist before performing/reporting AST (CMAST)"; 36/46 (78%) labs reported vancomycin S; 40/46 (87%) labs reported SXT S, 2 reported CMAST; 33/46 (72%) labs reported Nitrofurantoin S, 2 reported CMAST (Table 3 A-D).

Colony count, organism identification, and susceptibility testing to oxacillin, SXT, and vancomycin were correctly performed by at least 80 percent of reference laboratories and greater than 50 percent of all laboratories and were thus, determined to be suitable for grading.

Grading

Maximum grade: 20

Labs received a grade of 4 for reporting the correct colony count.

Participants reporting S. epidermidis were graded 4

A grade of 4 was given to each correctly reported susceptibility result:

- Oxacillin resistant
- Vancomycin susceptible
- SXT susceptible

Table 1. Colony count results

Reported x 10^6 cfu/L	Total	Grade
≥10 - ≥100	49	4
n/a, did not report culture	1	ungraded
n/a, no report due to shipping delay	1	ungraded
n/a, reported NG in culture	1	ungraded
sample not normally processed	2	ungraded
Total	**54**	

Table 2. Identification results

Reported	Total	Grade
Staphyloccocus epidermidis ± (coagulase- negative Staphylococcus)	40	4
coagulase-negative Staphylococcus	6	4
Staphylococcus epidermidis, unlikely pathogen/probable contaminant	2	4
10*8 Probable Contaminant	1	1
no growth	1	0
no report	1	0
shipping delay, no report	1	ungraded
sample not normally processed	2	ungraded
Total	**54**	

Identification methods: 27/49 labs used MALDI, 15 used Vitek 2, 2 used BD Phoenix, 1 Microscan and 4 only biochemical methods.

ASt methods: 32 labs used Vitek 2 +/- Kirby Bauer; 5 used BD Phoenix +/- KB; 1 lab used only KB and 2 labs used Microscan.

COMMENTS ON RESULTS

The identification results on this survey were very good. Most laboratories identified the isolate as *Staphylococcus epidermidis.* Some labs also used the less specific term of "coagulase negative staphylococci" which was deemed acceptable.

A few lab commented that this is a possible skin contaminant implying that clinical correlation is required.

There was complete agreement on the reporting of oxacillin, vancomycin and trimethoprim-sulfamethoxazole (SXT). While there was also agreement on reporting of nitrofurantoin, consensus requirements were not met and it was therefore not graded.

A few lab commented that a microbiologist approval would be needed prior to performing and reporting sensitivities.

ISOLATION AND IDENTIFICATION

Collection of a proper urine sample in this population is often problematic. Urine specimens should be obtained midstream by clean catch, or by in-and-out catheter when controlled voiding or cooperation is problematic.

Improper collection leads to specimen contamination by normal genitourinary flora, increasing the likelihood of false-positive urinalysis or misinterpretation of normal flora as pathogenic infection. Despite that, a study by Pallin and colleagues1 found that only 6% of participants had used proper midstream clean-catch technique and that 57% of the participants received no instruction on urine collection. [2]

Urinalysis is effective primarily for excluding UTIs; pyuria is sensitive but not specific for UTI, particularly among catheterized patients, in whom its presence is ubiquitous thus, while a positive result is necessary it is not sufficient to establish the diagnosis.[3]

Table 3. Susceptibility results

3A - Oxacillin	Total	Grade
R	38	4
no report	8	0
CMAST*	2	ungraded
n/a, reported as contaminant	1	ungraded
n/a, reported NG	3	ungraded
sample not normally processed	2	ungraded
Total	**54**	
3B - Vancomycin	**Total**	**Grade**
S	36	4
no report	8	0
CMAST*	2	ungraded
n/a, reported as contaminant	3	ungraded
n/a, reported NG	3	ungraded
sample not normally processed	2	ungraded
Total	**54**	
3C - SXT	**Total**	**Grade**
S	40	4
no report	4	0
CMAST	2	ungraded
n/a, reported as contaminant	3	ungraded
n/a, reported NG	3	ungraded
sample not normally processed	2	ungraded
Total	**54**	
3D - Nitrofurantoin	**Total**	**Grade**
S	33	ungraded
no report	11	ungraded
CMAST	2	ungraded
n/a, reported as contaminant	3	ungraded
n/a, reported NG	3	ungraded
sample not normally processed	2	ungraded
Total	**54**	

S. epidermidis is human skin commensal and an important opportunistic pathogen. Coagulase-negative staphylococci, including *S. epidermidis*, are a leading cause of hospital-acquired infections and they are often methicillin-resistant[4] and are associated with 2.5% of community acquired UTI (CAUTI).[5,6]

ANTIMICROBIAL SUSCEPTIBILITY

Antimicrobial susceptibility testing guidelines for coagulase negative staphylococci are outlined in CLSI. Primary testing and reporting for urines cultures can include oxacillin, tetracyclines, trimethoprim-sulfamethoxazole (SXT), vancomycin and nitrofurantoin.

Consultation with a microbiologist is recommended prior to reporting susceptibilities that would not be routinely reported.

CLINICAL RELEVANCE

Elderly patients are at particularly high risk for the development of UTIs. Contributing risk factors are incontinence, immobility, and cognitive impairment. [2]. In addition, correct diagnosis of UTI is challenging in the elderly population as they often lack typical signs and symptoms.[7]

UTI is the most common infection diagnosed in nursing home residents and it is the second most common infection in adult over 65 years old after respiratory infections. [8–10]

Although UTIs are more common in women, the incidence in men increases with age.

Diagnosis of UTI in older adults generally requires the presence of localized genitourinary symptoms, pyuria, and a urine culture with an identified urinary pathogen.

Distinguishing UTI from asymptomatic bacteriuria (ASB) in older adults is particularly important, as antibiotics are necessary for the treatment of symptomatic UTI, but not for ASB.[8]

Escherichia coli remains the most frequent pathogen identified in 75% to 82% of UTIs in this population. Other *Enterobacterales* also occur frequently, including *Klebsiella, Enterobacter* and *Serratia* species, as do urease-producing organisms, such as *Proteus mirabilis* and *Providencia stuartii*. *Pseudomonas aeruginosa* and *Candida albicans* are common in some populations, and gram-positive organisms, particularly enterococci and coagulase-negative staphylococci, are also frequently isolated. [11,12]

In this population, UTIs are the leading cause of bacteremia, hospitalization, decreased functional status, urosepsis, and even death.[13,14]

REFERENCES

1. Pallin DJ, Ronan C, Montazeri K, et al. Urinalysis in acute care of adults: Pitfalls in testing and interpreting results. *Open Forum Infectious Diseases*. 2014;1(1). doi:10.1093/ofid/ofu019
2. Detweiler K, Mayers D, Fletcher SG. Bacteruria and Urinary Tract Infections in the Elderly. *Urol Clin North Am*. 2015;42 (4):561-568. doi:10.1016/j.ucl.2015.07.002
3. Cortes-Penfield NW, Trautner BW, Jump RLP. Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. *Infect Dis Clin North Am*. 2017;31(4):673-688. doi:10.1016/j.idc.2017.07.002
4. Widerström M, Wiström J, Sjöstedt A, Monsen T. Coagulase-negative staphylococci: update on the molecular epidemiology and clinical presentation, with a focus on Staphylococcus epidermidis and Staphylococcus saprophyticus. *Eur J Clin Microbiol Infect Dis*. 2012;31(1):7-20. doi:10.1007/s10096-011-1270-6
5. Kline KA, Lewis AL. Gram-Positive Uropathogens, Polymicrobial Urinary Tract Infection, and the Emerging Microbiota of the Urinary Tract. *MicrobiolSpectr*. 2016;4(2):10.1128/microbiolspec.UTI-2012. doi:10.1128/microbiolspec.UTI-0012-2012
6. Hidron AI, Edwards JR, Patel J, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Annual Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infection Control & Hospital Epidemiology*. 2008;29(11):996-1011. doi:10.1086/591861
7. Nicolle LE. Urinary tract infections in the elderly. *ClinGeriatrMed*. 2009;25(3):423-436. doi:10.1016/j.cger.2009.04.005
8. Rowe TA, Juthani-Mehta M. Diagnosis and Management of Urinary Tract Infection in Older Adults. *InfectDisClinNorth Am*. 2014;28(1):75-89. doi:10.1016/j.idc.2013.10.004
9. Tsan L, Langberg R, Davis C, et al. Nursing home-associated infections in Department of Veterans Affairs community living centers. *American Journal of Infection Control*. 2010;38(6):461-466. doi:10.1016/j.ajic.2009.12.009
10. Beyer I, Mergam A, Benoit F, Theunissen C, Pepersack T. Management of urinary tract infections in the elderly. *Zeitschrift fur Gerontologie und Geriatrie*. 2001;34(2):153-157. doi:10.1007/s003910170080
11. Nicolle LE. Urinary tract pathogens in complicated infection and in elderly individuals. *JInfectDis*. 2001;183 Suppl 1 (Journal Article):5. doi:10.1086/318844
12. Scott MM, Liang SY. Infections in Older Adults. *Emerg Med Clin North Am*. 2021;39(2):379-394. doi:10.1016/j.emc.2021.01.004
13. Fried LP, Tangen CM, Walston J, et al. Frailty in Older Adults: Evidence for a Phenotype. *The Journals of Gerontology: Series A*. 2001;56(3):M146-M157. doi:10.1093/gerona/56.3.M146
14. Zeng G, Zhu W, Lam W, Bayramgil A. Treatment of urinary tract infections in the old and fragile. *World J Urol*. 2020;38 (11):2709-2720. doi:10.1007/s00345-020-03159-2