# Challenge M171-1

May 2017

Midstream urine: >100 x $10^6$ cfu/L *Klebsiella pneumoniae*

## HISTORY

A simulated midstream urine sample collected from a 7 year old female with frequency was sent to category A, B, and C laboratories.

Participants were expected to identify *Klebsiella pneumoniae*, report colony count and susceptibility results.

## CMPT QA/QC/STATISTICS

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

*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 10 days.

Organism identification, colony count, and antibiotic susceptibilities were 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%) processing laboratories reported 10 to ≥100 x $10^6$ cfu/L.

Identification: 12/12 (100%) processing laboratories reported *Klebsiella pneumoniae* ± subspecies *pneumoniae*.

Susceptibility testing: 12/12 (100%) processing laboratories reported the isolate resistant to ampicillin and susceptible to gentamicin and trimethoprim-sulfamethoxazole (SXT).

### MAIN EDUCATIONAL POINTS from M171-1

1. The current CLSI guidelines (M100-S27, 2017)[1] recommend using higher MIC breakpoint for cefazolin (Susceptible as ≤ 16 µg/mL instead of ≤ 2 µg/mL) for therapy of uncomplicated urinary tract infections due to *E. coli, K. pneumoniae* and *P. mirabilis*. The cefazolin results are used to predict results for oral cephem agents including cephalexin.

2. Systemic fluoroquinolones are not recommended as first –line systemic therapy in children.[2] They are associated with potentially permanent and disabling adverse effects of the tendons, muscles, joints, nerves, and CNS and should not be prescribed to patients who have other treatment options.[3,4]

Only 7/12 (58%) processing laboratories reported cefazolin/cephalothin/cephalexin S, 1 laboratory reported cephalothin I and cefazolin S, 1 laboratory reported cephalothin I, 1 laboratory reported cefazolin R and 2 laboratories did not report. Therefore, the results were ungraded due to lack of consensus.

1 laboratory indicated it does not normally process urine samples.

### Participants

Colony count (Table 1): 62/66 (94%) processing labs reported 10 to ≥100 x $10^6$ cfu/L and were graded 4.

Identification (Table 2): 63/66 (95%) processing labs reported *Klebsiella pneumoniae* ± subspecies *pneumoniae*.

**Table 1.** Colony count results

| Reported (x $10^6$) | Total | Grade |
|---|---|---|
| ≥100 | 32 | 4 |
| 10-100 | 30 | 4 |
| no count, reported mixed | 1 | 0 |
| no growth* | 1 | Ungraded |
| no report | 2 | 0 |
| snnp | 4 | ungraded |
| **Total** | **70** | |

* samples were delayed in transport for this lab

### Grading

**Maximum grade: 20**

Reporting 10 to100x$10^6$ cfu/L was graded 4.

Not reporting colony count, reporting mixed growth was graded 0.

Reporting *Klebsiella pneumoniae* was graded 4.

Reporting presumptive KES group and referring the isolate for further identification was graded 4.

Reporting mixed growth was graded 0.

Reporting the isolate resistant to ampicillin was graded 4.

Reporting the isolate susceptible to aminoglycosides and SXT was graded 4 for each agent reported.

No reporting susceptibility results was graded 0 for each agent no reported.

**Table 2.** Identification results

| Reported | A lab | B lab | C labs | Total | Grade |
|---|---|---|---|---|---|
| *Klebsiella pneumoniae* | 48 | 1 | 2 | 51 | 4 |
| *Klebsiella pneumoniae* subspecies *pneumoniae* | 12 | | | 12 | 4 |
| presumptive KES (*Klebsiella, Enterobacter* and *Serratia*) group, refer | | | 1 | 1 | 4 |
| Mixed growth of more than two organisms. | 1 | | | 1 | 0 |
| no growth* | | | 1 | 1 | ungraded |
| snnp | 3 | | 1 | 4 | ungraded |
| **Total** | **64** | **1** | **5** | **70** | |

* samples were delayed in transport for this lab

Susceptibility testing (Table 3): 60/66 (91%) processing labs reported the isolate resistant to ampicillin, while 61/66 (92%) and 63/66 (95%) reported it susceptible to Gentamicin and SXT respectively. These laboratories were given a grade of 4 for each correctly reported antibiotic. See Table 3A to C for grading.

***Suitability for Grading***

*A challenge is considered suitable for grading if agreement is reached by 80 percent of selected reference group and at least 50 percent of the participants.*

Organism identification, colony count, and susceptibility testing to ampicillin, SXT, and gentamicin 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. No consensus was reached for susceptibility to 1st generation cephalosporins (Table 4.) or nitrofurantoin, thus, these components were not graded.

## COMMENTS ON RESULTS

The performance on this survey, both for colony count and identification was very good with 94% reporting an acceptable colony count and 95% identified the organism as *Klebsiella pneumoniae* ± subspecies *pneumoniae*. One laboratory reported mixed growth with no count and another laboratory reported no growth.

The susceptibility testing results were generally good with 91% reported the isolate resistant to ampicillin, and 92% and 95% reported it susceptible to gentamicin and SXT respectively.

The susceptibility results of first generation cephalosporins were ungraded due to lack of consensus (Table 4). According to CLSI guide-

**Table 3A-C.** Susceptibility results

| 3A - Ampicillin | A lab | B lab | C labs | Total | Grade |
|---|---|---|---|---|---|
| Resistant | 57 | 1 | 2 | 60 | 4 |
| no report (tested R) | 1 | | | 1 | 0 |
| no report | 2 | | | 2 | 0 |
| n/a | 1 | | 1 | 2 | ungraded |
| refer / snnp | 3 | | 2 | 5 | ungraded |
| **Total** | **64** | **1** | **5** | **70** | |
| **3B - Aminoglycosides** | **A lab** | **B lab** | **C labs** | **Total** | **Grade** |
| Gentamicin Susceptible | 55 | 1 | 2 | 58 | 4 |
| Tobramycin Susceptible | 3 | | | 3 | 4 |
| high-level Gentamicin S | 1 | | | 1 | 0 |
| no report | 1 | | | 1 | 0 |
| n/a | 1 | | 1 | 2 | ungraded |
| refer/ snnp | 3 | | 2 | 5 | ungraded |
| **Total** | **64** | **1** | **5** | **70** | |
| **3C - SXT Results** | **A lab** | **B lab** | **C labs** | **Total** | **Grade** |
| Susceptible | 60 | 1 | 2 | 63 | 4 |
| n/a | 1 | | 1 | 2 | ungraded |
| refer, snnp | 3 | | 2 | 5 | ungraded |
| **Total** | **64** | **1** | **5** | **70** | |

**Table 4.** Susceptibility results for 1st generation cephalosporins

| 1st generation Cephalosporins | A lab | B lab | C labs | Grade |
|---|---|---|---|---|
| Cefazolin/Cephalothin/Cephalexin S | 44 | 1 | | ungraded |
| Cephalothin I | 6 | | | |
| Cefazolin/Cephalothin S | | | 2 | |
| Cephalothin I, Cefazolin S | 3 | | | |
| Cephalothin R, Cefazolin S | 3 | | | |
| Cefazolin R | 1 | | | |
| no report / n/a / snnp, refer | 7 | | 3 | |
| **Total** | **64** | **1** | **5** | |

lines,[1] a higher minimum inhibitory concentration (MIC) susceptible breakpoint (≤ 16 µg/mL) is used for cefazolin when treating uncomplicated UTIs due to *E. coli*, *K. pneumoniae* and *P. mirabilis*. The result of cefazolin MIC using this breakpoint is used to predict results for oral agents including cephalexin.

All labs reporting cephalothin should note that cephalothin has been deleted from the CLSI guidelines Table 2A-1 that suggests which oral agents should be considered for routine reporting on uncomplicated UTI due to Enterobacteriaceae. [1]

Although fluoroquinolones (FQ) are not recommended as first –line systemic therapy in children[2], 5 out of 12 processing reference laboratories reported FQ susceptibility, I lab reported a result with a comment*, and 6 reference laboratories did not report FQ susceptibility. 21 participants laboratories reported FQ susceptibility (mainly ciprofloxacin) without a comment, 4 reported a result with a comment*, 1 lab reported a comment* only and 33 participant laboratories did not report FQ susceptibility.

*Comment: *"Ciprofloxacin not reported for children <17 years of age."*

## ISOLATION and IDENTIFICATION

### Sample

The optimal sample for toilet-trained children is a midstream or clean catch sample. Obtaining urine samples from infants and younger children involves urethral catheterization or suprapubic aspiration. Samples should be delivered to the laboratory within 2 hours of collection otherwise they should be stored at 2-8°C for up to 24 hours.[5]

### Pyuria / Bacteriuria

Assessment of pyuria is important as it can aid to the differentiation between contamination, asymptomatic bacteriuria, and infection.

The preferred method of detection is hemocytometer analysis of uncentrifuged urine specimen where pyuria is defined by the presence of >10 white blood cells (WBCs)/$mm^3$. [6] The most common method using centrifuged urine sample has a poor predictive value as the centrifugation parameters are not standardized.[7]

UTIs without pyuria in children are rare except in children with febrile neutropenia.[8,9] It is also believed that Infants less than 2 months of age could have UTI without pyuria, although this might be due to contamination or asymptomatic bacteriuria rather than UTIs. [10]

### Colony count

Interpretation of urine culture results is based on the presence of pyuria, the number of cfus/L (colony count) and the method of specimen collection. The American Academy of Pediatrics (AAP) and the Canadian Paediatric Society (CPS) recommend a threshold of ≥$10^5$ cfu/mL (≥$10^8$ CFU/L) for clean catch/midstream urine samples and ≥5x$10^4$ CFU/mL (≥5x$10^7$ cfu/L) for in and out catheter urine samples in the presence of pyuria.[10,11]

## ANTIMICROBIAL SUSCEPTIBILITY

Empiric therapy of UTI should be based on local antibiogram profiles for uropathogens. Antibiotic agents widely used for empiric therapy in children include amoxicillin-clavulanate, cephalexin, and cefixime. SXT is becoming less acceptable due to higher rates of resistance.

## CLINICAL RELEVANCE

UTI is the most common bacterial infection in childhood. UTIs are more common in boys than girls in the first year of life (3.7% vs. 2%). The incidence changes to 3% for prepubertal girls and 1% for prepubertal boys.[12]

UTIs in previously well children with no antibiotic exposure are usually due to *Escherichia coli, Klebsiella pneumoniae*, *Enterobacter* spp, *Serratia spp or, mainly in adolescent females, Staphylococcus saprophyticus.*

UTI should be ruled out in infants and young children with unexplained fever or in older children with symptoms suggestive of UTI including dysuria, urinary frequency, hematuria, abdominal pain, back pain or new daytime incontinence.[10]

## REFERENCES

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