Pediatric Nephrology (2019) 34:1651–1653
https://doi.org/10.1007/s00467-019-04291-x

EDITORIAL COMMENTARY

Defining urinary tract infection by bacterial colony counts: a case for less than 100,000 colonies/mL as the threshold

Kjell Tullus [1]

Received: 17 May 2019 / Revised: 17 May 2019 / Accepted: 10 June 2019 / Published online: 20 June 2019

Many basic issues on making an accurate diagnosis of a urinary tract infection (UTI) are controversial still today. This might come as a surprise as UTIs are one of the most common bacterial infections in childhood. I will here debate, with Dr. Coulthard, which number of bacteria colony-forming units per milliliter (CFU/mL) is required for a diagnosis of a UTI. My opinion is that a rigid number of $\geq 10^5$ colony-forming units per milliliter (CFU/mL) risks missing 20% of true cases of UTI in small children [1].

History

The concept of defining a UTI by bacterial numbers in the urine and to use a cutoff level was suggested by Dr. Kass more than 60 years ago [2]. He introduced his new definition in a scientific study to be certain that he only included true cases of infection and he was aware that this cutoff did exclude some women with true infections and lower bacterial counts [3].

The level of $\geq 10^5$ CFU/mL was challenged already 30–40 years ago. Stamm noted that these criteria would exclude many women from a correct diagnosis of cystitis with only 51% identified when $\geq 10^5$ CFU/mL was used [4]. He recommended a very low level of $\geq 10^2$ bacteria/mL. Low counts of bacteriuria, $> 10^2$–10^4, were also found by Kunin in 45.8% of women with urinary symptoms [5].

What decides the bacterial numbers found in the laboratory?

The number of bacteria growing on the culture medium in the laboratory depends on many different factors. The incubation time of the bacteria in the urine bladder will define the number of cycles of bacterial replication and thus the number of bacteria in the child's urine. Frequent bladder emptying as in infants or in children with frequency as a cystitis symptom will thus reduce bacterial numbers. The mode of transportation of the bacteria to the laboratory is crucial to obtain a correct culture result. The bacteria can die during transport but also multiply markedly. Cooling is the most commonly used way to preserve the bacteria but different preservatives can be added to the sample.

Different kinds of agar plates are used in the laboratory. The most common are CLED, blood, and McConkey agar. They are promoting the growth of the bacteria commonly causing UTI while other bacteria that are found less often in UTIs might grow slowly or not at all on these media [6]. This is in most cases beneficial as these latter bacteria are less likely to cause a true infection. Unfortunately, when a UTI is truly caused by such an unusual bacteria then the likelihood of a urinary tract malformation is much higher and these infections are thus very important to diagnose [7].

A very drastic example showing the importance of transport and laboratory practices was recently seen in the DUTY study of 7163 children in general practice in the UK. These children had their urines sent simultaneously to two different laboratories: one NHS laboratory and one research laboratory. Two- to three-fold differences in the number of positive cultures were found between the two different laboratories [8].

What does research show us?

In a recent study, 430 infants were diagnosed with a symptomatic UTI with supra-pubic aspiration (SPA). In 83 (19%) of the infants, the bacterial cultures showed fewer than 10^5 CFU/mL [9]. In a further seven studies on 1587 children, mainly infants, 290 (18%) would have been misdiagnosed as not having a UTI if the conventional cutoff level had been

✉ Kjell Tullus
Kjell.Tullus@gosh.nhs.uk

[1] Great Ormond St Hospital London, London, UK

used. The false negative rate of the clean catch or bag culture in these studies ranged between 7 and 29% [10–16].

Dr. Coulthard claims that only studies where two parallel cultures were done can give us knowledge on this topic. This might be an optimal approach but would ignore the above eight very important studies.

What do modern guidelines recommend?

Most modern guidelines do not discuss this problem in any great detail. Different cutoff levels are however often recommended for samples collected with SPA, catheterized samples and urine collected outside of the child with a bag, urine pad, or a clean-catch sample. Non-invasive cultures typically are regarded as positive if they grow $\geq 10^5$ CFU/mL while the growth of any bacteria is regarded as significant if collected with a SPA. Recommendations for catheterized samples vary between 10^3 and 10^4 CFU/mL [17, 18]. Some guidance like that of the American Academy of Pediatrics recommends lower cutoff, 5×10^4 CFU/mL, for all cultures [19].

Does the cutoff level really matter?

Any test done in medicine will have false positive and false negative results. A cutoff limit of $\geq 10^5$ CFU/mL will have a low number of false positive cases; not too many children will be wrongly treated and investigated for a UTI [20]. But as many as 20% of children with a true UTI will show a false negative result and not in time get the treatment that they need and thus increasing their risks of developing post-infectious renal scarring.

Scientific studies will also become biased if the definition of true infection is incorrect. Many studies on DMSA uptake defects and blood inflammatory markers in small children show unexpected findings that partly can be explained by these problems.

Unfortunately, the opposite will become true if we lower the cutoff level for significant growth. Many more children will be falsely diagnosed with a UTI. This will lead to unnecessary treatment and investigations.

My recommendations

Dr. Coulthard shows interesting data but they are not enough for me to discard the evidence that I have presented above. It does, to me, however not make biological sense to base a medical diagnosis on a single cutoff level. Such strict levels do not exist anywhere else in medicine. I would still want to keep the present cutoff as the general recommendation for making the UTI diagnosis. It is very well established and helpful in most cases.

We doctors do however always need to be good clinicians. This means to use all important information, both clinical findings and results from urine and blood tests to make the best possible diagnosis. This will include symptoms and signs of any other infection, knowledge of the previous history, inflammatory markers, like CRP and procalcitonin, and urine findings of leucocytes and a positive nitrite test [21]. A low bacterial count will not stop me from making a diagnosis of UTI if the other findings are in favor of that diagnosis.

References

1. Tullus K (2016) Low urinary bacterial counts: do they count? Pediatr Nephrol 31:171–174
2. Kass EH (1957) Bacteriuria and the diagnosis of infections of the urinary tract; with observations on the use of methionine as a urinary antiseptic. AMA Arch Intern Med 100:709–714
3. Kass EH (1962) Pyelonephritis and bacteriuria. A major problem in preventive medicine. Ann Intern Med 56:46–53
4. Stamm WE, Counts GW, Running KR, Fihn S, Turck M, Holmes KK (1982) Diagnosis of coliform infection in acutely dysuric women. N Engl J Med 307:463–468
5. Kunin CM, White LV, Hua TH (1993) A reassessment of the importance of "low-count" bacteriuria in young women with acute urinary symptoms. Ann Intern Med 119:454–460
6. Hansson S, Svedhem A, Wennerstrom M, Jodal U (2007) Urinary tract infection caused by Haemophilus influenzae and Haemophilus parainfluenzae in children. Pediatr Nephrol 22:1321–1325
7. Tullus K (2019) Fifteen-minute consultation: why and how do children get urinary tract infections? Arch Dis Child Educ Pract Ed
8. Hay AD, Birnie K, Busby J et al (2016) The diagnosis of urinary tract infection in young children (DUTY): a diagnostic prospective observational study to derive and validate a clinical algorithm for the diagnosis of urinary tract infection in children presenting to primary care with an acute illness. Health Technol Assess 20:1–294
9. Swerkersson S, Jodal U, Ahren C, Hansson S (2014) Urinary tract infection in small outpatient children: the influence of age and gender on resistance to oral antimicrobials. Eur J Pediatr 173:1075–1081
10. Aronson AS, Gustafson B, Svenningsen NW (1973) Combined suprapubic aspiration and clean-voided urine examination in infants and children. Acta Paediatr Scand 62:396–400
11. Etoubleau C, Reveret M, Brouet D et al (2009) Moving from bag to catheter for urine collection in non-toilet-trained children suspected of having urinary tract infection: a paired comparison of urine cultures. J Pediatr 154:803–806
12. Hansson S, Brandstrom P, Jodal U, Larsson P (1998) Low bacterial counts in infants with urinary tract infection. J Pediatr 132:180–182
13. Hoberman A, Wald ER, Reynolds EA, Penchansky L, Charron M (1994) Pyuria and bacteriuria in urine specimens obtained by catheter from young children with fever. J Pediatr 124:513–519
14. Kanellopoulos TA, Vassilakos PJ, Kantzis M, Ellina A, Kolonitsiou F, Papanastasiou DA (2005) Low bacterial count urinary tract infections in infants and young children. Eur J Pediatr 164:355–361
15. Koskimies O (1995) Diagnostic accuracy of urinary tract infection and subsequent development of renal scars. J Pediatr 126:157–159

16. Ramage IJ, Chapman JP, Hollman AS, Elabassi M, McColl JH, Beattie TJ (1999) Accuracy of clean-catch urine collection in infancy. J Pediatr 135:765–767
17. Ammenti A, Cataldi L, Chimenz R et al (2012) Febrile urinary tract infections in young children: recommendations for the diagnosis, treatment and follow-up. Acta Paediatr 101:451–457
18. Mori R, Lakhanpaul M, Verrier-Jones K (2007) Diagnosis and management of urinary tract infection in children: summary of NICE guidance. BMJ 335:395–397
19. Roberts KB (2011) 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 128:595–610
20. Tullus K (2011) Difficulties in diagnosing urinary tract infections in small children. Pediatr Nephrol 26:1923–1926
21. Montini G, Tullus K, Hewitt I (2011) Febrile urinary tract infections in children. N Engl J Med 365:239–250