

Fever, Significant Pyuria and A Positive Urine Culture not Always A Urine Infection (UTI)

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ABSTRACT

One of the challenges in children is to appropriately diagnose a urinary tract infection (UTI). The definition of a UTI has been based on the presence of significant pyuria and a positive urine culture in a febrile child. 5 children presented having fever without focus and had urine tests done. They all showed significant pyuria. They did not receive antibiotics but had urine cultures sent. The urine cultures showed a significant growth in all children but the fever had subsided before the culture report was available. These children did not receive antibiotics and have remained well thereafter with no further problems in the next 6 months. We suggest that the clinical appearance of the child should dictate whether antibiotics are started when there is significant pyuria in a child having fever without focus. Mere presence of fever, significant pyuria and a positive urine culture does not always indicate a UTI.

Keywords: Urinary tract infection; Pyuria; Hypercalciuria

1. Introduction

Urinary tract infection (UTI) is one of the common problems seen in children. It is believed that 1% of children would have had a UTI by 8 years of age¹. The diagnosis of UTI is based on urine tests. Presence of significant pyuria and a significant growth on urine culture is considered diagnostic of a UTI. However it may not be that simple. Progression of symptoms added to the difficulties in obtaining and interpreting urine tests may suggest that the diagnostic criteria need to be qualified further. We present 5 cases below to make our case.

Case 1: A 6 month old boy presented with fever present for more than 2 days. He had been an otherwise healthy child with no previous problems. Though the fever was 38 degrees centigrade, in between fever he was a happy child. On examination, there was no focus identified for the fever. He had a urine microscopy done that revealed 10-15 pus cells/hpf (per high power field). A urine culture was sent. He was treated with paracetamol for fever but no antibiotics were given. The fever disappeared in the next 48 hours. The urine culture revealed a growth of 100000

organisms/ml of *Proteus mirabilis*. He did not receive antibiotics and has remained well over the next 6 months.

Case 2: A 5 month old boy presented with fever present for more than 2 days. He had otherwise been a healthy child with no previous problems. He had fever greater than 38 degrees Centigrade but remained well and happy between the episodes of fever. On examination, there was no focus identified for the fever. Urine microscopy revealed 25-30 pus cells/hpf. A urine culture was sent but he did not receive antibiotics as the fever seemed to be subsiding. The fever disappeared over the next 24 hours but the urine culture showed a growth of 100000 organisms/ml of *Klebsiella*. He did not receive antibiotics and remains well over the next 6 months.

Case 3: A 1 year old girl was seen for recurrent fever over the last 4 to 5 days. The fever was less than 38 degrees centigrade. She remained well between the episodes of fever. Examination revealed no focus. Urine microscopy revealed 15-20 pus cells/hpf. Urine culture was sent but no antibiotics were started. The fever settled in the next 48 hours but the urine culture revealed

100000 organisms/ml of E.coli. She did not receive antibiotics and has remained well over the next 6 months.

Case 4: A 6 year old girl presented with fever for 3 days that would reach 38 degrees centigrade. There were no urinary symptoms and examination revealed no focus for the fever. She used to remain well between episodes of fever. Urine microscopy showed 15-20 pus cells/hpf. She was prescribed antibiotics by her doctor but did not take them! A urine culture was sent. The fever settled in the next 24 hours. The urine culture revealed 100000 organisms/ml of E.coli. She did not receive antibiotics and remains well over that last 1 year.

Case 5: A 15 month old girl presented with fever for 3 days. The fever would reach 38 degrees centigrade. Between episodes of fever she remained well and playful. Urine microscopy revealed 6-8 pus cells/hpf. She did not receive antibiotics and her fever settled in the next 24 hours. Urine culture showed a growth of E coli 100000 organisms/ml and was reported as ESBL (extended spectrum beta lactamase) resistant variety. She did not receive antibiotics and has remained well over the next 6 months.

2. Discussion

Urine infections in children are common¹, and the greatest challenge remains about the diagnosis. The diagnosis of UTI is based on urine tests. Urine microscopy and culture are the 2 tests commonly relied upon to make a diagnosis of UTI. If both are 'positive', UTI is diagnosed. However that may be fallacious.

On urine microscopy, the number of leucocytes or pus cells is counted. Presence of more than 10 pus cells/cmm in an uncentrifuged sample or more than 5 pus cells /hpf in a centrifuged urine sample is considered significant pyuria. That is considered to make a UTI more likely. However, it is well known that significant pyuria may occur in many other conditions and not only UTI. Fever itself can cause significant pyuria as can inflammatory process anywhere else in the body like in other organ infections, any form of nephritis, presence of urinary calculi or hypercalciuria. Thus relying only on significant pyuria may not be right. The converse that absence of significant pyuria is a fairly good indicator of absence of UTI is increasingly found to be true and hence guidelines now suggest that there should be accompanying significant pyuria to make a diagnosis of UTI².

The recommendation is to start antibiotics in the presence of significant pyuria and fever without focus without waiting for the urine culture reports. As can be seen in the above cases, if antibiotics had been started, the disappearance of fever would have been ascribed to the action of antibiotics. That was clearly not the case. The fever disappeared without antibiotics in all the above children. What then about the 'positive' urine culture?

Urine is collected by different methods in children. The presence of a growth of 100000 organisms/ml of a single species is considered significant growth if the urine is collected as a mid-stream or clean catch sample. All these children had urine samples sent as a clean catch or mid-stream urine sample. Obviously, collection by a urinary catheter or suprapubic aspirate has a lower count that is considered as significant growth. (10,000 organisms/ml for a catheter sample and any growth for suprapubic aspirate).

Contamination of the urine sample is a major problem when collecting urine in children as a clean catch sample. In a study involving 50 children (25 boys and 25 girls) aged 12 days to 24 months, referred with a suspicion of UTI, urine was collected

by a mid-stream sample in 32 children (64%) and in a plastic bag in 18 children (36%). Hospital verifications of urine cultures were performed by suprapubic puncture culture in 24 children (48%) or by catheterisation of the urinary bladder in 26 (52%) children. UTI was confirmed in only 11 children of the 32 who had a positive urine culture by midstream urine sample. Of all the 18 bag urine culture positive results, none had an actual UTI on confirmation³! In fact, in a retrospective study that looked at records of 335 patients (137 with bacteriuria and 198 with negative urine cultures), only 34 patients (25% of patients with a positive urine culture) met the criteria for a symptomatic urine infection, 67 (49%) had asymptomatic bacteriuria and 36 patients (26%) had infection at a non-urinary site⁴! The risk of having a contaminated urine sample leading to a significant growth on urine culture remains high in any child.

At the same time, human microbiome studies are suggesting that normal bladders are not always sterile and asymptomatic bacteriuria is fairly common^{5,6}. In a study comparing the diagnosis of UTI in confirmed RSV-positive (Respiratory Syncytial Virus) infections based on urine culture, the rate dropped from 6.1 to 1.1 % by just using the new criteria for diagnosis of UTI, the conclusion being made that previously described risk of UTIs in these patients may represent asymptomatic bacteriuria or contaminated samples⁷! The guidelines for UTI also mention that the prevalence of asymptomatic bacteriuria in infants is 0.7% and 3 urine cultures from asymptomatic children showed the growth of similar organisms². Thus a positive urine culture would not be unusual in a child that does not have UTI. Diagnosing a UTI merely because of a positive urine culture would therefore lead to many children getting diagnosed with UTI when they don't have one.

How does one proceed then? We need to look at the clinical criteria that are used for sending a urine sample to diagnose UTI. The 2 major indications for sending a urine sample include fever without focus and the presence of urinary symptoms like dysuria, urgency etc. In the presence of urinary symptoms, irrespective of the presence or absence of fever, urine samples should be sent as long as UTI mimics like vulval redness or Detrusor instability have been ruled out (8). The problem arises in children having fever without focus. The proportion of children having UTIs who present as fever without focus has been gradually reducing as the criteria of diagnosing UTI have become more robust. Thus mere positivity of urine culture that was considered as UTI is no longer done so. In children aged 2 to 24 months, the percentage of children having UTI presenting as fever without focus has varied in different studies. In a study of 98 children between 5 to 31 months of age presenting with fever without focus, UTI was diagnosed in 9 out of 98 children (9%)⁹. In an old study, the rate of UTIs in 193 febrile infants was 4.1%. (10) Another study stated that amongst infants presenting with fever without focus, UTIs were confirmed in 3.5 to 5.5% infants. (11) It is now generally believed that about 5 to 7% of such children presenting with fever without focus are likely to have UTIs. So a majority of children presenting with fever without focus do not have UTIs and most of them have viral infections¹².

Even the revised guidelines for UTI by the American academy of Pediatrics for febrile children between 2 to 24 months of age has several important recommendations. The differentiation between a well child and a sick child determines the urine test. If the child looks sick, antibiotics are to be started but a urine sample has to be collected before starting antibiotics. However, if the child looks well, it is considered reasonable

to follow up the child till the fever disappears or a urine test becomes necessary. They also suggest looking at criteria for considering the risk of UTI to be high in the well child having fever without focus. Thus a urine sample is suggested to be sent later if the fever continues. The risk of UTI in children with fever without focus is presumed to be around 5% and in the low-risk group, probably much lower². Selecting the children who have fever without focus who may be at risk seems to be the logical solution. A predictive model¹³, looked at younger age (less than 1 year), high fever (more than 39 degrees centigrade), fever more than 2 days, white race etc and suggested that a urine test should be done only if 2 of the criteria were positive.

There is a case therefore to clinically decide when should a urine sample be sent and how to interpret it. A recent paper⁸, algorithm suggests the way forward. If the child presents with fever and urinary symptoms, the present practice of sending a urine sample and starting antibiotics (after giving the urine culture sample) in the presence of significant pyuria should continue.

However if the child presents only with fever without focus, one should clinically assess whether the child looks sick or looks well (playful between episodes of fever, sometimes during fever, no vomiting, not looking toxic). If the child looks sick, follow the same plan as for those with urinary symptoms. If the child looks well, then one should withhold antibiotics even when there is significant pyuria and the child should have watchful observation. If the fever disappears, one should not diagnose a UTI even if the urine culture is positive. The child should be observed carefully and started on antibiotics if there is recurrence of fever in the next few days.

However if the fever persists and the urine culture is positive, one should treat as a UTI. If the urine culture is negative but the fever persists, one should reassess the child to see if any other focus has developed. At any stage if the clinician feels the child is unwell, antibiotics should be started.

One of the worries that has made clinicians fearful is that delayed treatment could cause damage to the kidneys. A study whether early treatment of urinary tract infection prevented scarring looked at 278 infants (0.5 to 12 months of age) who presented with the first UTI and though the median time to start treatment was 2 days they looked at 2 groups. In the first group, treatment was started within 24 hours of onset of fever and the second group comprised children where the treatment was started 4 days or later from onset of fever. The conclusion drawn was that frequency of scarring in infants treated early or late did not differ and it appeared to be independent of that factor¹⁴. In another earlier paper, the authors were of the opinion that urinary tract infections per se do not cause end stage kidney disease¹⁵.

In 4 of the cases above, as the children looked well despite having fever without focus and significant criteria, antibiotics were withheld. In the other case, the parents did not give antibiotics even when prescribed! In all children fever settled down and they have remained well with no further problems. Thus the algorithm given below from a recent paper works really well. We need to be careful about the use of antibiotics with increasing antibiotic resistance that is being noted. It is time to further qualify the criteria for UTI based on the algorithm given below⁸.

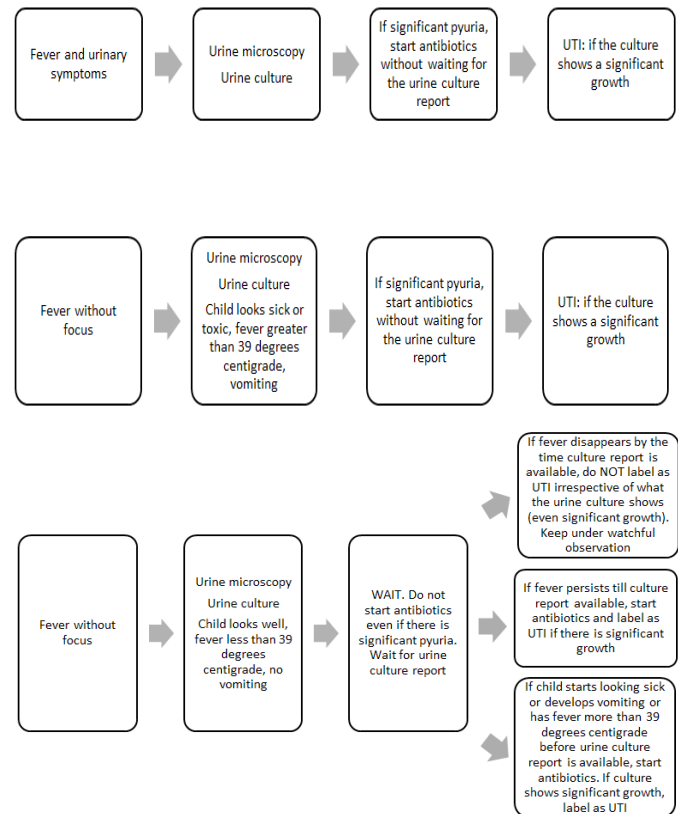


Figure 1: In a child with suspected UTI, if urine sample is sent early.

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