Rapid tests and urine sampling techniques for the diagnosis of urinary tract infection (UTI) in children under five years: a systematic review

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CRD summary
This review concluded that for the diagnosis of urinary tract infection (UTI), dipstick negative for both leucocyte esterase and nitrite or negative microscopic analysis for pyuria of a clean voided urine, bag or nappy/pad specimen may be used to rule out UTI, and that combinations of positive tests could similarly be used to rule in UTI. These conclusions are likely to be reliable.

Authors' objectives
To determine the accuracy of rapid tests for detecting urinary tract infection (UTI) in children under 5 years of age.

Searching
The authors searched 16 databases (including MEDLINE and EMBASE) from inception to between October 2002 and February 2003 without any language restrictions. The searches were updated in May 2004. In addition, 12 key journals were handsearched, reference lists were screened for additional references, and experts in the field were contacted for further published or unpublished material. Full details of the search were reported elsewhere (see Other Publications of Related Interest).

Study selection
Study designs of evaluations included in the review
Diagnostic cohort studies were eligible for inclusion.

Specific interventions included in the review
Studies evaluating microscopy or dipstick tests for the diagnosis of UTI, or evaluations of different urine sampling methods, were included in the review. Specific dipsticks tested for nitrite, leucocyte esterase (LE), glucose, protein, blood, or combinations of these.

Reference standard test against which the new test was compared
Studies were included if they used the reference standard of culture or culture combined with other tests. The included studies varied in terms of their definition of a positive test result.

Participants included in the review
Studies were selected if they included at least some children aged under 5 years with suspected UTI.

Outcomes assessed in the review
Studies were included if they provided sufficient information to construct a 2x2 table to calculate diagnostic accuracy estimates.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected titles and abstracts, with any disagreements resolved by consensus. One reviewer selected full papers for inclusion and a second reviewer checked their decisions.

Assessment of study quality
The included studies were assessed using the 14-item QUADAS (Quality Assessment of Diagnostic Accuracy Studies) checklist.
Data extraction
One reviewer extracted the data and a second reviewer checked the extraction. Key study details, including spectrum composition and 2x2 data, were extracted.

Methods of synthesis
How were the studies combined?
The sensitivity, specificity, positive and negative likelihood ratios (LR+ and LR-, respectively), and diagnostic odds ratios were calculated from 2x2 data for each test or test combination. Further analysis focused on combined LR+ and LR-, pooled using a random-effects model. Where multiple estimates of test performance were presented for the same test, the estimate most clinically similar to other studies was included in the meta-analysis.

How were differences between studies investigated?
Heterogeneity of the LRs was assessed using the Q statistic and by visual examination of forest plots. Sensitivity and 1 minus specificity were plotted in receiver operating characteristic space. Where there were sufficient data, heterogeneity was further investigated using regression analysis.

Results of the review
A total of 70 studies (the number of participants was unclear) were included in the review.

The included studies met a median of 8 of the 14 QUADAS validity items (range: 5 to 13).

Urine sampling (13 studies, 17 datasets).

For clean voided urine versus supra-pubic aspiration (5 studies), the pooled LR+ was 8.8 (95% confidence interval, CI: 2.6, 29.6) and the pooled LR- was 0.23 (95% CI: 0.18, 0.30). The pooled LR+ value was statistically heterogeneous (p<0.0001). There was insufficient data to establish the value of using urine samples from bags or pads/nappies.

Dipstick tests (39 studies, 107 datasets).

Studies of glucose dipstick testing showed generally high sensitivity and specificity. However, the CIs around pooled LRs were very large, indicating considerable uncertainty in these estimates.

Nitrite alone may be of use for ruling in, but not ruling out, disease: the pooled LR+ was 15.9 (95% CI: 10.7, 23.7) and the pooled LR- was 0.51 (95% CI: 0.43, 0.60).

LE alone appeared to be relatively poor for both ruling in and ruling out disease: the pooled LR+ was 5.5 (95% CI: 4.1, 7.3) and the pooled LR- was 0.26 (95% CI: 0.18, 0.36).

Combined nitrite and LE tests had the best LR-: the pooled LR+ was 28.2 (95% CI: 17.3, 46.0) and the pooled LR- was 0.20 (95% CI: 0.16, 0.26).

Data were insufficient to estimate the accuracy of dipstick tests for protein, blood, or combinations of three different tests.

Microscopy (39 studies, 101 datasets).

For pyuria alone, the pooled LR+ was 5.9 (95% CI: 4.1, 8.5) and the pooled LR- was 0.27 (95% CI: 0.20, 0.37).

Bacteriuria alone was considerably more useful than pyuria for ruling in and ruling out disease: the pooled LR+ was 14.7 (95% CI: 8.6, 24.9) and the pooled LR- was 0.19 (95% CI: 0.14, 0.24).

Pyuria or bacteriuria gave the lowest LR-: the pooled LR+ was 4.2 (95% CI: 2.3, 7.6) and the pooled LR- was 0.11 (95% CI: 0.05, 0.23).
Pyuria and bacteriuria gave the highest LR+: the pooled LR+ was 37.0 (95% CI: 11.0, 125.9) and the pooled LR- was 0.21 (95% CI: 0.13, 0.36).

**Authors' conclusions**
Dipstick negative for both LE and nitrite or negative microscopic analysis for pyuria of a clean voided urine, bag or nappy/pad specimen may be used to rule out UTI and exclude patients from further investigation. Combinations of positive tests could similarly be used to rule in UTI.

**CRD commentary**
This was a well-conducted review that answered a well-defined question, searched multiple sources to identify all the relevant evidence, and used appropriate methods to synthesise the included studies and investigate heterogeneity. Validity was assessed using an appropriate published set of criteria, and multiple reviewers were used at each stage of the review in order to minimise the potential for errors and bias. Consequently, the authors' conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that dipstick negative for both LE and nitrite or negative microscopic analysis for pyuria of a clean voided urine, bag, or nappy/pad specimen may be used to rule out UTI and exclude patients from further investigation, and that combinations of positive tests could similarly be used to rule in UTI and trigger further investigation.

Research: The authors recommended further research in specific areas of diagnosis of UTI. These were: urine sampling methods in younger children; accuracy and applicability of the glucose dipstick test; handling indeterminate nitrite and LE dipstick results; and accuracy of combined microscopy and dipstick testing.

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