Patients with recurrent EM sometimes recall being bitten by a tick at the site of recurrence, and regardless of whether a tick bite is recalled, residual anatomic evidence of the prior bite (the punctum) may be present [5–8]. Puncta are well described in patients with primary EM skin lesions [5–8] and have also been reported following the bites from a variety of other arthropods [9–12]. In one study, either re-collection of a tick bite at the EM site or the presence of a punctum in the EM lesion was documented in nearly 70% of a small group of patients with a primary EM [5]. It is extremely unlikely that a punctum would remain present in a putative relapse [2, 4]. The probability to be <.001.

A preliminary report of a molecular analysis of 6 patients with recurrent EM whose cultures were positive for Borrelia burgdorferi during both episodes showed that each episode was associated with a different strain of B. burgdorferi [13]. These data overwhelmingly argue for re-infection over relapse as the cause of the recurrent EM in these particular cases. Surprisingly, Stricker et al. [1] posit that, in all 6 cases, the original infection was caused by 2 different strains of B. burgdorferi, one of which responded to antibiotic therapy and the other of which was resistant. This singular interpretation was made despite the absence of published data demonstrating resistance of B. burgdorferi to the antimicrobial agents recommended to treat Lyme disease [14]. Indeed, patients with second and subsequent episodes of EM appear to respond very well to antimicrobial treatment [2] (R. Nadelman, unpublished observation; P. Krause, personal communication).

It is true that skin samples of EM lesions taken before the start of antimicrobial treatment may show PCR evidence of a second strain of B. burgdorferi in 12.5% [15] to 43.1% [16] of cases. However, amplification of a fragment of DNA does not necessarily indicate the existence of a viable organism. Less than 6% of cultures of EM demonstrate mixed infections [16]. However, even if these PCR results indicated true coinfections, it would be extremely improbable in all 6 of the evaluated cases that coinfections were present during the first episode of EM and that, in the second episode, the originally isolated strain of B. burgdorferi would fail to grow in culture (we calculate the probability to be <.001 for rates of coinfection of either 12.5% or 43.1%).

Acknowledgments

We thank Dr. Paul Visintainer, for assistance in calculating the probabilities, and Dr. Peter Krause, for sharing unpublished data.

Financial support. Dr. Wormser is supported in part by National Institute of Allergy and Infectious Diseases (RO3 AI 008275–101). Potential conflicts of interest. G.P.W. received a research grant from ImmuneKits and expects to receive a research grant from BioRad. R.B.N.: no conflicts.

Robert B. Nadelman and Gary P. Wormser
Department of Medicine, Division of Infectious Diseases, New York Medical College, Valhalla, New York.

References

1. Stricker RB, Corson AF, Johnson L. Reinfec-
2. Krause PJ, Foley DT, Burke GS, Christianson D, Closter L, Spidelman A. Tick-Borne Disease Study Group. Reinfec-
8. Malane MS, Grant-Kels JM, Feder HM Jr, Lug-
14. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and pre-
15. Seinost G, Golde WT, Berger BW, et al. In-
fection with multiple strains of Borrelia burg-

Reprints or correspondence: Dr. Robert B. Nadelman, New York Medical College, Dept. of Medicine, Div. of Infectious Diseases, Munger 245, Valhalla, NY 10595 (robert_nadelman@nymc.edu).

Clinical Infectious Diseases 2008; 46:950–1 © 2008 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2008/4606-0030$15.00 DOI: 10.1086/588872

Performance of the Urine Leukocyte Esterase and Nitrite Dipstick Test for the Diagnosis of Acute Prostatitis

To the Author—We read with great in-
terest the report by Koeijers et al. [1] evaluating the urine dipstick test in febrile male outpatients with urinary tract infection (UTI), and were surprised that the results were the opposite of those usually observed in female patients with uncomplicated cystitis.

We used the same approach in a nested study that included 136 inpatients with community-acquired acute prostatitis and systemic symptoms (fever in 86% of patients, painful prostate noted by digital rectal examination in 68%, a positive blood culture result in 20%) from a retrospective, multicenter study [2]. The bacterial titers in the 136 urine analyses were as follows: \( \geq 10^2 \) cfu/mL for 56 patients (41%), \( 10^3 \) cfu/mL for 15 patients (11%), \( 10^4 \) cfu/mL for 8 patients (6%), and \( 10^5 \) cfu/mL for 57 patients (42%). Of these 57 patients, 24 had received antibiotic treatment before analysis, and 50 had leukocyte counts of \( \geq 10^5 \) cells/mm\(^3\). Eighty-one percent of the isolated bacteria were nitrite-producing Enterobacteriaceae.

The performance findings for the dipstick urinary test are presented in table 1, as organized according to the bacteria load cutoff considered for the diagnosis of UTI in male subjects (either \( 10^3 \) or \( 10^4 \) cfu/mL). The best positive predictive values (94%–98%) were attained when both nitrites and leukocytes were detected, and the highest negative predictive values (65%–73%) were attained when either leukocytes or nitrites alone were detected.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte detection</td>
<td>81</td>
<td>71</td>
<td>89</td>
<td>57</td>
</tr>
<tr>
<td>Nitrite detection</td>
<td>55</td>
<td>94</td>
<td>97</td>
<td>42</td>
</tr>
<tr>
<td>Leukocyte and nitrite detection</td>
<td>50</td>
<td>97</td>
<td>98</td>
<td>40</td>
</tr>
<tr>
<td>Leukocyte or nitrite detection</td>
<td>87</td>
<td>69</td>
<td>89</td>
<td>65</td>
</tr>
</tbody>
</table>

Table 1. Performance of the urine dipstick detection of nitrites and leukocytes for the diagnosis of acute prostatitis.

We found that the dipstick urinary test had a high positive predictive value and a low negative predictive value for the diagnosis of acute febrile prostatitis, as Koeijers et al. [1] found for nonfebrile male patients with UTI. These performances were exactly the opposite of those usually observed for uncomplicated acute cystitis in women (i.e., high negative and low positive predictive values), for which recommendations usually agree that the test should be used to exclude infection [3, 4]. We agree with the conclusions of Koeijers and colleagues that, for symptomatic male patients, a positive nitrite test result should be considered indicative of a UTI and that a negative nitrite test result should not exclude the diagnosis of UTI, so that a midstream urine sample should be cultured. It is clear from the data from the study by Koeijers et al. [1] and from the data presented here that, for these patients, the sensitivity (55%–58%) and negative predictive value (42%–49%) are too low for the nitrite test result alone to be used to exclude the diagnosis of UTI in male subjects. Thus, unlike the diagnosis of uncomplicated acute cystitis in women, the dipstick test for the rapid detection of leukocytes and nitrites should be used to diagnose acute prostatitis and UTI in nonfebrile male subjects and not to exclude them.

However, Koeijers et al. [1] concluded that treatment should not be started when the nitrite test result is negative, pending the results of the urine culture. We think that this conclusion has to be balanced. Indeed, most of the male patients with UTI, like those described in our series, are febrile and require urgent antibiotic treatment because of a high risk of urosepsis and because of a poor tolerance of symptoms [3, 7]. In these cases, we would recommend starting antibiotic treatment after collection of the midstream urine sample, even when the dipstick test result comes back negative for nitrites. The urine dipstick test should be routinely performed for the management of UTI in male subjects, with awareness of its high positive and low negative predictive values.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Manuel Etienne, Martine Pestel-Caron, Pascal Chavanet, and François Caron

Departments of Infectious and Tropical Diseases and Bacteriology, Groupe de Recherche sur les Anti-microbiens, Rouen University Hospital, Rouen, and Department of Infectious and Tropical Diseases Department, Laboratoire des Maladies Infectieuses, Dijon University Hospital, Dijon, France

References


<table>
<thead>
<tr>
<th>Finding</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte detection</td>
<td>83</td>
<td>67</td>
<td>85</td>
<td>64</td>
</tr>
<tr>
<td>Nitrite detection</td>
<td>58</td>
<td>90</td>
<td>93</td>
<td>49</td>
</tr>
<tr>
<td>Leukocyte and nitrite detection</td>
<td>52</td>
<td>93</td>
<td>94</td>
<td>46</td>
</tr>
<tr>
<td>Leukocyte or nitrite detection</td>
<td>89</td>
<td>64</td>
<td>85</td>
<td>73</td>
</tr>
</tbody>
</table>

NOTE. NPV, negative predictive value; PPV, positive predictive value.
Reply to Etienne et al.

To the Editor—We read with great interest the letter by Etienne et al. [1], in which they describe the performance of the leukocyte and nitrite dipstick test in a male population presenting with acute prostatitis. It is reassuring that this study confirms the sensitivity and specificity that were obtained in our male population with acute, nonfebrile urinary tract infection (UTI) [2]. In the female outpatient population, the nitrite test also has a specificity of ~95% and a sensitivity of ~55%, resulting in a positive predictive value of 96% and a low negative predictive value [3, 4]. This result suggests that the dipstick test should be used in both female and male populations to diagnose UTI and not to exclude it. However, the positive predictive value of the nitrite dipstick test has varied in different studies with different populations tested. The same results have been reported for the leukocyte esterase activity test, in which there is an wide range of positive and negative predictive values [5].

The finding of a high positive predictive value when both the nitrite and leukocyte esterase activity tests were performed in a male population with symptoms of acute community-acquired prostatitis is interesting. In our population of male patients with nonfebrile UTI and female patients with an uncomplicated UTI [3], the leukocyte esterase activity did not have additional value in the diagnosis of UTI [3, 4]. It is possible that prostatitis results in a higher degree of pyuria and, thus, in more positive leukocyte esterase activity.

In our article, we recommended that nonfebrile male patients with symptoms indicative of UTI and a positive nitrite dipstick result should start empirical antibiotic therapy, pending the results of urine cultures. However, patients with a negative nitrite dipstick test result should refrain from antibiotic therapy, pending the urine culture data. However, we agree with Etienne et al. [1] that, in male and female patients with complicated UTIs, the negative predictive value of the dipstick test is not enough to warrant withholding antibiotic therapy in the event of a negative dipstick test result. The difference between their population (with symptoms indicative of acute prostatitis, high fever, and, in 20% of patients, a positive blood culture result) and our population (with symptoms of uncomplicated UTI) is immense. Although it has been stated that all UTIs in male patients are considered to be complicated, it is not clear (for either male or female populations) which percentage of uncomplicated UTIs become complicated. Both studies [1, 2] show a clear role for the urine dipstick test in the management of UTI in male patients, although the presentation of symptoms clearly leads to a different approach in the timing of start of antibiotic therapy.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

References


Reprints or correspondence: Dr. Annelies Verbon, Dept. of Medical Microbiology and Dept. of Internal Medicine, Div. of General Internal Medicine, Section of Infectious Diseases, Academic Hospital, Maastricht, The Netherlands (jverb @lmib.azm.nl).

Clinical Infectious Diseases 2008; 46:953 © 2008 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2008/4606-0032$15.00 DOI: 10.1086/528874

Buprenorphine Diversion: A Possible Reason for Increased Incidence of Infective Endocarditis among Injection Drug Users? The Singapore Experience

To the Editor—We read with interest the article by Cooper et al. [1] regarding the increased number of hospitalizations for illicit injection drug use–related infective endocarditis in the United States from 2000 through 2003. Since 2002, we have noted an increasing incidence of Staphylococcus aureus bacteremia (including endovascular infection) among persons who inject buprenorphine (Subutex; Schering-Plough) in Singapore. At the National...