crobial treatment of the original infection—too long a time interval to reasonably anticipate a relapse [2, 3]. In addition, 29 (90.6%) of 32 recurrences occurred during June–August—exactly the months in which reinfection would naturally occur [2, 4]. The P value for such seasonality occurring by chance alone is <.001.

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 recollection 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 of EM occurring after months to years. Thus, when present, a punctum in a recurrent EM lesion provides strong clinical evidence of reinfection.

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 reinfection 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with second and subsequent episodes of EM appear to respond very well to antimicrobial treatment [2] (R. Nadelman, unpublished observation; P. Krause, personal communication).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

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tion versus relapse in patients with Lyme dis
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tion with multiple strains of *Borrelia burgdorferi* sensu stricto in patients with Lyme dis

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 afebrile 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 results in 20%) from a retrospective, multicenter study [2]. The bacterial titers in the 136 urine analyses were as follows: \( \geq 10^3 \) cfu/mL for 56 patients (41%), \( 10^3 \)–\( 10^4 \) cfu/mL for 15 patients (11%), \( 10^4 \) cfu/mL for 8 patients (6%), and \( < 10^2 \) cfu/mL for 57 patients (42%). Of these 57 patients, 24 had received antibiotic treatment before analysis, and 50 had leukocyte counts of \( > 10^5 \) 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.

Two cutoff diagnostic bacteria loads (\( 10^3 \) and \( 10^4 \) cfu/mL) were tested, because this value remains controversial in the literature [5, 6]. We noticed minor variations in the performances of the dipstick urine test between the 2 cutoff values, likely because our patients had high bacteria loads.

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.

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### References


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

<table>
<thead>
<tr>
<th>Finding</th>
<th>Bacteria load, ( \geq 10^3 ) cfu/mL</th>
<th>Bacteria load, ( \geq 10^4 ) cfu/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity, %</td>
<td>Specificity, %</td>
</tr>
<tr>
<td>Leukocyte detection</td>
<td>81</td>
<td>71</td>
</tr>
<tr>
<td>Nitrite detection</td>
<td>55</td>
<td>94</td>
</tr>
<tr>
<td>Leukocyte and nitrite detection</td>
<td>50</td>
<td>97</td>
</tr>
<tr>
<td>Leukocyte or nitrite detection</td>
<td>87</td>
<td>69</td>
</tr>
</tbody>
</table>

**Note.** NPV, negative predictive value; PPV, positive predictive value.
7. Ulleryd P. Febrile urinary tract infection in
6. Lipsky BA, Ireton RC, Fihn SD, Hackett R, Ber-
dictive value of the nitrite dipstick test has
varied in different studies with different
populations tested. The same results have
been noted in previous studies with dif-
ferent populations. This result suggests that the dipstick test is useful to rule out infections:

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Reply to Etienne et al.

To the Editor—We read with great in-
terest 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 in-
fec tion (UTI) [2]. In the female outpatient
population, the nitrite test also has a spe-
cificity 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
should be used in both female and
male populations to diagnose UTI and not
to exclude it. However, the positive pre-
dictive 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 nitrate and leukocyte
esterase activity tests were performed in a
male population with symptoms of acute
community-acquired prostatitis is inter-
esting. In our population of male patients
with nonfebrile UTI and female patients
with an uncomplicated UTI [3], the
leukocyte esterase activity did not have ad-
ditional 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 an-
tibiotic 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 dip-
stick test is not enough to warrant with-
holding antibiotic therapy in the event of
a negative dipstick test result. The differ-
ence between their population (with
symptoms indicative of acute prostatitis,
high fever, and, in 20% of patients, a pos-
itive blood culture result) and our pop-
ulation (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 popula-
tions) which percentage of uncomplicated
UTIs become complicated. Both studies
[1, 2] show a clear role for the urine dip-
stick 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 anti-
biotic therapy.

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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 Staphy-
lcoccus aureus bacteremia (including end-
dovascular infection) among persons who inject buprenorphine (Subutex; Schering-
Plough) in Singapore. At the National