Clinical and Microbiological Determinants of Infection After Transrectal Prostate Biopsy

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(See the Editorial Commentary by Batura on pages 988–9.)

Background. Increasing numbers of infections following transrectal prostate biopsy (TPB) at our hospital led us to investigate clinical and bacterial risk factors to determine if the colonizing rectal Escherichia coli population is the source.

Methods. We performed an observational cohort study of men undergoing TPB (1 January 2010–6 February 2014) at the San Diego Veterans Affairs Medical Center. The primary outcome was clinically significant post-TPB infection. Rectal swabs were collected immediately before the biopsy and cultured selectively for fluoroquinolone-resistant gram-negative bacilli. Fluoroquinolone-resistant clinical and rectal E. coli isolates were compared using phylotyping, pulsed-field gel electrophoresis (PFGE) analysis, sequence typing, and virulence gene profiling.

Results. Rectal colonization with fluoroquinolone-resistant organisms (98% E. coli) was detected in 121 of 764 subjects (15.8%). Post-TPB infection was more common among fluoroquinolone-resistant-colonized subjects than non-colonized subjects (13/121 [10.7%] vs 8/649 [1.2%]; P < .001). Presence of fluoroquinolone-resistant colonizing E. coli was the most significant host characteristic associated with post-TPB infection (odds ratio, 4.5 [95% confidence interval, 1.2–18.2]; P = .03). Escherichia coli infection isolates (n = 18) did not differ from E. coli rectal culture isolates (n = 68) for any of 49 virulence genes or ST131 status (all P > .05). The rectal and clinical isolates of all 9 men with paired isolates had indistinguishable PFGE patterns and identical antimicrobial susceptibility profiles.

Conclusions. The rectal colonizing E. coli population is the source for most fluoroquinolone-resistant post-TPB infections, regardless of clonal background or virulence traits. Screening cultures can identify nearly all patients at risk for fluoroquinolone-resistant post-TPB infection.

Keywords. prostate; biopsy; infection; antibiotic resistance.

Prostate cancer is prevalent in industrialized countries and is most commonly diagnosed by transrectal ultrasound–guided prostate needle biopsy (TPB) [1, 2]. Historically, when done under the cover of recommended fluoroquinolone prophylaxis, TPB has had a low risk of infection (3%–5%) and sepsis (about 1%) [3, 4]. However, rates of post-TPB infection have increased recently, due mainly to fluoroquinolone-resistant Escherichia coli [3, 4]. Of concern is the epidemic E. coli lineage sequence type (ST) 131, which causes most fluoroquinolone-resistant E. coli infections in the United States today [4–8].

The rising incidence of TPB infections has led many urologists to switch to nonfluoroquinolone antibiotic prophylaxis, despite an absence of supporting evidence from clinical trials [9]. Others have adopted a transperineal biopsy route to avoid traversing the rectum; however, this can increase costs as the procedure usually involves monitored sedation anesthesia [9, 10]. Still others have used a preprocedure rectal swab culture to guide individualized prophylaxis, with apparent success.

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in small, nonrandomized studies [11–13]. This tailored approach is based on the unproven assumption that the organisms that cause post-TPB infections derive from the bacteria resident in the patient’s rectum and can be detected reliably with pre-TPB rectal cultures [14].

Our specific aims were to investigate (i) the association between fluoroquinolone-resistant *E. coli* rectal colonization and TPB infections, (ii) the clonal similarity of fluoroquinolone-resistant *E. coli* isolates from pre-TPB rectal cultures and post-TPB infections, and (iii) the virulence-associated characteristics of fluoroquinolone-resistant *E. coli* infection isolates, compared with colonization isolates.

**MATERIALS AND METHODS**

**Subjects**
Men presenting for TPB at the San Diego Veterans Affairs Medical Center from 1 January 2010 to 6 February 2014 underwent pre-TPB rectal culture as part of a quality improvement initiative. The standard pre-TPB prophylaxis regimen included a sodium phosphate enema the morning of the biopsy and 1 dose of ciprofloxacin 750 mg taken approximately 1 hour prior to TPB. If the practitioner deemed additional intramuscular antibiotic therapy necessary, this too was given 1 hour prior to TPB. One trained nurse practitioner performed most of the TPBs and collected a rectal swab immediately before placement of the rectal ultrasound probe for TPB. Although the culture was part of the biopsy protocol, it was not performed on every patient due to intermittent personnel shortages and temporary unavailability of selective media. Rectal swabs were processed in the hospital’s clinical microbiology laboratory as described below within 4 hours of collection.

Surveillance for post-TPB infections included a phone call to the patient from a nurse 2–3 days after TPB. Additionally, medical records were reviewed using a standardized instrument to extract epidemiological data and to identify infectious complications. Epidemiological data are listed in Table 1. Post-TPB infection was defined as presentation to an emergency department with lower urinary tract symptoms, plus fever and/or chills, within 7 days after TPB, irrespective of culture results. If the patient reported having presented elsewhere for post-TPB infection, we contacted that institution to obtain the clinical isolate(s), if available. Efforts were made to capture isolates from all patients who presented with TPB infection, whether or not they had a corresponding rectal culture, to provide as many post-TPB infection isolates as possible for genetic analysis.

**Detection of Fluoroquinolone-Resistant E. coli and Antimicrobial Susceptibility Testing**
For the first 100 enrolled patients, pre-TPB rectal swabs were collected in the urologist’s office at the time of initial pre-TPB

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**Table 1. Characteristics of 764 Men Undergoing Transrectal Prostate Biopsy, Stratified by Occurrence of Postbiopsy Infection**

<table>
<thead>
<tr>
<th>Epidemiological Variable</th>
<th>No Infection (n = 743)</th>
<th>Infection (n = 21)</th>
<th>P Value&lt;sup&gt;a,b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR)</td>
<td>65 (61–68)</td>
<td>67 (62.5–70)</td>
<td>.19&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>479 (64.2)</td>
<td>18 (85.7)</td>
<td>.49&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hispanic</td>
<td>34 (4.6)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>130 (17.4)</td>
<td>2 (9.5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>102 (13.7)</td>
<td>1 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m², median (IQR)</td>
<td>28.6 (25.7–32.3)</td>
<td>34 (27.6–36.3)</td>
<td>.16&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>1 (0–2)</td>
<td>1 (0–2)</td>
<td>.80&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetes</td>
<td>176 (23.8)</td>
<td>6 (28.6)</td>
<td>.61&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Previous prostate biopsy&lt;sup&gt;c&lt;/sup&gt;</td>
<td>153 (27.7)</td>
<td>2 (20.0)</td>
<td>.73&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hospitalized in the last year&lt;sup&gt;c&lt;/sup&gt;</td>
<td>47 (8.3)</td>
<td>3 (33.3)</td>
<td>.04&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Previous urinary tract infection&lt;sup&gt;c&lt;/sup&gt;</td>
<td>37 (6.6)</td>
<td>1 (11.1)</td>
<td>.46&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Received antibiotics in the last month&lt;sup&gt;c&lt;/sup&gt;</td>
<td>30 (5.3)</td>
<td>1 (11.1)</td>
<td>.39&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Additional antibiotics given at biopsy</td>
<td>156 (21.1)</td>
<td>4 (19.0)</td>
<td>.82&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Enema prior to biopsy</td>
<td>721 (97.4)</td>
<td>21 (100)</td>
<td>.46&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fluoroquinolone-resistant colonization&lt;sup&gt;d&lt;/sup&gt;</td>
<td>108 (14.5)</td>
<td>13 (61.9)</td>
<td>&lt;.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Data are presented as No. (%) unless otherwise indicated.

Abbreviation: IQR, interquartile range.

<sup>a</sup> Continuous variables: t test.

<sup>b</sup> Categorical variables: Fisher exact test.

<sup>c</sup> Fluoroquinolone-resistant rectal colonization, as indicated by a positive prebiopsy rectal culture.

<sup>d</sup> Data available for 75% (574/767) of subjects.
evaluation, typically 2–4 weeks prior to biopsy. Because of some unexpectedly long delays between screening and biopsy and the low rate of compliance with the culture procedure, only 65 of these were included in the study, and clinicians did not have access to the culture results. For all subsequent patients, cultures were collected at the time of biopsy by the single nurse practitioner who performed most biopsies. Rectal swabs were streaked onto locally prepared ciprofloxacin-supplemented (4 mg/L) MacConkey agar plates, which were quality-controlled using fluoroquinolone-susceptible and -resistant *E. coli* isolates.

From each plate with gram-negative bacterial growth, a representative colony of each distinct morphotype was selected for identification using the Vitek 2 instrument (bioMérieux, Durham, North Carolina) GN (gram-negative) identification cards. Antimicrobial susceptibility was assessed using the Vitek 2 and Clinical and Laboratory Standards Institute interpretative criteria [15]. Clinical isolates were identified and susceptibility was tested similarly to the rectal *E. coli* isolates. For isolates obtained from other hospitals, we confirmed the reported identification and susceptibility data. We determined the ciprofloxacin minimum inhibitory concentration (MIC) of all fluoroquinolone-resistant *E. coli* using Etest (bioMérieux) according to the manufacturer’s directions. A representative of each colonial morphotype encountered among the clinical and rectal *E. coli* isolates was stored at room temperature on a trypticase soy agar slant, pending molecular typing.

**Molecular Typing**

Fluoroquinolone-resistant *E. coli* isolates, whether rectal (ie, colonization) or clinical (ie, infection) isolates, were classified into the traditional major *E. coli* phylogenetic groups (A, B1, B2, D) and assessed for 49 virulence genes associated with extraintestinal pathogenic *E. coli* (ExPEC) by using established polymerase chain reaction (PCR)–based assays [16]. The virulence score was the number of virulence genes detected, adjusted for multiple detection of the *pap* (P fimbriae), *sfa/foc* (S and F1C fimbriae), and *kps* (group 2 capsule) operons. For group B2 isolates, ST131 status was defined by PCR-based detection of ST131-specific single-nucleotide polymorphisms (SNPs) in housekeeping genes *gyrB* and *mdh*. ST131 isolates were further tested for membership in the H30 ST131 subclone and its H30-Rx subset by PCR-based detection of clade-specific SNPs [17, 18].

**Pulsed-Field Gel Electrophoresis Analysis**

*XbaI* pulsed-field gel electrophoresis (PFGE) analysis was done according to a standardized protocol [6]. Using BioNumerics (Applied Maths), the PFGE profiles were compared with the PFGE profiles of previously encountered ST131 and non-ST131 isolates within a large private library (J. R. J.), using a Dice similarity value of ≥94% to classify profiles into discrete pulsotypes [6]. Dendrograms based on PFGE profiles were inferred according to the unweighted pair group method within Bionumerics.

**Study Design and Statistical Methods**

Three different comparisons were made to address the study aims. First, we determined the association of fluoroquinolone-resistant *E. coli* rectal colonization with TPB infections by comparing the infection rate among intestinal carriers (colonized) of fluoroquinolone-resistant *E. coli* to that among noncarriers (not colonized). Second, among men who had fluoroquinolone-resistant *E. coli* isolated from both the pre-TPB rectal culture and a post-TPB infection culture, we assessed the rectal and infection isolates for clonal similarity. Third, we compared colonization and clinical isolates of fluoroquinolone-resistant *E. coli* to try to identify characteristics that differentiated infection isolates from colonization isolates, using a subset of colonization isolates from patients who did not develop post-TPB infection and all the post-TPB infection isolates (both urine and blood cultures), whether or not the source patient underwent prebiopsy rectal culture.

Comparisons involving proportions were tested using Fisher or χ² tests, and those involving continuous variables were tested using *t* test. Univariable and multivariate odds ratios (ORs) were calculated using logistic regression analysis, and variables for inclusion in the model were selected based on having a *P* value <.2 in univariate analysis. A Bonferroni correction was used to reduce bias due to multiple comparisons. The criterion for statistical significance was *P* < .05.

**RESULTS**

**Rectal Culture and Post-TPB Infection**

From 1 January 2010 to 6 February 2014, according to administrative data, the San Diego Veterans Affairs Medical Center performed 1638 TPBs. Of these, 914 (60%) were preceded by a rectal culture, 146 (16%) of which yielded fluoroquinolone-resistant, gram-negative bacilli (Figure 1). (The incomplete capture resulted solely from logistical limitations; no selection criteria excluded any patient from undergoing prebiopsy rectal culture.) All positive rectal cultures yielded 1 or more morphotypes of fluoroquinolone-resistant *E. coli*. Two cultures additionally grew another fluoroquinolone-resistant organism (*Proteus mirabilis* and *Pseudomonas aeruginosa*, respectively). These organisms did not cause infection and were not included in the subsequent analyses. The institutional antibiogram documented a prevalence range of 32%–34% for fluoroquinolone resistance among clinical *E. coli* isolates from 2010 to 2014.

Complete clinical data (ie, epidemiological data, follow-up data, and rectal culture results) were available for 764 (83.5%) of the biopsy episodes. Of the corresponding 764 pre-TPB rectal cultures, 121 (15%) yielded a fluoroquinolone-resistant
organism, including 4 of 65 (6.2%) of those performed 1–2 weeks prebiopsy and 117 of 699 (16.7%) of those performed immediately prebiopsy ($P < .001$).

Twenty-one of the 764 (2.7%) patients with available clinical data presented to an emergency room with urinary tract infection within 72 hours of their biopsies (Figure 1). Of these 21 patients, 5 (25%) also had positive blood cultures. Demographic and clinical characteristics of the 21 patients with post–prostate biopsy infection are presented in Table 1. Of these 21 patients, 13 (62%) had pre-TPB rectal cultures that yielded a fluoroquinolone-resistant $E. coli$, and the remaining 8 (38%) did not. The post-TPB infection was due to fluoroquinolone-resistant $E. coli$ for all 13 (100%) of the rectally colonized patients compared with only 1 of the 8 (13%) patients with a negative pre-TPB rectal culture $E. coli$ ($P < .001$). The other 7 patients with a negative pre-TPB rectal culture were infected with a variety of fluoroquinolone-susceptible bacteria or had a sterile urine culture (Figure 1). Accordingly, the risk of post-TPB infection was significantly higher among intestinal carriers of fluoroquinolone-resistant $E. coli$ (13/121 [10%]) compared with noncarriers.

Figure 1. Study flow diagram shows the number of men presenting for prostate biopsy during the study period and their subsequent history within the study according to the performance and results of rectal culture, epidemiological data collection, and post–prostate biopsy infection. The source of patients for figures 2 and 3 is indicated. Abbreviations: $E. coli$, Escherichia coli; PFGE, pulsed-field gel electrophoresis; VA, Veterans Affairs.
(8/649 [1.2%]) (P < .001). In multivariable analysis, with adjustment for age and body mass index, both hospitalization in the last year for any cause (OR, 4.5; 95% confidence interval [CI], 1.1–19.4; P = .04) and colonization with fluoroquinolone-resistant E. coli (OR, 4.5; 95% CI, 1.2–18.2; P = .03) were significant risk factors for post-TPB infection (Table 2).

Supplemental Antibiotics

Overall, 160 of the 764 (20.9%) patients received supplemental prophylactic antibiotics, which was a single dose of ampicillin (1 g intramuscularly) for 94% (151/160). Supplemental antibiotic use was similarly frequent regardless of whether the prebiopsy rectal culture yielded fluoroquinolone-resistant E. coli —that is, 25.6% (31/121) if positive compared with 20.1% (129/643) if negative (P = .16). The infection rate likewise was similar among patients who did vs those who did not receive supplemental antibiotics, both for the overall population (2.5% vs 2.7%; P = .83) and specifically among the 121 whose rectal culture yielded fluoroquinolone-resistant E. coli (9.7% vs 11.1%; P = .83).

Genomic Relationships

Of the 121 fluoroquinolone-resistant E. coli rectal isolates with complete associated clinical data, the first 81 (67%) were selected for molecular analysis as representatives of the intestinal colonization group. According to PFGE analysis, these rectal isolates overall were quite diverse genomically (Figure 2). However, 51 of 81 (63%) belonged to ST131 and formed a well-resolved cluster separated from the non-ST131 isolates, which were more genomically heterogeneous than the ST131 isolates (Figure 2).

Of the 81 source patients for these fluoroquinolone-resistant rectal isolates, 11 (14%) developed post-TPB infection. ST131 was identified as a rectal colonizer with the same frequency among the 11 patients with infection (7/11 [64%]) as among the remaining 70 patients (44/70 [64%]). Of the 11 patients with infection, 9 had both a rectal isolate and an infection isolate available for a genomic comparison (Figure 3). Within each such matched pair, the clinical and rectal isolate had indistinguishable PFGE profiles, which contrasted with the considerable diversity of PFGE profiles across pairs (Figure 3) and among the rectal isolates generally (Figure 2). Interestingly, 1 man was coinfected with both a fluoroquinolone-resistant E. coli strain, which corresponded with the pre-TPB rectal isolate, and an unrelated fluoroquinolone-susceptible E. coli strain (patient F, strain 90; Figure 3). A second man was coinfected with 2 extended-spectrum β-lactamase–producing, fluoroquinolone-resistant E. coli strains, 1 of which corresponded with the prebiopsy rectal isolate (patient I, strain 75; Figure 3).

Bacterial Characteristics

We compared molecularly the 68 available fluoroquinolone-resistant rectal E. coli isolates from men who did not develop post-TPB infection with the 18 available fluoroquinolone-resistant clinical E. coli isolates from men who did develop post-TPB infection (of whom 10 underwent rectal surveillance and 8 did not). Among these 86 isolates, phylogenetic group B2 was the most common phylogroup overall and was similarly prevalent among colonization isolates and infection isolates (48/68 [71%] vs 14/18 [78%], respectively; P = .13). ST131 accounted for nearly all group B2 isolates (54/62 [87%]) and, like group B2, was similarly prevalent in the 2 source groups (44/68 [65%] vs 10/18 [56%] for colonization and clinical isolates, respectively; P = .59). Colonization and infection isolates also did not differ significantly according to the prevalence of any of the 49 tested virulence genes (Supplementary Figure 1) or aggregate virulence gene scores (median score, 13.5 vs 13.0 for colonization and infection, respectively; P = .73). The 54 fluoroquinolone-resistant ST131 E. coli isolates all represented the ST131-H30 subclone, and 7 (13%) of these represented the H30-Rx subset, which also did not differ in prevalence by source group (6/44 [14%] vs 1/10 [10%] for colonization and infection, respectively; P = .76; Figure 2).

DISCUSSION

In this 4-year observational study, which was done at a center where oral ciprofloxacin was used routinely for pre-TPB

Table 2. Multivariable Analysis of Epidemiological Variables as Predictors of Post–Prostate Biopsy Infection Among 764 Men Undergoing Prostate Biopsy

<table>
<thead>
<tr>
<th>Variablea</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.94 (0.85–1.05)</td>
<td>.27</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.01 (0.99–1.03)</td>
<td>.43</td>
</tr>
<tr>
<td>Hospitalization in the last year</td>
<td>4.52 (1.05–19.39)</td>
<td>.04</td>
</tr>
<tr>
<td>Fluoroquinolone-resistant colonizationb</td>
<td>4.59 (1.16–18.16)</td>
<td>.03</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio.

a Variables for inclusion in the model were selected based on having a P value < .20 in univariate analysis.

b Fluoroquinolone-resistant rectal colonization, as indicated by a positive prebiopsy rectal culture.

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Figure 2. Pulsed-field gel electrophoresis (PFGE) profiles of 81 fluoroquinolone-resistant pre–prostate biopsy rectal *Escherichia coli* isolates. The dendrogram was inferred according to the unweighted pair group method using Dice similarity coefficients, as derived from pairwise comparisons of XbaI PFGE profiles. Data columns, from left to right, indicate strain designation, whether the source patient developed a postbiopsy infection, pulsotype (with reference to a large private PFGE library: JRJ), ST131 status, and *E. coli* phylogenetic group. Dashes indicate negative results.
antimicrobial prophylaxis, 15% of men undergoing TPB carried fluoroquinolone-resistant rectal *E. coli* before biopsy. Multivariable analysis showed that such rectal carriers had a nearly 4.5-fold increased odds of post-TPB infection, which in all instances (13/13) involved fluoroquinolone-resistant *E. coli*, although 1 such patient was coinfected with fluoroquinolone-susceptible *E. coli*. Moreover, in the 9 cases that had both a fluoroquinolone-resistant prebiopsy rectal culture isolate and a clinical (urine or blood culture) isolate available for analysis, the 2 isolates corresponded precisely by PFGE and antimicrobial susceptibility testing. This molecular analysis provides, to our knowledge, the first direct evidence for the long-held but untested assumption that the patient’s own rectal microbiota is the source of most post-TPB infections. In turn, this suggests that rectal bacteria are implanted directly from the rectum into the blood, urine, and/or prostate by the prostate biopsy needle, and that the fluoroquinolone-resistant *E. coli* strains that are destined to cause post-TPB infection can be reliably identified in advance by rectal culture. Notably, rectal culture screening failed to identify rectal carriage in only 1 of the 14 men who

Figure 3. Pulsed-field gel electrophoresis (PFGE) patterns of paired clinical and rectal fluoroquinolone-resistant *Escherichia coli* isolates from 9 men with post–prostate biopsy infection. For all 9 patients, at least 1 rectal and 1 urine and/or blood isolate exhibited indistinguishable XbaI PFGE patterns, demonstrating genomic identity and supporting a rectal source for the clinical isolate. The 2 discrepant urine isolates are explained in the text.
developed postbiopsy infection with fluoroquinolone-resistant 
*Escherichia coli*. 

Despite the significantly higher infection rate among patients colonized with fluoroquinolone-resistant *E. coli*, approximately 90% of such colonized patients did not develop an infection. We tried to identify bacterial characteristics that might explain this phenomenon by comparing the colonization and infection isolates for phylogenetic group background, membership in ST131 (the single most prevalent *E. coli* lineage among clinical isolates from veterans across the United States) [18, 19], the H30 and H30-Rx ST131 subclones, and presence of ExPEC-associated virulence genes [19]. None of these characteristics differed in prevalence between strains that did or did not cause a post-TPB infection. ST131 is clearly antimicrobial resistant and by reputation is virulent [20]; however, non-ST131 bacteria were as likely to cause infection. Direct implantation of bacteria into host tissues by the biopsy needle could bypass host defenses and render unnecessary the virulence factors needed for typical ascending infection.

Although we identified no host factors associated with infection other than colonization with fluoroquinolone-resistant *E. coli* and prior hospitalization, unrecognized defects in innate or acquired immunity may have been present in patients who developed infection. TPB is known to transfer small numbers of bacteria into host tissues, usually without causing clinical disease [21]. The introduction of bacteria is necessary but not sufficient to cause disease, implying that in most patients host defenses clear these organisms before they can cause adverse sequelae. Early studies comparing ciprofloxacin to placebo documented post-TPB infection rates as high as 25% among placebo recipients [22]. In contrast, here the infection rate was only 2.7% (21/764), evidence that ciprofloxacin prophylaxis still was generally effective and should not be abandoned. We propose an individualized approach, in which choice of supplemental prophylactic antibiotic is guided by the results of a pre-TPB rectal culture that may improve prophylactic regimen efficacy while minimally increasing antibiotic usage. This hypothesis deserves rigorous testing in a well-designed, adequately powered randomized controlled trial.

Our study has strengths and limitations. Limitations include the retrospective, observational study design. Additionally, 40% of eligible patients did not have a rectal culture. Furthermore, most rectal cultures were done on the day of biopsy and so could not be used to modify the prophylactic regimen. On the other hand, the 65 patients who underwent rectal culture 1–2 weeks prior to biopsy (8.5% of 764 evaluable subjects) had a significantly lower prevalence of resistant colonization than did those who were cultured immediately prebiopsy. The basis for this phenomenon, which has several possible explanations, is unknown. Notably, another study found that rectal cultures taken 1–2 weeks prebiopsy correspond well with those taken immediately prior to biopsy [23].

Among study strengths, first was the standardized post-TPB follow-up, which included a routine phone call by a nurse to all biopsied patients. Second, the Veterans Affairs comprehensive electronic medical record system allowed us to search for all inpatient and outpatient medications, including supplemental (nonfluoroquinolone) antibiotics. Third, the extensive molecular characterization of study isolates, including for genomic background (phylogroup, ST131 status, pulsotype) and virulence traits, allowed an assessment of bacterial traits. Fourth, the study’s large sample size makes it one of the largest molecular epidemiological studies to date involving the TPB population.

**CONCLUSIONS**

Rectal colonization with fluoroquinolone-resistant *E. coli* is a significant risk factor, and nearly an absolute prerequisite, for fluoroquinolone-resistant post-TPB infection, when ciprofloxacin monotherapy is used for periprocedural prophylaxis. Nearly all post-TPB infections due to fluoroquinolone-resistant *E. coli* are caused by the pre-TPB colonizing rectal strain. Antimicrobial resistance and colonization fitness rather than intrinsic virulence likely determine which strains, including ST131, cause infection. Measures to prevent rectal colonization with fluoroquinolone-resistant *E. coli*, and/or to detect such strains in advance of TPB so that antibiotic prophylaxis can be adjusted appropriately, could help reduce the considerable morbidity and costs associated with post-TPB infection.

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**Table 3. Co-resistance Profiles of 121 Ciprofloxacin-Resistant *Escherichia coli* Rectal and Clinical Isolates From Men Undergoing Transrectal Prostate Biopsy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevalence of Resistancea, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>120 (99)</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>41 (34)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>31 (26)</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>22 (18)</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>20 (17)</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>18 (15)</td>
</tr>
<tr>
<td>Ceftiraxone</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Meropenem</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

a Drugs are listed in order according to resistance prevalence (high to low). 
b Intermediate is counted as resistant.
Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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References