American Journal of Epidemiology
Copyright © 2002 by the Johns Hopkins Bloomberg School of Public Health
All rights reserved
Vol. 156, No. 12
Printed in U.S.A.
DOI: 10.1093/aje/kwf159

Uropathogenic *Escherichia coli* Are More Likely than Commensal *E. coli* to Be Shared between Heterosexual Sex Partners

Betsy Foxman[1], Shannon D. Manning[1], Patricia Tallman[1], Richard Bauer[1], Lixin Zhang[1], James S. Koopman[1], Brenda Gillespie[2], Jack D. Sobel[3], and Carl F. Marrs[1]

[1] Center for Molecular and Clinical Epidemiology, Department of Epidemiology, The University of Michigan School of Public Health, Ann Arbor, MI.
[2] Center for Statistical Consultation and Research, University of Michigan, Ann Arbor, MI.
[3] Division of Infectious Diseases, Wayne State University School of Medicine, Detroit, MI.

Received for publication February 26, 2002; accepted for publication July 22, 2002.

Because uropathogenic *Escherichia coli* are better adapted than other *E. coli* to the urethra, periurethra, and vagina, the authors reasoned that uropathogenic *E. coli* would be more likely than commensal *E. coli* to be shared between sex partners. In this 1996–1999 Michigan study, the genetic identity of *E. coli* isolated from 166 women with *E. coli* urinary tract infection (UTI) and 94 women without UTI and their sex partners was determined by pulsed-field gel electrophoresis. Rectal isolates were considered uropathogenic *E. coli* if genetically identical to the urinary isolate causing UTI. All eight urinary isolates from men with UTI partners were identical to the *E. coli* found in the urine or vagina of their sex partner. When the 550 unique rectal *E. coli* isolates from couples were considered the unit of analysis, *E. coli* that caused UTI were nine times (odds ratio (OR) = 8.87, 95% confidence interval (CI): 5.41, 14.54) more likely than other *E. coli* to be shared between sex partners. Sharing occurred twice as frequently (OR = 1.87, 95% CI: 1.13, 3.08) if the *E. coli* had P pili or if the couples engaged in oral sex (OR = 2.09, 95% CI: 1.09, 4.00). Uropathogenic *E. coli* are more likely than commensal *E. coli* to be shared with a current heterosexual sex partner. Both sexual behaviors and a bacterial virulence factor, P pili, modified sharing.

disease transmission; *Escherichia coli*; sexual partners; urinary tract infections

Abbreviations: cfu, colony-forming unit; CI, confidence interval; OR, odds ratio; PFGE, pulsed-field gel electrophoresis; UTI, urinary tract infection.

It is widely accepted that the reservoir for urinary tract infection (UTI) is the human bowel flora and that most infections result from uropathogens moving into the bladder via the urethra (1). *Escherichia coli,* a universal bowel inhabitant, causes between 80 and 90 percent of outpatient UTI (1), although only a small fraction of *E. coli* are uropathogenic (2).

UTI occurs more frequently in women (17.5 percent incidence between ages 18 and 24 years) (3) than in men (0.5 percent incidence in the same age range) (4). The gender difference in the incidence of symptomatic infection is attributed in part to the shorter urethra of women and the proximity of the urethra to the anal opening and vaginal introitus (5). Although there are marked differences in disease incidence by gender, corresponding differences in gastrointestinal colonization rates are unlikely. *E. coli* are transmitted by the fecal-oral route and can be passed between persons via person-to-person direct contact or through a vehicle such as food or water. There has been some suggestion that uropathogens can be foodborne (6) and that UTI can be transmitted by direct person-to-person contact (7).

The incidence of symptomatic infection is associated with vaginal intercourse; spermicide, diaphragm, and condom use; and recentness of forming a relationship ("honeymoon cystitis") (8–11). One third of women have their first UTI by age 26 years, and cumulative incidence increases dramatically at the average age of initiating sexual activity (3).

We hypothesized that uropathogenic *E. coli* are transmitted between persons during sexual activity. Furthermore,

Correspondence to Dr. Betsy Foxman, Center for Molecular and Clinical Epidemiology, Department of Epidemiology, The University of Michigan School of Public Health, 109 Observatory Street, Ann Arbor, MI 48109-2029 (e-mail: bfoxman@umich.edu).

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

because uropathogenic *E. coli* are probably better adapted to the urethra, periurethra, and vagina than are other *E. coli*, we reasoned that *E. coli* would be more likely to be shared between sex partners when the woman has UTI than in couples in whom the woman does not have UTI. To test this hypothesis, we compared co-colonization rates among couples in whom the woman did or did not have UTI and investigated behavioral and bacterial virulence factors for co-colonization. In addition, we examined predictors of carrying the identical *E. coli* in vaginal and rectal flora among female study participants.

MATERIALS AND METHODS

Study design

We used a case-control design in which case couples were women with UTI and their most recent male sex partner and control couples were women without UTI and their most recent male sex partner. The outcome of interest was rectal-rectal co-colonization with genetically identical *E. coli* as determined by pulsed-field gel electrophoresis (PFGE).

Study protocol

Women with UTI and women without UTI were recruited from those women visiting the University of Michigan Health Service in Ann Arbor, Michigan, during the academic year (September–April) beginning in fall 1996 through spring 1999. Women aged 18–39 years were eligible if they had engaged in sexual activity—defined as vaginal, oral, or anal intercourse—with a male partner during the past 2 weeks, did not have diabetes, were not hospitalized or catheterized during the previous 2 weeks, and had not used antibiotics within the last 24 hours. Twenty-four hours without antibiotic therapy is sufficient for a uropathogen to grow in significant numbers in the urine. All women presenting to the Health Service Laboratory with urinary symptoms or for a throat culture were screened for eligibility and their willingness to participate in the study. Only one third of women presenting for a throat culture were eligible, primarily because they had not been sexually active in the previous 2 weeks or felt too ill to participate even if eligible. Therefore, during the last year of the study, we recruited from among women filling prescriptions at the Health Service Pharmacy to boost the number of uninfected women in the study. A full-time study recruiter interviewed all women for eligibility.

After giving their written consent to participate and have their medical records reviewed, eligible women collected a midstream urine specimen, a vaginal specimen (by using a tampon), and a rectal specimen by using a rayon swab. Studies by Onderdonk et al. (12) have demonstrated that vaginal cultures obtained by using tampons are comparable to those obtained from a vaginal swab. Participants completed a self-administered questionnaire including a detailed sexual history battery. They were then provided with a letter to give to their most recent male sex partner describing the study and inviting him to participate. As an incentive to participate, women and the participating sex partner were given monetary compensation.

To be eligible, men had to enroll within 7 days of their participating sex partner. After giving written consent to participate and have their medical records reviewed, they collected a random initial-void urine culture (10 ml) and a rectal specimen by using a rayon swab, and they completed a self-administered questionnaire. Without also testing a midstream urine culture, we could not rule out bladder involvement. However, bacteria isolates collected from a random initial void primarily reflect urethral flora; thus, in this paper we use the term "urethral" isolates. On the occasions in which partners were recruited together (women were not infrequently accompanied to the Health Service by their sex partner), they were seated in separate locations to ensure independent completion of the study questionnaire.

The study protocol was approved by the Institutional Review Board at the University of Michigan.

UTI definition

UTI was defined as a clinical diagnosis of UTI by a subject's treating physician, plus a urine culture positive for *E. coli* (>1,000 colony-forming units (cfu)/ml urine) in the presence of one or more urinary symptoms. The clinical diagnosis was confirmed by reviewing medical records.

Recruitment

Between fall 1996 and spring 1999, we identified 1,069 women with urinary symptoms and 552 with sore throats who were eligible for enrollment. A total of 434 (41 percent) of the women with urinary symptoms and 121 (22 percent) of the women with sore throats consented to participate. Almost one fifth of the women with urinary symptoms (20 percent) and women with sore throats (18 percent) refused because they anticipated that their sex partner could not be recruited. Thirteen percent of women with urinary symptoms and 32 percent of women with sore throats refused for other reasons, primarily lack of time or feeling too ill. During fall 1998 through spring 1999, we also recruited women without UTI by using an advertisement given to women presenting to the pharmacy. Of the 129 eligible women responding to the advertisement, 95 (74 percent) consented to participate. A total of 272/434 (63 percent) of consenting women with urinary symptoms and 152/216 (70 percent) of consenting women without urinary symptoms successfully recruited their sex partner.

Inclusions/exclusions

Of the 434 consenting, eligible women with urinary symptoms, 73 (17 percent) were excluded because they did not meet the UTI case definition. An additional 47 (11 percent) were excluded because their rectal specimen or that of their sex partner contained no gram-negative bacteria. Among the 216 consenting women without UTI (121 with sore throats and 95 recruited from the advertisement), 10 (5 percent) were excluded because they did not meet enrollment criteria and 40 (19 percent) were excluded because their rectal specimen or that of their sex partner contained no gram-negative bacteria. Of the remaining 166 women, 94 recruited their sex

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

partner. A total of 194 of the 434 consenting women with UTI who met the study criteria recruited their sex partner. Of these, 166 (86 percent) had UTI caused by *E. coli*, and their partner had *E. coli* in their rectal specimen. These 166 case couples and 94 control couples form the basis for the analyses presented in this paper.

Identification of bacteria

All urine specimens were inoculated, as described previously (7). Vaginal and rectal flora were isolated by inoculating tampons and rectal swabs onto Trypticase soy agar with 5 percent sheep blood and MacConkey agar. The predominant isolate on each plate and all morphologically distinct colonies were identified and were stored for further testing, as described by Plos et al. (13). Suspect gram-negative bacteria were identified by using the API-20E system (Biomerieux Vitek, Inc., Hazelwood, Missouri). All isolates were screened, by using the method of dot blot hybridization described previously (14), for the presence of 10 bacterial genes potentially associated with UTI: aerobactin (*aer*), group II capsule (*kps*MT), group III capsule (*cap*III), cytotoxic necrotizing factor 1 (*cnf*1), hemolysin (*hly*), outer membrane protein T (*omp*T), P-pili family of fimbriae (*pff*), DR-binding adhesins (*drb*), S fimbrial adhesin (*sfa*), and type 1 pili (*fim*).

Strain typing

To determine whether women and their sex partners were colonized with the identical *E. coli* or whether women carried identical strains at different anatomic sites, we used PFGE. Purification, rare-cutter restriction, and gel electrophoresis of minimally sheared *E. coli* DNA were performed, as described previously (7). We considered isolates to be identical if they differed by no more than one band. If identity was questionable, the gels were repeated. All gels were read by two independent readers; one was blinded to the UTI status of the participating woman. We considered as uropathogens case couples' rectal isolates that were genetically identical, as determined by PFGE, to the urinary isolate causing UTI.

Data analysis

The primary outcome of interest was the presence or absence of co-colonization (e.g., both sex partners carried the genetically identical *E. coli*, as determined by PFGE, in their bowel flora). The association between co-colonization and predictor variables was described by determining odds ratios and their 95 percent confidence intervals, and significance was tested by using chi-square statistics. To model the joint effects of variables on co-colonization, we fit a logistic regression model. Sexual behavior was reported by both partners; therefore, for partner analyses, if either partner reported engaging in a behavior, such as cunnilingus during the past 2 weeks, we considered both to have done so. The analysis was completed in two ways: 1) by using the couple as the unit of analysis and 2) by using the bacterial isolate as the unit of analysis. When the bacterial isolate was considered the unit of analysis, we included each unique isolate from the couple (co-colonizing isolates were included only once) and adjusted for clustering between isolates from the same couple by using generalized estimating equations (GEE).

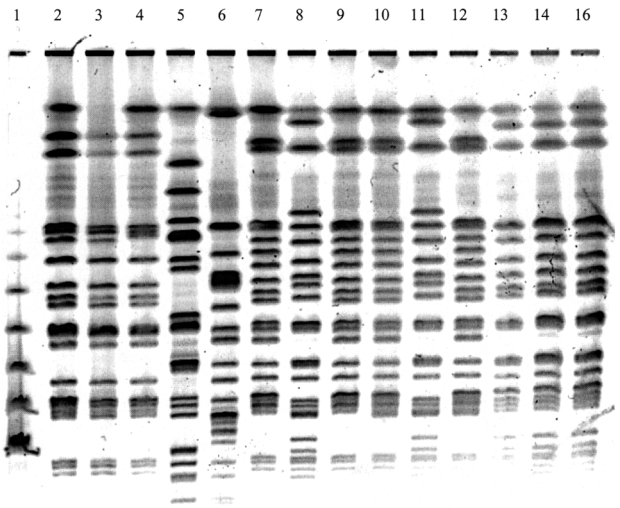


FIGURE 1. Pulsed-field gel electrophoresis of uropathogenic *Escherichia coli*, cut with restriction enzyme *NotI*, obtained from participants in a study of heterosexual transmission of urinary tract infection, Michigan, 1996–1999. Lane 1: DNA marker; lanes 2–4 and 7–9: urine, rectal, and vaginal isolates, respectively, from two female participants; lanes 5 and 6: rectal isolates from the most recent sex partner of the female in lanes 2–4; lanes 10–12: rectal isolates from the most recent sex partner of the woman in lanes 7–9; lanes 13 and 14: rectal and vaginal isolates, respectively, from a third female participant; lane 15: rectal isolate from her most recent sex partner.

RESULTS

Description of study population

Our analysis was limited to 166 case couples (heterosexual couples in which the woman had UTI caused by *E. coli*) and 94 control couples (heterosexual couples in which the woman did not have UTI). Women with UTI tended to be younger than women without UTI ($p = 0.11$) but were similar with respect to race/ethnicity ($p = 0.50$) (table 1). Male sex partners of women with UTI were significantly younger than partners of women without UTI ($p = 0.002$) but also were similar with respect to race/ethnicity ($p = 0.43$).

Colonization with *E. coli*

We compared the identity of *E. coli* isolated from within a subject or partnership by using PFGE (figure 1). Strains were considered identical if they differed by no more than one band. For example, lanes 7–9 in figure 1 are the urine, rectal, and vaginal isolates from a woman whose partner had three rectal isolates (lanes 10–12). The vaginal isolate (lane 9) is identical to one of her partner's rectal isolates (lane 10).

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

TABLE 1. Characteristics of 166 women with UTI* and 94 women without UTI, and of their most recent male sex partners, by UTI status of the woman, Michigan, 1996–1999†

Characteristic	Women				Men			
	UTI couples		Non-UTI couples		UTI couples		Non-UTI couples	
	No.	%	No.	%	No.	%	No.	%
Age (years)								
18–19	40	24	12	13	14	8	8	9
20–24	98	59	63	67	110	66	59	63
25–29	24	15	15	16	37	22	13	14
30–34	2	1	4	4	1	1	12	13
≥35	1	1	0	0	4	4	2	2
Race/ethnicity								
African American	7	4	4	4	6	6	5	5
Asian	20	12	6	6	18	11	5	5
Caucasian	122	74	71	76	125	75	70	74
Hispanic	9	6	6	6	8	5	5	5
Other	7	4	7	7	9	5	9	10

* UTI, urinary tract infection.

† Numbers do not sum to totals because of missing values, and percentages do not sum to 100 because of rounding.

Of the women with *E. coli*-mediated UTI, 123/166 (74 percent) had genetically identical strains in their urine and rectal isolates. Of the women without UTI, 8/94 (9 percent) had a urine culture positive for *E. coli*, and 5/8 (63 percent) of these cultures matched the rectal isolates. *E. coli* was found in the vaginas of 146/166 (88 percent) of the women with UTI and 26/94 (28 percent) of the women without UTI ($p < 0.001$). Twenty women with UTI and two women without UTI had two or more genetically distinct strains of *E. coli* in their vaginas. Of the women vaginally colonized, 110/146 (75 percent) of the vaginal isolates from women with UTI compared with 17/26 (65 percent) from women without UTI were genetically identical to one of their rectal *E. coli* isolates ($p = 0.29$).

The vaginal isolates matched the male's rectal flora in 54/146 (37 percent) of the UTI couples and 8/26 (31 percent) of the non-UTI couples. Eight (5 percent) male sex partners of women with UTI and one (1 percent) male sex partner of a woman without UTI had a urine culture positive for *E. coli*. All eight urethral isolates from men with UTI partners were identical to the *E. coli* found in the urine and vagina of their sex partner (except for the one woman not vaginally colonized). The urethral isolate from the partner of a woman without UTI matched an isolate from the woman's rectum. One male had more than 100,000 cfu/ml, although he was entirely asymptomatic; the others had less than 10,000 cfu/ml. Only two urethral isolates from partners of women with UTI matched an *E. coli* isolate from their own rectum. The urethral isolate from the partner of a woman without UTI did not match any isolates from his rectum.

Five men urethrally colonized with the same *E. coli* as that causing UTI in their sex partner returned for a second urine culture, and cultures for four were positive. Three carried the identical *E. coli,* as determined by PFGE, at both visits, which occurred 3–16 days later.

Co-colonization using the couple as the analysis unit

Comparison of co-colonization rates that include urinary isolates is biased because women with UTI by definition are colonized in the urinary tract. Thus, we excluded urinary isolates in our analysis of co-colonization and determined the number of couples that shared the genetically identical strain in their rectal flora (rectal-rectal co-colonization). This situation occurred among 36 percent of UTI couples compared with 25 percent of non-UTI couples ($p = 0.07$).

Rectal-rectal co-colonization rates were higher among UTI than non-UTI couples across the majority of characteristics measured; when they were not, the numbers were small (table 2). For both UTI and non-UTI couples, co-colonization rates did not vary by the UTI history of the woman, duration of the sexual partnership, or time since last engaging in sexual activity. However, both UTI and non-UTI couples engaging in cunnilingus had a greater odds of being co-colonized. Couples who reported using both condoms and spermicides had the lowest co-colonization rates. Most condom users also used spermicide, while few couples used spermicide alone.

To better understand the joint effects, we fit a logistic regression model predicting rectal-rectal co-colonization between sex partners (table 3, model 1) with cunnilingus, condom and spermicide use, and case couple status. These variables fit our underlying biologic model and were statistically significant in the bivariate analysis. After we adjusted for condom and spermicide use and for cunnilingus, rectal-rectal co-colonization in UTI couples was associated with

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

TABLE 2. Associations of selected characteristics with *Escherichia coli* co-colonization, Michigan, 1996–1999*,†

Characteristic	Rectal-rectal co-colonization between sex partners‡,§				Vaginal-rectal co-colonization within a woman¶			
	UTI couples		Non-UTI couples		UTI women		Non-UTI women	
	No.	%	No.	%	No.	%	No.	%
Total	166	36	94	25	166	66	94	18
Woman's age (years)								
18–19	40	35	12	25	40	70	12	33
20–24	98	39	63	22	98	67	63	19
≥25	27	26	19	32	27	59	19	5
Previous UTI history (woman)								
Yes	113	36	37	24	113	66	37	16
No	51	39	57	25	51	69	57	19
Antibiotic use in the past 2 weeks								
Yes	34	41	8	25	20	80	3	33
No	132	34	86	24	144	65	90	18
Type of sexual activity in the past 2 weeks								
Vaginal sex only	15	20	11	9	22	68	18	22
Vaginal sex and								
Fellatio only	25	24	14	7	30	63	15	13
Cunnilingus only	9	33	5	40	11	55	6	17
Both fellatio and cunnilingus	117	40	64	30	103	68	55	18
Spermicide and condom use in the past 2 weeks#								
None	60	48	56	23	60	70	56	16
Condom use alone	19	42	10	40	19	68	10	20
Spermicide use alone	4	0	3	33	4	75	3	33
Condom and spermicide use	83	27	25	20	83	63	25	20
No. of episodes of vaginal sex in the past 2 weeks								
1–3	39	39	44	21	39	67	44	14
4–5	30	18	21	33	30	70	21	14
6–8	49	29	12	25	49	61	12	25
≥9	47	45	17	24	47	70	17	29
Duration of relationship								
<3 months	37	32	9	33	37	70	9	22
3–6 months	32	38	16	0	32	53	16	19
6–12 months	37	49	18	39	37	60	18	28
1–2 years	22	27	23	35	22	77	23	22
≥3 years	28	25	25	20	28	71	25	8
Unknown	10	40	3	0	10	80	3	0
No. of days since last sexual activity**								
0–1	55	40	28	29	55	75	28	25
2	50	30	21	24	50	68	21	24
3–4	43	40	24	25	43	65	24	17
≥5	14	29	21	19	14	29	21	5

* Expressed as no. of participants with the characteristic and the percentage in the category with identical *E. coli* co-colonization.

† Numbers do not sum to totals because of missing values.

‡ Rectal-rectal co-colonization with *E. coli* among 166 women with urinary tract infection (UTI) and their most recent sex partner (UTI couples) and 94 women without UTI and their most recent sex partner (non-UTI couples).

§ Sexual behaviors were determined by using the combination of both partners' reports.

¶ Vaginal-rectal co-colonization with *E. coli* among women with UTI and women without UTI.

Determined by using the combination of both partners' reports.

** Mantel-Haenszel test for trend for vaginal-rectal colonization with identical *E. coli*: UTI women, $p = 0.006$; non-UTI women, $p = 0.07$.

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

TABLE 3. Logistic regression models predicting co-colonization with identical *Escherichia coli* (by using pulsed-field gel electrophoresis), by selected characteristics, Michigan, 1996–1999

	Coefficient (standard error)	*p* value	Odds ratio	95% confidence interval
*Model 1 predicting rectal-rectal co-colonization between sex partners**				
UTI couple vs. non-UTI couple	0.6682 (0.3049)	0.03	1.95	1.07, 3.55
Condom and spermicide use in the past 2 weeks†	–0.5897 (0.2958)	0.05	0.56	0.31, 0.99
Cunnilingus in the past 2 weeks	0.9411 (0.3684)	0.01	2.56	1.24, 5.28
Model 2 predicting whether an isolate colonizes both members of a couple‡,§				
Condom and spermicide use in the past 2 weeks†	–0.4398 (0.2891)	0.13	0.64	0.37, 1.14
Cunnilingus in the past 2 weeks	0.7380 (0.3302)	0.03	2.09	1.09, 4.00
Nonuropathogen¶ without P pili	Reference		1.0	
Uropathogen without P pili	1.7295 (0.3530)	<0.0001	5.64	2.82, 11.26
Uropathogen with P pili#	0.9652 (0.5126)	0.06	17.00	0.96, 7.17
P pili on a nonuropathogen	0.1386 (0.3602)	0.70	1.15	0.57, 2.33
*Model 3 predicting vaginal-rectal co-colonization within a woman***				
Women with UTI	2.1296 (0.3264)	0.0001	8.41	4.44, 15.95
Age of woman (years)	–0.0691 (0.0462)	0.14	0.93	0.85, 1.02
Time since last sex (days)	–0.2893 (0.0898)	0.001	0.75	0.63, 0.89

* Predicts co-colonization among 166 women with urinary tract infection (UTI) and their most recent sex partner (UTI couples) and 94 women without UTI and their most recent sex partner (non-UTI couples).

† Includes spermicidal condoms. Determined by using the combination of both partners' reports.

‡ Adjusted for clustering of behaviors within a partnership by using generalized estimating equations.

§ Uses isolate as the unit of analysis and predicts whether an isolate colonized both members of a couple (n = 550 isolates).

¶ Uropathogen defined as a rectal isolate genetically identical to the isolate causing UTI in the couple.

Coefficient, standard error, and p value for interaction term; odds ratio and 95% confidence interval for uropathogen and P pili relative to no uropathogen without P pili.

** Predicts co-colonization in the vagina and rectum of the 166 women with UTI and the 94 women without UTI.

twice the odds compared with rectal-rectal co-colonization in non-UTI couples. Couples engaging in cunnilingus also had twice the odds of co-colonization compared with those not reporting this practice. Couples using both condoms and spermicides had about half the odds of co-colonization (table 3) as couples using one or the other or neither of the two. When condom use and spermicide use were treated as separate variables rather than a single combined variable, condom use had no effect (odds ratio (OR) = 0.95, 95 percent confidence interval (CI): 0.46, 1.94), but spermicide had a notable, but statistically insignificant effect (OR = 0.50, 95 percent CI: 0.22, 1.14). Episodes of vaginal-penile intercourse were not associated with rectal-rectal co-colonization and thus were not included in the final model.

Co-colonization using the isolate as the analysis unit

For this analysis, we included all 550 unique *E. coli* isolates, as determined by PFGE, obtained from participating couples. There were 345 isolates from case couples; 124 (36 percent) had the same PFGE pattern as the isolate causing the UTI in the woman and were therefore classified as uropathogens. (One woman had two uropathogens, both also found in her rectal flora.) If the same isolate, as determined by PFGE, was found in both sex partners, it was included only once. The outcome for this analysis was whether the identical isolate, according to PFGE, was found in both members of the couples' rectal flora. Compared with commensal isolates, uropathogenic isolates were associated with 9.9 times (95 percent CI: 5.71, 17.19) the odds of being shared. Similar to the analysis in which the couple was considered the unit of analysis, oral sex (OR = 1.98, 95 percent CI: 1.08, 3.20) was positively associated with co-colonization. Using a condom and spermicide had a negative association with co-colonization, but the association was marginally significant only among uropathogens (uropathogenic isolate: OR = 0.51, 95 percent CI: 0.23, 1.11; commensal isolate: OR = 0.88, 95 percent CI: 0.39, 2.00).

All isolates had been screened previously by using dot blot hybridization for the presence of the genes encoding for 10 known uropathogenic virulence factors (14): aerobactin (*aer*), group II capsule (*kps*MT), group III capsule (*cap*III), cytotoxic necrotizing factor 1 (*cnf*1), hemolysin (*hly*), outer membrane protein T (*omp*T), P-pili family of fimbriae (*pff*), DR-binding adhesins (*drb*), S fimbrial adhesin (*sfa*), and type 1 pili (*fim*). The bacterial genes *hly* and *cnf*1 are linked physically: *cnf*1 never occurs without *hly*, although the reverse is not true. To determine whether the individual virulence factors were associated with co-colonization, we conducted a bivariate analysis followed by a stepwise

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

logistic regression model. We used both the backward and forward stepping methods including all virulence factors but *fim*, which was present on all isolates, and *cnf*1 because of its linkage with *hly*. Only P pili remained in the model, regardless of whether we used backward or forward stepping. Thus, we fit a final model (table 3, model 2) that included a marker for uropathogenicity, P pili, cunnilingus, and spermicide and condom use. Point estimates were similar to those from the crude analysis. However, we did observe a marginally statistically significant interaction between P pili and uropathogens. P pili had no effect (OR = 1.15, 95 percent CI: 0.57, 2.33) when present on a commensal isolate but were strongly associated with co-colonization when present on a uropathogen, suggesting a synergistic effect. The odds ratios for cunnilingus and for spermicide and condom use were similar to those observed in the couples analysis.

Vaginal-rectal co-colonization within a woman

Women with UTI were significantly more likely to be vaginally colonized with an *E. coli* identical to that found in their rectum (66 percent vs. 18 percent) (table 2). The frequency of carrying the same *E. coli* in the vagina and rectum decreased with time since last engaging in sexual activity. After our adjustment in a logistic regression model (table 3, model 3), women with UTI were 8.4 times (95 percent CI: 4.44, 15.95) more likely than women without UTI to have vaginal-rectal co-colonization with identical *E. coli* strains. The odds of vaginal-rectal co-colonization with the same organism decreased by 25 percent (OR = 0.75, 95 percent CI: 0.63, 0.89) with each day since vaginal intercourse.

DISCUSSION

Male-female rectal-rectal co-colonization with the genetically identical strain, as determined by PFGE, occurred in both UTI and non-UTI couples, but UTI couples had twice the odds of sharing the same *E. coli* strain after we adjusted for covariates associated with co-colonization. Furthermore, uropathogenic strains were associated with almost six times the odds of being shared, and sharing was even greater (OR = 17.0) if the uropathogen had P pili. Increased rectal-rectal co-colonization in UTI couples might be explained by the high levels of *E. coli* present in the urine of an infected woman, increasing the probability of transmission via direct contact. However, given that the presence of P pili increased the odds of sharing, it is likely that uropathogens have additional, yet unknown factors that enhance transmission. The higher rates of vaginal colonization among women with UTI might also be explained by the greater quantities of *E. coli* and the proximity of the urethra to the vagina.

The increased urethral colonization of males in UTI couples suggests that some of the transmission may have occurred through genital contact. Although the numbers were small, all eight urethral isolates from male sex partners of women with UTI were genetically identical to the *E. coli* found in their sex partner's urine and/or vaginal flora, but only two matched an isolate from their own rectum. Thus, it is possible that *E. coli* might be transmitted during vaginal intercourse from the male urethra to a woman's vagina and hence periurethral mucosa and subsequently ascend to the bladder. To do so, the inoculum must be sufficient to lead to colonization, and the male must carry it long enough to transmit the *E. coli* to another sex partner. Of the eight male sex partners of women with *E. coli* UTI who were urethrally colonized with *E. coli*, one had >100,000 cfu/ml. Three of the five males who returned for repeat cultures carried the identical *E. coli*, as determined by PFGE, at both visits, which occurred 3–16 days later. Persistent carriage or reinfection from the female to the male could not be differentiated. If the observed male urethral colonization represents persistent carriage, it is of sufficient duration that transmission to another sex partner might occur. Hence, intercourse could both transfer the pathogen and facilitate introduction of the uropathogen to the bladder. This observation is consistent with our previous follow-up study of women with a first UTI, in which condom use reduced the risk of reinfection with a new strain but not the same strain (15).

In our study, host behaviors as well as *E. coli* characteristics were important determinants of rectal-rectal co-colonization. Among both UTI and non-UTI couples, the incidence of rectal-rectal co-colonization was higher in couples engaging in cunnilingus. Using both condoms and spermicides decreased rectal-rectal co-colonization. This finding was true regardless of whether the couple or the isolate was used as the unit of analysis. Too few couples reported engaging in anal intercourse to enable any conclusions to be drawn. Condom use has been associated with increased risk of UTI (9, 16), but this effect may be due to trauma. Virtually all women who used spermicide did so with condoms; condom users alone had the same co-colonization rates as nonusers. Thus, the observed decrease in rectal-rectal co-colonization when both spermicide and condoms were used is probably attributable to spermicide use. Although spermicides are bacteriostatic, spermicides alone or in combination with a diaphragm increase vaginal colonization with *E. coli* (17). This is the first known report of an association of spermicide use with rectal-rectal co-colonization and therefore needs confirmation.

The adhesin P pili binds to glycolipids found on mucosal surfaces, including the urinary tract and bowel. The same qualities that make P pili important for ascending the urinary tract may enhance the ability of uropathogens to colonize the bowel flora. However, P pili are found in no more than half of all uropathogenic isolates. Thus, additional, yet unknown factors must be extant.

Our study has several limitations. First, our outcome was rectal-rectal colonization and not transmission. Because our study was cross-sectional, we could not prove that isolates were transmitted between couples, although the overall heterogeneity of PFGE patterns between couples compared with the homogeneity within couples suggests that transmission occurred. Prospective studies are required to address this point as well as the direction of transmission. Second, the response rate was somewhat lower than is desirable, probably reflecting the requirement that couples participate. Because one of the most common reasons for refusal was that the woman was hesitant to recruit her sex partner, we suspect that participation was biased toward more committed partnerships or partnerships in which the mone-

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014

tary incentive was more attractive. This possibility might have impacted the prevalence of the behaviors under study; for example, the variety or frequency of sexual behaviors might have been modified but should not have biased the association between these behaviors and co-colonization with the same *E. coli*.

ACKNOWLEDGMENTS

This work was supported by National Institutes of Health grant R01DK35368(BF).

This study would never had been completed without the assistance and support of the University of Michigan Health Service, Caesar Briefer, Director, and Charlotte Williams and all laboratory staff. The authors appreciate the assistance of Bonnie Andree and Lexie Bopp in recruiting study participants, Katie Neighbors in managing the data, and Alison Freeman and Natasha Ghazi in performing many pulsed-field gels.

REFERENCES

1. Kunin CM. Urinary tract infections. Detection, prevention, and management. 5th ed. Baltimore, MD: Williams & Wilkins, 1997.
2. Foxman B, Riley L. Molecular epidemiology: focus on infection. Am J Epidemiol 2001;153:1135–41.
3. Foxman B, Barlow R, d'Arcy H, et al. Urinary tract infection: estimated incidence and associated costs. Ann Epidemiol 2000; 10:509–15.
4. Krieger JN, Ross SO, Simonsen JM. Urinary tract infections in healthy university men. J Urol 1993;149:1046–8.
5. Hooton TM, Stapleton AE, Roberts P, et al. Perineal anatomy and urine-voiding characteristics of young women with and without recurrent urinary tract infections. Clin Infect Dis 1999; 29:1600–1.
6. Manges AR, Johnson JR, Foxman B, et al. Widespread distribution of urinary tract infections caused by a multidrug-resistant *Escherichia coli* clonal group. N Engl J Med 2001; 345:1007–13.
7. Foxman B, Zhang L, Tallman P, et al. Transmission of uropathogens between sex partners. J Infect Dis 1997;175:989–92.
8. Foxman B, Geiger A, Palin K, et al. First time urinary tract infection and sexual behavior. Epidemiology 1995;6:162–8.
9. Foxman B, Marsh JV, Gillespie B, et al. Condom use and first time urinary tract infection. Epidemiology 1997;8:637–41.
10. Foxman B, Chi JW. Health behavior and urinary tract infection. J Clin Epidemiol 1990;43:329–37.
11. Hooton TM, Scholes D, Hughes JP, et al. A prospective study of risk factors for symptomatic urinary tract infection in young women. N Engl J Med 1996;335:468–74.
12. Onderdonk AB, Zamarchi GR, Rodriguez ML, et al. Quantitative assessment of vaginal microflora during use of tampons of various compositions. Appl Environ Microbiol 1987;53:2774–8.
13. Plos K, Connel H, Jodal U, et al. Intestinal carriage of *P* fimbriated *Escherichia coli* and the susceptibility to urinary tract infection in young children. J Infect Dis 1995;171:625–31.
14. Foxman B, Zhang L, Palin K, et al. Bacterial virulence characteristics of *Escherichia coli* isolates from first-time urinary tract infection. J Infect Dis 1995;171:1514–21.
15. Foxman B, Gillespie B, Koopman, J, et al. Risk factors for second urinary tract infection among college women. Am J Epidemiol 2000;151:1194–205.
16. Fihn SD, Boyko EJ, Normand EH, et al. Association between use of spermicide-coated condoms and *Escherichia coli* urinary tract infection in young women. Am J Epidemiol 1996;144: 512–20.
17. Hooton TM, Roberts PL, Stamm WE. Effects of recent sexual activity and use of a diaphragm on the vaginal microflora. Clin Infect Dis 1994;19:274–8.

Downloaded from http://aje.oxfordjournals.org/ at Pennsylvania State University on April 21, 2014