

## Original Study

# Culture of Non-Genital Sites Increases the Detection of Gonorrhea in Women

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**Abstract.** *Study Objectives:* Although gonorrhea may infect the cervix, rectum, or pharynx of women, culturing non-cervical sites is rare outside of sexually transmitted disease (STD) clinics. This study aims to compare rectal and pharyngeal gonorrhea prevalence in adolescent and adult women and to calculate the percentage of cases that would be missed with cervical culture alone.

*Design:* Retrospective review of two laboratory databases.

*Setting:* STD clinic (2006–2007) and urban children's hospital (2003–2007).

*Participants:* Adolescent women (age 14–21, n = 16,039) in the hospital database; adolescent (n=525) and adult (age >21) women (n = 1424) in the STD database.

*Main Outcome Measures:* Prevalence of gonorrhea by group and culture source.

*Results:* Cervical plus additional culture was performed in 76% of adult STD, 52% of adolescent STD, and 2% of adolescent hospital samples. Pharyngeal gonorrhea prevalence in the adolescent hospital (3.5%) was similar to adolescent STD (6.8%,  $P = 0.1$ ) and adult STD (2.5%,  $P = 0.4$ ) samples. Rectal gonorrhea prevalence in adolescent hospital (2.9%) was lower than adolescent STD (13.4%,  $P = 0.01$ ) but not adult STD (5.2%,  $P = 0.6$ ) samples. Pharyngeal gonorrhea occurred in 0.6–3.4% and rectal gonorrhea in 0–2.7% of women with a negative cervical culture. Culturing only the cervix missed 20–40% of adult STD, 14–26% of adolescent STD, and 11% of adolescent hospital infected cases.

*Conclusions:* Pharyngeal gonorrhea is as high in adolescent women from a children's hospital as in adult women from an STD clinic. Without pharyngeal culture, 11–26% of infected adolescent women would be missed. Increased pharyngeal testing may impact the gonorrhea epidemic among adolescent women.

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**Key Words.** Women—Adolescent—Gonorrhea—Pharynx—Sexually transmitted disease

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### Introduction

Genital gonorrhea is a national public health concern because of its high prevalence and ability to cause serious sequelae among infected women. The national prevalence of 118 genital cases per 100,000 women in 2007 is much higher than the goal of 19 cases per 100,000 women set by Healthy People 2010.<sup>1,2</sup> Ominously, surveillance shows that between 2004 and 2007, the prevalence in Cincinnati has increased from 193 to 267 cases per 100,000 women. While over 95% of women with cervical gonorrhea are asymptomatic,<sup>3</sup> women with gonorrhea are at risk for serious consequences such as pelvic inflammatory disease<sup>4,5</sup> and disseminated gonococcal infections.<sup>6,7</sup> The high proportion of asymptomatic infections makes screening of “at risk” women necessary because untreated cases present risks to the patient and can lead to transmission to others. Thus, current guidelines recommend screening all sexually active women under age 26 for genital gonorrhea.<sup>8</sup>

In addition to the urogenital tract (cervix and urethra), gonorrhea can also infect the rectum and pharynx. In most of these cases, concurrent cervical infection is present. For example, older studies have shown that while up to 60% of adult women with cervical gonorrhea also have a positive rectal culture, isolated rectal infections are reported in 2–10% of cases.<sup>9,10</sup> Untreated rectal infections can lead to symptomatic proctitis and are a significant source of disease transmission for men who have sex with men. However, the consequences for women are not

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well defined. The overall prevalence of pharyngeal gonorrhea in women in older studies ranges from 2–5%, and up to 20% of women with cervical gonorrhea were co-infected at the pharynx.<sup>11–13</sup> However, isolated pharyngeal infection occurred in only 2–5% of infected women. The clinical importance of untreated pharyngeal infections in women is still unclear. Some studies have shown spontaneous resolution of pharyngeal infection.<sup>14,15</sup> However, other studies have shown that pharyngeal gonorrhea in women can be transmitted to a male partner during fellatio.<sup>12,13</sup> It is estimated that up to 2% of gonococcal urethritis cases result from fellatio.<sup>11</sup> In a 1989 study of adolescent women, routine pharyngeal culturing showed no isolated pharyngeal infections in a low risk (3.5% prevalence) population, and only 1% of infected women had isolated pharyngeal infections in a high risk (33% prevalence) population.<sup>16</sup> We could find no recent studies examining the benefit of screening for asymptomatic rectal and pharyngeal gonorrhea in adolescent women.

In Cincinnati's sexually transmitted disease (STD) clinic, providers obtain a comprehensive sexual history and routinely screen women for asymptomatic rectal and pharyngeal gonorrhea if a history of oral or anal sex is given. In other settings, providers vary in their ability to obtain a complete sexual history, and culture of non-genital sites is a matter of provider choice. In either setting, some patients may under-report oral or anal sexual practices. Therefore, it is possible that the pharynx or rectum could be a reservoir for gonorrhea that helps to maintain high rates of infection in young women in Cincinnati.

There are three main objectives for this study: First, we wish to update the estimates that are several decades old of oral and rectal gonorrhea prevalence in women. Second, in our city, with its known high prevalence of genital gonorrhea, we wish to compare the prevalence of cervical, pharyngeal, and rectal gonorrhea in three groups: adolescent women 14–21 years old and adult women over 21 years old attending an STD clinic, and adolescent women 14–21 years old seen at a children's hospital. Finally, we wish to determine if culturing the rectum and pharynx increases detection of gonorrhea in any of these groups above culture of the cervix alone. These findings may inform clinical decisions to offer screening for non-genital gonorrhea infections and may allow a cost-benefit analysis of expanded testing in the future. Such information may direct efforts to control the epidemic of gonorrhea in high-prevalence areas such as Cincinnati.

## Materials and Methods

This study was a retrospective review of de-identified data from two sources. We reviewed two years of data

(2006–2007) from an electronic clinical database at the local health department's STD clinic. From this database, we exported de-identified data that was limited to age, source of gonorrhea culture, and culture result. During this time frame, all gonorrhea testing was performed using culture, and nucleic acid amplification was not available. We stratified this sample into those aged 14–21 years (adolescent) and those aged  $\geq$  age years (adult). In addition, we reviewed 5 years of data (2003–2007) from the electronic data warehouse of an urban children's hospital that has an active adolescent clinic and large adolescent population. Data was de-identified and included only gender, age, race, source of gonorrhea culture, and culture result. Although gonorrhea testing using nucleic acid amplification became available during this review period, it was not widely used (<5% of cervical gonorrhea testing), and these results were not included in this database. The study was approved by the institutional review boards of both the health department and the children's hospital.

We generated descriptive frequencies of total proportion of positive gonorrhea cultures and stratified frequencies by source of specimen, age, and site of care. We estimated the clinical utility of additional cultures by calculating the percentage of infections that would be missed by cervical culture alone. For each estimate, we determined point estimates and 95% confidence intervals and performed chi-square tests to assess the statistical significance of any differences found.

## Results

From the STD clinic there were 1949 visits that included a cervical culture. Gender and race were not indicated in the STD database, so cervical culture was used as a proxy for female gender. Twenty-seven percent of women at the STD clinic ( $n=525$ ) were age 14–21, matching the children's hospital sample, and the remainder ( $n=1424$ ) were over age 21. From the children's hospital there were 16,039 patient visits made by adolescent and young adult females aged 14–21 years that included at least one cervical gonorrhea culture. These visit records comprise our three samples.

## Sample Characteristics

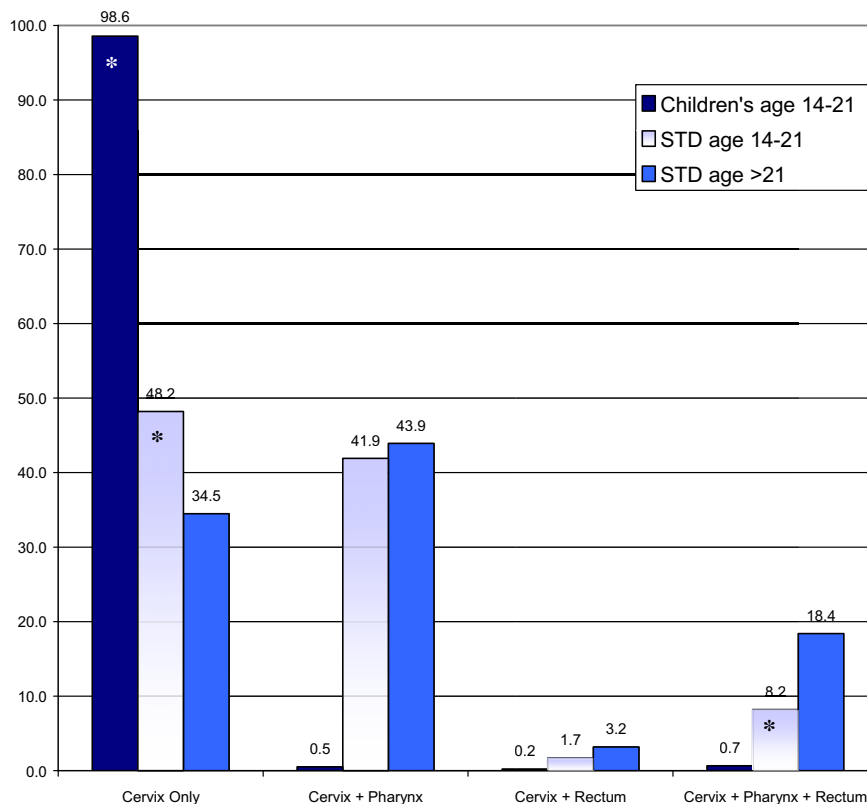
Women at the STD clinic were older than women at the children's hospital. The median age (range) for each group was as follows: Children's sample, 17.9 years (14–21); STD adolescent sample, 18.9 years (14–21); STD adult sample, 33.2 years (22–59), and these differences were significant at  $P < 0.01$  using Student's *t*-test. At the children's hospital, 76% of

patients were black, 21% white, and 3% other. Race data were not available from the STD clinic sample.

Practice patterns differed between the two sites, and by age (Fig. 1). The cervix was the only source cultured for 15,813 (98%) of women at the children's hospital. At the STD clinic, cervix was the sole source cultured for 253 of 525 (48%) of adolescent and 491 of 1424 (34%) of adult women. These differences were significant using a chi-square test at  $P < 0.01$ . At the STD clinic, adult women were more likely than adolescent women to be cultured at the cervix, pharynx, and rectum (262 of 1424 [18.4%] vs. 43 of 525 [8.2%],  $P < 0.001$ ). Only 109/16,039 (0.7%) women seen at the children's hospital were cultured at the cervix, rectum, and pharynx. The cervix and pharynx were both cultured for 220 of 525 (42%) of adolescent and 625 of 1424 (44%) of adult women at the STD clinic, which was not statistically different. However, when looking at any pharyngeal culture, adult women at the STD clinic were more likely receive a pharyngeal culture (887 of 1424, 62%) than adolescent women at the STD clinic (263/525, 50%) or adolescent women at the children's hospital (195/16,039, 1.2%; significant at  $P < 0.001$ ). Only 86 of 16,039 (0.5%) of women at the children's hospital were cultured at both the cervix and pharynx. The cervix and

rectum were both cultured for 9 of 525 (1.7%) of adolescent and 46 of 1,424 (43.2%) of adult women at the STD clinic, which was not statistically different. Only 31 of 16,039 (0.2%) of women at the children's hospital were cultured at both the cervix and rectum.

Point estimates and 95% confidence intervals for the prevalence of gonorrhea by anatomic source and site of care are displayed in Table 1. The prevalence of gonorrhea in the cervix did not differ between the children's hospital and the STD adolescent samples. However, the prevalence of cervical infection was significantly lower among adult women seen at the STD clinic (5.6%) compared to adolescents at either site. The prevalence of any pharyngeal gonorrhea among adolescent women seen in the STD clinic was similar to that seen in the children's hospital sample ( $P = 0.1$ ) but significantly higher than that seen in adult women at the STD clinic ( $P = 0.001$ ). Isolated pharyngeal infection (in the presence of a negative cervical culture) was highest among adolescent women seen in the STD clinic, compared to adult women in the STD clinic and adolescents seen at the children's hospital. However, this only reached statistical significance for the difference between adolescent and adult women at the STD clinic ( $P = 0.03$ ). Isolated rectal gonorrhea (in the presence of a negative



**Fig. 1.** Practice pattern: Distribution of sources of gonorrhea cultures by site of care and age. All women in the Children's Hospital sample were < age 22 ( $n = 16,039$ ). There were 525 women in the STD sample age 14–21, and 1424 women in the STD sample  $\geq$  age 22. Bars represent the percent of each culture pattern in each sample.

**Table 1.** Point Estimates and 95% Confidence Intervals for the Prevalence of Gonorrhea by Anatomic Source and Site of Care. *P* Values for the Difference in Prevalence Between Sites are Assessed by Fisher's Exact and Chi-square Tests

	Children's Hospital Age 14–21			STD Clinic Age 14–21			STD Clinic Over 21		
	Number Positive/ Number Tested	Gonorrhea Prevalence % (95% CI)		Number Positive/ Number Tested	Gonorrhea Prevalence % (95% CI)		Number Positive/ Number Tested	Gonorrhea Prevalence % (95% CI)	
Any cervix positive	1409 / 16039	8.8	8.3–9.2	49 / 525	9.3	6.8–11.8	80 / 1424	5.6	4.4–6.8
Any pharynx positive	7 / 195	3.5	1.0–6.2	18 / 263	6.8	3.8–9.9	22 / 887	2.5	1.4–3.5
Any rectum positive	4 / 140	2.9	0.1–5.7	7 / 52	13.4	3.9–23	16 / 308	5.2	2.7–7.7
Cervix negative/ pharynx positive	1 / 179	0.6	.01–1.7	8 / 237	3.4	1.4–6.5	11 / 841	1.3	0.7–2.3
Cervix negative/ rectum positive	0 / 130	0	0–28	1 / 45	2.2	0.1–12	8 / 295	2.7	1.2–5.3

\**P* values comparing CH age 14–21 to STD age 14–21.

†*P* values comparing STD over 21 to CH age 14–21.

‡*P* values comparing STD 14–21 to STD over 21.

cervical culture) occurred in 0–2.7% of women, and was not significantly different between the three samples.

To evaluate the utility of testing at non-cervical sites, we examined the subgroups of patients at the STD clinic and the children's hospital who were simultaneously cultured at multiple anatomic sites.

Of the children's hospital sample, 109 patients were cultured at all three sites, as shown in [Table 2](#). Cervical culture detected 8 cases of gonorrhea (prevalence 7.3%), and three subjects (37%) were co-infected at the rectum (2) or pharynx (1). However, the additional cultures did not identify any new infected cases. In 86 patients, both the cervix and the pharynx were cultured. The cervical culture detected 8 cases, and adding the pharyngeal culture detected five (62%) co-infections and one new case. The prevalence of infection was 10.5%. Cervical culture alone missed one of nine true infections (11%). There were 31 women who were tested at both the cervix and the rectum; two had cervical infections (6.5% prevalence), both (100%) were co-infected at the rectum, but no new cases were detected.

Among adolescent women age 14–21 tested at the STD clinic, 43 patients were cultured at all three anatomical sites. Cervical culture detected six cases and additional cultures detected five co-infections (85%) (two rectal only and three at both the rectum and pharynx), plus one isolated pharyngeal infection. The overall prevalence of infection was 16.3% and the proportion of cases missed by cervical culture alone was one of seven (14%). Among the subgroup of 220 patients who were cultured at both the cervix and the pharynx, the prevalence of gonorrhea was 12.3%. Cervical culture detected 20 cases and adding the pharyngeal culture detected seven (35%) concurrent infections and seven isolated pharyngeal infections without a cervical infection. Cervical culture alone would have missed 7 of 27 (26%) of truly infected patients. There were nine adolescent women at the STD clinic tested at both the cervix and the rectum, with a prevalence of 22% infected with gonorrhea. Cervical culture detected one case and adding the rectal culture detected one additional case. The cervical test alone would have missed 50% of infected women.

Among adult women over age 21 tested at the STD clinic, 262 patients were cultured at all three anatomical sites. Cervical culture detected 10 cases and additional cultures detected seven co-infections (70%) plus six rectal and one isolated pharyngeal infections. The overall prevalence of infection was 6.4% and the proportion of cases missed by cervical culture alone was seven of 17 (40%). There were 625 women who were cultured at both the cervix and the pharynx; 45 cases were detected for an overall gonorrhea prevalence of 7.2%. Cervical

**Table 2.** Estimates (and 95% Confidence Intervals) of the Proportion of Gonorrhea Cases that were Missed by Cervical Culture, by Culture Pattern, Site of Care, and Age

Sample Population	Sources Cultured	Individuals Tested	Total Infected Individuals N (%)	Infections Missed by Cervical Culture N (%)	95% CI (%)
Children's hospital < age 22	Cervix + Pharynx + Rectum	109	8 (7.3%)	0	
	Cervix + Pharynx	86	9 (10.5%)	1 (11%)	0.3–48%
	Cervix + Rectum	31	2 (6.5%)	0	
STD < age 22	Cervix + Pharynx + Rectum	43	7 (16.3%)	1 (14%)	0.3–58%
	Cervix + Pharynx	220	27 (12.3%)	7 (26%)	11–46%
	Cervix + Rectum	9	2 (22%)	1 (50%)	0.1–98%
STD ≥ age 22	Cervix + Pharynx + Rectum	262	17 (6.4%)	7 (40%)	18–67%
	Cervix + Pharynx	625	45 (7.2%)	9 (20%)	9–34%
	Cervix + Rectum	46	5 (10.8%)	2 (40%)	5–85%

culture detected 36 cases, and adding the pharyngeal culture detected nine (25%) concurrent infections and nine isolated pharyngeal infections without a cervical infection. Cervical culture alone would have missed 9 of 45 (20%) of infected women. There were 46 adult women at the STD clinic who were tested at both the cervix and the rectum, with a prevalence of 10.8% infected with gonorrhea. Cervical culture detected three cases and adding the rectal culture detected one co-infection and two additional cases. The cervical culture alone would have missed two of five (40%) of infected women.

## Discussion

We were surprised to discover that the prevalence of cervical and pharyngeal gonorrhea among adolescents seen in a children's hospital setting matched the rates of infection among adolescent women at an STD clinic. These findings are in contrast to those reported by Brown et al in a 1989 study.<sup>16</sup> Additionally, we showed that among women seen at an STD clinic, the prevalence of pharyngeal gonorrhea is higher in adolescent women (age 14–21) than in adult women (over age 21), even with a practice pattern where pharyngeal cultures are performed more often in adult women. In keeping with current knowledge and prior studies, we found a higher prevalence of cervical gonorrhea among adolescent women than in an adult STD population.

In all three samples, women with cervical gonorrhea had a high prevalence of co-infection at the pharynx (25–60%) and rectum (30–85%). Our results estimate that culturing a woman only at the cervix misses 20–40% of infected cases in adult women and 14–50% of adolescent women seen in an STD setting. Compared to culturing both the cervix and the pharynx, we found that culturing only the cervix missed an estimated 11% of truly infected adolescent women seen in a children's hospital setting. However, because

culturing the pharynx was rarely performed among adolescents, the 95% confidence interval around this point estimate is extremely wide (0.3–48%).

The prevalence of pharyngeal gonorrhea among women whose cervical culture is negative ranges from 0.6 to 3.4% in the three samples we studied. Data from the National Survey on Family Growth (2002) show that oral sex is common in adult and adolescent women: 80% of 18–24-year-old women and 90% of women age 25–29 report a history of oral sex with a male.<sup>17</sup> Giving oral sex provides an opportunity for pharyngeal gonorrhea infections. Even the lowest pharyngeal prevalence that we found is twice as high as the prevalence of genital gonorrhea reported in the general population (0.24%),<sup>18</sup> 30 times higher than the goal of 19 cases per 100,000 women set by Healthy People 2010<sup>2</sup> and as high as the prevalence of genital gonorrhea (0.4%) found among women age 18–26, which is the subgroup for whom routine annual screening is recommended.<sup>3</sup>

The prevalence of rectal gonorrhea was significantly higher for adolescent women seen in an STD setting than for the other two samples. However, data from the National Survey on Family Growth (2002) show that younger women ( $\leq$  age 24) are less likely to report anal sex than older women ( $\geq$  age 25).<sup>12</sup> The prevalence of concurrent rectal gonorrhea increases with the duration of cervical infection, because time increases the chance of perineal contamination.<sup>19</sup> Thus, one explanation may be that adolescent women seen in an STD clinic have less access to health care and a longer duration of cervical gonorrhea infections, leading to a higher prevalence of rectal infections from perineal contamination rather than from anal sex.

The practice pattern of which sites are cultured for gonorrhea at the children's hospital bears no relationship to reported sexual practices in adolescent women. This may be expected because there are no guidelines recommending gonorrhea culture of non-genital sites



for adolescent women. The distribution of anatomic sites cultured for women at the STD clinic reflects the reported distribution of sexual practices for adult women, but not for adolescent women. This suggests that in STD settings where questions regarding non-genital exposure and culturing of these sites are routine, adolescent women may be failing to accurately report their sexual behavior. In addition, the prevalence of infection did not differ by culture pattern at the children's hospital, suggesting that providers were not adept at identifying a subgroup of women for whom additional testing was indicated.

The study has several limitations. Despite the large databases, the actual sample sizes of adolescents tested at the rectum and pharynx are small, which limits statistical tests of association and produces wide confidence intervals. Not all patients were cultured at the cervix, rectum, and pharynx, and our data sources did not indicate why each patient received certain tests. Thus the choice of culture sites was biased by provider practice. A more complete study would compare universal screening of all three anatomical sites. Also, because Cincinnati has higher prevalence of gonorrhea than other areas of the country, our results may not apply to other places where the prevalence of gonorrhea is lower.

Several studies now suggest that non-culture methods such as nucleic acid amplification are better than culture for detection of pharyngeal and rectal gonorrhea.<sup>20,21</sup> However, these methods would also increase the costs of screening. In order to balance the need for better detection with cost control, future studies might consider combining specimens from several anatomic sources on a single culture or nucleic acid amplification test.

## Conclusions

Our data reflect current practices, where culturing of non-genital sites is routine in an STD clinic and rare in an adolescent population of women. In the STD clinic, culturing of the cervix, pharynx, and rectum increases the number of infected women detected over single cervical culture, and should be advocated. Because adolescent women may not report sexual behaviors as accurately as adult women, "routine" culturing of the pharynx and rectum may improve the detection of infected individuals. Given that the prevalence estimates of pharyngeal gonorrhea are similar for adolescents seen in a children's hospital and an STD clinic, that both are higher than the national prevalence of genital gonorrhea in adolescent women, and that pharyngeal gonorrhea is associated with disease transmission, the addition of pharyngeal cultures may be indicated for adolescent women. Such routine culturing might uncover a subset of women who are

contributing to the ongoing epidemic of gonorrhea in our community.

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