

# Clinical presentation of genital warts among circumcised and uncircumcised heterosexual men attending an urban STD clinic

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## Abstract

**Introduction**—A recent study comparing heterosexual men with and without confirmed sexually transmitted diseases (STDs) in an urban STD clinic showed that uncircumcised men were less likely than circumcised men to have genital warts detectable by clinical examination (adjusted odds ratio 0.7, 95% confidence interval 0.4, 0.9). Based on these initial findings we hypothesised that the appearance and anatomic distribution of genital warts, and possibly treatment response, may be different for circumcised and uncircumcised men.

**Methods**—The anatomic location, appearance, number of warts, and response to treatment was investigated through review of medical records of 459 heterosexual men with genital warts detected in 1988.

**Results**—Age- and race-adjusted estimates indicated that among men with genital warts, warts were detected much more commonly on the distal penis—that is, the corona, frenulum, glans or urethral meatus-, among uncircumcised men (26%) than among circumcised men (3%) (OR 10.0, 95% CI 3.9, 25.7). Where the appearance was specified, warts were more often described as condylomatous in uncircumcised men and slightly more often as papular in circumcised men. No significant difference between circumcised and uncircumcised men was seen in the number of return visits to the clinic for persistent warts after treatment with liquid nitrogen: 2.2 visits for 19 uncircumcised men and 2.3 visits for 149 circumcised men.

**Conclusion**—Circumcised men were more likely than uncircumcised men to have genital warts, but when present, warts were more often located on the distal portion of the penis among uncircumcised men. This paradox is not understood, but could reflect either non-specific resistance to proximal penile warts conferred by the foreskin, or heightened susceptibility to various HPV types in uncircumcised men, some of which may confer subsequent immunity to genital warts.

warts occur more commonly among uncircumcised men than among circumcised men.<sup>1-3</sup> However, in a recent study using the medical records of 2776 heterosexual men attending the Seattle-King County Sexually Transmitted Disease Clinic at Harborview Medical Center, the prevalence of genital warts among circumcised men (17.6%) exceeded that of uncircumcised men (11.0%) men, ( $p < 0.001$ ).<sup>4</sup> The relationship persisted after adjusting for age, race, other STDs, place of residence, and the number of sexual partners in the previous month. Also, circumcised men were more likely than uncircumcised men to report a history of previous warts (12.9% vs 7%,  $p < 0.001$ ). In contrast, uncircumcised men were more likely to have syphilis (OR 4.0, 95% CI 1.9, 8.4), and gonorrhoea (OR 1.6, 95% CI 1.2, 2.2). Our results may differ from those of previous studies because of our restriction to heterosexual men and our adjustment for more confounding variables. In view of these results, the present analysis was undertaken to characterise differences in the anatomic location, appearance, number, and apparent treatment response of genital warts based on circumcision status in this population.

## Methods

A review of heterosexual men seen in the Seattle-King County STD clinic in Seattle, Washington from January 1988 to December 1988 identified 463 men diagnosed clinically with genital warts. Details of this study have been reported.<sup>4</sup> Briefly, information was available on subject demographic characteristics, symptoms, sexual history, prior STDs, and clinical and laboratory diagnostic findings. Circumcision status was identified and recorded by the clinician.

For the present study, the medical records of 459 of the 463 men given a diagnosis of genital warts during 1988 were reviewed and information was abstracted on the location, number, and appearance of the exophytic warts (the medical records of four subjects were not available). The location of warts was categorised as distal penis (including the glans, coronal sulcus, urethral meatus, and frenulum), proximal penis (including the shaft and base of the shaft), both (distal and proximal), other (including scrotum, thighs, perianal area, and inguinal fold), or location not recorded. Four uncircumcised subjects had warts on the foreskin and were excluded from the analysis. Multiple locations that

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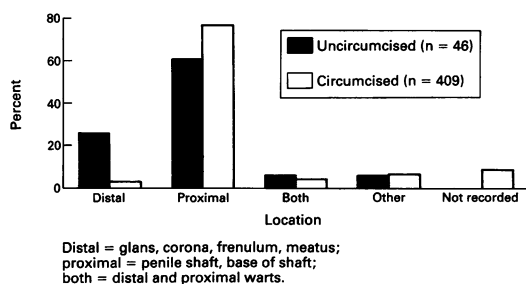
## Introduction

Previous studies have suggested that genital

Table 1 Characteristics of heterosexual men diagnosed with genital warts according to circumcision status, Seattle-King County STD clinic, 1988

Characteristic	Uncircumcised n = 46 (%)	Circumcised n = 409 (%)
Age (years)		
14-19	6 (13.0)	25 (6.1)
20-29	27 (58.6)	225 (55.0)
30-70	10 (21.7)	138 (33.7)
unknown	3 (6.5)	21 (5.1)
Race/ethnicity		
white	21 (45.7)	312 (76.3)
African-American	14 (30.4)	72 (17.6)
other	6 (13.0)	16 (3.9)
unknown	5 (10.9)	9 (2.2)
Number of sexual partners in previous month		
0	5 (10.9)	51 (12.5)
1	30 (65.2)	265 (64.8)
2+	9 (19.6)	70 (17.1)
unknown	2 (4.4)	23 (5.6)
Reported history of warts	11 (23.9)	162 (39.5)
Current complaint of genital lesions at this clinic visit	30 (65.2)	261 (63.8)

Figure Location of genital warts in heterosexual men, Seattle-King County STD Clinic, 1988.



included sites other than the penis were coded on the basis of the location of the penile warts, that is, a subject with warts on the glans and the inguinal fold was classified as distal penis. The appearance of warts was categorised as condylomatous, papular, other (verruca vulgaris), or appearance not recorded. The number of warts was categorised in three groups: 1, >1, or number not recorded.

Demographic and sexual characteristics of uncircumcised and circumcised men were compared. The number, anatomic distribution, and appearance of genital warts was also compared based on circumcision status. Among men with genital warts, age- and race-adjusted odds ratios relating circumcision status with the location, appearance, and

Table 2 Relationship between lack of circumcision and the anatomic location, appearance, and number of genital warts in heterosexual men, Seattle-King County STD clinic, 1988

	Uncircumcised n (%)	Circumcised n (%)	Crude odds ratio	Adjusted† odds ratio (95%CI)
Location				
proximal*‡	28 (61)	313 (77)	1.0	
distal§	12 (26)	12 (3)	11.2	10.0 (3.9, 25.7)
other/not recorded	6 (13)	84 (21)		
Appearance				
papule*	6 (13)	59 (14)	1.0	
condyloma	12 (26)	57 (14)	2.1	2.5 (0.8, 7.6)
other/not recorded	28 (61)	293 (72)		
Number				
1*	13 (28)	88 (22)	1.0	
>1	28 (61)	286 (70)	0.7	0.7 (0.3, 1.4)
other/not recorded	5 (11)	35 (9)		

\*referent category

†adjustment for age group (14-19, 20-29, 30+) and race/ethnicity (white, African-American, other).

‡proximal = penile shaft or base of shaft

§distal = coronal sulcus, frenulum, glans, urethral meatus.

number of warts were calculated by logistic regression analysis.<sup>5</sup> The response to treatment could not formally be compared in circumcised and uncircumcised men; clinic patients were generally advised to return for repeated treatment as long as warts persisted, but complete follow-up of all 459 men until the warts had resolved was not attempted by the clinic staff. Therefore, as a surrogate for treatment response, we compared the number of follow-up clinic visits at which persistent warts were detected among the 345 men treated with liquid nitrogen applications at the initial clinic visit. All analyses were done using SAS.

## Results

Among heterosexuals with genital warts (table 1), circumcised men were more likely than uncircumcised men to be 30 years or older, (33.7% vs 21.7%,  $p = 0.05$ ), white, (76.3% vs 45.7%,  $p < 0.001$ ), and to report a history of warts (39.5% vs 23.9%,  $p < 0.01$ ). No major differences were noted between circumcision groups with respect to the number of sexual partners in the previous month, and approximately two-thirds of both groups reported symptoms of genital lesions when specifically queried about lesions prior to examination.

The figure shows that the penile shaft, including the base of the shaft, was the most common location for genital warts in both circumcised and uncircumcised men. However, circumcised men were more likely to have warts in this location (77% vs 61%,  $p < 0.001$ ), whereas uncircumcised men were much more likely to have distal penile warts (26% vs 3%,  $p < 0.0001$ ).

Age- and race-adjusted results (table 2) comparing the presence of distal penile warts with proximal penile warts also indicate that distal warts are more likely in uncircumcised men (OR 10.0, 95% CI 3.9, 25.7). The presence of multiple wart lesions was unrelated to circumcision status. Condylomas were more likely than papules in uncircumcised men (OR 2.5, 95% CI 0.8, 7.6), but the appearance of warts was only specified for a small subset of subjects.

Approximately 50% of uncircumcised and circumcised subjects initially treated with liquid nitrogen for their genital warts did not return to the clinic for follow-up visits (table 3). Of those who returned, the mean number

Table 3 Clinic visits of heterosexual men with venereal warts treated with liquid nitrogen by circumcision status, Seattle-King County STD clinic, 1988

	Uncircumcised (n = 39)	Circumcised (n = 306)
Clinic visits		
follow-up visit with clearing of venereal warts	5 (13)	28 (9)
1 to 6 follow-up visits without clearing of venereal warts	14 (36)	121 (40)
no follow-up visits	20 (51)	157 (51)
Among those who returned to the clinic		
mean number of visits with warts detected	2.2	2.3

Table 4 Comparison in the anatomic distribution of genital warts in men seen at the STD clinic, Seattle, Washington, 1988, and St. Thomas' Hospital<sup>3</sup>, London, 1967-1970, and at the Mayo Clinic<sup>6</sup> Rochester, Minnesota, 1950-1978

Anatomic location of warts	Percentage of subjects affected				
	Seattle-King County-STD Clinic			St. Thomas' Hospital	Mayo Clinic*
	uncircumcised (n = 50)	circumcised (n = 409)	All cases (n = 459)	All cases (n = 191)	All cases (n = 246)
Frenulum, corona, and glans	30	6	8	52	10
Prepuce (all parts)	8	—	0.9	33	8
Urethral meatus	4	2	2	23	10
Shaft of penis	64	81	79	18	51
Other	12	14	14	10	38
Not recorded	2	9	8	—	—

\*includes patients seen at the only private practice group in Rochester during the study period.

of visits with warts detected was virtually identical between circumcision groups: 2.2 visits for uncircumcised men and 2.3 visits for circumcised men.

### Discussion

This review of medical records of heterosexual men found to have genital warts at our STD clinic in 1988 shows that warts were more likely to be distal, and to have a condylomatous appearance, among uncircumcised men than among circumcised men. However, the response of genital warts to liquid nitrogen application appeared comparable in the two groups.

In the present study, the foreskin itself was seldom affected, with only four subjects having warts on the inner or outer surface of the foreskin. These four subjects were excluded from the analysis since circumcised men do not have a comparable anatomic site at risk for infection; their inclusion would have elevated the positive relationship between uncircumcised status and distal penile warts.

A possible concern is the higher proportion of circumcised men (9%), compared with uncircumcised men (2%) who did not have the location of wart lesions recorded in their medical record. It could be argued that if most, or all, of these circumcised men actually had distal warts, the positive relationship between the presence of a foreskin and distal penile warts would disappear. However, even if we conservatively assume that all the circumcised men with unspecified wart locations (n = 38) had distal penile warts, there would still be a higher proportion of uncircumcised men with genital warts on the distal penis (OR 2.7, 95% CI 1.2, 5.4).

The relationship between the appearance of warts and circumcision status in this population is consistent with a study from St. Thomas' Hospital, which indicated that fleshy hyperplastic warts, or classic venereal warts, were most common on the glans and the inner lining of the foreskin among uncircumcised men.<sup>3</sup> The anatomic distribution of genital warts found in the present study, and in studies from St. Thomas' Hospital<sup>3</sup> and the Mayo Clinic,<sup>6</sup> are compared in Table 4. In contrast to both the present study and the Mayo Clinic study, distal penile warts were more common than proximal warts in the St. Thomas' Hospital study. This discrepancy could be due in part to the high percentage of

men who were uncircumcised in the St. Thomas' Hospital study (79%).

In contrast to our findings, a Canadian Army study found that uncircumcised status was more common among active duty men with warts than among recruits without warts.<sup>1</sup> However, differences between these two groups of Canadian men in age, sexual activity, and other factors could have strongly influenced the study results. Age-adjusted analyses from the Public Health Department Special Treatment Clinic in Perth, Australia, suggested uncircumcised men were more likely than circumcised men to have warts (OR 1.5, 95% CI 1.0, 2.4).<sup>2</sup> Discrepancies with our results could be due to our restriction to heterosexual men, our adjustment for confounding factors, and any systematic differences in health seeking behavior between circumcised and uncircumcised men residing in the two countries.

In summary, among heterosexual men at our STD clinic, uncircumcised men had a lower prevalence of genital warts than circumcised men, yet when warts occurred in uncircumcised men, they were more likely to be distal warts under the foreskin. It is possible that the less cornified epithelium of the distal penis within the preputial sac has increased susceptibility to HPV, including those types causing condylomas. A higher incidence of early subclinical, subpreputial HPV infection could promote immunity to subsequent penile condylomata. The series of men at our STD clinic may include a high proportion who have already experienced such an infection and acquired some immunity. Alternatively, the presence of the foreskin may confer nonspecific protection of the proximal penis from acquisition of HPV infection.

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