# Carcinoma In Situ of the Penis in a 76-Year-Old Circumcised Man

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The commonly believed notion that circumcised men cannot develop penile cancer can result in delays in diagnosis. Recent medical literature has failed to confirm the protective effect of circumcision on penile neoplasms. Physicians need to be aware that men circumcised after 1 month of age may be at higher risk for penile cancer than those never circumcised.

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commonly held misperception in modern medicine is that circumcised men cannot develop neoplasms of the penis.<sup>1</sup> This misperception can be traced to a single 1932 article by Wolbarst,<sup>2</sup> a procircumcision advocate who also proclaimed circumcision as the cure for everything from masturbation to epilepsy to infant death.<sup>3</sup> This often cited paper based its conclusion on gathered reports of penile cancer from hospitals. No attempt was made to confirm circumcision status, and no control group was employed. None of the cases of penile cancer occurred in Jewish men circumcised at birth, prompting Wolbarst to conclude that circumcision prevented penile cancer. Until recently, this conclusion has not been properly studied or challenged. As circumcision gained popularity early in this century, the number of circumcised men reaching the age when penile cancer becomes apparent is rapidly increasing. Concomitantly, the number of circumcised men with penile cancer is already beginning to increase.<sup>4</sup> The following report demonstrates the potential damage resulting from this misperception.

# CASE REPORT

A 72-year-old white man presented to his physician in August 1992 with several millimeters of what was described in the chart as "white erythema" on the right glans penis. The lesion had been treated by a wologist with "creams." The patient was referred again to the urologist, but delayed the appointment until his follow-up cystoscopy for a papillary, grade 2, transitional-cell bladder carcinoma, which had been diagnosed in 1984. The erythematous patch was noted on the glans again by his physician in May 1994. In August 1995, at the age of 76 years, the patient was referred to a dermatologist, whose biopsy showed a squamous cell carcinoma in situ (Bowen's disease). A wide local excision was performed. No further evidence of disease has been identified in the first 6 months of clinical follow-up.

Significant past medical history included nonrecurrent bladder carcinoma, left hemicolectomy in 1964 for colon adenocarcinoma, excision of a rectal tubulovillous adenoma in 1994, benign prostatic hypertrophy status post-transuretheral resection of prostate, prostatourethritis in 1965, and hepatitis A with jaundice in 1942. He has been followed at the Marshfield Clinic in Marshfield, Wisconsin, since 1928.

He is of German descent and has lived his entire life in Marathon County, Wisconsin, as a dairy farmer. He was married in 1951 and had no sexual relationships outside his marriage. He has a 23-packyear history of cigarette smoking but quit in 1959 and reports drinking an occasional beer. His circumcision status was not documented in the chart. After a review of the chart, the patient was contacted and he confirmed that he had been circumcised as long as he could remember.

# **DISCUSSION**

Cancer of the penis is an extremely rare malignancy with a predicted lifetime risk of 1 in 1437 men in the United States<sup>5</sup> and 1 in 1694 in Denmark,<sup>6</sup> representing 0.09% of all cancers and 0.16% of cancers in the

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## TABLE

### **Risk Factors for Developing Penile Cancer**

Risk Factor/Study	Odds Ratio*	95% Confidence Interval*
Phimosis <sup>7</sup>	35.20	11.43-108.39
Phimosis <sup>9</sup>	8.10	5.22-12.54
Difficulty retracting foreskin <sup>8</sup>	6.23	3.18-12.19
Smoking <sup>8</sup>	2.63	1.48-4.68
Smoking <sup>9</sup>	1.43	1.11-1.85
Genital warts <sup>7</sup>	27.63	3.46-220.45
Genital warts <sup>8</sup>	7.52	3.27-17.29
>30 sexual partners <sup>8</sup>	3.32	1.93-5.72
Previous genital condition <sup>7</sup>	2.05	1.05-4.01
Chewing tobacco <sup>9</sup>	2.80	2.07-3.80
Snuff	3.51	1.57-7.80
Late circumcision <sup>7</sup>	26.78	3.57-200.93
Late circumcision <sup>27</sup> †	7.81	1.20-51.00
Late circumcision <sup>8</sup>		
vs Never circumcised	1.16	0.63-2.17‡
vs Infant circumcision	3.55	1.75-7.20
Penile rash <sup>8</sup>	13.14	5.46-31.63
Penile tear <sup>®</sup>	6.24	3.41-11.44
Foreskin <sup>®</sup> - raw data	2.03	1.30-3.15
Age controlled for§	1.19	0.77-1.85‡
vs Infant circumcision	3.04	1.79-5.15

\*Calculated using data reported in original studies.

†No control group for this published series. Published rate of circumcision in Denmark<sup>a</sup> used to make calculations.

‡Not statistically significant.

§Calculations made adjusting control group for age.

male adult.<sup>5</sup> The risk factors for penile cancer (Table) include genital warts,<sup>7,8</sup> smoking,<sup>8,9</sup> past sexually transmitted diseases,<sup>7,10</sup> a sexual relationship outside marriage,<sup>7</sup> multiple sexual partners,<sup>8</sup> poor genital hygiene,<sup>7,8,11,12</sup> phimosis,<sup>7-10,13</sup> previous genital conditions (including urinary tract infection, genital warts, yeast infections, chlamydia, genital crabs, gonorrhea, genital herpes, syphilis, genital ulcers or sores),<sup>7</sup> penile rash (which lasted longer than 1 month) or penile tear,<sup>8</sup> chewing tobacco or areca nut, using snuff,<sup>9</sup> and postnatal circumcision.<sup>7,8</sup> Of these risk factors, a history of genital warts appears to be the most significant, leading experts to identify human papillomavirus (HPV) as the most common causative factor in penile cancer.<sup>14</sup>

Interestingly, genital warts are now more common in circumcised men,<sup>15</sup> and HPV-associated lesions are equally prevalent in circumcised and intact men. Penile intraepithelial neoplasia, although found rarely, is slightly more common in men with foreskins.<sup>16</sup> In one published series of 11 men with carcinoma in situ of the penis, 10 had been circumcised as infants.<sup>17</sup>

The role of circumcision in preventing penile cancer has recently been called into question.<sup>18</sup> In addition to several publications documenting penile cancer in circumcised men,<sup>19-26</sup> a recent case-control study of 110 men with penile cancer from the Pacific Northwest revealed that 41 (37%) had been circumcised.8 Relative to men circumcised at birth, the risk for penile cancer was 3.04 times as great among men who were never circumcised and 3.55 times as great among men who were circumcised after the neonatal period. The magnitude of risk for developing penile cancer was similar in smokers. but a history of multiple sexual partners or genital warts were the strongest risk factors (Table). While neonatal circumcision may play a small role in preventing penile carcinoma, 20% of the patients in this study were circumcised at birth.8 Unfortunately, this study did not control well for age. When the control group was properly adjusted for age, there was no difference between the case group and control group in circumcision status.

Circumcision performed after the new-

born period may increase the likelihood of penile neoplasms. In a Danish study, men with localized squamous cell carcinoma of the penis were 7.81 times as likely to have been circumcised after the newborn period as the general population.<sup>627</sup> Maden et al<sup>8</sup> demonstrated that men circumcised after the newborn period had a slightly higher risk of developing penile cancer when compared with men never circumcised and a significantly higher risk when compared with those circumcised at birth.<sup>8</sup>

In an epidemiologic study with both retrospective and prospective cases from China, 157 men with penile neoplasms were identified. Circumcised men were markedly more likely to develop penile cancer than controls.<sup>7</sup> The circumcision scar is often the focus of tumor formation.<sup>19</sup> In Africa an uncontrolled study found that all of the circumcised men who developed penile cancer were circumcised late in adolescence or adulthood.<sup>28</sup> Why the timing of circumcision is a significant factor is unclear.

For the circumcision status of the patient to be missing from the chart for the past 60 years is indefensible, but not uncommon. In a series of penile cancer patients from the Mayo Clinic, 15% did not have their circumcision status documented in the chart.<sup>14</sup> Because circumcision is so prevalent in the United States, a circumcised penis is often described as "normal" in medical records, thus providing no useful information.

In spite of the body of evidence to the contrary, several circumcision advocates still profess that penile cancer is "virtually eliminated" by neonatal circumcision.<sup>1,29-31</sup> Having been given access to respectable medical journals, their errant message has been adopted by many mainstream physicians.<sup>14</sup> The persistence and prevalence of this myth may be detrimental, as evidenced by the 3-year delay in this patient between the time the penile lesion was noted on physical examination and a biopsy was taken.

This patient had multiple previous neoplasms, which prompts us to speculate whether men who develop penile cancer may be more "cancer-prone." Do these "cancer-prone" men respond to stimuli (such as HPV) by forming a penile neoplasm, when the vast majority of men with similar exposure will not? Should occupational or environmental irritants also be considered? These questions suggest the need for further study.

Officials of the American Cancer Society do not recommend circumcision as a cancer preventive measure (personal correspondence, H. Shingleton and C.W. Heath, Jr, to Peter Rappo, MD, Feb 16, 1996). Recognizing that circumcised men can acquire penile cancer and are at equal or higher risk for HPV-associated lesions is the first step in preventing penile cancer. Screening for, recognizing, and treating these lesions as they develop on the penis as is currently performed on the uterine cervix may be the most responsible approach to controlling both cervical and penile cancer; however, the utility of such screening needs to be explored.<sup>16,32</sup> Persistent penile rashes are a highly significant risk factor for penile cancer<sup>8</sup> and should not be ignored.

Because of the absence of a national tumor registry in the United States, most of the epidemiological studies have been performed outside the United States. When the incidences of penile cancers from different countries are compared, the biggest factor appears to be indoor plumbing.<sup>33</sup> The downward trend in the incidence of penile cancer over the past 47 years in Denmark, where 1.6% of men are circumcised, has been partially attributed to better penile hygiene.<sup>6</sup> Ironically, Denmark, in spite of its low circumcision rate, currently has a lower incidence of penile cancer than the United States, where 60% to 80% of men are circumcised.

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#### REFERENCES

- 1. Schoen EJ. Urologists and circumcision of newborns. Urology 1992; 40:99-101.
- Wolbarst AL. Circumcision and penile cancer. Lancet 1932; 1:150-3.
- Wolbarst AL. Universal circumcision as a sanitary measure. JAMA 1914; 62:92-7.
- Van Howe RS. The detection of human papillomavirus deoxyribonucleic acid in intraepithelial, in situ, verrucous and invasive carcinoma of the penis [letter]. J Urol 1996; 155:2035.
- Wingo PA, Tong T, Bolden S. Cancer statistics, 1995. CA Cancer J Clin 1995; 45:8-30.
- Frisch M, Friis S, Kjaer SK, Melbye M. Falling incidence of penis cancer in an uncircumcised population (Denmark 1943-90). BMJ 1995; 311:1471.
- 7. Brinton LA, Li JY, Rong SD, Huang S, Xiao BS, Shi BG, et al. Risk factors for penile cancer: results from a case-control study in China. Int J Cancer 1991; 47:504-9.
- Maden C, Sherman KJ, Beckmann AM, Hislop TG, Teh CZ, Ashley RL, Daling JR. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. J Natl Cancer Inst 1993; 85:19-24.
- 9. Harish K, Ravi R. The role of tobacco in penile carcinoma. Br J Urol 1995; 75:375-7.
- Tan LB, Chiang CP, Huang CH. Clinical analysis of penile cancers among Chinese in Taiwan [in Chinese]. J Formos Med Assoc 1990; 89:66-9.
- Longombe AO, Lusi KM. Penile cancer in rural Zaire. Trop Geogr Med 1994; 46:366-7.
- Reddy CR, Raghavaiah NV, Mouli KC. Prevalence of carcinoma of the penis with special reference to India. Int Surg 1975; 60:474-6.
- Pec J Jr, Pec J Sr, Plank L, Plank J, Lazarova Z, Kliment J. Squamous cell carcinoma of the penis. Analysis of 24 cases. Int Urol Nephrol 1992; 24:193-200.
- Cupp MR, Malek RS, Goellner JR, Smith TF, Espy MJ. The detection of human papillomavirus deoxyribonucleic acid in intraepithelial, in situ, verrucous and invasive carcinoma of the penis. J Urol 1995; 154:1024-9.
- Cook LS, Koutsky LA, Holmes KK. Clinical presentation of genital warts among circumcised and uncircumcised heterosexual men attending an urban STD clinic. Genitourin Med 1993; 69:262-4.
- Aynaud O, Ionesco M, Barrasso R. Penile intraepithelial neoplasia. Specific clinical features correlate with histologic and virologic findings. Cancer 1994; 74:1762-7.
- Wade TR, Kopf AW, Ackerman AB. Bowenoid papulosis of the penis. Cancer 1978; 42:1890-903.
- Holly EA, Palefsky JM. Factors related to risk of penile cancer: new evidence from a study in the Pacific Northwest. J Natl Cancer Inst 1993; 85:2-4.
- Bissada NK, Morcos RR, el-Senoussi M. Post-circumcision carcinoma of the penis. I. Clinical aspects. J Urol 1986; 135:283-5.
- Bissada NK. Post-circumcision carcinoma of the penis: II. Surgical management. J Surg Oncol 1988; 37:80-3.
- Rogus BJ. Squamous cell carcinoma in a young circumcised man. J Urol 1987; 138:861-2.

- Boczko S, Freed S. Penile carcinoma in circumcised males. N Y State J Med 1979; 79:1903-4.
- Leiter E, Lefkovitis AM. Circumcision and penile carcinoma. N Y State J Med 1975; 75:1520-2.
- Onuigbo WI. Carcinoma of skin of penis. Br J Urol 1985; 57:465-6.
- Korczak D, Siegel Y, Lindner A. Verrucous carcinoma of the penis [in Hebrew]. Harefuah 1989; 117:436-7.
- Girgis AS, Bergman H, Rosenthal H, Solomon L. Unusual penile malignancies in circumcised Jewish men. J Urol 1973; 110:696-702.
- 27. Windahl R, Hellsten S. Laser treatment of localized squamous cell carcinoma of the penis. J Urol 1995; 154:1020-3.
- Magoha GA, Kaale RF. Epidemiological and clinical aspects of carcinoma of penis at Kenyatta National Hospital. East Afr

Med J 1995; 72:359-61.

- 29. Weiss GN, Weiss EB. A perspective on controversies over neonatal circumcision. Clin Pediatr Phila 1994; 33:726-30.
- Schoen EJ. Circumcision updated—indicated? Pediatrics 1993; 92:860-1.
- Schoen EJ. Neonatal circumcision and penile cancer: evidence that circumcision is protective is overwhelming. BMJ 1996; 313:46.
- Viladoms Fuster JM, Leira Juanos J. Papilomavirus humano en el varón [in Spanish]. Actas Urol Esp 1989; 13:343-6.
- Boon ME, Susanti I, Tasche MJ, Kok LP. Human papillomavirus (HPV)-associated male and female genital carcinomas in a Hindu population. The male as vector and victim. Cancer 1989; 64:559-65.