Carcinoma of the Penis

Lester Persky, M.D.
Jean deKernion, M.D.

Tumors of the penis are rare in North America, although they represent a significant health problem in the rest of the world. Proper hygiene and early circumcision undoubtedly account for the low incidence in certain countries; the role of smegma as an etiologic agent has been established, although a specific carcinogen has not been identified.

Over the past several decades, the approach to penile tumors has been modified. First, it is now recognized that there are true premalignant lesions, with variable potential for malignancy. Second, since dissemination of penile carcinoma occurs through both inguinal and iliac nodes, the surgical approach must encompass both areas. Third, adjuvant therapy in the form of radiation therapy and chemotherapy is becoming increasingly important as palliative, and sometimes curative, treatment.

Accompanying this information are several areas of controversy, such as the treatment of certain premalignant penile lesions, the advisability of "prophylactic" node dissection, and the use of radiation therapy. The following article presents the current management of penile tumors, emphasizing major controversies and discussing in detail the authors' experience in the treatment of squamous carcinoma.

Dr. Persky is Clinical Professor of Urology at Case Western Reserve University Hospital in Cleveland, Ohio.

Dr. deKernion is Professor of Urology and Chairman of the Department of Urology at U.C.L.A. School of Medicine in Los Angeles, California.

Precancerous Lesions

Leukoplakia

Chronic irritation has been incriminated in the etiology of leukoplakic changes of the penile and glanular epithelium. Although leukoplakia definitely has malignant potential, the precise incidence of malignant degeneration is uncertain, since few such lesions are followed clinically. Areas of leukoplakia have been described adjacent to squamous tumors in as many as 17 percent of specimens,[1] but it is not known if leukoplakia occurs first or simply coexists with the carcinoma. If the prepuce is involved, these lesions should be completely excised or circumcision should be performed. Careful follow-up is mandatory, since recurrence is not uncommon.

Erythroplasia of Queyrat

Since the description of this hyperplastic penile lesion by Queyrat in 1911,[2] many cases have been reported, and the lesion's propensity for malignant degeneration has become well recognized. It occurs on the dorsum of glans of the uncircumcised male as well-defined, velvety, red plaques, which may be very painful. The microscopic appearance is diagnostic, with hyperplasia of the strata corneum and germination, as well

as interpapillary acanthosis. There are mitotic figures throughout the epithelium, and the dermis is infiltrated by inflammatory cells. The clinical course varies; some lesions remain stable for years.

Erythroplasia is often considered a carcinoma in situ, and identical, therefore, to Bowen's disease. Regardless of the nomenclature, however, invasive carcinoma frequently develops,[1] and treatment is aimed at eradication of the lesions. Excision or partial amputation, if invasion is suspected, is usually effective; the incidence of recurrence is low. When surgery is refused or ill-advised, radiation therapy is sometimes curative.[3] Topical 5-fluorouracil (5-FU) has been reported to have been used successfully in three patients[4] and deserves further consideration in selected instances.

Bowen's Disease

Intraepithelial carcinoma of the penis is similar to that of other locations. Histologically, the disease is often almost identical to erythroplasia of Queyrat. Unlike erythroplasia, however, Bowen's disease is associated with distant visceral cancer in about 25 percent of patients and frequently occurs concomitantly in other areas.[5] These lesions should be completely excised, but they have a propensity for local recurrence.[6] The risk of metastases is very small and, to our knowledge, has not been reported in the literature.

Balanitis Xerotica Obliterans

Balanitis xerotica obliterans, a localized form of lichen sclerosis et atrophicus, may occur anywhere on the penis. It does not seem to be associated with smegma, but in many instances follows surgical trauma, such as meatotomy or circumcision. Microscopically, there is loss of the rete pegs, thinning of the epidermis, and homogenization of the collagen in the upper dermis. On gross inspection, the involved area is thin, scaly, and parchment-like, and may ulcerate or fissure. Pruritus and pain are not uncommon. The meatus is often involved, with extension into the fossa navicularis.

Treatment should be conservative, since malignant degeneration rarely occurs. Local excision is usually curative, and penectomy is necessary only for severe involvement of the glans or when cancer is strongly suspected.[7] Topical and intralesional steroids have been administered successfully when local excision was not feasible.[8,9]

Buschke-Loewenstein Tumor

Condyloma acuminatum giganticum, as described by Buschke and Loewenstein,[10,11] is histologically benign, but invades locally by compression and destruction. The confusion regarding recognition and management arises from the tumor's similarity to large, exophytic squamous carcinoma and its tendency for malignant change. It is frequently impossible to determine if inalignant degeneration has occurred or if the carcinoma coexists with the benign lesions.[12] Some lesions found to contain obvious cancer were probably primarily true exophytic carcinomas, rather than giant condylomas.[13] Conversely, penectomy has been performed for lesions thought to be malignant that were subsequently proven to be condylomas.[14]

Although multiple biopsies show that condyloma has no evidence of cancer, conservative therapy involving excision and cautery carries a definite risk. The known premalignant potential, the reported coexistence of cancer, and the incidence of mistaken diagnosis make limited penectomy advisable in most cases.[15] Node dissection is unnecessary unless invasive carcinoma is present. Radiation therapy is of no value,[16] and podophyllin is not effective for giant condylomas. Fulguration and excision may be attempted in young patients with limited involvement when the diagnosis is definite, but penectomy is usually necessary.[17]. Occasionally, laser therapy may be curative, as it is in other premalignant lesions.

Cancerous Lesions

Carcinoma In Situ

Malignant changes in the epithelium oc-

casionally occur with no evidence of invasion of the basement membrane. If untreated, most of these lesions will eventually become invasive. Carcinoma in situ should properly be classified as an early cancer.

Squamous Carcinoma

Epidermoid carcinoma is the most common form of penile cancer. It occurs primarily in underdeveloped countries where circumcision is not practiced. While carcinoma of the penis accounts for less than one percent of male cancers in the United States, it represents 12 percent of all cancers among the Hindus of India,[18] and is common in China and Africa.[19]

The association of penile cancer with poor hygiene and smegma has been well established. Chemical agents or venereal disease have not been incriminated in the etiology, and most patients do not have a history of trauma.

The usual presenting symptoms are phimosis of recent onset or the presence of a mass; urethral obstruction and bleeding rarely occur. Prognosis correlates well with the stage of the tumor, and early therapy is associated with good results. Many patients have advanced disease at diagnosis, however, either because of fear of penectomy or failure to recognize the lesion beneath a phimotic foreskin.

The tumor disseminates mainly through the profuse penile lymphatics by bloodborne metastases and by local invasion of the abdominal wall. Rapid regional node involvement is characteristic of the disease. New nodal metastases rarely appear after three years following therapy.

Basal Cell Carcinoma

Basal cell carcinoma of the penis is an extremely rare lesion; only 10 patients have been reported in the world literature.[20] This penile tumor resembles basal carcinoma located elsewhere, with well-defined, rolled borders and a depressed center. Metastasis occurred in only one patient. Local excision with adequate margins is sufficient treatment.

Melanoma

Fifty patients with malignant melanoma of the penis have been reported in the world literature. All were white, and their disease was of the melanotic variety. The most frequent site for this tumor is the glans, but it may arise anywhere on the penile shaft.[21]

Early recognition requires a high index of suspicion for all pigmented penile lesions. As in the treatment of melanoma in other areas of the body, adequate local excision with tumor-free margins is essential. Partial penectomy is probably sufficient for tumors of the distal penile skin, but total penectomy is necessary for glanular and deeply invasive lesions.[22] Bilateral node dissection should probably be performed in all cases, since more than 50 percent of patients have nodal metastases when first diagnosed.[21]

Dissemination of penile carcinoma occurs through both inguinal and iliac nodes.

The prognosis is guarded but improves if the regional nodes are negative, although local recurrence and metastases are common.[23] New methods of immunotherapy have not been used for penile melanomas, nor has chemotherapy been successful to date. Gojaseni and Nitiyant reported successful treatment of one patient with penectomy, node dissection, and melphalan.[24] Radiation therapy is probably not effective. Endolymphatic ^{131}I therapy has been employed with encouraging results in two patients with penile cancer.[25,26]

Mesenchymal Tumors

The stromal and connective tissues of the penis are unusual sources of cancer, but any histologic type may occur. Because of the rarity of these tumors, treatment is difficult to assess.

Only about 50 percent of mesenchymal tumors of the penis are malignant.

TABLE 1
THE JACKSON STAGING SYSTEM FOR CANCER OF THE PENIS[31]

Stage I	Tumor limited to the glans, penis, and/or prepuce.
Stage II	Invasion into the shaft or corpora, but without nodal or distal metastases.
Stage III	Tumor confined to the shaft, with proven regional node metastases.
Stage IV	Invasion from the shaft, with inoperable regional node involvement or distant metastases.

While benign tumors occur more frequently in the glans, cancers tend to arise in the shaft.[27] Sarcomatous tumors, especially fibrosarcoma and Kaposi's sarcoma, are the most common.[28] Kaposi's sarcoma is now seen in greater numbers with the advent of acquired immune deficiency syndrome. Leiomyosarcoma, malignant neural tumors, malignant hemangioendothelioma, and unclassified sarcomas have also been reported.

The natural history of these tumors is generally similar to mesenchymal tumors located elsewhere. Leiomyosarcomas vary in pleomorphism and frequently recur locally before metastases develop.[29] Fibrosarcomas tend to be of the more malignant histological type and to disseminate early. Hemangiomatous tumors usually have a good prospect for cure.

The treatment for a malignant mesenchymal tumor of the penis is total penectomy. Lymph node dissection is not indicated, since metastasis occurs primarily via the bloodstream. Small lesions of the glans should initially be excised for frozen section examination. Unless the diagnosis of an invasive tumor is certain, masses in the shaft should first be biopsied, preferably by needle biopsy. Occasionally, penectomy for a benign tumor can be avoided by this approach, and there is no evidence that the chance for cure is compromised.

Metastatic Tumors

Secondary cancers of the penis originate most commonly in the genitourinary tract. Bladder and prostate carcinomas account for over 50 percent of the primary sites, and 25 patients with metastases from the rectosigmoid have been reported. Distant metastases from the lung, pancreas, kidney, and ureter have also occurred, as well as several tumors originating in primary testicular neoplasms.[30] The presenting symptoms are frequently priapism or severe penile pain. Local excision and radiation therapy are seldom beneficial, but do occasionally relieve symptoms.

Treatment of Squamous Carcinoma: Authors' Experience

From 1954 to 1974, 77 patients with squamous cell carcinoma of the penis were treated at the teaching hospitals of Case

TABLE 2
RELIABILITY OF CLINICAL STAGING FOR CANCER OF THE PENIS

Stage	Number of Patients		Percentage Error
	Clinical Stage*	Histological Stage**	
I	26	31	19
II	12	19	38
III	33	21	36
IV	6	6	0

*Based on histological examination of primary tumor and clinical impression of groin nodes.
**Final diagnosis, after node biopsy or node dissection.

Western Reserve School of Medicine in Cleveland. All patients were followed for at least three years or until death. Ages ranged from 31 to 85 years, with an average of 63 years, although 12 patients were under 50. Only two patients (2.6 percent) had been circumcised as an adult.

The staging system recommended by Jackson[31] (Table 1) was used for all patients. An unusually large number of patients presented with advanced disease (Table 2). Only 39 percent had stage I tumors, compared with the usually reported figure of 50 to 65 percent, a reflection no doubt of the large percentage of indigent patients in our study's population.

Seventy-three patients underwent partial penectomy. For two patients, excisional biopsy was the primary treatment, and in two others, excision by circumcision was performed. There was one case of local recurrence, which occurred in a patient initially treated by partial penectomy. Local irritation occurred, and a small excrescence was biopsied and found to be carcinoma in situ. After undergoing further amputation, this patient has remained free of disease for the last several years. Figure 1 shows the technique of penectomy, which involves amputation 1.5 to 2 cm proximal to the primary lesion. The urethra is divided five to eight mm distal to the amputated corpora and spatulated to ensure an adequate orifice and minimize stricture formation.

A significant discrepancy was found between the initial clinical staging and the final histologic stage (Table 2). This was primarily due to the large number of patients with palpable inguinal nodes that proved to be free of metastases by node dissection or superficial inguinal node biopsy. In the entire series, 42 patients (55 percent) presented with palpable nodes, which was consistent with the usually reported incidence rate of 35 to 60 percent. Of these 42 patients, only 25 (60 percent) had proven nodal metastases. The problem of clinical assessment of the regional nodes is especially pertinent in patients with stages I and II disease, where there was a 36 percent (18 of 50 patients) incidence of false positives (Table 3).

The staging error was also increased by the number of patients with clinically negative nodes who were later shown to have groin metastases after adequate control of the primary. Six patients (one with

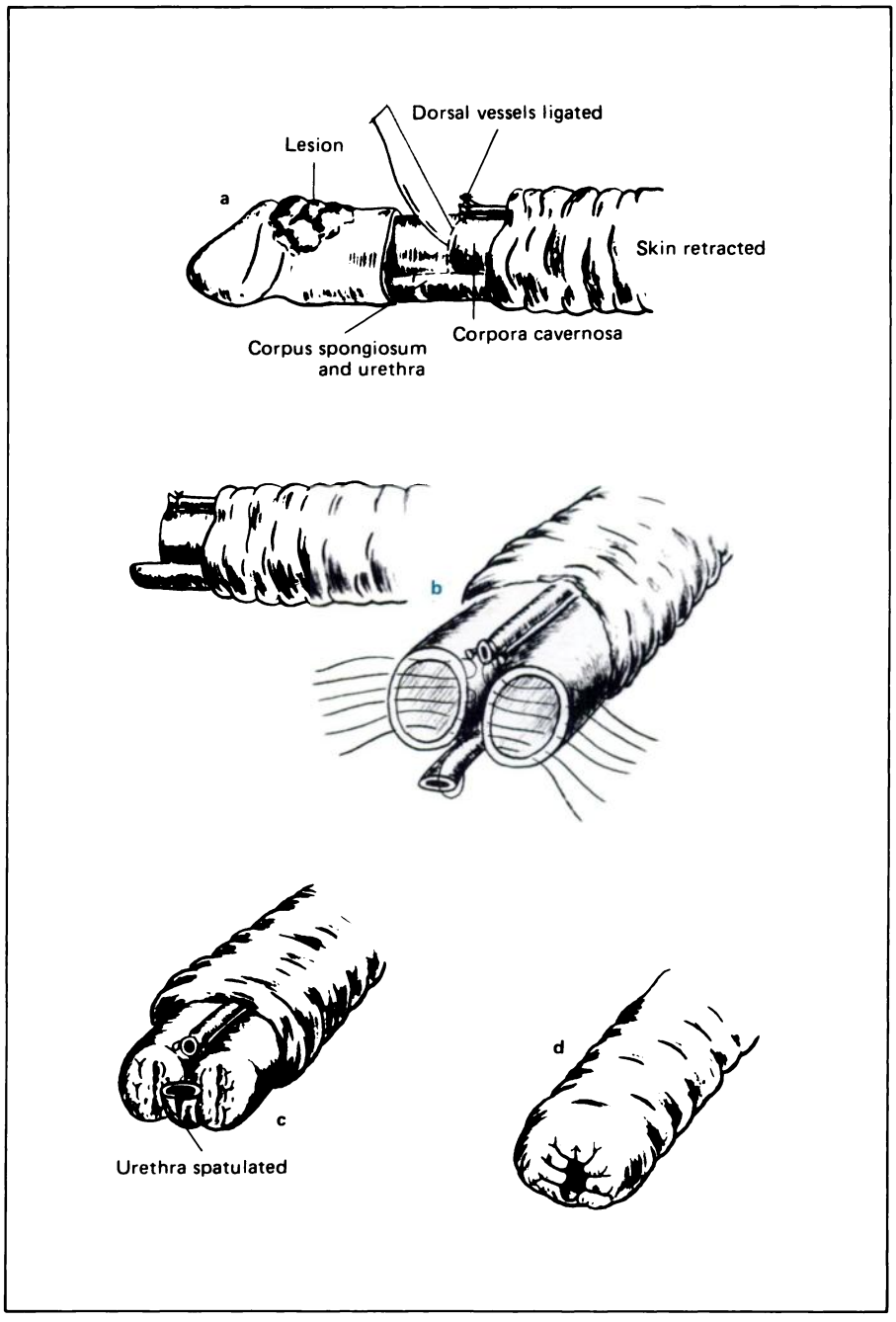

Fig. 1. Penectomy involves amputation 1.5 to two cm proximal to the primary lesion. The urethra is divided five to eight mm distal to the amputated corpora and spatulated to ensure an adequate orifice and minimize stricture formation.

stage I, and five with stage II) with clinically negative nodes subsequently died of metastases. One other patient with an invasive primary and palpable nodes had a negative node biopsy and was therefore categorized as stage II, but eventually developed groin metastases. Thus, a total of seven patients (nine percent) had negative nodes that subsequently proved to be cancerous, an experience similar to that of other investigators.

Survival rates correlated well with stage of disease (Table 3). The survival rate of 43 percent for patients with stage III lesions might have been greater had node dissection been performed in all patients.

Adjuvant therapy in the form of radiation therapy and chemotherapy is becoming increasingly important as palliative, and sometimes curative, treatment.

Six refused surgery, and one patient was inoperable because of severe fixation of the tumor and advanced disease of multiple systems. These seven patients died within one year. Twelve bilateral ilioinguinal node dissections were performed in this group of patients, of whom five were cured.

Three of the patients originally classified as stage II, who subsequently showed groin metastases, also underwent node dissection. The cure rate for all patients undergoing lymphadenectomy for histologically positive nodes was 55 percent.

All six patients who initially presented with distant metastases (stage IV) died within one year. Partial penectomy was performed for palliation; one patient received irradiation to the groin nodes, and one also received chemotherapy, without benefit.

Treatment of Primary Lesions

Adequate control of the primary tumor is essential for cure. Small tumors limited to the prepuce have been successfully treated by circumcision, but local recurrences have been reported. Small superficial tumors confined to the glans may also be treated effectively by laser therapy. Partial penectomy is indicated in every patient with invasive carcinoma, unless contraindicated by the patient's young age. The penis should be amputated two cm proximal to any visible tumor.

Although local recurrence is noted in a small percentage of patients treated by these methods, we found only one such case in the 74 patients in our series treated by penectomy or adequate local excision. It seems, therefore, that for lesions confined to the foreskin, the psychological trauma of penectomy can be avoided. Tumors of the glans penis should not be locally excised, however, since these lesions spread more rapidly to deep nodes through the profuse glandular lymphatics. In the Mayo Clinic series,[32] the recurrence rate for locally excised glandular lesions was 40 percent.

Total penectomy is associated with considerable psychological trauma and usually contributes little to the prognosis. However, lesions at the base of the penis or in the proximal shaft of the penis require complete excision to achieve tumor-free margins. Lesions that extend to the abdominal wall must be treated by penectomy with en bloc paniculectomy and bilateral node dissection, as originally described by Young.[33]

Radiation therapy has been proposed as a method of treating primary penile carcinoma and preserving the phallus. Grabstald and Kelley[34] treated 10 patients with primary penile cancers; local recurrence occurred in only one patient, who was subsequently successfully treated by partial penectomy. Krieg and Luk[35] similarly concluded that radiation therapy was the treatment of choice for early-stage primary lesions, achieving successful local control following surgery in 88 percent of patients and following radiation therapy in 75 percent (nine of 12 patients). This conclusion reflects less mutilation and distortion than seen with surgery. Two of

the patients who failed, however, were subsequently able to achieve local control after surgery. Daly et al[36] treated 22 patients with implants of iridium-131 wire, and achieved local control with conservation of the penis in 86 percent of patients. Forty-seven patients had chronic urethral stenosis requiring dilation, and severe penile necrosis occurred in two patients. Others have reported a significant increase of tumor recurrence after radiation therapy.[37,38]

Improved methods of delivering radiation to surface tumors either externally or by brachytherapy have made irradiation an acceptable treatment for some patients with penile carcinoma. The morbidity can be considerable, however, and seems to be increased with increasing size of tumor and increasing depth of invasion. Recurrence may be difficult to ascertain in the patient with extensive necrosis, and inflammatory response to irradiation may make assessment of the inguinal lymph nodes difficult. The penile shaft is conserved in most patients in recent series, but often at the expense of considerable deformity after such management of large lesions. In addition, the functional capacity of the penis is usually uncertain, especially in regard to the ability to have and sustain erections. Nonetheless, radiation therapy should be considered for young patients with small primary lesions that are not deeply invasive.

Treatment of Regional Lymph Nodes

Recognition of the significance of the regional lymph nodes in surgical treatment has led to the early use of node dissection in patients with cancer of the penis.[33,39] The penile lymphatics drain not only to the inguinal, but also to the deep iliac nodes and may involve both iliac regions by communications at the base of the penis.[40] Bilateral, ilioinguinal lymph node dissection, therefore, offers the best chance of cure for patients with invasive primary penile carcinoma, but at the expense of morbidity in some patients who have no lymph node involvement.

The advisability of lymph node dissection in patients with clinically positive inguinal adenopathy is generally accepted, and the increase in the survival rate after using this procedure has been well documented. Approximately 40 to 50 percent of patients with positive nodes can be cured by node dissection;[36,41] in untreated patients, death from metastases occurs uniformly within two to three years. The major current controversy concerns the issue of "prophylactic" node dissection versus observation and lymph node dissection only for patients with adenopathy. Since the rationale for immediate lymph node dissection must be based partially on the risk of lymph node involvement, this issue is best discussed in the context of the local stage of the primary lesion (see below). As shown in Table 3, deeply invasive lesions have a much higher incidence of lymph node metastases than do superficial lesions.

The association of penile cancer with poor hygiene and smegma is well established; chemical agents and venereal diseases have not been implicated in the etiology.

The identification of the sentinel lymph node according to Cabanas[42] should eliminate the need for prophylactic lymph node dissection. According to Cabanas's lymphangiographic and surgical studies, the first lymph node of drainage from penile cancer is located just superior and medial to the saphenofemoral junction in each groin. No patient with negative sentinel lymph nodes had positive inguinal or deep pelvic lymph nodes. In contrast, 20 percent of patients with positive sentinel nodes had more extensive lymph node involvement. All patients with proven inguinal lymph node metastases were found to have positive sentinel nodes.

This study suggested that the status of the regional lymph nodes could be accu-

rately predicted by simple excision of the sentinel node. This study, however, has not been confirmed by other authors. We know of one patient with a negative sentinel node biopsy who developed inguinal metastases; a similar case has been reported in the literature.[43] In Cabanas's original series of 31 patients, three failed to survive five years following a negative sentinel node biopsy. If they indeed died of cancer or with cancer, then this would suggest a 10 percent error, which is not dissimilar from the error based on clinical assessment alone. The significance of the sentinel node, therefore, should continue to be assessed, but its true reliability has not been firmly established.

Stage I

Although tumors that do not invade the corpora seldom metastasize, the presence of inguinal adenopathy is not uncommon with such lesions. Inflammation at the primary site is often considerable, and only nodes that are enlarged three weeks after surgical treatment of the primary tumor should be considered important. Persistent adenopathy was present in 32 percent of our stage I patients and 26 percent of those reported by Hardner et al.[37] All of our patients had pathologically negative nodes, and none had recurrent disease.

In spite of this high incidence of benign adenopathy, the specter of occult metastases has encouraged an aggressive approach to the management of regional nodes, even in the absence of corporal invasion. Kuruvilla et al[18] reported that 20 percent of patients with clinical stages I and II tumors actually had nodal involvement and that the clinical impression, therefore, was unreliable.

In our series, only one patient with a noninvasive tumor developed late lymph node metastases; the primary lesion in this patient, however, had not been adequately controlled. The highest incidence of late clinical manifestation of groin node metastases following adequate excision of noninvasive primary tumors was 11 percent (five of 43), reported by Hardner et al.[37] The authors recommended routine superficial node dissection to be extended to a deep dissection if the superficial nodes were positive.

This high incidence of metastases is not the usual experience,[41-44] and the high incidence of negative nodes makes routine ilioinguinal dissection for stage I tumors difficult to justify. The small but real risk of occult metastases, however, cannot be ignored, and the patient must be carefully examined at monthly intervals. Though the sentinel node approach has not been definitely proven, it is associated with minimal morbidity and may be a satisfactory procedure in this group of patients, combined with careful follow-up examinations.

Stage II

Invasion of the corpora cavernosa is associated with nodal metastases in a significant number of patients, and evidence suggests that regional metastases are more likely to occur than noninvasive lesions.[37,44] In our series, more than half the patients with invasive primary lesions had histologically proven lymph node metastases sometime during follow-up. This high incidence has encouraged us to perform routine lymph node dissection for persistent adenopathy when the primary tumor invades the corpora, even though about 25 to 30 percent of the specimens will be free of tumor.[18,41]

Again, the main controversy concerns the advisability of lymph node dissection when the primary lesion invades the shaft of the penis and the nodes are clinically negative. Proponents of prophylactic lymph node dissection emphasize the high percentage of clinically negative nodes that later become positive. Although this figure is reported to be as high as 16 to 20 percent,[18,37] Hanash et al reported a rate of only one percent.[1] In our series, one third of the patients with negative nodes and a stage II primary lesion developed inguinal metastases. Assuming even a modest incidence of occult lymph node metastases, routine prophylactic node dissection can be justified only if the procedure ultimately increases the length of survival. Central to

TABLE 3
CANCER OF THE PENIS:
SURVIVAL ACCORDING TO SURGICAL STAGING AND PRESENCE OF INGUINAL ADENOPATHY

Surgical Stage	Number of Patients	Clinical Impression of Groin Nodes	Biopsy-Proven Metastases (Number Biopsied or Excised)	Survived Three Years without Disease	
				Number	Percent
I	31	+10	0 (10)	10/10	100
		-21	0 (0)	20/21	95
II	19	+8	0 (8)	6/8	75
		-11	0 (0)	7/11	64
III	21	+7	4 (4)	2/4	50
		-14	8 (8)	3/8	38
IV	6	+6	0	0	0

The symbol + refers to clinical impression that nodes were tumor bearing.

The symbol - refers to clinical impression that nodes were non-tumor bearing.

*Six patients refused ilioinguinal node dissection.

this issue are both the patient's reliability in pursuing follow-up examinations and the impact of an expanded tumor burden on the prospect for cure by either surgery or radiation therapy.

Although it would seem that allowing regional metastases to enlarge until they become palpable would reduce the chances for surgical cure, the opposite has been suggested by Beggs and Spratt.[44] They reported that the number of patients who died of cancer because of delayed lymph node dissection was only one percent—approximately equal to the mortality rate of lymphadenectomy. Frew and colleagues found that of their patients in whom dissections were deferred until there was evidence of clinical adenopathy, none died of metastases.[45] Ekström and Edsmyr reported a cure rate of 50 percent in patients who had lymph node dissection only after appearance of adenopathy,[46] a rate higher than that for primary excision of involved nodes.

Catalona,[47] however, citing the 20 percent incidence of occult metastases and the low surgical morbidity with the use of modern surgical and postoperative techniques, recommends lymphadenectomy in patients with invasive primary lesions. He also notes the risk of developing incurable disease in patients with clinically negative lymph nodes. Our series emphasized the problem of improper follow-up. Undoubtedly, survival time is decreased in the patient who develops extensive lymph node disease, since the risk of local nonresectability and further regional and distant metastases has to be increased. Four patients with improperly staged lesions (one with stage I, three with stage III) subsequently developed groin metastases. Only two patients had lymph node dissection, and neither survived. All four patients died within two years.

The issue of whether prophylactic dissection is indicated has not been completely resolved. Patient compliance is clearly an important factor. Percutaneous fine needle aspiration of inguinal lymph nodes may play a role in management. Suspicious superficial nodes can easily be aspirated, and the cytology can be interpreted with a high degree of accuracy by the skilled pathologist.

Stage III

When inguinal lymph node metastases are clinically evident, pelvic and inguinal lymph node dissection are the rule. Because extensive lymph node involvement above the level of the external iliac vessels is almost never associated with surgical cure,[48] we do not use inguinal dissection in those cases. In the absence of pelvic disease, however, superficial and deep inguinal lymph node dissection is the treatment of choice. Bilateral dissection is generally indicated because of the decussation of the lymphatics at the base of the penis. Lymphadenectomy seems to be curative for this cancer, with five-year survival rates as high as 50 percent[41,44] following proper excision of involved inguinal nodes.

The issue of simultaneous versus staged bilateral lymph node dissections continues to be debated. The risk of positive nodes on the contralateral side is approximately 20 to 25 percent.[47] This rate approximates the risk of lymph node metastases in patients with invasive primary lesions and raises the same controversy about early lymph node dissection regardless of the clinical status of the opposite groin. Careful and frequent observation of the contralateral groin, however, has often spared the patient the need for a second operation.

Techniques of Ilioinguinal Node Dissection (Fig. 2)

Ilioinguinal node dissection has been performed with a number of different techniques. Whitmore advocates bilateral iliac dissection through a suprapubic incision with separate groin incision for the inguinal nodes.[49] We have dissected the groin nodes through vertical incisions extending through the groin crease. The complication rate is generally high, with a mortality rate reportedly as high as one to three percent. Necrosis of the skin flaps, wound infection, severe lymphedema, hemorrhage from the femoral vessels, and thromboembolitic

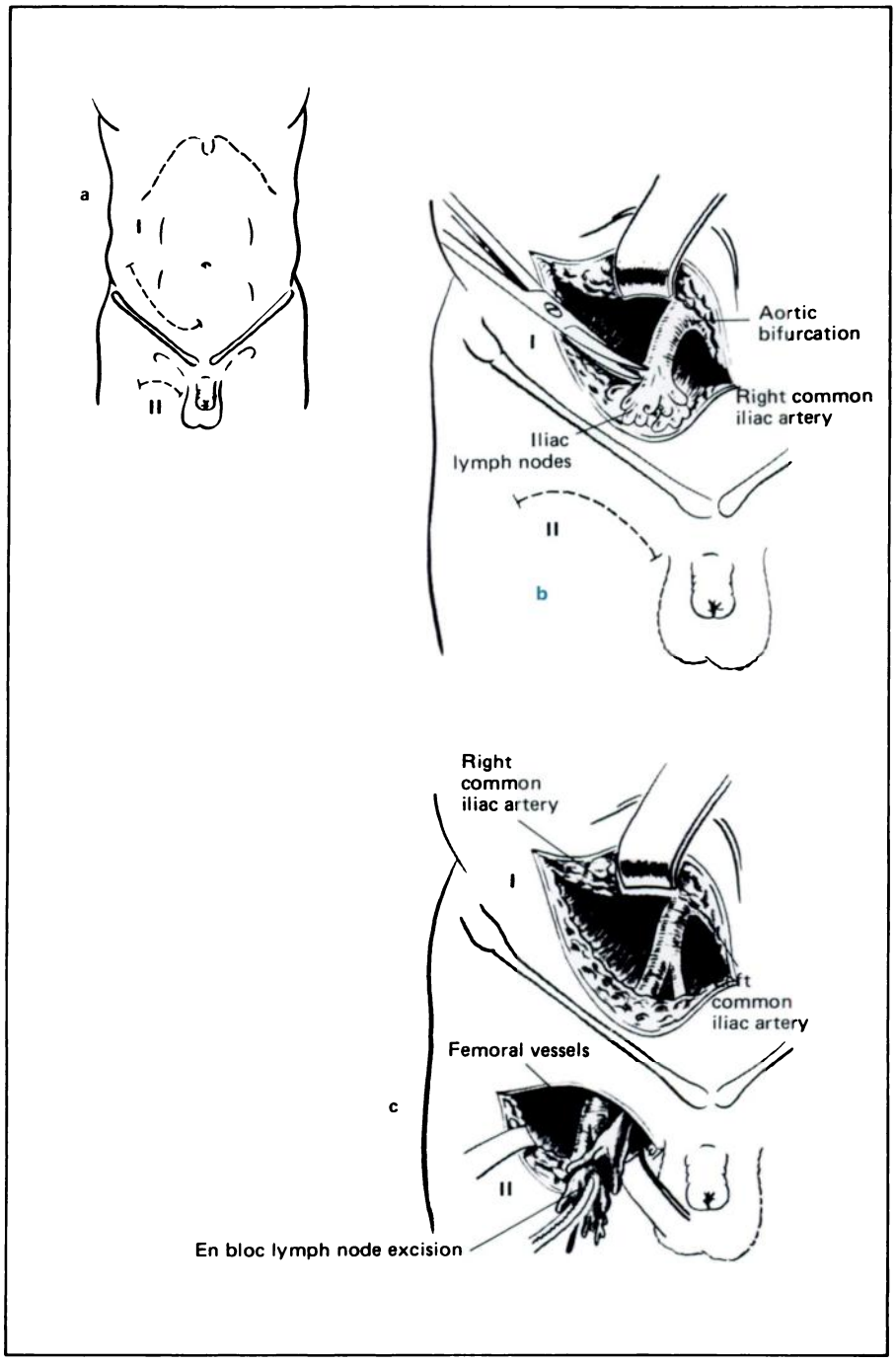

Fig. 2. Techniques of ilioinguinal node dissection.

disease are not uncommon. Recent changes in the surgical approach have decreased the incidence of complications, making the procedure a more acceptable option.

Because a major cause of complications is infection and necrosis of the skin flaps at the groin crease, we have abandoned the vertical ilioinguinal incisions. Although many approaches have been used successfully, we prefer to first perform a limited pelvic lymph node dissection through a suprapubic vertical incision. This limited dissection is similar to that performed in patients with prostate cancer and is seldom associated with severe lymphedema or other major problems. If the lymph nodes are extensively involved, we stop the procedure. Otherwise, a slightly curved transverse incision is made in the groin just below the inguinal ligament on the involved side.

After the skin flaps are developed, thorough ilioinguinal lymph node dissection can be completed. Morbidity has been markedly decreased by this approach, which also emphasizes preservation of subcutaneous tissue on the skin flaps and the transposition of the sartorius muscle over the femoral vessels. The skin flaps are secured to the underlying muscle with sutures, and the spaces drained with large suction catheters. Patients are kept in bed with their lower extremities elevated.[50] The value of minidose heparin or other perioperative prophylactic measures for phlebitis has not been established, but it seems reasonable to include controlled anticoagulation in this group of high-risk patients.

Radiation Therapy

Radiation therapy of the primary lesion has already been discussed. Although it is generally agreed that radiation therapy should not be the primary treatment of lymph node metastases, some evidence suggests that these metastases may be radiosensitive. Staubitz et al reported a five-year survival rate of 40 percent following inguinal radiation therapy in 10 patients with proven metastases.[51] The authors emphasized that the results of surgery in patients with positive nodes appear to be twice as good as those achieved with radiation therapy alone. Groin nodes that are fixed and usually considered inoperable, however, can occasionally be adequately resected following a course of radiation therapy.[52] Prophylactic radiation therapy to the inguinal lymph nodes has not proved advantageous.[12] Ekström and Edsmyr[46] reported a 16 percent incidence of groin metastases after prophylactic irradiation, a rate similar to what would be expected from the known incidence of occult metastases in patients with clinically negative nodes.

Chemotherapy

Bleomycin, which has shown activity in a number of squamous tumors, was reported by Ichikawa et al to be effective in metastatic carcinoma of the penis;[53] long-term palliation or cure, however, was not documented. Mathé reported one apparent cure with bleomycin,[54] although its efficacy as a single agent has been limited.

Methotrexate was recently shown to be very effective for patients with advanced carcinoma of the penis.[55] Sklaroff and Yagoda[56] treated eight patients with varying dosage schedules and produced either partial or complete remissions.

Using a combination of methotrexate, cisplatin, and bleomycin, we achieved complete regression of inoperable large inguinal metastases in two of three patients. Both responders are apparently cured, with no recurrence three and five years after chemotherapy followed by surgical excision. One patient had no viable tumor in the specimen. It is clear that the new chemotherapeutic agents are effective against metastatic penile cancer, although the necessary clinical trials cannot be conducted because of the small number of such patients in the US.

Treatment Guidelines

We have developed a treatment policy based on retrospective analysis of our series and the experience of other observers. First, the invasiveness of the primary tumor and the presence of palpable adenopathy are noted. The primary lesion is treated by par-

tial penectomy unless invasion of the base of the penis necessitates radical penectomy. Although we have not had experience with radiation therapy, the literature suggests a role for radiation therapy rather than partial penectomy for many patients.

In the absence of palpable lymph nodes, lesions that do not invade the corpora are treated locally; patients are followed closely for three to five years without lymph node biopsy unless the nodes become clinically significant. Excisional biopsy of the sentinel nodes may be appropriate. Patients with unequivocal firm lymph nodes undergo lymphadenectomy. Those with equivocal adenopathy are often helped by percutaneous fine-needle aspiration cytology.

Although it is generally agreed that radiotherapy should not be the primary treatment of lymph node metastases, evidence suggests that these metastases may be radiosensitive.

After excision or radiation therapy for lesions that invade the corpora, we advocate bilateral lymphadenectomy in patients with definite adenopathy. Many approaches are used, but we prefer a limited bilateral pelvic lymph node dissection. If the pelvic lymph nodes are not extensively involved, we perform a unilateral groin dissection through a separate transverse incision below the inguinal ligament. In the absence of clinically positive nodes in the patient with a deeply invasive primary lesion, we recommend lymphadenectomy as the safest procedure. In the thin patient who can be relied on to return for follow-up and in the patient who refuses lymphadenectomy, however, sentinel node biopsy and careful follow-up may be appropriate.

Summary

Most premalignant penile lesions should be completely locally excised. Giant condyloma frequently cannot be distinguished from fungating carcinoma and usually requires limited penectomy. Cancers other than epidermoid carcinomas are very rare and, except for basal cell carcinoma, have a generally poor prognosis. Prognosis of squamous cell carcinoma, however, depends on the stage of disease as determined by both local invasion and by involvement of inguinal nodes. The three-year survival rates for 55 patients were: stage I, 95 percent; stage II, 67 percent; stage III, 29 percent; and stage IV, zero percent. Most primary lesions were treated by partial penectomy, and no patient developed local recurrence. There is a significant discrepancy between initial clinical and histologic staging, due to the difficulty of determining lymph node metastases.

Current methods of radiation therapy indicate that it has a role for management of primary penile cancer, especially in young men with small lesions. The management of inguinal lymph nodes is still debated. Although the reliability of the sentinel node biopsy has not been established, it may be appropriate in patients with noninvasive primary lesions and no detectable inguinal metastases. The need for immediate or prophylactic lymph node dissection in patients with invasive primary tumors is controversial. Successful management depends on careful and frequent follow-up examinations, with early intervention for suspicious adenopathy. In view of the poor prognosis for advanced lymph node metastases, we prefer to use early lymph node dissection when the primary lesion is deeply invasive.

Limited bilateral pelvic lymph node dissection is associated with minimal morbidity and seems to be an appropriate prelude to groin dissection. Extensive pelvic metastases are a sign of incurability and abrogate the need for groin dissection. We prefer to perform the inguinal dissection at the time of lymph node dissection through a separate curve groin incision.

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