Epidermoid cancer of the vulva is essentially a cutaneous disease, modified by its site in a specialized epithelium that is subjected to rather special environmental, hormonal, infectious and functional factors. Vulvar cancer has a well-defined natural history and an "at risk" population that is beginning to be identified.\(^1\)\(^2\) It accounts for 3.5 percent of all gynecologic cancer.

In its natural course, this lesion progresses from dysplasia through intraepithelial neoplasia to invasive cancer as an inter-related function of time and the status of the patient's defense mechanisms. Therefore, a more advanced lesion is expected in a patient with the longest history of disease and the poorest immunologic response.\(^3\) Based on historical data, dysplasia and intraepithelial cancer may be present for 10 years or longer.\(^4\) An invasive lesion that is histologically well-differentiated may extend locally for a considerable time before metastases occur. As the size of the lesion increases, the incidence of lymph gland metastases also increases and survival progressively diminishes. Hence, the major prognostic factors are lesion size and regional lymph gland metastases. Clinical and biostatistical data confirm that a lesion size of three cm. and the presence of histologically proven regional (inguinal) lymph gland metastases are valid parameters for differentiating Stage I from Stage II epidermoid cancer of the vulva. The presence or absence of histologically proven regional (inguinal) lymph gland metastases was also a statistically valid factor for differentiating Stage II and Stage III cancers. Once regional metastases develop, the course becomes much more rapid and the prognosis correspondingly poor.\(^5\)\(^6\)

While a specific etiology cannot be delineated, there is evidence that an "at risk" group can be identified. At least one-third of patients with vulvar cancer have chronic vulvitis, within which neoplasia begins. The chronic vulvitis may be venereal or non-specific in origin, or it may be one of the dysplastic depigmented lesions of the vulva. These lesions have increased cellular activity, allowing for cellular aberration.\(^7\) It is also
currently speculated that the present treatment of herpetic vulvitis by photo-
dynamic inactivation could permit the development of neoplasia at a later
date.8 In addition, while vulvar cancer
not infrequently occurs in premeno-
pausal patients, its peak incidence is in
women over 50 years old. Therefore,
postmenopausal patients with chronic
vulvitis have the highest risk of dyspla-
sia and epidermoid cancer of the vulva.

Diagnosis
Patients should be routinely screened for
cutaneous venereal disease, metabolic
disorders and parasites. The diagnosis
must be confirmed histologically by
biopsies of high-yield vulvar areas.
Tumor and nevi are evaluated by excisi-
on biopsy; all ulcers are biopsied at the
advancing edge. (Table 1.)

In the past, patients were reluctant to
seek medical attention for vulvar lesions
and physicians were either reticent to
biopsy the vulva or indecisive on the
best and most productive areas to
biopsy. Simple injection of local anes-
thetic and the use of a small derma-
tologic punch make the procedure
simple and almost painless. If required,
the biopsy site can be closed with a
Dexon triple 0 suture.

Chromotaxic staining is useful in de-
lineating high-yield areas for biopsy.
One percent toluidine blue is painted on
the suspicious area of the vulva, allowed
to dry, and then decolorized with one
percent acetic acid. Abraded and healing
areas are artifacts of this technique and
can be ignored. (Figs. 1A. and 1B.)
Magnification with a good hand lens or by colposcopy is invaluable in assessing and following vulvar lesions. Colposcopy not only facilitates localization of preferred biopsy sites, but also allows photographic recording of these areas, a necessity for long-term follow-up. (Figs. 2A. and 2B.) Thus, this instrument has gained great favor.

Stage
Once a definitive diagnosis has established the presence of vulvar cancer, an organized treatment protocol is mandatory. (Flow Chart.) Staging becomes of paramount importance and depends on definite parameters of therapeutic and prognostic importance. We have found the FIGO staging method (Table 2) to be less than ideal and have substituted another system based on significant clinical and biostatistical data. FIGO is a Tumor, Node, Metastasis classification, utilizing an arbitrary two cm. lesion size and "palpable lymph nodes" as staging parameters. There is no consideration for in situ cancer and other significant factors. The recommended staging system (Table 3.) reflects the natural history of vulvar cancer and gives an orderly progression for therapy and prognosis. Patient groups have been proportionate and allow accurate transfer of information for retrieval and analysis of the data systems. This staging system conforms to that recently recommended for epidermoid cancer of the anus. Once the patient has been staged in this system, therapy decisions are facilitated.

Treatment
Stage 0
Several treatment variables for intraepithelial cancer must be noted. First, a completely accurate diagnosis depends on the certainty that there is no area of invasion. Hence, the entire lesion should be removed and serially sectioned. In most patients, however, this ideal is impractical because of the size of the lesion, its existence in multifocal sites and the financial deterrent to routine serial section examination in all but subsidized investigations. If, however, the entire lesion is removed as a biopsy, no further treatment is required unless the disease is not controlled.

Another variable is spontaneous regression in a younger pregnant patient. Finally, when neoplasia begins in an
area of chronic vulvitis, such as a venereal granuloma, treatment of the precursor introduces another variable into the complex problem of therapy evaluation. Topical treatment of Stage 0 cancer with a five percent 5-FU cream over a 10-week period has been effective in some patients treated in our Clinic for Vulvar Disease, and shows the promise expected in view of its success in treating skin cancer of the head and neck.3,8,9 The topical application of this agent is more effective in the immunologically competent patient.3 Incorporation of 5-FU into cellular RNA and its inhibition of DNA in the S phase of cell division seems to account for its anticancer action. It is also postulated that delayed hypersensitivity to 5-FU contributes to its anticancer activity.

Patients with State 0 vulvar cancer can be treated with five percent 5-FU cream and rebiopsied at intervals during and after therapy. If no histologic evidence of disease is present, routine follow-up is initiated. If disease remains, the patient can be retreated. However, if the cancer persists after two trials of 5-FU, and it is small and in one area only, local excision with serial sections of the specimen, examined to rule out invasive disease, can be successful. On the other hand, if the disease is persistent after 5-FU, and it is multifocal, vulvectomy is the treatment of choice. Again, careful examination should be performed to rule out invasion. If there is an area of invasion, therapy should conform to that necessary for Stage I disease and lymphadectomy added to the already performed vulvectomy.

Stages I, II and III
Stage I (three cm. lesion or less), Stage II (three cm. lesion or greater) and Stage III (lesion of any size with histologically proven lymph gland metastasis) are all treated by extended vulvectomy with inguinial and pelvic lymphadenectomy.

While many techniques of vulvectomy are satisfactory, an en bloc vulvectomy and inguinial lymphadenectomy should be used whenever possible. In our Center, pelvic lymphadenectomy is routinely performed simultaneously to vulvectomy, but as a separate procedure. There should be a tumor-free margin in the operative specimen; meticulous postoperative care is important. Blood loss should not be excessive, but...
Table 2.
Carcinoma of the Vulva
FIGO Method of Staging

T = Primary tumor

T1  Tumor confined to the vulva, two cm. or less in large diameter.
T2  Tumor confined to the vulva, more than two cm. in diameter.
T3  Tumor of any size with adjacent spread to the urethra and/or vagina
    and/or perineum and/or anus.
T4  Tumor of any size infiltrating the bladder mucosa and/or the rectal
    mucosa or both, including the upper part of the urethral mucosa
    and/or fixed to the bone.

N = Regional lymph nodes

N0  No nodes palpable.
N1  Nodes palpable in either groin, not enlarged, mobile (not clinically
    suspicious of neoplasm).
N2  Nodes palpable in either one or both groins, enlarged, firm and mobile
    (clinically suspicious of neoplasm).
N3  Fixed or ulcerated nodes.

M = Distant metastases

M0  No clinical metastases.
M1a  Palpable deep pelvic lymph nodes.
M1b  Other distant metastases.

Clinical Stage Groups

| Stage I |       | Stage IV |       |
|---------|-------|----------|-------|
| T1 N0 M0|       | T1 N3 M0 |       |
| T1 N1 M0|       | T2 N3 M0 |       |
| T2 N0 M0|       | T3 N3 M0 |       |
| T2 N1 M0|       | T4 N3 M0 |       |
| Stage II|       | T4 N0 M0 |       |
| Stage III|      | T4 N1 M0 |       |
| T3 N0 M0|       | T4 N2 M0 |       |
| T3 N1 M0|       | T1 N2 M0 |       |
| T3 N2 M0|       | All other conditions containing M1a or M1b |
| T1 N2 M0|       |

If cytology or histology of lymph nodes reveals malignant cells, the symbol + (plus)
should be added to N; if such examination does not reveal malignant cells, the
symbol – (minus) should be added to N.

if it occurs, early correction is obviously indicated. Antibiotic coverage is rou-
tine, as is drainage of the wound site. Early ambulation is practiced and silas-
tic urethral catheter drainage is maintained at least 72 hours. Wound dehis-
cence is a possible complication, best treated by Betadine whirlpool baths and
secondary closure. Grafting procedures are seldom necessary. The survival rates
with surgical treatment of invasive dis-
ease are excellent (91 percent); when re-
geonal metastases are present, the five-
year survival rate drops to 36 percent.
### Table 3.
Epidermoid Cancer of the Vulva
Proposed Staging Method

| Stage 0 | In situ cancer |
|---------|----------------|
| A. Single site | C*      |
|          | L**       |
|          | CL***     |
| B. Multiple sites | C |

**Stage I** = Invasive lesion (three cm. or less in greatest diameter)

| A. Single site | C |
| L |
| CL |
| B. Multiple sites | C |
| L |
| CL |

**Stage II** = Invasive lesion (greater than three cm.)

| A. Single site | C |
| L |
| CL |
| B. Multiple sites | C |
| L |
| CL |

**Stage III** = Invasive lesion with extension to superficial or deep inguinal lymph nodes (histologically proven).

| A. Unilateral lymph node involvement |
| B. Bilateral lymph node involvement |

**Stage IV** = Vulva lesion with involvement of contiguous organs and/or metastasis beyond regional lymph nodes.

| A. Contiguous organ involvement |
| B. Bony or distant metastases |
| A.&B. Both of the above |

*C = central (clitoral only). **L = lateral (labial, including fourchette). ***CL = combined.

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**Stage IV**

Stage IV cancer is divided into three substages of which only the first (substage A) can be treated surgically. Stage IV-A includes those patients with contiguous organ involvement, but without bony or distant metastases. In these patients, exenteration is necessary and has yielded an excellent overall survival rate. Patients without regional lymph gland involvement have five-year survival rates of 75 percent, but in those with lymph gland metastases, survival diminished to 22 percent in a composite
Vulvar Cancer Treatment Protocol Flow Chart

Vulvar Lesion
- Dark field
- STS
- Frei test
- Donovan body smear

Dx - Protocol
- Non-malignant
- Malignant
- Vulvectomy

Dx
- Stage 0 Ca in situ
- Stage I lesion < 3cm
- Stage II lesion > 3cm
- Stage III lymph gland metastasis

Rx
- Rx as indicated
- S-FU
- Rebiopsy
- No disease
- Persistent disease

Vulvectomy
- Vulvectomy, inguinal & pelvic lymphadenectomy
- Vulvectomy, exenteration, lymphadenectomy
- Individualization:
  a. Betatron Rx
  b. Systemic chemotherapy
  c. Palliation

Routine Followup

series. Bony or distant metastases are an absolute contraindication to vulvectomy or exenteration. Age carries a relative contraindication to surgery, since patients over 70 years old have a higher operative mortality and lacked five-year survivals. Palliative exenterations are not indicated.

Patients with Stage IV-B and IV-AB cancer are not candidates for surgical procedures. In this group, radiotherapy may play a role, and is often effective against squamous cell cancer of the vulva. However, the tumor bed tolerates irradiation poorly and there are significant complications. Even in early le-
sions, irradiation has not provided survival rates that approximate surgery. Most investigators conclude that, at best, radiation therapy is an alternative method of treatment.11,12

Results

Utilizing surgical treatment only and, correcting for autopsy-proven medical disease, excellent survival rates can be expected, unless the regional lymph glands are invaded. (Table 4.) In patients with regional disease, Stage III, survival drops to 36 percent. In some patients with contiguous organ involvement without regional lymph gland metastases, (Stage IV-A) excellent survival rates represent the effectiveness of surgical removal. Patients in subsets IV-B and IV-AB, as expected, exhibit the poorest prognosis.

Follow-up

The patient with vulvar cancer should be followed for the remainder of her life. Cancer should be continually searched for elsewhere. In 22 percent of our patients, a second cancer, usually of the genital tract, occurred. Full treatment of these cancers is warranted. An active rehabilitation program, especially for patients with advanced cancer, should be maintained and follow-up used for patient education and support.

Table 4.
Results of Treatment for Epidermoid Cancer of the Vulva

| Stage of Disease | Percent Survival |
|------------------|------------------|
| 0                | 100              |
| I                | 100              |
| II               | 83               |
| III              | 36               |
| IV               | 39               |
| IV-A             | 75               |
| IV-B             | 22               |
| IV-AB            | 0                |

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