Vagina

Protocol applies to all invasive carcinomas of the vagina.

Protocol revision date: January 2005
Based on AJCC/UICC TNM, 6th edition and FIGO 2001 Annual Report

Procedures
• Cytology (No Accompanying Checklist)
• Biopsy
• Vaginectomy
• Radical Vaginectomy

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For the Members of the Cancer Committee, College of American Pathologists

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the “Surgical Pathology Cancer Case Summary (Checklist)” portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with the document. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.
Summary of Changes to Checklist(s)

Protocol revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.
Surgical Pathology Cancer Case Summary (Checklist)

*VAGINA: Biopsy
(Note: Use of checklist for biopsy specimens is optional)

*Patient name:
*Surgical pathology number:

*Note: Check 1 response unless otherwise indicated.

*MACROSCOPIC

*Specimen Type
*___ Incisional biopsy
*___ Other (specify): ___________________________
*___ Not specified

*Tumor Site
*___ Upper third
*___ Middle third
*___ Lower third
*___ Not specified

*MICROSCOPIC

*Histologic Type (check all that apply)
*___ Squamous cell carcinoma
*___ Adenosquamous carcinoma
*___ Adenocarcinoma
    *___ Mucinous
    *___ Clear cell
    *___ Not otherwise specified
*___ Other (specify): ___________________________
*___ Carcinoma, type cannot be determined

* Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
*Histologic Grade
  * ___ Not applicable
  * ___ GX: Cannot be assessed
  * ___ G1: Well differentiated
  * ___ G2: Moderately differentiated
  * ___ G3: Poorly differentiated
  * ___ G4: Undifferentiated
  * ___ Other (specify): ___________________________

*Extent of Invasion
  * ___ Cannot be assessed
  * ___ Stromal invasion (specify if present)
  * ___ Muscle invasion (specify if present)

*Margins
  * ___ Not applicable
  * ___ Cannot be assessed
  * ___ Uninvolved by tumor
  * ___ Involved by tumor
    Specify site: ___________________________

*Additional Pathologic Findings (check all that apply)
  * ___ None identified
  * ___ Dysplasia
  * ___ Condyloma acuminatum
  * ___ Adenosis
  * ___ Other (specify): ___________________________

*Comment(s)

* Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2005
Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition
and FIGO 2001 Annual Report

VAGINA: Excisional Biopsy, Resection

Patient name:
Surgical pathology number:

**Note:** Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type

___ Excisional biopsy
___ Partial vaginectomy
___ Radical vaginectomy
___ Other (specify): ____________________________
___ Not specified

Tumor Site (check all that apply)

___ Upper third
  * ___ Circumferential
  * ___ Anterior
  * ___ Posterior
  * ___ Left lateral
  * ___ Right lateral

___ Middle third
  * ___ Circumferential
  * ___ Anterior
  * ___ Posterior
  * ___ Left lateral
  * ___ Right lateral

___ Lower third
  * ___ Circumferential
  * ___ Anterior
  * ___ Posterior
  * ___ Left lateral
  * ___ Right lateral

___ Not specified

Tumor Size

Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm
___ Cannot be determined (see Comment)

* Data elements with *asterisks* are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
MICROSCOPIC

Histologic Type (check all that apply)
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Adenocarcinoma
  * Mucinous
  * Clear cell
  * Not otherwise specified
- Other (specify): ____________________________
- Carcinoma, type cannot be determined

Histologic Grade
- Not applicable
- GX: Cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- G4: Undifferentiated
- Other (specify): ____________________________

Pathologic Staging (pTNM [FIGO])

Primary Tumor (pT)
- pTX [-]: Cannot be assessed
- pT0 [-]: No evidence of primary tumor
- pTis [0]: Carcinoma in situ
- pT1 [-]: Tumor confined to vagina
- pT2 [II]: Tumor invades paravaginal tissues but not to pelvic wall
- pT3 [III]: Tumor extends to pelvic wall
- pT4 [IVA]: Tumor invades mucosa of bladder or rectum and/or extends beyond true pelvis

Regional Lymph Nodes (pN)
- pNX: Cannot be assessed
- pN0: No regional lymph node metastasis
- pN1 [III]: Pelvic or inguinal lymph node metastasis (pT1-pT3)
- pN1 [IVA]: Pelvic or inguinal lymph node metastasis (pT4)
- pN1 [IVB]: Pelvic or inguinal lymph node metastasis (pT1-pT4, pM1)
Specify: Number examined: ___
Number involved: ___

Distant Metastasis (pM)
- pMX: Cannot be assessed
- pM1 [IVB]: Distant metastasis
  * Specify site(s), if known: ____________________________

* Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
Margins (check all that apply)
___ Cannot be assessed
___ Margins uninvolved by invasive carcinoma
   Distance of invasive carcinoma from closest margin: ___ mm
   Specify margin, if possible: ___________________________
___ Carcinoma in situ absent at margin
___ Carcinoma in situ present at margin
___ Margin(s) involved by invasive carcinoma
   Specify margin(s), if possible: ___________________________

*Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)
*___ Absent
*___ Present
*___ Indeterminate

*Additional Pathologic Findings (check all that apply)
*___ None identified
*___ Dysplasia
*___ Condyloma acuminatum
*___ Adenosis
*___ Other (specify): ___________________________

*Comment(s)

* Data elements with asterisks are not required for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.
Background Documentation

Protocol revision date: January 2005

I. Cytologic Material
A. Clinical Information
1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) pregnancy
      (2) uterine bleeding pattern, if abnormal
      (3) discharge per vagina
      (4) previous therapy (eg, hormonal, radiation, chemotherapy)
      (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs
         (Note A)
      (6) previous tumors and operations of possible relevance (Note B)
   b. Relevant findings (eg, radiologic studies, laboratory data) (Note C)
   c. Clinical diagnosis
   d. Operative findings
   e. Procedure (eg, vaginal pool aspiration, scraping of vaginal surface, fine-needle aspiration)
   f. Type(s) or site(s) of specimen(s)
B. Macroscopic Examination
1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of slides received, if appropriate
   c. Other (eg, cytologic preparation from tissue)
   d. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation (eg, smear, touch preparation)
3. Special studies (specify) (eg, immunocytochemistry)
C. Microscopic Evaluation
1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present (Note D)
   a. Histologic type, if possible (Note E)
   b. Other characteristics, as pertinent
3. Additional cytologic findings, if present
4. Results/status of special studies (specify)
5. Comments
   a. Correlation with intraprocedural consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate
II. Biopsy
   (Incisional or Excisional)
A. Clinical Information
   1. Patient identification
      a. Name
      b. Identification number
      c. Age (birth date)
   2. Responsible physician(s)
   3. Date of procedure
   4. Other clinical information
      a. Relevant history
         (1) pregnancy
         (2) uterine bleeding pattern, if abnormal
         (3) discharge per vagina
         (4) previous therapy (eg, hormonal, radiation, chemotherapy)
         (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs
            (Note A)
         (6) previous tumors and operations of possible relevance (Note B)
      b. Relevant findings (eg, radiologic studies, laboratory data) (Note C)
      c. Clinical diagnosis
      d. Operative findings
      e. Procedure (eg, excisional biopsy, needle biopsy)
      f. Type(s) or site(s) of specimen(s) (eg, apex, anterior, posterior, lateral wall, upper, middle, lower third)
B. Macroscopic Examination
   1. Specimen
      a. Unfixed/fixed (specify fixative)
      b. Number of pieces
      c. Size or size range
      d. Descriptive features
      e. Orientation, if designated by surgeon
      f. Results of intraoperative consultation
   2. Tumor
      a. Dimensions, if appropriate
      b. Descriptive features
   3. Margins, if pertinent
   4. Other lesions, if present
   5. Submit entire specimen for microscopic evaluation unless otherwise indicated
   6. Special studies (specify)
C. Microscopic Evaluation
   1. Tumor
      a. Histologic type (Note E)
      b. Histologic grade (Note F)
      c. Extent, including resection margins, if pertinent
      d. Other features of possible prognostic or therapeutic significance
   2. Additional pathologic findings, if present (specify), and relation to tumor, if pertinent (Note G)
      a. Dysplasia
      b. Carcinoma in situ
      c. Condyloma acuminatum
      d. Adenosis
      e. Other(s)
   3. Results/status of special studies (specify)
4. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

III. Vaginectomy
A. Clinical Information
   1. Patient identification
      a. Name
      b. Identification number
      c. Age (birth date)
   2. Responsible physician(s)
   3. Date of procedure
   4. Other clinical information
      a. Relevant history
         (1) pregnancy
         (2) uterine bleeding pattern, if abnormal
         (3) discharge per vagina
         (4) previous therapy (eg, hormonal, radiation, chemotherapy)
         (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs
            (Note A)
         (6) previous tumors and operations of possible relevance (Note B)
      b. Relevant findings (eg, radiologic studies, laboratory data) (Note C)
      c. Clinical diagnosis
      d. Operative findings
      e. Procedure (eg, partial vaginectomy)
      f. Type(s) or site(s) of specimens

B. Macroscopic Examination
   1. Specimen
      a. Organ/tissue(s) received
      b. Fixed/unfixed (specify fixative)
      c. Number of pieces
      d. Size (length/circumference/thickness)
      e. Orientation, if indicated by surgeon
      f. Descriptive features (inner and outer surfaces, wall)
      g. Results of intraoperative consultation
   2. Tumor
      a. Size
      b. Descriptive features
   3. Margins, if pertinent
   4. Additional pathologic findings, if present
   5. Tissue(s) submitted for microscopic evaluation
   6. Special studies (specify) (eg, staining with Schiller’s or Lugol’s solution) (Note H)

C. Microscopic Examination
   1. Tumor
      a. Histologic type (Note E)
      b. Histologic grade (Note F)
      c. Extent of invasion (Note I)
      d. Resection margins
      e. Other features of possible prognostic or therapeutic significance
2. Additional pathologic findings, if present, and relation to tumor, if pertinent (Note J)
   a. Dysplasia
   b. Carcinoma in situ
   c. Condyloma acuminatum
   d. Adenosis
   e. Other(s)
3. Results/status of special studies
4. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

IV. Radical Vaginectomy
   (Hysterectomy, Unilateral or Bilateral Salpingo-Oophorectomy, Lymphadenectomy or Sentinel Lymph Node Biopsy, Removal of Other Organs and Tissues)

A. Clinical Information
   1. Patient identification
      a. Name
      b. Identification number
      c. Age (birth date)
   2. Responsible physician(s)
   3. Date of procedure
   4. Other clinical information
      a. Relevant history
         (1) pregnancy
         (2) uterine bleeding pattern, if abnormal
         (3) discharge per vagina
         (4) previous therapy (eg, hormonal, radiation, chemotherapy)
         (5) prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs
            (Note A)
         (6) previous tumors and operations of possible relevance (Note B)
      b. Relevant findings (eg, radiologic studies, laboratory data) (Note C)
      c. Clinical diagnosis
      d. Operative findings
      e. Procedure
      f. Type(s) or site(s) of specimen(s)

B. Macroscopic Examination
   1. Specimen
      a. Organs/tissues received
      b. Unfixed/fixed (specify fixative)
      c. Measurements, if appropriate
      d. Orientation, if indicated by surgeon
      e. Results of intraoperative consultation
   2. Vagina
      a. Size (length, circumference, thickness)
      b. Descriptive features (inner and outer surfaces, wall)
      c. Tumor
         (1) size
         (2) descriptive features
      d. Resection margins, if pertinent
      e. Additional pathologic findings, if present
3. Uterine cervix
   a. Descriptive features (Note J)
      (1) appearance of ectocervix
      (2) appearance of endocervix
   b. Tumor, if present
      (1) descriptive features
      (2) size
      (3) extent
      (4) relation to vaginal tumor
   c. Additional pathologic findings, if present (specify)
4. Uterine corpus
   a. Descriptive features of endometrium, myometrium, and serosa
   b. Tumor, if present
      (1) measurements
      (2) location
      (3) relation to main tumor
   c. Additional pathologic findings, if present (specify)
5. Fallopian tube(s) (Note K)
   a. Descriptive features, including measurements
   b. Tumor, if present
      (1) measurements
      (2) location
      (3) relation to vaginal tumor
   c. Additional pathologic findings, if present (specify)
6. Ovary or ovaries
   a. Descriptive features
      (1) outer surface
      (2) sectioned surfaces
   b. Dimensions
   c. Tumor, if present
      (1) measurements
      (2) location
      (3) relation to vaginal tumor
   d. Additional pathologic findings, if present (specify)
7. Regional lymph nodes
   a. Number and size range at each designated location
   b. Tumor, if present
      (1) size
      (2) descriptive features
   c. Additional pathologic findings, if present (specify)
8. Other organ(s) or tissue(s) removed
   a. Type(s)
   b. Dimensions
   c. Descriptive features
   d. Tumor, if present
      (1) measurements
      (2) location
      (3) relation to vaginal tumor
   e. Other features of possible prognostic or therapeutic significance
9. Tissues submitted for microscopic evaluation (specify)
10. Special studies (specify)
C. **Microscopic Evaluation**

1. **Vagina**
   a. **Tumor**
      (1) histologic type (Note E)
      (2) histologic grade (Note F)
      (3) extent of invasion (Note I)
      (4) other features of possible prognostic or therapeutic significance
   b. **Status of resection margins**
   c. **Additional pathologic findings, if present, and relation to tumor, if pertinent** (Note G)
      (1) dysplasia
      (2) carcinoma in situ
      (3) condyloma acuminatum
      (4) adenosis

2. **Uterine cervix (see Cervix protocol if second primary tumor is present)**
   a. **Metastatic tumor, if present**
      (1) histologic type (Note E)
      (2) histologic grade (Note F)
      (3) extent of invasion
      (4) location and relation to vaginal tumor
   b. **Additional pathologic findings, if present, and relation to tumor, if pertinent**
      (1) dysplasia
      (2) carcinoma in situ
      (3) condyloma acuminatum

3. **Uterine corpus (see Endometrium protocol if separate primary tumor)**
   a. **Metastatic tumor, if present**
      (1) histologic type (Note E)
      (2) histologic grade (Note F)
      (3) location and relation to vaginal tumor
   b. **Additional pathologic findings, if present, and relation to tumor, if pertinent**
   c. **Portion uninvolved by tumor**

4. **Fallopian tube(s) (see Fallopian Tube protocol if separate primary)**
   a. **Metastatic tumor, if present**
      (1) histologic type (Note E)
      (2) histologic grade (Note F)
      (3) location and relation to vaginal tumor
   b. **Additional pathologic findings, if present**

5. **Ovary/ovaries (see Ovary protocol if separate primary)**
   a. **Metastatic tumor, if present**
      (1) histologic type (Note E)
      (2) histologic grade (Note F)
      (3) location and relation to vaginal tumor
   b. **Additional pathologic findings, if present**

6. **Regional lymph nodes (Note I)**
   a. **Location, if designated**
   b. **Tumor, if present**
      (1) histologic type, if different from vaginal tumor
      (2) histologic grade, if different from vaginal tumor
   c. **Additional pathologic findings, if present**
7. Other organ(s) or tissue(s) removed (see appropriate protocol for second primary)
   a. Metastatic tumor, if present (Note I)
      (1) location, distribution, and extent
      (2) histologic type, if different from main tumor
      (3) histologic grade, if different from main tumor
   b. Resection margins, if applicable
   c. Additional pathologic findings, if present
8. Results/status of special studies (specify)
9. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Prenatal DES Exposure
Prenatal exposure to diethylstilbestrol (DES) or related synthetic drugs were relatively common in the United States and other countries until 1971, when its relation to clear cell adenocarcinomas of the vagina and cervix led to proscription of these drugs by the Food and Drug Administration. From the 1970s to the turn of the 21st century, most patients with clear cell adenocarcinoma of the vagina had a history of DES exposure. As this cohort ages, the diagnosis has been less common, and most women with the diagnosis currently have no DES exposure history. A bimodal age peak for DES-related carcinoma has, however, been recently reported, and therefore a history of this type of prenatal drug exposure should alert the pathologist to the possible presence of those tumors and associated lesions.\(^1\)-\(^4\)

B. Prior Tumors and Operations
A history of dysplasia, carcinoma in situ or invasive carcinoma of the cervix as well as knowledge of its microscopic features may be essential in the determination whether a subsequent vaginal tumor is a recurrent or new tumor. Also, a history of a carcinoma higher in the female genital tract may influence the interpretation of a neoplasm that is detected in a specimen from the vagina. Prior pathology slides and reports should be obtained and reviewed if a review is deemed essential by the clinician or pathologist for optimal pathologic evaluation of the present specimen.

C. Clinical Findings and DES Exposure
Naked-eye examination, colposcopy, and iodine staining of the cervix and vagina may disclose a variety of changes highly suspicious of prenatal diethylstilbestrol (DES) exposure, such as cervical hypoplasia, pseudopolyp, or coxcomb deformity, and vaginal adenosis or ridge, any of which should alert the pathologist to examine carefully for DES changes.\(^1\)-\(^4\)

D. Bethesda Classification System of Cervical/Vaginal Cytology
For consistency in reporting, the cytologic classification proposed in The Bethesda System 2001 is recommended.\(^5\) Although this protocol does not preclude the use of other systems of classification, use of the Papanicolaou class designation system is strongly discouraged.
Cervical/Vaginal Cytology Classification (The Bethesda 2001 System)

**Negative for Intraepithelial Lesion or Malignancy**
- **Organisms**
  - *Trichomonas vaginalis*
  - Fungal organisms morphologically consistent with *Candida* spp
  - Shift in flora suggestive of bacterial vaginosis
  - Bacteria morphologically consistent with *Actinomyces* spp
  - Cellular changes associated with Herpes simplex virus

- Other non-neoplastic findings (optional to report, list not inclusive)
  - Reactive cellular changes associated with
    - inflammation (includes typical repair)
    - irradiation
  - Glandular cells status post hysterectomy
  - Atrophy

**Other**

**Epithelial Cell Abnormalities**

**Squamous Cell**
- Atypical squamous cells
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL)"
  - encompassing: HPV/mild dysplasia/VAIN I
- High grade squamous intraepithelial lesion (HSIL)
  - encompassing: moderate and severe dysplasia/ VAIN2/VAIN3/VACIS
  - with features suspicious for invasion (if invasion suspected)
- Squamous cell carcinoma

**Glandular Cell**
- Atypical
  - glandular cells (NOS or specify in comment)
  - glandular cells, favor neoplastic
- Adenocarcinoma
  - not otherwise specified (NOS)

**Other Malignant Neoplasms**
- Specify

# Cellular changes of HPV cytopathic effect, previously termed “koilocytosis,” “koilocytic atypia,” or “condylomatous atypia,” are included in the category of LSIL.

**E Histologic Type**
The World Health Organization (WHO) classification and nomenclature of vaginal tumors is recommended because of its wide acceptance.
WHO Classification
Precancerous Lesions and Carcinomas of the Vagina (Modified)

Squamous intraepithelial lesions  Vaginal intraepithelial neoplasia (VAIN)
  Mild dysplasia  VAIN 1
  Moderate dysplasia  VAIN 2
  Severe dysplasia  VAIN 3
  Carcinoma in situ  VAIN 3

Squamous cell carcinoma
  Keratinizing
  Nonkeratinizing
  Verrucous
  Warty (condylomatous)

Atypical adenosis
Adenocarcinoma
  Clear cell
  Endometrioid
  Mucinous
    Endocervical type
    Intestinal type
  Mesonephric
Adenosquamous carcinoma
Adenoid cystic carcinoma
Adenoid basal carcinoma
Carcinoid tumor
Small cell carcinoma
Undifferentiated carcinoma

F. Histologic Grade
No specific grading system for vaginal cancers is recommended. For the sake of uniformity, however, it is suggested that 4 grades be used, as shown below, with grades 1 to 3 assigned to carcinomas showing squamous or glandular differentiation while grade 4 (undifferentiated) applied to tumors with no differentiation. Microinvasive carcinoma is not, currently, a recognized entity in the vagina, in contradistinction to the cervix, and the term is therefore not used. Superficially invasive tumors which invade 3 mm or less and which do not manifest lymphovascular invasion (LVI) have a low incidence of lymph node metastasis.7

Grade X  Cannot be assessed
Grade 1  Well differentiated
Grade 2  Moderately differentiated
Grade 3  Poorly differentiated
Grade 4  Undifferentiated

G. Other Lesions
Squamous dysplasia or carcinoma in situ, adenocarcinoma in situ, or atypical adenosis, particularly if such changes are at the resection margin, may increase the frequency of recurrent tumor.
H. Staining of Mucosal Surface
Schiller’s or Lugol’s solutions stain glycogenated epithelium brown. Therefore, they stain glycogenated squamous epithelium and well-glycogenated tumors. The stains are useful in identifying sites of non-staining vaginal adenosis or immature squamous metaplasia of adenosis in patients exposed to diethylstilbestrol (DES), which may not be detectable before staining.

I. TNM and FIGO Stage Groupings
The TNM staging system for vaginal cancer endorsed by the American Joint Committee on Cancer (AJCC) and the International Union against Cancer (UICC), and the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO) are recommended.

By AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

TNM and FIGO Staging Systems for Vaginal Carcinoma

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>TNM</th>
<th>FIGO</th>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>(--)</td>
<td></td>
<td></td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>(--)</td>
<td></td>
<td></td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>0</td>
<td>I</td>
<td></td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>I</td>
<td></td>
<td>Tumor confined to vagina</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>I</td>
<td></td>
<td>Tumor invades paravaginal tissues but not to pelvic wall#</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>IV</td>
<td></td>
<td>Tumor extends to pelvic wall</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>IVA</td>
<td></td>
<td>Tumor invades mucosa of bladder or rectum and/or extends beyond the true pelvis (bullous edema is not sufficient to classify a tumor as T4)</td>
</tr>
<tr>
<td>(M1)</td>
<td></td>
<td>IVB</td>
<td></td>
<td>Distant metastasis (excludes peritoneal metastasis)</td>
</tr>
</tbody>
</table>

# Pelvic wall is defined as muscle, fascia, neurovascular structures, or skeletal portions of the bony pelvis.

Regional Lymph Nodes (N): TNM
NX   Regional lymph nodes cannot be assessed
N0   No regional lymph node metastasis
N1   Pelvic or inguinal lymph node metastasis
Distant Metastasis (M): TNM
MX  Distant metastasis cannot be assessed
M0  No distant metastasis
M1  Distant metastasis

Stage Groupings

<table>
<thead>
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<th>AJCC/UICC TNM</th>
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<td>Stage 0</td>
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<td>T3 N0, N1 M0</td>
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<td>Stage IVA</td>
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<td>Stage IVB</td>
<td>Any T Any N M1</td>
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</table>

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y,” “r,” and “a” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

The “a” prefix designates the stage determined at autopsy: aTNM.

Additional Descriptors

Residual Tumor (R)
Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

| RX  | Presence of residual tumor cannot be assessed |
| R0  | No residual tumor                             |
| R1  | Microscopic residual tumor                    |
| R2  | Macroscopic residual tumor                    |

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond
to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

**Vessel Invasion**
By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

**Lymphatic Vessel Invasion (L)**
- LX: Lymphatic vessel invasion cannot be assessed
- L0: No lymphatic vessel invasion
- L1: Lymphatic vessel invasion

**Venous Invasion (V)**
- VX: Venous invasion cannot be assessed
- V0: No venous invasion
- V1: Microscopic venous invasion
- V2: Macroscopic venous invasion

**Regional Lymph Nodes: Isolated Tumor Cells**
Isolated tumor cells (ITC) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITC found by either standard histologic examination, immunohistochemical stains (eg, cytokeratin), or nonmorphological techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be so identified. There is currently no guidance in the literature as to how these patients should be coded; until further studies are available, they should be coded as “N1” with a comment noting how the cells were identified.

**Sentinel Lymph Nodes**
The sentinel lymph node is the first node to receive drainage from a primary tumor. There may be more than 1 sentinel node for some tumors. If a sentinel node contains metastatic tumor, it indicates that other more distant nodes may also contain metastatic disease. If sentinel nodes are negative, other regional nodes are less likely to contain metastasis.

**J. Cervical Abnormalities**
Ectropion (erosion, eversion) of the cervix, which is characterized by the appearance of glandular (columnar) epithelium outside the external os of the cervix, is seen in approximately 90% of women exposed to diethylstilbestrol (DES) in utero (but is often seen in non-exposed women as well). Approximately one-third of patients exposed to DES have 1 or more gross structural abnormalities of the cervix.

**K. Fallopian Tubes**
The fallopian tubes are abnormal in some women exposed to diethylstilbestrol (DES) in the form of hypoplasia or defects demonstrated on hysterosalpingographic examination.
References

Bibliography