

# Ovary

**Protocol applies to all primary borderline and malignant surface epithelial tumors, germ cell tumors, and sex cord-stromal tumors.**

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

## Procedures

- **Cytology** (No Accompanying Checklist)
- **Incisional Biopsy** (No Accompanying Checklist)
- **Unilateral Oophorectomy**
- **Salpingo-oophorectomy**
- **Subtotal Resection or Removal of Tumor in Fragments**
- **Hysterectomy with Salpingo-oophorectomy**
- **Second-look Staging** (No Accompanying Checklist)

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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)

*Protocol revision date: January 2005  
Applies to primary borderline tumors, carcinomas,  
germ cell tumors, and sex-cord stromal tumors only  
Based on AJCC/UICC TNM, 6<sup>th</sup> edition  
and FIGO 2001 Annual Report*

### **OVARY: Oophorectomy, Salpingo-oophorectomy, Subtotal Oophorectomy or Removal of Tumor in Fragments, Hysterectomy with Salpingo-oophorectomy**

***Note: Applies to ovarian primary tumor. If bilateral tumors of 2 different histologic types are present, separate checklists should be used for each tumor.***

Patient name:

Surgical pathology number:

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

#### **MACROSCOPIC**

##### **Specimen Type (check all that apply)**

- Right oophorectomy
- Left oophorectomy
- Right salpingo-oophorectomy
- Left salpingo-oophorectomy
- Subtotal right oophorectomy
- Subtotal left oophorectomy
- Removal of tumor in fragments
- Hysterectomy with salpingo-oophorectomy
- Omentectomy
- Other (specify): \_\_\_\_\_
- Not specified

##### **Primary Tumor Site (check all that apply)**

- Diffuse bilateral ovarian involvement, primary site cannot be determined

##### Right Ovary

- Not applicable
- Parenchymal growth
- Growth on surface
- Uninvolved
- Not specified

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\* 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.

Left Ovary

- Not applicable
- Parenchymal growth
- Growth on surface
- Uninvolved
- Not specified

**Specimen Integrity (check all that apply)**

Right Ovary

- Not applicable
- Intact
- Ruptured
- Fragmented
- Other (specify): \_\_\_\_\_

Left Ovary

- Not applicable
- Intact
- Ruptured
- Fragmented
- Other (specify): \_\_\_\_\_

**Tumor Size**

Right Ovary (if applicable)

- Greatest dimension: \_\_\_ cm
- \*Additional dimensions: \_\_\_ x \_\_\_ cm
- Cannot be determined (see Comment)

Left Ovary (if applicable)

- Greatest dimension: \_\_\_ cm
- \*Additional dimensions: \_\_\_ x \_\_\_ cm
- Cannot be determined (see Comment)

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**MICROSCOPIC**

**Histologic Type (check all that apply)**

- Serous, borderline
- Serous, carcinoma
- Mucinous, borderline
- Mucinous, carcinoma
- Endometrioid, borderline
- Endometrioid, carcinoma
- Clear cell, borderline
- Clear cell, carcinoma
- Transitional cell, borderline
- Transitional cell, carcinoma
- Mixed epithelial, borderline  
Specify types: \_\_\_\_\_
- Mixed epithelial, carcinoma  
Specify types: \_\_\_\_\_
- Undifferentiated
- Granulosa cell
- Germ cell  
Specify type(s): \_\_\_\_\_
- Other(s) (specify): \_\_\_\_\_

**Histologic Grade**

- Not applicable
- GX: Cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- G4: Reserved solely for tumors in the undifferentiated category (WHO classification)

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**Pathologic Staging (pTNM [FIGO])**Primary Tumor (pT)

- \_\_\_ pTX [--]: Cannot be assessed  
 \_\_\_ pT0 [--]: No evidence of primary tumor  
 \_\_\_ pT1 [I]: Tumor limited to ovaries (1 or both)  
 \* \_\_\_ pT1a [IA]: Tumor limited to 1 ovary; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings  
 \* \_\_\_ pT1b [IB]: Tumor limited to both ovaries; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings  
 \* \_\_\_ pT1c [IC]: Tumor limited to 1 or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings  
 \_\_\_ pT2 [II]: Tumor involves 1 or both ovaries with pelvic extension and/or implants  
 \* \_\_\_ pT2a [IIA]: Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings  
 \* \_\_\_ pT2b [IIB]: Extension to other pelvic tissues. No malignant cells in ascites or peritoneal washings  
 \* \_\_\_ pT2c [IIC]: Pelvic extension and/or implants (T2a or T2b / IIa or IIb) with malignant cells in ascites or peritoneal washings  
 pT3 and/or N1 [III]: Tumor involves 1 or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis (including liver capsule metastasis) and/or regional lymph node metastasis  
 \_\_\_ pT3a [IIIA]: Microscopic peritoneal metastasis beyond pelvis  
 \_\_\_ pT3b [IIIB]: Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension  
 \_\_\_ pT3c and/or N1 [IIIC]: Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis  
 \_\_\_ Any T/Any N and M1 [IV]: Growth involving 1 or both ovaries with distant metastasis.

*Note: If pleural effusion is present, there must be positive cytology to assign a case to stage IV. Parenchymal liver metastasis is classified as stage IV.*

Regional Lymph Nodes (pN)

- \_\_\_ pNX: Cannot be assessed  
 \_\_\_ pN0: No regional lymph node metastasis  
 \_\_\_ pN1 [IIC]: Regional lymph node metastasis  
 Specify: Number examined: \_\_\_  
 Number involved: \_\_\_

Distant Metastasis (pM)

- \_\_\_ pMX: Cannot be assessed  
 \_\_\_ pM1 [IV]: Distant metastasis  
 \*Specify site(s), if known: \_\_\_\_\_

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**Implants (only applies to borderline tumors) (check all that apply)**

Not applicable/none sampled

Noninvasive (epithelial) implants

Not present

Present

Specify site(s): \_\_\_\_\_

Noninvasive (desmoplastic) implants

Not present

Present

Specify site(s): \_\_\_\_\_

Invasive implants

Not present

Present

Specify site(s): \_\_\_\_\_

**Summary of Organs/Tissues Microscopically Involved by Tumor (check all that apply)**

One ovary

Both ovaries

Omentum

Uterus

Peritoneum

Other organs/tissues

Specify all: \_\_\_\_\_

**\*Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**

\*  Absent

\*  Present

\*  Indeterminate

**\*Additional Pathologic Findings (check all that apply)**

\*  None identified

\*  Endometriosis

\*  Ovarian

\*  Extraovarian

\*  Endosalpingiosis

\*  Other(s):

\*Specify site(s) and type(s): \_\_\_\_\_

**\*Comment(s)**

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## Background Documentation

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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) currently pregnant
    - (2) abnormal uterine bleeding pattern
    - (3) previous therapy (hormonal, radiation, chemotherapy)
    - (4) previous tumors or operations of possible relevance
    - (5) family history of ovarian or breast cancer
  - b. Relevant findings (eg, radiologic studies, aspiration of cyst, laboratory data, ascites)
  - c. Clinical diagnosis
  - d. Procedure (eg, brushing, washing, other)
  - e. Operative findings (eg, rupture-preoperative, intraoperative, or postoperative)
  - f. Type(s) or site(s) of specimen(s)
    - (1) ascitic fluid
    - (2) peritoneal washings (specify site)
    - (3) brushings (specify site)
    - (4) cyst fluid (specify site)
    - (5) fine-needle aspirate (specify site)
    - (6) cytology preparation of tissue (touch preparation) (specify site)
    - (7) pleural fluid
    - (8) other

#### B. Macroscopic Examination

1. Specimen
  - a. Unfixed/fixed (specify fixative)
  - b. Number of slides received, if appropriate
  - c. Quantity and appearance of fluid specimen, if appropriate
  - d. Other (eg, tissue received for cytologic preparation)
  - e. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation (eg, smear, cytocentrifuge, touch or filter preparation, cell block)
3. Tissues submitted for special studies (specify) (eg, frozen tissue for immunohistochemistry, flow cytometry)

#### C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present
  - a. Histologic type, if possible (Note **A**)
  - b. Other characteristics, as pertinent
3. Additional cytologic findings, if present
4. Results/status of special studies (specify)
5. Pathologic stage

6. Comments
  - a. Correlation with intraoperative consultation, as appropriate
  - b. Correlation with other specimens, as appropriate
  - c. Correlation with clinical information, as appropriate

## II. Incisional Biopsy

### 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) currently pregnant
    - (2) abnormal uterine bleeding pattern
    - (3) previous therapy (hormonal, radiation, chemotherapy)
    - (4) previous tumors or operations of possible relevance
    - (5) family history of ovarian or breast cancer
  - b. Relevant findings (eg, radiologic studies, aspiration of cyst, laboratory data, ascites)
  - c. Clinical diagnosis
  - d. Procedure
  - e. Operative findings (eg, rupture-preoperative, intraoperative, or postoperative)
  - f. Type(s) or site(s) of specimen(s)

### B. Macroscopic Examination

1. Specimen
  - a. Fixed/unfixed (specify fixative)
  - b. Number of pieces, size or size range
  - c. Descriptive features
  - d. Orientation, if designated
  - e. Results of intraoperative consultation
2. Tissues submitted for microscopic evaluation
  - a. Submit entire specimen
  - b. Frozen section tissue fragment(s) (unless saved for special studies)
3. Tissues submitted for special studies (specify) (eg, frozen tissue for immunohistochemistry, flow cytometry)

### C. Microscopic Evaluation

1. Tumor, if present
  - a. Histologic type (Note **A**)
  - b. Histologic grade (Note **B**)
  - c. Invasion
  - d. Other features of possible prognostic or therapeutic significance
2. Additional pathologic findings, if present (specify); and relation to tumor, if pertinent
3. Results/status of special studies (Note **C**)
4. Pathologic stage
5. Comments
  - a. Correlation with intraoperative consultation, as appropriate
  - b. Correlation with other specimens, as appropriate
  - c. Correlation with clinical information, as appropriate

### III. Unilateral Oophorectomy or Salpingo-oophorectomy

#### 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) currently pregnant
    - (2) abnormal uterine bleeding pattern
    - (3) previous therapy (hormonal, radiation, chemotherapy)
    - (4) previous tumors or operations of possible relevance
    - (5) family history of ovarian or breast cancer
  - b. Relevant findings (eg, radiologic studies, laboratory data, ascites)
  - c. Clinical diagnosis
  - d. Procedure
  - e. Operative findings (eg, rupture-preoperative, intraoperative, or postoperative)
  - f. Type(s) or site(s) of specimen(s)
  - g. Identification of areas for special study
    - (1) rupture site(s)
    - (2) adhesions suspicious for tumor
    - (3) resection margin(s), if pertinent

#### B. Macroscopic Examination

1. Specimen
  - a. Organs/tissues received (specify)
  - b. Unfixed/fixed (specify fixative)
  - c. Number of pieces
  - d. Dimensions (measure attached tissues individually)
  - e. Orientation of specimen
  - f. Results of intraoperative consultation
2. Ovary or ovary-tube, if fused into single mass<sup>#</sup>

*# If fused ovary and tube are identifiable separately on sectioning, describe tumor in each, including relation to one another.*

  - a. Size, weight, or volume, as appropriate
  - b. Outer surface (describe)
    - (1) adhesions, roughening, granularity (largest dimension or proportion of total area involved)
    - (2) rupture (Note **D**)
  - c. Sectioned surface of specimen or opened cyst(s)
  - d. Tumor (Note **E**)
    - (1) location (Note **F**)
      - i. cortex
      - ii. medulla
      - iii. hilus
      - iv. combination
      - v. replaces specimen
    - (2) dimensions (and proportion of entire specimen, if appropriate)
    - (3) solid and cystic components
      - i. proportion of each
      - ii. number of cysts, if easily countable
      - iii. size range of each component

- iv. location(s), if pertinent
- v. contents of cyst(s)
- vi. lining of cyst(s)
- vii. papillary or polypoid excrescences
- viii. roughening, etc (largest dimension or proportion of total area involved)
- e. Identification of areas for special study (eg, rupture site[s], adhesions suspicious for tumor)
- f. Resection margin(s), if pertinent
- g. Additional pathologic findings, if present
- 3. Fallopian tube, if not fused with ovary into single mass
  - a. Tumor, if present
    - (1) size
    - (2) location and relation to ovarian tumor
    - (3) descriptive features
  - b. Additional pathologic findings, if present
- 4. Tissues submitted for microscopic evaluation (Note **G**)
- 5. Tissues submitted for special studies (specify) (eg, frozen tissue for immunohistochemistry, flow cytometry)

### C. Microscopic Evaluation

- 1. Ovary or ovary-tube, if fused into single mass
  - a. Tumor
    - (1) site(s) of origin (Note **H**)
    - (2) location (Note **F**)
    - (3) surface (if possible, distinguish origin on surface from invasion onto surface by subjacent tumor)
    - (4) extent of invasion in ovary
      - i. cortex
      - ii. medulla
      - iii. hilus
      - iv. combination
      - v. replaces specimen
    - (5) extent and distribution of invasion of tube, if involved
    - (6) low-power pattern (single mass, discrete nodules, etc) (Note **I**)
    - (7) histologic type (note mixtures) (Note **J**)
    - (8) histologic grade (Note **B**)
    - (9) venous/lymphatic vessel invasion (Note **K**)
    - (10) other features of possible prognostic or therapeutic significance
  - b. Status of any specially designated resection margins
  - c. Additional pathologic findings, if present (specify); and relation to tumor, if pertinent (Note **L**)
- 2. Fallopian tube, if not fused with ovary into single mass
  - a. Tumor
    - (1) site(s) of origin (Note **H**)
    - (2) location
    - (3) extent
    - (4) histologic type or grade, if different from that of ovarian tumor
    - (5) venous/lymphatic vessel invasion (Note **K**)
    - (6) other features of possible prognostic or therapeutic significance
  - b. Status of any specially designated resection margins
  - c. Appearance of epithelium adjacent to tumor (Note **H**)
  - d. Additional pathologic findings, if present (specify); and relation to tumor, if pertinent
- 3. Results/status of special studies (Note **C**)

4. Pathologic stage
5. Comments
  - a. Correlation with intraoperative consultation, as appropriate
  - b. Correlation with other specimens, as appropriate
  - c. Correlation with clinical information, as appropriate

#### IV. Subtotal Resection or Removal of Tumor in Fragments

##### 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) currently pregnant
    - (2) abnormal uterine bleeding pattern
    - (3) previous therapy (hormonal, radiation, chemotherapy)
    - (4) previous tumors or operations of possible relevance
    - (5) family history of ovarian or breast cancer
  - b. Relevant findings (eg, radiologic studies, laboratory data, ascites)
  - c. Clinical diagnosis
  - d. Procedure
  - e. Operative findings (eg, rupture-preoperative, intraoperative, or postoperative)
  - f. Type(s) or site(s) of specimen(s)
  - g. Identification of areas for special study
    - (1) rupture site(s)
    - (2) adhesions suspicious for tumor
    - (3) resection margin(s), if pertinent

##### B. Macroscopic Examination

1. Specimen
  - a. Organs/tissues received
  - b. Unfixed/fixed (specify fixative)
  - c. Number of pieces
  - d. Dimensions (measure organs and tissues individually)
  - e. Orientation of specimen
  - f. Results of intraoperative consultation
  - g. Outer surface (describe)
    - (1) adhesions, roughening, granularity (largest dimension or proportion of total area involved)
    - (2) rupture (Note D)
  - h. Sectioned surface of specimen or opened cyst(s)<sup>#</sup>  
*# If fused ovary and tube are identifiable separately on sectioning, describe tumor in each, including relation to one another.*
  - i. Tumor (Note E)
    - (1) location (Note F)
      - i. cortex
      - ii. medulla
      - iii. hilus
      - iv. combination
      - v. replaces specimen

- j. Dimensions (and proportion of entire specimen, if appropriate) of solid and cystic components
  - (1) proportion of each
  - (2) number of cysts, if easily countable
  - (3) size range of each component
  - (4) location(s), if pertinent
  - (5) contents of cyst(s)
  - (6) lining of cyst(s)
  - (7) papillary or polypoid excrescences
  - (8) roughening, etc (largest dimension or proportion of total area involved)
- k. Outer surface (describe)
- l. Identification of areas for special study
  - (1) rupture site(s)
  - (2) adhesions suspicious for tumor
  - (3) resection margin(s), if pertinent
- 2. Additional pathologic findings, if present
- 3. Tissues submitted for microscopic evaluation (Note **G**)
- 4. Tissues submitted for special studies (specify) (eg, frozen tissue for immunohistochemistry, flow cytometry)

### C. Microscopic Evaluation

- 1. Tumor
  - a. Site(s) of origin (Note **H**)
  - b. Location (Note **F**)
  - c. Surface (if possible, distinguish origin on surface from invasion onto surface by subjacent tumor)
  - d. Extent of invasion
    - (1) cortex
    - (2) medulla
    - (3) hilus
    - (4) combination
    - (5) replaces specimen
  - e. Extent and distribution in tube, if involved
  - f. Low-power pattern (single mass, discrete nodules, etc) (Note **I**)
  - g. Histologic type (note mixtures) (Note **J**)
  - h. Histologic grade (Note **B**)
  - i. Venous/lymphatic vessel invasion (Note **K**)
  - j. Other features of possible prognostic or therapeutic significance
- 2. Status of any specially designated resection margins
- 3. Additional pathologic findings, if present; and relation to tumor, if pertinent (Note **L**)
  - a. Endometriosis
  - b. Abnormalities of surface epithelium or surface epithelial inclusion glands or cysts
  - c. Others
- 4. Results/status of special studies (Note **C**)
- 5. Pathologic stage
- 6. Comments
  - a. Correlation with intraoperative consultation, as appropriate
  - b. Correlation with other specimens, as appropriate
  - c. Correlation with clinical, information, as appropriate

## V. Hysterectomy with Salpingo-oophorectomy and Removal of Attached and/or Unattached Organs or Tissues (Staging Procedure)

### 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) currently pregnant
    - (2) abnormal uterine bleeding pattern
    - (3) previous therapy (hormonal, radiation, chemotherapy)
    - (4) previous tumors or operations of possible relevance
    - (5) family history of ovarian or breast cancer
  - b. Relevant findings (eg, radiologic studies, laboratory data, ascites)
  - c. Clinical diagnosis
  - d. Procedure
  - e. Operative findings (eg, rupture-preoperative, intraoperative, or postoperative)
  - f. Type(s) or site(s) of specimen(s)
  - g. Identification of areas for special study
    - (1) rupture site(s)
    - (2) adhesions suspicious for tumor
    - (3) resection margins, if pertinent

### B. Macroscopic Examination

1. Specimen
  - a. Organs/tissues included
  - b. Unfixed/fixed (specify fixative)
  - c. Number of pieces
  - d. Dimensions (measure attached tissues individually)
  - e. Orientation of specimen
  - f. Results of intraoperative consultation
2. Ovary or ovary-tube if fused into single mass<sup>#</sup>

*# If fused ovary and tube are identifiable separately on sectioning, describe tumor in each, including relation to one another.*

  - a. Size, weight, or volume, as appropriate
  - b. Outer surface (describe)
    - (1) adhesions, roughening, granularity (largest dimension or proportion of total area involved)
    - (2) rupture (Note **D**)
3. Sectioned surface of specimen or opened cyst(s)
  - a. Tumor (Note **E**)
    - (1) location (Note **F**)
      - i. cortex
      - ii. medulla
      - iii. hilus
      - iv. combination
      - v. replaces specimen

- (2) dimensions (and proportion of entire specimen, if appropriate) of solid and cystic components
  - i. proportion of each
  - ii. number of cysts, if easily countable
  - iii. size range of each component
  - iv. location(s), if pertinent
  - v. contents of cyst(s)
  - vi. lining of cyst(s)
  - vii. papillary or polypoid excrescences
  - viii. roughening, etc (largest dimension or proportion of total area involved)
- b. Identification of areas for special study (eg, rupture site[s], adhesions suspicious for tumor, resection margin[s], if pertinent)
- c. Additional pathologic findings, if present
4. Fallopian tube, if not fused with ovary into single mass
  - a. Tumor, if present
    - (1) size
    - (2) location and relation to ovarian tumor
    - (3) descriptive features
  - b. Additional pathologic findings, if present
5. Contralateral ovary (Note **M**)
  - a. Size, weight, or volume, if appropriate
  - b. Outer surface (describe)
  - c. Sectioned surface
  - d. Tumor, if present (handle as for predominant ovarian mass)
  - e. Other lesions (specify)
6. Uterus
  - a. Descriptive features of endometrium, myometrium, and serosa
  - b. Tumor, if present
    - (1) descriptive features
    - (2) location (depth of myometrial invasion, if appropriate)
    - (3) relation to ovarian tumor (separate or adherent)
  - c. Other lesions, if present (specify)
7. Omentum (Note **G**)
8. Regional lymph nodes
  - a. Number and size range at each designated location
  - b. Tumor, if identifiable
  - c. Other lesions, if present (specify)
9. Other staging biopsy specimens (specify)
  - a. Tumor, if present
    - (1) descriptive features
    - (2) location
  - b. Other lesions, if present (specify)
10. Other organ(s) or tissue(s) removed
  - a. Type, dimensions, and other descriptive features
  - b. Tumor
    - (1) location and relation to ovarian tumor (separate or adherent)
    - (2) size and distribution within organ or tissue
  - c. Resection margins, if applicable
  - d. Other lesions, if present (specify)
11. Tissues submitted for microscopic evaluation (Note **G**)
12. Tissues submitted for special studies (specify) (eg, frozen tissue for immunohistochemistry, flow cytometry)

**B. Microscopic Evaluation**

1. Ovary or ovary-tube if fused into single mass
  - a. Tumor
    - (1) site(s) of origin (Note **H**)
    - (2) location (Note **F**)
    - (3) surface (if possible, distinguish origin on surface from invasion onto surface from subjacent tumor)
    - (4) extent of invasion in ovary
      - i. cortex
      - ii. medulla
      - iii. hilus
      - iv. combination
      - v. replaces specimen
    - (5) extent and distribution of invasion of tube, if involved
    - (6) low-power pattern (single mass, discrete nodules, etc) (Note **I**)
    - (7) histologic type (note mixtures) (Note **J**)
    - (8) histologic grade (Note **B**)
    - (9) venous/lymphatic vessel invasion (Note **K**)
    - (10) other features of possible prognostic or therapeutic significance
  - b. Status of any specially designated resection margins
  - c. Additional pathologic findings, if present (specify); and relation to tumors, if pertinent (Note **L**)
2. Fallopian tube if not fused with ovary into single mass
  - a. Tumor
    - (1) site(s) of origin (Note **H**)
    - (2) location
    - (3) extent
    - (4) histologic type or grade, if different from that of ovarian tumor
    - (5) venous/lymphatic vessel invasion (Note **K**)
    - (6) other features of possible prognostic or therapeutic significance
  - b. Status of any specially designated resection margin(s)
  - c. Appearance of epithelium adjacent to tumor (Note **H**)
  - d. Additional pathologic findings, if present (specify); and relation to tumor, if pertinent
3. Contralateral ovary (Note **M**)
  - a. Tumor, if present (handle as for predominant ovarian mass)
  - b. Additional pathologic findings, if present
    - (1) endometriosis
    - (2) abnormalities of surface epithelium
    - (3) surface epithelial glands or cysts (Note **L**)
4. Uterus
  - a. Tumor, if present (Note **N**)
    - (1) histologic type
    - (2) histologic grade
    - (3) location
    - (4) extent including depth of invasion of wall, if suspected to be primary in endometrium
    - (5) venous/lymphatic vessel invasion
  - b. Endometrium uninvolved by tumor
  - c. Additional pathologic findings, if present (Note **O**)

5. Omentum (Note **P**)
  - a. Tumor, if present
    - (1) histologic type, if different from ovarian tumor
    - (2) histologic grade, if different from ovarian tumor (Note **P**)
    - (3) invasive or noninvasive (Note **P**)
  - b. Additional pathologic findings, if present (Note **O**)
6. Regional lymph nodes (at each location, if separately designated)
  - a. Number
  - b. Number involved by tumor
    - (1) histologic type, if different from ovarian tumor
    - (2) histologic grade, if different from ovarian tumor (Note **P**)
  - c. Additional pathologic findings, if present (Note **O**)
7. Other staging biopsy specimens at each location, if so designated
  - a. Tumor, if present
    - (1) histologic type, if different from ovarian tumor
    - (2) histologic grade, if different from ovarian tumor (Note **P**)
  - b. Additional pathologic findings, if present (Note **O**)
8. Other organs or tissue removed
  - a. Tumor, if present
    - (1) location, distribution, and extent
    - (2) histologic type, if different from ovarian tumor
    - (3) histologic grade, if different from ovarian tumor (Note **P**)
  - b. Resection margins, if applicable
  - c. Additional pathologic findings, if present (Note **O**)
9. Results/status of special studies (Note **C**)
10. Pathologic stage
11. Comments
  - a. Correlation with intraoperative consultation, as appropriate
  - b. Correlation with other specimens, as appropriate
  - c. Correlation with clinical information, as appropriate

## VI. Second-look Staging

### 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) currently pregnant
    - (2) abnormal uterine bleeding pattern
    - (3) previous therapy (hormonal, radiation, chemotherapy)
    - (4) previous tumors or operations of possible relevance
    - (5) family history of ovarian or breast cancer
  - b. Relevant findings (eg, radiologic studies, laboratory data)
  - c. Clinical diagnosis
  - d. Procedure
  - e. Operative findings
  - f. Type(s) or site(s) of specimen(s)

**B. Macroscopic Examination**

1. Specimen
  - a. Organs/tissues received
  - b. Unfixed/fixed (specify fixative)
  - c. Number of pieces
  - d. Dimensions (measure attached tissues individually)
  - e. Orientation of specimens
  - f. Results of intraoperative consultation
2. Tumor
  - a. Size
  - b. Descriptive characteristics
3. Additional pathologic findings, if present
4. Tissues submitted for microscopic evaluation
  - a. Submit entire specimen
  - b. Frozen section tissue fragment(s) (unless saved for special studies)
5. Tissues submitted for special studies (specify) (eg, frozen tissue for immunohistochemistry, flow cytometry)

**C. Microscopic Evaluation**

1. Tumor
  - a. Site(s) of origin of tumor
  - b. Histologic type, if different from ovarian tumor
  - c. Histologic grade, if different from ovarian tumor (Note **P**)
  - d. Invasive vs noninvasive
  - e. Changes due to therapy, if present
2. Additional pathologic findings, if present (Note **O**)
3. Results/status of special studies (specify) (Note **C**)
4. 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. Histologic Type**

It is recommended that the World Health Organization (WHO) Classification and Nomenclature of Ovarian Tumors be used because of its wide acceptance.<sup>1</sup> An abbreviated form of this classification is shown below.

**WHO Classification of Malignant Ovarian Tumors**Surface Epithelial-Stromal Tumors<sup>#</sup>

Histologic Type (Epithelial Component)

- Serous
- Mucinous
- Endometrioid
- Clear cell
- Transitional (including Brenner)
- Squamous
- Mixed
- Undifferentiated

(Degree of Malignancy of Epithelial and/or Stromal Component)

Borderline (of low malignant potential)<sup>##</sup>

Malignant

Carcinoma

Sarcoma

Both (malignant mesodermal mixed tumor)

#### Germ Cell Tumors

Dysgerminoma

Yolk sac tumor (endodermal sinus tumor)

Immature teratoma

Mixed malignant germ cell tumors (specify types)

Cancer with dermoid cyst (specify type)

Other (specify)

#### Sex Cord-Stromal Tumors

Granulosa cell tumor

Other (specify)

# These tumors should be further subclassified according to the location of the neoplastic cells (eg, “cystadeno-,” “surface,” or both) and the quantity of their stromal component. When the stromal component predominates, “adenofibro-” appears in the diagnostic term. This addition may be important since malignant ovarian tumors in which the neoplastic cells are surrounded by abundant benign fibromatous tissue appear to have a better prognosis than those without such a component. Surface involvement by neoplastic cells elevates the substage in stage 1 cases and indicates a higher likelihood of extraovarian peritoneal involvement.

## Kurman and his group<sup>2</sup> have recently challenged the concept of borderline neoplasia, providing evidence that most so-called borderline tumors in the serous category should be designated “atypical proliferating” because they are rarely fatal, but that a small subset of serous borderline tumors with a micropapillary or cribriform pattern are fatal in a substantial number of cases, and should be designated “micropapillary carcinoma” even in the absence of invasion of the stromal component of the tumor. This proposal has not been widely accepted by gynecological pathologists,<sup>3-4</sup> however, satisfactory reproducibility of the histological distinction between the 2 proposed forms of serous borderline tumor has not yet been established. Evaluation of additional series of cases by other groups of investigators is warranted before change in the WHO terminology is considered.

Another proposal by several groups of investigators<sup>5-7</sup> is the reinterpretation of so-called mucinous borderline tumors of intestinal type associated with pseudomyxoma peritonei as metastatic tumors of intestinal (almost always appendiceal) type in almost all cases. This proposal should be considered by staging groups in the near future.

#### **B. Histologic Grade for Surface Epithelial Stromal Tumors**

Numerous grading systems, including architectural, nuclear, and combined architectural and nuclear systems, as well as schemas that incorporate additional features (eg, appearance of tumor margin, inflammatory cell reaction, and vascular space invasion) have been used for ovarian cancers. This protocol does not recommend any specific grading system since several types that have been evaluated have proved to have prognostic significance.<sup>8-10</sup> For the sake of uniformity, however, it is recommended that 3 grades be used, as shown below.

Grade X	Cannot be assessed
Grade 1	Well differentiated
Grade 2	Moderately differentiated
Grade 3	Poorly differentiated (tumors with minimal differentiation seen in very small foci)

*Note:* Grade 4 is reserved solely for tumors in the undifferentiated category (WHO classification).

### Epithelial Cancers

As a rule, both architectural and nuclear features are evaluated. The prognostic significance of the grading varies with the type of tumor.

Serous. Usually, architectural features parallel nuclear features (ie, the extent of gland and papillae formation versus the quantity of solid growth correlates with well versus moderate versus poor differentiation). Exceptions exist, however, such as certain tumors with a solid growth pattern in the form of small nests exhibiting a high degree of nuclear maturation and often containing numerous psammoma bodies.<sup>11</sup> Tumors in the latter category are assigned grade 1 despite their solid architecture.

Mucinous. Architectural and nuclear features are both evaluated. The most important determination, however, is whether the tumor is borderline or carcinoma (WHO).<sup>1</sup>

Many mucinous tumors that lack obvious stromal invasion contain cysts and glands lined by malignant instead of atypical epithelium. Such tumors have been designated “intraglandular carcinoma”<sup>12</sup> or borderline tumor “with intraepithelial carcinoma.” These tumors appear to have an excellent prognosis but one that appears to be slightly worse than that of borderline tumors lacking this feature.

Endometrioid. These tumors can be graded according to the system suggested for similar tumors of the uterine corpus.<sup>13</sup>

Grade 1:	5% or less of a non-squamous, solid growth pattern
Grade 2:	6% to 50% of the neoplasm has a solid non-squamous pattern
Grade 3:	More than 50% of the tumor shows a solid (non-squamous) growth pattern

Notable nuclear atypia, inappropriate for the architectural grade, raises the grade of a grade 1 or grade 2 tumor by 1 grade. Adenocarcinomas with squamous differentiation are graded according to the nuclear grade of the glandular component.

Clear cell. Although it is recommended that these carcinomas be graded with the use of general guidelines, many investigators have not been able to correlate the grade with the prognosis.

Transitional cell. Nuclear grading, with a 3-tiered grading scale, is recommended.<sup>14</sup>

Squamous cell. Histologic grading, using a 3-tiered grading-scale, is recommended.

### Borderline Tumors

Grading of ovarian borderline tumors may be done but has not been proved prognostically significant, stage for stage. There is some evidence, however, that

nuclear grading of associated peritoneal disease is prognostically important in cases of serous borderline tumors.<sup>15</sup>

### **Germ Cell Tumors**

Immature teratomas are graded on the basis of the quantity of embryonal elements, almost always neuroectodermal, that they contain.<sup>16</sup> Other primitive germ cell tumors are not graded.

### **Granulosa Cell Tumors**

Two groups of investigators<sup>17,18</sup> have found that nuclear grading is effective in determining prognosis.

### **C. Special Studies**

Special studies include histochemical and immunohistochemical staining, which are helpful diagnostically in occasional cases; flow cytometry; DNA image analysis; quantitative microscopy; hormone receptor studies; molecular genetic studies; chromosome analysis; and others. At present, the use of special studies for prognostic and therapeutic purposes remains controversial and is under continuing investigation.<sup>19-33</sup>

### **D. Rupture of Tumor<sup>8,9</sup>**

Site refers to the location of rupture within a complex tumor that may be partly benign, partly borderline, and partly invasive or partly mature and partly immature if the tumor is a teratoma. In such cases, it may be helpful to the gynecologist to know what component of the tumor has ruptured to formulate an opinion whether benign, borderline, or malignant cells may have spilled into the abdominal cavity.

### **E. TNM and Stage Groupings**

In view of the role of the pathologist in the staging of cancers, the staging system for ovarian cancer endorsed by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), as well as the parallel system formulated by the International Federation of Gynecology and Obstetrics (FIGO) are recommended.<sup>34-38</sup>

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 Ovarian Carcinoma<sup>#</sup>****Primary Tumor (T)**

TNM Category	FIGO Stage	Definition
TX	—	Primary tumor cannot be assessed
T0	—	No evidence of primary tumor
T1	I	Tumor limited to ovaries (1 or both)
T1a	IA	Tumor limited to 1 ovary; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings <sup>#</sup>
T1b	IB	Tumor limited to both ovaries; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings
T1c	IC	Tumor limited to 1 or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings
T2	II	Tumor involves 1 or both ovaries with pelvic extension and/or implants
T2a	IIA	Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings
T2b	IIB	Extension and/or implants to other pelvic tissues. No malignant cells in ascites or peritoneal washings
T2c	IIC	Pelvic extension and/or implants (T2a or T2b/IIA or IIB) with malignant cells in ascites or peritoneal washings
T3 and/or N1	III	Tumor involves 1 or both ovaries with confirmed peritoneal metastasis outside the pelvis (including liver capsule metastasis and/or regional lymph node metastasis [N1])
T3a	IIIA	Microscopic peritoneal metastasis beyond pelvis (no macroscopic tumor)
T3b	IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension
T3c and/or N1	IIIC	Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis
(M1)	IV	Distant metastasis (excludes peritoneal metastasis), including positive cytology in a pleural effusion or parenchymal liver metastasis

<sup>#</sup> The presence of nonmalignant ascites is not classified. The presence of ascites does not affect staging unless malignant cells are present.

**Regional Lymph Nodes (N): TNM Classification**

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

**Distant Metastasis (M): TNM Classification**

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis (excludes peritoneal metastasis)

**Stage Groupings**

TNM Stage Groupings				FIGO Stage
Stage IA	T1a	N0	M0	Stage IA
Stage IB	T1b	N0	M0	Stage IB
Stage IC	T1c	N0	M0	Stage IC
Stage IIA	T2a	N0	M0	Stage IIA
Stage IIB	T2b	N0	M0	Stage IIB
Stage IIC	T2c	N0	M0	Stage IIC
Stage IIIA	T3a	N0	M0	Stage IIIA
Stage IIIB	T3b	N0	M0	Stage IIIB
Stage IIIC	T3c	N0	M0	Stage IIIC
	Any T	N1	M0	Stage IIIC
Stage IV	Any T	Any N	M1	Stage IV

**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

**F. Location of Tumor**

If an ovarian tumor does not replace the parenchyma, its location within the ovary may provide a clue as to its origin and nature. For example, confinement to or centering of a tumor in the hilus generally favors metastatic carcinoma over primary carcinoma or an origin from some structure in the hilus. Also, location of a malignant component in a tumor that is predominantly benign may be important because a focal carcinoma extending to the external surface of a tumor is probably associated with a poorer prognosis than an otherwise similar focus located centrally. Distinction of origin on the surface of the ovary from invasion of an underlying carcinoma may be important in the decision to classify a tumor as either an ovarian or as a primary peritoneal tumor (see Note **O**).

**G. Suggestions for Sampling for Microscopic Examination****Surface Epithelium<sup>#</sup>**

The external surface of the ovary should be handled as gently as possible; rubbing or scraping it or allowing it to dry should be avoided.

<sup>#</sup> The surface epithelium and its inclusion glands and cysts and adjacent stroma are generally considered the source of most epithelial cancers of the ovary but have not been studied carefully by most pathologists. One reason is the great fragility of the surface epithelium, resulting in its absence in most microscopic specimens. Occasionally, dysplastic lesions and carcinoma can be identified in the surface epithelium and its inclusions if they are examined carefully. Gentle handling of the specimen and meticulous microscopic examination are especially important in patients who have had a prophylactic oophorectomy because of a family history of ovarian cancer with or without breast cancer or documentation of a BRCA mutation. It may be possible to detect tiny but potentially fatal carcinomas by careful examination of the ovaries from such patients.<sup>39</sup>

**Primary Tumor**

One section for each 1 to 2 cm of tumor largest dimension is generally recommended, with modification based on the degree of homogeneity or heterogeneity of the tumor and the difficulty of diagnosis.<sup>##</sup>

Some sections should include the ovarian surface closest to the tumor on gross examination, with the number depending on the degree of suspicion of surface involvement.

Adhesions of tumor, sites of rupture, and resection margins, if pertinent, should be sampled and labeled specifically if necessary for microscopic identification.

## Sampling Issues: The recommendation for the number of sections to be taken of an ovarian tumor that may be at least focally malignant is a general guideline, with the pathologist determining in each case how many sections are necessary. If a tumor is obviously malignant and homogeneous throughout on gross examination, large numbers of sections are not required in most cases. In contrast, if there is great variability in the gross appearance of the sectioned surfaces or opened cysts, and the presence or extent of malignant change cannot be easily determined on gross examination, it may be necessary to take large numbers of sections to sample the tumor adequately. Mucinous tumors, particularly those with solid areas, solid teratomas, and primitive germ cell tumors, often require especially careful gross examination and judicious and extensive sampling. Often, additional sampling of a tumor that poses a problem in differential diagnosis is more informative than special studies such as immunohistochemical staining.

### **Fallopian Tube(s)**

- One section of each, if no gross lesion is present.
- Representative sections of tumor, if present, to determine its distribution and the appearance of the adjacent epithelium (Note **F**).

### **Uterus**

- Tumor grossly present: sections necessary to determine its extent, including depth of invasion of myometrium if tumor possibly originated in endometrium, and to determine its relation to ovarian tumor (metastatic to, metastatic from, independent primary).

### **Omentum**

- Representative sampling of grossly identifiable tumor.
- Multiple representative sections when no tumor is detected grossly (see Note **P**).
- For borderline tumor or immature teratoma with grossly apparent implants, multiple sections of the implants (see Note **P**).

### **Lymph Nodes**

- Representative sections of grossly positive lymph nodes.
- If lymph nodes appear free of tumor, samples of every node in the specimen(s).

### **Other Staging Biopsy Specimens**

- Embed entirely unless grossly positive for tumor.
- If grossly positive, a representative section.

### **Other Organ or Tissue Removed**

- Sections adequate to determine presence or absence and location and extent of tumor, if present.
- Resection margins, if applicable.

### **H. Site(s) of Origin of Tumor**

When a tumor involves both the ovary and the fallopian tube, it may be difficult to determine the primary site of the tumor in some cases. Typically, the tumor predominates and is obviously primary in one or the other organ, almost always the ovary. Occasionally, however, the ovary and tube are fused to form a solid or cystic mass with destruction of most or all landmarks. In such cases the tumor is almost always designated a primary ovarian cancer because the frequency of ovarian cancer is much greater than that of tubal cancer. Finding what appears to be in situ carcinoma in the tube

adjacent to the main tumor mass is not always a reliable criterion for the diagnosis of a primary carcinoma of the tube since carcinoma that has extended into the tube can grow along its mucosal surface and closely simulate carcinoma in situ.

#### **I. Growth Pattern of Tumor**

Whether an ovarian cancer is growing as a single mass or in discrete nodules is 1 of several clues that it is primary or metastatic, respectively.<sup>40</sup> Many metastatic tumors that are not large enough to replace the ovary form 2 or more separate nodules, in contrast to primary cancers, which usually form single nodules or masses.

#### **J. Mixtures of Histological Types of Tumors**

If neoplasia of more than 1 cell type accounts for 10% or greater of a surface epithelial cancer, the tumor is diagnosed as one of mixed cell types. Therefore, it is important to identify and estimate the proportion(s) of various cell types within epithelial cancers.

Quantitation of various epithelial cell types within a specimen, as well as quantitation of tumor types within primitive germ cell tumors, may be important prognostically.<sup>14,41,42</sup>

Although unproven, it is reasonable to assume that the quantity of the more malignant elements in tumors that have varying combinations of benign, borderline, and carcinomatous components also has prognostic significance.

#### **K. Vessel Invasion**

Although the prognostic significance of vascular space invasion in ovarian cancer has not been demonstrated by multivariate analysis, studies of cancers in many other organs suggest that this finding might also be important in ovarian cancer. In addition, vascular space invasion is much more common in cancers that are metastatic to the ovary<sup>40</sup> and therefore is worth noting, particularly if there is doubt about the primary or metastatic nature of the tumor.

#### **L. Other Lesions**

The presence of other lesions, such as endometriosis and atypicality of surface epithelium or surface epithelial inclusion glands or cysts, is occasionally important in determining the origin of an ovarian cancer. Also, the presence of endometriosis, particularly if it is in continuity with an endometrioid cancer (either carcinoma or stromal sarcoma), is a very important clue as to the primary nature of the ovarian tumor in cases in which it may be difficult otherwise to exclude metastasis from a synchronous or asynchronous cancer of the uterine corpus.

#### **M. Contralateral Ovary**

“Contralateral ovary” refers to the ovary that is non-dominant, either because it is involved by a tumor that is similar to but smaller than the dominant ovarian tumor, or because it appears negative for tumor or contains only what appears to be metastatic tumor on gross examination. If the contralateral ovary contains only focal tumor, the gross and microscopic examination should concentrate on determining whether the tumor is independently primary or metastatic from the dominant ovary. Metastatic involvement is supported by the same criteria that are used to distinguish primary and metastatic cancers in general, such as the presence of multiple nodules, surface implants, and vascular space invasion, which favor metastasis.

#### **N. Uterine Tumor**

When carcinoma involves the ovary and uterus, it may be difficult to determine whether one is dealing with a primary ovarian carcinoma with spread to the uterus, vice versa, or independent primary tumors. This problem arises most commonly when the tumors in both organs are of endometrioid type but also exists occasionally when the tumors are of serous or other cell types. There are numerous criteria for determining which of the 3

alternative explanations for the coexistence of ovarian and uterine tumors is correct. The size and distribution of the tumors, the presence of a precancerous lesion in either organ (atypical hyperplasia of the endometrium, endometriosis or adenofibroma of the ovary), microscopic comparisons of the tumors, DNA ploidy findings, and molecular genetic studies of the 2 tumors have all been used to facilitate the differential diagnosis. Over-reliance on a single criterion, however, has resulted in a lack of consensus in the literature. The very good prognosis of endometrioid carcinomas confined to the uterine corpus and 1 or both ovaries, however, suggests that in most cases of this combination, the tumors are independently primary.

### O. Other Lesions

The occurrence of benign fallopian tube type epithelium in the peritoneum (endosalpingiosis) and in lymph nodes (mullerian inclusion glands, endosalpingiosis) has raised the possibility of multicentric origin of serous malignant tumors in the ovary and on the peritoneum or in lymph nodes. Therefore, it is important to identify the above benign lesions when they are present. Currently, serous cancers that are characterized by a grossly predominant mass on the peritoneum or in the omentum with no involvement of the ovary or with tumor in the ovary that invades to a depth of less than 5 mm are generally considered to be primary peritoneal cancers. An interesting finding in association with some serous borderline tumors of the ovary is an independent primary serous borderline tumor in a pelvic or para-aortic lymph node arising from a mullerian glandular inclusion.

### P. Omentum

In 1 study,<sup>43</sup> microscopic metastases were detected in 22% of grossly negative specimens of omentum, with a mean tumor diameter of 6.7 mm. Because of this type of experience, and because the finding of a single metastatic lesion on microscopic examination may alter the management of the patient, the omentum should be adequately sampled in those cases. In cases of serous borderline tumors and immature teratomas of the ovary, it is also suggested that multiple sections of grossly recognizable implants be taken, since the implants of these tumors may vary from noninvasive to invasive<sup>15</sup> and from mature to immature,<sup>44</sup> respectively. Identification of a single invasive or immature implant may alter the prognosis and therapy.

### References

1. Scully RE. *Histological Typing of Ovarian Tumours. World Health Organization International Histological Classification of Tumours*. Berlin: Springer Verlag; 1999.
2. Seidman JD, Kurman RJ. Ovarian serous borderline tumors: a critical review of the literature with emphasis on prognostic indicators. *Hum Pathol*. 2000;31:539-557.
3. Eichhorn JH. Ovarian serous borderline tumors with micropapillary and cribriform patterns. *Am J Surg Pathol*. 1999;23:397-409.
4. Kempson RL, Hendrickson MR. Ovarian serous borderline tumors: the citadel defended. *Hum Pathol*. 2000;31:525-526.
5. Young RH, Gilks CB, Scully RE. Mucinous tumors of the appendix associated with mucinous tumors of the ovary and pseudomyxoma peritonei: a clinicopathologic analysis of 22 cases supporting an origin in the appendix. *Am J Surg Pathol*. 1991;15:415-429.
6. Prayson RA, Hart WR, Petras RE. Pseudomyxoma peritonei: a clinicopathologic study of 19 cases with emphasis on site of origin and nature of associated ovarian tumors. *Am J Surg Pathol*. 1994;18:591-603.

7. Ronnett BM, Kurman RJ, Zahn CM, et al. Pseudomyxoma peritonei in women: clinicopathologic analysis of 30 cases with emphasis on site of origin, prognosis, and relationship to ovarian mucinous tumors of low malignant potential. *Hum Pathol*. 1995;26:509-524.
8. Vergote I, De Brabanter J, Fyles A, et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet*. 2001;357:176-182.
9. Trimble EL. Prospects for improving staging of ovarian cancers. *Lancet*. 2001;357:159-160.
10. Silverberg SG. Histopathologic grading of ovarian carcinoma: a review and proposal. *Int J Gynecol Pathol*. 2000;19:7-15.
11. Gilks CB, Bell DA, Scully RE. Serous psammocarcinoma of the ovary and peritoneum. *Int J Gynecol Pathol*. 1990;9:110-121.
12. Hoerl HD, Hart WR. Primary ovarian mucinous cystadenocarcinomas: a clinicopathologic study of 49 cases with long-term follow-up. *Am J Surg Pathol*. 1998;22:1449-1462.
13. Silverberg SG, Kurman RJ. Tumors of the uterine corpus and gestational trophoblastic disease. In: *Atlas of Tumor Pathology*. 3<sup>rd</sup> series. Fascicle 3. Washington, DC: Armed Forces Institute of Pathology; 1992.
14. Gershenson DM. Ovarian carcinomas with transitional cell carcinoma pattern. *Am J Clin Pathol*. 1990;93:457-465.
15. Bell DA, Weinstock MA, Scully RE. Peritoneal implants of ovarian serous borderline tumors: histologic features and prognosis. *Cancer*. 1988;62:2212-2222.
16. Norris HJ, Zirkin HJ, Benson WL. Immature (malignant) teratoma of the ovary: a clinical and pathologic study of 58 cases. *Cancer*. 1976;37:2359-2372.
17. Bjorkholm E, Pettersson F. Granulosa-cell and theca-cell tumors: the clinical picture and long-term outcome for the Radiumhemmet series. *Acta Obstet Gynecol Scand*. 1990;59:361-365.
18. Stenwig JT, Hazekamp JT, Beecham JB. Granulosa cell tumors of the ovary: a clinicopathological study of 118 cases with long-term follow-up. *Gynecol Oncol*. 1979;7:136-152.
19. Auersperg N, Edelson MI, Mok SC, Johnson SW, Hamilton TC. The biology of ovarian cancer. *Semin Oncol*. 1998;25:281-304.
20. Bell DA. Flow cytometry of ovarian neoplasms. In: Sasano N, ed. *Current Topics in Pathology. Gynecological Tumors. Recent Progress in Diagnostic Pathology*. Berlin: Springer-Verlag; 1992:337-356.
21. Berchuck A, Kohler MF, Bast RC Jr. Oncogenes in ovarian cancer. In: Ozols RF, ed. *Hematology/Oncology Clinics of North America. Ovarian Cancer*. Philadelphia, Pa: WB Saunders; 1992:813-827.
22. Brugghe J, Baak JPA, Wiltshaw E, Brinkhuis M, Majjer GA, Fisher C. Quantitative prognostic features in FIGO I ovarian cancer patients without postoperative treatment. *Gynecol Oncol*. 1998;68:47-53.
23. Burger CW, Prinssen HM, Baak JPA, Wagenaar N, Kanemans P. The management of borderline epithelial tumors of the ovary. *Int J Gynecol Cancer*. 2000;10:181-197.
24. DeSouza PL, Friedlander ML. Prognostic factors in ovarian cancer. In: Ozols RF, ed. *Hematology/Oncology Clinics of North America. Ovarian Cancer*. Philadelphia, Pa: WB Saunders; 1992:761-781.
25. Haapasalo H, Collan Y, Atkin NB. Major prognostic factors in ovarian carcinomas. *Int J Gynecol Cancer*. 1991;1:115-162.
26. Jacobs I, Lancaster J. The molecular genetics of sporadic and familial ovarian cancer. *Int J Gynecol Cancer*. 1996;6:337-355.

27. Kommoss F, Pfisterer J, Geyer H, Thome M, Sauerbrie W, Pflaiderer A Jr. Estrogen and progesterone receptors in ovarian neoplasms: discrepant results of immunohistochemical and biochemical methods. *Int J Gynecol Cancer*. 1991;1:147-153.
28. Lage JM, Weinberg DS, Huettner PC, Mark SD. Flow cytometric analysis of nuclear DNA content in ovarian tumors: association of ploidy with tumor type, histologic grade, and clinical stage. *Cancer*. 1992;69:2668-2675.
29. Ludescher C, Weger A-R, Lindholm J, et al. Prognostic significance of tumor-cell morphology, histopathology, and clinical parameters in advanced ovarian carcinoma. *Int J Gynecol Pathol*. 1990;9:343-351.
30. Pierett M, Cavalieri C, Conway PS, et al. Genetic alterations distinguish different types of ovarian tumors. *Int J Cancer*. 1995;64:434-440.
31. Sasano H, Garrett CT. Oncogenes in gynecological tumors. In: Sasano N, ed. *Current Topics in Pathology. Gynecological Tumors. Recent Progress in Diagnostic Pathology*. Berlin: Springer-Verlag; 1992:357-372.
32. Silverberg SG. Prognostic significance of pathologic features of ovarian carcinoma. In: Nogales F, ed. *Current Topics in Pathology. Ovarian Pathology*. Berlin: Springer-Verlag; 1989:109.
33. Trope C, Kaern J. DNA ploidy in epithelial ovarian cancer: a new independent prognostic factor? [Editorial] *Gynecol Oncol*. 1994;53:1-4.
34. Friedlander ML. Prognostic factors in ovarian cancer. *Semin Oncol*. 1998;25:305-314.
35. Greene FL, Page DL, Fleming ID, et al, eds. *AJCC Cancer Staging Manual*. 6<sup>th</sup> ed. New York, NY: Springer; 2002:275-284.
36. Sobin LH, Wittekind C. *UICC TNM Classification of Malignant Tumours*. 6<sup>th</sup> ed. New York: Wiley-Liss; 2002.
37. Heintz APM, Odicino F, Maisonneuve P, et al. Carcinoma of the ovary: FIGO Annual Report. *J Epidemiol Biostat*. 2001;6:107-138.
38. Wittekind CH, Henson DE, Hutter RVP, Sobin LH. *TNM Supplement. A Commentary on Uniform Use*. 2<sup>nd</sup> ed. New York: Wiley-Liss; 2001.
39. Bell DA, Scully RE. Early de novo ovarian carcinoma: a study of fourteen cases. *Cancer*. 1994;73:1859-1864.
40. Young RH, Scully RE. Metastatic tumors in the ovary: a problem-oriented approach and review of the recent literature. *Semin Diagn Pathol*. 1991;8:250-276.
41. Tornos C, Silva EG, Khorana SM, Burke TW. High-stage endometrioid carcinoma of the ovary: prognostic significance of pure versus mixed histologic types. *Am J Surg Pathol*. 1994;18:687-693.
42. Kurman RJ, Norris HJ. Malignant mixed germ-cell tumors of the ovary: a clinical and pathologic analysis of 30 cases. *Obstet Gynecol*. 1976;48:579-589.
43. Steinberg JJ, Demopoulos RI, Bigelow B. The evaluation of the omentum in ovarian cancer. *Gynecol Oncol*. 1986;24:327-330.
44. Robboy SJ, Scully RE. Ovarian teratoma with glial implants on peritoneum: an analysis of 12 cases. *Hum Pathol*. 1970;1:643-653.

### Bibliography

- Beahrs OH, Henson DE, Hutter RVP, Kennedy BJ, eds. *Manual for Staging of Cancer*. 4th ed. Philadelphia, Pa: JB Lippincott Company; 1992.
- Hendrickson MR, ed. *State of the Art Reviews. Surface Epithelial Neoplasms of the Ovary*. Philadelphia, Pa: Hanley & Belfus; 1993.
- Russell P, Farnsworth A. *Surgical Pathology of the Ovaries*. 2nd ed. Edinburgh: Churchill Livingstone; 1997.

Scully RE, Young RH, Clement PB. *Tumors of the Ovary, Maldeveloped Gonads, Fallopian Tube and Broad Ligament. Atlas of Tumor Pathology*. 3rd series. Fascicle 23. Washington, DC: Armed Forces Institute of Pathology; 1997.

Young RH, Clement PB, Scully RE. Pathology of the ovary. In: Sternberg SS, ed. *Diagnostic Surgical Pathology*. Vol. 2. New York: Raven Press; 1994:2195-2279.