

Trophoblast

Protocol applies to all gestational trophoblastic malignancies.

*Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition*

Procedures

- **Dilatation and Curettage**
- **Resection**

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Surgical Pathology Cancer Case Summary

*Protocol revision date: January 2004
Applies to invasive trophoblastic neoplasms only
Based on AJCC/UICC TNM, 6th edition*

TROPHOBLAST: Dilation and Curettage/Resection

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type

- Dilation and curettage
 Hysterectomy
 Radical hysterectomy
 Pelvic exenteration
 Other (specify): _____
 Not specified

Tumor Site

- Specify, if known: _____
 Not specified

Fetal Anomalies

- Cannot be determined
 Absent
 Present
 *Specify type: _____

Tumor Size

- Greatest dimension: ____ cm
 *Additional dimensions: ____ x ____ cm
 Cannot be determined (See Comment)

Other Organs Involved by Tumor (check all that apply)

- Not applicable
 Specify organ(s) with direct extension: _____
 Specify organ(s) with separate metastasis: _____

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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.

MICROSCOPIC**Histologic Type**

- Hydatidiform mole, complete
 Hydatidiform mole, partial
 Hydatidiform mole, invasive
 Choriocarcinoma
 Placental site trophoblastic tumor
 Epithelioid trophoblastic tumor
 Other (specify type): _____
 Malignant trophoblastic tumor, type cannot be determined

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

- pTX [--]: Primary tumor cannot be assessed
 pT0 [--]: No evidence of primary tumor
 pT1 [I]: Tumor confined to uterus
 pT2 [II]: Tumor extends outside of the uterus but is limited to the genital structures (adnexa, vagina, broad ligament)

Distant Metastasis (pM)

- pMX [--]: Metastasis cannot be assessed
 pM1a [III]: Tumor extends to the lungs with or without genital tract involvement
 pM1b [IV]: Tumor involves all other metastatic sites
 *Specify site(s), if known: _____

Margins

- Cannot be assessed
 Uninvolved by malignant tumor
 Distance of malignant tumor from closest margin: ____ mm
 Specify margin: _____
 Involved by malignant tumor
 Specify margin(s): _____

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

- Absent
 Present
 Indeterminate

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Fetal Tissue (Macroscopic or Microscopic)

Cannot be determined

Absent

Present

*Specify type: _____

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

* None identified

* Implantation site

* Other (specify): _____

***Comment(s)**

Background Documentation

Protocol revision date: January 2004

I. Dilatation and Curettage

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 (Note **A**)
 - (1) menstrual history
 - (2) week of pregnancy
 - (3) passage of tissue
 - (4) history of hydatidiform mole
 - b. Relevant findings (eg, size of uterus, ultrasound, human chorionic gonadotropin [hCG] level)
 - c. Clinical diagnosis
 - d. Procedure (eg, endometrial biopsy, dilation and curettage, spontaneous passage of tissue)
 - e. Anatomic site(s) of specimen(s) (eg, uterine corpus, cervix)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Size (aggregate dimensions if multiple, after separating tissue from blood)
 - c. Lesion/tumor
 - (1) dimensions
 - (2) descriptive features
 - (3) vesicles, with size of largest
 - (4) fetal tissue and anomaly
 - (5) firmness
 - (6) necrosis
 - d. Results of intra-procedural consultation
2. Tissue submitted for microscopic evaluation
 - a. Villous tissue
 - (1) representative samples, if abundant
 - (2) all, if sparse
 - b. Fetal tissue
 - c. Uterine tissue
3. Special studies (specify) (eg, immunohistochemistry, DNA analysis [specify type], oncogene analysis, karyotype analysis)

C. Microscopic Evaluation

1. Adequacy of specimen (if inadequate for evaluation, specify reason)
2. Tumor
 - a. Histologic type (Note **B**)
 - b. Presence in sharp curettage specimen
 - c. Presence in suction curettage specimen

3. Additional tissues or pathologic findings, if present
 - a. Implantation site
 - b. Endometrium
 - c. Myometrium
 - d. Cervix
 - e. Fetal tissues (cord, amnion, chorion, yolk sac)
 - f. Fetal anomalies, if present
4. Results/status of special studies
5. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, including hCG level, as appropriate

II. Resection

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 (Note **A**)
 - (1) menstrual history
 - (2) week of pregnancy
 - (3) passage of tissue
 - (4) history of hydatidiform mole
 - b. Relevant findings (eg, size of uterus, ultrasound, hCG level)
 - c. Clinical diagnosis
 - d. Procedure (eg, abdominal hysterectomy, radical hysterectomy with bilateral salpingo-oophorectomy, staging laparotomy, pelvic exenteration, other)
 - e. Anatomic site(s) of specimen(s) (eg, uterine corpus, cervix)

B. Macroscopic Examination

1. Specimen
 - a. Organ(s)/tissue(s) included
 - b. Unfixed/fixed (specify fixative)
 - c. Number of pieces
 - d. Dimensions
 - e. Orientation, if indicated by surgeon
 - f. Areas indicated by surgeon for specific microscopic evaluation
 - g. Results of intraoperative consultation
2. Tumor
 - a. Location (eg, corpus, fundus, cornu, isthmus, cervix)
 - b. Size
 - c. Descriptive characteristics (eg, villous tissue, exophytic, color)
 - d. Extent of invasion (Note **C**)
 - (1) into myometrium/serosa/parametrium/cervix
 - (2) invasion of other organ(s)/tissue(s)
 - e. Distance from margins
3. Additional pathologic findings, if present
 - a. Evidence of prior sampling or treatment at apparent site of lesion

4. Uterine corpus
 - a. Dimensions
 - b. Descriptive features of endometrium, myometrium, and serosa
 - c. Tumor
 - (1) descriptive features, including size, location, and extent
 - (2) relation to main tumor
 - d. Resection margins if, appropriate
 - e. Additional findings, if present
5. Uterine cervix
 - a. Descriptive features, including appearance of ectocervix and endocervix
 - b. Tumor
 - (1) descriptive features, including size, location, and extent
 - (2) relation to main tumor
 - c. Resection margins, if appropriate
 - d. Additional findings, if present
6. Vagina
 - a. Size (length, circumference, thickness)
 - b. Descriptive features, including inner and outer surfaces, wall
 - c. Tumor
 - d. Descriptive features, including size, location, and relation to main tumor
 - e. Resection margins, if appropriate
 - f. Additional findings, if present
7. Fallopian tube(s)
 - a. Dimensions
 - b. Descriptive features, including dimensions
 - c. Tumor
 - (1) descriptive features, including size, location, and extent
 - (2) relation to main tumor
 - d. Resection margins, if appropriate
 - e. Additional findings
8. Ovary(ies)
 - a. Descriptive features, including measurements, outer surface, and sectioned surface
 - b. Lesion/tumor
 - (1) descriptive features, including size, location, and extent
 - (2) relation to main tumor
 - c. Resection margins, if appropriate
 - d. Additional findings (eg, multiple luteinized follicle cysts)
9. Organ containing primary tumor (uninvolved component)
 - a. Dimensions
 - b. Descriptive features
 - c. Resection margins if appropriate
 - d. Additional findings, if present
10. Regional lymph nodes
 - a. Tumor
 - (1) size
 - (2) descriptive features
 - b. Additional findings, if present
11. Other organ(s) or tissue(s) removed (eg, omentum, staging biopsy specimens)
 - a. Type(s) or site(s)
 - b. Dimensions and other descriptive features

- c. Tumor
 - (1) descriptive features, including size, location, and extent
 - (2) relation to main tumor
- d. Resection margins if appropriate
- 12. Tissues submitted for microscopic evaluation
 - a. Primary tumor of uterus or other organ, adequate number to demonstrate the following:
 - (1) deepest myometrial invasion or extent of involvement
 - (2) distance from serosa or resection margin
 - (3) cornual/isthmic/cervical/parametrial involvement, if present
 - b. Other lesions
 - c. Grossly uninvolved tissue, as appropriate
 - d. Staging and lymph node specimens (at least 1 section of each)
 - e. Omentum (multiple sections whether or not grossly involved)
 - f. Vaginal cuff
 - g. Frozen section tissue fragment(s) (unless saved for special studies)
 - h. Other organs/tissues, as appropriate for gross/clinical indications
- 13. Special studies (eg, DNA flow cytometry, genetic studies such as karyotype analysis, image analysis, DNA polymorphism analysis)

C. Microscopic Evaluation

- 1. Organ primarily involved
 - a. Tumor
 - (1) histologic type (Note **B**)
 - (2) site
 - (3) extent of invasion (Note **C**)
 - (4) depth of invasion from endometrial junction/thickness of myometrium, or extent of primary tumor in other organs
 - (5) closest distance to serosa
 - (6) venous/lymphatic vessel invasion
 - b. Resection margins
 - c. Status of inked areas or areas designated by surgeon
- 2. Additional pathologic findings, if present
 - a. Implantation site, if present (endometrium, myometrium, cervix)
 - b. Fetal tissues (chorion, amnion, yolk sac)
 - c. Fetal anomalies, if present
- 3. Regional lymph nodes
 - a. Total number
 - b. Number involved by tumor
 - c. Other findings (eg, decidua)
- 4. Other organ(s) and tissue(s)
 - a. Tumor
 - (1) location
 - (2) extent
 - (3) relation to primary tumor
 - b. Resection margins, if appropriate
 - c. Additional findings (eg, decidua, hyperreactio luteinalis of ovaries)
- 5. Results/status of special studies (specify)
- 6. 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. Previous History

Previous slides should be reviewed by the pathologist if it is deemed necessary by the gynecologist or pathologist for optimal evaluation of the specimen.

B. Histologic Type

A modified World Health Organization (WHO) classification of gestational trophoblastic lesions is as follows¹⁻⁵:

Histologic Classification of Gestational Trophoblastic Lesions

Hydatidiform mole

 Complete[#]

 Partial^{##}

Invasive hydatidiform mole

Choriocarcinoma

Placental site trophoblastic tumor^{###}

Epithelioid trophoblastic tumor^{6, ###}

Trophoblastic lesions, miscellaneous

 Exaggerated placental site[^]

 Placental site nodule^{^^}

Unclassified trophoblastic lesions

[#] Usually diploid, 46 chromosomes; most commonly no fetal tissues unless with a twin gestation; villi markedly enlarged, hydropic, central cistern; prominent trophoblastic hyperplasia.

^{##} Usually triploid, 69 chromosomes; fetal tissues present; villi scalloped, have stromal trophoblastic inclusions; focal trophoblastic hyperplasia, usually of syncytiotrophoblast.

^{###} Malignant tumor of intermediate trophoblast.

[^] Benign lesion composed of seemingly increased intermediate trophoblast at the implantation site, most commonly seen in uterine curettage specimens. These lesions are benign and do not require staging.

^{^^} Retention of nodule(s) of benign intermediate trophoblast. These lesions are benign and do not require staging.

C. TNM and Stage Groupings

The 6th edition of the TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC),^{3,4} and the corresponding updated 2001 edition of staging system of the International Federation of Gynecology and Obstetrics (FIGO),⁵ are recommended as follows. Both are based not only on the anatomic extent of the tumor but on additional factors, including clinical and laboratory findings.

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 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. Gestational trophoblastic tumors do not have an N classification (see below).

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 category 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.

AJCC/UICC TNM Classification for Trophoblastic Tumors^{3,4}

Primary Tumor (T)

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- T1 Tumor confined to uterus
- T2 Tumor extends to other genital structures (vagina, ovary, broad ligament, fallopian tube) by metastasis or direct extension

Regional Lymph Nodes (N)

There is no regional nodal designation (N classification) in the staging of gestational trophoblastic tumors. Nodal involvement in these tumors is rare but has an extremely poor prognosis. Nodal metastases should be classified as metastatic M1b disease.

Distant Metastasis (M)

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis
- M1a Metastasis to lung(s)[#]
- M1b Other distant metastasis (eg, brain) with or without lung metastasis[#]

[#] Genital metastasis (vagina, broad ligament, ovary, fallopian tube) is classified as T2. Direct invasion or metastasis to any non-genital structure is classified using the M classification.

FIGO Staging for Gestational Trophoblastic Tumors (2001)⁵

Stage I	Tumor confined to the uterus
IA	Tumor confined to the uterus with low risk prognostic score
IB	Tumor confined to the uterus with high-risk prognostic score
Stage II	Tumor extends outside of the uterus but is limited to the genital structures (adnexa, vagina, broad ligament)
IIA	Tumor involving genital structures with low risk prognostic score
IIB	Tumor extends outside of the uterus but limited to genital structures with high-risk prognostic score
Stage III	Tumor extends to the lungs with or without known genital tract involvement
IIIA	Tumor extends to the lungs with or without genital tract involvement and with low risk prognostic score
IIIB	Tumor extends to the lungs with or without genital tract involvement and with high-risk prognostic score
Stage IV	Tumor involves all other metastatic sites
IVA	Tumor involves all other metastatic sites with low risk prognostic score
IVB	Tumor involves all other metastatic sites with high-risk prognostic score

Note: Stages I to IV are subdivided into A (low risk) and B (high risk) according to the prognostic score (see below).

Prognostic Score^{3,4}**pTM Pathological Classification**

The pT and pM categories correspond to the T and M categories.

Prognostic Factor	Prognostic Score			
	0	1	2	3
Age	<40	≥40		
Antecedent pregnancy	H. mole	Abortion	Term pregnancy	
Months from index pregnancy	<4	4 – <7	7 – 12	>12
Pretreatment serum hCG (IU/ml)	<10 ³	10 ³ – <10 ⁴	10 ⁴ – <10 ⁵	≥10 ⁵
Largest tumor size including uterus	<3 cm	3 – <5 cm	≥5 cm	
Sites of metastasis	Lung	Spleen, kidney	Gastrointestinal tract	Liver, brain
Number of metastasis		1 – 4	5 – 8	>8
Previous failed chemotherapy			Single drug	2 or more drugs

Risk Categories

Total prognostic score 7 or less is low risk (add “A” to FIGO Stage)

Total prognostic score 8 or more is high risk (add “B” to FIGO Stage)

Stage Groupings[#]

FIGO Stage	TNM Classification		Risk Factors
Stage I	T1	M0	unknown
Stage IA	T1	M0	low
Stage IB	T1	M0	high
Stage II	T2	M0	unknown
Stage IIA	T2	M0	low
Stage IIB	T2	M0	high
Stage III	Any T	M1a	unknown
Stage IIIA	Any T	M1a	low
Stage IIIB	Any T	M1a	high
Stage IV	Any T	M1b	unknown
Stage IVA	Any T	M1b	low
Stage IVB	Any T	M1b	high

[#]The T and M categories are defined to correspond to the FIGO Stages.

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 DescriptorsResidual 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

In summary, the following factors should be considered and noted in reporting:

1. Prior chemotherapy for known gestational trophoblastic tumors.
2. Benign placental site tumors (exaggerated placental site and placental site nodule) should be reported separately and are not staged.
3. Histological verification of disease is not required when the human chorionic gonadotropin (hCG) is abnormally elevated.
4. TNM and FIGO staging applies to choriocarcinoma, invasive hydatidiform mole, placental site trophoblastic tumor and epithelioid trophoblastic tumor.
5. In contrast to other sites, an N classification (regional lymph node status) does not apply to gestational trophoblastic tumors.

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