Uterus, Cervix, and Vagina

Biopsies

Cervical and vaginal biopsies consist of an epithelial surface and varying amounts of underlying stroma. Usually, no grossly identifiable lesion can be seen. The most important objectives are to orient the specimen so that perpendicular sections will be taken through the surface and to secure the specimen properly to ensure that small pieces are not lost. These tasks can be accomplished in several ways. If the specimen is large enough (i.e., greater than 0.4 cm), the tissue can be bisected perpendicular to the surface and marked with either mercurochrome or tattoo powder to indicate the surface to be cut. If the specimen is small, it can be secured between Gelfoam sponges, within fine-mesh biopsy bags, or it can be wrapped in tissue paper. The gynecologist may also submit the biopsy oriented mucosal side up on a mounting surface such as filter paper. In this case, instruct your histotechnologist to embed and cut the biopsy specimen perpendicular to the mounting surface. All biopsy specimens should be entirely submitted, and it is often useful to routinely request that multiple levels be examined by the histology laboratory.

Endometrial biopsies should be handled similarly to curettage specimens.

Curettings

Endocervical and endometrial curettings consist of multiple small fragments of epithelium, which are often admixed with blood and mucus. The surgeon may put the curettings on Telfa pads or directly into fixative. Scrape the Telfa pad carefully on both sides, and filter the fluid of the specimen container into a tissue bag to obtain all tissue fragments. Record the aggregate dimension, and note the percentage of tissue versus the percentage of blood and mucus. The entire specimen should be submitted either wrapped in tissue paper or within a fine-mesh biopsy bag. Even if no tissue is visible, the blood and mucus should still be submitted for histologic evaluation, as they may contain entrapped small epithelial fragments. Multiple levels are often useful in evaluating these specimens. For endometrial specimens, if the tissue obtained is not representative of functioning endometrium (e.g., endocervix, lower uterine segment, or surface endometrial epithelium only), this fact should be specified. If endometrial cancer is identified, estimate the percentage of the specimen involved by tumor.

Cervix

Loop Electrocautery Excisions

The loop electrosurgical excision procedure (LEEP) and large loop excision of the transformation zone (LLETZ) are electrocautery excisions of the cervical transformation zone that excise less tissue than the traditional cone biopsy. Their use is increasing in the treatment of squamous intraepithelial lesions. Depending on the type of loop used and on the depth of the excision, the specimen may be large enough to allow one to orient, open, and process it like a conventional



Loop Electrocautery Excisions of the Cervix

1. Orient the specimen by identifying the ectocervical and endocervical mar-

cone biopsy, as described later. However, many of these specimens arrive in the surgical pathology laboratory already fixed in formalin and/or in several pieces. The endocervical margin will sometimes be submitted separately, and an overall orientation may or may not be provided. If multiple fragments are submitted, identify the mucosal surface, and try to distinguish the smooth, gray squamous mucosa from the rugated, mucoid, tan endocervical mucosa. Divide the fragments into strips with sections perpendicular to the squamocolumnar junction. For shallow, saucer-shaped specimens, divide the specimen radially as illustrated. This is similar to slicing a pie. For small conical specimens that are already well fixed, divide the specimen into anterior and posterior halves, and section each half longitudinally as shown. Conceptually, cutting the biopsy this way is similar to the handling of the perpendicular sections of the distal urethral margins in a radical prostatectomy specimen. Note that in contrast to large cone biopsies, not all sections will demonstrate the cervical canal mucosa. Although cautery artifact may make the limits of resection of these specimens difficult to evaluate, it is always best to ink the mucosal margins and exposed stroma for histologic evaluation.

Cone Biopsy

A cervical cone biopsy is a conical excision of the cervical canal performed with either a laser or a surgical blade (cold knife excision). The wider part of the cone is the outer ectocervix, and the tapered end is the endocervical margin. Measure the length of the cone biopsy corresponding to the endocervical canal, the diameter at the ectocervical margin, and the diameter at the endocervical margin. By convention, the ectocervix is described as a clock face with the most superior midpoint of the anterior lip designated as 12 o'clock. This point is usually marked with a stitch by the gynecologist. After orienting the cone biopsy as if viewed *in situ*, ink the exposed fibrous stroma and the ectocervical mucosal margin. Use a different color to ink the endocervical mucosal margin. Make a longitudinal incision through the outer stroma to the inner canal at the 3-o'clock position, and open the specimen so that the inner mucosal surface is exposed. The convention of incising the cervix at either 3 or 9 o'clock is based

on the fact that most cervical lesions arise on the anterior and posterior surfaces, rather than laterally. Pin the specimen to either a wax or cork board with the epithelial surface upward, using pins placed through the stroma on both sides. Examine the mucosal surface, and look for any lesions, especially along the squamocolumnar junction.

After fixation, cut serial full-thickness sections perpendicular to the mucosal surface in the plane of the endocervical canal. Use the endocervical apex as a pivot, and angle the cuts to provide a continuous line from the endocervical mucosa to the ectocervical mucosa. These cuts will encompass the squamocolumnar junction and will demonstrate the extent of the transformation zone. The sections should be 0.2 to 0.3 cm wide and will end up being slightly wedge-shaped. All sections should be submitted sequentially and designated as to their clock-face orientation. As with other biopsies, multiple levels are often routinely requested.

Important Issues to Address in Your Surgical Pathology Report on the Cervix

- What procedure was performed, and what structures/organs are present?
- What grade of squamous intraepithelial lesion is identified?
- Is adenocarcinoma in situ present?
- Is the lesion focal, multifocal, or extensive? State the percentage or quadrants of tissue involved.
- Are the resection margins involved (endocervical, ectocervical or stromal)?
- Is evidence of invasion present? If so, what is the depth of invasion from the base of the epithelium, either surface or glandular, from which it arises (in millimeters)? What is the horizontal spread (in millimeters)? Is there any evidence of capillary–lymphatic space invasion?
- If no precursor lesion or invasive tumor is identified, what is the adequacy of the specimen (i.e., state the presence or absence of the squamocolumnar junction)?

Uterus

The uterus is removed for a wide variety of reasons. Common indications for hysterectomy



Maintain the clock-face orientation.

include uterine prolapse, leiomyomas, endometrial hyperplasia, cervical cancer, and endometrial cancer. Given the diverse nature of these processes and the variation in the appearance of the uterus due to the hormonal environment, it is important to know both the clinical indication for the surgery and the patient's reproductive status when evaluating a hysterectomy specimen.

The uterus is traditionally divided into two components: (1) the uterine corpus and (2) the uterine cervix. The uterine corpus (or body) extends from the superiorly located fundus to the point of maximal narrowing which corresponds to the location of the internal os. The right and left cornual regions are located superolaterally, at the insertion of the fallopian tubes. The inferior 1 to 2 cm of the corpus is referred to as the isthmus or lower uterine segment (LUS). This region is a "bridge" between the cervix and the uterus and demonstrates a gradual transition from endocervical to endometrial mucosa. The cervix encompasses the lower portion of the uterus, beginning at the internal os. The cervix is composed of an inner endocervical canal lined by columnar epithelium and a rounded outer ectocervix covered by squamous epithelium. The location of the squamocolumnar junction moves in and out of the cervical canal with age and parity. It is within this region that most intraepithelial lesions arise. Although the exact limits of this region are not visible grossly, the term "transformation zone" encompasses this entire transition area including the squamocolumnar junction.

This section provides an approach to the evaluation of hysterectomy specimens in four categories: (1) hysterectomies for nonmalignant disease, (2) hysterectomies for endometrial cancer, (3) radical hysterectomies for cervical cancer, and (4) pelvic exenterations with vaginectomies for vaginal cancer or recurrent cervical cancer.

Hysterectomy for Nonmalignant Disease

zpThe category of hysterectomy of nonmalignant disease includes hysterectomies for uterine prolapse, persistent abnormal bleeding, intractable pelvic pain, leiomyomas, and endometrial hyperplasia. The procedure can be performed either vaginally or abdominally. The fallopian tubes and ovaries may also be present. Orient the uterus by identifying the stubs of the round ligaments that insert anterior to the fallopian tubes. The ovaries should lie posteriorly. In addition, because the anterior peritoneum reflects onto the bladder, the anterior peritoneum does not extend as far inferiorly along the uterus as does the posterior peritoneum. Vaginal and abdominal hysterectomies may be distinguished by examining the peritoneal surface in the region of the posterior cul-de-sac. The peritoneum appears V-shaped in a vaginal and Ushaped in an abdominal hysterectomy specimen.

If the adnexa are present, remove them from the right and left cornual regions, and examine them separately (see Chapter 28). Weigh the uterus, and record the following measurements: fundus to ectocervix, cornu to cornu, and anterior to posterior. Measure the length of the cervix from the level of the internal os to the ectocervix and the diameter of the cervix from side to side and from anterior to posterior.

The uterus can now be evaluated with a systematic examination of each of its main components. Begin by examining the uterine serosa. Look for and describe any adhesions or small "powder burn" spots, which may signify endometriosis. These may be seen more frequently on the posterior aspect.

Next, evaluate the cervix. Note the shape of the external os, which is usually circular in nulliparous women and slit-like in parous women. Examine the ectocervix for any lacerations, scars, masses, ulcers, or cysts. Place a probe through the cervical canal and into the endometrial cavity. Beginning at the cervix, incise the uterus with a large blade using the probe as a guide to divide it into anterior and posterior halves. Another method for bivalving the uterus is to use a pair of scissors to cut along the lateral margins from the ectocervix to the cornu. Gently remove the excess mucus from the endocervical canal, and examine it for the presence of polyps. At this point, the uterus may be photographed and then pinned to a wax tablet for fixation. Be sure to avoid placing pins through the mucosal surfaces. After fixation, longitudinally section the cervix at 0.2- to 0.3-cm intervals, and evaluate the transformation zone and stroma.

Now, measure the thickness of the endometrium, and look for any unusual thickenings or polyps. Keep in mind the age and reproductive status of the patient. If the woman is postmenopausal, an endometrial thickness greater than



2 mm may signify a hyperplastic process. Conversely, a thick endometrium in a premenopausal woman may reflect only the normal secretory phase.

The myometrium is examined last. Make serial 0.5-cm-thick transverse cuts through the uterine corpus and lower uterine segment, and record the maximum myometrial thickness. Look for intramural leiomyomas or evidence of adenomyosis. Adenomyosis is usually more extensive in the posterior wall and may be recognized by a thickened wall with trabeculations and small hemorrhagic or cystic foci.

If no lesions are identified, standard sections of the uterus include longitudinal sections of the anterior and posterior cervix (including the transformation zone) and full-thickness sections of the anterior and posterior walls of the uterus to include endometrium, myometrium, and serosa. At our institution, sections of the anterior and posterior lower uterine segment regions are routinely submitted as well.

Additional sampling may also be required if the standard sections reveal either endometrial hyperplasia or a cervical intraepithelial lesion. In the case of endometrial hyperplasia, the entire endometrium may need to be evaluated to rule out an invasive process. Multiple thin strips of endometrium with only a small amount of underlying myometrium can be submitted in a limited number of tissue cassettes. If a highgrade squamous intraepithelial lesion is identified, the cervix should be processed and submitted as described for cone biopsies. For low-grade squamous intraepithelial lesions, a section from each quadrant may suffice.

The evaluation of a uterus with multiple leiomyomas deserves special mention. A leiomyomatous uterus is one of the most frequently encountered specimens, and the gross examination of these specimens is the key to their proper handling. Orient, weigh, measure, and section the uterus as described above. Record the number of nodules present and their size. Specifically state whether they are submucosal, intramural, or subserosal in location. All nodules should be sectioned at 1- to 2-cm intervals and examined grossly but not necessarily microscopically. Benign leiomyomas are firm and white with a whorled cut surface. Their border with the surrounding myometrium is smooth and well-circumscribed. If these criteria are met, representative sampling of each leiomyoma is

sufficient. Always include sections demonstrating the border between the leiomyoma and the surrounding myometrium or overlying endometrium. Any leiomyomas with areas of hemorrhage, necrosis, or softening need to be sampled more extensively. In these cases, the general rule of one section per 1 cm of tumor diameter should be followed. Smooth muscle tumors less than 5 cm do not need to be sampled, as they rarely metastasize, regardless of their microscopic appearance.

Important Issues to Address in Your Surgical Pathology Report on Hysterectomies for Non-Malignant Disease

- What procedure was performed, and what structures/organs are present?
- Cervix: Are any preinvasive or invasive lesions identified?
- Endometrium: Is the endometrium hyperplastic, atrophic, or functional? If functional, specify whether it is in the proliferative or secretory phase. Are any polyps present?
- Myometrium: Are any leiomyomas or regions of adenomyosis identified? Specify whether the leiomyomas are submucosal, intramural, or subserosal.
- Serosa: Are any adhesions or regions of endometriosis identified?

Hysterectomy for Endometrial Cancer

The approach to hysterectomies performed for endometrial cancer parallels the approach to hysterectomies for benign disease. Additional steps include inking the paracervical and parametrial soft tissue margins and evaluating the extent of the tumor.

Orient, weigh, and measure the uterus as described in the section on hysterectomies for benign disease, and ink the soft tissue resection margins around the cervical canal. Also, ink the parametrial tissue, which extends along the body of the uterus and into the broad ligament. Carefully examine the serosal surfaces for evidence of tumor extension. Ink these areas a different color



- Weigh and measure the uterus and cervix. Ink the paracervical and parametrial soft tissue
- margins.
- 3. Place a probe in the endocervical and endometrial canal. Bivalve the uterus into anterior and posterior halves with a long blade.
- 4. Longitudinally section the cervix, extending the incision upward through the LUS. Serially bread-loaf the uterine corpus with 0.5-cm transverse slices.
- 5. Describe the size, appearance, and location of the tumor.
- 6. Submit sections of tumor to demonstrate the maximum tumor thickness, anterior and posterior LUS sections, uninvolved endometrium, and anterior and posterior cervix. If the adnexa are present, submit sections of the ovary and fallopian tube with adjacent soft tissue.

for orientation. If the adnexa are present, remove them at their lateral insertions along the uterus. Make multiple transverse cuts through the ovary and fallopian tube, looking for evidence of either direct tumor extension or metastatic spread. Submit at least one section from each side to demonstrate the ovary and fallopian tube with adjacent soft tissue.

Bivalve the uterus by using a long, sharp knife guided by a probe placed through the cervical canal. Closely examine the endometrial cavity. Endometrial carcinomas can be shaggy, sessile tumors or polypoid masses arising from the surface of the endometrium. They may be either focal or diffuse. The sounding depth of the uterus from the external cervical os to the superior limit of the endometrial cavity may be measured, but it is no longer used in the staging of endometrial cancers. While the tumor is fresh, remove a portion to freeze for future molecular diagnostic tests if desired. The bivalved uterus may now be photographed and pinned to a wax tablet for fixation.

The dissection begins with longitudinal sectioning of the cervix. Extend these incisions through the lower uterine segment to include both endometrial and endocervical mucosal surfaces. Note whether or not the tumor grossly involves the endocervical mucosa and/or stroma. Submit a section of this region from the anterior and posterior halves to evaluate for tumor extension into the cervix, an important factor in determining the stage of the cancer. This step may also be accomplished by taking transverse sections of the upper endocervix and lower uterine segment. Next, serially bread-loaf the uterine corpus and lower uterine segment with transverse sections. Record the size, location, and appearance of the tumor. Describe the pattern of invasion. Does the tumor have a broad pushing front, an infiltrating finger-like pattern, or is it discontinuous? Measure the greatest depth of tumor invasion into the myometrium starting from the normal junction of the endometrium and the myometrium. In addition, measure the total myometrial thickness at this point, and specify the uninvolved distance from the deep tumor/myometrial junction to the serosa. When selecting sections for histologic analysis, include the deepest point of tumor invasion as well as the interface with grossly uninvolved endometrium. The best sections are those that show the full thickness from the endometrium to the serosa. Sometimes, however, the myometrium

may be too thick to fit in a standard-size tissue cassette. In these situations, divide the section into endometrial and serosal halves. Be sure to designate their relationship clearly in your summary of sections.

Lymph nodes from the pelvic and para-aortic regions may also be included as separate specimens. They can be handled in a routine manner for evaluation of metastatic disease.

Important Issues to Address in Your Surgical Pathology Report on Hysterectomies for Endometrial Cancer

- What procedure was performed, and what structures/organs are present?
- What is the size of the tumor?
- What are the histologic type and grade of neoplasm present?
- What is the maximum depth of tumor invasion (in millimeters)? (Measure from the normal endometrial/myometrial junction.)
- What is the total myometrial thickness at the deepest point of invasion (in millimeters)?
- What is the distance from the deepest tumor/ myometrial junction to the serosa (in millimeters)?
- Does the tumor extend through the serosa?
- Does the tumor involve the endocervix? (Specify surface glandular and/or stromal involvement.)
- Is capillary–lymphatic space invasion seen?
- Does the tumor involve the adjacent adnexa?
- Does the tumor involve any margins (cervical/ vaginal, right paracervical/parametrial, left paracervical/parametrial)? Give the distance of the tumor from closest margin (in centimeters).
- Does the tumor involve any lymph nodes? (Include the number of nodes involved and the number of nodes examined at each specified site.)

Radical Hysterectomy for Cervical Cancer

Radical hysterectomies are performed for early stage invasive squamous carcinomas and adenocarcinomas of the cervix. In addition to the



uterus and cervix, the specimen has attached parametrial/paracervical soft tissue and a vaginal cuff.

Begin by orienting, measuring, and weighing the uterus and cervix as described in the section on hysterectomies for benign disease. Also, measure the size of the attached parametrial/paracervical tissue and the length of the attached vaginal cuff. Note whether the shape of the cervix is rounded or barrel shaped. Ink the right and left parametrial/paracervical tissues, the anterior/ posterior soft tissue margins of the cervical canal, and the vaginal cuff margin. Remove the parametrial/paracervical tissue by shaving each side close to its lateral attachment on the cervix. Section this tissue at 0.3-cm intervals, and submit the entire tissue for histologic examination. Any identifiable lymph nodes may be dissected and separately designated.

Next, amputate the cervix at the level of the internal os, and open the canal with a longitudinal incision opposite the tumor. Pin it open, and fix it as you would a cone biopsy. Measure the maximum tumor width and length as well as the distance to the nearest vaginal margin. Examine the vaginal cuff. Unless the tumor is close to the vaginal margin, the margin may be removed with a 0.3-cm parallel shave and submitted as four designated quadrants. If the tumor closely approaches the vaginal margin, leave the vaginal cuff intact and take perpendicular margins to demonstrate the relationship of the tumor to the margin. Serially section the cervix at 0.3-cm intervals, and measure the maximum tumor thickness as well as the thickness of the cervical wall at that site. Occasionally, a cervical tumor may not be easily discernible as a result of prior surgery or therapy.

Now turn your attention to the uterine corpus. Take a transverse section of the lower uterine segment and bivalve the uterus into anterior and posterior halves. Examine the corpus with serial transverse sections as you would in any hysterectomy specimen.

Sections for microscopic analysis should be chosen to demonstrate the maximum thickness of the tumor and its interface with any normalappearing mucosa. If the tumor is not visible, the cervix with attached vaginal cuff should be entirely submitted as in a cone biopsy. The superior extent of the tumor can be documented by taking transverse sections of the upper endocervix and lower uterine segment. The inferior extent of the tumor is documented by taking sections of the cervical tumor that include the adjacent vaginal tissue. Margins to be evaluated include the left and right parametrial/paracervical tissues, submitted in their entirety, and the vaginal cuff. The anterior and posterior cervical soft tissue margins should be submitted to delineate the extent of the tumor in relationship to the bladder and rectum.

Lymph nodes are usually submitted separately by the surgeon from the right and left internal iliac, external iliac, obturator, pelvic, and paraaortic node groups. They can be handled in a routine manner for evaluation of metastatic disease.

Important Issues to Address in Your Surgical Pathology Report on Radical Hysterectomies for Cervical Cancer

- What procedure was performed, and what structures/organs are present?
- What are the histologic type and grade of the tumor?
- Are any associated precursor lesions present [cervical intraepithelial neoplasia (CIN) or ade-nocarcinoma in situ (AIS)]?
- What is the tumor size? Give horizontal spread (in millimeters) for microinvasive tumors and overall size (in centimeters) for gross tumors. State which quadrants of the cervix are involved.
- What is the maximum depth of invasion (in millimeters)? Measure from the base of the squamous or glandular epithelium from which it originates.
- What is the thickness of the cervical wall at the point of deepest tumor invasion (in millimeters)?
- Does the tumor involve capillary–lymphatic spaces?
- Does the tumor extend into the vagina, parametrial/paracervical tissue, uterus, or adnexa? Specify the extent of involvement and depth of invasion.
- Does the tumor involve any resection margins (vaginal, anterior and posterior cervical, and bilateral parametrial/paracervical)? If the tumor is close to but does not involve a resection

Total Pelvic Exenteration



margin, give the distance between the tumor and the margin (in millimeters).

• Is metastatic disease present? Record the number of lymph nodes with metastases and the number of lymph nodes identified by site.

Pelvic Exenterations Including Vaginectomies

Vaginectomies for vaginal cancer include a portion of vagina attached to the uterus and cervix. These specimens can be handled in the same manner as radical hysterectomies for cervical cancer, although the paracervical soft tissues may not be present. Note that a clinical history of prenatal diethylstilbestrol (DES) exposure is related to the presence of vaginal adenosis and clear cell adenocarcinoma of the vagina and cervix. Adenosis appears as a red, granular change on the normally smooth, white vaginal mucosa. Also look for structural abnormalities of the cervix and fallopian tubes associated with DES exposure. Important observations include the size of the tumor and the distance of the tumor to the vaginal margin. If the uterus has been previously removed, the resulting vaginal pouch can be opened along one side and handled in the same manner as a large skin excision. Sections should be taken so as to demonstrate the greatest depth of tumor invasion, the tumor with adjacent normalappearing mucosa, and the relationship of the tumor to the cervix. If the bladder is included with the uterus the resection is termed an *anterior* exenteration, and if the rectum is included the resection is termed a *posterior exenteration*. With these added structures, additional sections include documentation of the extent of tumor involvement of the bladder or rectal wall, and an evaluation of their respective surgical margins. Specifically, these include the urethral and ureteral margins for the bladder, and the proximal and distal bowel margins for the rectum.

Exenterations are also performed for centrally recurrent cervical cancer. Perhaps the most daunting specimen received in the surgical pathology laboratory is a total pelvic exenteration, which includes the bladder, uterus with attached adnexa, vagina, and rectum. The evaluation of these specimens uses both a separate and an integrated approach, as described in Chapter 8. Resection margins are best handled if each of the four main components (i.e., bladder, vagina, uterus, and rectum) is thought of separately. Appropriate examination of the central tumor involves demonstrating its *in situ* relationship to these surrounding organs.

When a total pelvic exenteration specimen is received for recurrent cervical cancer, do not panic. Instead, calmly note the organs present and their dimensions. Specifically, look for the ureters, urethra, bladder, uterus, fallopian tubes, ovaries, vagina, and rectum. Take shave sections of the vaginal, ureteral, and urethral margins. Take perpendicular sections from the proximal and distal rectal margins, providing ink for margin orientation. Next, ink all the exposed soft tissue that surrounds the cervix and tumor.

Fill the vagina with formalin-soaked gauze pads, and distend the bladder and rectum with formalin. Submerge the entire specimen in formalin, and fix it overnight. The fixed specimen may then be bisected in a sagittal plane to demonstrate the tumor and its relationship to surrounding structures. This is best accomplished by using probes in the urethra and uterine canal as midline guides. After the specimen has been sectioned, a diagram can facilitate the description of the tumor, including its extension. Take sections of the tumor to demonstrate invasion of the bladder. rectum, vagina, and/or paracervical tissue. Document the vaginal and paracervical soft tissue margins with perpendicular or shave sections. Last, dissect the soft tissue surrounding the cervix, and submit for histology a section of any lymph nodes found.

Important Issues to Address in Your Surgical Pathology Report on Pelvic Exenterations

- What procedure was performed, and what structures/organs are present?
- What is the site of origin of the tumor?
- What are the histologic type and grade of the tumor?
- What is the size of the tumor?
- What other organs are involved by the tumor? Specify the extent of tumor involvement into these structures. That is, does it reach the muscular wall, submucosa, or mucosa?

- Does the tumor infiltrate the capillary–lym-phatic spaces?
- Does the tumor involve any resection margins? Give the distance of the tumor from the closest margin (in centimeters).
- Does the tumor involve any lymph nodes? Include the number of nodes involved and the number of nodes examined at each specified site.
- Are any radiation effects present?