

Endometrial Cancer: Screening, Diagnosis, and Surgical Staging

Annekathryn Goodman and Barbara Goff

Abstract Through case studies, the authors point out environmental and hereditary factors that contribute to increased risk of developing endometrial cancer and how to apply screening modalities in pre- and postmenopausal women. Attention is drawn to certain anatomic abnormalities that prevent vaginal bleeding – the most common symptom related to cancer. Diagnostic tests that are available to pursue various aspects of the diagnosis in a sequential fashion are described, culminating in the endometrial biopsy. Recommendations for screening and diagnosis in the asymptomatic as well as the symptomatic patients are summarized. Surgical staging represents the final event in the diagnostic workup. Instances when such staging can be modified to deal with various comorbidities are delineated.

Keywords Endometrial cancer • Heredity • Screening • Endometrial biopsy • Surgical staging

Screening

Case Report 1

A 32-year-old thin, nulliparous woman presented with menorrhagia. The bleeding was unresponsive to birth control pill use. She had no other medical conditions. There was no family history of malignancies. She underwent a rollerball endometrial ablation. She did not have an endometrial biopsy done prior to this procedure. Three months later a hysterectomy was performed because of persistent bleeding.

A. Goodman(✉) and B. Goff

Division of Gynecologic Oncology, Gillette Center for Women's Cancers,
Massachusetts General Hospital, Boston, MA
e-mail: agoodman@partners.org

Her pathology showed a deeply invasive grade 2 endometrioid endometrial adenocarcinoma with metastases to a para-aortic lymph node.

While endometrial cancer is the most common malignancy of the female genital tract with 41,200 new cases and 7,350 deaths in 2006 (1), routine screening is not recommended. The rationale for the lack of massive screening is that symptoms develop at an early stage and the female genital tract allows easy access to the uterus for diagnostic evaluation. Therefore, the focus has been on efficient evaluation in the setting of symptoms.

There are certain groups of women who have an increased risk for the development of endometrial cancer. Evaluation of the endometrial cavity should be considered and a higher index of suspicion for the development of endometrial cancer should be entertained even in the absence of symptoms for these women. Table 1 summarizes the groups of women who are at increased risk for the development of endometrial cancer. Whether screening should be performed in asymptomatic women is controversial.

Any factor that increases the exposure to unopposed estrogen increases the risk of endometrial cancer (2). Premenopausal women who have had chronic anovulation will develop a build up of the endometrial lining (3). Women with polycystic ovarian syndrome will present with years of anovulation since their teenage years (4). Other causes of anovulation include thyroid disease, hyperprolactinemia, and certain exogenous drugs such as antipsychotics (5). Estrogen secreting ovarian tumors such as granulosa cell tumors and thecomas can lead to stimulation and the build up of the endometrial lining (6).

Table 1. Factors associated with increased risk of developing endometrial cancer

Premenopausal women
Endogenous estrogen exposure:
Anovulatory cycles
Polycystic ovarian syndrome
Morbid obesity
Estrogen secreting tumors
Hereditary syndromes:
Hereditary nonpolyposis colorectal cancer
BRCA1 mutation
Postmenopausal women
Endogenous estrogen exposure:
Morbid obesity
Estrogen secreting tumors
Cirrhosis of the liver
Exogenous estrogen exposure:
Exogenous estrogens without progestins
Tamoxifen use
Pelvic radiation
Hereditary syndromes:
Hereditary nonpolyposis colorectal cancer
BRCA1 mutation

Morbid obesity is a risk factor at all ages as these women have higher endogenous estrogens due to the aromatization of androgens to estradiol and the conversion of androstendione to estrone in peripheral adipose tissue (7). Use of exogenous estrogen without the balance of progesterone is associated with endometrial cancer (8). Women with liver disease who cannot adequately metabolize their endogenous or exogenous estrogens are also at risk for the development of endometrial malignancies (9).

Tamoxifen increases the risk of endometrial cancer two- to threefold (10). Tamoxifen effect on the endometrial lining is not seen before 2 years of use (11). However, the absolute risk of developing endometrial cancer while taking tamoxifen is 1.2/1,000 per year or only 6/1,000 after 5 years (12). Currently, the American College of Obstetrician Gynecologists (ACOG) does not recommend screening in asymptomatic women taking tamoxifen (13).

Women with breast or colon cancer may have a higher genetic risk of gynecologic malignancies. A careful family history will help guide the decision to evaluate the endometrium. Hereditary nonpolyposis colon cancer (HNPCC), an autosomal dominant syndrome, confers a 40–60% risk of endometrial cancer (14). Women with known HNPCC who are undergoing surgery for colorectal cancer should be counseled about the potential benefits of total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH–BSO) at the time of colorectal surgery (15). BRCA1 gene mutation, in addition to the well-known increased risk of ovarian cancer, has been associated with an increased endometrial cancer risk (16).

Pelvic radiation for other malignancies such as cervical or rectal cancer will increase the risk of uterine corpus cancers. The most common postradiation pelvic malignancy is adenocarcinoma of the endometrium (17).

Even in the absence of personal or family risk factors of endometrial cancer, all women with abnormal bleeding need to be evaluated for malignancy. Any vaginal bleeding in postmenopausal women regardless of the quantity needs to be evaluated. The risk of endometrial cancer in a 50-year-old woman with postmenopausal bleeding is 9%, 16% for a woman in her sixties, 28% for a woman in her seventies, and 60% for a woman in her eighties (18). Irregular bleeding in premenopausal women needs to be thoughtfully worked up. While hormonal irregularities, complication of pregnancy, and pelvic infection are other causes of premenopausal bleeding, the possibility of malignancy must be taken seriously. Twenty-five percent of all endometrial cancers occur in premenopausal women and 5% are found in women <40 years old (19).

Table 2 lists certain anatomical changes that may prevent the development of the warning sign of vaginal bleeding or impair the examiner's ability to fully evaluate the pelvic tract. Women who have developed cervical stenosis because of postmenopausal atrophy, or previous cervical procedures such as cryotherapy or cervical cone biopsies will not have an open cervical canal. On physical inspection, the examiner will see that a cutip or cytobrush cannot pass through the cervical os. Some women develop agglutination of the upper vagina secondary to atrophy, radiation, or infection. Certain congenital duplications of the lower genital tract such as a vaginal septum can also close off the uterus and not allow blood to exit the

Table 2. Anatomic abnormalities that prevent vaginal bleeding

Abnormality	Causes
Agglutinated Vagina	Postmenopausal atrophy Radiation Sequelae of infection (Toxic shock syndrome, Stevens-Johnson syndrome) Use of intravaginal Efudex cream
Cervical stenosis	Sequelae of therapy for cervical intraepithelial neoplasia (cryotherapy, cone biopsy, LEEP)
Vaginal septum	Congenital
Intrauterine synechia	Asherman's syndrome Endometrial ablation
LEEP loop electrosurgical excision procedure.	

vagina. Women who have had an endometrial ablation may develop a malignancy deep to the scar of ablation, which is not amenable to detection by biopsy. For all these women, it is important to evaluate the upper genital tract especially if they also have other risk factors discussed above.

Comment on Case Report 1

The 32-year-old woman had no known risk factors for endometrial cancer. However, she had abnormal bleeding that was not fully evaluated before trying the therapeutic intervention of ablating her endometrial lining. It is extremely important to perform an endometrial biopsy when bleeding is unexplained. Only 10% of all gynecologic cancers are associated with a known genetic risk. Endometrial cancers that are not associated with hyperestrogenism seem to have a more aggressive behavior.

Diagnostic Tests

Case Report 2

A 49-year-old woman presented with mid cycle spotting. She had had several abnormal pap smears showing atypical glandular cells over the last 5 years. Colposcopy and cervical biopsies had been normal. An endometrial biopsy showed a grade 2 endometrioid adenocarcinoma. She underwent a total abdominal hysterectomy (TAH), bilateral salpingo oophorectomy (BSO), and pelvic node biopsies. Her final pathology showed a polypoid carcinoma of the endometrium with superficial myometrial invasion. All staging biopsies were negative for tumor.

Evaluation of the uterus occurs with physical examination, visual inspection, cytologic and histologic evaluation, and radiologic imaging. Table 3 summarizes the different diagnostic tests that are available to study the uterus.

Physical examination includes visual inspection of the external genitalia. In the setting of abnormal bleeding, it is important to rule out the possibility of an extrauterine lesion. The vulva, periurethral region, and anus are examined. The vagina and cervix are evaluated. The cervix is assessed for stenosis, friability, and gross lesions. The vagina should also be palpated circumferentially to make sure that there are no nodules that may have been missed on visual examination. The uterus is palpated on bimanual examination. It should be evaluated for size, tenderness, and irregularities of shape. A rectovaginal examination allows the examiner to evaluate the cul-de-sac, the back wall of the uterus, and the adnexal structures.

While Papanicolaou smears were developed for screening of lower genital tract neoplasia, an occasional asymptomatic woman with endometrial carcinoma will

Table 3. Diagnostic tests for uterine corpus disease

Office procedures	Type of information
Physical examination	Origin of bleeding Cervical stenosis Uterine size, pelvic mass
Pap smear	Cytologic abnormalities of cervix, vagina Occasional information about upper tract disease
Endometrial biopsy	Endometrial lining
Hysteroscopy	Endometrial lining
Radiological procedures	Type of information
Transvaginal ultrasound	Endometrial stripe Uterine size Adnexal size, presence of cysts, masses
Sonohysterogram	Endometrial stripe Presence of submucosal fibroids, polyps, endometrial cavity masses
Pelvic MRI	Myometrial abnormalities Endometrial cavity Adnexal structures Invasion into parametria, vagina, bladder Pelvic nodal disease
Abdominopelvic CT scan	Ascites Pelvic and para-aortic adenopathies Intraparenchymal organ abnormalities Peritoneal and omental disease
Operative procedures	Type of information
Examination under anesthesia	Same as physical examination
Dilation and curettage	Endometrial lining
Hysteroscopy	Endometrial lining
Hysterectomy	Full pathologic analysis of the uterus

present with abnormal cytology. Cervical cytology is not a reliable screening test for endometrial cancer. However, endometrial cells seen on cervical cytology in women over 40 years of age can signify endometrial disease (20).

The risk of malignancy is increased twofold when atypical endometrial cells are seen on cervical cytology compared with benign appearing cells (21). In patients with endometrial cancer, suspicious cells on cervical cytology are associated with higher grade and more advanced stage disease (22). Some studies have not confirmed a higher risk of endometrial pathology in asymptomatic women with normal endometrial cells noted by cervical cytology screening (23).

Any abnormal uterine bleeding needs to be evaluated by endometrial biopsy. The accuracy of an office biopsy will be depending on the size of the endometrial lesion, the examiner's skills, the anatomy of the patient, and patient comfort. Small lesions, cervical stenosis with the inability to get deeply into the endometrial cavity, and distorting submucosal fibroids can all reduce the yield on office biopsies. Premedication with a nonsteroidal anti-inflammatory and the use of a paracervical block can help facilitate an office evaluation. An office hysteroscope can also increase the yield for diagnosing abnormalities. Many different types of office biopsy devices are thought to be effective diagnostic techniques (24). Table 4 lists some of the commercial devices that are available for outpatient endometrial biopsies.

If it is not possible to obtain an adequate sampling in the office because of patient distress, anatomic factors, or a discrepancy between normal office biopsy results and an abnormal imaging study (see below), a day surgical procedure should be scheduled. Under anesthesia, vaginal adhesions can be gently opened up. If cervical stenosis is a problem, an ultrasound can help safely guide the operator into the uterine cavity and avoid uterine perforation. Hysteroscopy combined with curettage of the endometrial cavity is recommended to avoid missing small lesions.

Imaging studies can be a helpful adjunct in the evaluation of endometrial pathology. In asymptomatic women, the addition of a transvaginal ultrasound can help determine the need for an endometrial biopsy. The stripe width varies with the menstrual cycle in premenopausal women. After the menopause, an endometrial stripe thickness >5 mm is usually considered abnormal (28). Tamoxifen can increase the incidence of a falsely thickened endometrial stripe because of tamoxifen-induced subendometrial edema (29). In addition, about 30% of women taking tamoxifen will develop endometrial polyps (30). A sonohysterogram can be helpful. Sterile saline is instilled into the endometrial cavity and then a transvaginal ultrasound is performed. The saline will reveal subtle irregularities such as small

Table 4. Commercial devices for endometrial biopsy

Device	Accuracy for diagnosis of endometrial cancer (%)	References
Novak curet	67–97	(25)
Pipelle (Unimar)	79–94	(26)
Vabra aspirator	80–98	(27)

Table 5. Endometrial cancer: recommendations for screening and diagnosis

Asymptomatic patient
No risk factors and normal physical examination: routine yearly follow-up
Risk factors of estrogen excess: transvaginal ultrasound
Tamoxifen use for >2 years: annual sonohysterogram
Genetic risk factors: annual endometrial biopsy
Abnormal physical examination: transvaginal ultrasound
Symptomatic patient
Office endometrial biopsy and transvaginal ultrasound
Dilation and curettage if unable to perform office biopsy or abnormal ultrasound

polyps and it will reduce the error in measuring the stripe thickness. Some authorities recommend proceeding directly to a sonohysterogram in the evaluation of women on tamoxifen (31).

A pelvic MRI is useful preoperatively to help determine depth of myometrial invasion in a known invasive cancer (32). It is about 70% accurate in predicting myometrial invasion. A CT scan can also help to evaluate the lymph node chains and check for upper abdominal disease. Neither of imaging tests is indicated in screening for, and the diagnosis of endometrial cancer. In general, CT scan is recommended preoperatively in women with papillary serous or clear cell histologies. Table 5 summarizes screening and diagnostic recommendations.

Comment on Case Report 2

This patient had repetitively abnormal glandular cells on cervical cytology. She also had unexplained midcycle bleeding. When her cervical evaluation with colposcopy returned with negative results, she should have undergone an endometrial biopsy. An ultrasound may have been helpful to pick up the large polypoid lesion within her endometrial cavity.

Surgical Staging

Case Report 3

A 35-year-old G3P3 woman with menorrhagia undergoes a total vaginal hysterectomy. The final pathology reveals a grade 3 endometrioid adenocarcinoma of the endometrium with inner one-third myometrial invasion. She is taken back to surgery and undergoes a laparoscopic BSO, pelvic and para-aortic lymph node dissection,

and pelvic washings. All staging biopsies are negative for cancer. She has a stage Ib grade 3 endometrial cancer diagnosis.

The staging of a cancer serves three main purposes. An internationally agreed upon numeric classification of extent of disease allows the collection of statistics and worldwide interpretation of treatment outcome and survival. A stage assignment for a particular cancer gives information about prognosis. Third, with the knowledge of stage, a particular treatment regimen that is based on solid collective experience can be recommended. A stage is assigned for the cancer at initial presentation and this stage assignment never changes. For instance, a woman who develops lung metastases after an initial diagnosis of stage IIb endometrial cancer does not have stage IV disease. Her cancer is described as Stage IIb with lung metastases.

Since 1988, endometrial cancer has been staged surgically (33). For endometrioid carcinomas a degree of differentiation is also documented. A grade 1 tumor has $\leq 5\%$ solid growth pattern of the glandular component. A grade 2 tumor has 6–50% solid growth pattern. Grade 3 tumors have $> 50\%$ solid component. Endometrioid type endometrial cancer spreads in a predictable manner (34). It first occurs by direct invasion into the myometrium. Spread can also progress into the cervix and then the vagina. Tumor cells can also migrate transtubally with implantation on the ovaries, uterine serosa, or with free-floating cells in the peritoneum. Involvement of lymphovascular spaces can lead to lymphatic spread. Tumor then can involve the organs of the upper abdomen, the inguinal lymph nodes, or extra-abdominal sites. Endometrial cancer can also spread hematogenously to involve the lungs. Surgical staging reflects this predictable behavior (*see* Table 6). While the rare subtypes have less predictable behavior, they are included in the FIGO endometrial cancer staging system. Clear cell and serous histologies commonly spread by transtubal route and follow the peritoneal fluid circulation in a manner similar to epithelial ovarian cancers (35). This spread frequently occurs while the primary cancer is small and noninvasive of the myometrium.

Table 6. Surgical staging of endometrial cancer

Stage	Site of tumor involvement	Substages
I	Uterine corpus	Ia: no myometrial invasion Ib: invasion of $<$ one half of the myometrium Ic: invasion \geq one half of the myometrium
II	Uterine cervix	IIa: endocervical gland involvement IIb: cervical stromal invasion
III	Pelvic Structures	IIIa: positive peritoneal cytology, serosal involvement or adnexal metastases IIIB: vaginal metastases IIIC: pelvic or para-aortic nodes
IV	Upper abdomen, extra-abdominal disease invasion outside the true pelvis	IVa: bladder or bowel invasion IVb: distant metastases including inguinal and intra-abdominal nodes

Operative Techniques for Staging

Laparotomy

The surgical approach chosen for removal of the uterus, tubes, and ovaries will be based on many factors. If a patient has had multiple prior surgeries, a history of peritonitis, diverticulitis, or abdominal radiation, an open approach may be judicious. A preoperative bowel preparation is an important addition to preoperative planning. The choice of the incision can be based on patient's body habitus, previous abdominal scars, and what surgery is planned. The classic incision for abdominal exploration is the low vertical incision, which can be extended as needed into the upper abdomen. Some surgeons prefer a slight paramedian approach to avoid compromising the structural integrity of the umbilicus. A low transverse incision is reasonable for grade 1 cancers where one is not planning to sample the high para-aortic nodal chains. This incision can be modified by the muscle cutting Maylard incision if more exposure is necessary. It is important not to compromise the blood supply to the skin by making a parallel incision to an old incision. As the skin and subcutaneous tissue is supplied by the superficial epigastric vessels that come in from a lateral position, a skin bridge between two incisions can develop necrosis. It is also important to understand the surgical techniques that have been performed previously when a woman has undergone a myofascial flap for breast reconstruction after breast cancer surgery. Commonly a mesh is placed after a TRAM flap. It is helpful to obtain advice about where to place the new fascial incision from the plastic surgeon who has done the previous surgery. This will reduce the risk of postoperative hernias.

Pelvic cytology is first collected by rinsing the pelvis with sterile saline and aspirating the fluid back. The abdomen is then carefully explored. After the uterus and both adnexa are removed, a decision about further staging is made. For grade 2 and 3 cancers, pelvic and para-aortic lymph node dissection should be performed. For grade 1 cancers, the uterus is sent to pathology for evaluation of the depth of invasion and then determine the need for lymph node dissection. Macroscopic examination of the fresh specimen correctly predicted depth of invasion in 87% of grade 1, 65% of grade 2, and 30% of grade 3 tumors (36). Lymph node dissection should be performed for deeply invasive grade 1 tumors.

Some investigators recommend staging all patients with endometrial cancer if technically feasible (37). Otherwise, potential pitfalls, seen in 15–20% of patients include: final pathology report with a higher grade than the preoperative endometrial biopsy and lack of accuracy in assessing depth of invasion for grade 2–3 tumors. Several studies have suggested a potential therapeutic benefit from lymphadenectomy as compared to lymph nodes sampling or no lymph node dissection (38).

Laparoscopy

A laparoscopically assisted vaginal hysterectomy with appropriate staging is an acceptable alternative to a laparotomy as long as the same information can be obtained (39). Uterine morcellation should not be performed because of the theoretical risk of seeding and spread of viable cancer cells.

Vaginal Approach

For patients who have multiple comorbidities, a simple vaginal hysterectomy without comprehensive surgical staging should be considered. The purpose of this surgery is to remove the uterus and stop bleeding. This surgery can be performed under spinal anesthesia. Vaginal hysterectomy with BSO is also appropriate for women with grade 1 minimally invasive tumors. It is not always technically possible to remove the ovaries through the transvaginal approach. As synchronous primary cancers of endometrium and ovary are found in 5–10% of women it is important to remove the ovaries if technically possible and medically safe to do so (40).

Comment on Case Report 3

The gynecologic oncology group demonstrated that 22% of women with clinical stage I disease had extrauterine spread (34). The patient had undergone a vaginal hysterectomy because of menorrhagia without an endometrial biopsy. With the discovery of a grade 3 cancer, it was crucial that she had undergone a second surgery to evaluate her ovaries and nodal status. With the diagnosis of a stage Ib endometrial cancer, she did not need postoperative whole pelvic radiation. She was at higher risk for vaginal recurrence and vaginal brachytherapy was recommended.

Conclusions

- An endometrial biopsy is the key diagnostic test for abnormal vaginal bleeding.
- Any positive findings on biopsy should be pursued further beyond physical examination and cytologic evaluation, selecting from a number of radiologic and operative procedures (see also Chapter 3).
- With a diagnosis of invasive endometrial cancer, the operative approach beyond hysterectomy should include thorough surgical staging.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ. Cancer Statistics 2006. *CA Cancer J Clin* 2006; 56:106–130.
2. Hale GE, Hughes CL, Cline JM. Endometrial cancer: hormonal factors, the perimenopausal “window at risk”, and isoflavones. *J Clin Endocrinol Metab* 2002; 87:3.
3. Coulam CB, Anneger JF, Kranz JS. Chronic anovulation syndrome and associated neoplasia. *Obstet Gynecol* 1983; 61:403.
4. Azziz R, Woods KS, Reyna R, et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab* 2004; 89:2745.
5. Schlechte J, Sherman B, Halmi N, et al. Prolactin-secreting pituitary tumors in amenorrheic women: a comparative study. *Endocr Rev* 1980; 1:295.
6. Outwater EK, Wagner BJ, Mannion C, et al. Sex cord-stromal and steroid cell tumors of the ovary. *Radiographics* 1998; 18:1523.
7. Siiteri PK. Adipose tissue as a source of hormones. *Am J Clin Nutr* 1987; 45:277.
8. Persson I, Adami H-O, Bergkvist L, et al. Risk of endometrial cancer after treatment with estrogens alone or in conjunction with progestogens: results of a prospective study. *BMJ* 1989; 298:147.
9. Zumoff B, Fishman J, Gallagher TF, Hellman L. Estradiol metabolism in cirrhosis. *J Clin Invest* 1968; 47(1):20–25.
10. Cohen I. Endometrial pathologies associated with postmenopausal tamoxifen treatment. *Gynecol Oncol* 2004; 94:256.
11. Suh-Burgmann EJ, Goodman A. Surveillance for endometrial cancer in women receiving tamoxifen. *Ann Intern Med* 1999; 131:127–135.
12. Fisher B, Constantino JP, Redmond CK, Fisher ER, Wickerham DL, Cronin WM. Endometrial cancer in tamoxifen treated breast cancer patients: findings from the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14. *J Natl Cancer Inst* 1994; 86:527–537.
13. ACOG Committee Opinion Number 232 April 2000-Tamoxifen and Endometrial Cancer.
14. Ollikainen M, Abdel-Rahman WM, Moisio AL, et al. Molecular analysis of familial endometrial carcinoma: a manifestation of hereditary nonpolyposis colorectal cancer or a separate syndrome? *J Clin Oncol* 2005; 23:4609.
15. Schmeier KM, Lynch HT, Chen L-M, et al. Prophylactic surgery to reduce the risk of gynecologic cancers in the Lynch Syndrome. *N Eng J Med* 2006; 354:261–269.
16. Levine DA, Lin O, Barakat RR, et al. Risk of endometrial carcinoma associated with BRCA mutation. *Gynecol Oncol* 2001; 80:395.
17. Kleinerman RA, Boice JD, Storm HH, et al. Second primary cancer after treatment for cervical cancer. *Cancer* 1995; 76:442–452.
18. Anderson B. Diagnosis of endometrial cancer. *Clin Obstet Gynecol* 1986; 13:739–750.
19. Pellerin GP, Finan MA. Endometrial cancer in women 45 years of age or younger: a clinicopathological analysis. *Am J Obstet Gynecol* 2005; 193:1640.
20. Cherkis RC, Patten SF, Jr, Andrews TJ, et al. Significance of normal endometrial cells detected by cervical cytology. *Obstet Gynecol* 1988; 71:242.
21. Cherkis RC, Patten SF, Jr, Dickinson JC, et al. Significance of atypical endometrial cells detected by cervical cytology. *Obstet Gynecol* 1987; 69:786.
22. DuBeshter B, Warshal DP, Angel C, et al. Endometrial carcinoma: the relevance of cervical cytology. *Obstet Gynecol* 1991; 77:458.
23. Chang A, Sandweiss L, Bose S. Cytologically benign endometrial cells in the papanicolaou smears of postmenopausal women. *Gynecol Oncol* 2001; 80:37.
24. Clark TJ, Mann CH, Shah N, Khan KS, Song F, Gupta JK. Accuracy of outpatient endometrial biopsy in the diagnosis of endometrial cancer: a systematic quantitative review. *BJOG: An Int J Obstet & Gynaecol* 2002; 109:313

25. Karlsson B, Granberg S, Wikland M, et al. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding – a Nordic multicenter study. *Am J Obstet Gynecol* 1995; 172:1488.
26. Decensi A, Fontana V, Bruno S, Gustavino C, Gatteschi B, Costa A. Effect of tamoxifen on endometrial proliferation. *J Clin Oncol* 1996; 14:434–440.
27. Love CDB, Muir BB, Scrimgeour JB, et al. Investigation of endometrial abnormalities in asymptomatic women treated with tamoxifen and an evaluation of the role of endometrial screening. *J Clin Oncol* 1999; 17:2050.
28. Schwartz LB, Snyder J, Horan C, Porges RF, Nachtigall LE, Goldstein SR. The use of transvaginal ultrasound and saline infusion sonohysterography for the evaluation of asymptomatic postmenopausal breast cancer patients on tamoxifen. *Ultrasound Obstet Gynecol* 1998; 11:48–53.
29. Manfredi R, Gui B, Maresca G, Fanfani F, Bonomo L. Endometrial cancer: magnetic resonance imaging. *Abdom Imaging* 2005; 30:626–636.
30. Novak E. A suction-curet apparatus endometrial biopsy. *JAMA* 1935; 104:1497–1498.
31. Behnamfar F, Khamehchian T, Mazoochi T, Fahiminejad T. Diagnostic value of endometrial sampling with pipelle suction curettage for identifying endometrial lesions in patients with abnormal uterine bleeding. *J Res Med Sci* 2004; 3:21–23.
32. Goldberg GL, Tsalacopoulos G, Davey DA. A comparison of endometrial sampling with the Accurette and Vabra aspirator and uterine curettage. *S Afr Med J* 1982; 61:114–116.
33. International Federation of Gynecology and Obstetrics. Annual report on the results of treatment in gynecologic cancer. *Int J Gynecol Obstet* 1989; 28:189–190.
34. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. *Cancer* 1987; 60:2035–2041.
35. Aquino-Parsons C, Lim P, Wong F, Mildenerberger M. Papillary serous and clear cell carcinoma limited to endometrial curettings in FIGO stage Ia and Ib endometrial adenocarcinoma: treatment implications. *Gynecol Oncol* 1998; 71:83–86.
36. Goff BA, Rice LW. Assessment of depth of myometrial invasion in endometrial adenocarcinoma. *Gynecol Oncol* 1990; 38:46–48.
37. ACOG Partice bulletin, number 65, August 2005. Management of Endometrial Cancer.
38. Kilgore LC, Partridge EE, Alvarez RD, Austin JM, Shingleton HM, Noojian F, III, et al. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. *Gynecol Oncol* 1995; 56:29–33.
39. Fowler JM. Laparoscopic staging of endometrial cancer. *Clin Obstet Gynecol* 1996; 39:669.
40. Soliman PT, Slomovitz BM, Broaddus RR, et al. Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. *Gynecol Oncol* 2004; 94:456.



<http://www.springer.com/978-1-58829-736-5>

Uterine Cancer

Screening, Diagnosis, and Treatment

Muggia, F.; Oliva, E. (Eds.)

2009, XI, 296 p., Hardcover

ISBN: 978-1-58829-736-5

A product of Humana Press