The endometrium demonstrates a wide spectrum of normal and pathologic appearances throughout menarche as well as during the prepubertal and postmenopausal years and the first trimester of pregnancy. Disease entities include hydrocolpos, hydrometrocolpos, and ovarian cysts in pediatric patients; gestational trophoblastic disease during pregnancy; endometritis and retained products of conception in the postpartum period; and bleeding caused by polyps, submucosal fibroids, endometrial hyperplasia, or endometrial adenocarcinoma. Other findings include tamoxifen-associated changes, intrauterine fluid collections, and endometrial adhesions. Although ultrasound (US) is almost always the first modality used in the radiologic work-up of endometrial disease, findings at sonohysterography, hysterosalphingography, magnetic resonance imaging, and computed tomography are often correlated with US findings. It is important to understand that the appearance of the endometrium is related to multiple factors, including the patient’s age, stage in the menstrual cycle, and pregnancy status and whether she has undergone hormonal replacement therapy or tamoxifen therapy. Accurate diagnosis requires that these factors be taken into account in addition to clinical history and physical examination findings.
Introduction

Endometrial abnormalities are common diagnostic challenges facing the radiologist and referring gynecologist. Ultrasound (US) is the primary imaging modality in this setting, but findings at sonohysterography and magnetic resonance (MR) imaging are often correlated with US findings. In this article, we review the current approach to endometrial imaging and demonstrate the spectrum of normal and pathologic findings in pediatric, premenopausal, pregnant, postpartum, and postmenopausal patients.

Pediatric Endometrium

Normal Appearance

Characteristic morphologic changes take place in the uterus and endometrium over time. At birth, the uterus is similar in size to the cervix (2.3–4.6 cm), and the endometrium generally appears as a thin, echogenic line (Fig 1) (1). Approximately one-fourth of neonates will have fluid collections within the endometrial cavity (1). On the other hand, hematocolpos and hematometrocolpos in adolescent girls are generally associated with an imperforate hymen without an increase in associated congenital anomalies. US demonstrates an echogenic, tubular, cystic midline mass with internal echoes representing fluid and debris (Fig 2) (3).

Pathologic Appearances

The most common pelvic masses in neonates include hydrocolpos, hydrometrocolpos, and ovarian cysts. Hydrocolpos is characterized by distention of the vagina. Hydrometrocolpos is characterized by dilatation of both the uterus and vagina (with the vagina usually being distended to a greater extent [2]) with serous fluid and possibly urine if there is a urogenital sinus. The endometrium is intrinsically normal, but the endometrial cavity is distended with fluid. Both hydrocolpos and hydrometrocolpos result from vaginal or cervical stenosis, hypoplasia, or agenesis (Meyer-Rokitansky-Kuster-Houder syndrome), which is often associated with congenital anomalies (1). US demonstrates a cystic midline mass with internal echoes representing mucoid material and cellular debris.

On the other hand, hematocolpos and hematometrocolpos in adolescent girls are generally associated with an imperforate hymen without an increase in associated congenital anomalies. US demonstrates an echogenic, tubular, cystic midline mass with internal echoes representing fluid and debris (Fig 2) (3).

Premenopausal Endometrium

Normal Appearance

During menstruation, the endometrium appears as a thin, echogenic line 1–4 mm in thickness (Fig 3) (4,5). The endometrium is usually best seen on endovaginal scans. Endometrial thickness is measured from echogenic border to echogenic border across the endometrial cavity on a sagittal midline image. Intraluminal blood or sheets of sloughed endometria may be identified. Once the proliferative phase of the menstrual cycle (days 6–14) begins, the endometrium becomes thicker (5–7 mm) and more echogenic relative to the myometrium, reflecting the development of glands, blood vessels, and stroma (5). In the late proliferative (periovulatory) phase, the endometrium develops a multilayered appearance with an echogenic basal layer and hypoechoic inner func-
tional layer, separated by a thin echogenic median layer arising from the central interface or luminal content (Fig 4). In this stage, the endometrium may measure up to 11 mm in thickness. The layered appearance usually disappears 48 hours after ovulation. During the secretory phase, the endometrium becomes even thicker (7–16 mm) and more echogenic (Fig 5) (4,5). This increased echogenicity is thought to be related to stromal edema and glands distended with mucus and glycogen. Stromal edema also accounts for the increased posterior acoustic enhancement that may be seen (5). The endometrium typically reaches a maximum thickness during the midsecretory phase (4). The appearances of normal and abnormal endometrium, such as in the setting of endometrial hyperplasia, may overlap. Cyclic ovarian changes parallel the endometrial changes in the follicular and luteal phases.

The MR imaging appearance of normal endometrium is best demonstrated on T2-weighted images because the uterus has homogeneous intermediate signal intensity with T1-weighted sequences. T2-weighted images delineate the uterine zonal anatomy. The normal endometrium is of uniformly high signal intensity, and the inner myometrium, or junctional zone, is of uniformly low signal intensity (Fig 6).

Figure 3. Normal premenopausal endometrium. Sagittal US image of the uterus obtained during menstruation shows a thin endometrial lining (arrow) with a trace of fluid.

Figure 4. Normal premenopausal endometrium. Sagittal US image of the uterus obtained during the late proliferative phase of the menstrual cycle demonstrates the endometrium with a multilayered appearance (arrows).

Figure 5. Normal premenopausal endometrium. Sagittal US image of the uterus obtained during the secretory phase of the menstrual cycle shows a thickened, echogenic endometrium ( cursors).

Figure 6. Normal premenopausal endometrium. T2-weighted MR image shows the normal endometrium (straight arrow) and junctional zone (curved arrow).
Appearance during Pregnancy

Transvaginal US is the primary modality for evaluation of an early intrauterine pregnancy (IUP). The appearance of an IUP depends on gestational age. The normal gestational sac can be seen at 4.5 weeks gestation and should be visualized when greater than 5 mm in length (6,7). The yolk sac should be visualized between 5 and 6 weeks gestation, and an embryo may be seen before 6 weeks gestation (8). The normal gestational sac appears as an oval or rounded anechoic space within the endometrium surrounded by a hyperechoic rim at least 2 mm in thickness, and the sac should grow at a rate exceeding 1.2 mm per day (8). It should be located in the upper or middle uterine segment, midway between the two apposed uterine walls (6). A low position in the endometrial cavity suggests an impending or ongoing miscarriage, a cervical ectopic pregnancy, or a fundal fibroid compressing the sac downward (8). The presence of placental flow in a cervical ectopic pregnancy or low-lying sac is useful in distinguishing these entities from an abortion in progress.

Prior to visualization of a yolk sac or embryo, two US signs assist in the diagnosis of a normal IUP. The intradecidual sign occurs before 5 weeks gestational age, when the sac is too small to indent or deform the central endometrial echo (9). The sac appears as a rounded, hyperechoic area surrounding a small anechoic area within the thickened decidua. After 5 weeks gestational age, the double decidual sac sign may be seen (Fig 7) (10). The double decidual sac sign appears as a hyperechoic ring about the sac surrounded by a second hyperechoic ring, with a hypoechoic line interposed between the two echogenic rings due to apposition of the endometrial walls.

Although many findings suggestive of or diagnostic for an ectopic pregnancy can be seen outside the uterine cavity (eg, living embryo, tubal ring sign, fluid in the cul-de-sac, adnexal mass), various endometrial changes may also be seen. A pseudogestational sac is an intrauterine finding that is seen in 10%–20% of ectopic pregnancies (11). It may range in appearance from anechoic fluid to echogenic material (in which case it is called a decidual cast) in the uterine cavity (Fig 8) and is related to the hormonal effects of the pregnancy. Apparent endometrial thickening in the setting of a positive pregnancy test may in fact represent an echogenic decidual cast in the endometrium, although retained products of conception (RPOC) may have a similar appearance. There is no associated double decidual sign.

The double decidual and intradecidual signs may not be seen in early abnormal IUPs, and their absence does not exclude a normal IUP. A
thin decidual reaction of less than 2 mm, an ab-
normally shaped sac, or a gestational sac in a low
uterine location suggests an abnormal pregnancy.
An empty gestational sac may represent a blighted
ovum (mean gestational sac diameter, >10 mm
[6,12]) (Fig 9), an early IUP, or the pseudogesta-
tional sac of an ectopic pregnancy (Fig 10). Ab-
sent fetal cardiac activity when the crown-rump
length is greater than 5 mm is indicative of em-
bryonic demise (13). RPOC may appear as an
ill-defined intrauterine collection with mixed
echogenicity.

Gestational trophoblastic disease is a prolifera-
tive disease of the trophoblast that may manifest
as a complete or partial hydatidiform mole, inva-
sive mole, or choriocarcinoma. A hydatidiform
mole, the most common form of gestational tro-
phoblastic disease, is noninvasive and usually
manifests in the second and third trimesters. This
type of mole distends and fills the endometrial
cavity without invading the myometrium. US
demonstrates a uterus that is enlarged for gesta-
tional age and filled with multiple small, hyper-
echoic areas 3–10 mm in diameter with good pos-
terior acoustic enhancement (Fig 11). The cysts
represent grossly swollen villi from trophoblastic
hyperplasia. During the first trimester, the molar
tissue may appear as a homogeneously echogenic
endometrial mass. In cases of partial molar preg-
nancy, part of the fetus will be identified. Doppler
US of the tissue may reveal trophoblastic flow
greater than 21 cm/sec (14).
Postpartum Endometrium

Normal Appearance

The normal US appearance of the postpartum pelvis includes uterine enlargement and an endometrial cavity less than 2 cm in anteroposterior diameter (15). The cavity wall has a variable appearance ranging from smooth, well-defined borders to irregular, heterogeneous linings, with considerable overlap between normal and abnormal cases (15). Small echogenic foci within the endometrial cavity may not be pathologic, instead representing retained membranes and clots not completely expelled with the placenta (15). Although the presence of intrauterine air, as demonstrated by tiny internal echoes at US or foci of very low attenuation at computed tomography (CT), is consistent with endometritis in the appropriate clinical setting, it may also be seen in up to 21% of healthy patients in the postpartum period (16). Clot and debris are seen in 24% of cases after delivery (17). The thickness of the endometrial stripe decreases with involution of the uterus during puerperium, and if the endometrial cavity remains thickened, complications such as RPOC or hypotonic uterus should be suspected.

Pathologic Appearances

Endometritis, the most common cause of fever in the postpartum period, complicates 2%–3% of vaginal deliveries and up to 85% of cesarean sections (18). It is also associated with prolonged labor, premature rupture of membranes, retained clots, and RPOC. Although the US appearance of the uterus and endometrium may be normal, findings may include a thickened, heterogeneous endometrium, intracavitary fluid, and intrauterine air (Fig 12).

Postpartum hemorrhage is most often caused by uterine atony and RPOC and complicates 1%–2% of vaginal deliveries (19). There can be considerable overlap in the US appearance of these two entities. They can be distinguished clinically because uterine atony is seen in the immediate postpartum period and RPOC usually causes hemorrhage or infection at a later date. A normal-appearing uterus and endometrial cavity
in the presence of postpartum hemorrhage indicates uterine atony, whereas an echogenic intracavitary mass is suggestive of RPOC (Fig 13a) (20). If the mass remains attached to the endometrium, a finding of high-velocity, low-resistance flow at color Doppler US is suspicious for RPOC. A peak systolic velocity of 21 cm/sec is used as the minimum threshold for the diagnosis of residual trophoblastic tissue (Fig 13b) (14). It should be noted that the lack of increased flow does not eliminate the possibility of RPOC. RPOC that are seen late after delivery may contain calcifications (Fig 14). MR imaging depicts RPOC as an eccentric, enhancing intrauterine mass. CT may not help distinguish between RPOC and intrauterine clot because both processes can appear as dense masses (21).

**Postmenopausal Endometrium**

**Normal Appearance**

The postmenopausal examination should take into consideration the patient’s clinical history (eg, vaginal bleeding) and whether she has undergone hormonal replacement therapy. The normal postmenopausal endometrium should appear thin, homogeneous, and echogenic. There is controversy regarding endometrial thickness with menopause. Although some authors have found
that endometrial thickness decreases with age (22,23), others believe there is no statistically significant change during menopause (24). In general, a double-layer thickness of less than 5 mm without focal thickening excludes significant disease and is consistent with atrophy (25–27). Homogeneous, smooth endometria measuring 5 mm or less are considered within the normal range with or without hormonal replacement therapy (28). The endometrium in a patient undergoing hormonal replacement therapy may vary up to 3 mm if cyclic estrogen and progestin therapy is being used (22). The endometrium will appear thickest prior to progestin exposure and thinnest after the progestin phase. Imaging should be performed at the beginning or end of a cycle of treatment, when the endometrium will be at its thinnest and any pathologic thickening will be most prominent. A patient undergoing unopposed estrogen therapy with endometrial thickening exceeding 8 mm should be considered for biopsy, whereas patients receiving progesterone in addition to estrogen can be rescanned at the beginning or end of the following cycle to determine if there has been a change in endometrial thickness (22).

**Postmenopausal Bleeding**

Causes of postmenopausal bleeding include endometrial atrophy (approximately 75% of cases), endometrial polyps, submucosal fibroids, endometrial hyperplasia, endometrial carcinoma (approximately 10%), and estrogen withdrawal (5). Imaging should take place immediately after bleeding has stopped, when the endometrium is presumed to be thinnest and any disease entity will be most prominent. Endometrial thickness less than 4–5 mm at transvaginal US generally excludes cancer (Fig 15) (27). The atrophic postmenopausal endometrium may also be appreciated at MR imaging (Fig 16). Any thickness greater than 5 mm in the setting of postmenopausal bleeding or any endometrial heterogeneity or focal thickening seen at transvaginal US should be investigated further with sonohysterography, biopsy, or hysteroscopy. Endometrial sampling in the gynecologist’s office can lead to false-negative results if a focal abnormality is not sampled.
Endometrial Polyps.—Endometrial polyps are a common cause of postmenopausal bleeding and are most frequently seen in patients receiving tamoxifen. Although endometrial polyps may be visualized at transvaginal US as nonspecific endometrial thickening, they are frequently identified as focal masses within the endometrial canal. Polyps are best seen at sonohysterography and appear as echogenic, smooth, intracavitary masses outlined by fluid (Fig 17) (29,30). Cystic spaces corresponding to dilated glands filled with proteinaceous fluid may be seen within the polyp (31). The polyp may be broad-based and sessile or pedunculated. The point of attachment should not disrupt the endometrial lining (30). Polyps may also be seen at hysterosalpingography as pedunculated filling defects within the uterine cavity (Fig 18) or at T2-weighted MR imaging as low-signal-intensity intracavitary masses surrounded by high-signal-intensity fluid and endometrium (Fig 19). Color Doppler US may be used to image vessels within the stalk. Fibroids or foci of endometrial hyperplasia or carcinoma can mimic a sessile polyp, and foci of atypical hyperplasia are sometimes found within polyps (30,32).

Submucosal Fibroids.—Uterine leiomyomas are benign soft-tissue tumors that occur in patients of all ages. Although their size and frequency increases with age, they may grow until menopause and then involute and are a cause of premenopausal uterine bleeding. They are commonly identified at US as hypoechoic solid
masses, but they may be heterogeneous or hyperechoic, depending on the degree of degeneration and calcification. Fibroids tend not to interrupt the endometrium unless they are submucosal in location. Submucosal fibroids may distort the uterine cavity with varying degrees of intracavitary extension and are best visualized at sonohysteroscopy (Fig 20). Hysteroscopy can depict only the intracavitary portion of the fibroid (33).
Determining the intracavitary extent of a leiomyoma is important for surgical management because hysteroscopic myomectomy can be performed if over one-half the volume of the mass is within the endometrial canal (34).

At hysterosalpingography, submucosal fibroids are seen as filling defects with enlargement or deformity of the uterine cavity (Fig 21). At T1-weighted MR imaging, fibroids appear isointense to hypointense relative to the myometrium, whereas at T2-weighted imaging they appear homogeneously hypointense or heterogeneously hyperintense when degeneration is present (Fig 22).

**Endometrial Hyperplasia.**—Endometrial hyperplasia is an abnormal proliferation of endometrial stroma and glands and represents a spectrum of endometrial changes ranging from glandular atypia to frank neoplasia. A definitive diagnosis can be made only with biopsy, and imaging cannot reliably allow differentiation between hyperplasia and carcinoma. Up to one-third of endometrial carcinoma is believed to be preceded by hyperplasia (35).

All types of endometrial hyperplasia (cystic, adenomatous, atypical) can cause diffusely smooth or, less commonly, focal hyperechoic endometrial thickening (Fig 23). The US appearance can simulate that of normal thickening during the secretory phase, sessile polyps, submucosal fibroids, cancer, and adherent blood clots, yielding potentially false-positive results (32). Endometrial hyperplasia is considered whenever the endometrium appears to exceed 10 mm in thickness, especially in menopausal patients (36), although it can be reliably excluded in these patients only when the endometrium measures less than 6 mm. Endometrial hyperplasia may also cause asymmetric thickening with surface irregularity, an appearance that is suspicious for carcinoma. Because endometrial hyperplasia has a nonspecific appearance, any focal abnormality should lead to biopsy if there is clinical suspicion for malignancy.

**Endometrial Adenocarcinoma.**—Endometrial adenocarcinoma is the most common invasive gynecologic malignancy, but thanks to early detection and treatment, it is not a leading cause of cancer deaths. US signs of endometrial carcinoma include heterogeneity and irregular endometrial thickening (Fig 24a). These signs are nonspecific and can be seen in endometrial hyperplasia as well as polyps, leading to biopsy of almost any irregularity in the setting of postmenopausal bleeding. However, polypoid tumors tend to cause more diffuse and irregular thickening than a polyp and more heterogeneity than endometrial hyperplasia (37). A more specific US sign is irregularity of the endometrium-myometrium border, a finding that indicates invasive disease. A small amount of fluid in the endometrial canal is likely related to benign cervical stenosis and does not require further evaluation. An intrauterine fluid collection in a postmenopausal patient, although possibly related to cervical stenosis, should raise concern for endometrial (or cervical) carcinoma.
The value of Doppler and color Doppler US in distinguishing benign from malignant endometrial disease is controversial. It has been suggested that low-impedance blood flow at Doppler US can be associated with malignancy (38). Increased focal vascularity may be seen at color Doppler US in both benign and malignant diseases of the endometrium. Significant overlap in Doppler indices (ie, peak systolic velocity, resistive index, pulsatility index) in benign and malignant endometrial processes reduces the value of Doppler US in characterizing endometrial masses. Color and power Doppler US may occasionally aid in determining the presence and extent of tumor invasion and ensuring that biopsies are directed toward regions with increased blood flow (5).

MR imaging is valuable in the evaluation of endometrial cancer. Endometrial carcinoma usually manifests as a mass that, relative to normal endometrium, is hypo- to isointense on T1-weighted images and hyperintense or heterogeneous on T2-weighted images. Although MR imaging is not helpful in differentiating endometrial carcinoma from hyperplasia, it is helpful in cancer staging. Tumors are staged on the basis of depth of myometrial invasion. T1-weighted gadolinium-enhanced MR imaging is helpful in demonstrating myometrial invasion because a carcinoma will enhance less than normal endometrium. Superficial invasion involves only the inner half of the myometrium, whereas deep invasion involves the outer half of the myometrium and beyond (Fig 24b). If the normal low-signal-intensity junctional zone is intact, myometrial invasion can most likely be excluded. If the junctional zone is thinned due to atrophy or distention from clot, fluid, or polypoid tumor and is not well visualized, the presence of myometrial invasion is indicated by loss of the normal endometrium-myometrium interface. An irregular interface suggests invasion. Both MR imaging and CT (Fig 24c) are useful in demonstrating extraterine spread and lymphadenopathy.

![Figure 24](image-url)
Tamoxifen has proestrogenic effects on the endometrium and is associated with an increased prevalence of endometrial hyperplasia, polyps, and carcinoma (39,40). Up to one-half of breast cancer patients who are treated with this medication may develop an endometrial lesion within 6–36 months (40). Therefore, any patient who develops bleeding while taking tamoxifen requires evaluation. Tamoxifen causes the endometrium to appear thickened, irregular, and cystic at US (Fig 25). The punctate cystic spaces may be secondary to reactivation of adenomyosis within the inner myometrium or to obstructed glands in the endometrium due to the drug’s weak estrogenic effects (41). It has also been reported that the degree of endometrial thickening corresponds to the duration of tamoxifen therapy (42).

Two MR imaging patterns associated with tamoxifen have been described (43). The first pattern manifests as homogeneous high signal intensity on T2-weighted images, contrast material enhancement of the endometrium-myometrium interface, and signal void within the endometrial lumen on T1-weighted images. This pattern was found to be associated with endometrial atrophy or proliferative changes. The second pattern manifests as heterogeneous signal intensity on T2-weighted images (Fig 26) and lattice-like enhancement traversing the endometrial canal on T1-weighted images. This pattern was found to be associated with polyps, and it is believed that the lattice-like appearance may represent enhancing interstices between cysts within a polyp. In addition, an enhancing stalk may be seen if the polyp is pedunculated.

**Tamoxifen-associated Changes**

Tamoxifen has proestrogenic effects on the endometrium and is associated with an increased prevalence of endometrial hyperplasia, polyps, and carcinoma (39,40). Up to one-half of breast cancer patients who are treated with this medication may develop an endometrial lesion within 6–36 months (40). Therefore, any patient who
Intrauterine Fluid Collections

Although a tiny amount of fluid within the postmenopausal endometrial canal may be considered normal (44), any significant fluid collection is abnormal and requires careful evaluation of the uterus and adnexal structures for associated findings. Intrauterine fluid collections are associated with both endometrial and cervical cancers (45–47). An obstructing tumor must be excluded even when cervical stenosis has been identified clinically. In premenopausal patients, fluid collections are most commonly associated with menstruation, early IUP, or the pseudogestational sac in an ectopic pregnancy. In prepubertal patients, fluid in the endometrial canal may be related to hematometrocolpos. Other benign causes of obstruction leading to intrauterine fluid production include polyps, infection, and submucosal fibroids. The fluid may range in appearance from hypoechoic to hyperechoic depending on whether it is composed of serum, mucin, or blood.

Endometrial Adhesions

Endometrial adhesions are posttraumatic or postsurgical in nature and can cause Asherman syndrome, which includes infertility, recurrent pregnancy loss, and amenorrhea. Adequate distention of the endometrial cavity seen at sonohysterography or hysterosalpingography is necessary for radiologic diagnosis. Sonohysterography may demonstrate synechiae as echogenic bands bridging the uterine cavity. If the bands are thick and fibrotic, they may prevent complete uterine distention. Hysterosalpingography will demonstrate similar findings, with incomplete filling of the endometrial cavity and numerous irregular filling defects (Fig 27). Sonohysterography or hysterosalpingography may also be used to document resolution following hysteroscopic lysis.

Intrauterine Contraceptive Devices

Intrauterine contraceptive devices (IUD) should lie within the endometrial cavity and serve to prevent implantation of the embryo. IUDs should be readily detected at US as highly echogenic structures with distal acoustic shadowing (Fig 28). Endovaginal US is useful when distinction between the IUD and normal endometrial stripe cannot be made transabdominally. Penetration of the myometrial wall by the IUD may also be seen at US. If US cannot help identify an IUD within the endometrial canal, conventional radiography or CT may be performed to determine whether it lies within the peritoneal cavity. If so, the diagnosis of perforation of the uterine wall can be made (4).

Conclusions

There are many different imaging appearances of the normal and abnormal endometrium. Although US is almost always the first modality used in the radiologic work-up of endometrial disease, the use of multiple imaging modalities is common. Whether using US, MR imaging, sonohysterography, or hysterosalpingography, radiologists must understand that the appearance of the endometrium is dynamic. They must take into account the patient’s age, stage in the menstrual cycle, and pregnancy status and whether she has undergone hormonal replacement therapy or tamoxifen therapy, in addition to clinical history and physical examination findings, to make an accurate diagnosis.
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References


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