Role of Endovaginal Sonography in the Diagnosis and Management of Ectopic Pregnancy¹

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Although diagnostic laparoscopy is still considered the standard reference in the diagnosis of ectopic pregnancy (EP), use of high-resolution endovaginal sonography, in conjunction with qualitative serum assays of the beta subunit of human chorionic gonadotropin (β-hCG), allows detection of earlier and smaller EPs. The most common endovaginal sonographic finding of EP (89%–100% of cases) is an extraovarian, round or elongated, solid tubal mass. A tubal ring (an extrauterine saclike structure) is the second most common finding (40%–68% of cases). Pelvic fluid may be present, but it is a nonspecific finding. An EP may have a pseudosac, which can be distinguished sonographically from the true gestational sac of an intrauterine pregnancy. Color Doppler techniques can complement endovaginal sonographic findings, but they should be performed only after a thorough real-time evaluation of the adnexal region. Current therapeutic options for EP include expectant management (ie, close follow-up), medical treatment (usually injections of methotrexate), and surgery. Accurate diagnosis with endovaginal sonography is the prerequisite to nonsurgical management, since surgery is the logical treatment if laparoscopy is used for diagnosis.


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INTRODUCTION
The prevalence of ectopic pregnancy (EP), which constitutes 1% of all pregnancies (1), has increased more than threefold in the past 2 decades. The risk factors associated with this increased prevalence include a history of pelvic inflammatory disease or endometriosis, prior tubal ligation or tuboplasty, current use of an intrauterine device, and pregnancies achieved through in vitro fertilization or gamete intrafallopian tube transfer (2). The current use of highly accurate diagnostic tests may account for part of this increase. For patients with a history of EP, the risk of subsequent EP increases 10-fold. Although the prevalence of EP has increased, the heightened awareness of clinicians, the development of highly accurate diagnostic tests, and improved therapeutic options have resulted in a dramatic reduction in deaths from this condition. One of these diagnostic tools is endovaginal sonography, which has been shown to have superior diagnostic accuracy for imaging EP compared with transabdominal sonography (3,4).

This article reviews the role that endovaginal sonography plays in both the diagnosis and management of EP and proposes an algorithm for achieving high accuracy in the diagnosis of EP. The diagnostic criteria used with endovaginal sonography, including Doppler analysis, and the pitfalls of this modality are discussed. In addition, the role of endovaginal sonography in expectant management and medical treatment, by both the systemic and transvaginal routes of methotrexate administration are presented.

PATHOLOGIC FEATURES OF EP
Seventy-five percent to 80% of EPs are located in the ampullary portion of the fallopian tube, 10%-15% in the isthmic or interstitial portion, 5% in the fimbrial end, and 2%-4% in the interstitial end; only 0.5% are ovarian in origin (5). Abdominal pregnancy (which almost always occurs in patients with a previous aborted or ruptured tubal pregnancy) and cervical pregnancy are considered very rare forms of EP. Decidual reaction at the site of implantation is uncommon. The products of conception may grow on the mucosal or serosal surface of the fallopian tube or in a mixed position (6,7). Most of the distortion and expansion of the fallopian tube is caused by bleeding into the wall and lumen rather than from the products of conception.

DIAGNOSIS OF EP
Diagnostic laparoscopy is still considered the standard reference for the diagnosis of EP, although this invasive approach has a reported false-negative rate of 3%-4% and a false-positive rate of 5% (8). The combined use of a rapid assay for the beta subunit of human chorionic gonadotropin (β-hCG) and high-resolution endovaginal sonography is the current noninvasive approach for diagnosing EP. Early investigation of both symptomatic and high-risk asymptomatic patients with use of serum β-hCG screening and endovaginal sonography has resulted in the detection of earlier and smaller EPs. More than two-thirds of EPs are now detected unruptured (7), compared with only one-quarter before 1978 (8). The current treatment approach to suspected EP has, therefore, changed from emergency surgery to more elective management.

Negative results from a qualitative serum β-hCG test indicate that EP is not present, except in rare cases of “chronic EP” (8). Therefore, in high-risk asymptomatic patients, use of endovaginal sonography is indicated only if the qualitative serum β-hCG test is positive.

At our institution, patients with suspected abnormal first-trimester pregnancy are first scanned by using the endovaginal approach, and the transabdominal approach is used only when the adnexal structures are inadequately visualized. This happens rarely and usually when the adnexal structures are located far from the vagina.
Endovaginal Sonographic Features

The presence or absence of an intrauterine pregnancy (IUP) should first be determined when an EP is suspected. A normal IUP can be identified at endovaginal sonography when the patient's serum β-hCG level is above 1,000 IU/L (Second International Standard [2ndIS] unit) (9). This discriminatory β-hCG level has not been validated for patients with multiple gestations. Therefore, it is theoretically possible that multiple intrauterine gestations are first seen when the patients have higher β-hCG levels. At institutions where the Third International Standard (or International Reference Preparation [IRP]) is used, the discriminatory values are double those of the 2ndIS. The presence of an IUP practically excludes the possibility of an associated ectopic gestation, which remains rare in the general population. However, patients with pregnancies acquired through assisted techniques have a reported prevalence of heterotopic pregnancy as high as 1.1% (10).

A double-sac sign is the earliest reliable indication of an IUP on endovaginal sonograms (Fig 1). The parietal decidua creates the outer ring, and the capsular decidua makes up the inner ring of the double sac (11). A true sac of IUP and a pseudosac of EP can be confidently distinguished on the basis of a typical double-sac sign (11).

Endovaginal Sonographic Features of EP

Endometrial Findings.—There is no endometrial finding diagnostic of an ectopic gestation. The endometrial thickness in EP varies from a thin endometrium, usually seen in patients with substantial vaginal bleeding, to a thick endometrium.

Thin-walled, simple-appearing decidual cysts, usually present at the junction of the endometrium and myometrium (Fig 2), are associated with EP (12). However, decidual cysts are also seen with IUP (Fig 3). The thin wall of a
Figures 5–7. (5) Pseudo tubal ring. Endovaginal sonogram demonstrates a hemorrhagic cyst of the ovary that contains debris (arrows), which mimics the appearance of an embryo. (Reprinted, with permission, from reference 15.) (6) EP with a tubal ring appearance. Endovaginal sonogram demonstrates a tubal ring (arrowheads) next to a less thick and less echogenic corpus luteum cyst (arrow). (7) EP of the fimbrial end of the fallopian tube seen as a tubal ring. Endovaginal sonogram demonstrates a tubal ring (arrowheads) next to a corpus luteum cyst (arrow) of the ovary. Note the similar appearance of the wall of the corpus luteum cyst and the EP. (Reprinted, with permission, from reference 15.)

decidual cyst helps differentiate it from the gestational sac of an IUP.

The endometrium may have a pseudosac appearance if an EP is present. The pseudosac of EP is caused by either the presence of intruterine fluid surrounded by a thick decidual reaction or a detached decidual reaction (decidual cast) containing fluid centrally (Fig 4). The presence of two layers of the decidua surrounding the sac fluid in an IUP (Fig 1) allows the true gestational sac of IUP to be differentiated from the pseudosac of EP, which has only one layer corresponding to the endometrial decidual reaction (Fig 4).

Figure 4. Pseudosac of EP. Endovaginal sonogram shows a fluid collection (arrow) surrounded by only one echogenic layer of endometrium (arrowhead); the latter characteristic allows the pseudosac to be distinguished from a true intrauterine sac, which has a double-layered appearance.
**Adnexal Findings.**—The presence of a live embryo outside the uterus is the only pathognomonic sign of EP, reported in 8%–26% of EPs detected on endovaginal sonograms (13,14). Unless a well-developed embryo is identified, a reliable diagnosis of EP cannot be confirmed, because debris in other cystic structures in the adnexa can mimic the content of the sac of an EP (Fig 5).

A “tubal ring,” an extraterine saclike structure, is the second most common finding of EP, reported in 40%–68% of cases at endovaginal sonography (13,14,16). Although some sacs of EP are seen as a thick echogenic tubal ring (Fig 6), most gestational sacs of EP do not have this typical appearance (Fig 7).

The equivalent of a surgically identified tubal mass is the most common endovaginal sono- graphic adnexal finding in patients with EP (13) (Fig 8). This finding has been reported in 89%–100% of cases diagnosed at endovaginal sonography (13,17–20), with a specificity of 92%–98.8% (17,18,20).

**Pelvic Fluid.**—Pelvic fluid may be present in patients with EP, regardless of its nature (intact, ruptured, or aborting). However, pelvic fluid is a nonspecific finding that is seen in other conditions that can clinically mimic EP, such as a ruptured ovarian cyst, pelvic inflammatory disease, and ovarian torsion. Retrograde passage of blood through the fallopian tube into the cul de sac is also seen in association with a bleeding IUP or even normal menstruation. Pelvic fluid has been observed on endovaginal sonograms in 63%–70% of EPs and 25%–31% of IUPs (21–23).

Intraperitoneal fluid in EP is usually echogenic and may be the only abnormal endovaginal sonographic finding of EP (22). Echogenic fluid, particularly in a moderate to large amount, is reported to have a high positive predictive value (86%–93%) for the diagnosis of EP in a patient with positive results from a serum pregnancy test (23).

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**Figure 8.** EP seen as a solid tubal mass in two different patients. Transverse (a) and longitudinal (b) endovaginal sonograms show solid tubal masses (arrowheads) lying next to the ovary (arrows).
Doppler Findings.—Doppler analysis can play a role in the assessment of EP because the presence of an IUP or an EP can be confirmed when a low-impedance placental flow is identified in the uterus or in an adnexal mass. Measurements of peak systolic velocity thresholds have been advocated to help differentiate a pseudosac of EP from a normal or abnormal IUP. Dillon et al (24) reported a sensitivity of 84% and a specificity of 100% in the detection of IUPs on the basis of an endometrial peak systolic velocity threshold of more than 21 cm/sec. The sensitivity and specificity of this finding have not been evaluated in any large series. Altieri et al (25) reported peak systolic velocity values in IUPs ranging from 8-30 cm/sec in the absence of an intrauterine sac to 10-60 cm/sec with a visible intrauterine sac. However, in practice, the presence of focal, significantly increased color vascularity of the endometrium with low-impedance flow in a patient with a positive pregnancy test suggests an IUP (Fig 9). This finding should be confirmed by follow-up examination when there is suggestion of early IUP or by dilation and curettage in the case of an abnormal IUP.

Two groups of investigators have recently reported that use of color duplex techniques with endovaginal sonography led to an increased sensitivity in the diagnosis of EP (26, 27). Pellerito et al (26) identified an extraterine “placental flow” with a resistive index of less than or equal to 0.6, and Emerson et al (27) reported a wide range of waveforms: from “peritrophoblastic flow” in some masses to very high systolic peaks with high-resistance flow in others. Their reported sensitivities increased from 54% and 71% at real-time imaging to 95% and 87% with the addition of color duplex techniques (26, 27). With the use of color duplex techniques, 2% and 16% of EPs that were not seen at the initial endovaginal sonographic examinations were identified. Although Doppler indexes of EP are generally in the low-impedance range, they can vary from very low to very
Figure 10. Very vascular EP. (a) Gray-scale endovaginal sonogram shows an inhomogeneous tubal mass (arrowheads) containing cystic areas (arrows). (b) Color Doppler image shows substantial vascularity of the tubal mass that corresponds to the cystic areas. (c) Pulsed Doppler waveform of the tubal mass reveals a high-velocity, low-impedance flow with a resistive index of 0.38, consistent with peritrophoblastic flow. (d) Duplex image of a different EP shows a very high resistant flow.

high impedance (Fig 10). Substantial overlap exists between the resistive index values of EP, which range from 0.18 to 0.58, and those of a corpus luteum cyst, which range from 0.30 to 0.50, reported in a series published by Taylor et al (28). Therefore, only resistive index values less than 0.3 allowed discrimination between an EP and a corpus luteum cyst in this series.

- **Accuracy of Endovaginal Sonography in Diagnosing EP**

There is a recent trend toward treating EP either medically or not at all (29-33). This approach requires a highly accurate noninvasive test for the evaluation of patients with suspected EP, since diagnostic laparoscopy, which is still considered the standard reference for the diagnosis of EP, naturally leads to surgical treatment of these patients.

Endovaginal sonography is currently the only available alternative to diagnostic laparoscopy for the diagnosis of EP. However, the reported sensitivities of endovaginal sonography vary from low values of 47.4% and 54% (23,26) to high values of 89%-100% (13,17-20). Low sensitivities are reported in series in which an extrauterine gestational sac (tubal ring) with or without a live embryo was identified as the only specific criterion for a diagnosis of EP. In
other series, any “adnexal mass” was used as a diagnostic feature, which explains their low accuracy. When the presence of an adnexal mass is identified without documenting its extraovarian location, there is a high number of false-positive diagnoses of EP.

Our main diagnostic criterion is the presence of a homogeneous or inhomogeneous, rounded or elongated, solid structure with or without cystic areas lying outside but usually in proximity to the ovary; we identify this structure as a tubal mass (13) (Fig 11). The emphasis should be on the extraovarian location of this finding to achieve a high accuracy. This structure may or may not show vascularity on color Doppler images. Brown and Doubilet (34), in a recent review of the literature combining 10 studies that included 565 EPs and 1,651 IUPs, found an 84.4% sensitivity, a 98.9% specificity, a 96.3% positive predictive value, and a 94.8% negative predictive value for the accuracy of endovaginal sonography in the diagnosis of EP on the basis of observing any adnexal mass except for a simple cyst or an intraovarian lesion.

We use color Doppler techniques mostly as a complementary addition to endovaginal sonographic findings. The tubal mass is rarely seen only on color Doppler images (26,35). However, the products of conception contained in the tubal mass produce color vascularity, which allows it to be differentiated from a blood-filled tube or a pelvic hematoma. The finding of a placent al flow pattern of very low resistance (generally a resistive index of $<0.5$ [28]) in the tubal mass favors the diagnosis of EP.

- **Technical Aspects of Endovaginal Sonography for Highly Accurate Detection of EP**

Our preferred initial approach to examining patients in whom an EP is clinically suspected is to perform endovaginal sonography when the patient has an empty bladder. The ovaries must first be located to help detect an EP in the adnexal region. The extraovarian location of the EP can be recognized during real-time examination under most circumstances, since the majority of EPs lie between the ovary and the cornu of the uterus. An exophytic corpus luteum cyst may be difficult to differentiate from a tubal mass. On these occasions, dynamic scanning is performed with a bimanual approach, with one hand controlling the transducer and one hand palpating the abdomen suprapubically. Another technique used to differentiate between the
Figure 12. EP seen only with suprapubic sonography. (a) Endovaginal sonogram reveals a corpus luteum cyst (arrow), but the adnexal region was thought to be suboptimally visualized. (b) Suprapubic sonogram demonstrates an EP with a gestational sac (curved arrows) lying adjacent to the ovary (straight arrows).

Figure 13. Role of follow-up endovaginal sonography in the confirmation of EP. (a) Initial endovaginal sonogram shows a very small saclike structure (arrowheads) in the vicinity of the ovary (arrows). Distinction of an EP from an exophytic ovarian cyst was not definite at this point. (b) Follow-up endovaginal sonogram obtained after 72 hours helps confirm the presence of EP by showing its increasing size (arrowheads). Also, dynamic scanning at this point demonstrated the extraovarian location of the sac.

two conditions is to confirm the independent movement of the tubal mass and the ovary while tapping the ovary with the endovaginal transducer. The cul de sac region should also be examined, since some EPs fall into this space, presumably because of their weight. Suprapubic examination should be performed when the adnexal region is suboptimally visualized, which usually occurs when the patient is obese, when the uterus lies horizontally (placing the tubal regions far from the vagina), or when interfering bowel gas obscures the adnexal regions. However, a suprapubic examination is rarely required, and, in the few cases we have encountered, the EP was evident at the suprapubic examination performed when the patient had an empty bladder (Fig 12).

Some EPs may be attached to the ovary when substantial adhesions are present. If the diagnosis of an adherent EP or exophytic ovarian cyst cannot be confirmed by using dynamic scanning or color duplex techniques and the patient is stable, a follow-up examination is performed (Fig 13). The rapid change in the appearance of the ovarian cyst often allows these two conditions to be differentiated.
Because the addition of color Doppler techniques decreases the resolution of real-time imaging and because the prominent vascularity in the adnexa could obscure a small tubal mass, color Doppler studies should be performed after a thorough real-time imaging evaluation of the adnexal region.

**Nonvisualization of EP at First Examination**

Five percent to 18% of EPs are detected or confidently diagnosed only at the follow-up examinations (18–20). This will occur when the tubal mass is not seen at the initial examination or the adnexal finding is not definite for EP, when indication of an IUP is not present on endovaginal sonograms, and when the serum \( \beta \)-hCG level is less than 1,000 IU/L (2ndIS).

During follow-up examinations, performed every 24–48 hours, one of the following possibilities could arise: (a) a definite tubal mass is detected; (b) an IUP appears; (c) the serum \( \beta \)-hCG level increases to above 1,000 IU/L and an IUP is not seen, in which case an EP is assumed to be present even if it is not detected on endovaginal sonograms; or (d) the serum \( \beta \)-hCG level continues to drop, which indicates the presence of an aborted or aborting EP or IUP. With the availability of endovaginal sonography, diagnostic laparoscopy or dilation and curettage is not commonly required for the assessment of patients with possible EP.

**Pitfalls**

Potential pitfalls in the diagnosis of EP (ie, entities that can mimic an EP) at static imaging include paratubal or mesenteric cysts (Fig 14), hydrosalpinx or tubo-ovarian abscesses (Fig 15), pedunculated fibroids (Fig 16), loops of bowel, and ovarian cysts. The thick tubal ring of an EP (except in the late stages of spontaneous resolution) allows it to be differentiated from paratubal and mesenteric cysts. Although an uncomplicated hydrosalpinx has an elongated tubular appearance, it is predominantly cystic and does not contain echoes. A tubo-ovarian ab-

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**Figures 14–16.** (14) Paratubal cyst mimicking an EP gestational sac. Endovaginal sonogram shows a cystlike structure (curved arrow) lying next to the ovary (straight arrows). This cystic structure has a thin wall compared with the expected thick tubal ring of an EP. (15) Pyosalpinx mimicking a tubal mass of an EP. Longitudinal endovaginal sonogram shows a pyosalpinx (arrowheads). The very long, tubular nature of these structures at real-time imaging, a negative serum \( \beta \)-hCG level, and the clinical presentation of the patient help distinguish this condition from EP. (16) Subserosal fibroid. Endovaginal sonogram shows an oval solid structure (curved arrows), which was separate from the ovary but attached to the uterus (straight arrows). The patient had a negative serum \( \beta \)-hCG level.
can be helpful for differentiating between a corpus luteum cyst and a tubal mass, a substantial overlap exists between the resistive index values of EP and corpus luteum cyst. In a group of 45 EPs that we diagnosed by using endovaginal sonography, the resistive indexes of the EPs ranged from 0.15 to 1.6, whereas those for the corpus luteum cysts varied from 0.39 to 0.7. In our series, a resistive index less than 0.39 had a positive predictive value of 100% but a sensitivity of only 15% in the diagnosis of EP (Atri M., unpublished data, Dec 1995). Other series have reported similar results (36,37).

Another potential pitfall is a distended blood-filled tube, which develops secondary to retrograde passage of blood to the tube from an aborting IUP or normal menstruation (Fig 18). The presence of color Doppler vascularity in a tubal mass at endovaginal sonography allows it to be distinguished from a blood-filled tube.

**Localization of EP**

Most EPs are identified next to the ovary at endovaginal sonography. The close relationship of an ampullary or fimbrial EP to the ovary should not be the only factor in differentiating it from an isthmic EP, although an EP lying close to the uterus and far from the ovary is

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**Figure 17.** Ovarian cyst simulating an EP. (a) Gray-scale endovaginal sonogram shows a saclike structure (arrowheads) with a thick rind lying adjacent to the ovary (arrows). (b) Pulsed Doppler image of the saclike structure demonstrates a low-impedance flow with a resistive index of 0.40. The patient's serum β-hCG level was negative, and the structure appeared to move with the ovary, indicating the presence of a functional ovarian cyst.

**Figure 18.** Tubal mass presumably caused by retrograde passage of blood into the fallopian tube. Endovaginal sonogram shows an extraovarian solid tubular structure (arrowheads) that was nonvascular. Pelvic fluid is present (arrow). Serum β-hCG level was negative.
more likely to be isthmic. Interstitial EPs are located close to the uterus and can be recognized on endovaginal sonograms from the extension of the myometrium to their border or periphery (Fig 19). Extension of the endometrial lining to the periphery of the ectopic conceptus helps localize interstitial EP (38). The presence of ovarian tissue surrounding an EP suggests the diagnosis of ovarian EP (Fig 20). However, in the absence of definite embryonal elements or a fetal heart, differentiation of an EP from a corpus luteum cyst may be difficult.

**Prediction of Rupture**
A poorly defined complex adnexal mass and a moderate-to-large amount of pelvic fluid are common findings with a ruptured EP (13,21,39) (Fig 21). In our experience as well as that of others (13,21), the presence of a well-defined EP does not preclude its rupture. An EP most likely has not ruptured if an adnexal mass and moderate-to-large amount of pelvic fluid are not seen (13). Conversely, a substantial amount of pelvic fluid in an EP is not always a reliable indicator of rupture. Despite a moderate-to-large amount of pelvic fluid seen at preoperative endovaginal sonography, the tubes were intact at surgery in 46% of 39 EPs in the series of Frates et al (21) and 50% of 14 EPs at our institution (Atri M, unpublished data, Dec 1995) (Fig 22). Tubal hemorrhage with or without spontaneous abortion of EP is responsible for substantial pelvic fluid in the absence of tubal rupture.

**MANAGEMENT OF EP**
Surgery has been and still is the traditional treatment for EP. In a review of the literature, Carson and Buster (40) reported that of the patients treated with laparoscopic surgery, 86% subsequently had patent fallopian tubes, with 66% of the patients becoming pregnant and 23% of these pregnancies being ectopic.

Current treatment options for EP include "expectant management" (ie, close follow-up with no treatment unless treatment becomes necessary), medical (nonsurgical) treatment, and surgery (29,30,41,42). Because a much higher number of EPs are now being detected as intact or unruptured, the clinical picture of EP has changed dramatically from that of a drastic, life-threatening condition requiring immediate care to that of a more benign entity that can be evaluated and managed in a timely manner. Noninvasive diagnosis by means of endovaginal sonography is the prerequisite to the nonsurgical management of EP, since surgery is the logical treatment of choice if laparoscopy is needed for diagnosis.
Medical Treatment of EP

Different substances have been used for the medical treatment of EP, including prostaglandin F2α, potassium chloride, hypertonic glucose, and methotrexate (42-46). Among these substances, methotrexate is the most widely used agent. Methotrexate is administered both locally by the transvaginal, laparoscopic, and transcervical approaches (29,45,47) and systemically by intramuscular injection (48). In the initial regimens for systemic administration of methotrexate, several injections were required, which caused some side effects. Transvaginal injection prevented these systemic side effects (49). New regimens for systemic intramuscular administration of methotrexate consist of a single-dose treatment, which results in infrequent side effects (32,48). Stovall and Ling (32) reported a 94% overall success rate in a group of 120 patients treated with intramuscular methotrexate; the success rate dropped to 86% for those patients who presented with a live embryo. Patients may develop abdominal pain during the first week after systemic methotrexate treatment, presumably because of the aborting EP. In a literature review of 306 patients treated with systemically administered methotrexate compared with 295 patients in whom the agent was injected directly, the mean success rate was 94% versus 83%, mean tubal patency after treatment was 81% versus 88%, and the mean subsequent pregnancy rate was 71% versus 82.5%, with 11% of those pregnancies being ectopic in the systemic injection group versus 6% in the direct injection group (39).

The main criteria for the medical treatment of EP are: (a) a stable patient, (b) a growing EP as indicated by the presence of a live embryo or a rising level of serum β-hCG (15% increase in...
Figure 23. Advanced and vascular growing EP treated with transvaginal injection of methotrexate under US guidance. (a, b) Gray-scale (a) and color Doppler (b) endovaginal sonograms show an advanced EP containing an embryo on the day of methotrexate injection. (c) Color Doppler endovaginal sonogram demonstrates the remaining tissue (arrowheads) after long-term follow-up. (Reprinted, with permission, from reference 29.)

...in 24–48 hours), and (c) no indication of rupture at endovaginal sonography. Some authors have recommended that medical treatment be used only for EPS 3.5 cm in diameter or smaller (32). In our first series of patients with EPS treated with transvaginal injection of methotrexate, 19 (76%) of 25 were successfully treated (29) (Fig 23). The remaining six patients underwent surgery because of abdominal pain the day after the injection (four cases) and because of abdominal pain and vaginal bleeding that developed at a later date despite dropping serum ß-hCG levels (two cases). Of these six patients, only one had a ruptured EP. We considered a 15% or more decline in the serum ß-hCG level in the 48 hours after transvaginal injection to be proof of a successful treatment. However, Stovall and Ling (32) observed a transient increase in the serum ß-hCG level initially after intramuscular methotrexate injection. Therefore, they recommended repeating the quantitative serum ß-hCG assay on days 4 and 7 after the injection. If the serum ß-hCG level decreases from day 4 to day 7, the patient has responded positively to the treatment (32).

In our series of patients with EP treated with a transvaginal injection of methotrexate, the success rate did not vary substantially, regardless of the initial ß-hCG level or the EP appearance, vascularity, or size (29). Despite a positive response to treatment, the EPs increased in size in 63% of our patients and became more vascular during the course of resolution in 68% (29) (Fig 24). The amount of fluid in the cul de sac may also increase because of the trauma of injection, an aborting conceptus, or ovulatory bleeding from a new cycle (29). During the resolution, the EP may develop cystic areas (29) (Fig 25).
Follow-up of an EP treated with transvaginal injection of methotrexate. (a) Endovaginal sonogram obtained at the time of presentation shows a tubal mass (cursors) containing a gestational sac (arrow). (b) Follow-up endovaginal sonogram demonstrates cystic areas (arrowheads) that developed in the interim.

EP treated with transvaginal injection of methotrexate. (a) Color Doppler endovaginal sonogram demonstrates a tubal mass (arrowheads) on the day of methotrexate injection. (b) Color Doppler endovaginal sonogram obtained 10 days later shows the same EP (arrowheads), which has increased in vascularity and size. (c) Color Doppler endovaginal sonogram shows the remaining tissue (cursors) after long-term follow-up. (Reprinted, with permission, from reference 29.)
Local injection of the EP, as in our series, was attempted primarily because of the side effects caused by multiple systemic injections. Local injection has now mostly been replaced by a single-dose systemic injection of methotrexate because the latter has a comparable success rate and no significant side effects. This newer technique is used except in rare cases, such as patients with heterotopic pregnancy in whom systemic injection cannot be used, patients who refuse to receive a systemic injection, or patients in whom there is a contraindication to the systemic use of methotrexate.

Although routine use of endovaginal sonography is not indicated during the resolution of EP, if the patient develops new symptoms, follow-up endovaginal sonography is helpful in determining the cause. Endovaginal sonography can reveal some of the causes of pain related to EP, including an increase in the size of the EP or bleeding into the cul de sac during resolution, development of a transient hydrosalpinx, development of an ovarian hemorrhagic cyst, and rupture of the EP.

The long resolution time of EP, regardless of the approach used for administering the methotrexate (systemically or directly), is the main drawback of medical treatment. In one series, the resolution period of the tubal mass was always slower than the rate at which the serum β-hCG level reached zero (33). In our series, the maximum time for the serum β-hCG level to reach zero was 69 days, compared with 147 days for the tubal mass to resolve completely (29).

- **Expectant Management**

The improved sensitivity of current diagnostic tests probably accounts for part of the increased prevalence of EPs, since some of these would have spontaneously resolved had they remained unrecognized. Spontaneous resolution of EP has been documented in a number of reports (30,41,50). The main criterion for choosing expectant management for a patient with EP diagnosed by means of endovaginal sonography is the patient’s lack of symptoms or minimal symptoms. The EP is generally small (<3–4 cm in diameter), with no indication of a live embryo or rupture at endovaginal sonography. The initial indication for expectant management is either a minimal or no rise in the serum β-hCG level or a decline of more than 15% in 24–48 hours (30,41). We previously documented 13 spontaneously resolved EPs that ranged in size from 1 to 3.5 cm; in all cases, the patients had serum β-hCG levels of less than

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**Figure 26.** Expectant management of EP in two different patients. (a) Initial endovaginal sonogram reveals a solid tubal mass ( cursors). (b) Initial endovaginal sonogram demonstrates a gestational sac (inner cursors) in the EP (outer cursors).
Figure 27. Expectant management of an advanced interstitial EP. (a) Endovaginal sonogram shows an interstitial EP (arrows) containing a well-developed embryo (arrowheads). (b) Color Doppler image shows moderate color vascularity. (c) Follow-up endovaginal sonogram shows some residual mass of mixed cystic and solid components (arrows) attached to the uterus (arrowheads).

1,000 IU/L 2ndIS (30), a characteristic that has been reported by another group of investigators (41). These 13 cases constituted 24% of all cases of EP seen during that period at our institution. Sonographic findings revealed that EPs that spontaneously resolved tended to be less advanced (ie, the tubal mass appeared largely solid without a gestational sac) and less vascular than the growing EPs (30) (Fig 26). However, since this series was reported, we have documented more advanced and more vascular EPs accompanied by higher initial serum β-hCG levels that also spontaneously resolved, including a case of advanced interstitial EP (Fig 27). In our recent prospective study to evaluate possible predictors of spontaneous resolution, the EPs of older gestational age and with higher resistive index values were more likely to resolve spontaneously (51). The less advanced and less vascular EPs also spontaneously resolved more frequently. Korhonen et al (50) have suggested that upper limits for size (4 cm) and serum β-hCG levels (2,000–3,000 IU/L [IRP]) be used as criteria for selecting expectant management for a patient. As seen with medical treatment, an EP can increase in vascularity and size, and pelvic fluid may develop and even increase in quantity during spontaneous resolution (30).

BASING THE DIAGNOSIS AND MANAGEMENT PROTOCOL SOLELY ON ENDOVAGINAL SONOGRAPHY AND SERUM β-HCG LEVELS

Endovaginal sonography is a readily available, cost-effective, and indispensable tool in the diagnosis and management of EP. Consequently, noninvasive endovaginal sonography with its high sensitivity and specificity is well suited for replacing the routine use of invasive procedures such as culdocentesis, dilation and curettage, and diagnostic laparoscopy.
Ankum et al (52) have recently shown that the combined use of endovaginal sonography and serial assays of serum β-hCG levels now challenges the pivotal role of diagnostic laparoscopy, even rendering it obsolete. In their prospective study in which a serum β-hCG cut-off level of 1,500 IU/L (IRP) and endovaginal sonography were used, they obtained a sensitivity of 97% and a specificity of 95% for differentiating among three categories of pregnancies: IUP, EP, and trophoblast in regression (intra- or extrauterine).

At our institution, over the past 5 years, we have based the diagnosis and selected management protocol of EP on a combination of serum β-hCG levels and endovaginal sonographic findings. We have designed an algorithm for diagnosis and for choosing the appropriate management approach (Fig 28) in which endovaginal sonography has replaced laparoscopy, dilation and curettage, and culdocentesis as the main diagnostic tool. This algorithm is based on three premises. (a) In a small percentage of patients with a positive pregnancy test, the pregnancy may not be localized during the first radiologic examination when the findings are indeterminate or the examination is negative. A follow-up endovaginal sonographic examination may reveal an EP or IUP. (b) The absence of an IUP at endovaginal sonography, accompanied by a serum β-hCG level above 1,000 IU/L (2ndIS) and no significant bleeding, or a serum β-hCG level reaching 1,000 IU/L (2ndIS) during follow-up and no IUP indicate the presence of EP, even if it is not visualized at endovaginal sonography (in practice this rarely occurs). (c) If the serum β-hCG level drops and there is no indication of an EP or an IUP, the patient is assumed to have a regressing trophoblast, located either outside or within the uterine and will be treated expectantly.

Figure 28. Algorithm for the diagnosis and management of EP. EVS = endovaginal sonography. f/u = follow up.
CONCLUSION
Endovaginal sonography has substantially changed the diagnostic approach to EP. The combination of a highly sensitive serum \( \beta \)-hCG test and highly accurate endovaginal sonography can now potentially replace invasive procedures (e.g., diagnostic laparoscopy, dilation and curettage) used to evaluate patients with suspected EP. With the increasing interest in the conservative nonsurgical management of EP, endovaginal sonography can have a role in both the selection and follow-up of these patients.

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