Ultrasound Evaluation during the First Trimester has become an important diagnostic tool to establish the site and status of the early pregnancy.

Clinical Indications for First Trimester Obstetric Sonography:

1.) Exclusion of Ectopic pregnancy: Primarily by identification of intrauterine implantation.

2.) Confirm ongoing pregnancy in the setting of vaginal bleeding and pain (Threaten Abortion).

3.) Establish gestation age and EDC (due date) when menstrual history inadequate (First trimester ultrasound gestational age estimates most accurate).

4.) In treatment of infertility, early ultrasound confirms intrauterine location (ectopic location common) and establishes number of embryos (high incidence of multiple gestation).

Section 2: Natural history of early pregnancy.

Timing of Early Pregnancy:

1.) Menstrual Age: The traditional duration of pregnancy dates from the first day of the last Menstrual period an average of 40 weeks to delivery. This period is made up of:
Pre-ovulatory (follicular) phase of the Ovarian cycle: 13-14 days ending with ovulation of oocyte from ovary into the peritoneal (fimbriated) end of the fallopian tube. Variation typically less than 3 days, occasionally 5-7 days.

Oocyte migration: The oocyte migrates into the tube, with fertilization in the tube within 24 hours, typically about day 14.

Fertilization and Zygote migration: The Zygote migrates from tube into the fundal uterus with implantation on day 22-25.

Implantation: With implantation, trophoblastic HCG production gains access to maternal circulation and sensitive pregnancy tests turn positive, this event occurs 3-5 days prior to the first missed period. The local morphology of the implantation site (by ultrasound imaging) whether in intrauterine or ectopic location.

Growth and Development: Following implantation, 37 weeks of progressive differentiation and growth result in the mature fetus.

Early pregnancy loss: About 18% of zygotes do not implant, and about 32% of implantations spontaneous abort near the onset of the next Menstrual period (Menstrual Abortion). Only about 1/2 of zygotes persist as a clinical (symptomatic or noticeable) pregnancy. Compared to this early period, the later phases of pregnancy result in relatively little additional loss.
The pace of the early gestational process and the high prevalence of lost and ectopic gestations create a clinical need to make imaging assessments in the first trimester. The high resolution, safety, and ease of performance make ultrasound the procedure of choice.

**Section 3: Anatomic Structure of the Early Pregnancy**

The recently implanted embryonic cell mass forms an interface with the endometrial decidua, the the trophoblastic cell layer identified as the chorionic layer. The cell mass actually implants into the substance of the decidua, and the overlying decidua covers the implanted mass. Because of this the early development of the gestation appears to occur within the decidua layer, and enlarges to fill the endometrial cavity later.

Following implantation, a cavity or sac develops which lies inside the chorionic layer. This subchorionic layer contain the yolk sack (secondary) and the embryonic disk (early embryonic cell mass) surrounded by it's own small amniotic cavity.

At about 5 weeks the gestational sac shows a well defined yolk sac within the chorionic cavity (extraembryonic coelom). The embryo and amniotic cavity very small. The gestational sac grows at a rate of about 1mm per day. As a rule of thumb, the menstrual age in days can be estimated by adding 30 days (first appearence of sac) to the sac size in mm (1mm = 1 day)
As gestation progresses, the embryo and amniotic cavity grow rapidly and crowd out the chorionic cavity, and subsequently bulge into and then fill the endometrial (subchorionic) cavity.

By high resolution ultrasound examination these structures can be clearly delineated:
As the Gestation enlarges, the portion of the chorionic trophoblast destined to form the placenta enlarges and remains in intimate apposition to the underlying decidua (decidua basalis). The portion of the chorion on the cavity side of the gestation expands to form as the decidua capsularis, which comes into contact with the lining of the free endometrial cavity, now called the decidua parietalis.

Anatomic Points important to Ultrasound Interpretation are:

1.) True gestational sacs implant into the endometrial lining, and are seen eccentric to the endometrial canal. Fluid collections within the canal are not true gestational sacs.

2.) The Gestational sac and yolk sac (secondary yolk sac) are seen beginning at 4.5-5 weeks, before a recognizable embryo is seen.

3.) As the gestation enlarges into the endometrial cavity, only the early placenta need be in tight contact with the decidua. Small amounts of bleeding into the cavity are commonly seen, and may surround much of the
gestational sac, but if the decidua basalis remains intact, the gestation can and usually does continue to develop normally.

**Section 4: Early Ultrasound Findings in Normal Pregnancy**

*Ultrasound findings in the normal First Trimester Pregnancy:*

The visualization of early structures benefits from high resolution technique. In most cases, ultrasound probes designed to operate in the vagina provide the best resolution, and a necessary whenever definitive diagnosis cannot be made by standard scanning.

1.) Early Ultrasound appearance: The earliest visible gestational sac is seen at 4.5 weeks as an echogenic ring, with a tiny central hypoechoic area.

![Very Early, Sac with echogenic chorion HCG 1000-3000 4.5wk](image)

The Nearly horizontal line beneath the sac is the endometrial cavity. Note the gestational sac lies outside the cavity, embedded in the decidua (lining). This eccentric position is called the intradecidual sign, seen in intrauterine implantations, and different from fluid collections in the endometrial cavity which can be seen in both intrauterine and ectopic pregnancies. The presence of fluid in the canal in ectopic gestation carries the risk of mis-identification as an intrauterine pregnancy, and is referred to as a pseudogestational sac. Pseudosacs never show the intradecidual sign however. (See Ectopic Pregnancy Section for more information.

2.) Gestational Age Estimate: Measurement of the mean gestational sac diameter is an effective estimate of gestational age, used between 5 and 5.7-6weeks. The accuracy in this period is about +/-5 days. As soon as an identifiable embryo crown-rump length (CRL) is measurable (5.7-6 weeks), it should be used. This is because later gestational sac measurements may not reflect the embryonic size (or even its presence), but the embryonic CRL directly reflects embryonic growth. Tables of Mean Sac Size may be used, or as a rule of
3.) Yolk Sac: The secondary yolk sac is the first element seen in the gestational sac. Because it is reliably seen early, usually be 5 weeks, it is a critical landmark identifying a true gestation sac. Yolk sac should be seen in normal pregnancy when Mean Sac Diameter is 20 mm by transabdominal scan, and 8-mm by high resolution vaginal imaging.

It is a spherical membrane, quite echogenic and readily seen.
4.) Embryo:

The embryo is first seen on high resolution scans as a thickening on the margin of the yolk sac. It may be seen at 2-4 mm Crown-Rump Length (CRL - Longest Axis) corresponding to 5.7-6.1 weeks gestational age. With high-resolution, the heartbeat is seen as a regular flutter in the embryo, first evident at 5mm CRL(6.2 week.). Thus it is possible to see healthy embryos without heartbeats. In such cases, a follow-up study in 5-7 days will almost always demonstrate the heartbeat in healthy embryos. The presence of a heartbeat is a very positive prognostic sign.

By High resolution vaginal scanning, embryos should be seen at Mean Sac Diameters (MSD) of 18mm, with lower resolution abdominal scanning, embryos should be seen with MSD of 25mm.
Important Aspects of Normal Pregnancy Ultrasound:

Early Structures are small and benefit from High Resolution Vaginal Probe Scanning.

Gestational Sac first appears in the substance of the decidua (intradecidual) at 4.5 weeks, and should be seen in virtually all normal 5 week intrauterine pregnancies.

The yolk sac is a definite evidence of a true gestational sac, first seen at 5 weeks. It is a landmark to the early embryo, which develops along it's outer margin. Yolk sac should be seen when sac is 8-10mm. MSD by vaginal probe, or 20 mm. MSD by abdominal probe.

By vaginal probe high resolution scanning the embryo is first seen between 5.7-6.1 weeks, with heartbeat appearing at 6.2 weeks. Small normal embryos may not have a heartbeat. Embryo should be seen by High resolution scan at 18mm MSD, or 25 mm MSD by abdominal scan.

Section 5: Ultrasound Correlation with Measurement of Human Chorionic Gonadotrophin (HCG)

Serum Human Chorionic Gonadotropin and First Trimester Ultrasound:

The laboratory measurement of Serum Human Chorionic Gonadotropin has become an integral part of the evaluation of First Trimester Pregnancies.

When done to qualitatively detect the presence of a pregnancy, highly sensitive assays allow confident exclusion of pregnancy, even in ectopic locations.

When done quantitatively, HCG values allow rough but useful estimation of gestational age. Combined with ultrasound findings, HCG measurements allow systematic evaluation of 1st Trimester complications including pregnancy loss, ectopic pregnancy, gestational trophoblastic tumors, and ovarian hyperstimulation associated with Hormonal induction of ovulation.

1.) Standards:
Because HCG assays have been standardized by at least three standards, the significance of a given quantitative level (mIU/ml) has changed over the years.

Between 1964 and 1982, standardization used the Second International Standard (2nd IS). This standard was less pure and assays based on it are about 1/2 the values obtained with later standards. Thus if older clinical studies are used, it is imperative that the standardization be checked.

More recently the WHO First International Reference Preparation and the Third international Standard have been used, which yield results about twice as high as the classic (2nd IS) articles on HCG correlation.

Values listed in this section reflect later results unless otherwise specified.

**Earliest Ultrasound Detection and HCG:**

The occurrence of positive qualitative evidence of pregnancy occurs shortly after implantation at about 23-28 days (menstrual). The first ultrasound evidence of pregnancy occurs at about 32-35 days.

In instances where menstrual history is vague, bleeding or pain during this time may lead to concern for a more advanced ectopic or failing pregnancy. Since the HCG is positive, and no intrauterine pregnancy is seen, an erroneous diagnosis of ectopic pregnancy may be made.

To avoid this confusion, it is usual to define a minimum quantitative level of HCG at which intrauterine pregnancy should be seen by ultrasound.

With transabdominal scanning, this will correspond to about 5 weeks gestational age, and 3600 mIU/ml (1 IS - Corresponds to 1800 by older 2IRP) is the usual level chosen. Because the resolution of abdominal scanning is less than that of vaginal scanning, and much more dependent on body size (worse in large persons). We now use it only to identify larger and therefore easier gestations. Whenever an absent or questionable sac is found, vaginal scanning is always performed.

With high-resolution vaginal scanning, a value of 2000 mIU/ml (1 IS, 3rd IRP) may be used. Although it is common to see pregnancies at levels below this level (1000-2000), at these lower levels, confidence is too low to intervene surgically.

Using this"discrimination" level, in patients with no high resolution ultrasound evidence of an intrauterine pregnancy, a level greater than 2000 mIU/ml is considered presumptive evidence of an early ectopic pregnancy.

Patients with similar ultrasound findings and lower HCG levels are considered indeterminate, and a follow-up HCG and ultrasound are done, usually in 3-7 days. Follow-up is generally a safe policy, since ectopic pregnancies with such low HCG values generally do not rupture immediately, but whenever clinical findings are concerning, laparoscopic evaluation must be considered.

**Recent Spontaneous Abortion:**

Another pitfall occurs when a recent complete spontaneous abortion has occurred. If the lost pregnancy is relatively advanced, the starting HCG value may be many times the discrimination level (e.g. 8 week pregnancy - HCG = 30,000-100,000 mIU/ml.). In this setting, a substantial serum HCG level may remain, but ultrasound may show no evidence of the recently lost pregnancy. These finding may allow a erroneous presumptive diagnosis of ectopic pregnancy may be considered.
In most cases, the passage of products of conception per Vagina will identify this situation. In addition less than 10% of spontaneous abortions result in substantial elevation of HCG. None the less, when the situation occurs, a decision to perform laparoscopy to exclude ectopic or delay 6-12 hours to follow-up the serum HCG value must be made.

The Following Table lists the correlation between Serum HCG values as measured by the old Standard with gestational age and mean gestational sac measurement. Remember to multiple the HCG values X 2 to use the table with more modern HCG assays.

### Table A-6. RELATION BETWEEN MEAN SAC DIAMETER, MENSTRUAL AGE, AND HUMAN CHORIONIC GONADOTROPIN

<table>
<thead>
<tr>
<th>Mean Gestational Sac Diameter (mm)</th>
<th>Predicted Age (wk) Range = 95% CI*</th>
<th>Predicted hCG (mIU/mL) Range = 95% CI†</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>5.0 (4.5–5.5)</td>
<td>1,164 (629–2,188)</td>
</tr>
<tr>
<td>3</td>
<td>5.1 (4.6–5.6)</td>
<td>1,377 (771–2,589)</td>
</tr>
<tr>
<td>4</td>
<td>5.2 (4.8–5.7)</td>
<td>1,629 (863–3,036)</td>
</tr>
<tr>
<td>5</td>
<td>5.4 (4.9–5.8)</td>
<td>1,932 (1,026–3,636)</td>
</tr>
<tr>
<td>6</td>
<td>5.5 (5.0–6.0)</td>
<td>2,165 (1,126–4,256)</td>
</tr>
<tr>
<td>7</td>
<td>5.6 (5.1–6.1)</td>
<td>2,704 (1,465–4,990)</td>
</tr>
<tr>
<td>8</td>
<td>5.7 (5.3–6.2)</td>
<td>3,199 (1,749–5,852)</td>
</tr>
<tr>
<td>9</td>
<td>5.9 (5.4–6.3)</td>
<td>3,785 (2,085–6,670)</td>
</tr>
<tr>
<td>10</td>
<td>6.0 (5.5–6.5)</td>
<td>4,478 (2,483–8,075)</td>
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<tr>
<td>11</td>
<td>6.1 (5.6–6.6)</td>
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<tr>
<td>12</td>
<td>6.2 (5.8–6.7)</td>
<td>6,267 (3,502–11,218)</td>
</tr>
<tr>
<td>13</td>
<td>6.4 (5.9–6.8)</td>
<td>7,415 (4,145–13,266)</td>
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<td>14</td>
<td>6.5 (6.0–7.0)</td>
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<td>6.6 (6.2–7.1)</td>
<td>10,379 (5,766–18,682)</td>
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<td>6.7 (6.3–7.2)</td>
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<td>17</td>
<td>6.9 (6.4–7.3)</td>
<td>14,528 (7,964–26,501)</td>
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<td>18</td>
<td>7.0 (6.5–7.5)</td>
<td>17,188 (9,343–31,621)</td>
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<tr>
<td>19</td>
<td>7.1 (6.6–7.6)</td>
<td>20,337 (10,951–37,761)</td>
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<tr>
<td>20</td>
<td>7.3 (6.8–7.7)</td>
<td>24,060 (12,820–45,130)</td>
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<td>21</td>
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<tr>
<td>24</td>
<td>7.8 (7.3–8.2)</td>
<td>47,138 (24,067–93,325)</td>
</tr>
</tbody>
</table>

**Section 6: Early Pregnancy Failure - Anembryonic Gestation (Blighted Ovum)**

**Anembryonic Gestation (Blighted Ovum):**

Development of a normal appearing gestational sac without and embryo. This likely occurs as a result of early embryonic death, with continued development of the trophoblast. The sac may reach considerable size. The empty sac contains no distinguishing structures. Nearly half of spontaneous abortions occur without an embryo.

When small, the sac cannot be distinguished from the early normal pregnancy.
When larger, it must be distinguished from an endometrial fluid collection associated with ectopic pregnancy (pseudo-gestational sac), and hemorrhage (subchorionic) causing false enlargement of a smaller normal sac.

**Key Findings in Anembryonic Gestation:**

The sac must be intradecidual in position, and spherical in shape to be distinguished from the angular endometrial pseudosac. Detailed, high resolution scanning is used to distinguish a smaller normal sac complicated by hemorrhage.

The sac must be of sufficient size that the absence of normal embryonic elements is established.

**By High Resolution Vaginal Scanning** a sac >13 mm MSD (Mean Sac Diameter) with no yolk sac is often considered abnormal, but occasional normal pregnancies do not show yolk sac up to 20mm.

**By Lower Resolution Abdominal Scanning** a sac >20 mm. MSD with no yolk sac is abnormal. Vaginal Scanning to improve certainty should then be done.

**By High Resolution Vaginal Scanning** a sac >18 mm. MSD without an embryo is often considered abnormal, however normal sacs up to 20 mm. may show no embryo.

**By Lower Resolution Abdominal Scanning** a sac >25 mm. MSD without an embryo is abnormal. At this sac size, if subsequent Vaginal Scan also negative, anembryonic nature is virtually assured.

These criteria have been shown to be sufficiently specific to render the diagnosis of pregnancy failure of the anembryonic type. Since there is no addition risk, many centers believe it prudent to offer the mother a follow-up study in 7-10 days exclude error. Such errors are unlikely however.
Additional Findings:

In addition to Absent yolk sac and embryo, several associated finding have been described:

Thin Decidual Reaction (<2 mm.)

Weak Decidual Echo Amplitude

Low Uterine Position

Irregular Contour

Each of these elements has been shown to be useful, however it is the sac size and content that are key to this diagnosis. The more subjective nature of these findings make them subject to bias as well.

Section 7: Bleeding in Early Pregnancy - Threatened Abortion

Threatened Abortion: Bleeding in the First Trimester.

Vaginal bleeding occurs during the first 20 weeks in nearly 25% of clinical pregnancies. Since almost half of these pregnancies will be lost, it is a source of great concern, and a major indication for ultrasound examination.

Incomplete Spontaneous Abortion (Embryo Dead):

In many cases, the embryo will have already died, persistent chorionic function maintains a positive HCG assay. Expulsion of the sac is often delayed several days, though it may be seen to slowly migrate from the initial fundal location toward the uterine cervix.

The Living Embryo and threatened abortion:

The presence of an embryonic heartbeat is highly reassuring. When visualized by Low Resolution Abdominal sonography, more than 90% of pregnancies continue. Visualization by high resolution vaginal sonography is associated with a 70% continuance rate. The apparent discrepancy is because the heartbeat is a stronger positive sign in the larger more advanced embryos seen by transabdominal scanning.

The rate of pregnancy loss with positive heartbeat varies with gestational age and the presence of vaginal bleeding:

- Heartbeat at < 6 week., With bleeding 33% are lost, 16% are lost if no bleeding present
- Heartbeat at 7-9 week., With bleeding 10% are lost, 5% are lost without bleeding present
- Heartbeat at 9-11 week., With bleeding 4% are lost, 1-2% are lost without bleeding present.

The prognosis for the living embryo improves as gestation proceeds.
Associated Findings in threatened Abortion:

Subchorionic Bleeding:

Often visible as endometrial fluid surrounding the external (Decidua Capsularis) aspect of the gestational sac. As long as the placental (Decidua Vera) interface of the gestational sac and decidua remain intact, the pregnancy often continues. From the standpoint of Hemorrhage volume (Estimated from formula Length (cm) X Height (cm) X Depth (cm) X 0.52 = Volume ml), less then 75-200 ml. is often associated with continued development.

Slow Heartbeat:

Embryonic heart rate < 85 BPM is a negative prognostic sign, but is less reliable in small embryos.

Small Sac:

When the mean sac diameter (MSD) exceeds Crown Rump Length (CRL) by less then 5 mm., loss rate is 80%, however this "small sac" sign occurs only 2% of the time.

Conclusions:

When Yolk Sac in small sac is seen (< 13 mm.), and particularly when heartbeat is seen in larger sacs, expectant management will identify a substantial majority of successful pregnancies, even in the face of vaginal bleeding.

Section 8: Ultrasound Evaluation of Suspected Ectopic Pregnancy

General Information:

Ectopic pregnancy results from implantation outside the body and fundus of the uterus.

Although ectopic pregnancies occur everywhere from the cervix to the upper abdomen, 97 percent occur in the fallopian tube.

The clinical importance of ectopic pregnancy stems from the high mortality of ruptured ectopic pregnancy (0.1%) and the relatively high and increasing incidence of such pregnancies.

Clinical presentation includes:

Pelvic Pain
Bleeding
Adnexal Mass
Missed menstrual period

The occurrence of these signs and symptoms is not universal however, and ectopic pregnancy is potentially serious condition that is notoriously difficult to exclude clinically.

In recent years, the sensitivity of Serum HCG assays has improved such that virtually all ectopic pregnancies yield a positive result. Routine HCG measurement in patients with pelvic pain, vaginal bleeding, and unexplained adnexal mass allows confident definition of patients at risk for ectopic pregnancy.
**Risk Factors:**

The rate of ectopic pregnancy is increased in patients with tubal disease:

- Previous Salpingitis
- Previous Tubal Reconstruction
- Previous Contralateral Ectopic Pregnancy (Nearly 20%)
- Previous Tubal Ligation (Pregnancy uncommon 1:1000, but high rate of tubal location)
- Infertility (Increased rate of tubal damage).

**Ultrasound Evaluation:**

There are two important observations in ectopic pregnancy:

1. Direct visualization of ectopic gestation:

   Ideally, ultrasound can directly localize the gestation outside the uterus. In practice, difficulties in visualizing the adnexa and distortion of the gestation sac mean only 25-60% display unequivocal ectopic gestations. Because of this, the adnexal findings are usually considered of secondary importance (except when a definite embryo or yolk sac can be shown). More about adnexal findings later.

2. Absence of intrauterine gestation.

   Because the uterus is reliably seen at high resolution in all patients, any intrauterine pregnancy of sufficient size will be seen by ultrasound.

   *The most important single observation in evaluation of suspected ectopic pregnancy is the presence or absence of an intrauterine pregnancy.*

   Since the co-existence of both intrauterine and ectopic pregnancy is rare (1 in 4-30,000), in most cases the presence of an intrauterine pregnancy reduces the probability of ectopic gestation below the level of clinical concern.

   None the less, it is good practice to carefully evaluate the adnexa for alternative causes of pelvic pain, and to identify the rare heterotopic twin pregnancy.

3. Criteria for presumptive diagnosis of Ectopic pregnancy:

   Positive Serum HCG and absence of detectable intrauterine pregnancy when:

   a.) Gestation of 5 week menstrual age or more. Gestations of less than 5 weeks are not reliably seen by ultrasound. Since menstrual age is not 100% accurate, verification by serum HCG levels above the "discrimination" level of 2000 mIU/ml. (1 IS, 3rd IRP) suggests that an intrauterine gestation below the ultrasound detection threshold is present.

   Note: In this case, diagnostic laparoscopy is often indicated because of a high probability of ectopic pregnancy. None the less, as many as 35% of patients with a value of 2000 units and negative ultrasound will have ongoing intrauterine pregnancy. Because of this, negative ultrasound and HCG > 2000 units should not be the basis for therapeutic termination, such as methotrexate injection, but only further diagnostic maneuvers.

   b.) No clinical evidence of recent complete spontaneous abortion. In this setting a small number (about 10%) will have residual serum HCG values despite recent complete spontaneous loss of an intrauterine pregnancy.

   This presumptive diagnosis should lead to Laparoscopic visualization of the tubes, with appropriate therapy.
4.) In patients with shock or very severe pain: Ultrasound examination should not be done if it introduces appreciable delay. In this life-threatening situation, a low-risk "unnecessary" negative Laparoscopic study is preferable to possible serious morbidity or death which may result from delayed intervention.

5.) Ultrasound Findings in Intrauterine Pregnancy:
The structure of gestational sacs is similar in ectopic and intrauterine positions.

At 4.5-5 weeks gestational age, the gestational appears as small hyperechoic ring implanted into the adjacent tissue or decidua, eccentric to the endometrial canal. This finding alone is not definitive since occasional endometrial cysts may give a similar appearance. Early sac often demonstrate a second ring or decidual cast, constituting the "double decidual cast sign". These intradecidual sacs are the earliest suggestion of intrauterine pregnancy, but not 100% diagnostic until yolk sac or embryo appear:

The intradecidual eccentric position is important because fluid collections in the endometrial canal are common (25%) in ectopic pregnancy. These "pseudogestational sacs" do not lie in the decidua, and are concentric with the canal. The pseudosacs below were associated with ectopic gestation.

Adnexal Imaging in Ectopic:
The hyperechoic chorion ring is also the hallmark of small ectopic gestation, in which the small ring is identified in the adnexa.
More advanced ectopic pregnancies in the 7.5-9 week range may come to lie in the central area of the pelvis. If the covering tube is thickened, this ectopic may resemble the uterine fundus, and displace a small true fundus posteriorly. Be sure to identify the uterine cervix and link it to the gestation in the fundus in every case. This will avoid mis-identifying a tubal pregnancy as intrauterine as seen here:

Since ovulation extrudes the ovum out of the ovarian capsule, ectopic gestation are only rarely located inside the ovary (<1%). This is important, because corpus luteal cysts inside the ovary are a physiologic element of all pregnancies. Their irregular often cystic character may lead to confusion. If a cystic structure can be localized in the ovary, it is very unlikely to represent an ectopic pregnancy.

**Basic Radiology Imaging Lectures**