A 28-year-old nulligravida presented to the emergency department with a two day history of lower abdominal pain. Initially the pain was dull and diffuse, but it had progressed to a sharp sensation in the right lower quadrant. She stated that she was currently menstruating and has a regular 28-day menstrual cycle. However, upon further questioning, her last menstrual period (LMP) was 45 days ago and this period was lighter than usual. Physical examination revealed normal vital signs (HR 86, BP 114/72, RR 19, SpO2 99%, temperature 37.8°C) and tenderness to palpation in the right lower quadrant. Pelvic examination demonstrated right adnexal fullness. She had a remote history of Chlamydia trachomatis infection, but was otherwise healthy. A serum β-hCG was 2400 mIU/mL; therefore, a transvaginal ultrasound was performed (Figure 1).

**What is the most likely diagnosis?**

A. Appendicitis  
B. Ectopic Pregnancy  
C. Torsion of an ovarian cyst  
D. Gestational trophoblastic disease  
E. Early normal intrauterine pregnancy

Figure 1. Transvaginal ultrasound (TVUS) demonstrating (A) Sagittal view of the uterus and (B) Transverse view of the right adnexa.
Diagnose This: Female with Lower Abdominal Pain

Overview
Ectopic pregnancy occurs when a zygote implants in a location other than in the uterus. Over 95% of spontaneous ectopic pregnancies occur in the fallopian tube and other anatomic locations are mainly associated with the use of assisted reproductive technology (ART). \(^1,2\) When left untreated, ectopic pregnancies can rupture resulting in massive hemorrhage, infertility and even death. \(^1\) With the advent of TVUS technology and β-hCG assays, pregnancy-related death from ruptured ectopic pregnancy has decreased dramatically. \(^1,2\) However, with an incidence of 2%, ectopic pregnancy still contributes to 9% of pregnancy related deaths and is a leading cause of death in the first trimester. \(^1,2\) Hemorrhage is the most likely cause of death in 85-92% of cases. \(^2\)

Clinical Features
High risk factors for an ectopic pregnancy are often additive and include previous ectopic, previous tubal surgery or ligation, tubal pathology and current intrauterine device (IUD) use. \(^1\) Moderate risk factors include infertility, previous cervicitis, history of pelvic inflammatory disease (PID), multiple sexual partners and smoking. However, over 40% of women who present with an ectopic may not have these factors on history. \(^2\) A strong risk factor is that of PID or previous tubal disease from sexually transmitted infections, and STI rates have increased over the past 30 years. \(^2\) Indeed, Chlamydia trachomatis is thought of as the most common organism involved in acute salpingitis. \(^2\)

The classic presentation for an ectopic pregnancy includes vaginal bleeding, abdominal and/or pelvic pain as well as a tender adnexal mass; however, only 50% of patients present with this triad of symptoms. \(^1\) Additional symptoms include nausea, fatigue, cramping and amenorrhea, which often mimic a normal early intrauterine pregnancy or miscarriage. \(^1,2\)

It is important to explore the history of presenting illness fully as pain can progress from dull to sharp to no pain at all, as in tubal rupture, which decreases luminal distention but can also cause serious hemorrhage. The symptoms of hemoperitoneum may be even more difficult to localize and in severe cases, blood contact with the diaphragm can cause phrenic nerve irritation, thus shoulder pain. \(^2\) It is also valuable to document any history of prior tubal surgery, pelvic infections, infertility and types of contraception. \(^2\)

On exam, abdominal tenderness is the most common finding and is usually but not limited to being unilateral. Approximately 40% of ectopic cases are associated with a palpable adnexal mass. \(^3\) In cases of massive hemorrhage, rebound tenderness, guarding, rigidity in addition to orthostatic hypotension, narrowed pulse pressure and cardiovascular collapse may occur. \(^1,2\)

Imaging Findings and Diagnosis
Once a positive β-hCG is obtained, the differential diagnosis is narrowed to those of gynecologic in origin: normal intrauterine pregnancy, abnormal intrauterine pregnancy, spontaneous abortion, molar pregnancy and finally, an ectopic pregnancy. TVUS is highly useful for distinguishing these entities, especially when the β-hCG is above the discriminatory zone. \(^1\) This zone is the β-hCG level over which a gestational sac should be visualized on TVUS if an intrauterine pregnancy is present. In most hospitals, a β-hCG above 1500 or 2000 IU/L is considered above the discriminatory zone threshold. Therefore, a clinical diagnosis of an ectopic pregnancy can be made if the β-hCG is above the discriminatory zone and there is no evidence of an intrauterine pregnancy on TVUS. \(^3\)

TVUS allows the uterus to be imaged in both sagittal and transverse planes and has no ionizing radiation. In the event that an ectopic pregnancy is not visualized on TVUS, transabdominal imaging may be performed to provide a wider anatomical view as a negative TVUS does not rule out ectopic pregnancy. \(^1\)

TVUS can rule out an ectopic pregnancy if an intrauterine pregnancy is seen (gestational sac with a yolk sac or an embryo) or can rule in an ectopic pregnancy if a pregnancy at an ectopic site is seen. A pseudogestational sac may be visualized in 10-20% of cases. \(^1,2\) (Figure 2A). In the context of a positive β-hCG and concern for an ectopic pregnancy, any adnexal finding besides a corpus luteum should be considered suspect. \(^1\) To better differentiate possible adnexal masses, colour Doppler may be useful. In a tubal ectopic pregnancy, the gestational sac will have an increased blood supply, resulting in a “ring of fire” or hypervascular appearance on Doppler \(^4\) (Figure 3A). It is
important to ensure that the mass is visualized separate from the ovary as the corpus luteum can demonstrate a similar appearance. However, in 15-35% of ectopic pregnancies, no adnexal mass will be visualized on initial TVUS.

It is helpful to confirm that the adnexal mass is inside the ovary or arising from it in an exophytic manner. This can help exclude the presence of an ectopic as intraovarian ectopic pregnancies account for less than 1% of cases (Figure 2B). In addition, the tubal ring of an ectopic is more echogenic than that of ovarian parenchyma and it is highly specific. Ectopic pregnancy is a primary cause of hemoperitoneum in a woman of child-bearing age and it is demonstrated by free fluid on TVUS. Hemoperitoneum in relation to a positive β-hCG has a positive predictive value of over 85% for ectopic pregnancy (Figure 3B).

Management
The goals of treatment are to avoid tubal rupture, hemorrhage and death. Unstable vital signs are an indication for surgical therapy and a CBC, blood type and cross-match should be retrieved. In eligible cases, medical therapy with methotrexate via intramuscular dose has decreased patient morbidity by eliminating risks associated with surgery and anesthesia in addition to reduced costs associated with hospitalization. Following either surgical or medical therapy, there is the risk of persistent trophoblastic tissue. Therefore, serial β-hCG titres must be evaluated until they are no longer detectable. WinRh0® should be administered if the patient is Rh negative.

References