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### Ectopic Pregnancy

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The incidence of ectopic pregnancy (EP) has been rising from 4.5 per 1000 pregnancies to 19.7 per 1000 in 1992. This increase has been attributed to both a rise in the prevalence of EP risk factors and increased early diagnosis (transvaginal ultrasound and ultra-sensitive  $\beta$ HCG testing.) Only 33% of patients with an EP will have a future pregnancy progress to a live birth and 6-7% of maternal deaths are caused by EP.

**Risk Factors:** There are two mechanisms responsible for risk factors: a disruption in the tubal transport of the embryo or tubal damage. A tubal surgery/sterilization, prior ectopic, and history of pelvic infections all cause tubal damage and are associated with an increased risk of ectopic. A prior tubal surgery has the highest risk (21-fold common adjusted odds ratio of EP), while a prior ectopic pregnancy and tubal infection have increased risks of six to eight fold, and two to four fold, respectively.<sup>1</sup> An IUD alone should raise your suspicion for an EP as it acts as an obstacle to normal implantation. However, the mere use of an IUD as birth control, and likewise the use of oral contraceptives, does not predispose a patient to having an EP. Other risk factors include cigarette smoking, vaginal douching, previous pelvic or abdominal surgery, multiple sexual partners, in-vitro fertilization, DES exposure in-utero, and early age at first intercourse.<sup>1</sup>

A physical exam alone during the first trimester is rarely useful unless the os is open, products of conception are found at the os, a uterine size larger than 8 weeks, or the presence of heart tones on doppler makes the diagnosis of ectopic less likely, but it still may be present! Ten percent of EP have no pain with rupture, while only 10% have an adnexal mass on exam.<sup>4</sup> Frequently a patient's body habitus further interferes with an examination. Other symptoms of an ectopic include: abdominal pain (80-100% of patients with an ectopic), amenorrhea (75-95%), vaginal bleeding (50-80%), dizziness/fainting (20-35%), urge to defecate (5-15%), pregnancy symptoms (10-25%), and passage of tissue (5-10%). Signs of an EP include: adnexal tenderness (75-90%), abdominal tenderness (80-95%), adnexal mass (50%), uterine enlargement (20-30%), orthostatic changes (10-15%), and fever (5-10%).

With such insensitive physical findings, the importance of laboratory and ultrasonography increases immensely. A serum quantitative  $\beta$ HCG should also be sent if there is a high clinical suspicion of an ectopic or if the patient's urine  $\beta$ HCG is positive. Normal pregnancies have  $\beta$ HCGs that increase by 67% in 48 hours for the first 6-7 weeks of a pregnancy; 15% of normal pregnancies have abnormal doubling times, while 17% of EP have normal doubling times.<sup>3</sup> Therefore, it is recommended to check a second  $\beta$ HCG in 48 hours if the patient is stable provided there is appropriate followup. The result of the initial quantitative  $\beta$ HCG will determine the subsequent work up and the utility of the ultrasound. With a  $\beta$ HCG level of 1500 or 6500<sup>3</sup> for transvaginal and abdominal ultrasonography, respectively, an intrauterine pregnancy should be visualized reliably. With beta levels above these values, the diagnosis is less of a diagnostic dilemma. Below these levels, an ultrasound

is still helpful. An ectopic gestation will not produce  $\beta$ HCG at the same rate as a normal pregnancy and therefore may never produce a  $\beta$ HCG within the discriminatory zone. There are many case reports of ruptured ectopics with  $\beta$ HCG level under 100 or even less than 10 (negative qualitative test.)

While  $\beta$ HCG and ultrasonography are community standards for the detection of an EP, serum progesterone levels are the most controversial. Progesterone is produced by the corpus luteum in response to the presence of a pregnancy. In contrast to  $\beta$ HCG, progesterone levels change little in the first 8-10 weeks of gestation; after 10 weeks, the progesterone level starts falling. A serum progesterone level of more than 25ng/ml excludes an EP with 98% sensitivity; a level less than 5ng/ml identifies a non-viable pregnancy with near 100% sensitivity.<sup>3</sup> However, ACOG does not support the use of a single progesterone level to determine viability. In addition, a study found that 2% of EPs have progesterone levels over 25ug/ml. The use of this test will remain controversial until more prospective studies are completed.

While surgical intervention is the mainstay of therapy for EP, the use of Methotrexate (folate antagonist) has provided an alternative of medical management. Contraindications to its use include: obvious signs of rupture, adnexal mass greater than 3-4cm,  $\beta$ HCG > 2000mIU/ml, evidence of cardiac activity, and/or suspected heterotopic pregnancy.<sup>2</sup> Two dosing regimens exist, the more widely used single dose and variable dosing. While the single dose is more convenient, it is slightly less successful (88% success vs. 96%).<sup>2</sup> The single dose regimen is 50mg/m<sup>2</sup> IM with a repeated dose on 7 if the  $\beta$ HCG is greater than day number 4. In the variable dosing schedule, the patient receives 1mg/kg IM on days 1,3,5,7 and leucovorin on days 2,4,6,8. Remember to check Rh give Rhogam accordingly. A common side effect of this medication is transient pelvic pain, frequently occurring between days 3 to 7 and lasting 4-12 hours. It is difficult to differentiate between successful abortion and tubal rupture. Patients without orthostatic hypotension or decrease in packed-cell volume are frequently observed for 24 hours.

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