

ECTOPIC PREGNANCY
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March, 2001

1. **General Considerations:**

- Constitutes one of the true emergencies which can be seen in a primary care setting
- May be the only life-threatening disease whose prevalence (1-2% of pregnancies in the USA in 1992) is increasing while mortality is decreasing. This phenomenon is largely explained by advances in early diagnosis.
- Ectopic pregnancy is the major cause of maternal death in the first trimester accounting for 9-13% of all maternal deaths (approx 30-40 deaths per year in the USA)
- Fatalities are highest in teenagers and non-whites

2. **Predisposing Factors:** Any process which damages the tube will predispose to ectopic pregnancy.

High Risk

- **Tubal surgery**
- **Sterilization (esp after electrocoagulation procedures)**
- **Previous ectopic pregnancy (increases in proportion to the number of previous ectopic pregnancies)**
- **In-utero exposure to DES (absent or minimal fimbriae, small os, and fallopian tubes which are shorter and thinner than normal)**
- **Use of IUD (if pregnancy occurs, there is a strong probability that it will be ectopic)**
- **Documented tubal pathology (prior PID, endometriosis or previous surgery)**

Moderate Risk

- **Infertility treatment (proper fertilized ovum transport through the fallopian tube may be adversely influenced by human menopausal gonadotropin)**
- **Previous genital infections**
- **Multiple sexual partners**

Slight Risk

- **Previous pelvic/abdominal surgery**
- **Cigarette smoking**
- **Vaginal douching**
- **Age < 18 yrs at first intercourse**

3. Most Common Implantation Sites

- **95% occur in the fallopian tubes**
- **Others in ovary, abdomen**
- **Interstitial or cornual position of uterus can be involved**

4. Natural History of Ectopic Pregnancy

- **10-50% abort or are absorbed**
- **The rest rupture, re-implant, or are surgically or medically removed.**
- **Time of rupture depends partially on implantation site**
- **Ampulla, isthmus (most common) rupture 4th-12th week**
- **Interstitial (rarer) rupture later, during 8th-16th week**
- **Tubal and intrauterine pregnancies can co-exist (1:6000-1:30,000)**

5. Presenting Symptoms:

- ***** Classic Triad***: Pain, amenorrhea, then vaginal bleeding**
- **All three are present in 2/3 of patients. Some patients present with no pain and only abnormal bleeding.**

- **Pain:**
 - Present in 90-99%
 - Can be anywhere including upper abdomen
 - Referred to shoulder or back in 10-20%
 - Severity:
 - Less severe implies tubal distension or localized bleeding
 - More severe implies rupture. Usually aggravated by motion. Rupture can be precipitated by straining with BM, intercourse, or repeated pelvic exams!

- **Amenorrhea:**
 - Present in 65-75%
 - Time since LMP usually 6-10 weeks

- **Vaginal bleeding**
 - Present in 75%
 - Usually scanty and dark brown
 - If profuse, consider cornual or interstitial pregnancy

- **Other pregnancy symptoms such as breast engorgement, morning sickness are uncommon**

- **GI symptoms can occur and include nausea, vomiting, urge to defecate, abd cramping. GI sx are often associated with misdiagnosis. In a study of fatal ectopic pregnancies, 80% had GI sx.**

- **Dizziness occurs in 33% of ectopics.**

6. Physical Findings:

- **Vital Signs:**
 - Most patients have normal vital signs
 - Hypovolemia is present in 10-20%
 - Low grade fever may occur in 5-10%, occasionally hi fever

- **Abdominal/Pelvic exam:**
 - Abdominal tenderness is usually present (75%)
 - Localized tenderness is usually associated with unruptured ectopics
 - Generalized or rebound tenderness or signs of peritonitis accompany rupture.

- Adnexal or cervical motion tenderness found in 75-90%
- Adnexal mass found in 50%
- Cul-de-sac fullness in 33-60%
- Uterine enlargement may be found in 30% secondary to placental hormone influence. The fundal height may even correspond to expected size for an intrauterine pregnancy, 6-8 weeks. Finding an enlarged uterus does not rule out ectopic!

7. Diagnostic Tests:

General

- Almost all ectopics are dx'd between 5-12 weeks' gestation
- The identification of the implantation site of an embryo earlier than 5 weeks' gestation is beyond the resolution of current diagnostic techniques

Blood Tests:

- Beta-hCG should be positive. <1% of ectopics have beta < 10 mIU/ml.
- Urine hCG is as good as serum but a dilute urine (sp gr < 1.015) decreases the reliability of the urine test. Urine hCG is a qualitative test, not a quantitative test but can be useful in establishing whether a pregnancy is present.
- Beta-hCG rises exponentially in early normal pregnancy and should double every 1.4-2.1 days, with a minimum 66% rise in 2 days.
- In an intrauterine pregnancy, the serum beta-hCG should double in 48 hrs!!

Radiologic Tests:

- Transabdominal ultrasound
- Much less sensitive than transvaginal ultrasound
- Rarely visualizes the ectopic.
- May exclude intrauterine pregnancy
- May visualize peritoneal or cul-de-sac fluid
- ***Best Use of Transabdominal Ultrasound:
 - When beta-hCG > 5500-6500 mIU/ml (approx 6 menstrual weeks), approx 90% of intrauterine pregnancies can be visualized as a gestational sac
 - Absence of an intrauterine pregnancy indicates an ectopic in 90% of cases
 - The problem is: only 25-40% of ectopics have beta-hCG > 6000

- **Transvaginal Ultrasound**
- **Visualizes intrauterine gestational sac at 1000-2000 mIU/ml (4-5 menstrual weeks)**
- **May visualize an adnexal mass**
- **Diagnostic Algorithm: (from Barnhart, Esposito, Coutifaris, see references and figure at end of this article)**
 - **The most efficient way to rule out an ectopic pg is to confirm an IUP by US (sensitivity and specificity approach 100% in a gestation > 5.5 weeks). The identification of an ectopic pg is much less sensitive and less specific; therefore most diagnostic algorithms focus on diagnostic and surgical procedures for women who do not have a viable IUP.**
 - **Because women may have irregular bleeding early in pregnancy, the exact age of gestation is often unknown. In this case the beta-hCG level can be used as a surrogate marker for gestational age by a concept known as the discriminatory zone (DZ). When the DZ is > than a defined level (based on the expertise of the ultrasonographer and the equipment used; must be determined for each institution), the pg is advanced enough that an IUP can be visualized by ultrasound with 100% sensitivity**
 - **The DZ varies from institution to institution (1500-2000 mIU/ml). For MCV, using the best equipment and the most experienced ultrasonographers in the OB/Gyn Dept, it approaches 1500 although it has not been validated here. (personal communication, Dr. John Pierce). Other centers use a DZ of 1800-2000 which is more conservative. Therefore, the diagnostic algorithm for the pregnant pt with pain and vaginal bleeding looks like this:**
 1. **If hCG > 1800, transvaginal US is done. If IUP seen, pt is followed closely clinically. If no IUP is seen or if the US suggests either spontaneous miscarriage or ectopic pg, the pt goes to the OR for D & C. If products of conception obtained, miscarriage is confirmed. If no products of conception, laparoscopy is done to visualize the fallopian tubes.**
 2. **If hCG < 1800, transvaginal US is frequently nondiagnostic. Then the clinically stable pt is followed with serial quantitative beta-hCGs. Once the beta has reached the DZ, US is performed again and the sequence in # 1 occurs. If the beta shows an abnormal rise (should double in 48 hrs), plateaus, or declines, then the pt goes to the OR for D & C as above. If the pt is clinically unstable and unable to tolerate any delay while serial b-hCGs are followed, she is taken immediately to laparoscopy.**

8. Treatment:

Expectant Management

- **Because many ectopic pregnancies resolve spontaneously, some gynecologists recommend expectant management for:**
- **Adnexal masses < 4 cm**
- **No adnexal cardiac activity**
- **Cul-de-sac fluid < 100 cc**
- **Falling hCGs**
- **Expectant management success rates vary from 47-100% if the above criteria are met**

Surgical

- **Laparotomy has been replaced by operative laparoscopy**
- **Linear salpingostomy is recommended for ampullary ectopics**
 - **the standard laparoscopic operation when the ectopic mass is unruptured and measures > 4 cm by ultrasound**
 - **a longitudinal incision is made over the bulging antimesenteric border of the implantation site**
 - **products of conception are removed with forceps or by suction.**
 - **hemostasis is achieved and the incision is left to heal**
- **Segmental resection is necessary if the ectopic is located in the isthmus; microsurgical anastomosis may be accomplished either intraoperatively or at a later date. The tubal lumen is narrower in the isthmus; therefore, the isthmus is predisposed to more severe damage and greater rates of proximal obstruction.**
- **Ruptured ectopics are usually treated by salpingectomy which can be accomplished laparoscopically as long as the patient is hemodynamically stable.**
- **Interstitial (cornual) ectopics are difficult to treat laparoscopically; laparotomy is often required.**
- **Subsequent pregnancy rates after laparoscopic treatment of an ectopic pregnancy approaches 50-65%. The repeat ectopic pregnancy rate is 15%.**
- **Laparoscopic salpingectomy is preferred for women who do not desire to become pregnant again.**
- **Persistent ectopic pregnancy occurs in 5-20% of cases and results from incomplete removal of trophoblastic tissue. It is diagnosed when follow-up beta-hCGs plateau or rise. These can usually be treated with a single-dose of systemic methotrexate (50 mg/m²).**

- **Follow-up:**
 - Weekly beta-hCG until < 5.0 IU/L
 - No sex, pelvic exam or US until resolved
 - Single dose MTX (see above) for persistent ectopic pregnancy

Medical

- **Methotrexate (MTX) is an anti-metabolite that inhibits folic acid reductase, interfering with DNA synthesis and cell multiplication. Actively proliferating trophoblasts are highly susceptible to MTX.**
- **Advantages of MTX: lower cost, faster recovery, higher subsequent fertility than with surgery**
- **Contraindications to MTX:**
 - Hepatic dysfunction (SGOT 2x nl)
 - Renal disease (Cr > 1.5)
 - Active peptic ulcer disease
 - Blood dyscrasia (WBC < 3,000, Plt < 100,000)
 - Poor patient compliance
- **MTX is used to treat ectopic pregnancy if the sac < 4 cm and there is no fetal cardiac activity**
- **There are two commonly used MTX regimens:**

1. **Variable dose: MTX 1 mg/kg IM, alternate days (d 1,3,5,7)**

Leucovorin 0.1 mg/kg IM, alternate days (d 2,4,6,8)

Continue until beta-hCG falls 15% in 48 h or four doses of MTX

2. **Single dose: MTX 50 mg/m² IM**

Repeat dose if beta-hCG on d 7 d 4

- **Follow-up:**
- **Weekly beta-hCG until < 5.0 IU/L**
- **No sex, pelvic exams or US until resolved**
- **Repeat course for persistent ectopic pregnancy**

9. SPECIAL NOTE TO STUDENT HEALTH PROVIDERS:

1. **Maintain a high index of suspicion in women of reproductive age who have abdominal pain, even if the sx seem to be GI in origin.**

2. A urine pregnancy test should be ordered if there is any possibility that unprotected intercourse has occurred.
3. Be aware that the differential diagnosis includes:
 - Spontaneous abortion
 - Ovarian cyst (can co-exist with intrauterine pregnancy)
 - PID (usually has negative beta-hCG)
 - Appendicitis (can co-exist with intrauterine pregnancy)
 - Dysfunctional uterine bleeding (beta-hCG negative)
 - GI disorder
4. If the patient has a positive hCG, pelvic pain +/- vaginal bleeding, she should be referred immediately to a gynecologist. If she has no insurance, she should be referred to the MCV ER.

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