

Introduction:

- Following fertilization and fallopian tube transit, the blastocyst normally implants in the endometrial lining of the uterine cavity
- Implantation outside of the uterine endometrium is considered an ectopic pregnancy
- Ectopic pregnancies account for 0.5-1.5% of all first trimester pregnancies in the US
- Earlier diagnosis improves maternal survival rates through:
 - *B-hCG assays*
 - *Transvaginal sonography*

Tubal pregnancy

- 95% of ectopic pregnancies implant in the fallopian tube
 - *Ampulla* – 70%
 - *Isthmic* – 12%
 - *Fimbria*- 11%
 - *Interstitial tube pregnancies* 2%
- 5% are nontubal ectopic pregnancies, sites include:
 - *Ovary*
 - *Peritoneal cavity*
 - *Cervix*
 - *Prior C- section scar*
- Occasionally a multifetal pregnancy one implanting normally in the uterine endometrium and one pregnancy implanting in an ectopic location – termed: **heterotopic pregnancies**
 - Natural incidence 1:30,000
 - With assisted reproductive technologies 9:10,000

Risk factors:

- Prior tubal pregnancy:
 - *Risk is increased x5*
- Tubal ligation procedures
- Endometriosis
- Congenital tubal anomalies (especially, diethylstilbestrol exposure in utero)
- Smoking- mechanism is unclear
- History of an STD or tubal infection can distort normal tubal anatomy
- For example; one episode of salpingitis can be followed by a subsequent ectopic pregnancy in up to 9%
- Intrauterine devices- important to note that they do not increase the risk of ectopic pregnancies compared to the general population, however they increase the RELATIVE risk of the presence of a pregnancy outside of the uterine cavity

Potential outcomes of a tubal pregnancy

- The lack of a submucosal layer allows the fertilized ovum to burrow through the epithelium
- The zygote comes to lie near or within the muscularis which is invaded by a rapidly proliferating trophoblast
- The embryo or fetus in an ectopic pregnancy is often absent or stunted
- Outcomes include:
 - *Tubal rupture – the associated expanding pregnancy and hemorrhage can tear the fallopian tube*
 - *Tubal abortion – pregnancy may pass out of the distal fallopian tube (depends on the original location of implantation of the ectopic pregnancy- distally is more favored)*
 - *Pregnancy failure with resolution- spontaneous failure and reabsorption*

Clinical manifestations

- Earlier patient presentation and precise diagnostic technology allow for a better outcome and identification of an ectopic pregnancy before rupture occurs
- Delayed presentation triad:
 - *Delayed menstruation*
 - *Pain*
 - *Vaginal bleeding/ spotting*
- Tubal rupture:
 - *Lower abdominal and pelvic pain – sharp stabbing pain*
 - *Abdominal palpation illicit tenderness*
 - *Cervical excitation test is painful*
- Posterior vaginal fornix may bulge due to blood collection in the rectouterine cul-de-sac. It may also present as a tender boggy mass felt beside the uterus

clinical manifestations

- Uterus may be enlarged due to hormonal stimulation
- Symptoms of diaphragmatic irritation may be present due to hemoperitoneum
 - *Neck or shoulder pain especially upon inspiration*
- 60-80% of women report vaginal spotting or bleeding
 - *Response to moderate bleeding will not change vital signs significantly. However, slight rise in BP or a vasovagal response resulting in bradycardia and hypotension may occur.*
 - *If BP will fall and pulse will rise if significant hemorrhage and hypovolemia is present*
 - *CBC will show a significant drop in hematocrit and possibly varying degrees of leukocytosis*

Multimodality diagnosis

- Long list of differential diagnoses of the presentation of an ectopic pregnancy need to be addressed as well
 - *Overlapping symptoms of an intrauterine pregnancy*
 - *Miscarriage*
 - *Round ligament pain*
 - *Adnexal diseases: torsed ovarian masses, salpingitis, tuboovarian abscess*
 - *Appendicitis*
 - *Cystitis*
 - *Renal stones*

Diagnosis:

- Physical findings
- Transvaginal sonography
- Serum B-hCG level measurements: initial, and the subsequent pattern of rise or decline
- Surgical diagnosis:
 - *D&C*
 - *Laparoscopy – if hemodynamically stable*
 - *Laparotomy - if hemodynamically unstable*

Transvaginal sonography

- An intrauterine gestational sac is usually visible between 4-5 weeks.
- The yolk sac appears between 5-6 weeks
- Fetal pole with cardiac activity is detected at 5-6 weeks
- In an ectopic pregnancy
 - *A trilaminar endometrial pattern can be diagnostic*
 - *The adnexa need to be visualized and if a yolk sac, embryo or fetus is identified then an ectopic pregnancy is confirmed*
 - *Hypoechoic fluid collections may suggest an early intrauterine gestational sac but may also be present with ectopic pregnancies*

Hemoperitoneum

- Presence of blood in the peritoneal cavity is identified using sonography and/ or culdocentesis
- Presence of a hypoechoic fluid collecting in the retrouterine cul-de-sac then surrounds the uterus as it fills the pelvis
- With significant intrabdominal hemorrhage, blood will collect in Morison pouch near the liver. So free fluid in this pouch is not seen until it reaches 400 ml and more

Medical management

- Traditionally involves the antimetabolite Methotrexate
 - *Folic acid antagonist*
 - *Leads to arrested DNA, RNA and protein synthesis*
 - *MTX is highly effective against rapidly proliferating tissue such as trophoblast*
 - *Does not lead to a decrease in the ovarian reserve, but pregnancy should be avoided up until 6 months to avoid fetal malformations and miscarriages*
 - *Drawbacks:*
 - Bone marrow suppression
 - GI mucosa and respiratory epithelium disruption
 - Directly toxic to hepatocytes

TABLE 19-1. Medical Treatment Protocols for Ectopic Pregnancy

	Single Dose	Multidose
Dosing	One dose; repeat if necessary	Up to four doses of both drugs until serum β -hCG declines by 15%
Medication dosage		
Methotrexate	50 mg/m ² BSA (day 1)	1 mg/kg, days 1, 3, 5, and 7
Leucovorin	NA	0.1 mg/kg days 2, 4, 6, and 8
Serum β-hCG level	Days 1 (baseline), 4, and 7	Days 1 (baseline), 3, 5, and 7
Indication for additional dose	If serum β -hCG level does not decline by 15% from day 4 to day 7 Less than 15% decline during weekly surveillance	If serum β -hCG level declines <15%, give additional dose; repeat serum β -hCG in 48 hours and compare with previous value; maximum four doses
Surveillance	Once 15% decline achieved, then weekly serum β -hCG levels until undetectable	
Methotrexate Contraindications		
Sensitivity to MTX	Intrauterine pregnancy	Immunodeficiency
Tubal rupture	Peptic ulcer disease	Hepatic, renal, or hematologic dysfunction
Breastfeeding	Active pulmonary disease	

BSA = body surface area; β -hCG = β -human chorionic gonadotropin; MTX = methotrexate; NA = not applicable.
Data from American Society for Reproductive Medicine, 2013.

Patient selection for the MTX protocol

- Asymptomatic
- Motivated
- Compliant
- Preferably a low initial serum B-hCG
- Will present for follow up

Surgical management

- Laparoscopy and laparotomy : offer direct visualization of the fallopian tubes and pelvic structures – provides easy transition to definitive operative therapy
- Overall, tube patency and number of subsequent uterine pregnancies do not differ between these two routes
- Laparoscopy vs laparotomy mostly depend on the hemodynamic status of the patient
- Desire to maintain future fertility should be addressed prior to surgery and taking into consideration the patency of the contralateral tube to decide between:
 - *Salpingostomy*
 - *Salpingectomy*

Salpingostomy

- Used to remove a small unruptured pregnancy
- 10-15 mm incision is made on the antimesenteric border of the fallopian tube over the location of the ectopic to extrude the products
- Usually followed by flushing out using high pressure irrigation to remove trophoblastic tissue
- Small bleeding sites are controlled with needlepoint electrocoagulation
- Incision is left to heal by secondary intention
- Serum B-hCG are used to monitor response post-op

Salpingectomy

- Tubal resection may be used for both ruptured and unruptured ectopic pregnancies to minimize the rare recurrence of pregnancy in the tubal stump
- This process moves serially from the proximal mesosalpinx to its distal extent under the tubal ampulla.
- Most tubal ectopic pregnancies are small. Accordingly, they can be held firmly by grasping forceps and drawn up into one of the accessory site cannulas. Larger tubal ectopic pregnancies may be placed in an endoscopic sac to prevent fragmentation as they are removed through the laparoscopic port site.
- Irrigation and suction while moving the patient from Trendelenburg to reverse Trendelenburg position should be performed to dislodge any