ECTOPIC PREGNANCY AND OTHER EARLY PREGNANCY EMERGENCIES

ECTOPIC PREGNANCY:

- OCCURS WHEN A CONCEPTUS IS IMPLANTED OUTSIDE OF THE UTERINE CAVITY

PATHOPHYSIOLOGY:

- ECTOPIC PREGNANCY OCCURS WHEN THE ZYGOTE IMPLANTS IN ANY LOCATION OTHER THAN THE UTERUS
  - Vast majority occur in the fallopian tube
  - Extratubal sites:
    - Abdominal cavity
    - Cervix
    - Ovary
- A normal placenta is uncommon in ectopic pregnancy
- Conditions causing damage to the fallopian tube pose the highest risk for ectopic

Table 101-1 Major Risk Factors for Ectopic Pregnancy
Pelvic inflammatory disease
History of tubal surgery
Use of intrauterine device
In utero exposure to diethylstilbestrol
Assisted reproduction techniques
Previous ectopic pregnancy

- Pregnancy in a patient with prior tubal surgery for sterilisation is assumed to be an ectopic pregnancy until proven otherise
- HOWEVER → >50% of ectopics occur in patients without recognised RF

CLINICAL FEATURES:

- HISTORY:
  - Classic triad of symptoms:
    - Abdominal pain
    - Vaginal bleeding or spotting
    - Amenorrhoea
      - PPV of this triad is low and is more common in those with threatened miscarriage
  - Ectopic pregnancy should be considered in all women of childbearing age who present with abdominal or pelvic complaints or with unexplained signs or symptoms of hypovolaemia
  - Abdominal pain is MOST COMMON → 90% cases. Pain is due to tubal distention or rupture → classically the pain is lateralised, sudden, sharp and severe
  - No missed menses is reported in 15% cases

- Although bleeding is often scant → heavy bleeding DOES NOT EXCLUDE ECTOPIC
  - Differential for bleeding in early pregnancy → ectopic, miscarriage (any form), impantation bleeding, cervicitis, cervical polyp or ectropion/ectropion plus GU/GIT bleeding

- PHYSICAL EXAMINATION:
  - Highly variable in ectopic
  - In cases of ruptured ectopic, patients present in shock with peritoneal signs and adnexal mass/tenderness
  - Relative bradycardia may present due to VAGAL STIMULATION
  - THERE IS POOR CORRELATION BETWEEN VOLUME OF HAEMOPERITONEUM AND VITAL SIGNS IN RUPTURED ECTOPIC
  - Fever is rare
  - In more common scenario of UNRUPTURED ECTOPIC → vital signs, pelvic exam etc may all be normal
    - Foetal heart tones or tissue extruding form cervical os are reliable in excluding ectopic

DIAGNOSIS:

- DIFFERENTIAL DIAGNOSIS IS OUTLINED BELOW:

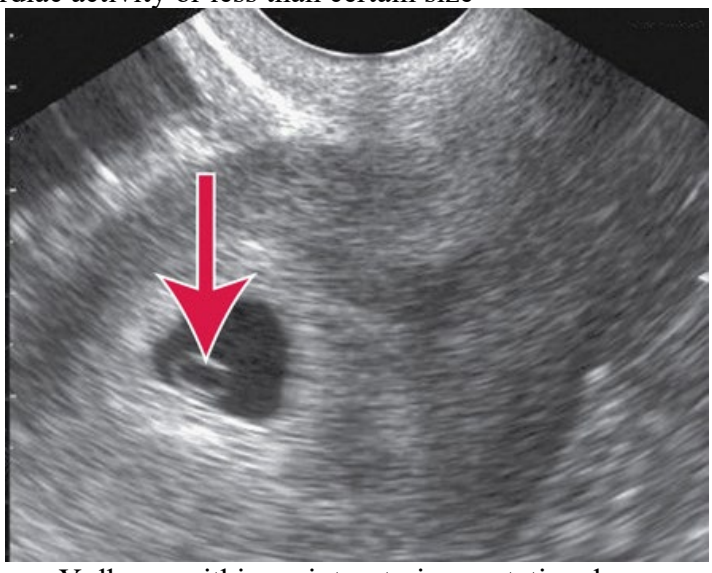
Table 101-2 Differential Diagnosis of Ectopic Pregnancy

All Patients	Pregnant Patients
Appendicitis	Normal (intrauterine pregnancy)
Inflammatory bowel disease	Threatened abortion
Ovarian pathology	Inevitable abortion
Cyst	
Torsion	
Pelvic inflammatory disease	Molar pregnancy
Endometriosis	Heterotopic pregnancy*
Sexual assault/trauma	Implantation bleeding
Urinary tract infection	Corpus luteum cyst
Ureteral colic	

Heterotopic pregnancy = IUP plus ectopic

- PREGNANCY TESTING:
  - Diagnosis of pregnancy is central to the diagnosis of possible ectopic
  - Tests currently rely on β-subunit of HCGH → released into urine → urine tests (qualitative) are reported as positive when the β--HCG concentration is >20 units/mL and >10 in serum
  - → at this level, the false negative rate will not be >1% for urine and 0.5% for serum
    - Dilute urine may cause a false negative test, especially early
    - The sensitivity of serum is ~100%

- LAB TESTS AND ECTOPIC PREGNANCY:
    - Definitive diagnosis of ectopic is made by either direct visualisation (laparoscopy/laparotomy) or US
    - Differences in dynamics of β-HCG production in normal and pathologic pregnancy are useful in the diagnosis of ectopic pregnancy
        - Early in normal pregnancy, β-HCG rise rapidly until 9-10 weeks and then plateau, but βHCG in nonviable pregnancies and treated ectopics will DECLINE
        - HOWEVER → no single β-HCG level can reliably distinguish between a normal and a pathologic pregnancy
        - Absolute levels of βHCG and DOUBLING TIME are longer in ectopic and other abnormal pregnancy (normal doubling time ~2 days)
        - Thus, in stable patients, serial measurements of βHCG are therefore used to either heighten or lower the suspicion for ectopic pregnancy
    - Progesterone levels → secreted by the ovaries and placenta during pregnancy → absolute levels are lower in pathologic pregnancies and fall when a pregnancy fails → considerable overlap in level between normal and pathologic pregnancy
- ULTRASOUND AND ECTOPIC PREGNANCY:
    - Primary goal of US in suspected ectopic is to determine if an IUP is present
    - US findings may also be useful in planning therapy when an ectopic is discovered → noninvasive therapies are reserved for ectopics with no cardiac activity or less than certain size



Yolk sac within an intrauterine gestational sac

- It has previously been assumed that if an IUP exists, the diagnosis of ectopic pregnancy has been excluded. This assumption is based on the historical incidence of HETEROTOPIC PREGNANCY OCCURING ONCE PER 30,000 PREGNANCIES → no longer a safe assumption → 1 in 3,000 in general population due to rise in IVF

    - One study showed 4% ectopic rate amongst IVF population, with 2 of 29 being heterotopic
- Advances in US have allowed earlier detection of IUP/ectopic, but is operator-dependent
    - Transabdominal first, and if that is not diagnostic, then proceed to TV scan
    - When US reveals an unequivocal IUP and no other abnormalities, then ectopic is effectively excluded unless the patient is at high risk for heterotopic pregnancy
    - Signs suggestive of ectopic:

Table 101-4 Ancillary US Findings Suggestive of Ectopic Pregnancy in High-Risk Patients

Ancillary Findings	Risk of Ectopic Pregnancy (%)
Small amount of free pelvic fluid	52
Echogenic adnexal mass	70
Moderate/large amount of free pelvic fluid	86
Any mass plus echogenic fluid	97

- The discriminatory zone is the level of β-HCG at which findings of IUP are expected → TV ~1000 units/mL, TA scanning → ~6000
    - Ectopic can occur even with very low levels of HCG (~500)

INVASIVE DIAGNOSTIC TECHNIQUES:

- Laparoscopy → in those with nondiagnostic US and suspected ectopic.
- Low false negative rates and can be therapeutic

TREATMENT OF ECTOPIC PREGNANCY:

- Can be divided into surgical, medical and expectant approaches
- SURGICAL:
    - Laparoscopy is preferred → if unruptured, salpingostomy preferred over salpingectomy
    - Salpingostomy is associated with higher rates of persistent and recurrent ectopic, but is also associated with higher rates of subsequent IUP by allowing preservation of the fallopian tube
        - Need to assess for persistent ectopic after laparoscopy salpingostomy → weekly HCG
    - Laparoscopy/laparotomy for ruptured → laparotomy if unstable
- MEDICAL TREATMENT:
    - METHOTREXATE → the only drug currently recommended as a medical alternative to surgical treatment → inhibitis cell division in rapidly growning tissues (e.g. in the trophoblast)
        - Failure rate is 14.3% when pre-treatment levels are >5000 (c/W 3.7% for levels < 5000)
        - Most common side effects are abdominal pain → represents a clinical dilemma ?pain due to rupture

        - Prognostic factors associated with higher failure rate for methotrexate → higher HCG, greater tubal diameter, severe abdominal pain and foetal cardiac activity
- REFRAIN FROM SEXUAL INTERCOURSE FOR 14-21 DAYS AFTER TREATMENT, AS IT MAY INCREASE RATES OF RUPTURE
- RHESUS SEROCONVERSION AND ?ANTI-D:
    - Alloimmunisation can occur with as little as 0.1mL of foetal blood admixing with the mothers → current guidelines suggest treating with anti-D

DISPOSITION AND FOLLOW UP:

- Unstable patients with suspected ectopic should receive resuscitation, urgent consultation and operative intervention → ED US may be valuable even in unstable patients, as it should not interfere with resuscitation and rapid transfer to OT
- Stable patients with β-HCG levels above the discriminatory zone and an empty uterus on US, with/without findings of ectopic → presumed to have an ectopic

OTHER CAUSES OF BLEEDING IN THE FIRST 20 WEEKS OF PREGNANCY:

Table 101-5 Common Causes of Bleeding during the First Trimester of Pregnancy
Abortion
Ectopic pregnancy
Gestational trophoblastic disease
Implantation bleeding (physiologic)

ABORTION:

- PATHOPHYSIOLOGY/EPIDEMIOLOGY:
    - Spontaneous abortion is loss of pregnancy before 20 weeks (or <500g)
    - Estimates of incidence is 20-40% of pregnancies
    - Approximately 75% occur <8/40
    - Most common association is chromosomal anomaly:
        - Other causes → advanced maternal age, prior poor obstetric history, concurrent medical disorders, previous miscarriage, infection, smoking
- TERMINOLOGY:

Table 101-6 Spontaneous Abortion Terminology	
Terminology	**Definition**
Threatened abortion	Pregnancy-related bloody vaginal discharge or frank bleeding during the first half of pregnancy without cervical dilatation
Inevitable abortion	Vaginal bleeding and dilatation of the cervix
Incomplete abortion	Passage of only parts of the products of conception
	More likely to occur between 6–14 wk of pregnancy
Complete abortion	Passage of all fetal tissue, including trophoblast and all products of conception before 20 wk of conception
Missed abortion	Fetal death at <20 wk without passage of any fetal tissue for 4 wk after fetal death
Septic abortion	Evidence of infection during any stage of abortion

- **BLEEDING, WITH OR WITHOUT ABDOMINAL PAIN IS THE MOST COMMON PRESENTING COMPLAINT**
- DIAGNOSIS:
    - Further information → amount of bleeding as pads used per hour, LMP, PMH, past obstetric history
    - Consider pelvic exam → less common currently
    - Diagnosis of pregnancy is central to diagnosis of abortion
    - Also need to take FBC, blood group and antibody screen
    - An abnormally high βHCG suggests advanced pregnancy, multple gestion, gestational trophblastic disease or (rarely) ovarian tumour
    - US is useful to rule out ectopic and to aid as prognostic tool for foetal viability → also diagnoses retained products of conception
- TREATMENT:
    - Threatened abortion can be safely discharged if close follow up is ensured
    - No proven effectiveness in bed rest, and generally speaking, miscarriage cannot be avoided
    - Incomplete abortion → consider D+C
    - Those with nonviable foetus can either be admitted or discharged, depending on their comfort → advise to retun if there is heavy bleeding, pain or fever
    - ALL PATIENTS WHO ARE RH-NEGATIVE AND HAVE VAGINAL BLEEDING DURING PREGNANCY SHOULD BE TREATED WITH ANTI-D

SEPTIC ABORTION:

- A spontaneous or other abortion complicated by pelvic infection → fever, abdominal pain, vaginal discharge, vaginal bleeding and recent pregnancy → most commonly due to retained products of coneption, therapeutic abortion and introduction of bacteria → US plus fluid resuscitation, broad-specturm antibiotic and early obstetric consultation for evacuation of the uterus

GESTATIONAL TROPHOBLASTIC DISEASE:

- Broad spectrum → uncomplicated partial hydatidiform molar pregnancy to STAGE IV CHORIOCARCINOMA WITH CEREBRAL METASTASES

    - It is a neoplasm that arises in the trophoblastic cells of the placent, occurring in 1 in 1700 pregnancies
    - Risk of 1% after one molar pregnancy and up to 23% after two
- Symptoms → vaginal bleeding (75%) and hyperemesis (26%)
- Because not all molar pregnancies are found on US, send all tissue from D+C for testing
    - HCG that fail to fall should prompt assessment for persistent or metastatic disease (to lungs, liver and brain) → prognosis for most is good

IMPLANTATION BLEEDING:

- OCCURS AS THE EMBRYO IMPLANTS INTO THE VASCULAR UTERINE DECIDUAL TISSUE
- Can be scant or like menstrual bleeding and usually occurs at 5-6 weeks.

N+V OF PREGNANCY AND HYPEREMESIS GRAVIDARUM:

EPIDEMIOLOGY:

- N+V generally seen in first 12 weeks of pregnancy and affect 60-80% of women, most cases are mild and aetiology is unknown (?HCG effect)
- Severe N+V in pregnancy is known as HYPEREMESIS GRAVIDARUM and is defined as intractable vomiting with weight loss, volume depletion and lab values showing hypokalaemia or ketonaemia → occurs in 2% of pregnancies
    - Women who lose >5% of pre-pregnancy body weight have an increased risk of intrauterine growth restriction and low-birth-weight infants

CLINICAL FEATURES:

- Findings are normal usually except for signs of volume depletion
- Send blood for FBC< EUC, UA
- Ketonaemia is important as an early sign of starvation but ketonaemia is not directly harmful to the foetus
- Presence of abdominal pain in hyperemesis is unusual and should prompt consideration of another diagnosis

TREATMENT:

Treatment for most women is nonpharmacological. Reassurance of a good prognosis and dietary modification (small, frequent, high-carbohydrate, low-fat meals; avoiding dehydration; taking a multivitamin supplement) are often all that is necessary. Ginger (in doses equivalent to 1 to 2 g of powdered ginger daily) may be helpful. Adequate sleep is important, as fatigue exacerbates symptoms. Other nondrug therapy includes P6 acupressure.

If these nonpharmacological measures are ineffective, try:

pyridoxine 25 to 50 mg orally, up to 4 times daily (uncategorised by TGA).

If mild or moderate nausea and vomiting persists, use:

pyridoxine 25 to 50 mg orally, 4 times daily (uncategorised by TGA)

PLUS EITHER

1 **doxylamine 12.5 to 25 mg orally, at night (TGA category A)**

OR

1 **promethazine 10 to 25 mg orally, 3 to 4 times daily (TGA category C)**

OR

1 **metoclopramide 10 mg orally, 3 times daily (TGA category A)**

OR

1 **prochlorperazine 5 to 10 mg orally, 3 to 4 times daily (TGA category C).**

If this treatment is unsuccessful, trial pyridoxine with one of the other drugs listed above.

If the response is still unsatisfactory, try:

ondansetron tablet or wafer 4 to 8 mg orally, 2 to 3 times daily (TGA category B1).

For patients unable to tolerate oral drugs (including ondansetron wafers), use:

1 **metoclopramide 10 mg IM or IV, 8-hourly (TGA category A)**

OR

2 **ondansetron 4 to 8 mg IV, 8- to 12-hourly (TGA category B1)**

OR

2 **prochlorperazine 25 mg rectally, once or twice daily (TGA category C) or prochlorperazine 12.5 mg IM, 8-hourly (TGA category C)**

OR

2 **promethazine 12.5 to 25 mg IM, 4- to 6-hourly (TGA category C).**

- **IV REHYDRATION to replete volume and reverse ketonuria**
- Discharge with antiemetics, there is no clear drug of choic
- If intractable, patient may benefit from systemic steroids
- Consider admission if weight loss >10%, diagnosis uncertain, intractable vomiting, persistent electrolyte anomalies after attempts at correction