Bleeding in early pregnancy

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Definition:

- It’s bleeding through the genital tract during pregnancy before the age of viability. (24 -28 ws)

Causes:

1. Abortion
2. Ectopic pregnancy
3. Gestational trophoblastic disease (Molar pregnancy)
4. Local gynecological causes

Abortion

Definition:

- Abortion is defined as the spontaneous **or** induced termination of pregnancy before the age of fetal viability. (⬅ So What is that?)
- It's the age at which the fetus can withstand extra-uterine life.

Definition (cont.):

- The National Center for Health Statistics, the Centers for Disease Control and Prevention, and the World Health Organization all define abortion as **pregnancy termination before 20 weeks' gestation or with a fetus born weighing < 500 g.**

Definition (cont.):

- However many western countries consider the age of viability to be **24 weeks**.
- **In Egypt**, age of viability is **28 weeks.**

Definition (cont.):

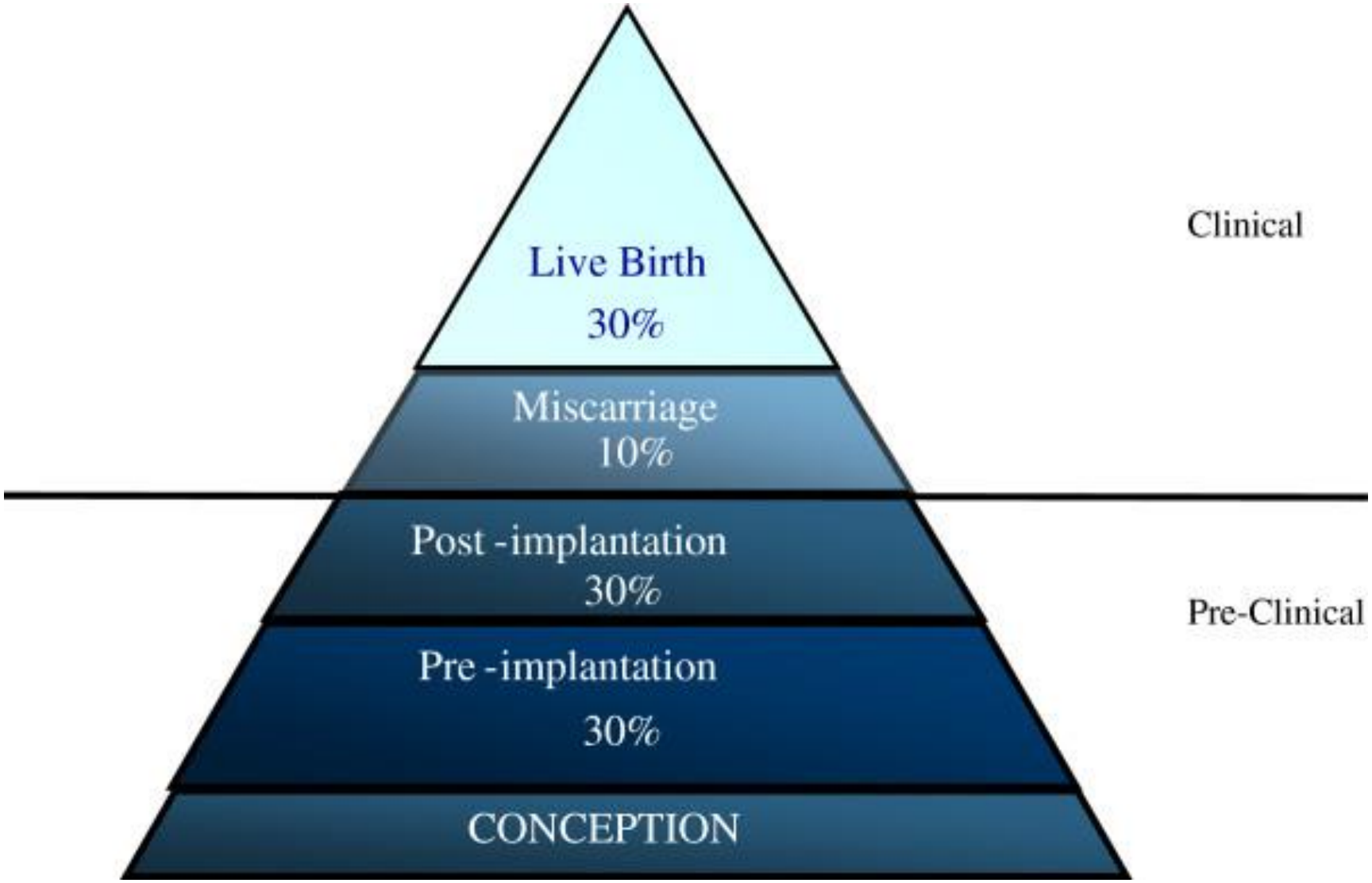
- The most common cause of **bleeding in early pregnancy.**
- Spontaneous or Induced.
- 1st trimester or 2nd trimester. (before or after 12 weeks gestation)

Definition (cont.):

- The word abortion derives from the Latin *aboriri*—to miscarry, It thus is appropriate that miscarriage and abortion are terms used interchangeably in a medical context.
- But because popular use of abortion by lay persons implies a deliberate intact pregnancy termination, many prefer **miscarriage or pregnancy loss** for spontaneous fetal loss.

Incidence

- The spontaneous miscarriage rate varies between from **10% to 20%.**
- 10% refers to late recognition of pregnancy and 20% refers to research involving routinely testing for pregnancy before 4 weeks or 4 weeks after the last menstrual period.


Live Birth
30%
Miscarriage
10%
Post -implantation
30%
Pre -implantation
30%
CONCEPTION
Clinical
Pre-Clinical

Incidence (cont.)

- More than 80 % of spontaneous abortions are 1st trimester abortions.
- 2nd trimester is estimated at 1.5 to 3 %, and after 16 weeks, it is only 1 % (of all clinically recognized pregnancies)
- First-trimester bleeding doubles the incidence of second-trimester loss.

Etiology:

Fetal Factors:

1. Anembryonic pregnancy. (about half of all 1st trimester abortions).

   These could be euploid or aneuploid.

   Frequently called (Blighted ovum).

2. Aneuploidy: (Most common cause in 1st trimester). Could be in embryonic and anembryonic pregnancies.

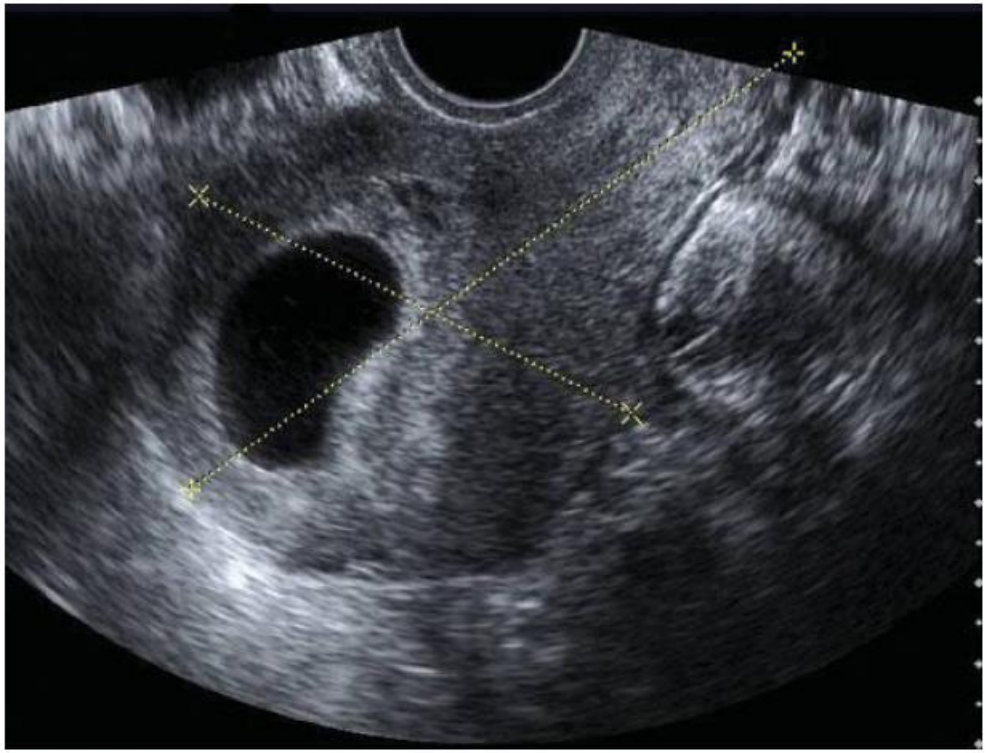


FIGURE 18-4 Transvaginal sonogram displays a large anechoic sac consistent with an anembryonic gestation. Calipers measure uterine length and anteroposterior thickness in a sagittal plane.

TABLE 18-1. Chromosomal Findings in First-Trimester Abortuses

Chromosomal Studies	Incidence Range (%)
Embryonic	~50
Euploid	
46,XY and 46,XX	45 to 55
Aneuploid	
Autosomal trisomy	22 to 32
Monosomy X (45,X)	5 to 20
Triploidy	6 to 8
Tetraploidy	2 to 4
Structural anomaly	2
Anembryonic (blighted ovum)	~50

Data from Eiben, 1990; Kajii, 1980; Simpson, 1980, 2007.

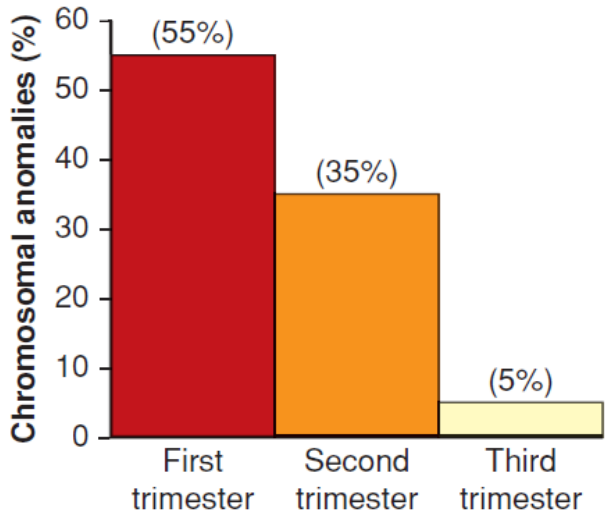


FIGURE 18-1 Frequency of chromosomal anomalies in abortuses and stillbirths during each trimester. Approximate percentages for each group are shown. (Data from Eiben, 1990; Fantel, 1980; Warburton, 1980.)

Etiology (cont.):

- **Autosomal trisomy** is the most frequently identified chromosomal anomaly. Although most trisomies result from *isolated nondisjunction*, balanced structural chromosomal rearrangements are found in one partner in 2 to 4 percent of couples with recurrent miscarriages.
- Trisomies have been identified in abortuses for all except chromosome number 1, and those with **13, 16, 18, 21 and 22 are most common.**

Etiology (cont.):

- **Monosomy X (45,X)** is the single **most frequent specific** chromosomal abnormality. This is *Turner syndrome*, which usually results in abortion, but liveborn females are described. Conversely, *autosomal monosomy* is rare and incompatible with life.
- **Triploidy** is often associated with hydropic or molar placental degeneration. The fetus within a partial hydatidiform mole frequently aborts early, and the few carried longer are all grossly deformed.
- **Tetraploid** fetuses most often abort early in gestation, and they are rarely liveborn.
- **Chromosomal structural abnormalities** infrequently cause abortion.

Etiology (cont.):

Maternal Factors:

1. Age: extremes of age.
2. Infections: (eg, rubella virus, cytomegalovirus, Listeria infection, toxoplasmosis, malaria, brucellosis, human immunodeficiency virus (HIV), dengue fever, influenza).
   - Bacterial vaginosis is related to 2nd trimester abortion.
3. Corpus luteum deficiency.

Etiology (cont.):

Maternal Factors:

4. Uterine factor:

   - Congenital: Depending on their anatomy, some may increase risks for early miscarriage, whereas others may cause midtrimester abortion or preterm delivery. Unicornuate, bicornuate, and septate uteri are associated with all three types of loss.

TABLE 18-5. Estimated Prevalence and Pregnancy Loss Rate for Some Congenital Uterine Malformations

Uterine Anomaly[a]	Proportion of All Anomalies (%)	Pregnancy Loss Rate (%)[b]
Bicornuate	39	40–70
Septate or unicornuate	14–24	34–88
Didelphys	11	40
Arcuate	/	
Hypo- or aplastic	4	

[a]Estimated overall prevalence 1:200 women.
[b]Includes first- and second-trimester losses.
Data from Bradshaw, 2012; Buttram, 1979; Nahum, 1998; Reddy, 2007; Valli, 2001.

Etiology (cont.):

Maternal Factors:

4. Uterine factor:

- Acquired:
  - Submucous Fibroid.
  - Endometrial polyp.
  - Iatrogenic (Intra-uterine adhesions e.g. Asherman's syndrome).

Etiology (cont.):

Maternal Factors:

4. Uterine factor:

- Incompetent cervix: (characterized classically by painless cervical dilatation in the second trimester. It can be followed by prolapse and ballooning of membranes into the vagina, and ultimately, expulsion of an immature fetus).
    - Congenital : DES exposure.
    - Acquired: (Iatrogenic or due to birth trauma) previous cervical trauma such as dilatation and curettage, conization, cauterization, or amputation has been implicated.

Etiology (cont.):

Maternal Factors:

5. Polycystic ovary syndrome.
6. Diabetes mellitus. (poorly controlled)
7. Hypothyroidism.
8. Antiphospholipid antibody syndrome.
9. SLE.
10. Renal diseases.
11. Obesity.

Etiology (cont.):

<u>Maternal Factors:</u>

- Exogenous factors include the following:
  - Tobacco
  - Alcohol
  - Cocaine
  - Caffeine (high doses)
  - Environmental toxins (e.g.: Arsenic, lead, formaldehyde, benzene, and ethylene oxide and DDT)

Etiology (cont.):

- Paternal Factors:
- Chromosomal abnormalities in sperm reportedly had an increased abortion risk.
- Increasing paternal age was significantly associated with increased risk for abortion in the Jerusalem Perinatal Study. This risk was lowest before age 25 years, after which it progressively increased at 5-year intervals.

Clinical types:

- Missed abortion
- Threatened abortion
- Inevitable abortion
- Incomplete abortion
- Complete abortion
- Medical abortion
- Septic abortion
- Habitual abortion/Recurrent miscarriage/Recurrent pregnancy loss

Clinical types of abortions:

Type	Clinical findings	Ultrasound findings	Management
Missed abortion	Cervix closed/ No bleeding/ No pain/ Symp. Of pregnancy disappear	Anembryonic pregnancy Fetal pole with no cardiac pulsations	Expectant management or Active termination either medical or surgical
Threatened abortion	Cervix closed ± minimal bleeding or pain	Intrauterine gestational sac± fetal pole + cardiac pulsations	Expectant management, support to the mother, bed rest
Inevitable abortion	Cervix open ± bleeding or pain	Intrauterine gestational sac± fetal pole ± cardiac pulsations	Observant management, maintain good general condition.
Incomplete abortion	Possibly open cervix ± bleeding or pain	Heterogenous intrauterine content > 15 mm in diameter	Expectant management vs. medical ttt (ecobolics) or surgical ttt +maintain good general condition.
Complete abortion	Cervix closed with minimal or no bleeding or pain.	Empty uterus < 15 mm endometrial thickness	Expectant management, support to the mother

What is recurrent pregnancy loss (RPL).

- RPL has been defined in many ways by different organizations.
- **ASRM** (2012) : **two** or more failed clinical pregnancy.

Ideally threshold of 3 or more should be used for epidemiologic studies, but start clinical evaluation after 2 losses.

- **RCOG** (2014) : spontaneous loss of **three or more consecutive** pregnancies before age of viability.
- **ESHRE** (2017) :"A diagnosis of Recurrent Pregnancy Loss (RPL) **could** be considered after the loss of **two** or more pregnancies."

Why 2 and not 3?

- Will facilitate research, shared decision-making and psychological support to couples. In addition, testing for APS, a treatable sub-diagnosis of RPL, can be performed after two losses.

Why not consecutive?

- NO difference in **prognosis** of unexplained RPL, prevalence of **APS**, prevalence of carrier state of **chromosomal anomalies.**
- About 10% of RPL couples will have 2 or more non-consecutive losses, so **these cases will be underdiagnosed**.

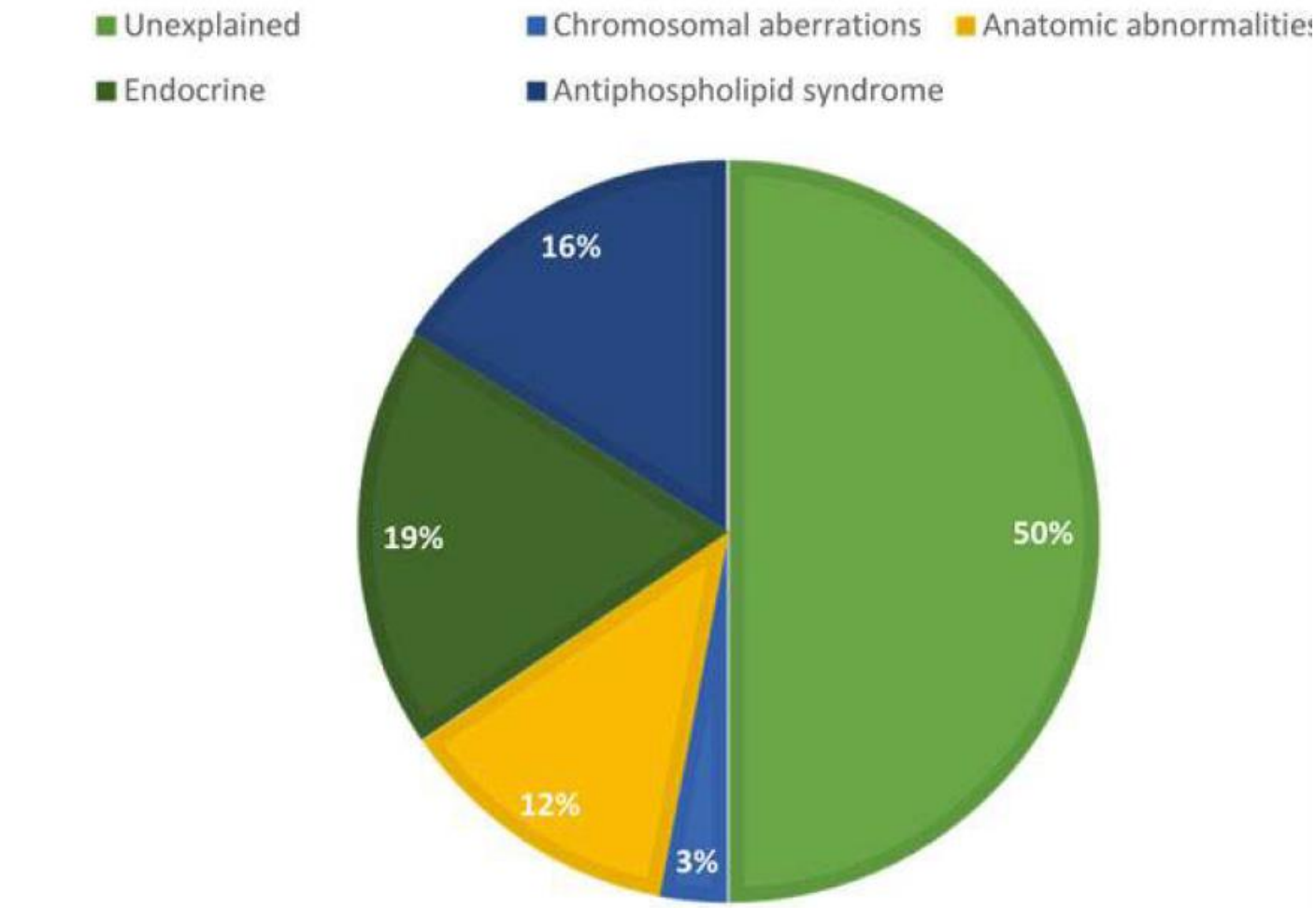


Fig. 1.3 Etiology of RPL

ASRM 2012

International Consensus Classification criteria for the antiphospholipid syndrome (APS) (23, 24).

APS is present if one of the following clinical criteria and one of the laboratory criteria are met.

Clinical criteria

1. Vascular thrombosis
2. Pregnancy morbidity
   a. One or more unexplained deaths of morphologically normal fetuses after the 10^{th} week of gestation by ultrasound or direct examination of the fetus.
   b. One or more premature births of a morphologically normal neonate before the 34^{th} week of gestation because of eclampsia or severe pre-eclampsia or recognized features of placental insufficiency.
   c. Three or more unexplained consecutive spontaneous abortions before the 10^{th} week of gestation with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded.

Laboratory criteria

1. Lupus anticoagulant present in plasma on two or more occasions at least 12 weeks apart, or
2. Anticardiolipin antibody of IgG or IgM isotype in serum or plasma present in medium or high titer (>40 GPL or MPL or $> 99^{th}$ percentile), on two or more occasions at least 12 weeks apart, or
3. Anti-β_2 glycoprotein-I antibody of IgG and/or IgM isotype in serum or plasma (in titer greater than the 99^{th} percentile), present on two or more occasions at least 12 weeks apart.

Practice Committee. Recurrent pregnancy loss. Fertil Steril 2012.

Diagnosis

- Clinical
- Ultrasound
- HSG
- Hysteroscopy
- MRI
- Cytogenetics
- Hormonal profile
- HbA1C

Treatment

1. Expectant management: could be tried in recently diagnosed miscarriage and case is stable.
2. Medical termination: Patient is anxious or expectant management is unacceptable. If there's a need for accelerated termination for fear of deterioration of general condition due to bleeding.
3. Surgical termination: In emergency situations where abrupt evacuation of uterine content is necessary or in case of failed medical termination.

Treatment

1. Medical treatment:
    1. Prostaglandin E1 analogue (MISOPROSTOL): dose according to clinical situation and gestational age.

<13 weeks' gestation	13–26 weeks' gestation
Pregnancy termination[a,b,1] 800µg sl every 3 hours *or* pv*/bucc every 3–12 hours (2–3 doses)	**Pregnancy termination**[1,5,6] 13–24 weeks: 400µg pv*/sl/bucc every 3 hours[a,e] 25–26 weeks: 200µg pv*/sl/bucc every 4 hours[f]
Missed abortion[c,2] 800µg pv* every 3 hours (x2) *or* 600µg sl every 3 hours (x2)	**Fetal death**[f,g,1,5,6] 200µg pv*/sl/bucc every 4–6 hours
Incomplete abortion[a,2,3,4] 600µg po (x1) *or* 400µg sl (x1) *or* 400–800µg pv* (x1)	**Inevitable abortion**[g,2,3,5,6,7] 200µg pv*/sl/bucc every 6 hours
Cervical preparation for surgical abortion[d] 400µg sl 1 hour before procedure *or* pv* 3 hours before procedure	**Cervical preparation for surgical abortion**[a] 13–19 weeks: 400µg pv 3–4 hours before procedure >19 weeks: needs to be combined with other modalities

Treatment

1. Medical treatment:

    2. Methotrexate.

    3. Mifepristone (antiprogesterone) .

    (These 2 are usually used in combination with misoprostol)

TABLE 18-9. Regimens for Medical Termination of Early Pregnancy

Mifepristone/Misoprostol

[a]Mifepristone, 100–600 mg orally followed by:

[b]Misoprostol, 200–600 μg orally or 400–800 μg vaginally, buccally, or sublingually given immediately or up to 72 hours

Methotrexate/Misoprostol

[c]Methotrexate, 50 mg/m^2 BSA intramuscularly or orally followed by:

[d]Misoprostol, 800 μg vaginally in 3–7 days. Repeat if needed 1 week after methotrexate initially given

Treatment

1. Surgical treatment:
    A. First trimester:
        1. Dilatation and evacuation.
        2. Vacuum aspiration.
    B. Second trimester:
        1. Intrauterine balloon catheter.
        2. Hysterotomy.

Treatment

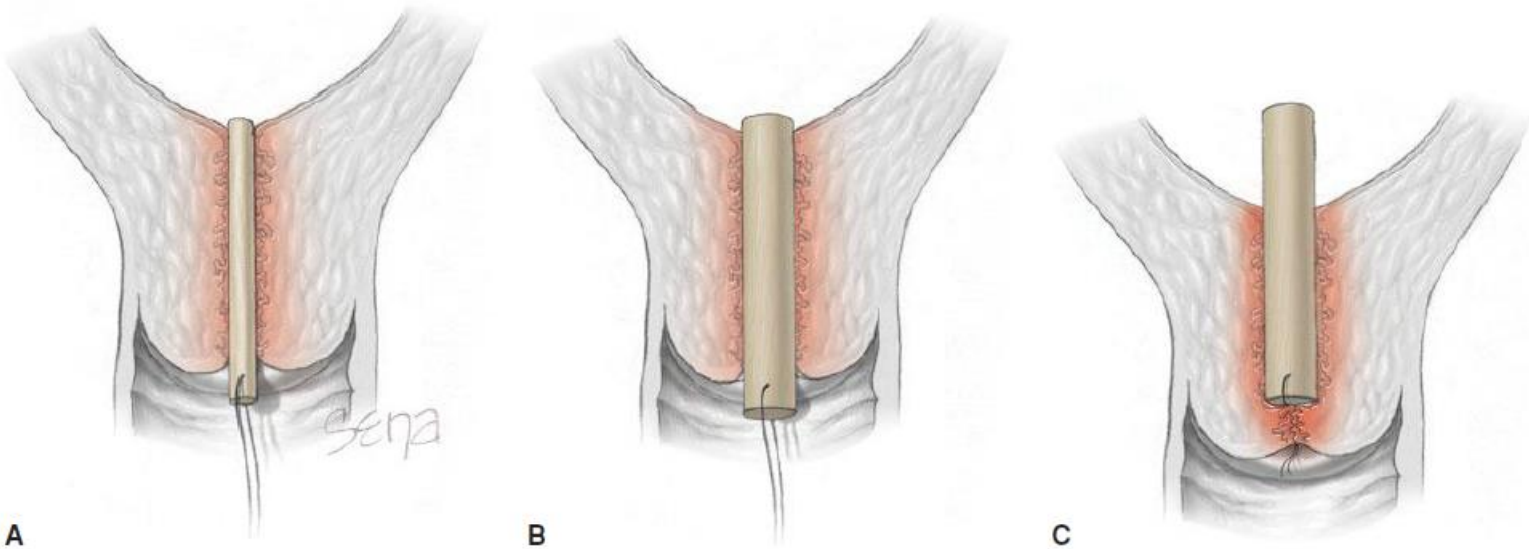


FIGURE 18-7 Insertion of laminaria before dilatation and curettage. **A.** Laminaria immediately after being appropriately placed with its upper end just through the internal os. **B.** Several hours later the laminaria is now swollen, and the cervix is dilated and softened. **C.** Laminaria inserted too far through the internal os; the laminaria may rupture the membranes.

Treatment

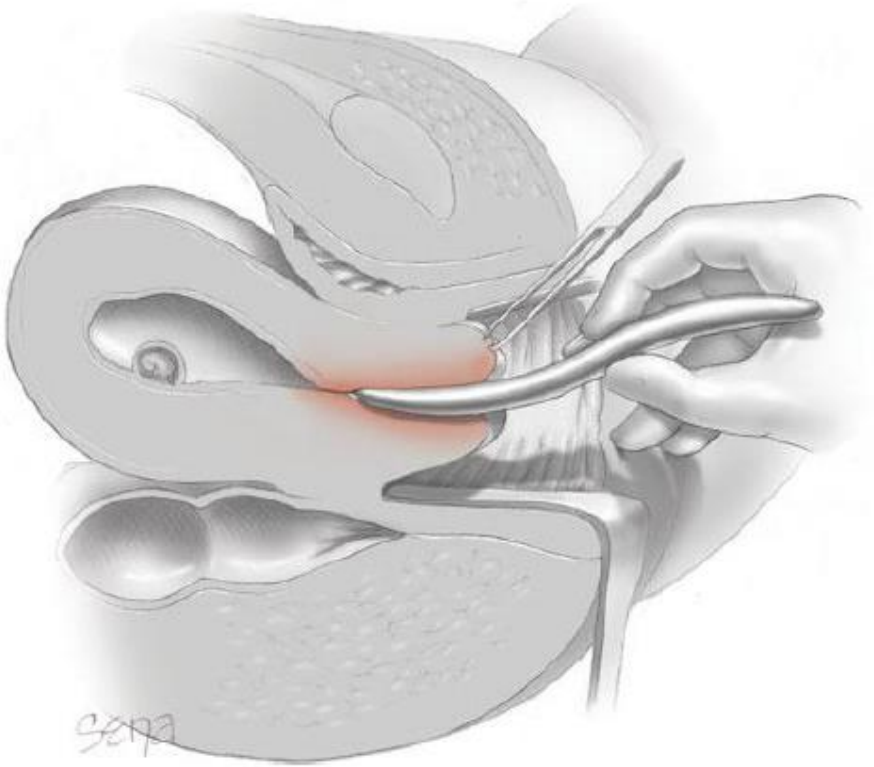


FIGURE 18-9 Dilatation of cervix with a Hegar dilator. Note that the fourth and fifth fingers rest against the perineum and buttocks, lateral to the vagina. This maneuver is an important safety measure because if the cervix relaxes abruptly, these fingers prevent a sudden and uncontrolled thrust of the dilator, a common cause of uterine perforation.

Treatment

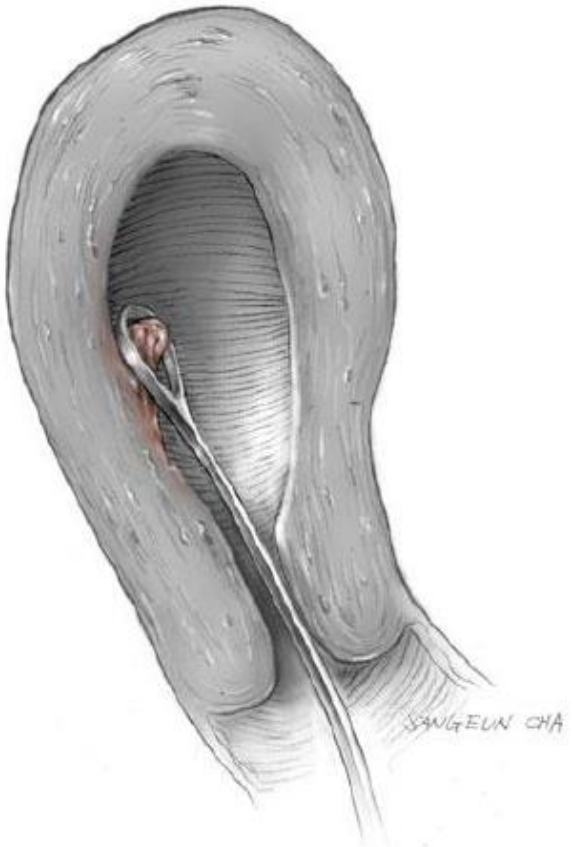


FIGURE 18-11 A sharp curette is advanced into the uterine cavity while the instrument is held with the thumb and forefinger as shown in Figure 18-9. In the movement of the curette, only the strength of these two fingers should be used. (From Word, 2012, with permission.)

Treatment

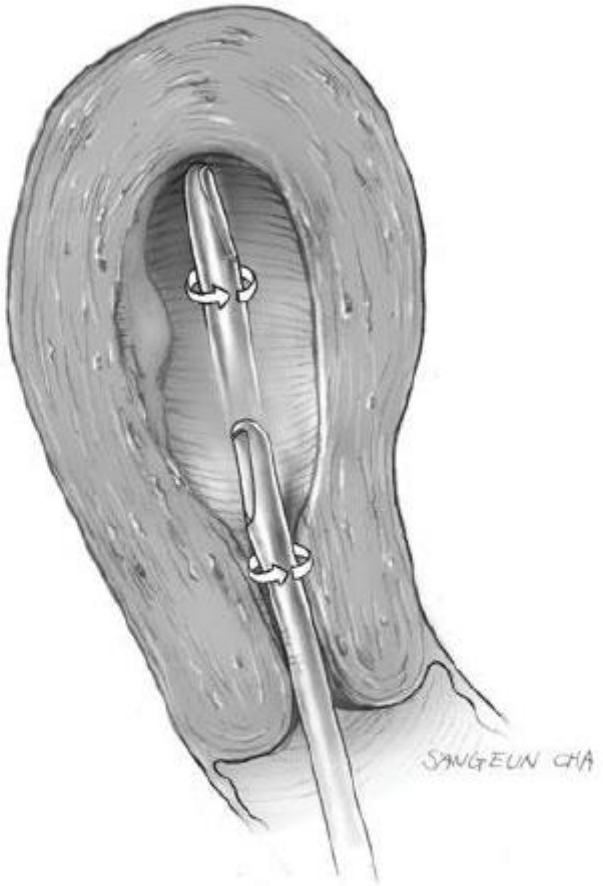


FIGURE 18-10 A suction curette has been placed through the cervix into the uterus. The figure shows the rotary motion used to aspirate the contents. (From Word, 2012, with permission.)

Cervical incompetence

- Mainly is a cause of second trimester abortion or preterm labour.
- Diagnosis during current pregnancy through pv examination (cervical shortening and dilatation). Or through U/S examination showing cervical shortening with or without funneling .
- Diagnosis by history of painless cervical dilatation and rapid progress of labour or second trimester abortion in a previous pregnancy.
- In-between pregnancy by HSG or the passage of No. 8 Hegar dilator without resistance (all subjective).
- Treatment options : Progesterone, Cerclage either prophylactic or rescue “emergency” cerclage (controversial).

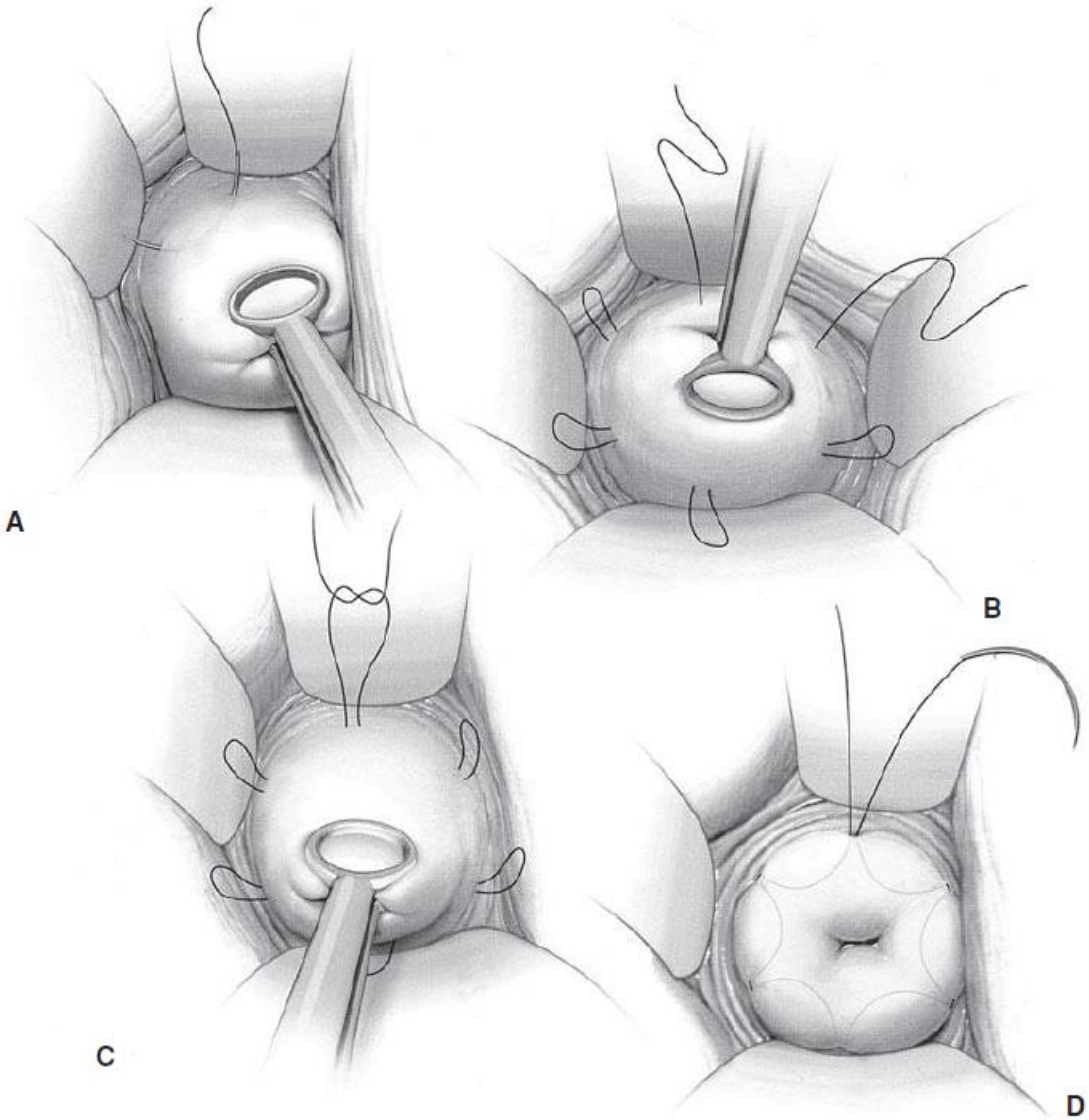


FIGURE 18-5 McDonald cerclage procedure for incompetent cervix. **A.** Start of the cerclage procedure with a No. 2 monofilament suture being placed in the body of the cervix very near the level of the internal os. **B.** Continuation of suture placement in the body of the cervix so as to encircle the os. **C.** Encirclement completed. **D.** The suture is tightened around the cervical canal sufficiently to reduce the diameter of the canal to 5 to 10 mm, and then the suture is tied. The effect of the suture placement on the cervical canal is apparent. A second suture placed somewhat higher may be of value if the first is not in close proximity to the internal os.

cervix into the uterus. The figure shows the rotary motion used to aspirate the contents. (From Word, 2012, with permission.)

Treatment

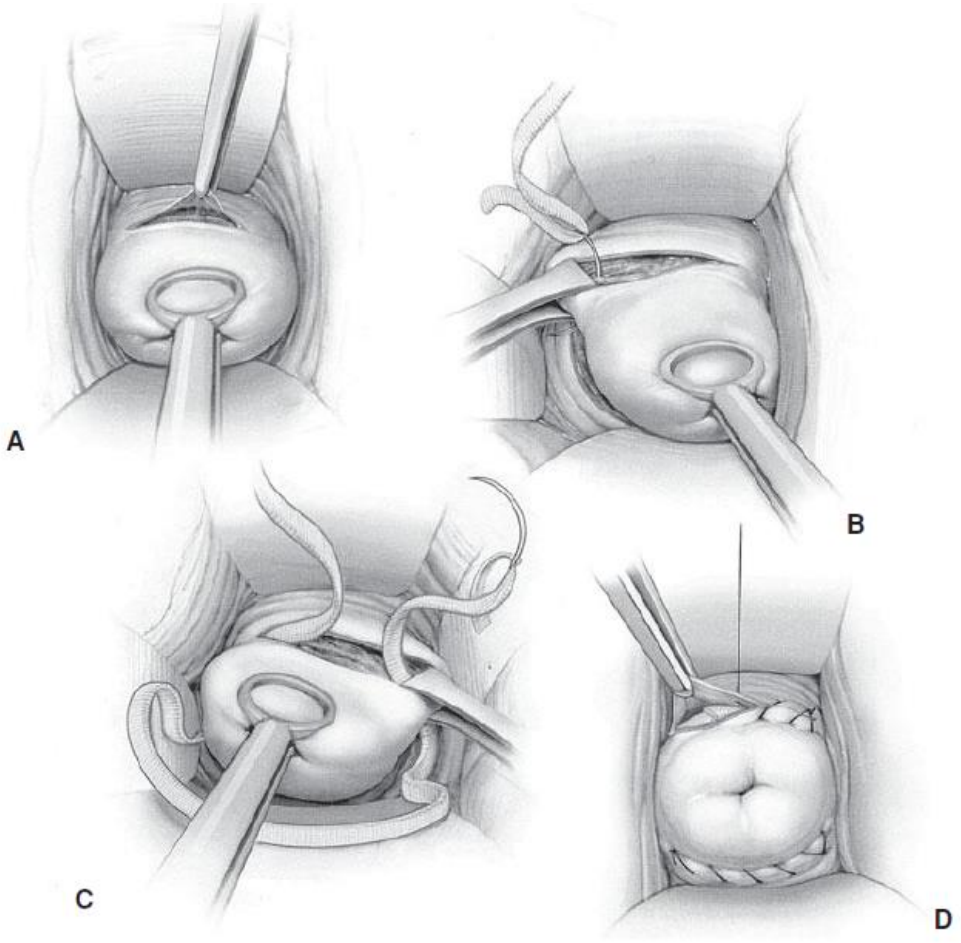


FIGURE 18-6 Modified Shirodkar cerclage for incompetent cervix. **A.** A transverse incision is made in the mucosa overlying the anterior cervix, and the bladder is pushed cephalad. **B.** A 5-mm Mersilene tape on a swaged-on or Mayo needle is passed anteriorly to posteriorly. **C.** The tape is then directed posteriorly to anteriorly on the other side of the cervix. Allis clamps are placed so as to bunch the cervical tissue. This diminishes the distance that the needle must travel submucosally and aids tape placement. **D.** The tape is snugly tied anteriorly, after ensuring that all slack has been taken up. The cervical mucosa is then closed with continuous stitches of chromic suture to bury the anterior knot.

Ectopic pregnancy

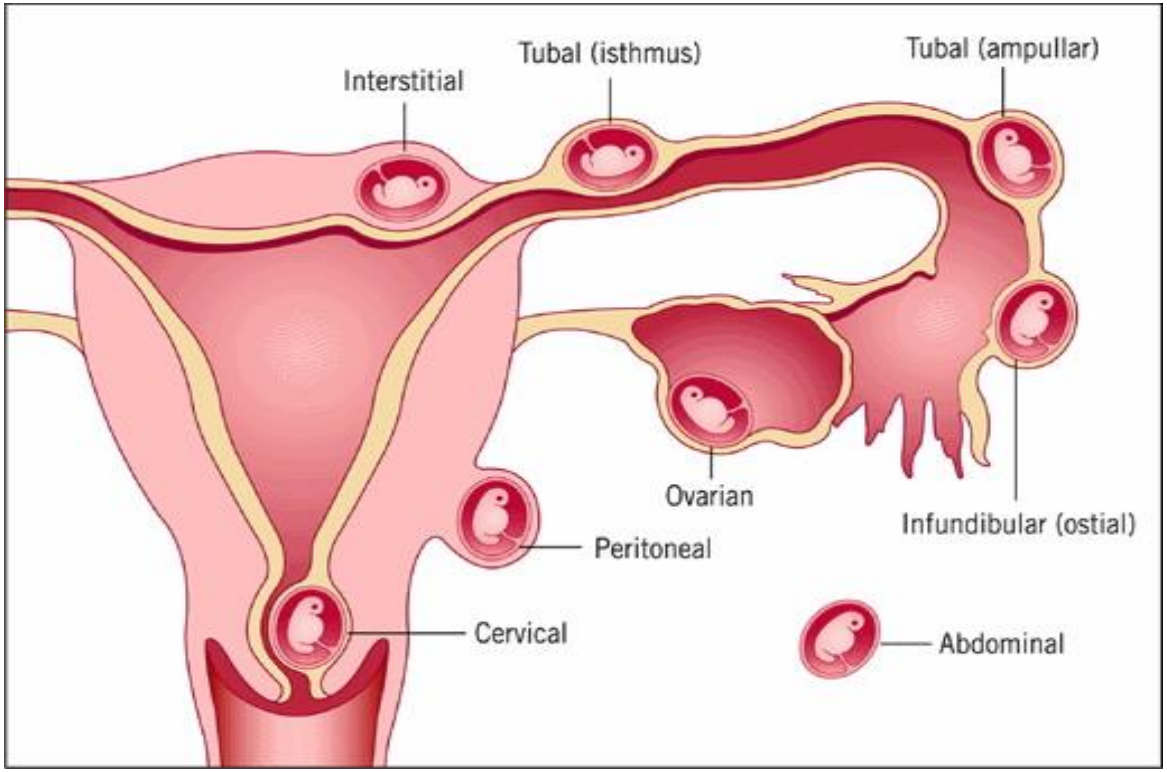
Ectopic pregnancy

- **Definition:** Pregnancy outside the uterine cavity.

- **Types:**
  - Most common site is the fallopian tubes (95%)
  - Other possible site: Ovary, cervix, CS scar, uterine cornu, Abdominal …..

- **Incidence:** 1:100-1:200

Sites:


Interstitial
Tubal (isthmus)
Tubal (ampullar)
Ovarian
Infundibular (ostial)
Peritoneal
Cervical
Abdominal

Risk factors:

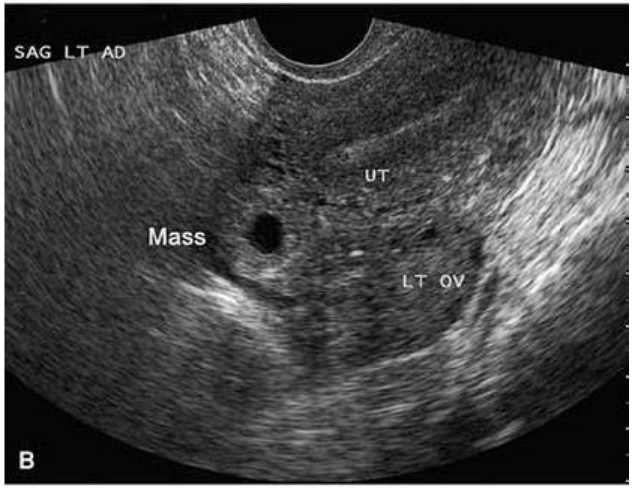
- Prior tubal surgery.
- Prior ectopic.
- History of PID.
- Current IUD use.
- DES exposure.

Clinical picture

- Difficult to diagnose because symptoms often mirror those of a normal early pregnancy. These can include missed periods, breast tenderness, nausea, vomiting, or frequent urination.
- The first warning signs of an ectopic pregnancy are often **pain** and/or **vaginal bleeding.**
- One important clinical sign is **cervical motion tenderness** and adnexal tenderness.
- Sometimes the case is presented with shock due to internal haemorrhage following ruptured ectopic pregnancy.

Investigations

- Ultrasound:
  - shows empty uterine cavity.
  - Adnexal mass could be seen. (Ring of fire on doppler)
  - May show peritoneal collection denoting internal hemorrhage.
  - In rare occasions there could be heterotopic pregnancy.
- Serum Beta hCG:
  - If level is above 2000 mIU, a GS must be seen intrauterine by TVS. (known as discriminatory level or zone).
  - If less repeat after 48-72 hrs. for comparison as long as maternal condition is controlled.
- Laparoscopy:
  - Sometimes diagnosis could only be made by laparoscopy which can be both diagnostic and therapeutic.


SAG LT AD
UT
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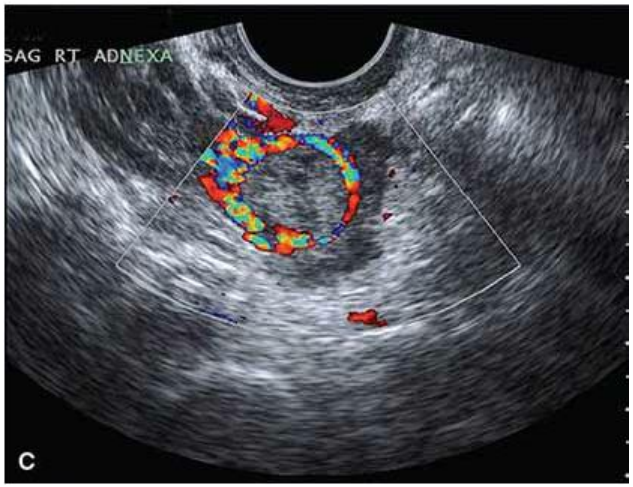
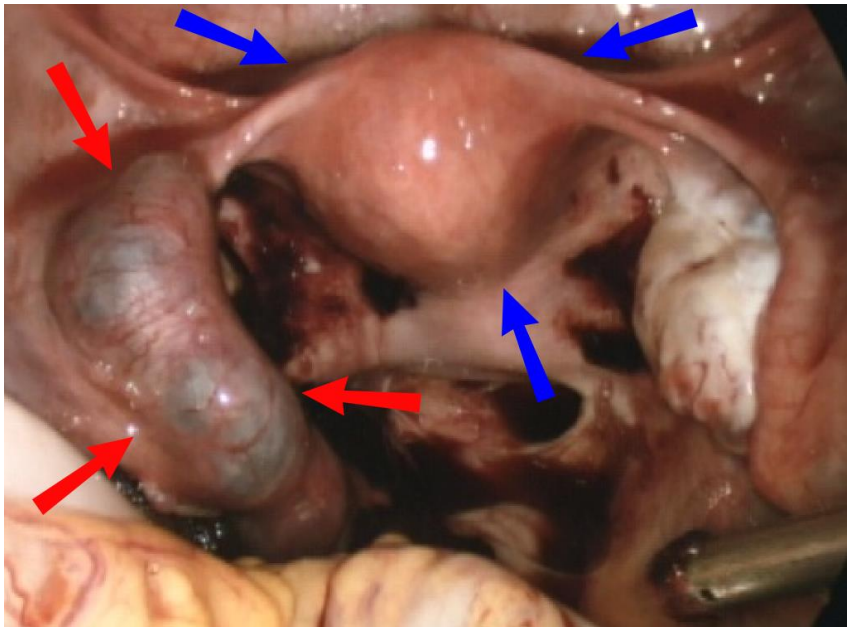

SAG RT ADNEXA
C



Differential Diagnosis:

- Threatened abortion
- Acute or chronic PID
- Ovarian cysts (torsion or rupture)
- Acute appendicitis

- Some cases end up with no definite diagnosis and termed: Pregnancy of unknown location (PUL)

Fate of ectopic pregnancy

1. Tubal abortion.

2. Tubal rupture.

MANAGEMENT OF ECTOPIC PREGNANCY

1. **Hemo-dynamically unstable**
   - Surgical : → **salpingectomy (preferred),** salpingotomy or salpingostomy (only if one tube or the other tube looks unhealthy with future desire of pregnancy)

     laparoscopic or via Laparotomy

2. **Hemo-dynamically stable** :
   - **Medical :**
     - Pre-requisites: Asymptomatic, small ectopic, low Bhcg levels, undisturbed.
     - Methotrexate: single or multiple doses (If multiple must be combined with folinic acid “leucovorin rescue”) Dose: 50 mg/m2 IM
     - Disadvantages: Needs observation, side effects of the drug.

   - **Conservative** - only if haemo-dynamicaly stable, asymptomatic, suggestive of tubal miscarriage. (non popular line of management).

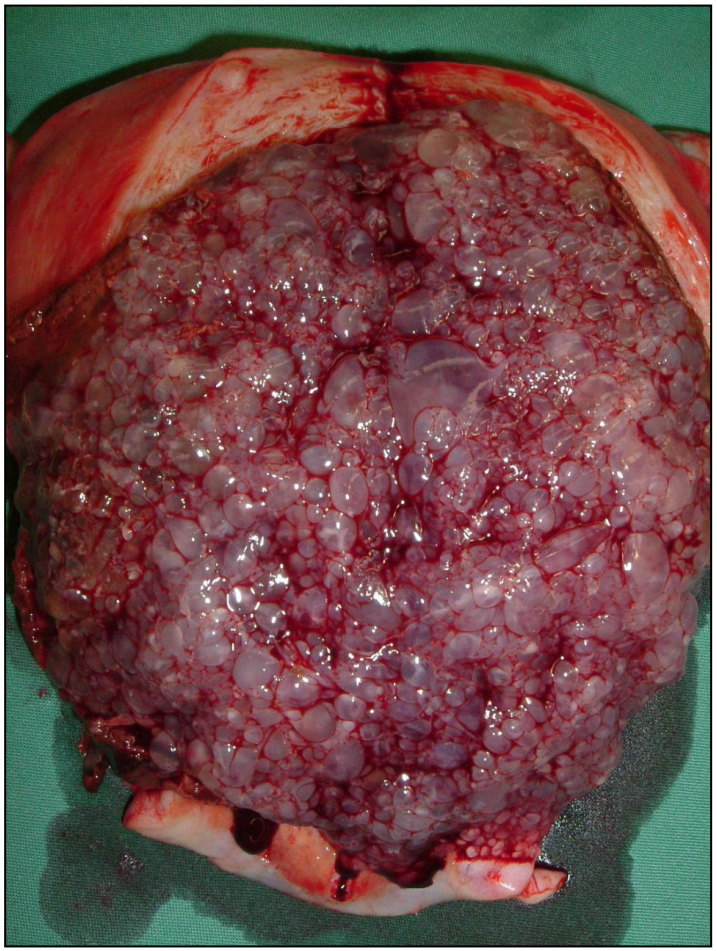
   - **Surgical** option is also valid option especially in case of failed medical ttt and still rising or plateauing b-hCG.

Molar pregnancy

الحمل العنقودي

Molar pregnancy

- Molar pregnancy or hydatidiform mole is a relatively rare condition in which tissue around a fertilized egg (trophoblasts) that normally would have developed into the placenta instead develops as an abnormal cluster of cells.
- This grapelike mass forms inside of the uterus after fertilization instead of a normal embryo.
- Incidence: 1:1000

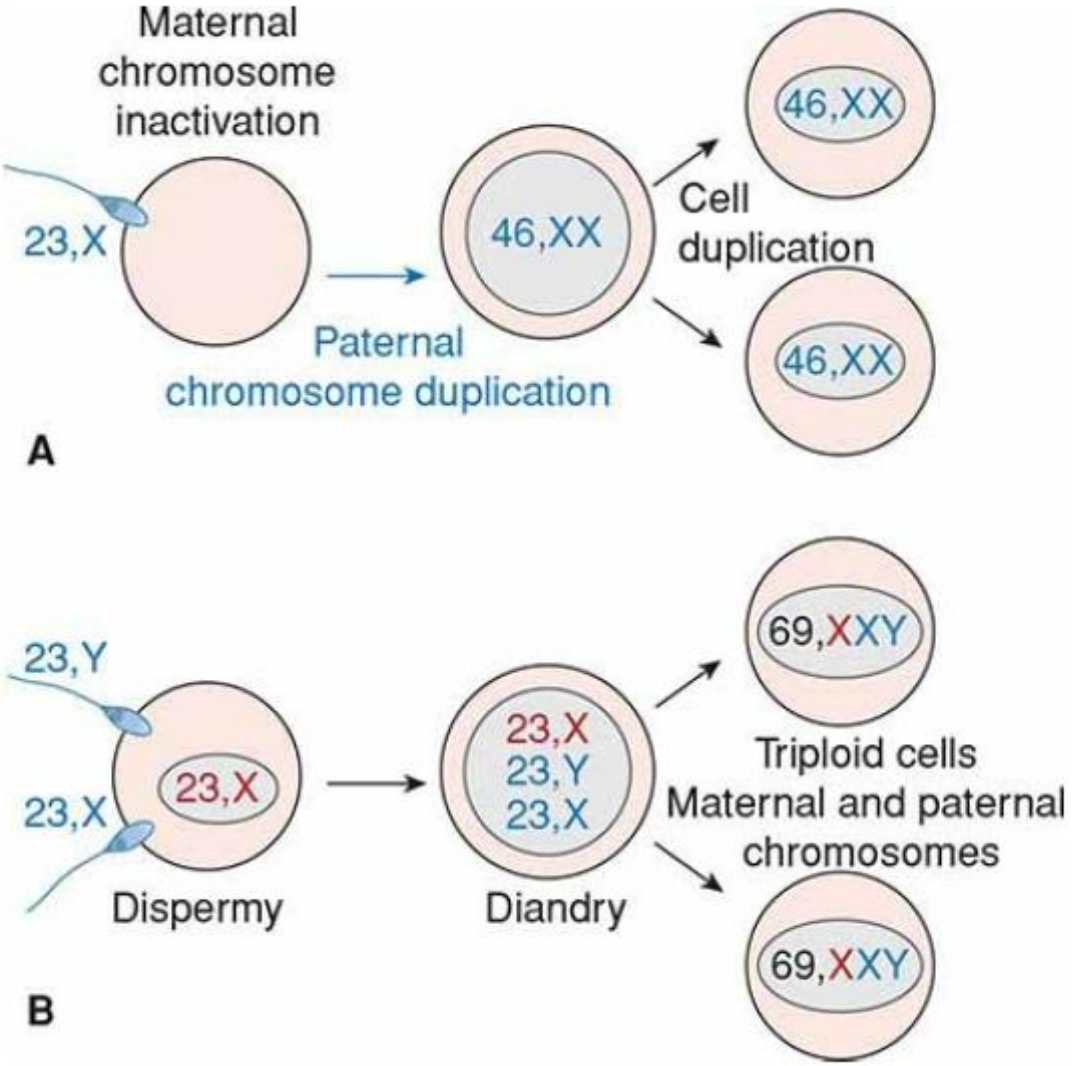


Types:

- Complete mole:
  - Consists of diffuse hydropic villi with trophoblastic hyperplasia.
  - This is diploid, derived from sperm duplicating its own chromosome following fertilization of an ‘empty’ ovum.
  - This is mostly 46XX with no evidence of fetal tissue.
  - Source is paternal. (Failed maternal chromosome activation with duplication of the paternal chromosomal material).

Types:

- Partial mole:
  - Consists of hydropic and normal villi.
  - This is triploid (69XXX, XXY, XYY) with one maternal and two paternal haploid sets.
  - Most cases occur following two sperms fertilizing an ovum, and a fetus may be present.



Typical pathogenesis of complete (A) and partial mole (B).

Risk factors for hyatidiform mole

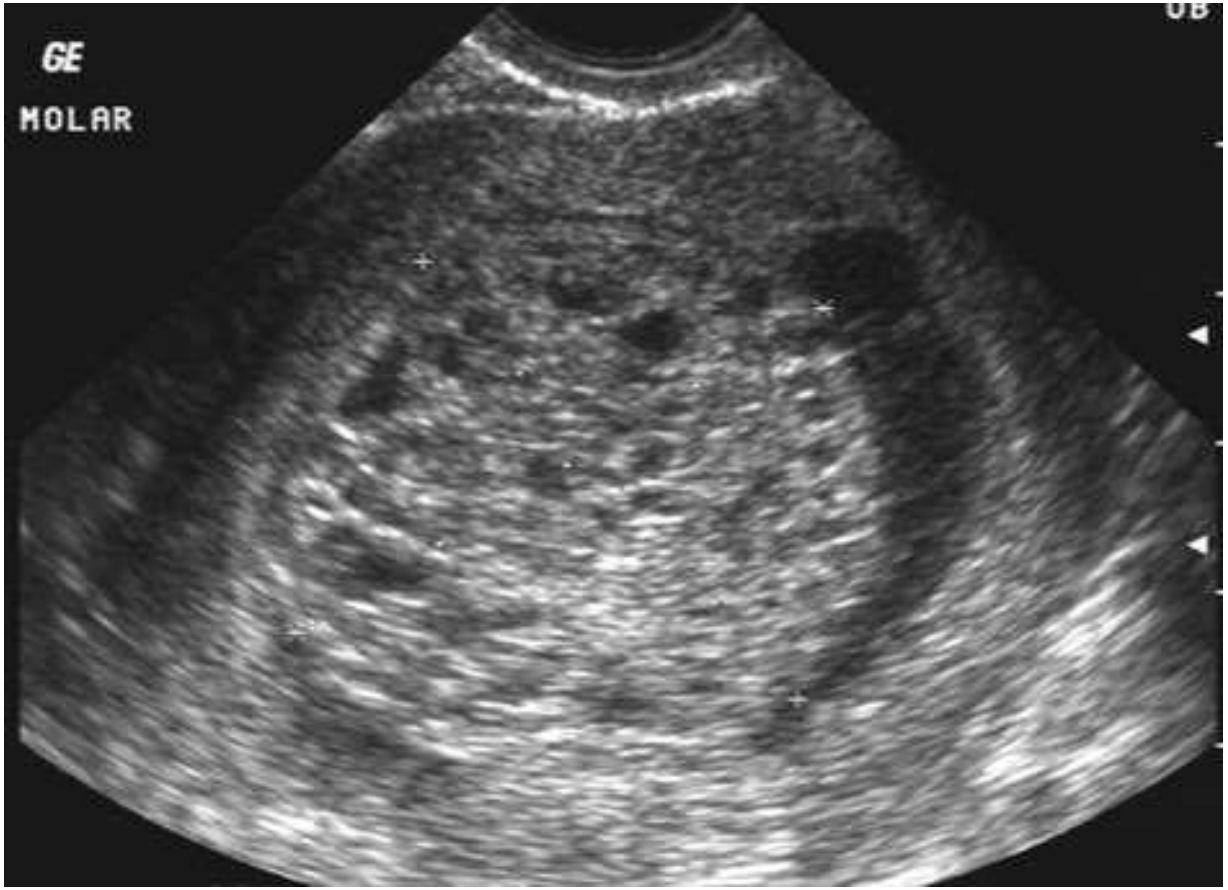
- Age:
  - extremes of reproductive life (>40yrs and <15yrs of age) in complete moles, not partial moles.
- Ethnicity:
  - x2 higher in east Asia, particularly Korea and Japan.
- Previous molar pregnancy:
  - x10 higher risk of developing future molar pregnancy.

Clinical picture

- Irregular first-trimester vaginal **bleeding** (>90%).
- **Uterus large** for dates (25%).
- **Pain** from large theca lutein cysts (20%) resulting from ovarian hyperstimulation by high hCG levels.
- Vaginal **passage of vesicles** containing products of conception (10%) or prune juice discharge.
- Exaggerated **pregnancy symptoms**; hyperemesis (10%)
- **Hyperthyroidism** (5%)
- **Early pre-eclampsia** (5%).

Investigations

- Serum B-hCG:
  - excessively high with complete moles
  - levels may be within the normal range for partial moles.
- Ultrasound:
  - Complete mole: Snowstorm appearance of mixed echogenecity, representing hydropic villi and intrauterine haemorrhage. Large theca lutein cysts.
  - Partial mole: Fetus may be viable, with signs of early growth restriction or structural abnormalities.
- Chest X-ray: To exclude metastasis to the lungs.
- Thyroid function testing.


GE
MOLAR
OB

Management:

- Complete mole:
  - Surgical evacuation (Suction evacuation) is advisable and should be performed by an experienced surgeon as risks of uterine perforation and hemorrhage are significant.
  - Oxytocin may be required to reduce the risk of hemorrhage.
- Partial mole:
  - Surgical evacuation is preferable, unless the size of fetal parts necessitates medical evacuation.
- Histological examination of products of conception is essential to confirm diagnosis.

Management:

- Hysterectomy: is a preferable choice in women with advanced maternal age, completed their family and who have complete mole for fear of malignant transformation.

Specialist follow-up for molar pregnancy

- Serum hCG should be checked weekly until levels are normal.
- Then Follow-up hCG monthly for 6 months.
- Barrier methods for contraception until bhCG is normal are preferred, then COCs throughout the follow up period.
- Either increasing or persistently plateaued levels mandate evaluation for trophoblastic neoplasia. If the woman has not become pregnant, then these levels signify increasing trophoblastic proliferation that is most likely malignant.

Persistent GTD

- Risk of requiring chemotherapy is 15% after a complete mole and 0.5% after a partial mole.
- Chemotherapy is indicated if:
  - Serum hCG levels >20,000 IU/L at 4wks after uterine evacuation.
  - Static or rising hCG after uterine evacuation in absence of new pregnancy.
  - Persistent symptoms, e.g. uterine bleeding and/or abdominal pain.
  - Evidence of metastases.
  - Histological diagnosis of choriocarcinoma.

Prognosis

- With effective registration and treatment program, cure rate is high (98–100%) with low chemotherapy rates (5–8%).
- Recurrence rate is low (1/55).
- Women should be advised not to conceive until hCG level has been normal for 6mths.
- hCG levels should be checked 6 and 10w after each subsequent pregnancy.

Gestational trophoblastic neoplasia (GTN)

- This group includes invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor.
- These tumors almost always develop with or after some form of recognized pregnancy. Half follow hydatidiform mole, a fourth follow miscarriage or tubal pregnancy, and another fourth develop after a preterm or term pregnancy.
- **Risk factors**: - Complete mole - bhCG > 100,000 mIU/ml - Old maternal age. -Uterine size that is large for gestational age - Theca-lutein cysts >6 cm. -Slow decline in β-hCG levels post evacuation.

Gestational trophoblastic neoplasia (GTN)

- These placental tumors are characterized by their aggressive invasion into the myometrium and tendency to metastasize.
- The most common finding with GTN is irregular bleeding associated with uterine subinvolution.
- The bleeding may be continuous or intermittent, with sudden and sometimes massive hemorrhage.
- Myometrial perforation from trophoblastic growth may cause intraperitoneal hemorrhage.
- In some women, lower genital tract metastases are evident, whereas in others only distant metastases are found with no trace of uterine tumor.

Anatomical Staging	
Stage I	Disease confined to the uterus
Stage II	GTN extends outside of the uterus but is limited to the genital structures (adnexa, vagina, broad ligament)
Stage III	GTN extends to the lungs, with or without known genital tract involvement
Stage IV	All other metastatic sites

Modified World Health Organization (WHO) Prognostic Scoring System[a]

Scores[b]	0	1	2	4
Age (years)	<40	≥40	—	—
Antecedent pregnancy	Mole	Abortion	Term	—
Interval after index pregnancy (mo)	<4	4–6	7–12	>12
Pretreatment serum β-hCG (mIU/mL)	$<10^3$	10^3 to 10^4	10^4 to 10^5	$\geq 10^5$
Largest tumor size (including uterus)	<3 cm	3–4 cm	≥5 cm	—
Site of metastases		Spleen, kidney	GI	Liver, brain
Number of metastases	—	1–4	5–8	>8
Previous failed chemotherapy drugs	—	—	1	≥2

[a]Adapted by FIGO.
[b]Low risk = WHO score of 0 to 6; high risk = WHO score of ≥7.
β-hCG = beta human chorionic gonadotropin; GI = gastrointestinal; GTN = gestational trophoblastic neoplasia.
Adapted with permission from FIGO Committee on Gynecologic Oncology: Current FIGO staging for cancer of the vagina, fallopian tube, ovary, and gestational trophoblastic neoplasia, Int J Gynaecol Obstet 2009 Apr;105(1):3–4.

Gestational trophoblastic neoplasia (GTN)

- Treatment is mainly by **chemotherapy** +/- surgery.
- Single agent like methotrexate or actinomycin –D could be used.
- Combination therapy like EMA-CO, which includes etoposide, methotrexate, actinomycin D, cyclophosphamide, and Oncovin (vincristine) is used in high-risk cases.
- In selected cases, adjuvant surgical and radiotherapy may also be employed.

Follow up of GTN

- With either low- or high-risk disease, once serum β-hCG levels are undetectable, sero-surveillance is continued for 1 year.
- During this time, effective contraception is crucial to avoid any teratogenic effects of chemotherapy to the fetus and to mitigate confusion from rising β-hCG levels caused by superimposed pregnancy.

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Thank you