Ministry of Higher Education and Scientific Research
Al- Mustansiriyah University
College of Pharmacy
Department of Clinical Pharmacy

Hospital Training Manual
Obstetric and Gynecology ward

For
5th Year Students
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Aknowldegment

Great thanks and deep appreciations
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CONTENT

<u>Note:</u> The medical conditions included in this manual are the most admitted to the ward

Patient Data sheet

Patient Name Age: Sex: date of admission:
Weight: Height: BMI:

Chief Compliant (CC):

- History Of Present Illness (HOPI):

- Past Medical History(PMH):

- Past Surgical History(PSH):
- Medication history:

- Drug Allergy:
- Review of other system
- CNS
- CVS
- GIS
- RS
- GUT
- **Vital Signs:** BPPR(pulse rate)

RR (respiratory rate) Temp. (Temperature)

- Investigation:

- Lab. Data :

- U/S(ultrasound):

- Morning Tour Night Tour Treatment

- Morning Tour Night Tour Treatment

Problem identification
Medical /pharmaceutical problem

Problem 1:

Problem 2:

Problem 3:

Problem 4:

Problem	**Pharmaceutical care plan**
No.1:	Clinical outcomes &objectives Pharmacist interventions
No.2:	Clinical outcomes &objectives Pharmacist interventions
No.3:	Clinical outcomes &objectives Pharmacist interventions

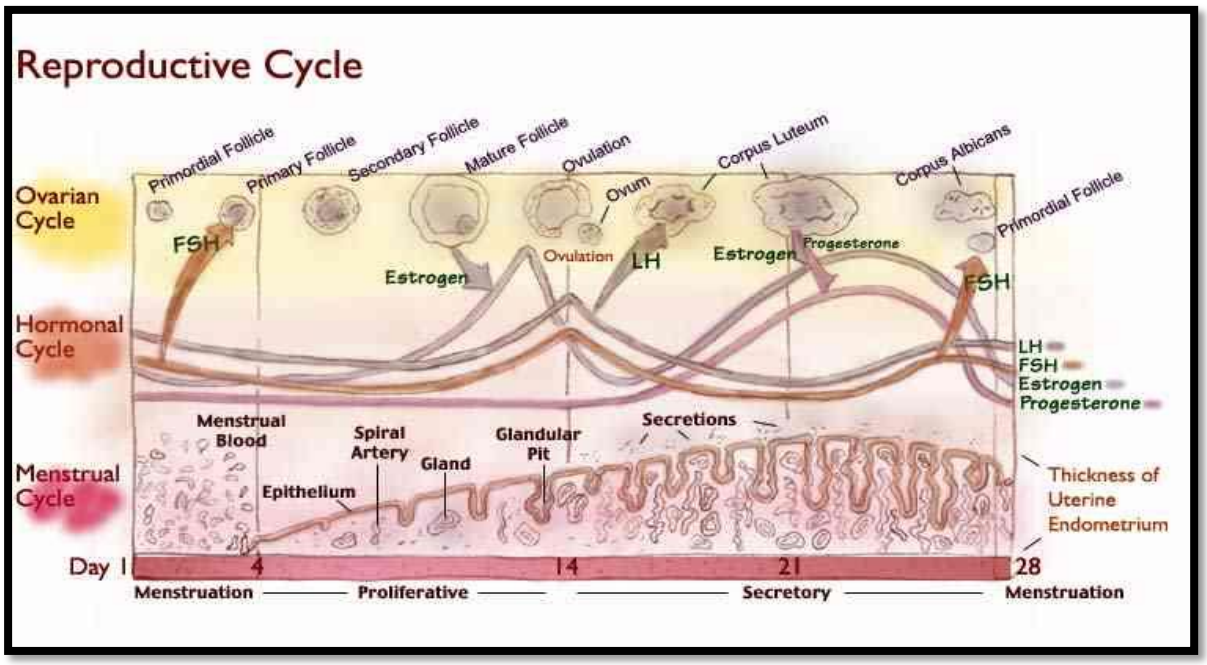
Part –A-

Obstetrics

Terminology

In medicine, gravidity refers to the number of times a woman has been pregnant.

1. Parity: is the no. of live birth at any age or stillbirth after 24 weeks of gestation.
2. Nullipara: a woman who has never delivered a fetus or fetuses beyond 20 weeks of gestation.
3. Gravida:a is the total no. of pregnancy regardless of how they ended (abortion, normal pregnancy).
4. Nullgravida: a nulligravida or gravida 0 is a woman who has never been pregnant.
5. Primigravida: a primigravida or gravida 1 is a woman who is pregnant for the first time or has been pregnant one time.
6. Elderly primigravida: an elderly primigravida is a woman in her first pregnancy, who is at least 35 years old.
Example: a woman who has 2 complete abortions and 1 normal pregnancy may be termed as G3P1A2.

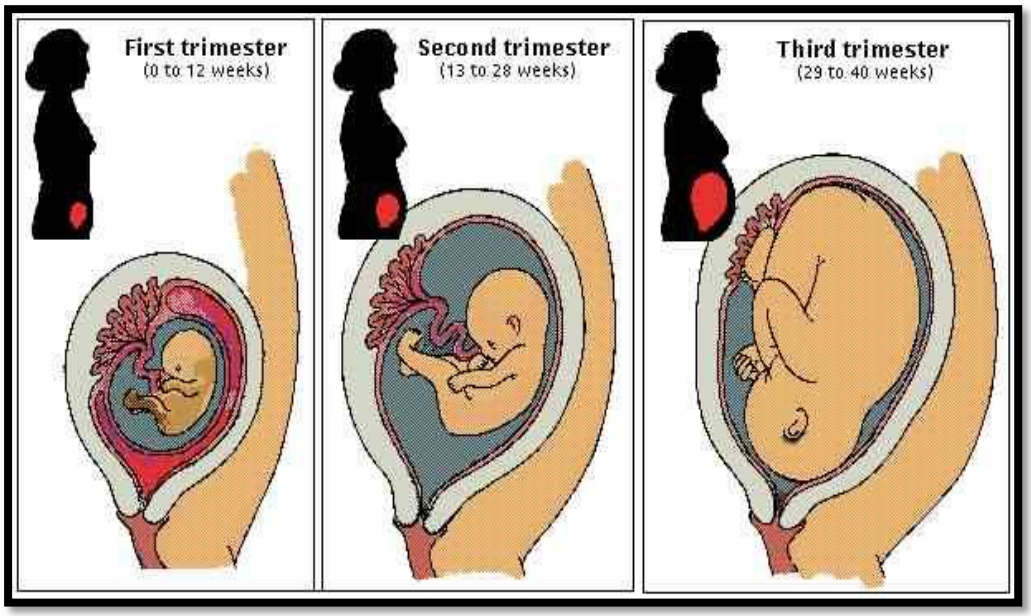


Obstetrical Abbreviations

-Expected Date of Delivery **(EDD)**
- First Missed Period **(FMP)**
- Last Menstrual Period **(LMP)**
- Fetal Movement **(FM)**
- Poly Cystic Ovary Syndrome **(PCOS)**
- Neural Tube Defect **(NTD)**
- Fetal Life **(FL)**
- Pregnancy Test **(PT)**
- Caesarean Section **(C/S)**
- Normal Vaginal Delivery **(NVD)**
- Premature Uterine Contractions **(PUC)**
- Respiratory Distress Syndrome **(RDS)**

Trimesters of Pregnancy

The human gestation period is 36-42 weeks, and is divided into three stages called trimesters. Each trimester is three months. The stages of development are the pre-embryonic, embryonic and fetal. The pre-embryonic stage is when the fertilized ovum consolidates, and it lasts for 17 days post conception. The major organ systems are formed during the embryonic stage (18-56 days), with maturation, development and growth continuing during the fetal stage (18-38 weeks).



A. First trimester of pregnancy

- First trimester pregnancy is the early stage of pregnancy from conception to 12 weeks gestation, or about 14 weeks from the first day of the last normal menstrual period (LNMP).
- During this stage pregnant may experience the dreaded morning sickness and sore and enlarged breasts. During the first trimester, growth and development in mother and fetus cause many changes to occur.
- A woman may notice no period or a light period; blue lines under the skin over her breasts and abdomen; waistline expansion; breasts that grow larger protruding nipples. food aversions and cravings; heartburn and indigestion; fatigue; tender breasts; complexion problems; a need to urinate often ; constipation; headaches, dizziness, or faintness. During the first trimester, both the mother's body and the fetus are changing rapidly.
- The most dramatic changes and development occur during the first trimester. During the first eight weeks, a fetus is called an embryo. The embryo develops rapidly and by the end of the first trimester it becomes a fetus that is fully formed, weighing approximately 1/2 to one ounce and measuring, on average, three to four inches in length.

B. Second trimester of pregnancy

- This second stage of pregnancy lasts until the end of the seventh month and is many times the easiest stage of pregnancy as most women will art to regain some of their energy.
- Women may notice the abdomen begins to swell. By the end of the second trimester, the uterus is near the rib cage; the skin on the abdomen and breasts stretches.
- Stretch marks may be visible; movements made by the fetus. Known as quickening, this often occurs sometime around weeks 6 to 20; a dark line forming from the navel down to the middle of the abdomen; brown, uneven marks on the face or other changes in skin pigment; darkening of the area around the nipples.
- In the fetus, growth continues quickly from now until birth. Organs such as the heart and kidneys develop further, eyebrows and finger nails form, the skin is wrinkled and covered with fine hair, periods of activity and quiet occur as the fetus moves, kicks, sleeps, and wakes. The fetus has now developed all its organs and systems and will now focus on growing in size and weight.
- During the second trimester, the umbilical cord continues to thicken as it carries nourishment to the fetus. However, harmful substances also pass through the umbilical cord to the fetus, so care should be taken to

avoid alcohol, tobacco, and other known hazards. During the second trimester, both the mother's body and the fetus continue to grow.

- The second trimester is the most physically enjoyable for most women. Morning sickness usually abates by this time and the extreme fatigue and breast tenderness usually subsides. These changes can be attributed to a decrease in levels of human chorionic gonadotropin (hCG) hormone and an adjustment to the levels of estrogen and progesterone hormones.

C. Third trimester of pregnancy

- The third trimester of pregnancy generally spans weeks 28 through 40, though healthy babies may be born a bit sooner or later. Although most women undergo many of the same physical changes during this time, no two pregnancies are alike.
- The fetus is continuing to grow in weight and size and the body systems finish maturing. The mother may feel more uncomfortable now as she continues to gain weight and begins to have false labor contractions (called Braxton-Hicks contractions).

Normal Pregnancy and Prenatal Care

A. Pregnancy Signs and Symptoms

1. Nausea and vomiting:

- Recurrent nausea and vomiting during the 1st trimester occurs in about one-half of pregnancies.
- The etiology of this problem is not clear but hormonal and emotional factors have been investigated.
- Symptoms can be mild or so severe that the patient becomes dehydrated and risks electrolyte imbalance and caloric malnutrition, this condition is known as Hyperemesis gravidarum that required hospitalization.
- Management include nonpharmacological measures as avoidance of fatty or spicy foods, eating small, more frequent meals, drinking ginger teas, inhaling peppermint oil vapors, wearing motion sickness.
- Bands on the wrists and increasing rest periods each day. Pharmacological therapy in severe cases include administration of pyridoxine, a variety of antihistamins, promethazine, metoclopramide, more recently intravenous droperidol and diphenhydramine.

2. Heartburn:

- Heartburn is a reflux esophagitis caused by both mechanical factors (enlarging uterus displacing the stomach above the esophageal sphincter) and hormonal factors (by progesterone).
- Management include non-pharmacological therapy avoidance of acidic and spicy foods, decreasing the amount of food and liquid at each meal, limiting food and liquid intake before bedtime, sleeping a semi-Fowlers position or propped up on pillows.
- Pharmacological therapy includes use of liquid forms of antacids H2-receptor inhibitors.

3. Constipation:

- Progesterone-induced relaxation of the intestinal smooth muscle .peristalsis and increase bowel transit time is the causative factor of constipation.
- Dietary management includes increased fluids and liberal intake of foods. Iron salts may exacerbate the problem.
- Enemas, laxative, and strong cathartics should be avoided.

4. Ptyalism:

Ptyalism is the increased production of saliva, probably induced by the consumption of starch. It is cured by reducing carbohydrate intake.

5. ***Varicosities and Hemorrhoids:***

- Varicosities most often occur in the lower extremities but may be seen in the vulva as well.
- Contributing factors include genetic predisposition, advanced maternal age, increased parity, and prolong standing.
- Treatment includes avoidance of garments that constrict at the knee and upper leg, support stocking, and increased periods of rest with the legs elevated.
- Hemorrhoids, Varicosities of the rectal veins, are due to mechanical compression by the enlarging uterus, as well as from constipation and straining at stool. Treatment includes OTC topical preparations, cool sitz baths, and stool softeners.

6. Leg Cramps:

- Almost half of all pregnant women suffer from recurrent painful spasms of the muscles of the lower extremities, especially the calves.
- Leg cramps are more frequent at night and usually occur during the 3rd trimester. Treatment include massage and placing the affected muscle(s) on stretch relieves the cramps when occur.

7. *Backache:*

- Most pregnant women experience lower backache as pregnancy progresses.
- These are usually alleviated by minimizing the amount of time spent standing, by increasing rest, by wearing a specially designed support belt over the lower abdomen, and by taking an analgesic such as paracetamol.

8. Headache:

- Muscle tension headaches may occur intermittently.
- Headaches during the 2nd and 3rd trimesters are not an expected symptom of pregnancy.

9. Urinary Frequency:

Urinary Frequency occurs mostly during the 1st trimester, as the enlarging uterus compresses the bladder, and again during the last weeks, as the fetal head descends into the pelvis.

10. Leukorrhea:

An increase in the amount of vaginal discharge is physiologic and suspected during pregnancy. Douching has no place in the treatment

11. Syncope:

- Venous pooling in the lower extremities increases as the pregnancy regresses. This can lead to dizziness or lightheadedness, especially after standing upright abruptly or for long periods of time.
- Other causes include dehydration, hypoglycemia, and the taunting of blood flow to the stomach after eating a large meal.

Laboratory Evaluation

1. Maternal Serum Screening Tests:

A. Amniocentesis (also referred to as ***amniotic fluid test or AFT):***

- Is a medical procedure used in prenatal diagnosis of genetic abnormalities and fetal infections, in which a small amount of amniotic fluid, which contains fetal tissues, is extracted from the amnion or amniotic sac surrounding a developing fetus, and the fetal DNA is examined for genetic abnormalities.
- The three most common abnormalities tested for are Down syndrome, Trisomy 18 and spina bifida.
- Amniocentesis can be performed as soon as sufficient amniotic fluid surrounds the fetus to allow a sample to be recovered relatively safely, usually no earlier than the 14th week of pregnancy.
- Often, genetic counseling is offered in conjunction with amniocentesis.

B. Chorionic Villus Sampling (CVS):

- Is a form of prenatal diagnosis to determine chromosomal or genetic disorders in the fetus.
- It entails getting a sample of the chorionic villus (placental tissue) and testing it.
- The advantage of CVS is that it can be carried out 10-13 weeks after the last period, earlier than amniocentesis (which is carried out at 15-18 weeks).

Indications: Possible reasons for having a CVS can include:

- Mother's age of 35 years or greater
- Increased nuchal translucency or other abnormal ultrasound findings
- Family history of a chromosomal abnormality or other genetic disorder
- Parents are known carriers for a genetic disorder

C. Alfa-fetoprotein (AFP or MSAFP) test:

- Is a maternal blood test done in the second trimester that checks for a protein normally secreted by the fetal liver.

- The levels of this protein alert the obstetrician to the possibility of a chromosomal abnormality, such as Down syndrome or the presence of twins. Abnormal AFP levels may also indicate developmental problems in the fetus, such as neural tube defects like spina bifida or defects in the abdominal wall of the fetus.
- An abnormal AFP may also simply mean that your due date has been miscalculated. Therefore, an abnormal AFP indicates the need for further testing. AFP testing is often done in concert with testing for other markers, such as hCG, estriol and inhibin, three hormones produced by the placenta.

2. Screening for Gestational Diabetes:

- The 1-hour, 50-g oral glucose screen is used to detect glucose intolerance in pregnancy. Routine screening is performed on all patients between 24 and 28 weeks gestation.
- The significance of GDM lies not in an increased risk of fetal loss but in the risk of excessive fetal growth with its attendant birth-related morbidities.

3. Researching for Rh Antibodies:

All Rh-ve women who are unsensitized at the beginning of pregnancy should be retested at approximately 26-28 weeks gestation. If the antibody screen remains -ve , the mother should receive Rho(D) immune globulin .

4. Screening for Bacterial Vaginosis

- Bacterial vaginosis(BV) is a condition in which the normal flora of the vagina(speciaaly lactobacilli) are reduced in number and replaced by overgrowth of anaerobic organisms.
- Some studies have linked BV with an increased incidence of preterm labor, endometriosis and premature rupture of the membranes.

5. ***Testing for Group B Streptococci (GBS):***

- GBS are part of the normal vaginal flora and implicated in preterm labor, as well as in amnionitis, endometriosis, and wound infection in

the mother. Vertical transmission during labor or delivery may result in generalized sepsis in the newborn and related long-term morbidity or neonatal death.

- Cultures obtained at 35-37 weeks gestation from the lower third of the vagina and perianal area. Culture+ve women are treated during labor with antibiotic prophylaxis to prevent fetal-neonatal GBS infection.

Nutrition in pregnancy

The overriding principle of good nutrition is that there is a positive linear relationship between maternal weight gain and newborn weight and that pre-pregnant maternal body mass index can affect fetal weight independently of the amount gained by the mother during pregnancy.

1. ***Folic acid:*** Folate is needed to make DNA and RNA (the building blocks of cells), is a B vitamin that occurs naturally in food, folate-deficient women who become pregnant are at greater risk of giving birth to low-weight, premature infants with neural tube defects, which can result in the malfunction of the spine (spina bifida), skull and brain. The Recommended Dietary Allowance (RDA) for folate equivalents for pregnant women is 600 micrograms.

2. ***Iron:*** iron is essential for the manufacture of red blood cells that carry oxygen around the body. During pregnancy iron is needed in larger amounts because the mother's blood volume increases and the baby's blood is also developing. Lack of iron can cause anemia, which means the red blood cells are not able to carry enough oxygen around the body leaving you tired and less able to fight off infections. Anemia during pregnancy can persist after the birth of the baby and can also affect the baby's iron stores. The dose is 200 mg tid.

3. ***Calcium:*** Total serum calcium decreases gradually thought pregnancy. Substantial increases in absorptive efficiency and positive balance begin in the 1st trimester. This must represent maternal accumulation of calcium, since the fetal calcium content is negligible at this time. It is possible that calcium added to maternal bone during early pregnancy is transferred to the fetus in later gestation. Calcium supplementation is not necessary in women with a diet that includes adequate dairy foods. Absent this, Calcium supplementation may be used on as may be used on as-needed basis to meet the recommended dietary allowance (RDA) of 1200 mg May during pregnancy.

4. ***Zinc:*** Zinc is a trace mineral. A zinc deficiency may be teratogenic in humans. Zinc levels in amniotic fluid correlate with antimicrobial activity, suggesting that zinc plays a role in protecting against intrauterine infection. Low dietary intake of zinc has been associated with IUGR. The RDA during pregnancy is increased from 15 to 20 mg /day.

5. ***Vitamin D:*** Most vitamin D is synthesized from a precursor in the skin after exposure to UV light from the sun and relatively few foods are good sources of the vitamin. If supplementation with vitamin D is indicated, care should be considered. In human pregnancy, high maternal intake of vitamin D was implicated as the cause of a syndrome that included mental and physical retardation and hypercalcemia. 400-500IU vitamin D supplementation have been reported to be safe and adequate.

6. ***Vitamin A:*** Vitamin A appears to be important for fetal growth and poor maternal vitamin A status was associated with preterm birth, intrauterine growth retardation (IUGR), and decreased birth weight. Vitamin A may be important for lung growth. However an excess leads to teratogenicity mainly in the 1st trimester as CNS abnormalities (hydrocephalus or micricephaly), CVS abnormalities, facial abnormalities and altered growth.

Teratology and Drugs in Pregnancy

A teratogen*:* is an agent that interferes with the normal growth and development of the fetus, and is used to describe drugs or chemicals that cause major or gross birth defects.

The food and Drug Administration (FDA) lists five categories of labeling for drug use in pregnancy.

Category A: no fetal risk shown in controlled human studies.

Category B: no human data available and animal studies shown no fetal risk or animal studies show a risk but human studies do not show fetal risk.

Category C: no controlled studies on fetal risk available for humans or animals or fetal risk shown in controlled animal studies but no human. data available (benefit of drug use must clearly justify potential fetal risk in this category).

Category D: studies show fetal risk in humans (use of drug may be acceptable even with risks such as in life threatening illness or where safer drugs are ineffective).

Category X: risk to fetus clearly outweighs any benefits from these drugs.

Social Drug Exposure

1. Smoking: Smoking is associated with decreased birthweight and increased prematurity. Risks of complications and of the associated perinatal loss increase with the no. of cigarettes smoked. Discontinuation of smoking or reduction in the no. the no. of cigarettes smoked during pregnancy can reduce the risk of complications and perinatal mortality, especially in women at high risk for other reasons.

2. Alcohol: Fetal alcohol syndrome has been reported in offspring chronically alcoholic mothers and includes the features of gross physical retardation that begins prenatally and continues after birth.

3. Caffeine: There is no evidence of any teratogenic effect of caffeine in humans. Concomitant consumption of caffeine with cigarette smoking may increase the risk of low birth weight. Maternal coffee intake decreases iron absorption and may increase the chance of anemia.

Pregnancy Loss and Spontaneous Abortion

- **Abortion** is the termination of pregnancy by any means, resulting in the expulsion of an immature, nonviable fetus.
- The term "miscarriage," although imprecise, has been used for all types of pregnancy losses up to a gestational age of 20 to 22 weeks.
- The term miscarriage is used often in the lay language and refers to spontaneous abortion.
- An abortion can be either spontaneous or induced loss of an early pregnancy. The period of pregnancy prior to fetal viability outside of the uterus is considered early pregnancy. Most consider early pregnancy to end at 20-24 weeks' gestation.
- Although spontaneous abortion has multiple etiologies, chromosome abnormalities are present in up to 60% of abortuses in some studies.
- For all types of abortion differential diagnosis is needed for condition with similar symptoms (ex: ectopic pregnancy, Hydatidiform mole, Benign and malignant lesions of the genital tract…etc).
- For all types of abortion RHoGAM (300 mg) is administered to Rh-negative, un-sensitized patients.

1- Threatened abortion

Clinical Manifestations

- Vaginal bleeding, with or without menstrual-like cramps, in the first 20 weeks of pregnancy is the most common manifestation of threatened abortion.
- There is frequently no history of passage of tissue or rupture of membranes.
- Physical exam is normal, except that the speculum exam may reveal a small amount of bleeding with a closed cervix and no more than mild discomfort.

Treatment

- Traditional treatment is bed rest and abstinence from intercourse and it is more rational for late threatened abortions (after 12 weeks of gestation).
- Symptoms are best managed on an outpatient basis with hospital admission reserved for heavy bleeding and/or pain relief.
- The patient should be advised about possible progression of threatened abortion to incomplete abortion, i.e. increasing bleeding, pain etc. therefore come back if the bleeding gets worse.

Medications

- There is no evidence that any hormones or medications alter or improve the outcome of threatened abortion in the first and early second trimester.
- Medications given during the period of organogenesis (days 18 to 55 after conception) may have teratogenic effects on the fetus. This may need to be balanced with the health of the mother.
- Progesterone is prescribed in 13-40% of women with threatened miscarriage. Progesterone is the main product of the corpus luteum, and giving Progesterone is expected to support a potentially deficient corpus luteum gravidarum and induce relaxation of a cramping uterus although progesterone does not seem to improve outcome in women with threatened miscarriage. However, local application of a progestogen was found to subjectively decrease uterine cramping more rapidly than bed rest alone in one small study.

- Example of progesterone giving for threatened abortion: Dydrogesterone (Duphaston ®) 10 mg tab (2-3 tab/ day).

2- Incomplete abortion

Incomplete abortion is the partial expulsion of the products of conception before the 20th week of gestation.

Clinical Manifestations

- Heavy bleeding associated with cramping labor like lower abdominal pains.
- The cervix is softened and open (admits a finger tip), or tissue (fetus or membrane) is passed.
- Speculum examination reveals a dilated internal os with tissue present in the vagina or endocervical canal

Treatment

I. Stabilization

- If the patient has signs and symptoms of heavy bleeding, at least one large-bore intravenous catheter suitable for blood transfusion (16 gauge or larger) is started immediately, if she has unstable vital signs.
- Ringer lactate or normal saline with 30 U oxytocin per 1000 mL is started at 200 mL/h and increased if necessary to obtain uterine tone (the uterus is less sensitive to oxytocin in early pregnancy). Such doses may depress urine output because of the antidiuretic hormone–like activity of oxytocin and should be discontinued as soon as appropriate.
- Product of conception (POC) should be removed from the endocervical canal and uterus with ring forceps or suction. This maneuver often dramatically decreases the bleeding.
- In a health centre, commence antibiotics and either insert Misoprostol 4 tabs vaginally or transfer for dilation and curettage (D & C) if there is significant continuing bleeding.
- In the hospital setting all incomplete abortions should be evacuated as soon as possible after admission this prevents blood

loss and the possibility of infection getting in to cause septic abortion.

II. Cervical ripening agents

- Cervical ripening agents aid in patient comfort and reduce the difficulty of uterine evacuation procedures.
- Available cervical ripening agents include Misoprostol, Mifepristone, and osmotic dilators.
- When given at least 2 to 3 hours prior to procedure, Misoprostol produced better results with fewer side effects when administered vaginally or sublingually rather than orally.
- However, when compared with Mifepristone, 200 mg, given 24 hours prior to the evacuation procedure, the use of Misoprostol by any route was less effective.
- For medical management of women with an incomplete abortion and a uterus less than 12 weeks in size Misoprostol (Cytotec®) 600 µg orally or 400 µg sublingually is used. Doses can be repeated every 3 hours for up to three total doses.

III. Curettage

- Before 10 weeks, the fetus and placenta are commonly expelled together, but later they are delivered separately. In many cases, retained placental tissue remains in the cervical canal, allowing easy extraction from an exposed external os with ring forceps. If unsuccessful, a suction curettage effectively evacuates the uterus.
- Curettage is performed carefully but systematically with a suction instrument.
- Vacuum curettage may be faster and result in less blood loss with advanced gestations.

III. Post curettage

- The patient is observed for several hours. Repeat blood count is ordered if bleeding has been excessive or if there is temperature greater than 38°C. One might also observe in the hospital setting.
- Avoid coitus, douching, or the use of tampons for 2 weeks.
- Oral ferrous sulfate is prescribed if blood loss has been moderate.
- Analgesics are rarely required.
- Follow-up is scheduled in 2 weeks.

3- Complete abortion

Complete abortion refers to a documented pregnancy that spontaneously passes all of the products of conception. Before 10 weeks, the fetus and placenta are often expelled simultaneously.

Clinical Manifestations

- Typically, a history of vaginal bleeding, abdominal pain, and passage of tissue exists.
- After that the passage of product of conception (POC) appears to be complete and bleeding is minimal. The cervix may be closed or minimally dilated and the uterus, on examination, is well contracted and small.
- The examination reveals some blood in the vaginal vault; a closed cervical os; and no tenderness of the cervix, uterus, adnexa, or abdomen.
- The ultrasound demonstrates an empty uterus.

Treatment

- Observation without surgical intervention is appropriate if the patient's vital signs are stable and no fever is present. The passage of tissue appears to be complete and bleeding is minimal.
- Check β-hCG weekly until levels indicate resolution of the pregnancy.

4- Missed abortion

Missed abortion is defined as the retention of product of conception (POC) after death of the fetus. There is no definition of the length of time of retention of the POC.

Clinical Manifestations

- The pregnant uterus fails to enlarge as expected.
- Amenorrhea may persist, or intermittent vaginal bleeding, spotting, or brown discharge may occur.

- Disseminated intravascular coagulopathy (DIC) may rarely develop with a missed abortion that extends for more than 4 or 5 weeks.

Treatments

I. Dilation and curettage (D&C)

- D&C is available for missed abortions that are less than 12 to 14 weeks' gestation by fetal size on ultrasound. If the cervix is not dilated, then preoperative dilation is accomplished with laminaria or prostaglandin cervical-dilating agents.

II. Dilation and evacuation (D&E)

- D&E is available for missed abortions greater than 14 weeks' gestation by fetal size on ultrasound. The D&E procedure is used rather than D&C when there are fetal bones and associated risk for uterine perforation
- Although surgery is the most rapid mode of treatment, surgical treatment may rarely result in uterine perforation requiring additional surgery, intrauterine adhesions and scarring, or cervical trauma with subsequent cervical incompetence.

III. Misoprostol

For missed abortion, misoprostol can be increased to 800 µg vaginally or 600 µg sublingually. Doses can be repeated every 3 hours for up to three total doses.

Misoprostol may be used for <u>outpatient treatment of missed or incomplete abortion</u> in patients with:

- Stable vital signs
- No evidence of infection
- Good reliability
- Fetus measuring less than 13 weeks' gestation
- POC with no fetal pole on transvaginal ultrasound

5- Habitual abortion

Habitual abortion, also known as recurrent pregnancy loss (RPL), is defined as three or more consecutive spontaneous abortions of clinical, pre-viable pregnancies (documented by ultrasound or histopathology).

Etiology

Up to 75% of cases of RPL will not have a clearly defined etiology. General etiological categories of RPL include anatomic, immunological, genetic, endocrine, and infectious factors.

I. Uterine anatomic defects that are implicated causes (note that if one of these anatomic causes is found, it should be treated before proceeding with other treatments):

- Double uterus
- Septate uterus
- Asherman syndrome
- Endometrial polyps
- Leiomyomas that impinge on the endometrial cavity

II. Cervical anatomic defects:

- Incompetent cervix (15 weeks and beyond)
- Antiphospholipid syndrome (APS) is the only immunological condition in which pregnancy loss is a diagnostic criterion for the disease. Up to 15% of patients with RPL may have APS.
- Genetic abnormalities: Approximately 4% of couples with RPL have a major chromosomal rearrangement (vs. 0.7% of the general population); usually a balanced translocation.

III. Other possible causes that are less well documented:

- Endocrine factors such as thyroid dysfunction, luteal phase defect, hyperprolactinemia, and
- Some infections, such as *Listeria monocytogenes, Toxoplasma gondii*, and cytomegalovirus, are known to cause sporadic pregnancy loss, but no infectious agent has been proven to cause RPL.
- Maternal–fetal human leukocyte antigen (major histocompatibility complex).

Treatment

- There is no generalized treatment for habitual abortion. Specific treatment is directed to any identified causes.
- Whether low-dose aspirin (60 to 80 mg/d), low-dose heparin, or prednisone (20 to 60 mg/d) improves outcomes is controversial and

depends on the specific etiology of each patient's series of habitual abortion.

- When indicated for specific thrombophilias, subcutaneous low-dose heparin and aspirin have been shown to have equally successful outcomes, with fewer complications compared with prednisone.

Type of Abortion		Vaginal bleeding	Abdominal pain/cramps	Cervical Os changes	Ultrasound U/S findings
1-	Threatened Abortion	Mild bleeding	Mild	Closed cervical Os	Either live, intra-uterine pregnancy or there is no fetal heart movement.
2-	Incomplete Abortion	Heavy bleeding+ passage of POC	Cramping labor like lower abdominal pains	Dilated, Open cervical Os	U/S confirms that some of the products of conception are still present in the uterus.
3-	Complete Abortion	**Hx:** Heavy bleeding + passage of POC. **On presentation:** mild bleeding	**Hx:** Cramping labor like lower abdominal pains **On presentation:** mild pain	**Hx:** Dilated, Open cervical Os **On presentation:** Closed cervical Os	U/S demonstrates an empty uterus
4-	Missed Abortion	No vaginal bleeding or minimal sometimes	No abdominal pain	No cervical Os changes	U/S showed nonviable fetus and that fetal heartbeat is not observed or heard at the appropriate time.

Gestational Disorders

A. Gestational Diabetes

- Gestational Diabetes (GD) is the most common type of diabetes complicating pregnancy, and most patients are obese.
- The women with GD have a normal oral glucose tolerance test (OGTT) when she is not pregnant, so her disease usually is mild.
- Pregnancy is associated with increased tissue resistance to insulin, resulting in increased levels of blood insulin as well as glucose and trigclyerides.
- These changes are due to placental lactogen and elevated circulating esterogens and progesterone.

Risk factors for gestational diabetes mellitus (GDM)

1. Maternal age greater than 30 years.
2. Previous macrosomic, malformed, or stillborn infant.
3. GDM in a previous pregnancy.
4. Family history or diabetes.
5. Maternal obesity.
6. Persistent glucosuria.
7. Chronic use of certain drug such as β-agonists or corticosteroids.

Maternal Problems

1. Hypoglycemia: occurs during the first half of pregnancy due to increased insulin sensitivity.
2. Hyperglycemia: occurs during the second half of pregnancy.
3. Urinary tract infection (UTI).
4. Hypertension: the abnormal blood vessels of pregnant women with DM can lead to the development of hypertension in the later weeks of gestation since the abnormal endothelium cannot produce enough prostacyclin to antagonize the elevated angiotensin II vasopressor levels.
5. Hydromnios: excess amounts of aminotic fluid can occur with DM especially if glucose is poorly controlled since maternal hyperglycemia produces fetal hyperglycemia and fetal glucosuria.
6. Retinopathy.

Infant Problems

1. Spontaneous abortion.
2. Congenital abnormalities: CVS and CNS most affected systems
3. Respiratory distress: since hyperglycemia interferes with ability of cortisol to accelerate surfactant production.
4. Hypoglycemia: since the fetus exposed to high glucose levels coming across the placenta from a hyperglycemic mother reacts by producing large amounts of insulin in an attempt to reduce glucose.
5. Macrosomia: more than 4 kg.
6. Hypocalcemia.
7. Hyperbilirubinemia: results from a higher hematocrit developed in utero especially if oxygen availability is decreased.
8. Perinatal mortality: since acute deprivation caused by glucose binding to Hb or sudden shifts in water and electrolytes with glucose movements have been suspected.

Screening and Diagnosis for GDM

- ❖ Two different protocols are presently advocated for the screening and diagnosis of GDM:
- **The one-step diagnostic protocol** has been proposed by the World Health Organization (WHO)
  - A 2-hour 75-g oral glucose tolerance test (OGTT) is performed with measurement of plasma glucose values at 1- and 2-hour post glucose challenge (unless fasting blood glucose (FBG) exceeds 92 mg/dL since this is diagnostic of GDM).
  - This protocol has the advantage of a single set of criteria for screening and diagnosis.
  - The patient should perform the test after fasting overnight for at least 8 hours.
  - The test is considered abnormal and diagnostic for GDM if any single serum glucose value meets or exceeds the following cutoffs:
  - Fasting plasma glucose (FPG) ≥92 mg/dL (5.1 mmol/L)
  - One-hour post challenge ≥180 mg/dL (10.0 mmol/L)
  - Two-hour post challenge ≥153 mg/dL (8.5 mmol/L).
- **Two-step diagnosis protocol** is commonly used in North America and is endorsed by the American College of Obstetricians and Gynecologists. Note that the two-step approach was not developed to

diagnose diabetes in pregnancy, but rather, to identify women "at risk" for developing diabetes later in life.

Management

1. Diet control.
2. Insulin therapy:

- All patients taking oral hypoglycemic agents should immediately be transitioned to insulin therapy, preferably before conception. (A possible exception is (Glucophage®) use in patients with poly cystic ovarian syndrome (PCOS) and infertility).
- The insulin regimen is individualized based on the type of DM, glucose control, and gestational age.
- Insulin absorption is most effective when injected into the subcutaneous tissue in the **abdomen**.

Table 'Commonly Prescribed Insulins during Pregnancy

Type	Example	Category	Onset	Peak	Duration	Appearance
Rapid-acting (analogs)	Humalog (lispro)	B	<15 min	1–2 h	4–6 h	Clear
Bolus or for meals	NovoLog (aspart)	B	<15 min	1–2 h	4–6 h	Clear
Short-acting	Apidra (glulisine)	C	<15 min	1–2 h	4–6 h	Clear
Short-acting (regular)	Humulin	B	½–1 h	2–4 h	6–8 h	Clear
Usually for IV use	Novolin		½–1 h	2–4 h	6–8 h	
Intermediate-acting (NPH)	Humulin N	B	1–2 h	4–6 h	12 h	Cloudy
Basal insulin	Novolin N		1–2 h	4–6 h	12 h	
Long-acting (analog) Basal insulin	Lantus (glargine)	C	1.5 h	Flat, maximum effect 5 h	24 h	Clear
Long-acting (analog) Basal insulin	Levemir (detemir)	B	1 h	Flat, maximum effect 5 h	12–24 h	Clear

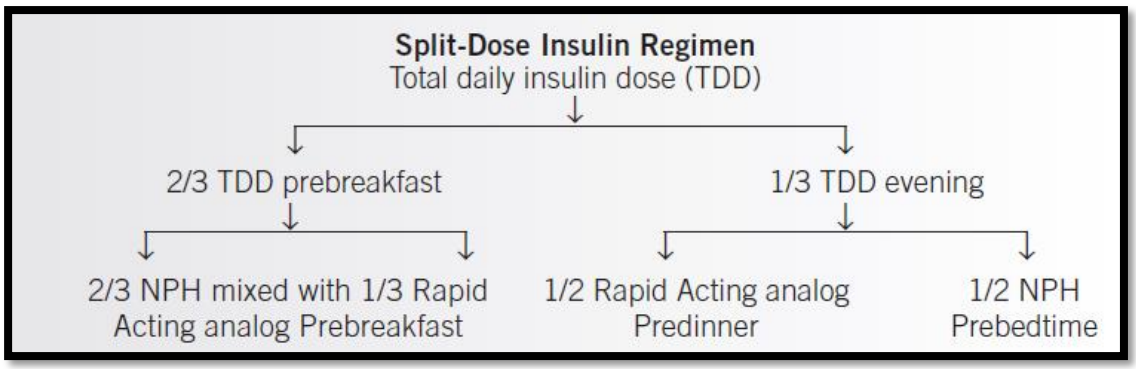
Intermediate-acting and long-acting insulins are usually given before bedtime (HS).
Lantus is generally not recommended for use in pregnancy.
Rapid-acting insulin (Humalog/NovoLog) is used in the CSII pump.

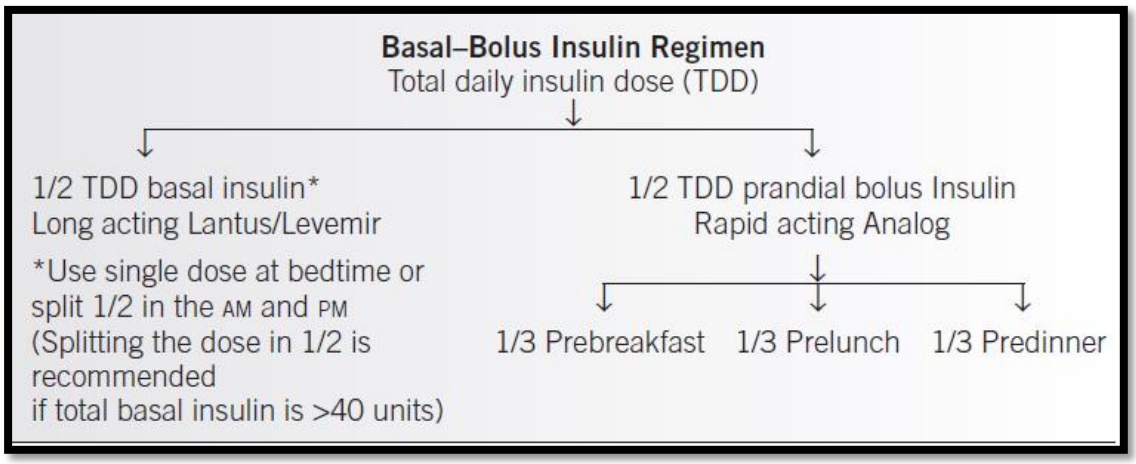
- To calculate the initial 24-hour total daily dose (TDD) insulin requirement, the health care provider should use the patient's current weight and the number of weeks of gestation.
- Table below includes dosing recommendations for women with DM1, DM2, and GDM.

Table Calculating Split-Dose Weight-Based Insulin

Weeks of gestation	TDD
Week 1–18	0.7 unit/kg
Week 18–26	0.8 unit/kg
Week 26–36	0.9 unit/kg
Week 36–40	1 unit/kg
For obesity >150% of DBW	1.5–2 unit/kg
Week 0–6 postpartum	0.4 unit/kg

Calculate TDD as above (kg = maternal weight in pounds/2.2)





- If a patient experiences nocturnal hypoglycemia (less than 60 mg/dL), the evening regimen of rapid-acting and intermediate-acting insulin may be split to give the rapid-acting before dinner and intermediate-acting insulin before the important bedtime snack.
- The goal is to first achieve normal AM fasting values and then focus on the rest of the glucose profile.
- If nocturnal hypoglycemia is identified, patients should have the evening dose of intermediate- or long-acting insulin reduced. Delaying NPH administration until bedtime may help minimize nocturnal hypoglycemia. Otherwise, the caloric intake (especially protein) at the bedtime snack may be increased.

B. Hypertensive Disorder of Pregnancy

I. Gestational hypertension

Is defined as a persistent systolic blood pressure level of 140 mm Hg or greater or a diastolic blood pressure level of 90 mm Hg or greater that

occurs on two occasions 4 hours apart after 20 weeks of gestation in a woman with previously normal blood pressure.

II. Chronic hypertension

- Patients with a persistent elevation of blood pressure to at least 140/90 mm Hg on two occasions before 20 weeks' gestation, and patients with hypertension that persists for more than 6 weeks postpartum.
- Complications related to chronic hypertension include superimposed preeclampsia, fetal growthrestriction, pre-term birth, and placental abruption. The risk of developing one of these complicationscorrelates with the degree of maternal blood pressure elevation; the higher the blood pressure, thegreater the risk of one of these complications.

III.PREECLAMPSIA

Preeclampsia: a syndrome of gestational hypertension plus end-organ manifestations including proteinuria [proteinuria defined as urinary excretion of 0.3 g protein or more in a 24-hour urine specimen or a protein/creatinine ratio ≥0.3 mg/DL].

In the absence of proteinuria, new-onset hypertension with thrombocytopenia (less than 100,000 platelets/mL) or renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL) or impaired liver functions (transaminases twice the upper limits of normal concentration) constitute diagnostic criteria of preeclampsia. There are only two types of preeclampsia: **mild and severe.**

Risk Factors for preeclampsia
a-Antiphospholipid syndrome
b- Nulliparity
c-Multiple gestation
d-Previous pregnancy with preeclampsia
e-Family history of preeclampsia or eclampsia
f-Preexisting hypertension or renal disease
g-Pre-gestational diabetes
h-Age over 40
i-Raised BMI

j-Molar pregnancy k-Obesity l-Raised diastolic blood pressure (>80 mmHg)

Symptoms of pre-eclampsia

- Mild preeclampsia: high blood pressure, water retention, and protein in the urine.
- Severe preeclampsia: severe headaches, blurred vision, inability to tolerate bright light, fatigue, nausea/vomiting, urinating small amounts, pain in the upper right abdomen, shortness of breath, and tendency to bruise easily, and/or urinating very infrequently.

Evaluations

Maternal Evaluation	**Fetal Evaluation**
Laboratory Evaluation •Hematocrit and platelet count once per week • Liver function tests once per week •Twenty-four–hour urine collection at diagnosis for total protein excretion and creatinine clearance or a protein/creatinine ratio to confirm the diagnosis	• Daily fetal movement assessment (kick counts) •Non stress test (NST) twice weekly • Biophysical profile if nonreactive NST •Amniotic fluid volume assessment weekly •Ultrasound evaluation of fetal growth every 3 weeks.

Treatment of Preeclampsia

1-Delivering the baby

Once the diagnosis of preeclampsia has been made, definitive therapy in the form of delivery is the desired goal because it is the only cure for the disease

2-Rest: it is common practice to admit women with pre-eclampsia to hospital, particularly if it is severe.

3-Drug therapy

A. ***Magnesium sulphate:*** mothers with pre-eclampsia are given magnesium sulphate, decrease the risk of developing eclampsia. Magnesium sulphate is an anticonvulsant, but prevents eclampsia

much better than other types of anticonvulsants which are used for epilepsy. It does not affect the outcome of the baby, but the risk of serious consequences to the mother are much reduced.

B. ***Anti-platelet agents*** (almost exclusively aspirin) as prevention of pre-eclampsia shows that these agents moderately reduce the risk of pre-eclampsia and its complications with no apparent increase in the risk of hemorrhage. Aspirin is indicated for women at high risk of pre-eclampsia at a dose of 150mg/day.

C. ***Medication:*** drugs to reduce blood pressure may be an option for a while if pre-eclampsia is not too severe. If the blood pressure is reduced it may help to allow the pregnancy to progress further before delivering the baby.

Medication used in Mild to moderate hypertension

[Chronic hypertention, Gestational hypertension, preeclampsia]

- A number of antihypertensive have been shown to be safe and effective during pregnancy in controlling maternal blood pressure.
- Treatment of elevated blood pressure with antihypertensive reduces the risk of maternal morbidities related to hypertension but does not reduce the risk of fetal complications such as intrauterine growth restriction, and placental abruption.

1-First line agent

α-adrenergic agonists

- **Methyldopa** has been studied extensively and is recommended by many as the first-line antihypertensive agent in pregnancy. It is a centrally acting alpha-adrenergic agonist that appears to inhibit vasoconstricting impulses from the medullary vasoregulatory center and decrease sympathetic tone, and therefore can have many side effects, including sedation and impaired sleep patterns.
- One potential side effect is that it may cause mild elevations of liver enzymes, which can lead to diagnostic confusion with HELLP syndrome.
- Although it is relatively safe, methyldopa is not a potent BP lowering agent. A positive direct Coombs' test may be seen, usually after 6–12 months of therapy.

- Hemolytic anemia may occur in these patients and is an indication to stop the medication. Fever, liver function abnormalities, granulocytopenia, and thrombocytopenia are rare side effects.
- The total daily dosage of 500 mg to 2 g is administered in 2–4 divided doses

2- **Second line agents**

These agents should be used when monotherapy with methyldopa is insufficient or when women are unable to tolerate methyldopa.

A- Calcium channel blockers

- **Nifedipine** is a calcium channel blocker that has been used during pregnancy for tocolysis and treatment of hypertension. Several reports suggest that nifedipine use is safe during pregnancy;
- When nifedipine is used for treatment of chronic hypertension during pregnancy, the long acting formulation (Procardia XL, Adalat CC) may improve patient compliance. The principal benefit of this agent is once-daily dosing.
- The usual starting dose is 30 mg daily. If necessary, the dose may be increased to 60–90 mg daily. The neuro-muscular-blocking action of magnesium may be potentiated by simultaneous calcium channel blockade; therefore, nifedipine should be used with caution in patients receiving magnesium sulfate.
- The sublingual route of administration is associated with unpredictable blood levels and should be avoided.

B- Oral hydralazine

- Hydralazine is safe throughout pregnancy, although the occurrence of maternal and neonatal lupus-like syndromes have been reported.
- Hydralazine is more frequently used as an infusion for the treatment of acute severe hypertension.

***3*- Third line agents**

A- β-blockers

- β-blockers are safe throughout pregnancy and there is wide experience with oxprenolol and labetalol.
- Labetalol is becoming one of the favored therapies for hypertension in pregnancy. It is a non-selective beta blocker that antagonizes beta and alpha-1 receptors, the beta blockade/ alpha-blockade ratio is 7:1.

- Its side effects include fatigue, decreased exercise tolerance, as well as bronchospasm in individuals with reactive airway disease.
- It is available in both oral and intravenous forms, so it may be used for both outpatient and inpatient management
- The usual starting dose is 100 mg twice per day (BID), and the dose can be increased weekly to a maximum of 2400 mg daily. Titration increments should not exceed 200 mg BID.
- Atenolol has been shown to have minimal effects on systolic BP in preeclampsia women, and it is also associated with intrauterine growth retardation

B- α- Adrenergic blockers

- α- adrenergic blockers are still avoided in the first half of pregnancy because of concerns about growth restriction and are viewed as third line agents for the treatment of hypertension in pregnancy.
- The safety and efficacy of prazosin in pregnancy has been demonstrated. Doxazosin appears to be safe, although data are limited.

C- Thiazide diuretics

- Thiazide diuretics are used infrequently in pregnancy. The drugs do not appear to be teratogenic and although such drugs abbreviate the plasma volume expansion associated with normal pregnancy, this has not been proven to impair fetal growth.
- The obstetric community remains reluctant to use these antihypertensive agents because of concern about potentiating the plasma volume contraction, which occurs with pre-eclampsia.
- However, women with chronic hypertension who, before conception, responded well to a thiazide diuretic, could have the drug reinstituted in pregnancy but it should be withdrawn if pre-eclampsia develops.

Note: Use of angiotensin-converting enzyme inhibitors (enalapril, captopril) during pregnancy is associated with fetal hypocalvaria, renal defects, anuria, and fetal and neonatal death. These agents are contraindicated in pregnancy.

SEVERE PREECLAMPSIA

• The clinical course of severe preeclampsia is usually characterized by progressive deterioration in both maternal and fetal status.

• Most of the fetal or neonatal complications are related to intrauterine fetal growth retardation, placenta abruption, or prematurity.

Diagnosis

1• Blood pressure ≥160 mm Hg systolic or ≥110 mm Hg diastolic on two occasions atleast 4 hours apart with the patient on bed rest.

2• Persistent occipital or frontal headaches, Cerebral or visual disturbances.

3• Severe and persistent epigastric or right upper quadrant abdominal pain.

4• Pulmonary edema or cyanosis.

Management

• Initiating delivery

• **All patients with severe preeclampsia** should be admitted to the labor and delivery area for close observation of maternal and fetal condition and provided steroids for lung maturity if less than 34 weeks' gestation during initial evaluation and with the decision for delivery.

• All patients should receive intravenous magnesium sulfate to prevent convulsions.

• Control of maternal blood pressure within a safe range

Control of Severe Hypertension [chronic hypertention, Gestational hypertension, preeclampsia]

• The objective of treating severe hypertension is to prevent maternal cerebrovascular accidents and congestive heart failure

• Labetalol

Parenteral labetalol has a rapid onset of action and produces a smooth reduction in blood pressure with rare overshoot hypotension.it is contraindicated in patients with a greater than first-degree heart block.

Labetalol is administered in intermittent intravenous boluses of 20 to 80 mg.

• Hydralazine

Hydralazine is a direct arteriolar vasodilator.Intravenous hydralazine has an onset of action of 10 to 20 minutes.Hydralazine is administered in intermittent bolus injections with an initial dose of 5 mg. Blood pressure should be recorded every 5 minutes.

If an adequate reduction in blood pressure is not achieved 20 to 30 minutes after the initial dose, then a repeat dose of 5 mg for a maximum of 25 mg/h.

• Nifedipine

Nifedipine improves renal function with a beneficial effect on urine output when treating preeclampsia in the postpartum period.

Nifedipine is administered 10 to 20 mg orally every 4 hours.

Profound reductions in blood pressure with nifedipine can be partially reversed by the slow intravenous administration of calcium gluconate.

• Sodium nitroprusside

Sodium nitroprusside relaxes arteriolar and venous smooth muscle by interferingwith both influx and the intercellular activation of calcium.Onset of action is immediate, and duration of action is very short (1 to 10 minutes).

Because preeclamptic patients have a propensity for depleted intravascular volume, they are especially sensitive to its effects. The initial infusion dose should therefore be 0.2 μg/kg/min, rather than 0.5 μg/kg/min as is standard in nonpregnant patients.

Cyanide and thiocyanate are products of metabolism of this drug with potential deleterious effects for the fetus.

Complications of pre-eclampsia

1. Eclampsia.
2. Liver, kidney, and lung problems.
3. A blood clotting disorder.
4. A stroke.
5. Severe bleeding from the placenta.
6. *Hellp* syndrome occurs in about 1 in 5 women who have severe pre-eclampsia. Hellp stands for 'haemolysis, elevated liver enzymes and low platelets' which are some of the medical features of this severe form of pre-eclampsia.

Patients with HELLP syndrome may present with a variety of signs and symptoms, including

• Epigastric or right upper-quadrant abdominal pain

• Nausea or vomiting

• Nonspecific viral syndrome–like symptoms
• History of malaise for the past few days before presentation

For the baby The poor blood supply in the placenta can reduce the amount of nutrients and oxygen to the growing baby.On average, babies of mothers with pre-eclampsia tend to be smaller. There is also an increased risk of stillbirth.

Eclampsia: is a type of seizure (convulsion) unrelated to other cerebral conditions during pregnancy which is a life-threatening complication of pregnancy. About 1 in 100 women with pre-eclampsia develop eclampsia. So, most women with pre-eclampsia do not progress to have eclampsia. However, a main aim of treatment and care of women with pre-eclampsia is to prevent eclampsia and other possible complications.

Treatment of Eclampsia

- If the patient is convulsing, should be turned on her side to prevent aspiration and to improve blood flow to the placenta. Fluid or food is aspirated from the glottis or trachea. The seizure may be stopped by giving IV bolus of magnesium sulphate ,There are several regimens of magnesium sulfate used to prevent convulsions. The most commonly used is an intravenous loading dose of 6 g of magnesium sulfate ($MgSO4·7H2O$) prepared as 6 g diluted in 150 mL D5W or lactated Ringer solution is administered via infusion pump over 20 to 30 minutes.
- If the patient develops recurrent convulsions after the initial infusion of magnesium sulfate, a further dose of 2 g can be infused over 5 to 10 minutes.On completion of the magnesium sulfate loading infusion, a maintenance infusion of 2 to 3 g/h is used.
- Magnesium blood level are then checked every 4-6 hr and the infusion rate adjusted Urinary output is checked hourly and the patient assessed for signs of possible magnesium toxicity such as loss of tendon reflexes or decrease in respiratory rate and depth, which can be reversed with calcium gluconate.

If magnesium toxicity is suspected, the following steps should be taken:

1-The magnesium sulfate infusion should be discontinued.

2-Supplemental oxygen should be administered.

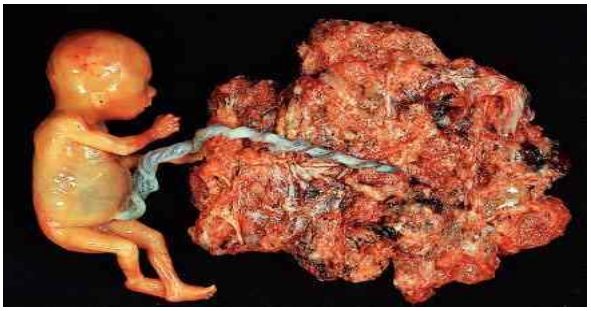
3-A serum magnesium level should be assessed.

4-If magnesium toxicity is recognized, 10 mL of 10% calcium gluconate is administered (1 g total) intravenously. This medication must be given slowly (i.e., 2 to 5 mL/min) to avoid hypotension, bradycardia, and vomiting.

-Calcium competitively inhibits magnesium at the neuromuscular junction, but its effect is only transient because the serum concentration is unchanged. Symptoms of magnesium toxicity can recur following calcium gluconate administration if the magnesium level remains elevated.

• At delivery, neonatal side effects of maternal administration of magnesium sulfate include; Hypotension, Hypotonia, Respiratory depression, Lethargy, Decreased suck reflex.

C. Gestational Trophoblastic Disease (Hydatidiform Mole &Choriocarcinoma)



Gestational trophoblastic disease is a spectrum of disorders that includes hydatidiform mole, invasive mole, and choriocarcinoma.

Causes

HM, or molar pregnancy, results from abnormal fertilization of the oocyte (egg). It results in an abnormal fetus. The placenta grows normally with little or no growth of the fetal tissue. The placental tissue forms a mass in the uterus. On ultrasound this mass often has a grape-like appearance, as it contains many small cysts.

Chance of mole formation is higher in older women. A history of mole in earlier years is also a risk factor.

Molar pregnancy can be of 2 types:

- Partial molar pregnancy. There is an abnormal placenta and some fetal development.
- Complete molar pregnancy. There is an abnormal placenta and no fetus.

Partial moles tend to follow a benign course, while complete moles have a greater tendency to become choriocarcinomas.

Symptoms

Symptoms of a molar pregnancy may include:

- Abnormal growth of the uterus, either bigger or smaller than usual
- Severe nausea and vomiting
- Vaginal bleeding during the first 3 months of pregnancy
- Symptoms of hyperthyroidism, including heat intolerance, loose stools, rapid heart rate, restlessness or nervousness, warm and moist skin, trembling hands, or unexplained weight loss
- Bilaterally enlarged cystic ovaries are sometimes palapable ,as a result of ovarien hyperstimulation due to excess of hCG.
- Symptoms similar to preeclampsia that occur in the first trimester or early second trimester, including high blood pressure and swelling in the feet, ankles, and legs (this is almost always a sign of a hydatidiform mole, because preeclampsia is extremely rare this early in a normal pregnancy)

Choriocarcinoma may be manifested by continued or recurrent uterine bleeding after evacuation of a mole or following delivery, abortion, or ectopic pregnancy. The presence of an ulcerative vaginal tumor, pelvic mass, or evidence of distant metastatic tumor may be the presenting observation. The diagnosis is established by pathologic examination of curettings or by biopsy.

Tests done may include:

1-hCG (quantitative levels) blood test
2-Abdominal or vaginal ultrasound of the pelvis
3-Chest x-ray
4-CT or MRI of the abdomen (imaging tests)
5-Complete blood count (CBC)

6-Blood clotting tests
7-Kidney and liver function tests

Laboratory findings

A serum hCG(above 40,000 mU/mL) or a urinary hCG value in excess of 100,000 units/24 h increases the likelihood of hydatidiform mole.

Imaging

Ultrasound has virtually replaced all other means of preoperative diagnosis of hydatidiform mole. A pregnancy ultrasound will show a snowstorm appearance with an abnormal placenta, with or without some development of a baby.A preoperative chest film is indicated to rule out pulmonary metastases of trophoblast.

Treatment

The uterus should be emptied as soon as the diagnosis of hydatidiform mole, removal of the abnormal tissue with a dilation and curettage (D & C) will most likely be suggested. D & C may also be done using suction. This is called suction aspiration (The method uses a suction cup to remove contents from the uterus). A hysterectomy (surgery to remove the uterus) may be an option for older women who DO NOT wish to become pregnant in the future.

Sometimes a partial molar pregnancy can continue. A woman may choose to continue her pregnancy in the hope of having a successful birth and delivery. However, these are very high-risk pregnancies. Risks may include bleeding, problems with blood pressure, and premature delivery (having the baby before it is fully developed). In rare cases, the fetus is genetically normal. Women need to completely discuss the risks with their provider before continuing the pregnancy.

Ovarian cysts should not be resected nor ovaries removed; spontaneous regression of theca lutein cysts will occur with elimination of the mole.

If malignant tissue is discovered at surgery or during the follow-up examination, chemotherapy is indicated.

Thyrotoxicosis indistinguishable clinically from that of thyroid origin may occur. While hCG usually has minimal TSH-like activity, the very high hCG levels associated with moles result in the release of T_3 and T_4 and cause hyperthyroidism. Patientsthyrotoxic on this basis should be stabilized with

(3-blockers prior to induction of anesthesia for their surgical evacuation. Surgical removal of the mole promptly corrects the thyroid overactivity.

Follow up:

After treatment, the hCG level should be followed. It is important to avoid another pregnancy and to use a reliable contraceptive for 6 to 12 months after treatment for a molar pregnancy. This time allows for accurate testing to be sure that the abnormal tissue does not grow back. Women who get pregnant too soon after a molar pregnancy are at high risk of having another molar pregnancy.

Prognosis:

Most HMs are noncancerous (benign). In some cases of complete HM, moles can become invasive. These moles can grow deep into the uterine wall and cause bleeding or other complications.In very few cases of complete HM, moles develop into a choriocarcinoma. This is a fast-growing cancer. It is usually successfully treated with chemotherapy, but can be life threatening.

Possible Complications

Complications of molar pregnancy may include:

- Change to invasive molar disease or choriocarcinoma
- Preeclampsia
- Thyroid problems
- Molar pregnancy that continues or comes back

D. Seizure disorders

- Epileptic women contemplating pregnancy who have not had a seizure for 5 years should consider a pre pregnancy trial of withdrawal from treatment. Those with recurrent epilepsy should use a single drug with blood level monitoring.
- valproate is contraindicated during pregnancy; phenytoin and carbamazepine may be teratogenic in the first trimester and should not be used unless absolutely necessary.
- Phenobarbital is considered the drug of choice. Serum levels should be measured in each trimester and dosage adjustments made to keep serum levels in the low normal therapeutic range.

- Pregnant women taking phenobarbital and phenytoin should receive vitamin supplements, including folic acid and vitamin D, throughout pregnancy. Vitamin K, 10-20 mg/d, is administered during the last month to help prevent bleeding problems in the newborn, who is at risk of bleeding tendencies due to decreased levels of clotting factors such infants should receive an injection of vitamin K- 1 mg subcutaneously immediately after delivery, and should have clotting studies 2-4 hours later.
- Breast-feeding is not contraindicated for infants of mothers taking anti-seizure medications.

E. Thyroid Disease

- Thyrotoxicosis during pregnancy may result in fetal anomalies, late abortion, or preterm labor and fetal hyperthyroidism with goiter.
- Thyroid storm in late pregnancy or labor is a life-threatening emergency.
- Radioactive isotope therapy must never be given during pregnancy. The anti-thyroid drug of choice is propylthiouracil, which acts to prevent further thyroxine formation by blocking iodination of tyrosine.
- There is a 2- to 3-week delay before the pretreatment hormone level begins to fall. The initial dose of propylthiouracil is 100-150 mg three times a day; the dose is lowered as the euthyroid state is approached.
- It is desirable to keep free T_4 in the high normal range during pregnancy. A maintenance dose of 100 mg/d minimizes the chance of fetal hypothyroidism and goiter.
- Maternal hypothyroidism even subclinical hypothyroidism manifested only by elevated levels of TSH may adversely affect subsequent neuropsychological development of the child.
- Mothers with known or suspected hypothyroidism should have the TSH level measured at the first prenatal visit. Replacement therapy with levothyroxine should be adjusted to maintain levels of TSH in the normal range.

F. Urinary Tract Infection

- The urinary tract is especially vulnerable to infections during pregnancy because the altered secretions of steroid sex hormones and the pressure exerted by the gravid uterus upon the ureters and bladder cause hypotonia and congestion and predispose to urinary stasis.
- Labor and delivery and urinary retention post-partum also may initiate or aggravate infection. *Eschrichia coli* is the offending organism in over two-thirds of cases.
- From *2%* to 8% of pregnant women have asymptomatic bacteriuria, which some believe to be associated with an increased risk of prematurity. It is estimated that pyelonephritis will develop in 20-40% of these women if untreated.
- A first-trimester urine culture is indicated in women with a history of recurrent or recent episodes of urinary tract infection. If the culture is positive, treatment should be initiated as a therapeutic measure. Nitrofurantoin (100 mg twice daily), Ampicillin (500 mg four times daily), and Cephalexin (500 mg four times daily) are acceptable medications for 3-7 days.
- Acute pyelonephritis requires hospitalization for intravenous administration of antibiotics until the patient is a febrile; this is followed by a full course of oral antibiotics.

G. Anemia

Anemia in pregnancy is defined as a Hb below 10 g/dl or hematocrit below 30%.

Plasma volume increases 50% during pregnancy, while red cell volume increases 25% causing lower HB and hematocrit values, which are maximally changed around the 24^{th}-28^{th} weeks. Anemia is very common in pregnancy causing fatigue, anorexia, dyspnea and edema.

A. Iron deficiency anemia: many women enter pregnancy with reduced iron stores resulting from heavy menstrual periods, previous pregnancies, breast-feeding, or poor nutrition. It is difficult to meet the increased requirement for iron through diet and anemia often develops unless iron supplements are given. RBCs may not become hypochromic and microcytic until the hematocrit has fallen significantly. Treatment consists of a diet containing iron-rich foods and 60 mg of elemental iron 3 times daily with meals. Iron is best absorbed if taken with a source of vitamin C.

B. Folic acid deficiency anemia: folic acid deficiency is the main cause of macrocytic anemia in pregnancy, since vitamin B12 deficiency anemia is rare in the childbearing years. The daily requirements of folic acid doubles from 0.4mg -0.8 mg in pregnancy.

Twin pregnancies, infections, malabsorption, and use of anticonvulsants such as phenytoin can precipitate folic acid deficiency. The anemia may first be seen in the puerperium owing to the increased need for folate during lactation. Good sources of folate in food are leafy green vegetables, orange juices, peanuts and beans. Cooking and storage of food destroy folic acid.

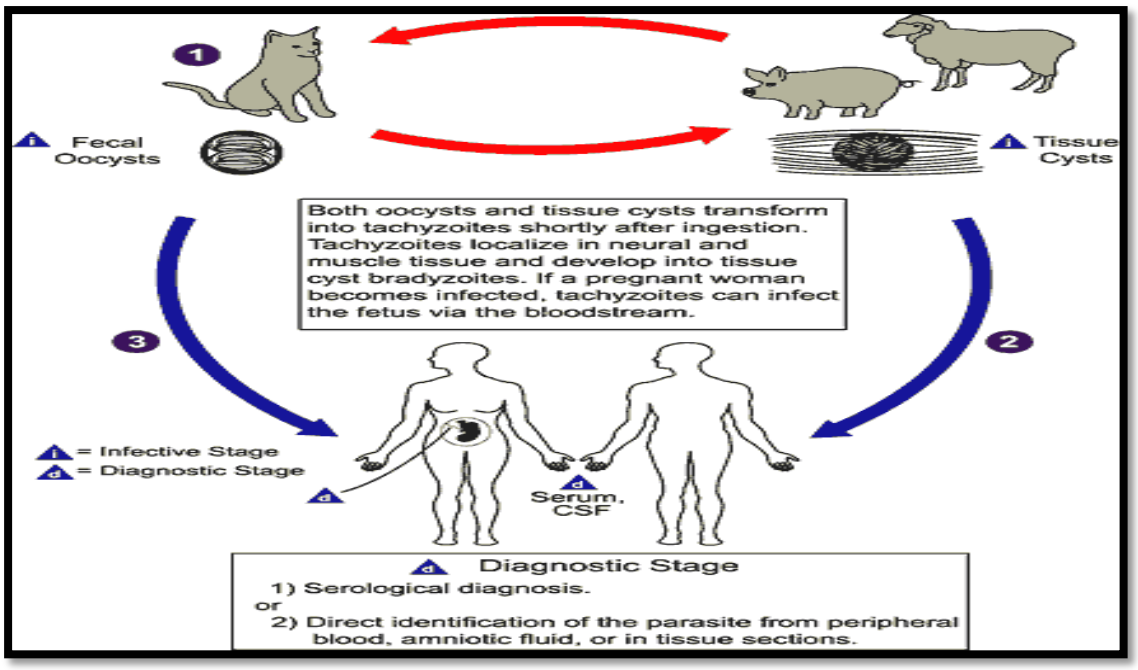
Toxoplasmosis

Toxoplasmosis is an infection caused by the protozoal parasite *Toxoplasmagondii.*

Transmission

Toxoplasmosis is not passed from person-to-person, except in instances of mother-to-child (congenital) transmission and blood transfusion or organ transplantation. People typically become infected by three principal routes of transmission.

1. Foodborne
2. Animal-to-human (zoonotic)
3. Mother-to-child (congenital)
4. Rare instances.



1- Foodborne transmission

The tissue form of the parasite (a microscopic cyst consisting of bradyzoites) can be transmitted to humans by food. People become infected by:

- Eating undercooked, contaminated meat
- Accidental ingestion of undercooked, contaminated meat after handling it and not washing hands thoroughly (*Toxoplasma* cannot be absorbed through intact skin)
- Eating food that was contaminated by knives, utensils, cutting boards, or other foods that had contact with raw, contaminated meat

2-Animal-to-human (zoonotic) transmission

- Cats play an important role in the spread of toxoplasmosis. They become infected by eating infected rodents, birds, or other small animals. The parasite is then passed in the cat's feces in an oocyst form, which is microscopic.
- Cats can shed millions of oocysts in their feces for as long as 3 weeks after infection. Mature cats are less likely to shed *Toxoplasma* if they have been previously infected. A *Toxoplasma*-infected cat that is shedding the parasite in its feces contaminate the soil or water in the environment as well.

3- Mother-to-child (congenital) transmission

- A woman who is newly infected with *Toxoplasma* during pregnancy can pass the infection to her unborn child (congenital infection). The woman may not have symptoms, but there can be severe consequences for the unborn child, such as diseases of the nervous system and eyes.
- Incidence and severity vary with the trimester of gestation during which the mother acquired the infection in which 10-20% (1^{st} trimester),30-54%(2^{nd} trimester), 60-65%(3^{rd} trimester) may occur.
- Congenital infection occurring in the 1^{st} trimester is the most severe. 89-100% of infections in the 3^{rd} trimester are asymptomatic and risk to the fetus is not correlated with symptoms in the mother.

4- Rare instances of transmission

- Organ transplant recipients can become infected by receiving an organ from a *Toxoplasma*-positive donor.
- Rarely, people can also become infected by receiving infected blood via transfusion. Laboratory workers who handle infected blood can also acquire infection through accidental inoculation.

Symptoms

Healthy people (non-pregnant)

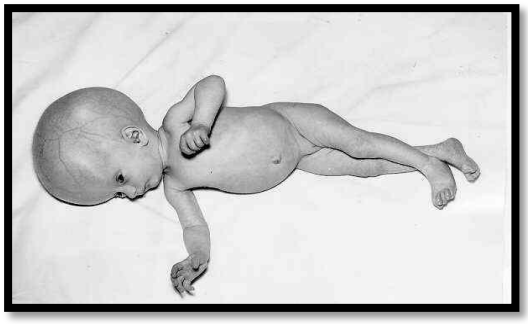
Healthy people who become infected with *Toxoplasma gondii* often do not have symptoms because their immune system usually keeps the parasite from causing illness. When illness occurs, it is usually mild with "flu-like" symptoms (e.g., tender lymph nodes, muscle aches, etc.) that last for weeks to months and then go away. However, the parasite remains in their body in an inactive state. It can become reactivated if the person becomes immunosuppressed.

Mother-to-child (congenital)

Results from acute infection acquired by the mother within 6-8 weeks before conception or during gestation.the mother can pass the infection to her unborn baby (congenital transmission). The damage to the unborn child is often more severe the earlier in pregnancy the transmission occurs. Potential results can be

- a miscarriage
- a stillborn child
- a child born with signs of toxoplasmosis (e.g., abnormal enlargement or smallness of the head)

Infants infected before birth often show no symptoms at birth but may develop them later in life with potential vision loss, mental disability, and seizures.



Persons with ocular disease

Eye disease (most frequently retinochoroiditis) from *Toxoplasma* infection can result from congenital infection or infection after birth by any of the modes of transmission . Eye infection leads to an acute inflammatory lesion of the retina, with retinochoroidal scarring. Symptoms of acute disease include: eyepain, sensitivity to light (photophobia), tearing of the eyes, blurred vision.

The eye disease can reactivate months or years later, each time causing more damage to the retina. If the central structures of the retina are involved there will be a progressive loss of vision that can lead to blindness.

Persons with compromised immune systems

Persons with compromised immune systems may experience severe symptoms if they are infected with *Toxoplasma* while immune suppressed. For example, HIV-infected person can have symptoms that include fever, confusion, headache, seizures, nausea, and poor coordination.

Diagnosis

- The diagnosis of toxoplasmosis is typically made by serologic testing. A test that measures immunoglobulin G (IgG)

is used to determine if a person has been infected. If it is necessary to try to estimate the time of infection, which is of particular importance for pregnant women, a test which measures immunoglobulin M (IgM) is also used along with other tests such as an avidity test.

- Diagnosis can be made by direct observation of the parasite in stained tissue sections, cerebrospinal fluid (CSF), or other biopsy material. These techniques are used less frequently because of the difficulty of obtaining these specimens.
- Molecular techniques that can detect the parasite's DNA in the amniotic fluid can be useful in cases of possible mother-to-child (congenital) transmission.
- Ocular disease is diagnosed based on the appearance of the lesions in the eye, symptoms, course of disease, and often serologic testing.

Treatment

A. Acute infection in pregnancy: treatment should be started immediately and risk of fetal infection reduced by 60% with treatment. In 1st trimester treatment is done with spiramycin 3g orally in 3-4 divided doses per day or sulfadiazine 4 g orally in 4 divided doses. In the 2nd and 3rd trimesters, sulfadiazine as above plus pyrmethamine 25 mg orally /day plus lucovorin 5-15 mg orally /day or spiramycin as in the same dose mentioned above.

B. Congenital infection: sulfadiazine 50mg/kg orally bid plus pyrimethamine 2 mg/kg orally for 2 days then 1mg/kg orally 3 times weekly plus lecoverin 5-20 mg orally 3 times weekly for 12 months as minimum duration of treatment.

Prevention

Prevention is most important in seronagative pregnant women and include cooking meat to 66 C◦ and cooking eggs, no drinking of unpasteurized milk, washing hands thoroughly after handling raw meat, washing kitchen surfaces that come in contact with raw meat, washing fruits and vegetables and avoiding contact with materials potentially contaminated with cat feces.

Erythrocyte Immunization (Rh Disease)

- Erythroblastosis fetalis (i.e., hemolytic disease of the newborn) is caused by an incompatibility between fetal and maternal blood.
- The Rh-negative mother becomes immunized by exposure to Rh-positive fetal erythrocytes during pregnancy or delivery, and antibodies formed by the mother pass through the placenta to the fetal circulation, where they react with the Rh-positive fetal erythrocytes, causing a hemolytic anemia.

Factors influencing Rh immunization

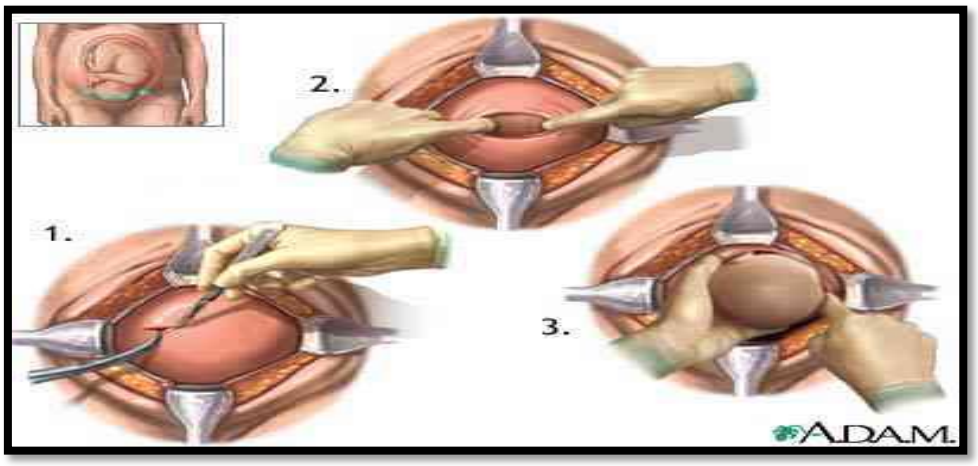
1. Aminocentesis
2. Threatened abortion, placenta previa, placental abruption
3. Abdominal truma
4. External version
5. Fetal death
6. Sinusoidal fetal heart tracing
7. Multiple pregnancies
8. Cesarean section
9. Anemic infant

Treatment

- Passive immunization against hemolytic disease of the newborn is achieved with Rho(D) immune globuline, a purified concentrate of antibodies against Rho(D) antigen.
- The Rho(D) immune globuline (one vial of 300 mcg IM) is given to the mother within 72 hours after delivery (or spontaneous or induced abortion or ectopic pregnancy).
- The antibodies in the immune globuline destroy fetal Rh-positive cells so that the mother will not produce anti- Rho(D), during her next Rh-positive gestation, erythroblastosis will be prevented.
- An additional safety measure is the administration of immune globulin at the 28^{th} week of pregnancy, the passive antibody titer that results is too low to significantly affect an Rh-positive fetus. The maternal clearance of the globulin is slow enough that protection will continue for 12 weeks.

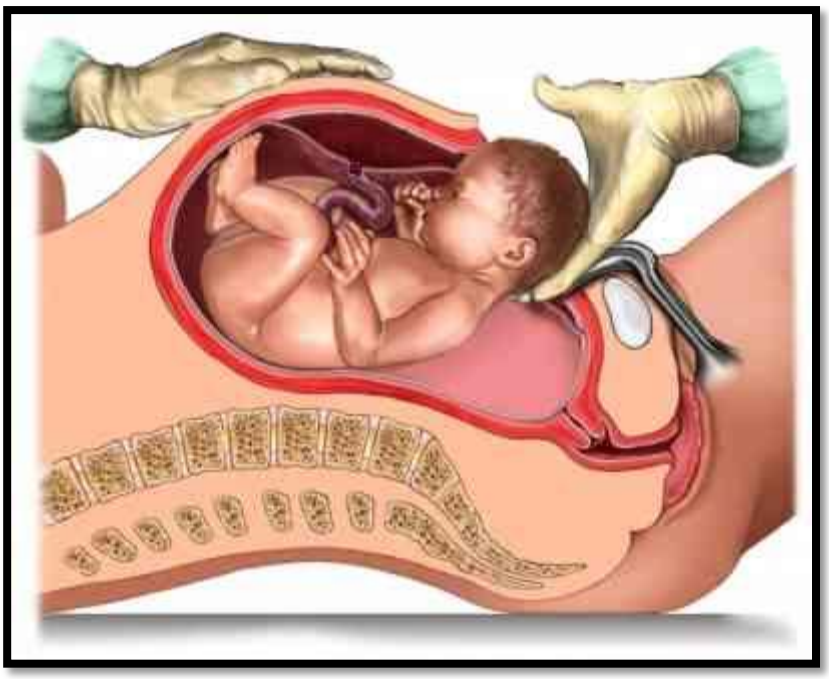
Caesarean section (C/S)

Cesarean section is a term used to describe the delivery of a vaiable fetus through an incision in the abdominal wall and the uterus.
The majority of cesarean sections are performed for fetal indications, a few are soly for maternal reasons, and some benefit both fetus and mother.



Common indications for cesarean delivery

1. Precious (high risk) Fetus
2. Prolonged labour or a failure to progress (dystocia)
3. Apparent fetal distress
4. Aapparent maternal distress
5. Complications (pre-eclampsia, active herpes)
6. Catastrophes such as cord prolapse or uterine rupture
7. Mmultiple births
8. Abnormal presentation (breech or transverse positions)
9. Failed induction of labour
10. Placental problems (placenta praevia, placental abruption or placenta accreta)
11. Umbilical cord abnormalities (vasa previa, multi-lobate including bi-lobate and succenturiate-lobed placentas, velamentous insertion)
12. Contracted pelvis
13. Sexually transmitted infections such as genital herpes (which can be passed on to the baby if the baby is born vaginally, but can usually be treated in with medication and do not require a c-section)
14. Previous caesarean section prior problems with the healing of the
15. Perineum (from previous childbirth or Crohn's Disease).



Complications of C-section

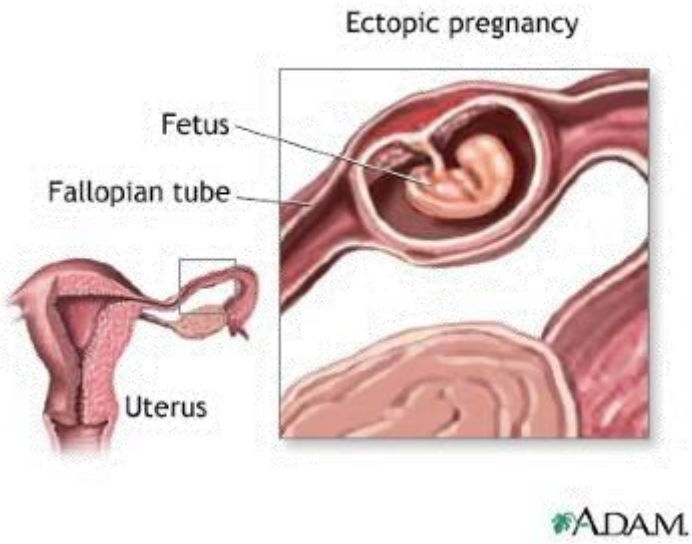
- Most of the serious complications associated with cesarean section are not due to the operation itself. Instead, the complications arise from the indication for the cesarean section.
- For example, a woman whose placenta separates prematurely (placental abruption) may require an emergency cesarean section.
- Under these circumstances, complications arise primarily from the placental abruption itself.Fortunately, serious complications are rare.
- However, the following minor complications can occur in women having cesarean sections

1. Infection
2. Bleeding
3. Atony
4. Lacerations
5. Placenta Accreta
6. Blood Clots

Ectopic Pregnancy

Definition

An ectopic pregnancy is one in which the fertilized ovum implants at any site other than the endometrial cavity. The fallopian tube is the most common site, accounting for more than 95% of ectopic pregnancies, but other implantation sites include the cervix, abdominal cavity, and ovary.



Etiology

A number of risk factors for ectopic pregnancy have been identified including the following conditions:

- Salpingitis. Approximately 50% of ectopic pregnancies can be attributed to a history of salpingitis. Chlamydial salpingitis may pose a greater risk than gonorrheal infection.
- Prior ectopic pregnancy
- Peritubal adhesions following postabortal infections, appendicitis, or endometriosis.
- Tubal surgery, including tubal ligation, and tubal reconstruction for fertility.
- Intrauterine device. Intrauterine devices (IUDs) are highly effective at preventing intrauterine pregnancy. Thus, any pregnancy in an IUD user is more likely to be tubal.
- Progestin-only contraceptives. Users of progestin-only oral contraceptives as well as injectable progestins are at increased risk

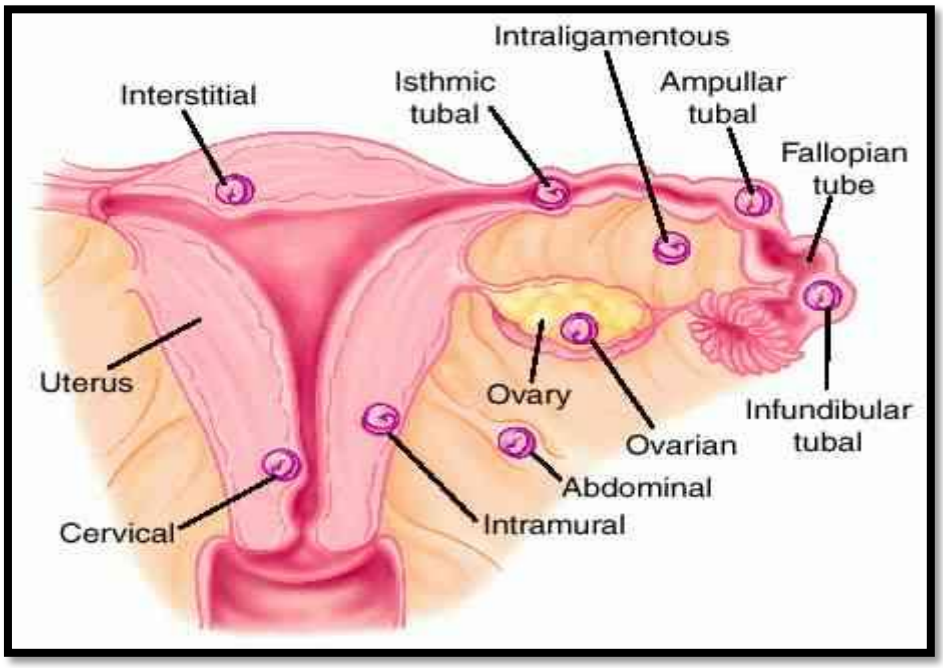
of ectopic pregnancy if pregnancy occurs, possibly because of altered tubal motility.

- History of infertility.
- Increased maternal age.

Clinical Findings

A. **Symptoms and signs:** they may be acute or chronic.

1. ***Acute (40%):*** Severe lower quadrant pain occurs in almost every case. It is sudden in onset, lancinating, intermittent, and does not radiate. Backache is present during attacks. Shock occurs in about 10%, often after pelvic examination. At least two-thirds of patients give a history of abnormal menstruation; many have been infertile.
2. ***Chronic (60%):*** Blood leaks from the tubal ampulla over a period of days, and considerable blood may accumulate in the peritoneum. Slight but persistent vaginal spotting is reported, and a pelvic mass can be palpated. Abdominal distention and mild paralytic ileus are often present.



B. Laboratory findings

1. *Human chorionic gonadotropin (hCG) hormone:* if normal intrauterine pregnancy (IUP), 85% have doubling time of 2 days. If abnormal gestation, will show < 66% increase of QhCG within 2

days. However, 13% of ectopic pregnancies have a normal doubling time.

2. *Progesterone:* decreased production in ectopic pregnancy, < 5 ng/ml strongly predictive of abnormal pregnancy. If > 25 ng/ml strongly predictive of normal pregnancy.
3. *Drooping hematocrit (Hct) associated with tubal rupture.*
4. Leukocytosis.

C. Imaging

- In U/S presence of intrauterine pregnancy (IUP) rules out ectopic pregnancy.
- If QhCG >6000mIU/ml, should see IUP on abdominal scan, and QhCG>1500mIU/ml for transvaginal scan.
- Findings on U/S in ectopic pregnancy include empty uterus, adnexal mass, Cul-de-sac fluid, fetal sac in tube and fetal cardiac activity in adnexa.

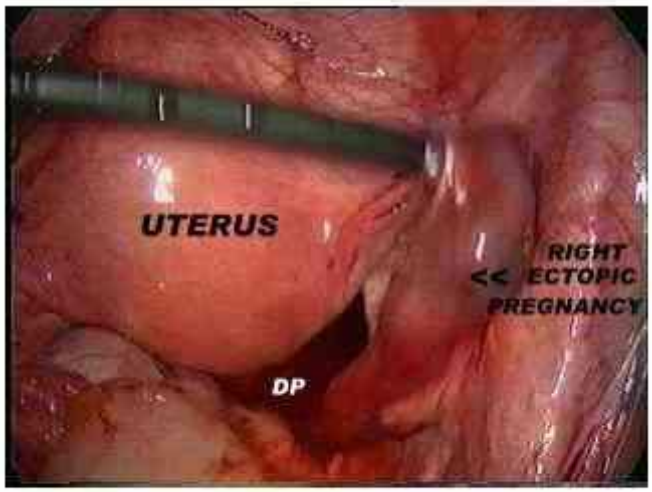


Figure 12:
Right Ectopic Pregnancy

D. **Special examination**

- With the advent of high-resolution transvaginal ultrasound used in evaluation of possible ectopic pregnancy.
- Laparoscopy is the surgical procedure of choice both to confirm an ectopic pregnancy and in most cases to permit pelviscopic removal of the ectopic pregnancy without the need for exploratory laparotomy.

Treatment

- Ectopic pregnancies can present as life-threatening emergencies. The patient presenting in shock with an acute abdomen should be stabilized and taken to surgery immediately.
- Fluid resuscitation must be carried out immediately.
- Laboratory tests needed are minimal. Blood should be drawn for hematocrit and cross matched for four units of red cells.
- A β-hCG level should be obtained, but it is not necessary to wait for the results. The patient should be taken to surgery as quickly as possible.

1- Surgical management

• Surgical options are operative **laparoscopy** or **laparotomy**.

- The first choice for surgical management is operative laparoscopy with either salpingostomy or salpingectomy.
- Laparotomy is reserved for specific indications.

• **Laparoscopic** salpingostomy is the procedure of choice in most circumstances. Salpingectomy is selected if future fertility is not desired (e.g., ectopic pregnancy after tubal ligation) or if rupture has destroyed the tube.

• **Laparotomy** should be performed if laparoscopy is unsatisfactory because of:

1. extensive adhesions
2. If the patient becomes unstable
3. If there are medical limitations to laparoscopy.

- After conservative surgery (when the tube is not removed), weekly β-hCG levels should be obtained until they are less than negative (values vary by laboratory).
- If there is concern about the completeness of removal of the pregnancy, postoperative prophylactic methotrexate using the single-dose regimen significantly decreases the rate of persistence.
- Early detection of trophoblastic persistence is facilitated by persistently elevated or rising β-hCG levels.

2- **Medical management**

- Medical management has the advantage of avoiding surgery with its attendant risks.
- Patients who are clinically stable with a small, unruptured ectopic pregnancy may be offered medical management with systemic methotrexate, a folic acid antagonist that preferentially inhibits rapidly replicating cells such as trophoblast.
- In properly selected patients, methotrexate is 75% to 85% effective in resolving ectopic pregnancy, with the remaining women requiring surgery.

Criteria for medical management (Methotrexate) include:

1. Hemodynamic stability
2. Gestational sac less than 3.5 cm in diameter
3. β-hCG at diagnosis less than 5000 IU
4. No ultrasound fetal cardiac activity
5. Minimal hemoperitoneum
6. No underlying liver or renal disease
7. No blood dyscrasia
8. Not breast-feeding
9. Ability to have regular follow-up.

• Pretreatment complete blood count and platelet count, β-hCG level, and liver and renal function tests should be obtained.

• Methotrexate is given in either single-**dose** or **multidose** regimens (Table 7-4).

- The two regimens have been widely studied for treatment of ectopic pregnancy and both are acceptable.
- The **multidose regimen** has a lower failure rate; however, the risk of complications including diarrhea, abnormal liver function, and stomatitis is greater with the multidoseregimen.
- The **single-dose regimen** is slightly less successful, requiring a second dose in up to 20% of women; however, there is a lower incidence of side effects.
- The failure rate of either regimen increases when a live embryo, a high initial β-hCG level, or a large adnexal mass is present.

- **Follow-up after methotrexate** includes measurement of β-hCG on days 4 and 7 after the single dose.
- The day 4 level is usually increased over baseline due to lysis of trophoblast.
- The day 7 level should be at least 15% less than the day 4 level or the dose may be repeated. Repeat dosing may also be required if β-hCG levels increase or plateau.
- Levels of β-hCG should be followed weekly until reaching a non-pregnant level (threshold will vary by laboratory).
- Surgical intervention is rarely required but may be needed to manage severe pain, hemorrhage, or treatment failure.

Table 7-4 Methotrexate for Ectopic Pregnancy

	Single-dose regimen	Multidose regimen
Protocol	50 mg/m² IM	1 mg/kg IM days 1, 3, 5, 7 until β-hCG drops Leucovorin 0.1 mg/kg days 2, 4, 6, 8
Follow-up	β-hCG days 4, 7, then weekly	β-hCG each day until >15% drop, then weekly
Success rate	88% 70% single dose 85% two doses	93% 10% single dose 25% two doses 50% ≥4 doses
Side effects	10%–25%	15%–35%

Preterm Labor

Risk factors for preterm labor

1. Twin pregnancy
2. Uterine abnormalities
3. Vaginal fibronectin
4. Age and race: increased age will increase the incidence of preterm labor. Black people have a short gestational period and their infants are of lower weight per week of age
5. Prior preterm labor
6. Urinary tract infection (UTI)
7. Bacterial vaginosis

8. Vaginal pH >4.5

Signs of preterm labor

- Uuterine contractions and cramps
- Vaginal discharge
- Bleeding
- Backache
- Leaking of amniotic fluid

Treatment of preterm labor

1. Bed rest

2. Hydration: 500 ml of balanced electrolyte solution, such as Ringers lactate IV over 30 min.peroid. Hydration is continued at a rate of at least 125 ml/hour.

3. Tocolytics

A. Magnesium sulfate: as high conc. have been shown to decrease uterine activity. The dose is 6 g IV as bolus dose in 250 ml of sol. over 30 min. period; the infusion is then maintained at 2-4 g /hr.

B. β- Mimetic drugs: like ritodrine as it causes uterine relaxation is administered IV and slowly titrated upward until a response is achieved. The dose is 100 µ /min. IV, with increases of 50 µ/min.every 10 min to a max of 350ug/min.

4. Glucocorticosteroid: these drugs are administered for the reduction of respiratory distress syndrome in preterm infants. The mechanism by which these drugs decrease lung disease is enzyme induction in type II pneumocytes of increased production of surfactant, which in turn reduces alveolar surface tension. All women between 24 and 34 weeks of pregnancy at risk for preterm delivery are candidates for antenatal corticosteroid therapy.

Treatment should consist of either tow doses of 12 mg of Betamethasone IM 24 hours apart or 4 doses of 6 mg of Dexamethasone IM 12 hours apart. Some benefit begins at 24 hours, with a maximum benefit at 48 hours after imitation of therapy and lasting for 7 days. Treatment is given weekly until fetal maturity.

5. *Group B Streptococcus treatment:* Premature infants are very susceptible to early GBS infections. So the use of Pencillin is recommended.

6. Calicum Channel Blockers: these drugs have been used for preterm labor as Nifedipine, Nicardipine and Verapamil as they inhibit contractions. Dosage of nifedipine is 10-20 mg every 4-6 hours orally sublingually in the first hour, followed by 60-160 mg/day of slow-release nifedipine.

Prevention of pre-term labor

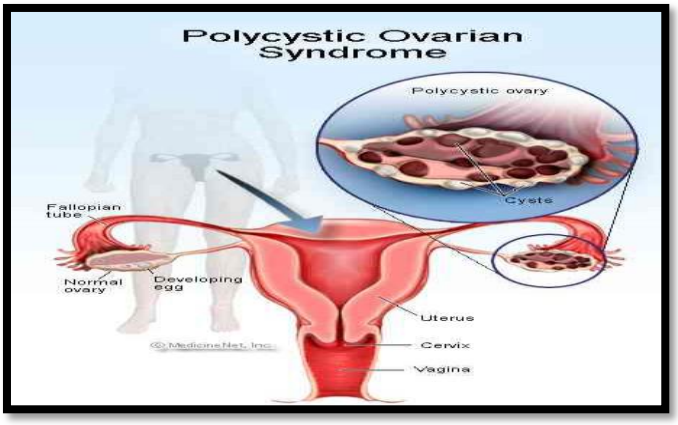
- Progesterone
- Studies have demonstrated that progesterone given to women with a *history of spontaneous preterm birth* can effectively decrease the incidence of recurrent preterm birth in a subsequent pregnancy.
- The optimal formulation for this indication has not been identified, but the most commonly used agent, based on data from the largest clinical trial, is 17-Hydroxyprogesterone caproate.
- Dose: 250 mg IM weekly initiated at 16 to 20 weeks of gestational age and continued until 37.

Part –B-

Gynecology

Poly Cystic Ovary Syndrome

- Polycystic ovary syndrome (PCOS), previously known as Stein-Leventhal syndrome, is a disorder in which numerous benign cysts form on the ovaries under a thick, white covering.
- It is most common in women under 30 years old.
- Elevated serum LH concentrations and an increased serum LH: FSH ratio result either from an increased GnRH hypothalamic secretion or less likely from a primary pituitary abnormality. This results in dysregulation of androgen secretion and increased intraovarian androgen, the effect of which in the ovary is follicular atresia, maturation arrest, polycystic ovaries, and anovulation.
- Hyperinsulinemia is a contributing factor to ovarian hyperandrgenism, independent of LH excess. A role for insulin growth factor (IGF) receptors has been postulated for the association of PCOS and DM. Imbalance of these hormones prevents the ovaries from releasing an egg each month. It also results in an increased production of the male hormone testosterone by the ovaries.



Symptoms of PCOS

- Amenorrhea (no menstrual period), infrequent menses, and/or oligomenorrhea (irregular bleeding).

- Oligo or anovulation (infrequent or absent ovulation).
- Hyperandrogenism.
- Infertility
- Cystic ovaries
- Enlarged ovaries.
- Obesity or weight gain.
- Insulin resistance, hyperinsulinemia, and diabetes.
- Dyslipidemia (lipid abnormalities).
- Hypertension.
- Hirsutism.
- Alopecia
- Acne/Oily Skin/Seborrhea
- Acanthosisnigricans (dark patches of skin, tan to dark brown/black).

Diagnoses

A. *Biochemical analysis:* Fasting comprehensive biochemical and lipid panel,2-hour GTT with insulin levels (also called IGTT), LH:FSH ratio, serum total testosterone level, Sex Hormone Binding Globulin (SHBG) level, serum androstenedione level, serum prolactin level and serum TSH, T4,T3 level.

B. *Imaging studies:* pelvic U/S (or CT scan) reveals the presence of 2-fold-5-fold ovarian enlargement with a thickened tunica albuginea, thecal hyperplasia, and 20 or more subcapsullar follicles from 1-15 mm in diameter.

Treatment

1. ***Metabolic derangements***: diet and exercise in patients with PCOS who are obese, endocrine-metabolic parameters markedly improve after 4-12 weeks of dietary restriction. Their SHBG levels rise and free testosterone levels fall by 2-fold. Serum insulin and IGF-1 levels also decrease. Weight loss in patients with PCOS who are obese is associated with a reduction of hirsutism and a return of ovulatory cycles in 30% of women. A moderate amount of daily exercise increases of levels of IGF-1 binding protein and decreases IGF-1 levels by 20%. Modest weight loss of 2-5% of total body weight can help restore ovulatory menstrual periods in obese patients with PCOS. A daily 500-1000 calorie deficit with 150 minutes of exercise per week can cause ovulation.

Investigational Therapies

- New evidence suggests that using medications which lower insulin levels in the blood may be effective in restoring menstruation and reducing some of the health risks associated with PCOS.
- Lowering insulin levels also helps to reduce the production of testosterone, thus diminishing many of the symptoms associated with excess testosterone: hair growth on the body, alopecia (scalp hair loss), acne, and, possibly, cardiovascular risk.
- Metformin improves insulin resistance and decrease hyperinsulinemia in patients with PCOS. The usual starting dose is 500 mg given orally twice a day. A decrease in body fat will lower the conversion of androgens to esterone thereby help restore ovulation.
- Pioglitazone (Actos®) and Rosiglitazone (Avandia®) are insulin-sensitizing agents that improve glucose tolerance and insulin resistance.

2. ***Anovulation:*** metformin can reduce hyperinsulinemia and hyperandrogenemia in PCOS. Metformin combined with clomiphene resulted in ovulation in 76% of patients compared with 42% in patients who received clomiphene alone. Metformin also has a small but beneficial effect on metabolic syndrome at a dose of 500 mg 3 times daily for 3-6 months. Management of unfertilized patients with PCOS includes the usage of clomiphene. Other, more aggressive, treatments for infertility (including injection of gonadotropin hormones and assisted reproductive technologies) may also

be required in women who desire pregnancy and do not become pregnant on clomiphene therapy.

3. Hirsutism

A. *Hair removal:* short-term non-pharmacologic treatments of hirsutism include shaving and use of chemical depilatories and/or bleaching cream.. Weight reduction decreases androgen production in women who are obese; therefore, losing weight can slow hair growth.

B. *Oral contraceptives*: women who do not wish to become pregnant can be effectively treated for hirsutism with oral contraceptives. Oral contraceptives slow hair growth in 60-100% of women with hyperandrogenemia. Therapy can be started with a preparation that has a low dose of estrogen and a nonandrogenic progestin. Preparations that have norgestrel and levonorgestrel should be avoided because of their androgenic activity.

C. *Spironolactone:* antiandrogens, such as spironolactone, are effective for hirsutism. Spironolactone 50-100 mg twice daily is an effective primary therapy for hirsutism. Because of its potential teratogenic effects, spironolactone should be prescribed with an oral contraceptive. Adverse effects of spironolactone include GI discomfort, and irregular menstrual bleeding (which can be managed by adding an oral contraceptive).

D. *Flutamide:* 250 mg daily or finasteride 5 mg daily.

E. *Eflornithine:* Eflornitliine (Vaniqa®) is a topical cream that can be used to slow the hair growth. Eflornithine works by inhibiting ornithine decarboxylase, which is essential for the rapidly dividing cells of hair follicles.

4. Menstrual irregularity : this is treated with an oral contraceptive, which not only inhibits ovarian androgen production but also increases SHBG production.

5. Surgical Care: surgical management is aimed mainly at restoring ovulation.

Placental problems

Role of placenta

The placenta is an organ that develops in the uterus during pregnancy. This structure provides oxygen and nutrients to the growing baby and removes waste products from the baby's blood. The placenta attaches to the wall of the uterus, and the baby's umbilical cord arises from it. In most pregnancies, the placenta attaches at the top or side of the uterus.

Factors affect placental health

Various factors can affect the health of the placenta during pregnancy, some modifiable and some not. For example:

- **Maternal age.** Certain placental problems are more common in older women, especially after age 40.
- **Premature rupture of the membranes.** During pregnancy, baby is surrounded and cushioned by a fluid-filled membrane called the amniotic sac. If the sac leaks or breaks before labor begins, the risk of certain placental problems increases.
- **High blood pressure.** High blood pressure can affect the placenta.
- **Twin or other multiple pregnancy.** pregnant with more than one baby, might be at increased risk of certain placental problems.
- **Blood-clotting disorders.** Any condition that either impairs blood's ability to clot or increases its likelihood of clotting increases the risk of certain placental problems.
- **Previous uterine surgery.** If woman had a previous surgery on her uterus, such as a C-section or surgery to remove fibroids, she at increased risk of certain placental problems.
- **Previous placental problems.** A placental problem during a previous pregnancy might be at increased risk of experiencing it again.
- **Substance abuse.** Certain placental problems are more common in women who smoke or use illegal drugs, such as cocaine, during pregnancy.
- **Abdominal trauma.** Trauma to the abdomen — such as from a fall or other type of blow to the abdomen — increases the risk of certain placental problems.

The most common placental problems

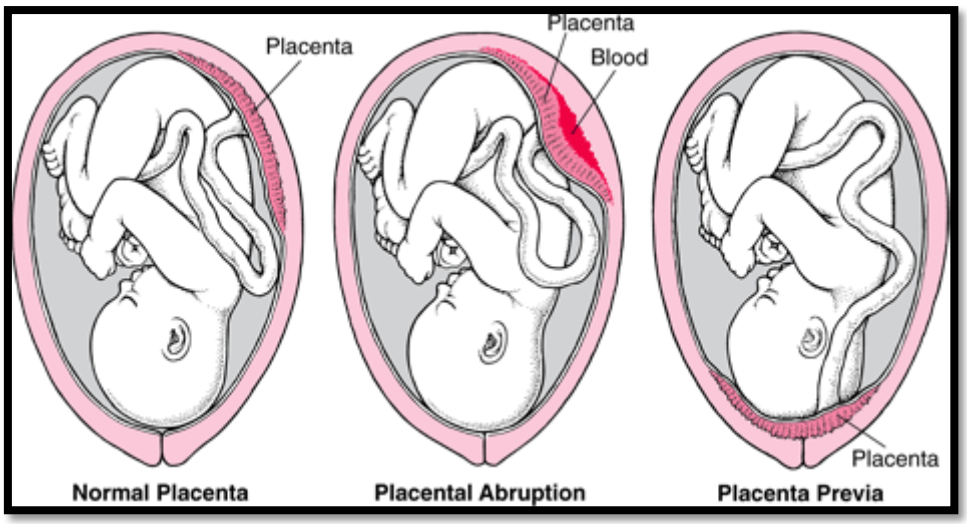
During pregnancy, the most common placental problems include placental abruption, placenta previa and placenta accreta. These conditions can cause potentially heavy vaginal bleeding. After delivery, retained placenta is also sometimes a concern.

- **Placental abruption (abruptio placentae).** If the placenta peels away from the inner wall of the uterus before delivery — either partially or completely — it's known as placental abruption. Placental abruption can cause varying degrees of vaginal bleeding and pain or cramping. It might also deprive the baby of oxygen and nutrients. In some cases, early delivery is needed.

- **Placenta Previa.** This condition occurs when the placenta partially or totally covers the cervix — the outlet for the uterus. Placenta previa is more common early in pregnancy and might resolve as the uterus grows. Placenta previa can cause severe vaginal bleeding before or during delivery. A C-section delivery usually is required if the placenta previa is present at the time of delivery.

- **Placenta accreta.** This condition occurs when the blood vessels of the placenta grow too deeply into the uterine wall. Placenta accreta can cause vaginal bleeding during the third trimester of pregnancy and severe blood loss after delivery. Treatment might require a C-section delivery followed by surgical removal of the uterus (abdominal hysterectomy). More-aggressive forms of this problem can also occur if the placenta invades the muscles of the uterus (placenta increta) or if the placenta grows through the uterine wall (placenta percreta).

- **Retained placenta.** If the placenta isn't delivered within 30 to 60 minutes after childbirth, it's known as retained placenta. Retained placenta might occur because the placenta becomes trapped behind a partially closed cervix or because the placenta is still attached to the uterine wall — either loosely (adherent placenta) or deeply (placenta accreta). Left untreated, a retained placenta can cause severe infection or life-threatening blood loss in the mother.



Female infertility

According to the World Health Organization (WHO), infertility can be described as the inability to become pregnant, maintain a pregnancy, or carry a pregnancy to live birth.[3] A clinical definition of infertility by the WHO is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse."

Infertility can further be broken down into primary and secondary infertility. Primary infertility refers to the inability to give birth either because of not being able to become pregnant, or carry a child to live birth, which may include miscarriage or a stillborn child. Secondary infertility refers to the inability to conceive or give birth when there was a previous pregnancy or live birth.

Factors Affect Fertility:

Hypothalamic-pituitary factors

- Hypothalamic dysfunction
- Hyperprolactinemia

Ovarian factors

- Chemotherapy with certain agents has a high risk of toxicity on the ovaries.

- Polycystic ovary syndrome
- Anovulation. Female infertility caused by anovulation is called "anovulatory infertility", as opposed to "ovulatory infertility" in which ovulation is present.
- Premature menopause
- Menopause
- Luteal dysfunction
- Gonadal dysgenesis (Turner syndrome)
- Ovarian cancer

Tubal (ectopic)/peritoneal factors

- Endometriosis
- Pelvic adhesions
- Pelvic inflammatory disease (PID, usually due to chlamydia)
- Tubal occlusion
- Tubal dysfunction
- Previous ectopic pregnancy

Uterine factors

- Uterine malformations
- Uterine fibroids
- Asherman's Syndrome
- Implantation failure without any known primary cause. It results in negative pregnancy test despite having performed e.g. embryo transfer.

Previously, a bicornuate uterus was thought to be associated with infertility, but recent studies have not confirmed such an association.

Cervical factors

- Cervical stenosis
- Antisperm antibodies
- Non-receptive cervical mucus

Vaginal factors

- Vaginismus
- Vaginal obstruction

Appendix

Some drugs used in obstetrics and gynecology

Drug name	***Trdae name®***	***Indications***	***Mechanism of action***	***Dosage form(s)***	***Dose and duration of therapy***
Clomifene	*Clomide*	*Anovulatory infertility*	*Antiesterogenic action (partial esterogen agonist)*	*50mg/tab.*	*1 tab. Daily for 5 days starting within about 5th day of the cycle*
Tamoxifen	*Nolvadex*	*Anovulatory infertility, breast cancer(BC)*	*Antiesterogenic action (partial estradiol inhibitor)*	*10, 20 mg/ tab.*	*Infertility: 20 mg/day on days 2,3,4,5 of the cycle; 20/day in BC*
Letrozole	*Femara*	*BC in postmenopausal women*	*Aromatase inhibitor (an enzyme required for esterogen synthesis)*	*2.5 mg/ tab*	*1 tab./day*
Human Chorionic Gonadotophin(hCG)	*Pregnyl*	*Infertility in women with hypopitutarism*	*Increase FSH, LH secretion cause induction of ovulation*	*1500,5000 mg/amp.*	*By IM use according to patient´s response*
Human Menopausal Gonadotrophins(hMG) contain	*Pergonal*	*Women infertility with hypopitutarism*	*Stimulant of FSH , LH to stimulate the ovaries to produce eggs*	*FSH 75 units, LH 75 units/vial*	*By IM use according to patient´s response*

FSH, LH					
FSH	*Gonal –F*	*Women infertility with hypopitutarism*	*Stimulant of FSH to stimulate the ovaries to produce egg*	*FSH 75 units units/vial*	*By IM, SC use according to patient´s response*
Bromocriptin	*Parlodel*	*Treatment of hypogonadism , galactorrhea , infertility*	*Stimulate dopamine receptors and reduce prolactine release*	*2.5 mg/tab.*	*1-2 times daily at bed time and increased gradually according to patient´s response*
Cabergolin	*Dostinex*	*Same as bromocriptine*	*Same as bromocriptine*	*0.5mg/tab.*	*1 mg/week as asingle dose or 2 divided doses in different days*
Goseleine	*Zoladex*	*Endomertiosis and BC*	*Gondorelin analogue stimulate the production of estrogen which then suppressed by body´s feedback mechanism*	*3.6 mg/syringe*	*By S.C. inj. 3.6 mg/28 day(max. 6 months)*
Leuprorelin	*Lupron depot*	*Endomertiosis and BC*	*Gondorelin analogue stimulate the production of*	*3.75 mg /1 ml syringe*	*By S.C. inj. 3.75 mg as a single dose repeat*

			estrogen which then suppressed by body´s feedback mechanism		*monthly (max. 6 months)*
Medroxyprogesterone	*Provera, Depoprovera*	*Contraception, endometriosis*	*A progersteronean algoue*	*2.5, 5 ,10 mg/tab.; 150 mg/ml inj.*	*1-2 tab tid ; deep IM inj. Within 5 days of cycle and last for 12 weeks.*
Northisterone	*Primolute - N*	*HRT, Contraception, endometriosis*	*A progersteronean algoue*	*5 mg/tab.*	*2-3 tab./day in divided doses*
Conjugated esterogen	*Premarin*	*Menopausal symptoms, osteoporsis prophylaxis, HRT*	*A mixture of esterogen hormones substitute the loss of esterogen and alleviates the menopausal symptoms*	*6.25, 1.25 mg/tab.*	*1 tab. /day*
Estradiol + progesterone	*Trisequens*	*Menopausal symptoms, osteoporsis prophylaxis, HRT*	*esterogen hormones substitute the loss of esterogen and alleviates the menopausal symptoms, progestine(reduce the esterogen-*	*12 blue estradiol 2 mg; 10 whilte estradiol 2mg and northisteron 1mg; 6 red estradiol 1*	*blue tab./day from day 5 of the cycle then 1 tab. day in sequence*

			induced risk of endometriosis),selective inhibition of pituitary function results in ovulation inhibition	*mg*	
Dydrogesteron	*Duphastone*	*Recurrent miscarriage, endometriosis*	*A progesterone analogue*	*10 mg/tab.*	*2-3 tab./day*
Progesterone	*Cyclogest pessaries; Gemstone inj.; Crinone vaginal gel*	*Cyclogest : premenstrual syndrome and natal depression; Gestone : recurrent miscarriage due to inadequate luteal phase; Crinone : infertility due to inadequate luteal phase*	*Its action on the womb lining causes it to thicken in preparation for the fertilized egg to implant; it supports the placenta and prevents the uterus from spontaneously aborting the fetus*	*Cyclogest: 200,400 mg pessaries; Gestone: 50 mg/ml amp.; Crinone 90 mg/aaplication*	*Cyclogest :200-400mg vaginally or rectally; Gestone deep IM inj. 5-10 mg/day for 5-10 days; Crinone: 1 application vaginally*
Methylergometrine	*Methergin*	*Induction of utrinecontactions and minimize postpartum haemorrhae*	*Ergot alkaloid act as blood vessels constrictor to decrease mother blood loss*	*0.5 mg/tab.; 0.5 mg/ml amp.*	*By IM inj. According to patient´s condition*

Tranxemic acid	*Cyklokapron*	*Reduce haemorrhage and stop vaginal bleeding*	*Antifibrinolytic agent stops bleeding*	*500 mg/tab.; 100 mg/ml amp.*	*2-3 times /day according to the case*
Oxytocin	*Pitocin*	*Induce labour*	*A hormone release from the posterior lob of pituitary to induce utrine contractions*	*5 units/ml amp., 10 units/ml amp.*	*By slow IV inj. According to patient´s condition*
Misopristol	*Cytotec*	*Induce medical abortion*	*PG cause vaginal bleeding*	*0.2 mg/tab.*	*By mouth or vaginal route according to the case*
Isoxsopurine	*Duvadilan*	*Uterine relaxant*	*Vasodilator, increase blood flow*	*10,20 mg/tab.*	*1 tab.twice daily*
Danazol	*Danol*	*Endometriosis therapy; benign fibrocystic breast disease*	*A synthetic androgen hormone, inhibit pituitary gonadotropins(ES and PG)*	*100,200 mg/ cap*	*Endometriosis 200-800 mg in divided doses; BC 300 mg in divided doses*

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