

## History of the Patient

**A- Patient demography:** (age, weight and height).

**B- Obstetric history:** this required definition of some terms:

**1- Parity:** is the number of live birth at any age or stillbirth after 24 weeks of gestation<sup>(1)</sup>.

**2- Nullipara:** describes a woman who has never delivered a fetus or fetuses beyond 20 weeks of gestation<sup>(2)</sup>.

**3- Multipara:** describes a woman who has had two or more deliveries past 20 weeks of pregnancy<sup>(2)</sup>.

**4- Gravida:** is the total number of pregnancies regardless of how they ended<sup>(1)</sup> (abortion, ectopic, normal pregnancy, hydatiform mole)<sup>(2)</sup>.

**5- Nullgravida:** a woman who has never been pregnant<sup>(2)</sup>.

**6- Primigravida:** a woman who has been pregnant once<sup>(2)</sup>.

e.g. a woman who has had two spontaneous abortions and three normal intrauterine pregnancies may be described as G<sub>5</sub> P<sub>3</sub> A<sub>2</sub>.

**C-Usual menstrual cycle history**<sup>(2)</sup>

1- Age when period began (menarchae).

2- Regularity of cycle.

3- Duration of each period, length of cycle and first day of last period.

e.g. 13 5/28 regular: meaning that the period began at age of 13 years, last for 5 days and occur every 28 days.

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## An Overview of Pregnancy<sup>(3)</sup>

**A- Signs and symptoms associated with pregnancy:**

The signs of pregnancy can vary. Early signs can include nausea, breast tenderness, frequent urination, fatigue and headaches. Later signs can include heartburn, backache, constipation and fatigue.

**1- Nausea and vomiting:** Nausea predominantly affects women during the first three months of pregnancy. Hormonal changes are an attributing factor. **Hyperemesis gravidarum** is an extreme form of vomiting in pregnancy which can result in admission to hospital.

2- **Increased need to urinate:** An increased need to urinate occurs early on as well as during the last few weeks of pregnancy when it is caused by the increased pressure on the bladder from the uterus.

3- **Headache:** Headache occurs more frequently in pregnancy.

4- **Feeling hot and sweaty** because of increased cardiac output and peripheral vasodilation.

5- **Dizziness and fainting.**

6- **Fatigue.**

7- **Varicose veins and hemorrhoids.**

8- **Epistaxis:** Epistaxis (nose bleeding) is more common in pregnancy, but is generally not serious.

9- **Hypertension and pre-eclampsia** (see page 15).

10- **Thromboembolism:** Thromboembolism is six times more likely in pregnancy and it is the leading cause of maternal death in the United Kingdom. Around half of cases occur in the first three months of pregnancy.

11- **Oedema:** Oedema is common in normal pregnancies, affecting more than 80 per cent of women.

12- **Breathlessness.**

13- **Heartburn:** Heartburn is particularly common in the later stages of pregnancy.

14- **Appetite and weight gain:** In the early stages, appetite may be lost but the majority of pregnant women will experience increased appetite at some stage during their pregnancy. Many women also develop cravings or aversions for certain foods. Weight gain averages around 12kg.

15- **Constipation and haemorrhoids.**

16- **Backache.**

17- **Leg cramp** is common in pregnancy, mostly at night.

18- **Hyperpigmentation** and stretch marks increased pigmentation is probably due to hormonal changes. This diminishes after pregnancy.

## **B- Prenatal period**

1- Pregnancy is usually divided into **three trimesters** each one approximately 13 weeks<sup>(2)</sup>.

2- Prenatal period is the development of the baby in the uterus and it is approximately 40 weeks. This is divided into<sup>(2)</sup>:

A- **Embryonic period:** is the first 8 weeks.

B- **Fetal period:** during 9-26 weeks.

C- **Perinatal period:** from 27 week till delivery.

## C- EDD

The EDD is calculated by adding nine calendar months and seven days (around 280 days in total) to the date of the first day of the last menstrual period (LMP)<sup>(3)</sup>. (the period from fertilization of the ovum to birth is given as 40 weeks from LMP (gestation being regarded as 38 weeks)<sup>(4)</sup>.

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### Some Commonly Used Abbreviations in Obstetrics

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

References:

1- Geoffrey Chamberlain. Obstetric by Ten Teachers. 8<sup>th</sup> edition. 2006.

2- Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.

3- Melanie Every, and Claire Hallam . Overview of Pregnancy. The Pharmaceutical Journal (Vol. 270) 8 February 2003. Pages: 194-196.

4-Pregnancy care. Chemist & Druggist 14 June 2003 . pages: 19-22.

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## Screening Tests and Investigations

### 1- Pregnancy Tests

The urine test rely on the detection of human chorionic gonadotropin (HCG) produced by the placenta. hCG levels increase shortly after implantation<sup>(1)</sup> (expected to become positive 3 days after implantation<sup>(2)</sup>), approximately double every 48 hours, reach a peak at 50-75 days, and fall to lower levels in the second and third trimesters. Laboratory and home pregnancy tests use antibodies specific for hCG. These tests are performed on urine <sup>(1)</sup>, (first morning specimen is recommended <sup>(2)</sup>) and are accurate at the time of the missed period or shortly after it<sup>(1)</sup>.

### 2- Ultrasound

A- **Transvaginal ultrasound:** is commonly used during the first trimester to determine accurate date of pregnancy as well as fetal location and number, placenta location in relation to internal cervical os<sup>(3)</sup> (a low-lying placenta may complicate birth<sup>(4)</sup>) and also to determine the cervical length to identify patient at risk of preterm labor<sup>(3)</sup>.

**B- Transabdominal ultrasound:** Is utilized after 16 weeks of gestation<sup>(3)</sup> (At this point the fetus is sufficiently large for all the major systems to be examined for any defects<sup>(4)</sup>) to evaluate the fetus for structural abnormality and provide information about fetal well being. In the third trimester, transabdominal ultrasound is useful in assessing fetal growth, fetal heart rate evaluation, fetal breathing activity, fetal movement and amniotic fluid<sup>(3)</sup>.

**C- Doppler sonography** which can precisely record fetal heart pulsation<sup>(3)</sup> and measure the velocity profile of blood flowing through fetal vessel, and allows for characterizing of vascular impedance<sup>(3)</sup>. An abnormal test signifies that the fetus is growth-retarded due to uteroplacental insufficiency<sup>(4)</sup>.

### 3- Alpha-feto-protein test

### 4- Amniocentesis

### 5- Chorionic villus sampling (CVS)

### 6- Laparoscopy

#### References:

- 1-Lawrence M. Tierney. Current Medical Diagnosis & Treatment, 45<sup>th</sup> edition (2006)
  - 2-Frances Fischbach. A manual of laboratory and diagnostic tests. 6<sup>th</sup> edition. 2000
  - 3-Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.
  - 4-Melanie Every, and Claire Hallam . Overview of pregnancy. The Pharmaceutical Journal (Vol. 270) 8 February 2003. Pages: 194-196.
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## Abortion (Miscarriage)

**Abortion:** Is the termination (spontaneous or induced) of established pregnancy before 20 weeks of gestational age<sup>(1)</sup>.

More than 60% of spontaneous abortions result from chromosomal defects due to maternal or paternal factors; about 15% appear to be associated with maternal trauma, infections, dietary deficiencies, diabetes mellitus, hypothyroidism, or anatomic malformations. There is no reliable evidence that abortion may be induced by psychic stimuli such as severe fright, anger, or anxiety. In about one-fourth of cases, the cause of abortion cannot be determined <sup>(2)</sup>.

**Note:** By the ultrasonographic examination, the gestational sac can be identified at 5-6 weeks from the LMP, a fetal pole at 6 weeks, and fetal cardiac activity at 6-7 weeks. Serial observations are often required to evaluate changes in size of the embryo. A small, irregular sac without a fetal pole with accurate dating is diagnostic of an abnormal pregnancy<sup>(2)</sup>.

### Types of abortion:

#### 1- Threatened (مهدد) abortion:

A- It refers to intrauterine bleeding before the 20<sup>th</sup> week of gestation, with or without uterine contraction, without cervical dilatation (i.e. closed cervix), and without

expulsion of the products of conception (POC)<sup>(3)</sup>. The pregnancy continues<sup>(2)</sup>, but about 25-50% of threatened abortions eventually result in loss of pregnancy<sup>(1)</sup>.

#### B-Management

1- Ultrasonic examination to determine whether the fetus is present if so, whether it is alive<sup>(1)</sup>.

2- Place the patient at bed rest for 24-48 hours<sup>(2)</sup> (or until 2 day after red loss has ceased<sup>(1)</sup>) followed by gradual resumption of usual activities, with abstinence from coitus and douching. Hormonal treatment with progesterone is contraindicated<sup>(2)</sup> (controversial)<sup>(3)</sup>. Other therapy (e.g., tocolytics) is even more questionable<sup>(3)</sup>.

3- If the patient is anxious and restless, diazepam 2 mg TID is recommended<sup>(1)</sup>.

### 2- Inevitable (حتمي) abortion:

A- It is the intrauterine bleeding before the 20<sup>th</sup> gestational week, with continued cervical dilatation but without expulsion of the POC<sup>(3)</sup>.

The passage of the products of conception is considered inevitable<sup>(2)</sup>.

#### B- Management

1- The uterus usually expels its content unaided<sup>(1)</sup>.

2- Analgesic such as Pethidine 100 mg may be injected<sup>(1)</sup>.

3- If bleeding is heavy Ergometrine 500 mcg can be given<sup>(1)</sup>.

### 3- Incomplete abortion:

A- It is the expulsion of some but not all of the POC before the 20<sup>th</sup> gestational week<sup>(3)</sup>.

Some portion of the POC (usually placental) remains in the uterus. Only mild cramps are reported, but bleeding is persistent and often excessive<sup>(2)</sup>.

#### B- Management

1- Insert IV line for fluid therapy or blood transfusion to prevent complication<sup>(1)</sup>.

2- Prompt removal (under appropriate pain control) of any products of conception remaining within the uterus is required to stop bleeding and prevent infection<sup>(2)</sup>.

### 4- Complete abortion

It is the expulsion of all the POC before the 20<sup>th</sup> gestational week. Pain ceases, but spotting may persist for a few days<sup>(3)</sup>.

### 5- Missed abortion

A- Missed abortion occurs when the embryo dies but the POC are retained in the uterus for several weeks or months<sup>(1)</sup>.

Symptoms of pregnancy disappear. There is a brownish vaginal discharge but no free bleeding. Pain does not develop<sup>(2)</sup>.

#### B- Management

1- Evacuate the conception surgically by aspiration is the method of choice for a missed abortion<sup>(2)</sup>.

2- Prostaglandin E2 vaginal suppositories are an effective alternative<sup>(2)</sup>.

## 6- Recurrent (Habitual:معتاد) abortion

It is the spontaneous, consecutive (تعاقب) loss of 3 or more nonviable pregnancies<sup>(3)</sup>.

Recurrent abortion occurs in about 0.4-0.8% of all pregnancies. Abnormalities related to recurrent abortion can be identified in approximately half of the couples. If a woman has lost three previous pregnancies without identifiable cause, she still has a 70-80% chance of carrying a fetus to viability. If she has aborted four or five times, the likelihood of a successful pregnancy is 65-70%. Recurrent abortion is a clinical rather than pathologic diagnosis. The clinical findings are similar to those observed in other types of abortion (see above)<sup>(2)</sup>.

### Treatment

#### A. Preconception therapy<sup>(2)</sup>:

Preconception therapy is aimed at detection of maternal or paternal defects that may contribute to abortion. A thorough general and gynecologic examination is essential.

1- Polycystic ovaries should be ruled out.

2- A random blood glucose test and thyroid function studies (including thyroid antibodies) should be done.

3- Detection of lupus anticoagulant and other hemostatic abnormalities (proteins S and C and antithrombin III deficiency) and an antinuclear antibody test may be indicated.

4- Endometrial tissue should be examined to determine the adequacy of the response of the endometrium to hormones.

5- The hysteroscopy or hystero-graphy used to exclude congenital anomalies.

6- Chromosomal analysis of both partners rules out balanced translocations (found in 5% of infertile couples).

#### B. Postconception Therapy

Provide early prenatal care and schedule frequent office visits. Complete bed rest is justified only for bleeding or pain. Empiric sex steroid hormone therapy is contraindicated<sup>(2)</sup>.

### Prognosis:

The prognosis is excellent if the cause of abortion can be corrected<sup>(2)</sup>.

### References:

1- Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.

2- Lawrence M. Tierney. Current Medical Diagnosis & Treatment, 45<sup>th</sup> edition (2006).

3- Martin L. Pernoll, M.D. Benson & Pernoll's. Handbook of Obstetric and Gynecology. 10<sup>th</sup> edition 2001.

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## Teratogenicity of Drugs

Congenital malformations can be defined as: non-reversible functional or morphological defects present at birth.

### The Risk of Teratogenicity

Several factors determine the effects teratogenic drugs may have on the fetus during pregnancy, (Table 1).

The duration of exposure and gestational age at exposure are very critical in the determination of teratogenic potential. During the period from conception to 2 weeks, there is a relative resistance to drug effects. Usually exposure during

Table 1<sup>(1)</sup>.

#### Factors That Determine the Effects of Teratogens

- 1-Dose reaching fetus
- 2-Point in development when drug exposure occurs
- 3-Duration of exposure
- 4-Environmental factors
- 5-Susceptibility of the fetus

this time produces an “all or none” effect; that is, the zygote dies from exposure to the teratogen, or it is unaffected. The remainder of the first trimester is the most critical time for organ malformation<sup>(1)</sup>. Weeks 4 through 10, the period referred to as embryogenesis or organogenesis, is the most likely time for major congenital malformations to occur. Unfortunately, this is also a time when many women are unaware of their pregnancy. Drugs that reach the embryo at this point may produce abortion, no effect at all, an anatomic defect (teratogenesis), or a subtle metabolic or functional defect that may not be detected until later in life. During the second and third trimester, known as fetogenesis, drugs are less likely to be associated with major malformations, but they may influence neurologic development, growth, physiologic and biochemical functioning, mental development, and reproduction. Little is known about the exact time of the greatest risk for teratogenesis<sup>(1)</sup>.

### Teratogenic Effects

The most common teratogenic effects attributed to drugs are shown in table 2.

Some drugs, such as warfarin, phenytoin, and alcohol, cause a group of effects specific for exposure to that agent (Fetal warfarin syndrome, fetal alcohol syndrome, and fetal hydantoin syndrome).

**FDA Classifications of Drug Risk**  
The Food and Drug Administration (FDA) instituted a rating system for drugs marketed after 1980 based upon their safety for use in pregnancy<sup>(1)</sup>. These categories are listed in Table 3.

Table 2<sup>(1)</sup>.

#### Effects of Teratogens on the Fetus

- 1-Spontaneous abortion
- 2-Defects in development
- 3-Malformations (major or minor)
- 4-Intrauterine growth retardation
- 5-Mental retardation
- 6-Carcinogenesis
- 7-Mutagenesis (causing genetic mutation)

## Known Teratogens and Their Effects

The most recognized teratogens and the most dangerous time for exposure during pregnancy are shown in table 4. For more specific information on teratogenic potential or safe use during pregnancy, the reader is referred to reference no. 2.

### Social Drugs:

Social or recreational drugs such as alcohol, caffeine, and nicotine may also be part of fetal exposure.

1- The heavy use of alcohol during pregnancy has been shown to lead to fetal alcohol syndrome, a pattern of defects including craniofacial defects, mild to moderate retardation, growth retardation, cardiac defects, and skeletal abnormalities. Since there are no known safe levels of alcohol during pregnancy, pregnant women should stop drinking alcohol completely during this period<sup>(1)</sup>.

2- Caffeine has not proven to have a direct teratogenic effect in humans. Studies of caffeine use have suggested that heavy use (more than 7 or 8 cups of coffee daily) may be associated with perinatal complications, such as stillbirth, preterm birth, spontaneous abortion or low birth weight infants. The patients may be advised to limit their caffeine intake to perhaps one cup of coffee or its equivalent daily.

3- Smoking cigarettes has been linked to lower birth weight infants, and there may be an increased incidence of spontaneous abortion, stillbirth, preterm birth, and sudden infant death syndrome (SIDS) in the children of mothers who smoke during pregnancy.

Table 3 <sup>(1)</sup> .	
FDA Classification of Teratogenic Drug Risk	
Category	Description of Risk
A	No fetal risk shown in controlled human studies
B	No human data available and animal studies show no fetal risk or Animal studies show a risk but human studies do not show fetal risk
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)
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)
X	Risk to fetus clearly outweighs any benefits from these drugs

Table 4 <sup>(3)</sup>			
Known Teratogens and Their Effects			
No	Drug class	Trimester of Risk	Comment
1	ACE-I and Angiotensin-II receptor antagonists	1,2,3	Potential teratogen: cause renal tubular dysplasia, skull hypoplasia & oligohydramnios.
2	Alcohol	1, 2	Regular use is teratogen (cause fetal alcohol syndrome )
3	Aminoglycoside	2,3	Potential damage of VIII cranial nerve (auditory) might cause hearing loss.
4	Amiodarone	2, 3	Complication reported: hypothyroidism & neonatal goitre.

5	Androgens	1, 2, 3	Masculinisation of female fetus
6	Benzodiazepine	1,2, 3	Avoid regular use might cause neonatal withdrawal syndrome, hypothermia & hypotonia.
7	Beta-blockers	2, 3	May cause intra-uterine growth restriction, neonatal hypoglycaemia, and bradycardia.
8	Carbamazepine	1, 3	Teratogen risk of neural tube defect (NTD) & risk of neonatal hemorrhage due to vitamin K deficiency.
9	Carbimazole	2, 3	Neonatal goitre and hypothyroidism, might cause fetal malformation
10	Chloroamphenicol	3	Neonatal gray syndrome
11	Iron (parenteral)	1	Avoid in first trimester.
12	Lithium	1,2,3	Congenital defect (tricuspid valve malformation).
13	NSAID	3	With regular use closure of fetal ductus arteriosus, pulmonary hypertension of newborn & delay duration of labor.
14	Methotrexate	1,2,3	Teratogenic.
15	Phenytoin	1,3	Congenital malformation (fetal hydantoin syndrome), vitamin K deficiency causing neonatal bleeding.
17	Quinolones	1,2,3	Avoid, erosion of cartilage and arthropathy
18	Statins	1,2,3	Avoid, congenital anomalies reported.
19	Sulfonylurea	3	Neonatal hypoglycemia.
20	Tetracycline	1,2,3	Affect skeletal development, result in permanent yellow-brown staining of teeth.
21	Valproic acid	1, 3	Risk of NTD, craniofacial anomalies.
22	VIT A High dose	1	Excessive doses (>25000U/day) may be Teratogen.
23	Warfarin	1, 2, 3	Teratogen, fetal and neonatal hemorrhage.

## References

- 1-Mary C. Gurnee, Mario F. Sylvestri, Teratogenicity of Drugs. US pharmacist.
- 2-Drugs in Pregnancy and Lactation. 6th ed. 2001. Briggs GG, et al. (ويتوفر على شكل CD)
- 3-BNF : 67.

## Common Complications of Pregnancy

### A- Liver and Gastrointestinal Diseases in Pregnancy

#### 1-Nausea and Vomiting

General Considerations: Nausea and vomiting begin soon after the first missed period and cease by the fifth month of gestation. Up to three-fourths of women complain from nausea and vomiting during early pregnancy, with the vast majority noting nausea throughout the day. This problem exerts no adverse effects on the pregnancy and does not presage other complications<sup>(1)</sup>.

Persistent, severe vomiting during pregnancy -hyperemesis Gravidarum- can be disabling and require hospitalization (can lead to metabolic acidosis, ketosis, hypovolemia, electrolyte disturbance & weight loss)<sup>(2)</sup>. Thyroid dysfunction can be associated with hyperemesis Gravidarum, so it is advisable to determine thyroid-stimulating hormone (TSH) and free T<sub>4</sub> values in these patients<sup>(1)</sup>.

## **Treatment**

A-Mild Nausea and vomiting: Reassurance and dietary advice (eating small but frequent meals, avoid greasy or spicy food, .....). Antiemetics, antihistamines, and antispasmodics are generally unnecessary to treat nausea of pregnancy. Vitamin B<sub>6</sub> (pyridoxine), 50-100 mg/d orally, is non-toxic and may be helpful in some patients<sup>(1)</sup>.

B- Hyperemesis gravidarum: Hospitalize the patient with complete bed rest<sup>(1)</sup>.

Protocol for the management of hyperemesis gravidarum includes:

A- Fluid therapy: Normal saline 1 L + 20-40 mmol KCl 8 hourly.

B- Anti-emetic therapy: possible regimens include<sup>(3)</sup> :

1- Cyclizine 50 mg orally, im, iv, tid.

Note: Novidoxine ® tablet contains 25 mg Cyclizine and 50 mg B6.

2- Prochlorperazine (stemetil®) 5 mg orally tid , or 12.5 mg im, iv, tid.

3- Metoclopramide (plasil ®) 10 mg orally, im, iv, tid.

4- Chlormpromazine (Largactil ®) 10-25 mg orally tid, or 25 mg im, tid.

5- Ondansetron 4-8 mg orally or iv q8h can be used for further refractory cases.

## **2- Gastro-esophageal Reflux Disease (GERD):**

About two-third of women experience GERD or heart burn during and commonly in third trimester. Reflux of gastric contents lead to heart burn (aggravated by meal and recumbent position), water brash and dyspepsia<sup>(3)</sup>.

Treatment

Non-pharmacological approach<sup>(2)</sup>.

1- Eating small but frequent meals

2- Avoid recumbent position especially after meal & to use extra pillow to elevate head when sleeping.

Pharmacological approach:

1- Antacid therapy (taken 1-3 hr after meal & at bed time)<sup>(2)</sup>.

2- Histamine 2-Receptor antagonists: like Ranitidine (Zantac) 150 mg BID in refractory case<sup>(2)</sup>.

3- Metoclopramide maybe helpful also<sup>(3)</sup>.

4-Proton Pump Inhibitors (PPI): like Omeprazole 20-40mg can be use and appear safe from limited data<sup>(3)</sup>.

## **3- Acid Aspiration Syndrome (Mendelson's Syndrome)<sup>(2)</sup>**

The pregnant patient in labor is at an increase risk of acid aspiration because of

1- Delay gastric emptying.

2- Increase gastric acidity.

3- Increase intra-abdominal & intragastric pressure.

These factors make regurgitation more likely.

Therefore women in the labor should be advised to eat light meal before coming to hospital.

Liquid antacid such as Maalox suspension is given every 3-4 hr during labor.

#### 4- Obstetric Cholestasis (Intrahepatic cholestasis of pregnancy):

This is a liver disease specific to pregnancy. Characterized by pruritus affecting the whole body but particularly the palms and soles, and abnormal liver function tests. It most commonly occurs in the third trimester of pregnancy and any woman with pruritus without rash should have liver function tests<sup>(3)</sup>

Management:

1- Current guideline suggest that in the absence of premature labour, delivery should be induced at 37-38 weeks<sup>(3)</sup>.

2- Vitamin K should be given to the mother (10 mg orally) from there time of diagnosis to reduce the postpartum hemorrhage<sup>(3)</sup>.

3- Control of symptoms may be achieved by a combination of antihistamines and emollient. And these are insufficient, Ursodeoxycholic acid (UDCA) (300 mg 2-3 times per day)<sup>(2,3)</sup>.

Following delivery, liver function tests return to normal. Recurrent of obstetric cholestasis is in subsequent pregnancies exceeds 90%<sup>(3)</sup>.

References:

1- Lawrence M. Tierney. Current Medical Diagnosis & Treatment, 45<sup>th</sup> edition (2006) .

2- Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.

3- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.

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#### B- Diabetes mellitus in pregnancy

The pregnancy may be complicated by maternal diabetes mellitus where:

A- Women with pre-existing diabetes (and are classified as either IDDM or NIDDM )

B- Those developing carbohydrate intolerance during pregnancy (usually during third trimester) and are classified as Gestational Diabetes Mellitus (GDM) <sup>(1)</sup>.

Diagnosis<sup>(2)</sup>:

The American Diabetes Association suggests the following targets for women who develop gestational diabetes during pregnancy. More or less stringent glycemic goals may be appropriate for each patient.

- Before meal (preprandial): 95mg/dl or less.
- 1 h after meal (postprandial): 140mg/dl or less.
- 2 h after meal (postprandial): 120mg/dl or less.

#### Complications of GDM

1- Fetal: Medical problems encountered in infants born to diabetic mothers (whether GDM or pre-existing g DM ) are shown in the following table 1 <sup>(3)</sup>:

**Table 1: Medical Problems Encountered in Infants Born to Diabetic Mothers**

1- Macrosomia (large babies: greater than 4 kg)

2- Hypoglycemia

3- Intrauterine growth retardation

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- 4- Late fetal death
- 5- Cardiomyopathy (asymmetric septal hypertrophy)
- 6- Pulmonary hypertension
- 7- Idiopathic respiratory distress syndrome (RDS)
- 8- Hyperbilirubinemia
- 9- Hypocalcemia and hypomagnesemia
- 10- Thrombosis and abnormal clotting

## 2-Maternal:

A- Complications of GDM to pregnant women include<sup>(4)</sup>:

- 1- Pre-eclampsia and gestational hypertension.
- 2- Preterm labor.
- 3- Recurrent vulvo-vaginal infection (thrush, UTI .....).
- 4- Long-term development of diabetes mellitus.
- 5- Increased incidence of operative delivery (like Caesarean section).

B- Complications of preexisting diabetes to pregnant women include<sup>(4)</sup>:

- 1- Pre-eclampsia and gestational hypertension.
- 2- Preterm labor.
- 3- Recurrent vulvo-vaginal infection (thrush, UTI .....).
- 4- Increased incidence of operative delivery (like Caesarean section).
- 5- Exacerbation of pre-existing disease (retinopathy, nephropathy, and cardiac disease).

## Management:

A- Pregnant woman with preexisting diabetes:

- 1- The aim is to maintain glucose level within these ranges and to avoid hypoglycemia and hyperglycemia<sup>(4)</sup>.
- 2- Most patients with pre-pregnancy diabetes are taking insulin, and this therapy must be maintained during pregnancy<sup>(4)</sup>.
- 3- For those on oral antidiabetic agents, it is advisable to convert them on insulin, because of the possible teratogenic effects and insulin facilitates a more effective manipulation of requirements as pregnancy progresses<sup>(4)</sup>.
- 4- In addition to insulin therapy, dietary advice is essential as it makes glycemic control with insulin easier<sup>(4)</sup>.

B- Pregnant woman with GDM:

- 1- The aim is to maintain fasting glucose level below 100 mg/dL (about 5.5 mmol/dL), below 125 mg/dL (about 7 mmol/dL) for 2 hours post-prandial glucose level, and to avoid hypoglycemia and hyperglycemia<sup>(4)</sup>.
- 2- Glucose control can be achieved through<sup>(4)</sup>:
  - 1- Dietary control.
  - 2- Insulin Therapy<sup>(5)</sup>: If dietary control does not reduce hyperglycemia sufficiently to reach the recommended glucose levels, insulin therapy is needed<sup>(5)</sup>.

(Note: many practitioners will try to control glucose using dietary method for 2 weeks prior to switching to insulin)<sup>(4)</sup>.

The initial starting insulin dose should be based on existing weight. And a total daily insulin dose of 0.5 to 0.7 units/kg is given. Two thirds of this dose is usually given in the morning and one third in the evening. Also, one third of each dose is given as rapid-acting insulin and the remaining dose as intermediate. The second dose may be divided so that rapid-acting insulin is given at supertime and intermediate at bedtime<sup>(5)</sup>.

#### C-Delivery:

The most common risk with GDM is macrosomia (large babies), which can lead to birth injuries. Clinical judgment often becomes the determinant on whether a Cesarean delivery is appropriate <sup>(5)</sup>.

وهناك بروتوكول خاص باستعمال الأنسولين أثناء الولادة في مصدر رقم ١

#### References:

- 1- Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.
  - 2- Pharmacotherapy Principles & Practice.
  - 3- Lincy S , Charlene Offiong . Pregnancy in a Diabetic Patient .US pharmacist
  - 4-David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.
  - 5- M. Saljoughian. Gestational Diabetes . U.S. Pharm. 2004;9:HS-3-HS-HS.
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## C- Pre-eclampsia

#### Definitions:

**1-Pre-eclampsia** is a disorder of pregnancy characterized by hypertension (blood pressure (BP) >140/90 mmHg) and clinically significant proteinuria (protein in urine >300 mg/24 h) developing after 20 weeks of gestation<sup>(1)</sup>.

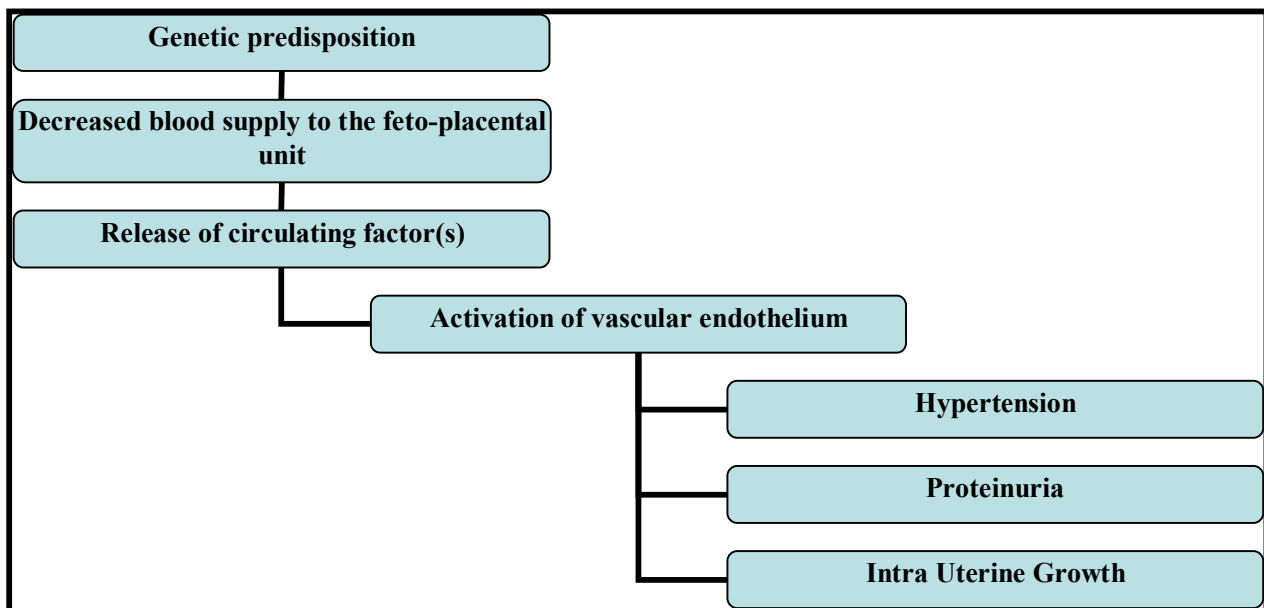
**2-Eclampsia:** is a convulsion occurring in women with established Pre-eclampsia, in the absence of other neurological or metabolic causes<sup>(2)</sup>.

**3-Chronic hypertension** is defined as BP elevation (BP >140/90 mmHg) that has persisted since before conception or 20 weeks of gestation<sup>(1)</sup>.

**4-Gestational hypertension** refers to hypertension that develops in previously normotensive women after 20 weeks of gestation without other symptoms of pre-eclampsia<sup>(1)</sup>.

#### Pre-eclampsia

**Etiology:** Although the primary events leading to pre-eclampsia are still unclear, there are cascade of events leads to the clinical syndrome:



### Sign and Symptoms of Pre-eclampsia<sup>(2)</sup>:

Symptoms: may be asymptomatic, headache, visual disturbance, and epigastric pain.

Signs: Elevation of BP, edema.

### Investigations for Pre-eclampsia:

The diagnosis and severity of pre-eclampsia-eclampsia can be measured with reference to the six major sites in which it exerts its effects: the central nervous system, the kidneys, the liver, the hematologic and vascular systems, and the fetal-placental unit. By evaluating each of these areas for the presence of mild to moderate versus severe pre-eclampsia, the degree of involvement can be assessed, and an appropriate management plan can be formulated, (Table 1)<sup>(5)</sup>.

### Management

The only cure for pre-eclampsia is delivery of the fetus & while it is the best treatment for the mother, it is not always the best option for the fetus because prematurity is the leading cause of neonatal mortality & morbidity. Therefore, if the patient were > 34 week of gestation she would delivered of her fetus. While women with severe pre-eclampsia or eclampsia should be delivered after a period of stabilization, regardless of the gestation age of the fetus<sup>(4)</sup>.

A-Mild to moderate pre-eclampsia

1-For mild to moderate pre-eclampsia-eclampsia, bed rest is the cornerstone of therapy. This increases central blood flow to the kidneys, heart, brain, liver, and placenta and may stabilize or even improve the degree of pre-eclampsia-eclampsia for a period of time. Bed rest may be attempted at home or in the hospital. Prior to making this decision, the provider should evaluate the following six sites to make an assessment about the severity of disease, (Table 1)<sup>(5)</sup>:

Table 1: Indicators of mild to moderate versus severe pre-eclampsia-eclampsia.

Site	Indicator	Mild to Moderate	Severe
Central nervous system	Symptoms and signs	Hyperreflexia Headache	Seizures Blurred vision Scotomas Headache Irritability
Kidney	Proteinuria	0.3–5 g/24 h	>5 g/24 h or catheterized urine with 4+ protein
	Uric acid	↑ > 4.5 mg/dL	↑↑ > 4.5 mg/dL
	Urinary output	> 20–30 mL/h	< 20–30 mL/h
Liver	AST, ALT, LDH	Normal	Elevated LFTs Epigastric pain Ruptured liver
Hematologic	Platelets Hemoglobin	> 100,000/mcL Normal range	< 100,000/mcL Elevated
Vascular	Blood pressure	< 160/110 mm Hg	> 160/110 mm Hg
	Retina	Arteriolar spasm	Retinal hemorrhages
Fetal-placental unit	Growth restriction Oligohydramnios Fetal distress	Absent May be present Absent	Present Present Present
AST = aspartate aminotransferase; ALT = alanine aminotransferase; LDH = lactate dehydrogenase; LFTs = liver function tests.			

2-Antihypertensive therapy should be use especially if diastolic BP reaches 100 mmHg

a- Methyldopa (aldomet ®) is centrally acting  $\alpha_2$  agonist. It is the most commonly used antihypertensive for hypertension during pregnancy. Usual dose is 750mg /day i.e. (250mg q 8 h) increase to 2-3gm/day<sup>(4)</sup>.

Adverse effect: Lethargy, somnolence, drowsiness & potential depression<sup>(4)</sup>.

b-  $\beta$ -adrenergic blocker:

Labetalol (Trandate ®) which is  $\alpha$  and  $\beta$  blocker. This agent has good safety record in pregnancy<sup>(2)</sup>. Daily dose is 400-800mg<sup>(4)</sup>.

c- Calcium channel blocker(CCB).

Administration of CCB nifedipine appears to be safe and is used commonly to treat hypertension during pregnancy particularly severe hypertension unresponsive to standard treatment but some adverse effect reported (flushing, headache & reflex tachycardia & ankle edema)<sup>(4)</sup>.

## B-Severe Pre-eclampsia

Symptoms are more dramatic and persistent. The blood pressure is often quite high, with readings over 160/110 mm Hg. Thrombocytopenia (platelet counts < 100,000/mcL) may be present and progress to disseminated intravascular coagulation. Severe epigastric pain may be present from. The HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) is a form of severe Pre-eclampsia<sup>(5)</sup>.

Mean arterial pressure (MAP): calculated as diastolic blood pressure + [(systolic diastolic)/ 3] is used to guide management and most protocols recommend the use of IV antihypertensive therapy if the MAP is > 125 mmHg <sup>(3)</sup>.

IV labetalol or hydralazine are most common drugs used<sup>(2)</sup>. If one agent is ineffective, or if the side effect occur (e.g. tachycardia with hydralazine), the other agent can be used <sup>(3)</sup>.

1- Hydralazine: Hydralazine (given IV) is the most commonly used treatment of severe hypertension in pre-eclamptic women. Since it is a potent vasodilator, hydralazine may increase a patient's risk of decreased intervillous blood flow and thus may impair uteroplacental perfusion. Consequently, some clinicians pretreat patients with plasma volume expansion (colloids) in an effort to prevent hypotension and fetal distress <sup>(1)</sup>.

Dosing regimen (many regional protocols) for example:

Bolus dose of 5 mg IV if the mean arterial pressure (MAP) remains > 125 mmHg, followed by a further boluses of 5 mg (every 20-30 minutes) up to a cumulative dose of 15 mg. Once the MAP is < 125 mmHg, an infusion of 10 mg /hour is commenced, doubling (if necessary) at 30 minutes intervals, until a satisfactory response or a dose of a 40 mg/hour is attained<sup>(3)</sup>.

2-Labetalol (given IV) is currently recognized as a second-line antihypertensive agent for treatment of severe hypertension in pre-eclamptic women and is reserved for use when target blood pressure is not achieved with hydralazine. It should not be administered to patients with asthma or congestive heart failure, as it is a nonselective beta-receptor antagonist <sup>(1)</sup>.

Dosing regimen (many regional protocols) for example :

Bolus dose of 20 mg IV if the mean arterial pressure (MAP) remains > 125 mmHg, followed at 10-minutes intervals by 40, 80, 80 mg boluses up to a cumulative dose of 220 mg. Once the MAP is < 125 mmHg, an infusion of 40 mg /hour is commenced, doubling (if necessary) at 30 minutes intervals, until a satisfactory response or a dose of a 160 mg /hour is attained<sup>(3)</sup>.

3-Nifedipine (Adalat ®): is also common choice to treat severe hypertension during pregnancy. Nifedipine 10 mg cap is given orally every 30-60min until the diastolic BP decrease < 110mmHg<sup>(4)</sup>.

## **C-Eclampsia:**

The occurrence of seizures defines eclampsia. The other abnormal findings of severe pre-eclampsia are also observed with eclampsia<sup>(5)</sup>. It is associated with high mortality rate<sup>(4)</sup>.

1- Magnesium sulphate is the drug of choice for the prevention of recurrent seizures in eclampsia. Regimens may vary between hospitals. Calcium gluconate injection is used for the management of magnesium toxicity <sup>(6)</sup>.

Prevention of seizure recurrence in eclampsia, initially by intravenous injection over 5-15 minutes, 4 g, followed by intravenous infusion, 1 g/hour for at least 24 hours after last seizure; if seizure recurs, additional dose by intravenous injection, 2 g (4 g if body-weight over 70 kg) <sup>(6)</sup>.

Urinary output is checked hourly and the patient assessed for signs of possible magnesium toxicity such as loss of deep tendon reflexes or decrease in respiratory rate and depth, which can be reversed with calcium gluconate <sup>(5)</sup>. 1g (10ml of 10% calcium gluconate) should be given iv over 3 minutes<sup>(4)</sup>.

2-Diazepam (valium®) 10 mg is suitable alternative<sup>(4)</sup>.

3-Phenobarbital (luminal®) also can be used<sup>(4)</sup>.

If seizure does not resolve by medical intervention, termination of pregnancy is recommended <sup>(4)</sup>.

### **Additional Points in management**

Premature delivery of the fetus is often required in severe pre-eclampsia. Therefore, corticosteroid should be given to enhance fetal lung maturity<sup>(3)</sup>.

If immaturity is present, corticosteroids dexamethasone 12 mg, two doses intramuscularly 12 hours apart) can be administered to the mother. Fetuses between 26 and 30 weeks of gestation can be presumed to be immature, and corticosteroids should be given <sup>(5)</sup>.

### **The Role of Prophylaxis**

A-low dose of aspirin (e.g. 75mg/day) : use to reduce the incidence of pre-eclampsia but it increases the incidence of abruptio-placenta, therefore low dose of aspirin use only in high risk group (e.g. those with previous pre-eclampsia , multiple gestation or those with chronic hypertension, DM )<sup>(2,3,4)</sup>.

2-Vitamin C and E (act as anti-oxidants) and calcium:

Clinical trials published in recent years have investigated various treatments for pre-eclampsia.

Many studies have shown that the use of vitamin C and E (act as anti-oxidants) or calcium reduce the likelihood of pre-eclampsia but the subject is of an ongoing trial<sup>(3)</sup>.

### **References:**

- 1- Christina Song. Preeclampsia-Eclampsia, Pathogenesis, Diagnosis and Treatment. US pharmacist
  - 2- Geoffrey Chamberlain. Obstetric By ten teachers. 8<sup>th</sup> edition. 2006.
  - 3- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.
  - 4- Neville F. Hacker Essentials of Obstetric and Gynecology. 4<sup>th</sup> edition. 2004.
  - 5- Lawrence M. Tierney. Current Medical Diagnosis & Treatment, 45<sup>th</sup> edition (2006) .
  - 6-BNF 67.
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## **D-Preterm Labor**

### **Definitions:**

In pregnancy, **term** refers to the period from 37-41 weeks of gestation, with **preterm** occurring between the 24-36 weeks of gestation<sup>(1)</sup>.

Preterm labour can be divided into three gestational periods<sup>(1)</sup>:

A- Mildly preterm birth: births at 32-36 weeks.

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- B- Very preterm birth: births at 28-31 weeks.  
C- Extremely preterm birth: births at 24-27 weeks.

### Etiology

- 1- Spontaneous preterm birth (idiopathic).
- 2- Infections (like bacterial vaginosis).
- 3- Over distension (like in multiple pregnancy).
- 4- Vascular (like antepartum hemorrhage and abruption).
- 5- Intercurrent illness (serious infections like pyelonephritis, pneumonia, ...)

### Risk factors (للاطلاع )

Non-modifiable (major) 1-previous preterm birth 2-Twin pregnancy 3-uterine abnormality	Non-modifiable (minor) 1-Parity = 0 or >5 2-Teenager having second or subsequent Babies.
modifiable 1-Smoking 2-Body mass index < 20 (underweight)	Factors in current pregnancy: 1-recurrent antepartum hemorrhage 2-intercurrent (e.g. sepsis ) 3-any surgery

### Clinical Finding<sup>(1,2)</sup>:

The diagnosis of preterm labour is difficult in the absence of advanced dilatation.

- 1- Symptoms such as low back pain or cramping are often cyclical.
- 2- Vague compliance such as pelvic pressure or increased vaginal discharge are usually common.
- 3- The co-existence of vaginal bleeding is serious mark.

### Management:

1-Management of asymptomatic high risk women:

A- Bacterial vaginosis: Bacterial vaginosis has been associated with an increased risk of preterm birth. Oral 5-7 days course of metronidazole or clindamycin significantly lower the risk of preterm birth, by 60% in high risk women positive for bacterial vaginosis<sup>(1,2)</sup>.

B- Asymptomatic bacteriuria: Asymptomatic bacteriuria carry an increased risk for preterm birth. This risk is reduced significantly by appropriate antibiotic course<sup>(1,2)</sup>.

C-Group B streptococcal genital colonization: Group B streptococcal genital colonization has been linked to prematurity. Therefore mother at risk of preterm delivery should be screened for Group B streptococcal genital colonization, if positive, then a appropriate antibiotics course should be offered<sup>(1,2)</sup>.

D-Lifestyle modification: There is no evidence that lifestyle modification improve outcomes. And in some studies hospitalization for bed rest led to an increase in preterm birth<sup>(1,2)</sup>.

## 2-Management of symptomatic women:

A- Steroid: Current evidence shows that a single course of maternal steroid (2 injections 12-24 hours apart) given between the 28 and 32 weeks' gestation and received within 7 days of delivery results in a marked neonatal outcome (mainly due to the reduction in the neonatal respiratory distress syndrome (RDS)), maximum benefit from the injection is seen after 48 hours.

However courses received less than 48 hours, or more than 7 days, as well as courses given below 28 weeks are still lead to benefits<sup>(1, 2)</sup>.

B-Tocolytics (Drugs that inhibit uterine contraction): There little evidence about the benefit of tocolytics agents like (ritodrine, Beta-agonists, Oxytocin antagonist (atosiban), magnesium sulphate, nifedipine (10-20 mg orally every 6 hours), and glyceryl trinitrate (GTN)). Therefore the use of tocolytics is usually inappropriate if steroids have been given and intensive care cots are available<sup>(1,2)</sup>.

### References:

1- Geoffrey Chamberlain. Obstetric by Ten Teachers. 8<sup>th</sup> edition. 2006.

2- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence-based text for MRCOG.2004.

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## E-Prevention of Hemolytic Disease of the Newborn

The antibody anti-Rh<sub>0</sub> (D) is responsible for most severe instances of hemolytic disease of the newborn. If an Rh<sub>0</sub>(D)-negative woman carries an Rh<sub>0</sub>(D)-positive fetus, she may develop antibodies against Rh<sub>0</sub>(D) when fetal red cells enter her circulation during small fetomaternal bleeding episodes in the early third trimester or during delivery, abortion, ectopic pregnancy, abruptio placentae, or other antepartum bleeding problems<sup>(1)</sup>.

This antibody, once produced, remains in the woman's circulation and poses the threat of hemolytic disease for subsequent Rh-positive fetuses. Passive immunization against hemolytic disease of the newborn is achieved with Rh<sub>0</sub>(D) immune globulin, a purified concentrate of antibodies against Rh<sub>0</sub>(D) antigen. The Rh<sub>0</sub>(D) immune globulin (one vial of 300 mcg I.M) is given to the mother within 72 hours after delivery (or spontaneous or induced abortion or ectopic pregnancy)<sup>(1)</sup>.

The antibodies in the immune globulin destroy fetal Rh positive cells so that the mother will not produce anti-Rh<sub>0</sub>(D). During her next Rh-positive gestation, of hemolytic disease of the newborn will be prevented. An additional safety measure is the administration of the immune globulin (300 mcg of anti-D immunoglobulin) at the 28<sup>th</sup> 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<sup>(1)</sup>.

### References:

1-Lawrence M. Tierney. Current Medical Diagnosis & Treatment, 45<sup>th</sup> edition (2006) .

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## **F-Toxoplasmosis**

*Toxoplasma gondii*, the cause of toxoplasmosis, is an intracellular protozoan parasite<sup>(1)</sup>.

### **Epidemiology and etiology:**

The definitive host of this organism is the domestic cat. Transmission may occur transplacentally (from the mother to fetus), by ingestion of raw or undercooked meat containing protozoan cysts, or by exposure to oocysts in soil contaminated with cat faeces<sup>(1)</sup>.

### **Congenital Toxoplasmosis:**

Congenital toxoplasmosis arises almost exclusively when the mother develops a primary infection during gestation. Congenital infection almost never develops from latent toxoplasmosis acquired before pregnancy<sup>(2)</sup>.

The risk of fetal infection depends on when maternal infection occurs where it rises throughout gestation from about 10% during the first trimester to about 60% during the third trimester<sup>(2)</sup>.

### **Presentation**

Adults and adolescents with primary infection are generally asymptomatic. Therefore specific treatment for non-pregnant adults and adolescents is not required<sup>(1)</sup>.

The consequences of fetal infection also depend on when infection occurs

A-Early fetal infection can result in more severe sequelae: (Congenital chorioretinitis, cerebral calcification, hydrocephalus, ....), spontaneous abortion is common<sup>(1)</sup>.

B- Late fetal infection can result in less severe sequelae: The majority of infants are born without any obvious problems<sup>(1)</sup>.

**Diagnosis:** By serological tests<sup>(1)</sup>.

### **Management:**

A- The prevention of congenital toxoplasmosis is of major importance:

1- Pregnant women should minimize contact with cats<sup>(2)</sup>.

2- They should wash their hands after contact with cats<sup>(2)</sup>.

3- In addition, pregnant women should wash all fruits and vegetables before eating them and should not eat undercooked meat<sup>(2)</sup>.

B- If maternal infection is confirmed, the macrolide antibiotic Spiramycin (in a 3 weeks course of 2-3 gm /day)<sup>(3)</sup> should be administered to reduce the likely of fetal infection (reduced by about 60%). Spiramycin should be started as soon as maternal infection has been confirmed, as the longer the delay the greater risk of fetal damage<sup>(1)</sup>.

C-Termination of pregnancy is also an option if infection occurs early in gestation or if there is an ultrasound evidence of congenital infection<sup>(1)</sup>.

**References:**

- 1- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.
- 2- David C. Dale. Infectious Diseases: The Clinician's Guide to Diagnosis, Treatment, and Prevention. 2003)
- 3-Geoffrey Chamberlain. Obstetric By ten teachers. 8<sup>th</sup> edition . 2006.
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## Labor

**False labor:** during the last 4-8week of gestation, the uterus undergoes irregular contraction that are painless and they are not associated with progressive cervical dilation or effacement<sup>(1)</sup>.

**Stages of labor:** there are three stages of labor:

**A-First stage:** consists of two phases:

- 1- Latent phase during which cervical effacement & early dilation occur<sup>(1)</sup>.
- 2- Active phase more rapid cervical dilation occurs with strong regular uterine contraction<sup>(1)</sup>.

**B-Second stage:** starts with complete cervical dilation & end with the delivery of the fetus<sup>(1)</sup>.

**C-Third stage** of labor is the time between delivery of fetus & the delivery of placenta<sup>(1)</sup>.

### References:

- 1- Neville F. Hacker Essentials of Obstetric and Gynecology. 4<sup>th</sup> edition 2004.
- 

## Induction and Augmentation of labour

**Induction:** is the process whereby labour is initiated by artificial mean<sup>(1)</sup>.

**Augmentation:** is the artificial stimulation of labour that has begun spontaneously<sup>(1)</sup>.

### Common Indications for induction of labour:

- 1- Post dates (i.e. 12 days or more beyond EDD)<sup>(2)</sup> (pregnancy passing 41 weeks)<sup>(3)</sup>.
- 2- Pre-labour spontaneous rupture of the membrane<sup>(3)</sup>.
- 3- Maternal request<sup>(3)</sup>.
- 4- Maternal disease: like: diabetes mellitus, hypertensive /renal diseases<sup>(3)</sup>.
- 5- Pregnancy-related conditions: like: Pre-eclampsia, placental abruption<sup>(3)</sup>.
- 6- Fetal conditions: like: Intrauterine growth restriction<sup>(3)</sup>.

**Induction and Augmentation of labour are done either:**

A- Mechanically by special procedures.

B- Pharmacologically (through administration of prostaglandin E2 like Dinoprostone & E1 Like misoprostol (cytotec ®)) or low dose oxytocin<sup>(1)</sup>.

1-Dinoprostone is available as vaginal tablets, pessaries and vaginal gels for the induction of labour. The intravenous solution is rarely used; it is associated with more side-effects.

2-Oxytocin (Petocin ®, Syntocinon ®) is administered by slow intravenous infusion to induce or augment labour. Uterine activity must be monitored carefully and hyperstimulation avoided. Large doses of oxytocin may result in excessive fluid retention.

3-Misoprostol is given orally or vaginally for the induction of labour.

### **Guidance for induction of labour**

1-Dinoprostone is preferable to oxytocin for induction of labour in women with intact membranes, regardless of parity or cervical favorability<sup>(4)</sup>.

2-Dinoprostone or oxytocin are equally effective for the induction of labour in women with ruptured membranes, regardless of parity or cervical favorability<sup>(4)</sup>.

3-Oxytocin should not be started for 6 hours following administration of vaginal prostaglandins; when used to induce labour, the recommended dose of oxytocin by intravenous infusion is initially 1 mU (0.001 U) - 2 mU (0.002) units/minute increased at intervals of at least 30 minutes until a maximum of 3-4 contractions occur every 10 minutes (0.012 units/minute is often adequate); the maximum recommended rate is 32 mU/minute<sup>(4)</sup>.

Note: Oxytocin should be used in standard dilutions of 10 units/500 mL (infusing 3 mL/hour delivers 1 mU/minute) or, for higher doses, 30 units/500 mL (infusing 1 mL/hour delivers 1mU/minute) <sup>(4)</sup>.

### **References**

1- Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.

2- Geoffrey Chamberlain. Obstetric by Ten Teachers. 8<sup>th</sup> edition 2006.

3- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence-based text for MRCOG.2004.

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## **Obstetric Hemorrhage**

### **A-Antepartum hemorrhage**

Vaginal bleeding in the third trimester complicates about 4% of all pregnancies. The main causes are:

#### **1-Placenta Praevia**

A-Definition: is defined as the presence of placental tissue over or near the internal cervical os<sup>(1)</sup>. It is graded in two ways as either grade 1- 4 or major/minor<sup>(2)</sup>.

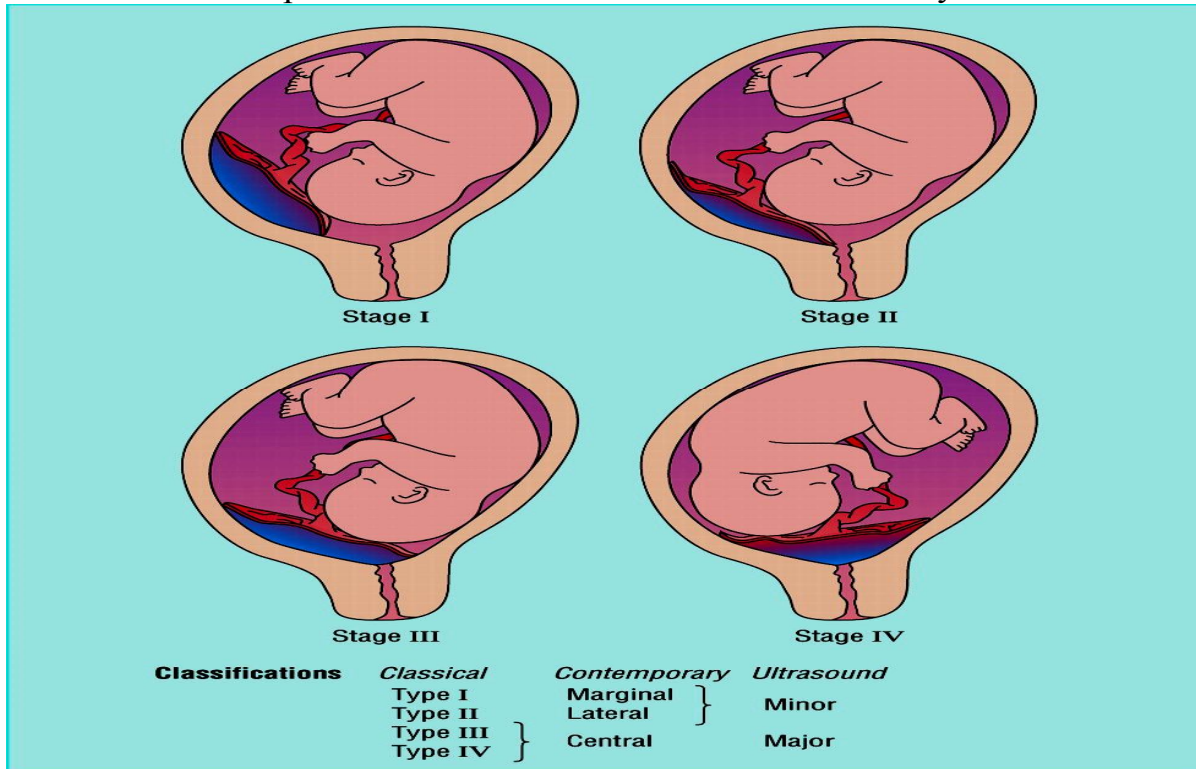
1- Grade one: The placental edge is in the lower uterine segment but does not reach the internal os<sup>(2)</sup>.

2- Grade two: The placenta reach the edge of the lower uterine segment but does not cover the internal os<sup>(1)</sup>.

3- Grade three: The placenta cover the internal os and is asymmetrically situated<sup>(1)</sup>.

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4- Grade four: the placenta cover the internal os and is centrally situated<sup>(2)</sup>.



The grades 1 and 2 represent the minor placenta praevia while the grades 3 and 4 are the major<sup>(2)</sup>.

### B- Predisposing factor of placenta praevia:

Predisposing factor of placenta praevia are <sup>(3)</sup> :

- 1- Multiparity.
- 2- Increasing maternal age.
- 3- Prior placenta praevia.
- 4- Multiple gestations.

### C-Presentation:

Placenta praevia usually presents with painless vaginal bleeding<sup>(2)</sup>.

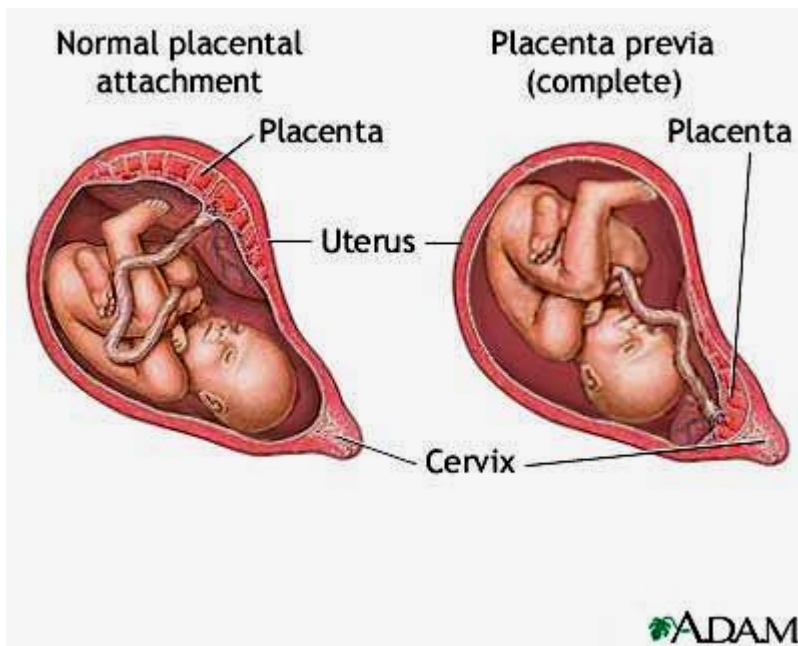
### D-Diagnosis

Diagnosis is done by ultrasound <sup>(3)</sup>.

### E-Management

Management depends on the severity of bleeding and the gestational age of the fetus<sup>(3)</sup>.

- 1-With preterm pregnancy, the goal is to attempt to obtain fetal maturation without compromising the mother health<sup>(3)</sup>.
- 2-If the bleeding is excessive, the delivery must be accomplished by Cesarean section irrespective of gestation<sup>(3)</sup>.



#### References:

- 1-Fortner, Kimberly B.; Szymanski, Linda M.; Fox, Harold E.; Wallach, Edward E. Johns Hopkins Manual of Gynecology and Obstetrics, 3<sup>rd</sup> edition. Copyright ©2007 Lippincott Williams & Wilkins
- 2- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence-based text for MRCOG.2004.
- 3-Neville F. Hacker Essentials of Obstetric and Gynecology. 4<sup>th</sup> edition 2004.

## 2-Apruptio Placenta (Placental abruption)

**A-Definition:** Abruption is defined as bleeding following premature separation of normally sited placenta<sup>(1)</sup>.

#### B-Risk factors

- 1- Maternal hypertension<sup>(2)</sup>.
- 2- Trauma<sup>(2)</sup>.
- 3- Polyhydramnios with rapid uterine decompression<sup>(2)</sup>.
- 4- Premature rupture of the membrane<sup>(2)</sup>.
- 5- Smoking<sup>(2)</sup>.
- 6- Previous abruption<sup>(1)</sup>.

#### C-Presentation:

The patient presents with painful vaginal bleeding in association with uterine tenderness, hyperactivity and increased tone<sup>(2)</sup>.

#### D-Diagnosis:

The diagnosis of placenta abruption is primarily a clinical one<sup>(1)</sup>. Ultrasound (U/S) detect only 2% of abruption <sup>(2)</sup>.

#### E-Complications<sup>(3)</sup>:

1-Effects on the mother: Hypovolemic shock, disseminated intravascular coagulation (DIC), acute renal failure and maternal mortality.

2-Effect on the fetus: Perinatal mortality and Intrauterine growth restriction.

### **F-Management**

1-If the abruption is small, fetus is uncompromised and the mother is well, conservative management may be utilized<sup>(1)</sup>.

2-Vaginal delivery is the preferred method of delivery for a fetus that has died secondary to placental abruption<sup>(4)</sup>.

3-Cesarean section is indicated when fetal compromise is present and the fetus is likely to survive<sup>(1)</sup>.

### **References:**

1-David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.

2-Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.

3-Geoffrey Chamberlain. Obstetric By ten teachers. 8<sup>th</sup> edition . 2006.

4-e-medicine.Abruptio placenta.

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## **3-Uterine Rupture**

Classically rupture is characterized by intense abdominal bleeding & some vaginal bleeding<sup>(1)</sup>.

Sometimes it is possible to repair the uterus, but frequently the only safe forward is hysterectomy<sup>(2)</sup>.

### **References:**

1-Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004-2-Ten teachers.

2- Geoffrey Chamberlain. Obstetric By ten teachers. 8<sup>th</sup> edition . 2006.

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## **B-Postpartum Hemorrhage (PPH)**

### **Definitions:**

**1-Primary postpartum hemorrhage:** is defined as blood loss in excess of 500 ml from the genital tract following (but within 24 hours) of the delivery of the baby<sup>(1)</sup>.

If the blood loss is greater than 1000 ml or 1500 ml, it considered massive postpartum hemorrhage<sup>(1)</sup>.

**2-Secondary postpartum hemorrhage:** is the blood loss from the genital tract of volume greater than expected after the first 24 hours but within the first 6 weeks of delivery<sup>(1)</sup>.

### **Etiology:**

**A-Primary postpartum hemorrhage** caused by:

1-Uterine atony (when the uterus is not contracted) (anesthesia, marked uterine distention, prolonged or excessive oxytocin administration<sup>(2)</sup>. It is the major cause of postpartum hemorrhage and account for about 90% of cases<sup>(3)</sup>.

2-Placental problems (abruptio placenta, placenta praevia, incomplete placental separation)<sup>(2)</sup>.

3-laceration(s) of the birth canal, rupture of the uterus, or mismanagement of the third stage of labour<sup>(2)</sup>.

**B-Secondary postpartum hemorrhage** is usually due to retained products of conception (like placental tissue) (which can be removed by curettage)<sup>(2, 4)</sup>.

### Complications:

The complications of postpartum hemorrhage include shock, anemia, infection and disseminated intravascular coagulation (DIC) ( a life threatening complication of massive hemorrhage <sup>(2, 4)</sup>.

### Treatment:

Significant PPH is an obstetric emergency.

1- Obtain a CBC, coagulation panel, blood type and cross match.

2- Ensure an open IV line.

3- Closely monitor further blood loss and vital signs.

4-Initiate appropriate blood component replacement (fresh frozen plasma, packed platelets , ....)

5- Manually deliver the partially separated placenta.

6-Explore the uterus, and carefully remove any retained products of conception (this may require uterine curettage).

7-To reverse uterine atony after placental recovery: by performing gentle uterine massage. And by giving uterotonic drugs (oxytocin). If that fails to slow bleeding, consider the addition of prostaglandins or ergometrine. (See Uterotonics below).

8-Hysterectomy or ligation of uterine arteries or hypogastric arteries may be lifesaving in certain extreme cases.

### Uterotonics:

A-Suggested dosage of Uterotonics <sup>(1)</sup>:

Uterotonic	Route of administration	Dosage
Oxytocin	I.V	Bolus dose of 5 IU, followed by infusion of 40 IU in 40 mL of saline run at 10 mL/hour.
Syntometrine ®(ergometrine maleate 500 µg, oxytocin 5 u./mL)	I.M	1 mL
Ergometrine	I.V /I.M	250-500 mcg
Carboprost	I.M	250 mcg every 15 -90 min(total cumulative dose is 2 mg ) ( i.e. 8 doses)
Misoprostol	Rectally	800 mcg
Gemeprost	Intrauterine	1-2 mg.

## Puerperal Sepsis

**Definition:** Puerperal Sepsis is define as a temperature of 38 C<sup>0</sup> or higher that occur for more than 2 consecutive days (exclusive of first postpartum day) during the first 10 postpartum days<sup>(1)</sup>.

**Etiology:** Streptococci, staphylococci, clostridia, coliform bacteria, or Bacteroides are the pathogens most often identified<sup>(2)</sup>.

**Signs and Symptoms**<sup>(1,2)</sup>: Pyrexia, tachycardia, malaise, headache, anorexia, & increasing uterine tenderness.

### Management

1- IV fluids are administered to maintain electrolyte and fluid balance<sup>(2)</sup>.

2- Antibiotic therapy of puerperal infection usually follows two major principles:

A- Early antibiotic treatment should be institute

B- The antibiotic should provide anaerobic coverage, Therefore the use of :

(Clindamycin 600mg q12h or q8h + ampicillin 500- 1000mg q6d) OR

(Clindamycin 600mg q12h 0r q8h + gentamicin 80mg q8h)

Above regimen provide better first line coverage<sup>(1)</sup>.

3-When a pelvic thrombophlebitis or thromboembolism is suspected, heparin therapy should be instituted <sup>(1)</sup>.

4-The presence of pelvic abscess demand surgical drainage<sup>(1)</sup>.

### References:

1- Neville F. Hacker Essentials of Obstetric and Gynecology .4<sup>th</sup> edition .2004.

2- Martin L. Pernoll, M.D. Benson & Pernoll's. handbook of Obstetric and Gynecology . 10<sup>th</sup> Edition.2001.

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## Caesarean Section

**Definition:** Caesarean section refers to an operation that is performed to deliver the baby via a transabdominal route.

### Some of the indications for Caesarean section:

1-Patient has a previous history of Caesarean section.

2-Baby is too big to pass safely through the vagina.

3-The baby's buttock or feet enter the birth canal first instead of the head, this is called breech position.

4-The baby's shoulder enter the birth canal first instead of the head this is called shoulder or transverse position.

5-Labour is too slow or stops (no dilation of cervix after time is finish).

6-There are problems with the placenta (placenta praevia or abruption) which may cause dangerous bleeding during vaginal delivery.

7-Mother has infection like genital herpes.

8-Twins, triplets or more.

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9-Baby has problem during labor (such as a slow heart rate) this is called fetal distress.

10-Mother has DM or high BP.

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## Ectopic Pregnancy

Ectopic pregnancy is derived from the Greek word *ektopos*, meaning out of place, and it refers to the implantation of a fertilized egg in a location outside of the uterine cavity, including the fallopian tubes <sup>(1)</sup> (About 98% of ectopic pregnancies are tubal<sup>(2)</sup>), cervix, ovary, cornual region of the uterus, and the abdominal cavity.

This abnormally implanted gestation grows and draws its blood supply from the site of abnormal implantation. As the gestation enlarges, it creates the potential for organ rupture because only the uterine cavity is designed to expand and accommodate fetal development.

Ectopic pregnancy can lead to massive hemorrhage, infertility, or death <sup>(1)</sup>.

Any condition that prevents or retards migration of the fertilized ovum to the uterus can predispose to an ectopic pregnancy, including a history of infertility, pelvic inflammatory disease,

ruptured appendix, and prior tubal surgery. Combined intrauterine and extrauterine pregnancy (heterotopic) may occur rarely <sup>(2)</sup>.

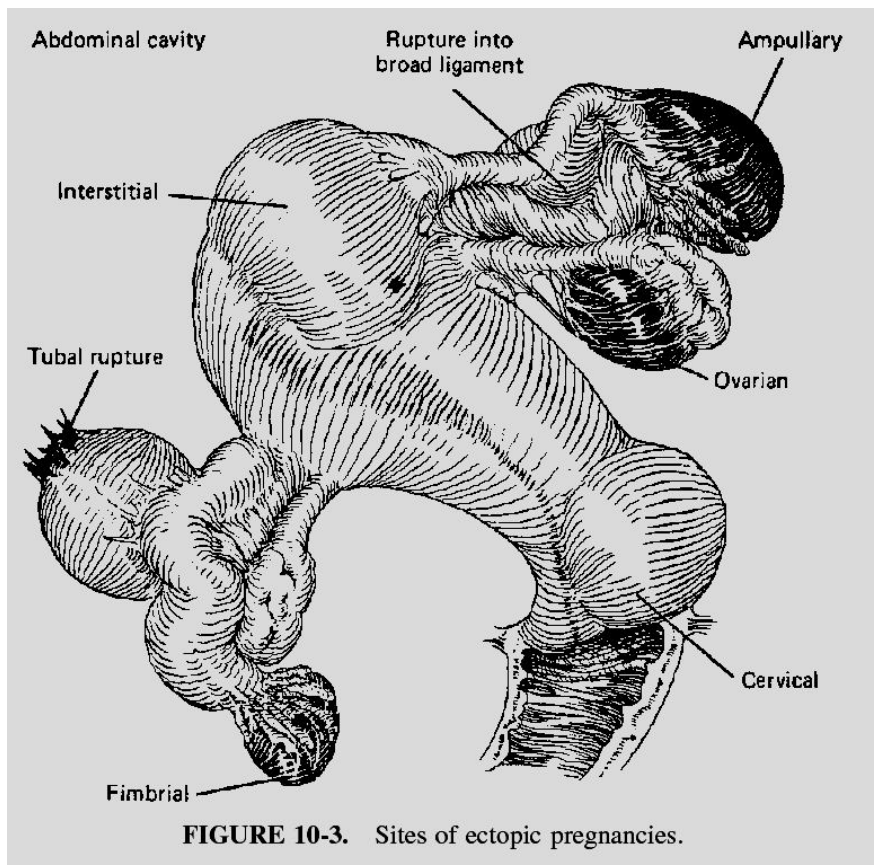


FIGURE 10-3. Sites of ectopic pregnancies.

### Etiology<sup>(1)</sup>:

The following risk factors have been linked with ectopic pregnancy:

- 1-Pelvic inflammatory disease (The most common cause is infection caused by *Chlamydia trachomatis*).
  - 2-History of prior ectopic pregnancy.
  - 3-History of tubal surgery and conception after tubal ligation.
  - 4-Use of fertility drugs (clomiphene citrate or injectable gonadotropin) or assisted reproductive technology.
  - 5-Use of an intrauterine device.
  - 6-Increasing age, smoking, and others.
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**Diagnosis:****A-Clinical Findings**

The classic clinical triad of ectopic pregnancy is pain (secondary to tubal distention or rupture), amenorrhea, and vaginal bleeding. Unfortunately, only 50% of patients present typically. Some patients may be collapsed and shocked from bleeding<sup>(1,3)</sup>.

**B-Laboratory Findings**

Blood studies may show anemia. Quantitative serum pregnancy tests will show levels generally lower than expected for normal pregnancies of the same duration. If pregnancy tests are followed over a few days, there may be a slow rise or a plateau rather than the near doubling every 2 days associated with normal early intrauterine pregnancy or the falling levels that occur with spontaneous abortion<sup>(2)</sup>.

**C-Imaging**

Ultrasonography can reliably demonstrate a gestational sac 6 weeks from the LMP and a fetal pole at 7 weeks if located in the uterus. An empty uterine cavity raises a strong suspicion of extrauterine pregnancy, which can occasionally be revealed by endovaginal ultrasound. Specified levels of serum hCG have been reliably correlated with ultrasound findings of an intrauterine pregnancy. For example, an hCG level of 6500 mU/mL with an empty uterine cavity by transabdominal ultrasound is virtually diagnostic of an ectopic pregnancy. Similarly, an hCG value of 2000 mU/mL or more can be indicative of an ectopic pregnancy if no products of conception are detected within the uterine cavity by transvaginal ultrasound<sup>(2)</sup>.

**D-Special Examinations**

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<sup>(2)</sup>.

**Treatment**

When a patient with an ectopic pregnancy is unstable or when surgical therapy is planned, the patient is hospitalized. Blood is typed and cross-matched. Surgical treatment is definitive<sup>(2)</sup>.

In a stable patient, a single dose methotrexate IM (50 mg/m<sup>2</sup> or approximately 1mg/kg)<sup>(4)</sup> is acceptable medical therapy for early ectopic pregnancy<sup>(2)</sup>.

Iron therapy for anemia may be necessary during convalescence. Give Rh<sub>0</sub>(D) immune globulin (300 mcg) to Rh-negative patients<sup>(2)</sup>.

**Prognosis**

Repeat tubal pregnancy occurs in about 12% of cases. This should not be regarded as a contraindication to future pregnancy, but the patient requires careful observation and early ultrasound confirmation of an intrauterine pregnancy<sup>(2)</sup>.

**References:**

1-E.medicines.

2- Lawrence M. Tierney. Current Medical Diagnosis & Treatment, 45th Edition (2006) .

- 3- Martin L. Pernoll, M.D. Benson & Pernoll's. handbook of Obstetric and Gynecology .10<sup>th</sup> Edition.2001.
- 4- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.
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## **Endometriosis**

Endometriosis is a common disease that can affect any menstruating woman from the time of her first period to menopause. In this disease, the endometrial tissue that lines the inside of the uterus (the endometrium), becomes implanted outside the uterus, possibly on the fallopian tubes, ovaries, or pelvic area. Endometrial tissue rarely spreads beyond the pelvic region <sup>(1)</sup>.

### **Pathophysiology:**

During the menstrual cycle, hormones signal the lining of the uterus to thicken to prepare for possible pregnancy. If a pregnancy does not occur, the hormone levels decrease, causing the thickened lining of the uterus to shed. This produces bleeding that exits the body through the vagina, i.e., the monthly period<sup>(1)</sup>.

When endometrial tissue is located in other parts of the body, it continues to act in its normal way: It thickens, breaks down, and bleeds each month as the hormone levels rise and fall. However, because there is nowhere for the blood from this misplaced tissue to exit the body, it becomes trapped and may lead to the growth of cysts. Cysts, in turn, may form scar tissue and adhesions. This process will cause pain in the area of the misplaced tissue, usually the pelvis, especially during menstruation. The formation of scars and adhesions on ovaries or fallopian tubes can prevent pregnancy<sup>(1)</sup>.

### **Sign and symptoms:**

Some women with endometriosis have no signs or symptoms, but others may have pelvic pain and severe cramping that may begin before and extend several days into the monthly period and that may include lower back and abdominal pain. Some women may experience occasional heavy periods or bleeding between periods<sup>(1)</sup>. Painful menstrual periods or noncyclic pelvic pain is a common symptom of endometriosis.

When menstruation ends permanently with menopause or temporarily with pregnancy, the signs and symptoms of endometriosis stop. The disease can return again after pregnancy when menstruation resumes<sup>(1)</sup>.

### **Underlying Cause**

The exact cause of endometriosis is not yet known<sup>(1)</sup>.

## **Risk Factors**

Endometriosis is more likely to occur in women who have not had children than in women who have. Some women may have an inherited tendency to develop endometriosis<sup>(1)</sup>.

## **Diagnosis**

Before making a diagnosis of endometriosis, the clinician will perform a pelvic exam to check for any abnormalities, such as cysts on the reproductive organs or scars behind the uterus. Other tests for physical clues of endometriosis include ultrasound, laparoscopy, and blood tests<sup>(1)</sup>.

## **Complications**

The major complication of endometriosis is infertility. Approximately 30 to 40% of women with endometriosis are infertile. Endometriosis can produce adhesions that can prevent the egg from traveling through the fallopian tube to the uterus for fertilization. It may also inhibit the mobility of the fallopian tube and impair its ability to pick up the egg<sup>(1)</sup>.

## **Treatment**

**Pharmacotherapy:** Endometriosis is treated with medications or surgery. The method chosen will depend on the severity of the signs and symptoms and whether the patient hopes to become pregnant<sup>(1)</sup>.

A-Ibuprofen or other NSAIDs: Typically help ease painful menstrual cramps. However, if taking the maximum dose does not provide full relief, the patient may need to try another treatment to manage the symptoms.

B-Supplemental hormones are effective in reducing or eliminating the pain of endometriosis, since it is the rise and fall of hormones during a woman's menstrual cycle that causes endometrial implants to thicken, break down, and bleed. There are several hormonal options for treating endometriosis:

1- Oral contraceptives help control the hormones responsible for the buildup of endometrial tissue each month. Taking the pill long-term can reduce or eliminate the pain of endometriosis. Most women also have lighter and shorter menstrual flow when they are taking the pill. The combined oral contraceptive pills are the main hormonal drug used.

In women with endometriosis-associated pain, the pill needs to be taken daily continuously or daily for blocks of three to four months, followed by a break of one week, during which time the patients will have a light period.

2-Another treatment for endometriosis, gonadotropin-releasing hormone agonists (Buserelin) Leuporelin acetate, and Nafarelin, Goserelin (Triptorelin, (Gn- RH) and antagonists (Cetrorelix and Ganirelix) block the production of ovarian-stimulating hormones. This action prevents menstruation and dramatically lowers estrogen levels, causing endometrial implants to shrink. Gn-RH agonists and antagonists can force endometriosis into remission during treatment and sometimes for months or years afterward. These drugs create an artificial menopause that can

lead to troublesome side effects, such as hot flashes and vaginal dryness. A low dose of estrogen may be taken along with these drugs to decrease such side effects. 3-The gonadotropin inhibitor danazol (Danol ®) blocks the production of ovarian-stimulating hormones, preventing menstruation and the symptoms of endometriosis. It also suppresses the growth of the endometrium. However, danazol may not be the first choice for treatment because it can cause unwanted side effects, such as acne and facial hair. Gestrinone has general actions similar to those of danazol and is indicated for the treatment of endometriosis <sup>(2,3)</sup>.

4-An injectable drug, medroxyprogesterone acetate (Depo-Provera®) is effective in halting menstruation and the growth of endometrial implants, thereby relieving the signs and symptoms of endometriosis. It acts by thinning and compacting endometrial tissue, and its side effects include weight gain and depressed mood.

**Surgery:** Although hormone therapies are normally effective in reducing or eliminating symptoms of endometriosis, they prevent pregnancy. For women who want to have children, surgery to remove implants may increase the chances for pregnancy. In addition, the surgery may also alleviate severe pain from endometriosis. Surgery removes endometrial growths, adhesions, and scar tissues without removing the reproductive organs.

In severe cases of endometriosis, a total hysterectomy and the removal of both ovaries may be the best treatment. Hysterectomy alone is also effective, but removing the ovaries ensures that endometriosis will not return. Either type of surgery is typically considered a last resort, especially for women still in their reproductive years.

**Reference:**

1-M. Saljoughian. Understanding Endometriosis and Its Treatment. US Pharm. 2005;9:HS-5-HS-8.  
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## Heavy and Irregular Menstruation

**Definitions:**

Menorrhagia: heavy (usually more than 80 ml/period) regular blood loss occurring over several consecutive cycles. Regular heavy bleeding without an identified local cause is also called Dysfunctional Uterine Bleeding (DUB) <sup>(1)</sup>.

**Treatment**

A-Non-Hormonal therapy: For women with menorrhagia requiring non-hormonal therapy, antifibrinolytic drugs (e.g. tranexamic acid (cyklokapron®)) is used for the reduction of blood loss. While the NSAIDs (like mefenamic acid) for the associated menstrual pain <sup>(1)</sup>.

B-Combined Oral Contraceptives (COC): COCP is effective for menorrhagia (reduce both the pain and bleeding) provided that there are no contraindications <sup>(1)</sup>.

C-Progestogens: Cyclical progestogens are effective for menorrhagia when given for 21 days out of 28 days (between the day 5 and 26 of cycle), (e.g. norethisterone

(Primolut N®) 5 mg tid for 21 days<sup>(1)</sup>. (BNF give different time dosage 5 mg 3 times daily for 10 days to arrest bleeding; to prevent bleeding 5 mg twice daily from day 19 to 26)<sup>(2)</sup>.

Also, continuous high dose progestogens (e.g. depot preparations like medroxyprogesterone acetate (Depo-Provera®)) are also effective if they induce amenorrhea<sup>(1)</sup>.

D-other second line agents includes: Danazol, Gestrinone, and gonadotropin-releasing hormone agonists<sup>(1)</sup>.

E-Surgery: Like hysterectomy when other alternatives have failed<sup>(1)</sup>.

#### References:

1- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.

2-BNF

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## Polycystic Ovarian Syndrome

**Definition**<sup>(1)</sup>: Any woman with at least two of the following three criteria are said to PCOS:

1-Evidence of hyperandrogenism (biochemical or clinical). Most commonly hirsutism, acne and crown pattern baldness.

2-Ovulatory dysfunction: amenorrhea , oligomenorrhoea (menstruation occurring at an interval >35 days).

3-Morphological polycystic ovaries.

#### **Etiology**<sup>(2)</sup>:

1-there have been many theories about the cause of PCOS. Around 40 per cent of sufferers have raised levels of LH and 30 per cent have raised levels of testosterone. LH stimulates the ovary to produce testosterone and consistently raised levels of LH can prevent ovulation.

2-Insulin resistance: Recent evidence has suggested that the principal underlying disorder may be insulin resistance with the resultant raised serum insulin concentrations stimulating excess ovarian androgen production. Excess circulating insulin also reduces the production of proteins that bind sex hormones, increasing the free testosterone levels.

3-Obesity: A high body mass index could also be a cause or effect. Increased weight can lead to increased serum insulin concentrations and, as described above, increased free testosterone levels.

4-There may be a genetic factor but this remains controversial.

#### **Sign and symptoms:**

The most common symptom is infertility, which occurs in 75% of patients. Other manifestations of PCO include hirsutism (70%), menstrual irregularities (amenorrhea 50%, functional bleeding 30%, and dysmenorrhea 25%), obesity (40%), insulin resistance, and virilization (20%)<sup>(3)</sup>.

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**Treatment:****A-Lifestyle:**

Weight loss in women with elevated BMI is an effective management strategy in women with PCOS<sup>(1)</sup>.

**B-Anovulation and Infertility (if pregnancy is desired):**

1-Clomifene citrate and Tamoxifen is an effective treatment for anovulation in PCOS<sup>(1)</sup>. Current recommendation being not to exceed 6 months of continuous therapy<sup>(1)</sup>.

2-Gonadotrophin therapy: Recombinant FSH and human menopausal gonadotrophin are both effective for ovulation induction in women with clomifene-resistant PCOS<sup>(1)</sup>.

3-As recent evidence has suggested that insulin resistance may be a cause and not an effect of PCOS, then treating insulin resistance has the potential to be the most appropriate action<sup>(1)</sup>. Metformin (Glucophage ®) has been the most commonly used drug in clinical trial<sup>(1,2)</sup>. (initially 500 mg with breakfast for 1 week, then 500 mg with breakfast and evening meal for 1 week, then 1.5–1.7 g daily in 2–3 divided doses<sup>(4)</sup>). However, this use still requires further evaluation and is still unlicensed<sup>(1)</sup>.

**C-Management of skin manifestations and hyperandrogenism<sup>(1)</sup>:****1-Acne:**

Mild acne: Topical agents like benzyl peroxide, azelaic acid, clindamycin lotion, erythromycin gel.

Mild: it may require oral antibiotics such as tetracyclines or erythromycin.

Severe: Oral isotretinoin.

**2-Hirsutism:**

A-Combination of oral contraceptive pill and cyproterone acetate (anti-androgen)

B-Spironolactone: oral aldosterone antagonist with anti-androgenic properties.

C-Flutamide: Anti-androgenic agent

D-Finasteride: (5- $\alpha$  reductase inhibitor).

**Long-Term Health Implications of PCOS<sup>(1)</sup>:**

1-Incrteased incidence of multiple pregnancy with subsequent increase in Perinatal mortality and morbidity.

2-Increased incidence of gestational DM and pregnancy-induced hypertension.

3-Increased incidence of endometrial and ovarian cancer.

**References:**

1- David M. Luesley and Philip N. Baker. Obstetric and Gynecology. An evidence – based text for MRCOG.2004.

2- Bad hair day. Chemis t& Druggist 7 June 2003 : 21-24.

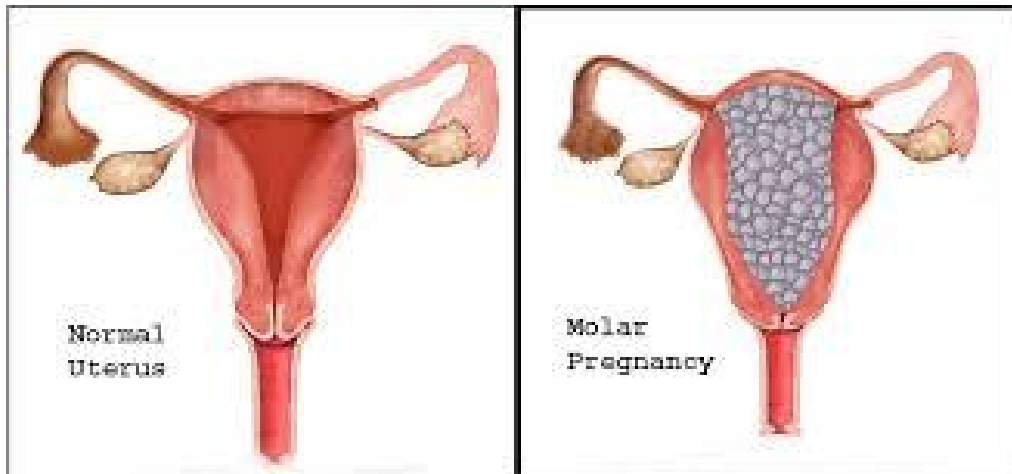
3- Martin L. Pernoll, M.D. Benson & Pernoll's. handbook of Obstetric and Gynecology .10<sup>th</sup> Edition.2001.

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## Molar Pregnancy

Molar pregnancy is an abnormal form of pregnancy in which a non-viable fertilized egg implants in the uterus and will fail to come to term. A molar pregnancy is a non-cancerous (benign) tumor that develops in the uterus that has swollen chorionic villi. These villi grow in clusters that resemble grapes. A molar pregnancy can develop when fertilized egg had not contained an original maternal nucleus. The products of conception may or may not contain fetal tissue. Molar pregnancies are also called gestational trophoblastic disease (GTD), hydatidiform mole or simply referred to as a “mole”.



Molar pregnancy can either be complete or partial, Complete molar pregnancies have only placental parts (there is no baby), and form when the sperm fertilizes an empty egg. Because the egg is empty, no baby is formed. The placenta grows and produces the pregnancy hormone, hCG.

**Partial Mole** occurs when the mass contains both the abnormal cells and an embryo that has severe birth defects. In this case the fetus will be overcome by the growing abnormal mass rather quickly.

### Risk factors for a molar pregnancy:

- Women over the age of 40
- Women who have had a prior molar pregnancy
- Women with a history of miscarriage

### Symptoms:

- Vaginal spotting or bleeding
- Nausea and vomiting
- Develop rare complications like thyroid disease
- Early preeclampsia (high blood pressure)
- Increased hCG levels
- No fetal movement or heart tone detected

**Diagnosis:** by pelvic examination that may reveal a larger or smaller uterus, enlarged ovaries, and abnormally high amounts of hCG and ultrasound (will often show a “cluster of grapes” appearance).

**Treatment:** A molar pregnancy can't continue as a normal viable pregnancy. To prevent complications (in order to avoid the risks of choriocarcinoma), the molar tissue must be removed either by:

- 1- Dilation and curettage (D&C).
- 2- Hysterectomy.

Patients are followed up until their serum human chorionic gonadotrophin (hCG) level has fallen to an undetectable level. Invasive or metastatic moles (cancer) may require chemotherapy and often respond well to methotrexate (MTX) or EMA/CO therapy.

The majority of women with persistent trophoblast disease after a molar pregnancy will fall into the low-risk treatment group and start chemotherapy with intramuscular methotrexate combined with oral folinic acid rescue as shown in the box below. The first cycle of treatment is given as an inpatient, with the following cycles administered closer to home. Women with an initial pretreatment hCG of >1000 IU/l may stay as inpatients for longer as they have a higher risk of bleeding: the larger tumors shrink rapidly with the initiation of chemotherapy.

a) Methotrexate/folinic acid treatment schedule	
Day 1	methotrexate 50 mg IM at noon
Day 2	folinic acid 15 mg orally at 6 p.m.
Day 3	methotrexate 50 mg IM at noon
Day 4	folinic acid 15 mg orally at 6 p.m.
Day 5	methotrexate 50 mg IM at noon
Day 6	folinic acid 15 mg orally at 6 p.m.
Day 7	methotrexate 50 mg IM at noon
Day 8	folinic acid 15 mg orally at 6 p.m.
b) EMA/CO chemotherapy	
Week 1	
Day 1	dactinomycin 0.5 mg IV etoposide 100 mg/m <sup>2</sup> IV methotrexate 300 mg/m <sup>2</sup> IV
Day 2	dactinomycin 0.5 mg IV etoposide 100 mg/m <sup>2</sup> IV folinic acid 15 mg orally 12 hourly × 4 doses, starting 24 hours after commencing methotrexate
Week 2	
Day 8	vincristine 1.4 mg/m <sup>2</sup> (maximum 2 mg) cyclophosphamide 600 mg/m <sup>2</sup>
IM = intramuscularly; IV = intravenously	

The use of folinic acid as a supplement is because MTX is classified as an antimetabolite due to its antagonistic effect on folic acid metabolism (folate antagonist). Many patients treated with MTX experience mucosal, gastrointestinal, hepatic or haematologic side effects. Supplementation with folic or folinic acid (a reduced folic acid) during treatment with MTX may ameliorate these side effects and minimize its toxicity.

## Some Drugs that are Used in Obstetric and Gynecology<sup>(1)</sup>

**1-Clomifene** (clomiphene) citrate (Clomid® citrate 50 mg tablet)

Anti-oestrogens used in female infertility caused by anovulation (oligomenorrhoea or secondary amenorrhoea). Dose : 50 mg daily for 5 days, starting within about 5 days of onset of menstruation (preferably on 2nd day) or at any time if cycles have ceased; second course of 100 mg daily for 5 days may be given in absence of ovulation; 3 courses should constitute adequate therapeutic trial .

**2-Dydrogesterone** (Duphaston ® 10mg tablet)

Progesterone analogue used in: Endometriosis, dysfunctional uterine bleeding, dysmenorrhoea, amenorrhoea, and premenstrual syndrome .

It may be used in the following but not recommended: Infertility, irregular cycles, and recurrent miscarriage (habitual abortion).

**3-Norethisterone** (Primolut N® 5 mg tablet): Progesterone analogue used in: Endometriosis, dysfunctional uterine bleeding, dysmenorrhoea, amenorrhoea, premenstrual syndrome and postponement of menstruation.

**4-Medroxyprogesterone Acetate** (Provera®: 2.5, 5 and 10 mg tablets, Depo-Provera® 150 mg injection) Progesterone analogue used orally in: dysfunctional uterine bleeding , secondary amenorrhoea, endometriosis, progestogenic opposition of oestrogen HRT.

Depo-Provera® 150 mg injection used as a contraceptive for about three months.

**5-Methyl ergometrine** (methergin ®) tablet 125mcg, injection: 200 mcg /mL (1 mL ampoule). Use in the prevention and treatment of post partum hemorrhage.

**6-Oxytocin** (Pitocin®) 10 IU / mL (1 mL ampoule) use to induce or augment labour and the prevention and treatment of post partum hemorrhage.

**7-Tamoxifen** (10 and 20 mg tablet) used in breast cancer, and anovulatory infertility.

**8-Human Chorionic Gonadotrophin; HCG** (Pregnyl ® Injection, 500-unit amp, 1500-unit amp 5000-unit amp) is used in the treatment of infertility in women with proven hypopituitarism or who have not responded to clomifene.

**9-Pergonal**® injection contain 75 units of FSH, and 75 units of human LH) is used in the treatment of infertility in women with proven hypopituitarism or who have not responded to clomifene. lutropin alfa (Recombinant human LH ) Injection, 75-unit Luveris®.use like pergonal®.

**10-Conjugated oestrogens** (Premarin® 652 mcg, and 1.25 mg tablets) use as a Hormone replacement therapy (HRT) for a alleviating menopausal symptoms.

**11-Trisequens** ® tablets: 12 blue tablets of estradiol 2 mg; 10 white tablets of estradiol 2 mg, norethisterone acetate 1 mg and 6 red tablets of estradiol 1 mg. use as a hormone replacement therapy (HRT) for a alleviating menopausal symptoms.

**12-Danazol** (Danol®100 mg, 200 mg cap). It is licensed for the treatment of endometriosis and for the relief of severe pain and tenderness in benign fibrocystic breast disease where other measures have proved unsatisfactory.

**13-Bromocriptine** (Parlodel® 2.5 mg tablet): is used for the prevention of lactation in galactorrhoea.

14-**Cabergoline** (Dostinex ® 0.5 mg tablet) has actions and uses similar to those of bromocriptine, but its duration of action is longer.

15-**Goserelin** (Zoladex® 3.6 mg injection): Gonadorelin analogues are used in the treatment of endometriosis, precocious puberty, infertility and breast cancer.

16-**Buserelin, Leuprorelin acetate, Nafarelin, Triptorelin**: Gonadorelin analogues are used in the treatment of endometriosis, precocious puberty, infertility and breast cancer.

17-**Tranexamic acid** (Cyklokapron®, Exacyl® 500 mg tablet, and 500 mg /5 mL injection). It is used to stop vaginal bleeding.

18-**Isoxsuprine** (Duvadilan® 10 mg and 20 mg tablet): uterine relaxant.

**Reference:**

1-BNF 67

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