

MEDSTAR

CLINICAL GUIDE AND SYNOPSIS

FIRST EDITION

OBSTETRICS AND GYNECOLOGY



PREPARED BY

MEDICAL STUDENTS OF 2008 E.C BATCH

JIMMA UNIVERSITY, ETHIOPIA



FOR
REVISION
ONLY

MEDSTAR CLINICAL GUIDE AND SYNOPSIS GYNECOLOGY AND OBSTETRICS

FIRST EDITION

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JUMC 2008E.C. MEDICAL STUDENT BATCH

Preface

The first edition of *MEDSATR CLINICAL GUIDE AND SYNOPSIS TO OBSTETRICS AND GYNECOLOGY (OBGYN)* is one of the three similar works, which include similar sister documents for Internal medicine and Pediatrics. It is prepared as a gift for our fellow medical students to be a guide through their clinical year attachments. As its name suggest, we are hoping it will be like a star in the sky showing directions to “med-travellers” through their journey into becoming a qualified doctors.

The guide is mainly prepared by combining our ward experience and the detailed science on the textbooks for the major cases in obstetrics and gynecology. Unlike its sister documents in the other attachments, ours is mostly case oriented, this is due to the limited number of major chief complaints in OBGYN (it is not uncommon to find multiple major cases with similar chief complaints). The management plans for the major cases is mainly taken from the Jimma University OBGYN Management Guideline.

For history and physical examination in OBGYN we strongly recommend you to read, *Introduction to Obstetrics and Gynecology diagnosis, by Dr. Asheber Gaym*. You should also check the simplified format for history taking and physical examination prepared by Jimma Medical Center OBGYN Department.

In conclusion, we would like to say, we have tried to make this guide as readable as possible. This work is just a start, and without doubt there will be some flaws in the document, but we are going to add more details and include more cases in the coming edition. So in the meantime we hope these documents might came handy as additional source for our fellow medicos in understanding OBGYN.

We have prepared an Email address and Telegram bot link so that we could get your feedback on the book and come up with a better second edition in upcoming years.

Email address: MEDSTARcomment@Gmail.com

Telegram bot link: @MedstarCommentsBot

The Contributors

Prepared by Jimma University Medical Students of 2008 E.C. Batch

ACKNOWLEDGMENT

We would like to express our sincere gratitude to the medical students who have sacrificed their time in relentlessly committing to this book. And we are grateful to Dr. Asfaw of Jimma University OBGYN department, for his invaluable, comments and suggestions for some of the cases of this book.

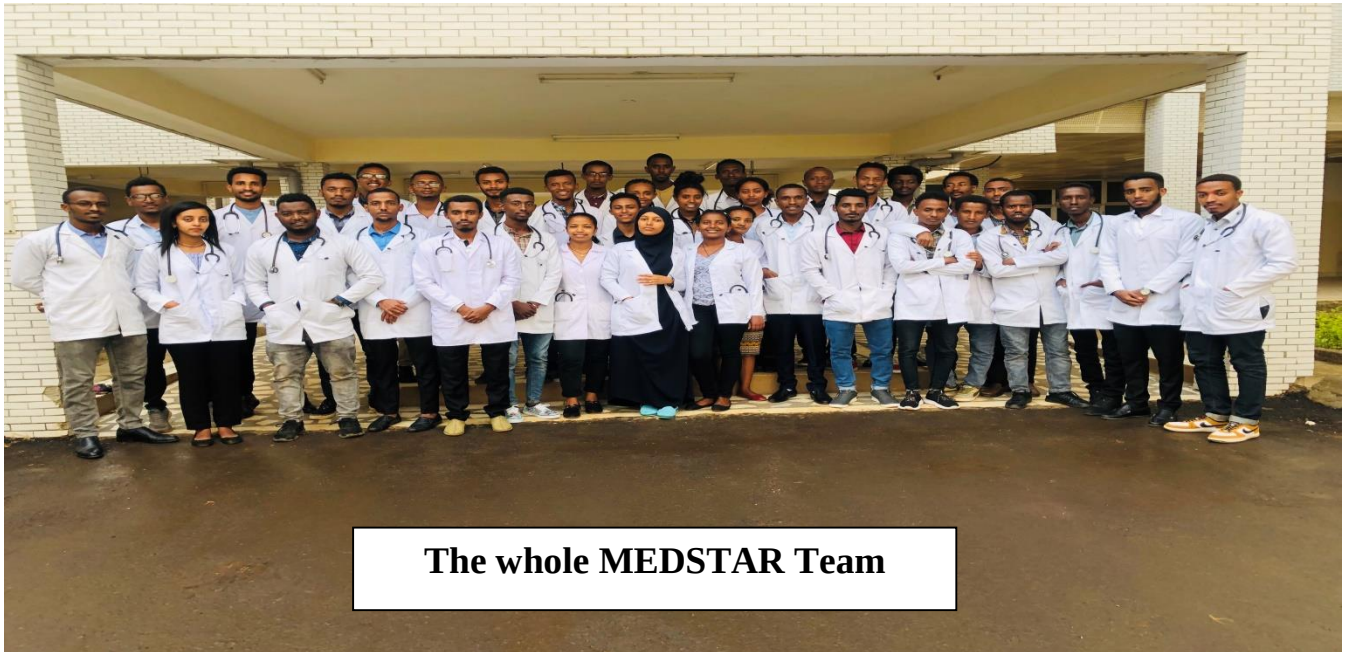
Special thanks are due to all Jimma University medical students who have been taking part by commenting on the cases, getting the right resources and helping us build this book to guide you in need.

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SECTION ONE

OBSTETRICS

CHAPTER 1

HYPERTENSIVE DISORDERS OF PREGNANCY (HDP)

HDP are one of the most common obstetric complications, affecting 5-10% of all pregnancy.

- Along with hemorrhage and infection it forms the deadly triad during pregnancy as a cause of maternal mortality.

DEFINITION AND CLASSIFICATION

Hypertension (HTN) is diagnosed empirically when appropriately[#] taken blood pressure exceeds 140mmHg systolic or 90mmHg of diastolic.

- The blood pressure must be observed at least on two occasions 4hrs apart but not more than 7days apart.
- [#]appropriate BP measurement include,
 - 1) Avoiding smoking, caffeine and exercise for 30min prior to measurement
 - 2) Patient should sit quietly for 5min (10min, old JUSH guideline) in a chair with feet on the floor.
 - 3) Measurement is taken from right arm at the level of the heart
 - 4) Using appropriate BP cuff size
 - Width of the inflatable bladder of the cuff should be about 40% of the upper arm circumference (about 12-14cm in the average adult)
 - Length of the inflatable bladder should be about 80% of the upper arm circumference(almost long enough to encircle the arm)

- The standard cuff is 12X23cm, appropriate for arm circumference up to 28cm
- 5) The 5th Korotkoff sound is used for diagnosis
 - Generally, avoid factors that will falsely or temporarily increase the BP, like:-
 - smaller cuff size
 - a loose cuff or a bladder that balloons outside the cuff
 - taking stimulants within the 30min prior to measurement
 - stressful environment
 - sitting with legs crossed
 - On the contrary larger cuff size and taking antihypertensive medications will decrease BP measurement.
 - *Read more on the steps and techniques of BP measurement on Bates Guide to Physical Examination 12ed.*

NB, we don't necessarily need both the systolic and diastolic BP to be elevated to diagnose HTN; elevation of one of them is enough for diagnosis

Severe HTN is when sustained elevation of SBP of ≥ 160 mmHg or DBP of ≥ 110 mmHg is observed on two occasions for at least 4hrs apart but not more than 7days

Proteinuria: Can be diagnosed before or during pregnancy, and it is defined as:

- ≥ 0.3 g protein in 24hr urine collection, or
- Protein: creatinine(P/C) ratio of ≥ 0.3 , or
- A dipstick measurement of $\geq 1+$ on two occasions

The concentration of urinary protein is influenced by contamination with vaginal secretions, blood, bacteria, or amniotic fluid. It also varies with urine specific gravity and pH, exercise, and posture.

- It usually appears after HTN, but it may also appear before HTN too

Edema: Is defined as an excessive weight gain of >1.8kg in 1wk in the second or third trimester. It may be the first sign of the potential development of PE

According to ACOG (2013) there are four types of hypertensive disorders during pregnancy

1. Gestational HTN (GH)
2. Preeclampsia eclampsia syndrome (PE-E syndrome)
3. Chronic essential HTN
4. Preeclampsia-superimposed on chronic HTN

Delta HTN

Normally during the first and second trimester of pregnancy the blood pressure declines to a nadir at 24-26wks of gestations and then rises afterward (mainly due to the decreased systemic vascular resistance, which is one of the physiologic changes during pregnancy).

Some pregnant women may have more than usual increment in BP especially after 32wks of gestation who by term has substantially high BP, but still under 140/90mmHg. The term delta HTN is used to describe this acute rise in BP

Some of these women will go on to have obvious PE, eclampsia or HELLP syndrome.

GESTATIONAL HTN

- Is an elevated BP without proteinuria or signs/symptoms of preeclampsia related end organ dysfunction that is diagnosed for the first time after 20 weeks of pregnancy and resolves by 12 weeks postpartum
- It is the **most frequent cause of HTN during pregnancy**

- The incidence ranges from 6-29% in nulliparous women and from 2-4% in multiparous, the incidence increases in multiple gestation.

Almost half of these women develop PE syndrome. The likelihood of progression to PE depends on gestational age (GA) at the time of diagnosis, with higher rates if the onset of HTN is before 35wks of gestation. Fortunately, most cases of GH develop at or beyond 37wks of gestation.

GH is divided in to two: Mild GH and Severe GH

- Criteria for the diagnosis of mild GH

- Systolic blood pressure >140 mm Hg but <160 mm Hg and diastolic blood pressure >90 mm Hg but <110 mm Hg
- Proteinuria of <300 mg per 24hr collection
- Platelet count of >100,000/mm³
- Normal liver enzymes
- Absent maternal symptoms
- Absent intrauterine growth restriction and oligohydramnios by ultrasound

- Criteria for the diagnosis of severe GH (see gabbe 7th edition, but there is some confusion about whether severe GH is separate thing or it is just PE)

The overall pregnancy outcome of GH depends on GA at time of diagnosis and the type of GH.

- Most cases of mild GH which develop after 37wks of gestation usually have similar outcome as normotensive pregnancy, other than higher rate of induction of labor.
- Women with severe GH has increased risk of maternal and perinatal morbidities, (greater than those with mild PE), including placental abruption, preterm delivery, and delivery of small for gestational age baby

Some reclassify GH as transient hypertension, if evidence of PE doesn't develop and the BP returns to normal by 12 weeks postpartum.

PREECLAMPSIA (PE)

PE refers to the new onset of hypertension and proteinuria or hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation in a previously normotensive woman.

Incidence:

- ranges from 2-7% in otherwise healthy nulliparous women which is generally mild, with onset near term or during labor (in 75% of cases)

NB, on Williams Obstetrics 25th Ed, the incidence is slightly different, 3-10% for nulliparous and 1.4 -4% for multiparous women

PE is categorized as, PE with severity features and PE without-severity features

Criteria for Preeclampsia with Severity Features

Preeclampsia, with severe features, is defined when either disorder is present in association with any of the following abnormalities:

- **SBP $\geq$ 160 mm Hg or DBP $\geq$ 110 mm Hg** on two occasions at least 4 hours apart while the patient is on bed rest or once if the patient has received prior antihypertensive therapy.
- **New-onset persistent cerebral symptoms:** headaches or visual disturbances
- **Impaired liver function** as indicated by abnormally elevated liver enzymes (at least twice the upper limit of normal [ULN]); severe, persistent right upper quadrant or epigastric pain that is unresponsive to medications and not accounted for by an alternative diagnosis; or both
- **Pulmonary edema** (often develop in postpartum)
- **Thrombocytopenia** (platelet count $<100,000/\mu\text{l}$)

- **Progressive renal insufficiency** (serum creatinine >1.1 mg/dl); some guidelines also include doubling in the patient's base line creatinine in absence of other renal diseases.

NB, the amount of proteinuria (≥ 5 gm in a 24hr urine specimen or $\geq 3+$ on dipstick), oliguria, and presence of intrauterine growth restriction (IUGR) or fetal growth restriction (FGR) by ultrasound have been **removed** as criteria for the diagnosis of severe disease.

Even though HTN is considered to be the hallmark of PE, some patient with PE may present with signs of PE without HTN, - and it is referred to as **atypical PE**.

- The criteria for atypical preeclampsia include gestational proteinuria or FGR plus one or more of the following:
 - Severity features of preeclampsia without hypertension: hemolysis, thrombocytopenia, elevated liver enzymes,
 - Early signs and symptoms of PE-E syndrome earlier than 20 weeks, (seen in patient with molar pregnancy, hydropic degeneration of chorionic villi and antiphospholipid antibody (APA) syndrome and
 - Late postpartum PE-E syndrome (>48 hours postpartum but less than six weeks after delivery).

RISK FACTORS OF PE

- **Nulliparity**, (limited sperm exposure)
- **Age** <20yrs or >40yrs
- **Race**, (higher in the Black population because of genetic predisposition)
- **Pregnancy with the aid of artificial reproductive technology**
 - Use ART increase risk because:
 - Increase chance that the women is >40yrs, nulliparous or obese with PCOS
 - Increase possibility of multiple gestation,
 - It pregnancy with donated gametes or embryos

- **Multifetal gestation** (increase risk to 13%)
- **Obesity/gestational diabetes mellitus** (BMI $\geq 35\text{kg/m}^2$ increase risk to 13.3%)
- **PE in previous pregnancy**
 - In women with severe PE in previous pregnancy, around 21% will have severe PE in the subsequent pregnancy.
 - The earlier PE is diagnosed in the index pregnancy, the greater the likelihood of recurrence.
- **Preexisting medical-genetic conditions**
 - Chronic hypertension
 - Renal disease
 - Type 1 DM
 - Antiphospholipid antibody syndrome
 - Factor V Leiden mutation
- **Interpregnancy interval >7 years**
- **Family history of preeclampsia**
- **Woman born small for gestational age**
- **Poor outcome in previous pregnancy**
 - ✓ Fetal growth restriction (FGR), placental abruption (PA), fetal death
- **Paternal factors** (men who fathered one preeclamptic pregnancy were nearly twice as likely to father a preeclamptic pregnancy with a different woman)
- ⇒ **Smoking**, unlike its effect in many obstetric and gynecologic abnormalities, carry a *reduced risk* for hypertension during pregnancy, because it up-regulates placental adrenomedullin expression which regulates volume homeostasis

ETIOPATHOGENESIS

- The etiology of PE remains unknown, but different theories have tried to explain it.

- Any satisfactory theory concerning the origins of preeclampsia must account for the observation that gestational hypertensive disorders are more likely to develop in women with the following characteristics:-
- Are exposed to chorionic villi *for the first time*
 - Are exposed to a *superabundance of chorionic villi*, as with twins or hydatidiform mole
 - Have preexisting *conditions associated with endothelial cell activation or inflammation*, such as diabetes, obesity, cardiovascular or renal disease, immunological disorders, or hereditary influences
 - Are *genetically predisposed* to hypertension developing during pregnancy.

A fetus is not a requisite for preeclampsia to develop. And, although chorionic villi are essential, they don't need to be intrauterine.

Regardless of the precipitating etiologies, the cascade of events leading to the PE syndrome is characterized by abnormalities that result in vascular endothelial damage with resultant *vasospasm, transduction of plasma and ischemic & thrombotic sequelae*.

The mechanisms that are currently considered important in explaining the pathogenesis of PE include:

- Placental implantation with abnormal trophoblastic invasion of uterine vessels
- Immunological maladaptive tolerance between maternal, paternal (placental), and fetal tissues
- Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy
- Genetic factors including inherited predisposing genes and epigenetic influences.

Abnormal trophoblastic invasion

During normal implantation the uteroplacental (UP) arteries are formed by the action of migratory interstitial and endovascular trophoblasts in to the walls of the spiral arterioles, this transform the UP arteries in to low resistance, low pressure and high flow system.

These trophoblast induced changes extend all the way from intervillous space to the origin of spiral arteries (to inner 3rd of myometrium). These changes are effected in two stages:

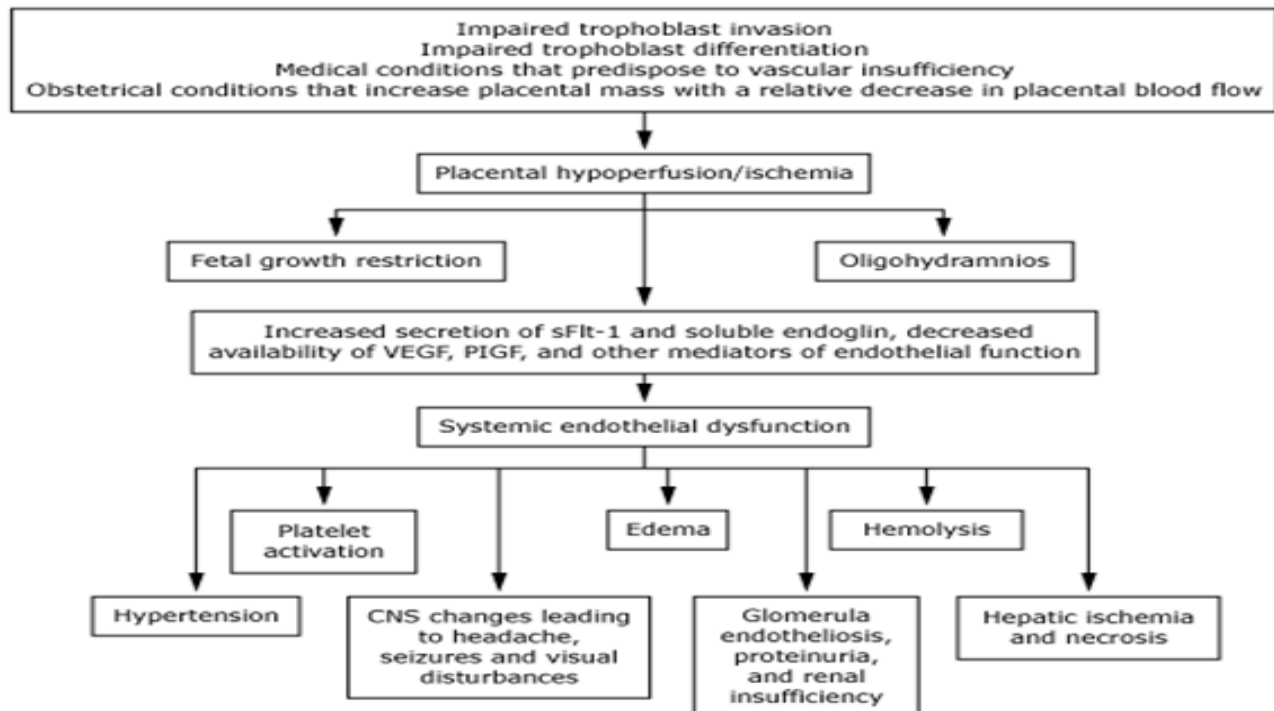
- ✓ 1st wave involve decidua segment of the arteries and occur in 1st trimester
- ✓ 2nd wave involving the myometrium segment and occur in 2nd trimester (after 16th week)

In pregnancies complicated with PE these changes are *limited to the decidua segment*, leaving the myometrial segments as high pressure and low flow system, resulting in limited UP blood flow(→Placental ischemia and FGR).

The pathogenesis of PE is divided into two artificial stages:-

- Asymptomatic Placental Stage
 - Caused by faulty endovascular trophoblastic remodeling
- Symptomatic Maternal Stage
 - Causes by the changes in stage one
 - Is susceptible to modification by preexisting maternal conditions that are manifested by endothelial cell activation or inflammation, such as cardiovascular or renal disease, DM, immunologic disorders... hence they are risk factors!

The following diagram shows a model for Pathogenesis of PE



PATHOPHYSIOLOGIC CHANGES IN PE

Hematological changes

- Thrombocytopenia
 - NB**, once it developed thrombocytopenia usually continues to worsen, so delivery is recommended
- Hemolysis, (Microangiopathic Hemolysis)
- HELLP syndrome

Renal changes

- Reduced renal perfusion and GFR (up to 25% below normal pregnancy)
- Oliguria,
 - NB**, Intensive IV fluid therapy is not indicated as a treatment for preeclamptic women with oliguria, unless urine output is diminished from hemorrhage or fluid loss from vomiting or fever

- Proteinuria, may develop late, for example, approximately 10-15% of HELLP syndrome and 17% of patient with eclampsia don't have proteinuria at the time of presentation.
- Increased urine sodium level
- Increased serum creatinine and uric acid level
- AKI in patients with comorbid hemorrhage with hypovolemia and hypotension (for example, in patient with severe placenta abruption)

NB, PE is the most common cause of AKI in pregnancy

HELLP syndrome

Criteria to establish the diagnosis of HELLP syndrome

- Hemolysis (at least two of the following)
 - ✓ Peripheral blood smear showing schistocytes, or burr cells
 - ✓ Serum Bilirubin $\geq 1.2\text{mg/dl}$
 - ✓ Low serum haptoglobin
- Severe anemia (Microangiopathic Hemolytic Anemia) unrelated to blood loss
- Elevated liver enzymes
 - ✓ ALT/AST at least twice the ULN (upper limits of the normal)
 - ✓ LDH $>600\text{U/L}$ ($>2\text{x}$ the ULN)
- Low platelets

Based on the platelet count HELLP syndrome is classified in to 3 classes

- ✓ Class I, platelet count $< 50,000/\text{mm}^3$
- ✓ Class II,,,,,,,,,,,,,,,,,,,,, $50,000 - 100,000/\text{mm}^3$
- ✓ Class III,,,,,,,,,,,,,,,,,,,,, $100,000 - 150,000/\text{mm}^3$

(See the rest of the pathophysiological changes on Williams 25th, only few are mentioned here)

CLINICAL MANIFESTATIONS OF PE

The clinical findings of PE can manifest as either a maternal syndrome or a fetal syndrome

Maternal syndrome

- The maternal syndrome of PE represents a clinical spectrum with major differences between near term PE without demonstrable fetal effects and PE that is associated with low birth weight and preterm delivery. Maternal manifestations include:
 - Symptoms
 - Headache (severe, global type, which is unresponsive to NSAIDs)
 - Blurring of vision, or less commonly double vision and blindness (from retinal detachment)
 - Right upper quadrant or Epigastric pain
 - Swelling of the face or vulva
 - Vaginal bleeding
 - Nausea/vomiting
 - Difficulty of breathing
 - Signs
 - Elevated BP, (**NB**, BP could be normal and patient still can have PE)
 - Facial (generalized) edema
 - Signs of pleural effusion and ascites
 - RUQ tenderness
 - Mental status change (confusion to coma, *result of cerebral edema*)
 - Hyperreflexia
 - Laboratory findings
 - Proteinuria
 - MAHA, Thrombocytopenia
 - Elevated serum AST/ALT, LDH, creatinine and bilirubin level
 - Findings of DIC

Fetal manifestations include: - Oligohydramnios, FGR, Abruptio, Vascular stillbirth and Preterm delivery

PREDICTION AND PREVENTION OF PE

- ACOG recommends the use of only risk factors for identifying women considered to be at risk for PE and None of the interventions suggested in the book (Gabby 7th ed) offer significant benefit in preventing PE

ECLAMPSIA

- *Eclampsia* is defined as the development of convulsions (generalized tonic-clonic) or unexplained coma during pregnancy or postpartum in patients with signs and symptoms of PE.
- In the western world, the reported incidence of eclampsia ranges from 1 in 2000 to 1 in 3448 pregnancies.
- Eclampsia can develop antepartum, intrapartum (most of the time) or postpartum (in around 10% of cases, mostly within 48hr of delivery)
 - *Late postpartum eclampsia* is defined as eclampsia that occurs after 48 hours but before 4 weeks of delivery.
 - Eclampsia that occurs before the 20th week of gestation is generally associated with molar or hydropic degeneration of the placenta with or without a coexistent fetus

Diagnosis

- The diagnosis of eclampsia is secure in the presence of generalized edema, hypertension, proteinuria, and ***convulsions***.

- At least one of the following occur in 59-75% of cases
 - Persistent occipital or frontal headache
 - Blurring of vision (blindness is seen in up to 10-15% of eclamptic patients, and it is mainly due to occipital lobe edema)
 - Photophobia
 - Epigastric or right upper quadrant pain
 - Altered mental status
- CT scan or MRI of the brain is not necessary for the diagnosis and management of eclampsia. However, it is indicated for patients with:
 - ✓ Focal neurologic deficit or prolonged coma
 - ✓ Atypical presentations
 - Onset <20wk of gestation or >48hr postpartum
 - Eclampsia refractory to adequate therapy
- Differential diagnosis for eclampsia (see Gabby 7th Ed, p692)

Maternal and fetal outcomes of eclampsia

Maternal (with incidence): - placental abruption (PA, 7-10%), DIC (7-10%), Pulmonary edema (3-5%), AKI (5-9%) Aspiration pneumonia (2-3%) and Cardiopulmonary arrest (2-5%)

Feta or perinatal: - Prematurity, PA, Severe FGR, Preterm delivery, is about 50% and about 25% occur before 32wks of gestation

Prevention of eclampsia

Can be:-

- **Primary:** by preventing the development and /or progression of PE,
- **Secondary:** by using pharmacologic agents that prevent convulsions in women with established PE.
- **Tertiary:** by preventing subsequent convulsions in women with established eclampsia

Some of the recommended preventive therapies include:

- close monitoring (in-hospital or outpatient),
- use of antihypertensive therapy to keep maternal BP below a certain level (< severe range or to normal values),
- timely delivery, and prophylactic use of magnesium sulfate during labor and immediately postpartum in those considered to have PE
- Prophylactic MgSO₄ is recommended only for women who are hospitalized with the established diagnosis of PE. MgSO₄ is associated with a significantly lower rate of recurrent seizures and a lower rate of maternal death than that observed with other agents, like diazepam.

NB, *about 31-87% of eclampsia is considered unpreventable*

CHRONIC HYPERTENSION IN PREGNANCY AND SUPERIMPOSED PE

Chronic HTN: Is defined as an elevated BP that is present prior to conception or is diagnosed before 20th week of gestation, or HTN that persist for more than 12wks postpartum.

- The frequency of chronic hypertension in pregnancy is estimated at 1% to 5%.

Women with chronic hypertension are at increased risk for superimposed PE.

Maternal and Perinatal Risks

Maternal: increased risk for the development of superimposed PE, PA (0.7% -2.7% in those with mild HTN and 5% -10% in those with severe or high-risk HTN), and FGR

Perinatal: perinatal mortality (3-4x greater), premature delivery and a growth restricted infant

Superimposed PE

The overall rate of superimposed PE is 25% (14% to 28% in mild HTN and 50% to 79% in severe HTN), the rate is not affected by maternal age, race, or presence of proteinuria early in pregnancy.

Recommended criteria to diagnose preeclampsia in women with preexisting medical conditions

Conditions	Criteria
Hypertension only	Proteinuria of ≥ 300 mg per 24hr or thrombocytopenia.
Hypertension plus proteinuria (renal disease or class F diabetes)	Worsening severe hypertension plus proteinuria and either ▪ new onset of symptoms ▪ thrombocytopenia, or ▪ elevated liver enzymes

MANAGEMENT OF PE-E SYNDROME

Management of PE

Management of PE depends on the severity of PE and the GA. It can be an expectant and definitive management.

NB, termination of pregnancy is the only cure for PE

Antepartum management**Mild preeclampsia**

Managed as outpatient

➤ Expectant management

- follow up
 - Urine protein every other day
 - BP measurement daily
 - Weight measurement every other day
 - Fetal movement count daily
 - ANC follow up twice weekly
 - CBC and liver enzymes during each ANC visit
 - NST and serial fetal growth and amniotic fluid evaluation
- The patient should be reminded to report any sign of severity if developed during the expectant management period.

NB, if expectant management is undertaken after 37 weeks, the patient should understand that the only known benefit is a possible reduction in the rate of cesarean birth.

➤ Indication for delivery (definitive mgt)

- GA is ≥ 40 wks or ≤ 28 wks
 - 37–40 weeks, if cervical status is favorable, induction is initiated. If the cervical status is unfavorable, pre-induction cervical ripening agents are used as needed
 - Abnormal antepartum testing
 - If evidence of worsening preeclampsia is seen
- ✎ Prophylactic intrapartum magnesium sulfate is indicated to prevent convulsions.

Severe preeclampsia

Severe preeclampsia *mandates hospitalization.*

➤ Expectant management

- Is given until development of maternal or fetal indications for delivery or until achievement of fetal lung maturity or 34 weeks' gestation.
- Acute BP control and maintenance of BP below severe level
- IV MgSO₄ is begun to prevent convulsions for the first 24-48 hours, anticonvulsant should be discontinued if no indications for delivery develop
- Corticosteroids to accelerate fetal lung maturity (Dexamethasone 6mg IM BID four doses) and delivery after 48 hours
- Follow up with preeclampsia chart
- Laboratory evaluation includes a platelet count, liver enzymes, and serum creatinine.
- Fetal evaluation includes fetal heart monitoring, a BPP, and fetal growth assessment

Antihypertensive therapy

The aim of this therapy is to keep the SBP between 140 & 160mmHg and DBP between 90 & 110mmHg.

Acute blood pressure control

- Hydralazine (peripheral vasodilator) 5–10 mg IV. The onset of action is 10–20 minutes, and the dose can be repeated in 20–30 minutes if necessary (**maximum of 60 mg IV or 300 mg PO in 24 hours**)
- Labetalol (Beta blocker) 5–20 mg by slow IV push. The dose can be repeated in 10–20 minutes
- Nifedipine (calcium channel blocker) 5–10 mg orally. The dose can be repeated in 20–30 minutes, as needed

Maintenance antihypertensive therapy

- Methyldopa up to 4gm/day PO in divided doses depending on the response
- Nifedipine 10-20mg PO every 6hrs

We normally do not use diuretics as an antihypertensive medication in PE. Use of potent loop diuretics can *further compromise placental perfusion* because it result in redistribution of the intravascular volume, which most often is already reduced in severe preeclampsia. Therefore, before delivery, diuretics are not used to lower blood pressure.

NB, we use antepartum furosemide or similar drugs solely to *treat pulmonary edema*.

Neuroprophylaxis—Prevention of Seizures

- Magnesium sulfate (MgSO_4)
 - Is the most preferred and effective anticonvulsant prophylaxis
 - Its neuroprotective effect is proposed to be through the following mechanisms:
 - reduced presynaptic release of the neurotransmitter glutamate
 - blockade of glutamatergic N-methyl D-aspartate (NMDA) receptors
 - potentiation of adenosine action
 - improved calcium buffering by mitochondria, and
 - blockage of calcium entry via voltage-gated channels
 - Dosage
 - IV loading dose of 4gm over 20–60 minutes and 10gm IM half on each buttock, followed by a maintenance dose of 3gm/hour IV or 5gm IM in alternate buttocks every 4 hours. If convulsion occurs after MgSO_4 is started, give 2gm MgSO_4 IV.

➤ Toxicity

- Is dependent on the plasma magnesium level
 - Loss of deep tendon reflexes occurs at 8 to 10 mEq/L
 - Respiratory paralysis at 10 to 15 mEq/L
 - Cardiac arrest at 20 to 25 mEq/L
 - In the event of these adverse effects MgSO_4 should be discontinued and Calcium gluconate (10 mL of 10% solution) should be given.
 - Urine output is monitored, and the magnesium dose is adjusted accordingly to prevent hypermagnesemia (UOP <30 ml/hour → reduce MgSO_4 dose to half).
- Other than preventing seizure, MgSO_4 also has, (1) inhibitory effect in uterine contraction(at higher plasma concentration), (2) protective effect against the development of cerebral palsy in very-low-birth weight newborns, and (3) relieving effect on headache and blindness

➤ Contraindications

- Hypermagnesemia
 - Hypocalcaemia
 - Skeletal muscle disorders, progressive muscle weakness with carcinoma
 - Severe renal impairment
 - Myasthenia gravis and Allergies
- In absence of magnesium sulfate one may use diazepam 30mg/1000ml D5W 30 drops per minute and 10mg IV bolus if convulsion occurs.

➤ Indications for definitive management (delivery)

- The gestational age is ≥ 34 wks
- Fetal pulmonary maturity is confirmed,
- When there is imminent risk for eclampsia (persistent severe symptoms)
- Multi-organ dysfunction
- Severe IUGR (< 5 th percentile)
- Suspected placental abruption
- Non-reassuring fetal testing

Intrapartum management

- If there are no contraindications to labor, *vaginal delivery is the preferred approach.*
- Cervical ripening agents and oxytocin are used as needed.
- Prophylactic anticonvulsant
- To avoid pulmonary edema, total IV fluids should not exceed 100 mL/hour.
- Pain control is achieved with regional anesthesia or with intramuscular or IV narcotic analgesics.
- The use of either epidural, spinal, or combined techniques of regional anesthesia is the method of choice during cesarean delivery.

Postpartum Management

- Close monitoring of BP, of symptoms consistent with severe disease, and accurate measurements of fluid intake and urinary output.
- Magnesium sulfate should be continued for at least 24 hours.
- Antihypertensive medications are discontinued if the BP remains below the hypertensive levels for at least 48 hours.

- 5 days of oral furosemide therapy (20 mg/day) enhances recovery and reduces the need for antihypertensive therapy in women with severe preeclampsia.
- If neurologic symptoms exist, brain imaging (if available) is undertaken to rule out the presence of cerebral pathology.

MANAGEMENT OF ECLAMPSIA

- Anticonvulsants – MgSO_4 (same dosage as in severe PE)
 - Alternative supplementary anticonvulsant medication include
 - Intravenous barbiturate (given slowly).
 - Midazolam or lorazepam may also be given in a small single dose, but prolonged use is avoided because it is associated with a higher mortality rate from aspiration pneumonia
 - Acute BP control
 - Supportive management to patients with loss of consciousness
 - Deliver the baby after the patient is stabilized
- N.B. mere presence of eclampsia is not an indication for CD.*

SAMPLE HISTORY

Chief Compliant: Headache of 2days duration

HPP:

This is a 19yrs old primigravida lady whose LNMP was on 19-4-12EC (reliable) making the EDD on 24-1-13EC and gestational age of 33⁺²wks(on 12-12-12EC, date of clerking). Menses was regular, coming every 28-30days and lasting for 3-4days, she usually used 2-3 tampons per day, and flow wasn't associated with clot or any abdominal discomfort. She used to take injectable contraception for two years, but stopped 6month before she saw her last period.

She suspected she was pregnant after her period was delayed for two weeks and when she started to have nausea & vomiting, which was usually in the mornings, then she went to the local health center, where urine pregnancy test was done and she was told that she was pregnant, (**NB.** if she remembers, write the specific date the test was done, and if ultrasound was done write the gestational age too), and She was told to return after 3months to start her ANC follow up. She has 4 ANC visits at () local health center.

Her first ANC visit was when she was around 4month pregnant, (**NB.** for all visits write specific date if she has a card or if she remembers correctly). On this visit history was taken, weight, height and BP were measured, and abdominal examination was done. Blood and urine sample were taken. She doesn't remember any of the specific results, but she was told that everything was fine. She was given an injection on her arm and a red tablet to take 1 tablet per day. (Write "iron supplement" if she knows what it is) and was told to return after 1month.

Her 2nd, 3rd and 4th visits were on 5th, 6th, and 7th months of pregnancy respectively (some seniors may expect you to write each visit separately even though it is going to be pretty much a repetition).

Similar examination and lab investigation (only urine) were done, and all were uneventful. 2nd injection was given on the 2nd visit and red tablet was given in all the visits.

She started to feel fetal movements at around 4-5month of pregnancy(if she remembers ask exact date of fetal quickening) and it has been increasing even since and it is a rolling and kicking type. The pregnancy was wanted, planned and supported. She hasn't made any significant change in her diet after she became pregnant. Her staple diet was injera made of teff with shiro wot 3 times per day, meat on holidays and fruit and vegetables at least once per week.

Currently she is presented with a persistent global type of headache of 2days duration, which hasn't improved even if she started taking medications for headache that she found in the house. Associated with this she also has swelling on her face, both hands and both legs, the swelling started from the leg and progress upward. After admission she was told that she has an elevated blood pressure and she was given medications. Now the headache and the swelling over her face and her hands have disappeared, **otherwise:-**

Danger signs

She has no history of blurring of vision, ABM or LOC

She has no history of epigastric pain, or right upper quadrant pain.

She has no history of vaginal bleeding, or vaginal discharge, high grade fever

She has no history of excessive vomiting

She has no history of cough, or shortness of breath

She has no history of urinary frequency, decreased urine output or pain during urination

She has no history of passage of liquor or pushing down pain

Risk factors

She has no previous history of hypertension, diabetes mellitus.

She has no history of use of artificial reproductive technology

She has no history of bleeding disorders

She has no family history of similar complaints

DDx (for the headache)

She has no history of neck stiffness or fever (meningitis)

She has no history of eye pain or redness of the eye (glaucoma)

She has no history of sleep disturbance, or worsening of headache at awakening or during bending, coughing or straining (brain tumor)

She has no history of head trauma, vomiting or abnormal body movement (Subarachnoid hemorrhage, which is usually referred by the patient as “the worst headache ever”, with sudden onset, *thunderclap headache*)

She has no history of fever, pain in the jaw or tongue during chewing or ringing sensation in the ears (Temporal Arteritis)

Physical examination

Vital signs: BP=> 165/105mmHg, Pulse, RR, temp, Weight, height and BMI... normal

Abdominal examination

❖ Inspection

- The abdomen is symmetrically distended and moves with respiration (sometimes the abdomen might appear asymmetrical in pregnant ladies, more on the right side(because of the sigmoid colon on the left side, which occupy the space))
- The umbilicus is flat
- There is midline hyperpigmentation (linea nigra) and purplish marks in the lower abdomen (striae grvida)
- There is no scar or distended veins over the abdomen
- Hernia sites are free

❖ Palpation

- Superficial palpation: There is no tenderness, rigidity, or superficial mass
- Deep palpation: No organomegaly or deep mass
- Obstetric palpation
 - Fundal palpation:
 - The fundus is 6 fingers above the level of the umbilicus: - 32 weeks
 - The fundus is occupied by a soft bulky, irregular, non-ballotable mass: -breech
 - Lateral palpation
 - The longitudinal axis of the fetus is in line with the mother's longitudinal axis, -longitudinal lie
 - There is a regular or smooth surfaced, hard mass on the right side of the abdomen, -the back
 - Pelvic palpation
 - The occiput (hard ballotable mass) is palpated in the lower uterine pole: - cephalic presentation
 - The anterior shoulder is 5 fingers above the symphysis pubis: - floating
 - The cephalic prominence is opposite to the side of the back: - flexed attitude.

❖ **Percussion:** No shifting dullness or fluid thrill

❖ **Auscultation:** FHB is 140bpm heard on the right side

Musculoskeletal system: Grade II bilateral pitting edema

Assessment: *Early preterm pregnancy (33⁺²weeks) + PE with severity feature (headache) + Primigravida*

- Why early preterm? => Because of the GA determined from reliable LNMP, if she doesn't know her LNMP with certainty and told you only duration of amenorrhea, (1) your diagnosis will simply be **2nd or 3rd trimester pregnancy**, and (2) you have to include **unknown LNMP** on the assessment.

Investigation

- CBC (anemia, or thrombocytopenia)
- BG (blood group, Rh)
- Urinalysis (proteinuria, bacteriuria, UTI?)
- VDRL (Venereal Disease Research Laboratory)
- PICT (Provider-Initiated Counseling and Testing)
- Liver function test
- Serum creatinine
- Serum LDH
- Abdominal Ultrasound (fetal growth and BPP)
- Coagulation profile (if thrombocytopenia or elevated liver enzymes)

Functions of obstetric ultrasound include:-

- Diagnosis of pregnancy
- Gestational age determination
- Placental localization
- Amniotic fluid volume determination
- Fetal wellbeing assessment
- Fetal sex identification
- Confirmation of fetal viability
- Fetal weight estimation
- Diagnosis of:-
 - fetal growth restriction
 - congenital anomaly
 - multiple gestation
 - molar pregnancy
 - uterine and adnexal pathology
- *See details on obstetric ultrasound and other investigation in obstetrics on Introduction to Obstetric and Gynecological diagnosis, Asheber Gaym (M.D.)*

Management plan

- ✓ See antepartum management of severe PE above

CHAPTER 2

ANTEPARTUM HEMORRHAGE (APH)

APH or late pregnancy bleeding is vaginal bleeding during pregnancy after 28th wks and before the delivery of the fetus (the last fetus in case of multiple pregnancies).

Incidence: 2 – 3 % of all pregnancies

Classes of hemorrhage and the physiologic response

Normal physiologic adaptations and changes during hemorrhage

- In normal physiology when 10% of circulatory blood volume is lost, vasoconstriction occurs in both arterial and venous compartments in order to maintain blood pressure and preserve blood flow to essential organs.
- As blood loss reaches 20% or more of the total blood volume, increase in systemic vascular resistance can no longer compensate for the lost intravascular volume and blood pressure decreases → cardiac output falls → poor end organ perfusion and finally cardiogenic shock will ensue.

Hemorrhage classification and physiologic response

Class	Acute blood loss (ml)	% lost	Response
I	1000	15	Dizziness, palpitation, minimal BP change, narrow pulse pressure
II	1500	20-25	Tachycardia, tachypnea, sweating, weakness
III	2000	30-35	Significant tachycardia and tachypnea, restlessness, pallor and cool extremities
IV	≥2500	40	Cardiogenic shock, air hunger, Oliguria or anuria.

NB, it is important that you know these classes with the response, because it will help you to estimate the blood loss in initial assessment of the patient

CAUSES OF THIRD-TRIMESTER BLEEDING

Differential diagnosis for third trimester vaginal bleeding

1. Placental causes	2. Non-placental causes	
Abruptio placentae	Bloody show	
Placenta previa	Uterine rupture	
Vasa previa	Bleeding diathesis	
Placenta membranacea	Local causes ~5%	Cervicitis
		Cervical ca.
		Cervical polyp
		Leech infestation
		Vulvo-vaginal abnormalities
Circumvallate placenta	3. Unknown/Undetermined* causes ~25%	

***Undetermined causes:** is to indicate that causes of APH other than local causes are ruled out but the local causes are not ruled out yet, because of the need to wait 48hr after last vaginal bleeding episode to perform speculum examination.

***Unknown causes:** no identified causes after performing all the necessary physical examination, including speculum examination and investigations.

Most common once are:

- Bloody show associated with cervical change
This cervical bleeding is the consequence of effacement and dilation of the cervix, with tearing of small vessels.
- Abruptio placentae (AP)
- Placenta previa
- Vasa previa

NB, The most common cause of APH is bloody show. And the most common cause of pathologic cause of APH is AP

PLACENTAL ABRUPTION

Placental abruption (PA), or abruptio placentae (AP), refers to the premature separation of a normally implanted placenta from the uterus after 20 weeks of gestation but prior to delivery of the last fetus.

MECHANISM OF BLEEDING

- AP is commonly due to rupture of defective maternal vessels in decidua basalis causing separation of the placenta.
- In rare cases it can be due to disruption of fetal-placental vessels.

These factors cause bleeding which in turn results in a decidual hematoma which promotes placental separation, destruction of placental tissue and a loss of maternal-fetal surface area for nutrient and gas exchange.

INCIDENCE

- The overall incidence of placental abruption is approximately 1 in 100 births.

- About 1/3rd of all APH can be attributed to PA. And 40-60% of abruptions occur prior to 37 weeks of gestation.

RISK FACTORS OF AP

- Increasing parity and maternal age (incidence in primigravida ~1%, multigravida ~2.5%)
- Maternal substance use
 - Cigarette smoking (40% increased risk), Cocaine abuse (10% higher risk)

- Trauma

Blunt or penetrating trauma to the gravid abdomen has been associated with placental abruption. After a minor trauma, the risk for placental abruption is between 7% and 9%, whereas the risk may be as high as 13% after severe injury.

The two most common causes of maternal trauma are motor vehicle crashes and domestic abuse. With motor vehicle crashes, uterine stretch, direct penetration, and placental shearing from acceleration-deceleration forces are the primary etiologies of trauma-related placental abruption

- Maternal diseases
 - Hypertension (5 fold increased risk), Hypothyroidism, Asthma
- Preterm premature rupture of membranes; in 2-5% , abruption occurs
- Rapid uterine decompression associated with multiple gestation (3 fold higher risk) and polyhydramnios
- Uterine and placental factors
 - Anomalies, Synechiae, Fibroids, Cesarean scar, Abnormal placental formation and Chronic ischemia
- Prior abruption (risk of recurrence 5-17%, after two consecutive abruptions risk of recurrence rises to ~25%)
- Hyperhomocysteinemia

CLINICAL MANIFESTATION

Several factors determine the clinical manifestations of placental abruption. These factors include:

- (1) The temporal nature of the abruption (acute vs. chronic),
- (2) Clinical presentation; Overt (80%) vs. concealed (20%), and
- (3) Severity

An acute, overt abruption typically presents with

- vaginal bleeding,
- abdominal pain, and
- uterine contractions

As placental separation worsens, uterine tenderness, tachysystole, fetal heart rate (FHR) patterns consistent with hypoxia, and fetal death may occur.

The amount of vaginal bleeding correlates poorly with the extent of placental separation and its potential for fetal compromise. In fact, concealed abruption occurs in 10% to 20% of cases.

Chronic abruption may be insidious in its presentation and is often associated with ischemic placental disease. Typically, these cases present with intermittent, light vaginal bleeding and evidence of chronic placental inflammation and dysfunction, such as oligohydramnios, fetal growth restriction, preterm labor, premature preterm rupture of membranes (PPROM), and PE.

With severe abruptions more than 50% of the placental surface area separates. In these scenarios, maternal compromise in the form of consumptive coagulopathy may result from the triggering of the clotting cascade by hemorrhage and extensive thrombin deposition
→ i.e. DIC (~10% of cases)

DIAGNOSIS

- Placental abruption is primarily a clinical diagnosis that is supported by radiographic, laboratory, and pathologic studies.

Clinically: Any findings of vaginal bleeding, uterine contractions, abdominal and/or back pain, or trauma should prompt an investigation for potential placental abruption. Port wine discoloration of liquor and non-reassuring fetal status can also be indicative.

Radiological (Ultrasound): for the diagnosis of placental abruption identified less than 2% of cases.

- Early hemorrhage is typically hyperechoic or isoechoic,
- Resolving hematomas are hypoechoic within 1 week and sonolucent within 2 weeks of the abruption.

Acute hemorrhage may be misinterpreted as a homogeneous thickened placenta or fibroid.

There are three predominant locations for placental abruption:-

- **subchorionic** (between the placenta and the membranes)
- **retroplacental** (between the placenta and the myometrium)
- **preplacental** (between the placenta and the amniotic fluid)

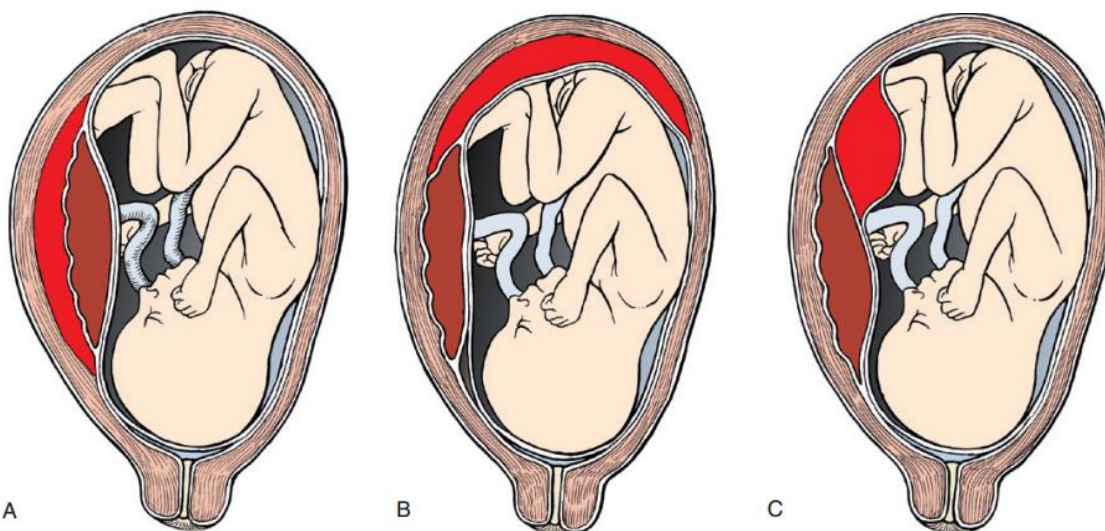


Figure 1 A) Retroplacental abruption B) Subchorionic abruption C) Preplacental abruption

NB, Retroplacental hematomas are associated with a worse prognosis for fetal survival than subchorionic hemorrhage. And the size of the hemorrhage is predictive of fetal survival; the greater the size, the greater the fatality.

Laboratory findings: Hypofibrinogenemia and evidence of consumptive coagulopathy may accompany severe abruption.

Pathologic studies: Macroscopic inspection of the placenta may demonstrate adherent clot, depression (due to missing cotyledons) of the placental surface and bleeding into myometrium causing **Couvellaire uterus**.

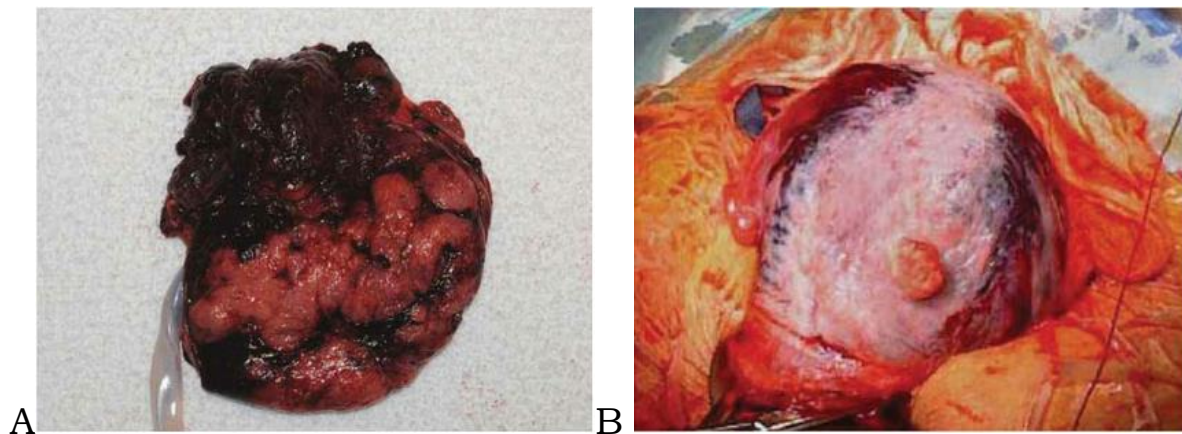


Figure 2, A. Partial placental abruption with a dark adherent clot. B. Couvellaire uterus from total placental abruption after CD

COMPLICATIONS OF PLACENTAL ABRUPTION

Maternal complications	Fetal complications
Blood loss	Intrauterine growth restriction (IUGR)
Consumptive coagulopathy	Oligohydramnios
Need for transfusion	Prematurity
End organ damage	Hypoxemia
Cesarean delivery	Still birth
Death	

Grading of abruptio placentae:

- Grade 0: Retrospective diagnosis of abruption
- Grade 1: Vaginal bleeding
- Grade 2: Vaginal bleeding, concealed hemorrhage, uterine tenderness, NRFHR
- Grade 3: Vaginal bleeding, shock, extensive concealed hemorrhage, uterine tenderness, IUFD
 - ✓ Grade 3 A: With no coagulopathy
 - ✓ Grade 3 B: With coagulopathy

MANAGEMENT OF AP

All cases should be admitted.

- Asses hemodynamic status, then
 - ⇒ IV line to be opened
 - ⇒ Fetal wellbeing monitoring
 - ⇒ HCT, BGP & Rh, platelets, fibrinogen, PT, aPTT

Grade 1:

Conservative management

- ⇒ Steroid in < 34 weeks of gestation
- ⇒ Keep in ward till bleeding subsides
- ⇒ Tocolysis in < 33 weeks of gestation
- ⇒ Follow maternal V/S, bleeding, uterine contraction & tenderness, FHB, kick count, BPP, fetal growth

Indications for delivery: Term, IUFD, malformed fetus, NRFHR, advanced labor, excessive bleeding

Grade 2 – 3:

- Asses maternal hemodynamic status, then stabilize the mother, then
 - ⇒ Maintain U.O.P > 30 ml/hr & HCT > 30%

- ⇒ Platelets (6U) transfusion if thrombocytopenia
- ⇒ FFP if fibrinogen < 100mg/dl
- ⇒ Delivery
 - Vaginal: Amniotomy & induction with oxytocin
 - C/d for uncontrolled hemorrhage & other obstetric indications
- ⇒ Hysterectomy; if uncontrolled hemorrhage occurs
- ⇒ Couvelaire uterus---Uterotonic agents, hysterectomy if unresponsive

PLACENTA PREVIA

Placenta previa is defined as the presence of placental tissue over or adjacent to the cervical os.

Recent revised classification of placenta previa consists of two variations:

- (1) **True placenta previa**; in which the internal cervical os is covered by placental tissue, and
- (2) **Low-lying placenta**; in which the placenta lies within 2 cm of the cervical os but does not cover it.

INCIDENCE

The overall reported incidence of placenta previa at delivery is 1 in 200 births. In the second trimester, placenta previa may occur in up to 6% of pregnancies.

Placental migration has been used to explain this “resolution” of placenta previa that is noted near term. Three theories have been suggested to account for this phenomenon:

- **1st theory**: as the pregnancy advances, the stationary lower placental edge relocates away from the cervical os with the development of the lower uterine segment.

- The lower uterine segment has been noted to increase from 0.5 cm at 20 weeks to more than 5 cm at term.
- **2nd theory:** the placenta-free uterine wall has been proposed to grow at a faster rate than the uterine wall covered by the placenta.
- **3rd theory: (*trophotropism*);** the growth of trophoblastic tissue away from the cervical os toward the fundus, results in resolution of the placenta previa.

ETIOLOGY OF PP

- Exact cause is unknown

Theories include:

- 1) Dropping down theory
- 2) Persistence of chorionic activity
- 3) Defective decidua
- 4) Big surface area of placenta

RISK FACTORS

- **Intrinsic maternal factors**
 - Increasing parity (Grand multipara 5% risk, Nulliparous women~ 0.2% risk)
 - Advanced maternal age (If age >35 , 4 fold increase risk, if age>40, 9 fold increase risk)
 - Maternal race (higher rates in Asian women)
- **Extrinsic maternal factors**
 - Cigarette smoking (as high as 3 fold increased risk)
 - Cocaine use
 - Residence at higher elevation (increased placental surface area due to decreased uteroplacental oxygenation)
 - Infertility treatments
- **Fetal factors**
 - Multiple gestations

- Male fetus (due to larger placental size and delayed implantation of the blastocyst)
- **Prior placenta previa** (8 fold increased risk)
- **Prior uterine surgery and cesarean delivery.**
 - PP incidence increases with the numbers of cesarian deliveries (CD). It occurs in 0.9% of women with one prior CD, in 1.7% of women with two prior CDs, and in 3% of those with three or more CDs.
 - In patients with four or more cesarean deliveries, the risk for placenta previa has been reported to be as high as 10%.

CLINICAL MANIFESTATION

Placenta previa typically presents as painless vaginal bleeding in the second or third trimester.

- Between 70% and 80% of patients with placenta previa will have at least one bleeding episode, and from those with bleeding,
 - One third of women will present before 30 weeks of gestation,
 - One third between 30 and 36 weeks, and
 - One third after 36 weeks.
- About 10% to 20% of patients present with uterine contractions before bleeding, and
- Fewer than 10% remain asymptomatic until term.

Time of bleeding in placenta previa is during:

- 1. Lower uterine segment formation**
- 2. Fetal head engagement**
- 3. Manipulation upon physical examination (eg. PV)**
- 4. Labor**

DIAGNOSIS

Whenever there is uterine bleeding after mid-pregnancy, placenta previa or abruption are always considered.

NB, PP should not be excluded until sonographic evaluation has clearly proved its absence.

Radiology (ultrasound):

- Transabdominal (diagnostic accuracy of at least 95%) and
- Transvaginal (diagnostic accuracy that approaches 100%) ultrasound provide the best means for diagnosing placenta previa.

If a true placenta previa or low-lying placenta is diagnosed in the second trimester, repeat sonography should be obtained in the early third trimester at 32 weeks.

More than 90% of placenta previa cases diagnosed in the second trimester resolve by term.

MANAGEMENT

- ⇒ Admit all ladies with APH secondary to placenta previa at time of diagnosis.
- ⇒ Resuscitation based on clinical condition.
- ⇒ Vaginal & rectal examinations are absolutely contraindicated.
- ⇒ Monitor closely maternal & fetal conditions.
- ⇒ HCT, BG & Rh, cross-match at least two units of blood
- ⇒ Decide on conservative management versus immediate delivery
 - **Indications for immediate delivery:**
 - Term pregnancy, IUFD, fetal growth restriction, NRFS, excessive bleeding, gross fetal congenital malformation which may not be compatible with life, lady in labor.

▪ Route of delivery

- depends on the type of placenta previa and presence of other obstetric indications:
- Low lying & anterior marginal → vaginal delivery
- Partialis, totalis, & posterior marginal → c/d
- Excessive bleeding, NRFS, other indications → c/d

⇒ In absence of any of the above indications to deliver the fetus, conservative management is instituted till an indication comes to picture.

▪ Conservative management in preterm lady includes:

- Bed rest (in hospital)-----No place for outpatient management
- Dexamethasone 6mg IM Q 12 hours for a total of 4 doses
- Follow: Maternal V/S, vaginal bleeding, uterine contractions, fundal height, FHB, kick count, BPP, serial HCT.
- Deliver at 37 completed weeks of gestation after maturity is confirmed

⇒ Double setup examination:

- Is used in areas where U/S is not widely available/not done by experienced people.
- It is important to decide on mode of delivery
- The procedure include:-
 - Prep and client to operation room
 - Everything must be ready for delivery
 - Speculum examination is done gently to rule out local causes & see the cervical status → then gentle digital vaginal examination is done to check for presence of placenta between fornices & presenting part, cervical dilatation & effacement, presence of placenta through open cervix.

MORBIDLY ADHERENT PLACENTAS

- Morbidly adherent placenta (a.k.a accrete syndromes) describes aberrant placentation characterized by abnormally implanted, invasive, or adhered placenta.

Classified by the depth of trophoblastic growth, as:-

1. **Placenta accrete;** indicates that villi are attached to the myometrium
2. **Placenta increta;** villi actually invade the myometrium, and
3. **Placenta percreta;** defines villi that penetrate through the myometrium and to or through the serosa.

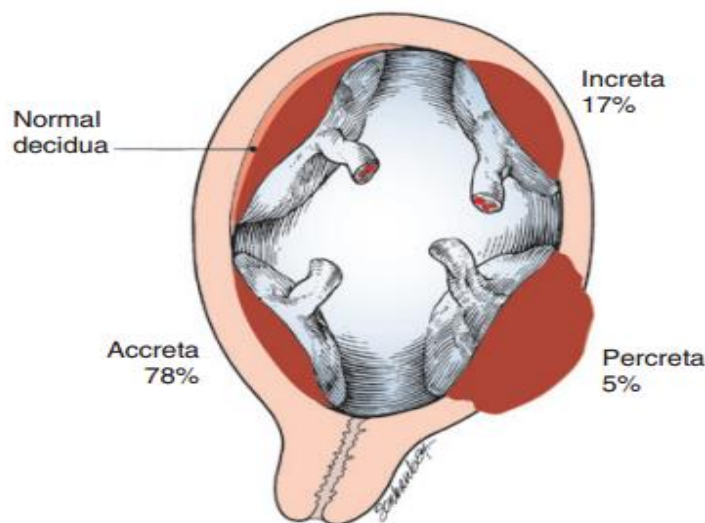


Figure 3. Uteroplacental relationships found with invasive placentation

INCIDENCE

The prevalence of accrete syndromes was 3.7 per 1000 births—1 per 270

RISK FACTORS

- Placenta previa
- Prior cesarean delivery

A classical hysterotomy incision has a higher risk for a subsequent accrete placenta

Risk of placenta accreta with placenta previa and prior cesarean delivery

Number of prior cesarean deliveries	Placenta accrete risk (%)
0	3
1	11
2	40
3	61
≥4	67

- Increasing parity and maternal age
- Submucosal uterine fibroids
- Curettage or endometrial ablation

CLINICAL MANIFESTATION

- In cases of first- and second-trimester accrete syndromes, there is usually hemorrhage that is the consequence of coexisting placenta previa. Such bleeding will typically prompt evaluation and management.
- In some women who do not have an associated previa, accreta may not be identified until third-stage labor when an adhered placenta is encountered. Unfortunately, imaging modalities are less than perfect to identify all of these placentas early.
- Hematuria can be a feature of placenta percreta with bladder invasion.

DIAGNOSIS

Radiographic techniques: Ultrasound is the preferred radiographic modality for the diagnosis of placenta accreta. Findings suggestive of placenta accreta include:

- A loss of the normal hypoechoic retroplacental myometrial zone,
- thinning and disruption of the uterine serosa–bladder wall interface,
- focal exophytic masses within the placenta, and numerous intraplacental vascular lacunae

Laboratory findings: Placenta accreta has been associated with unexplained elevations in maternal serum α -fetoprotein (MSAFP).

Pathologic studies: Placenta accreta is confirmed by the pathologic examination of a hysterectomy specimen.

MANAGEMENT

- Because of its associated risk for massive postpartum hemorrhage, placenta accreta accounts for a large percentage of peripartum hysterectomies.

When performing the surgery, it is recommended that the uterus be incised above the placental attachment site and that the placenta be left in situ after clamping the cord because disruption of the implantation site may result in rapid blood loss.

- Timing of delivery depends upon clinical circumstances; however, most authorities favor delivery at 34^{0/7} to 35^{6/7} weeks with or without antenatal corticosteroid administration.
- Adequate IV access with two large-bore catheters and ample blood product availability are mandatory.

⇒ In specific circumstances, uterine conservation may be attempted. These situations include focal accreta, desired future fertility, and fundal or posterior placentae accrete.

VASA PREVIA

- Vasa previa is defined as the presence of fetal vessels over the cervical os.
- These fetal vessels lack protection from Wharton jelly (velamentous cord insertion) and are prone to rupture and compression. When the vessels rupture, the fetus is at high risk for exsanguination.

INCIDENCE

- The overall incidence of vasa previa is 1 in 2500 deliveries; however, data have shown a range from 1 in 2000 to 1 in 5000 deliveries.

RISK FACTORS

- Bilobed and succenturiate-lobed placentas
- Pregnancies that result from assisted reproductive technology (ART)
- Multiple gestations
- History of second-trimester placenta previa or low-lying placenta.

CLINICAL MANIFESTATIONS

- Most cases of vasa previa presented after rupture of membranes with acute onset of vaginal bleeding from a lacerated fetal vessel. If immediate intervention was not provided, fetal bradycardia and subsequent fetal death occurred.
- Recently, many cases of vasa previa are diagnosed antenatally by ultrasound. In rare cases, pulsating fetal vessels may be palpable in the membranes that overlie the cervical os.

DIAGNOSIS

- Vasa previa is often diagnosed antenatally by ultrasound with color and pulsed Doppler mapping. Transabdominal and transvaginal approaches are most often used.

MANAGEMENT

- When diagnosed antenatally, vasa previa should be managed similarly to placenta previa.
- If an intrapartum diagnosis of vasa previa is made, expeditious delivery is needed. Immediate neonatal blood transfusion is often required in these circumstances.

SAMPLE HISTORY

Chief complaint: Vaginal bleeding of 1 hour duration

HPP

This is a 30 years old G4P3 (all alive) mother whose LNMP was on 22/05/2011EC (reliable) making the EDD on 27/02/2012EC and gestational age of 36+1 weeks (on 30/01/2012) EC, date of clerking). Menses was regular coming every 26-28 days, lasting for 3-4 days. She used 2-3 sanitary pads per day, menses has no clots associated and she has no abdominal discomfort. She has no history of contraceptive use. She doesn't remember the exact date she felt fetal movement but claimed that she still feels the kicks and it's increasing through time.

She suspected she was pregnant when she missed her menses and went to a nearby health center where the diagnosis of her pregnancy was confirmed by a urine pregnancy test, (write the exact date of urine pregnancy test or ultrasound if done and if she can recall).

She had total of four ANC visits at a local health center. First visit was at 3 month of pregnancy (write exact date if available), where history was taken, weight, height and blood pressure was measured, and abdominal examination was done. Blood and urine test was done, she doesn't remember any results, she was told everything was fine. She was given an injection on her left upper arm and a red round tablet to take once daily. She was appointed after a month.

Same physical examinations and investigation (only urine examination) were done on her 2nd, 3rd and 4th visits and they were all uneventful. She had another injection on her left upper arm on the 2nd visit and had a red round tablet refill in all the visits.

The pregnancy was not planned but is wanted and supported by her family. She hasn't made any significant changes in her diet after she got pregnant.

Her staple diet is Injera made of teff with shiro wot 3 times a day, fruits and vegetables occasionally and meat on rare occasions.

Currently she presented with a sudden onset of vaginal bleeding which was bright red, non-clotting and odorless. The blood soaked her underwear and dress. It was not associated with abdominal pain, gush of fluid or decreased fetal movement.

She has no history of easy fatigability, blurring of vision, ringing in the ears or palpitation (symptoms of anemia).

Otherwise:

Danger signs

She has no history of cough, or shortness of breath

She has no history of vision disturbances, ABM or LOC

She has no history of epigastric pain, or right upper quadrant pain.

She has no history of headache

She has no history of excessive vomiting

She has no history of urinary frequency, decreased urine output or pain during urination

She has no history of passage of liquor or pushing down pain

Risk factors

She has no history of trauma to the abdomen

She has no history of cigarette smoking or alcohol drinking

She has no history of infertility treatment

She has no history of twinning

She has no history of gynecologic operations

She has no similar previous history

DDx

She has no history of post-coital bleeding (Cervical ca.)

She has no history of river water contact (Leech infestation)

She has no history of bleeding from other sites (Autoimmune disorders like ITP)

She has no history of vaginal discharge, genital burning sensation (cervicitis)

PHYSICAL EXAMINATION

V/S: BP, pulse, RR, T^o, Weight, Height, BMI.....normal

HEENT: Pale conjunctiva

Abdominal examination: thorough examination,

(See the Preeclampsia history in chapter 1 to know how to write findings in obstetric palpation)

Pelvic examination (avoid Per Vaginal examinations unless placenta previa has been ruled out)

Assessment: *Late preterm pregnancy + APH secondary to R\O Placenta previa*

CHAPTER 3

POSTPARTUM HEMORRHAGE (PPH)

DEFINITION AND INCIDENCE

- There multiple definitions to PPH from different source/institutions. The different definitions include:-
 - **PPH**: is defined as
 1. Excessive bleeding following delivery (>500 ml in vaginal delivery, >1000 ml in CD and twin vaginal deliveries, >1500 ml following cesarean hysterectomy)
 2. A drop in Hct > 10% from baseline
 3. Bleeding that makes a patient symptomatic and/or results in signs of hypovolemia (best definition)
 4. Blood loss of > 15% of the total estimated blood volume

NB, hemorrhage may occur before, during, or after delivery of the placenta

Incidence

- PPH complicates 4 to 6% of all deliveries
- World's leading cause of maternal mortality
 - Accounts for 25% of all maternal deaths worldwide & 60% in developing countries
 - The worst thing about PPH is its short duration from onset to maternal mortality if not managed

- Major killers in maternity (enemies of Obstetrician, if u will) and their timing till death
 - PPH---2hrs
 - APH--- 12hrs
 - Ruptured uterus--- 1 day
 - Eclampsia---- 2 days
 - Obstructed labor--- 3 days
 - Sepsis ---6 days
- Hence PPH is an obstetric EMERGENCY

Normal Physiologic Mechanisms Preventing PPH

- Constriction of interlacing myometrial fibers that surround the blood vessels supplying the placental implantation site
- Formation of firm clots at mouth of vessels(placental bed) which occurs as result of increased viscosity and hypercoagulability of blood

CLASSIFICATION

- PPH can be classified temporally as:-
 - Primary (early) PPH
 - Secondary (late) PPH

Early PPH

- Blood loss during the first 24hrs after delivery.
- Account for 98% PPH cases

Etiology

- The etiologies for early PPH can easily remembered as the ***five Ts***
 - **T**one (uterine atony)
 - **T**rauma (genital tract laceration and Uterine rupture)
 - **T**issue(retained placenta and amniotic membranes)
 - **T**hrombin(coagulopathy) ,and
 - **T**raction(uterine inversion)

1) Uterine atony (50%)

- Failure of the uterus to contract sufficiently
- Risk factors:
 - excessive manipulation
 - general anesthesia (halothane)
 - uterine over distention (twin, polyhydramnios, big fetus)
 - prolonged labor
 - oxytocin induction/augmentation
 - previous PPH
 - precipitate labor
 - grandmultiparity

2) Retained products of conception (5%-10%)

- Retained products of conception-->uterine atony-->PPH
- Diagnosis-
 - when spontaneous expulsion of the tissue has not occurred within 30 to 60 minutes of delivery
- Risk factors:
 - retained placenta
 - succenturate lobe
 - morbid adherence
 - mismanagement of third stage of labor

3) Genital tract Laceration (20%)

- The most common lower genital tract lacerations are perineal, vulvar, vaginal, and cervical.
- Upper genital tract lacerations are typically associated with broad ligament and retroperitoneal hematomas.
- Risk factors:
 - Episiotomy extension
 - instrumental deliveries
 - precipitate labor
 - fetal malpresentation or macrosomia
 - delivery through undilated cervix
 - prior cerclage placement
 - shoulder dystocia
- Inspection of placenta and fetal membranes after delivery for completeness.
- Manual exploration of uterine cavity is both diagnostic and therapeutic

4) Uterine rupture

- Complete nonsurgical disruption of all uterine layers
- Uterine rupture is most common in women with a scarred uterus, including those with prior cesarean delivery and myomectomy.

Risk of uterine rupture after CD

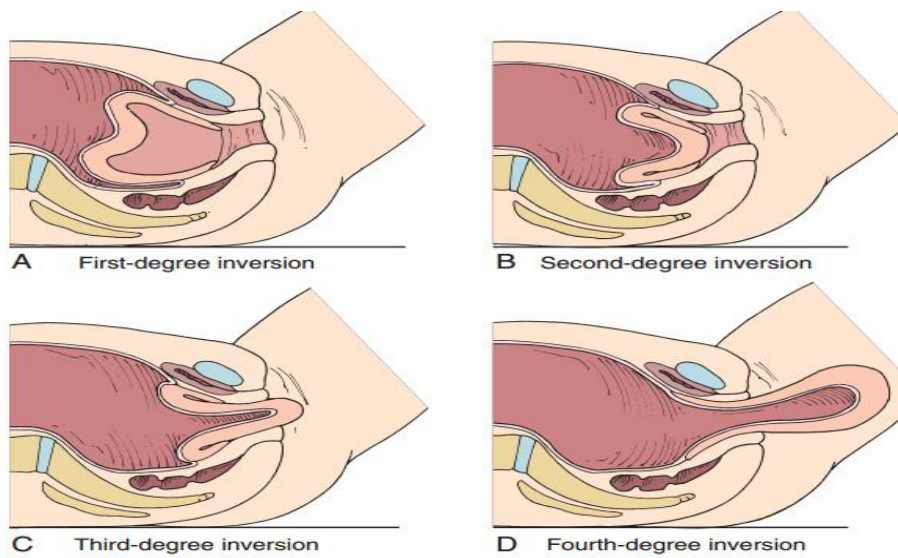
INCISION OF PRIOR CESAREAN DELIVERY	UTERINE RUPTURE RISK (%)
Classical	2-6
T or J shaped	2-6
Low vertical	2
Low transverse	0.5-1

➤ **Clinical manifestations**

- Fetal:
 - Fetal bradycardia with or without preceding variable or late decelerations-most common(33-70%)
 - Loss of fetal station in labor
- Maternal:
 - acute vaginal bleeding,
 - constant abdominal pain or uterine tenderness,
 - change in uterine shape,
 - cessation of contractions,
 - hematuria (if extension into the bladder has occurred), and
 - signs of hemodynamic instability

➤ **Uterine inversion**

- Collapse of the fundus into the uterine cavity, and it is classified by degree and timing.
- It is classified it to:
 - Three, based on timing:-
 - Acute (within 24 hours of delivery)
 - Subacute (>24 hours postpartum but <4 weeks)
 - Chronic (>1 month postpartum)
 - Four, based on degree of inversion:-
 - First degree (incomplete)
 - Second degree (complete)
 - Third degree (prolapsed)
 - Fourth degree (total)



- The two most commonly proposed etiologies are:
 1. Excessive umbilical cord traction with a fundally attached placenta and
 2. Fundal pressure in the setting of a relaxed uterus
- Risk factors include:-
 - uterine over-distention
 - fetal macrosomia
 - rapid labor and delivery
 - congenital uterine malformations
 - uterine fibroids
 - invasive placentation
 - retained placenta
 - short umbilical cord
 - use of uterine-relaxing agents
 - nulliparity
 - manual placental extraction
 - Ehlers-Danlos syndrome

- Clinical manifestation
 - Depend on by degree and timing.
 - Incomplete-subtle in its clinical findings,
 - Complete-brisk vaginal bleeding- inability to palpate the fundus abdominally, and maternal hemodynamic instability
- **Coagulopathy**
 - **Acquired**
 - Idiopathic thrombocytopenic purpura
 - Thrombocytopenia with preeclampsia
 - HELLP syndrome
 - Disseminated intravascular coagulation
 - Dead fetus in utero -Severe infection/sepsis
 - Placental abruption
 - Amniotic fluid embolus
 - Severe hemorrhage
 - Iatrogenic-anticoagulant administration
 - **Hereditary**
 - Von Willebrand's disease
 -

Late PPH

- Blood loss between 24hrs and 6wks after delivery
- Unlike primary PPH, bleeding usually is not catastrophic

Etiology

- Uterine infection
- Retained products of conception
- Placental site subinvolution
- Coagulopathy

Uterine infection

- If the mother has fever, uterine tenderness, and/or a foul-smelling discharge without massive bleeding, then endometritis should be suspected.

Uterine sub-involution

- Arrest/retardation of the uterus to go back to its original size and position
- Normally, uterine involution occurs in 4 weeks Postpartum
- After 2 weeks postpartum, uterus should be in pelvic cavity
- **Causes:-**
 - Infection
 - Retained placental fragments
 - Abnormal healing of the thrombosed vascular sinuses at the placental site

Clinical features of PPH

Symptoms

- Vaginal bleeding-continuous trickling of blood or copious flow or passage of huge blood clots
- It may be concealed and accumulate in the uterus or broad ligament, in such cases it is important to look for symptoms of hypovolemia/anemia
 - lightheadedness
 - weakness
 - palpitations
 - diaphoresis
 - restlessness, confusion
 - air hunger
 - syncope

Physical examination**G/A and V/S**

- Signs of shock, depend on the amount of bleeding and pre-deliver Hb levels (see the classes of hemorrhage and the physiologic response of the body to each class on the APH section above)

Abdominal examination findings

- The uterus can be:-
 - flabby and soft → atonic uterus
 - over distended → uterus filled with blood clots
 - ✓ Squeezing it leads to gush of clotted blood pervaginum
 - firmly contracted → trauma
 - atonic (non-contractile), tender and changing in shape → Uterine rupture
 - ✓ loss of station of the fetal presenting part PV examination is also indicative of uterine rupture
 - Soft and larger than expected for the time during Puerperium → Uterine subinvolution

Pervaginal examination findings

- dark red blood → atonic uterus
- bright red blood → trauma
- Cervical laceration, paraurethral tears → lower tract causes

Bimanual examination-palpation of uterine fundus in the lower uterine segment or within the vagina → uterine inversion

COMPLICATION

PPH is a major cause of maternal morbidity, including catastrophic sequelae:-

- Death
- Hypovolemic shock and organ failure: renal failure, stroke, myocardial infarction, postpartum hypopituitarism (Sheehan syndrome)
- Fluid overload (pulmonary edema, dilutional coagulopathy)
- Abdominal compartment syndrome
- Anemia
- Transfusion-related complications
- Acute respiratory distress syndrome
- Anesthesia-related complications
- Sepsis, wound infection, pneumonia
- Venous thrombosis or embolism
- Unplanned sterilization due to need for hysterectomy- control intractable PPH
- Asherman syndrome (related to curettage if performed for retained products of conception)

Management

Management Goal

- Restore or maintain adequate circulatory volume to prevent hypoperfusion of vital organs
- Restore or maintain adequate tissue oxygenation
- Reverse or prevent coagulopathy
- Eliminate the obstetric cause of PPH

The first step in management of PPH is call for help. The management is a race with time; every available practitioner should be involved

Evaluation of persistent bleeding

- If vaginal bleeding persists after delivery of the placenta, aggressive treatment should be initiated
- Search for the cause of bleeding and initiate definitive management
- STEPS:
 1. Compress manually the uterus and insert IV catheter
 2. While doing that obtain assistance
 3. Obtain blood (type and cross match)
 4. Check blood for clotting to rule out coagulopathy
 5. Begin fluid or blood replacement
 6. Carefully explore the uterus
 7. Inspect the cervix and vagina

Measures to Control Bleeding**1. Manual exploration of the uterus**

- Is done if PPH occurs after:
 - Vaginal delivery following previous c/d
 - Intrauterine manipulation (version, extraction)
 - Malpresentation
 - When abnormal uterine contour has been noted prior to delivery
- Ensure whole placenta is delivered and intact uterus.
- Uterine rupture detected by manual exploration in PPH requires laparotomy

2. A. Bi-manual compression and massage

- Most important step in controlling atonic PPH
- Immediate bimanual compression for 20-30min

B. Uterotonic agents

- Oxytocin 20-40u/L of crystalloid at a rate of 10-15ml/min
- Methylergonovine 0.2mg IM if mother is not hypertensive

3. Curettage

- It should be performed under ultrasound guidance.
- This is likely to reduce the rate of perforation, will allow identification of placental tissue, and confirm that this tissue has been evacuated

4. Operative Management

- The patient's wish of childbearing should be clear
- If can't be ascertained the operator assumes that childbearing is to be retained
- If possible, spouse/family could be informed
- 4a. Pressure occlusion of the abdominal aorta
 - Immediate temporary control of pelvic bleeding
 - To provide time to treat hypotension
 - To identify source of bleeding
 - Pressure occlusion can be maintained for several minutes without sequelae
- 4b. Uterine artery ligation
 - 90% of supply to the uterus is from uterine artery
 - Direct ligation of uterine artery is successful (75-90%) if bleeding is from uterus
- 4c. B-Lynch Brace Suture
 - An alternative to vessel ligation
 - Used in cases of atony or percreta
- 4d. Internal iliac artery ligation
 - Most commonly used method to control severe PPH
 - Exposure can be difficult (big boggy uterus or hematoma)
- 4e. Condom tamponade technique
 - With aseptic precautions, a sterile rubber catheter fitted with a condom is introduced into the uterus.
 - The condom is inflated with 250-500 ml normal saline, according to need.

- The condom catheter is kept for 24-48 hours, depending upon the initial intensity of blood loss, and gradually deflated when bleeding ceased.

5. Hysterectomy

- It is the definitive method of controlling PPH
- It is the procedure of life saving

PROGNOSIS

- PPH has a recurrence rate of approximately 10% in future pregnancies
- Maternal deaths are due to:
 - 1) Underestimation of blood loss
 - 2) Inadequate blood and fluid replacement
 - 3) Delay in operative intervention

PREVENTION

Antenatal:-

- Good and early ANC
- Treatment of anemia and malnutrition
- Early detection and prompt treatment of high risk factors

Intrapartum:-

- Avoid home delivery
- keep blood grouped and cross matched
- Active management of third stage of labor(**AMTSL**)
- Avoid prolonged or obstructed labor

Postpartum:-

- Close observation in 4th stage of labor
- Evaluation of placenta and membranes
- Exploration of genital tract for trauma

NB, Risk factors do not predict PPH

- Only about 10% of women with any of the risk factors develop PPH and over two-thirds have no identifiable risk factors

Hence ***all pregnancies are at risk of PPH***

AMTSL

- Is the main stay in prevention of PPH
- Its components are:-
 - 1) Oxytocin 10 IU IM within one minute of delivery of the last baby
 - 2) Controlled cord traction (CCT) to deliver the placenta (Brandt-Andrew maneuver)
 - If placenta is not delivered with CCT or cord is severed, do manual removal of placenta.
 - 3) Uterine massage every 15 minutes for the first 2 hours after delivery

CHAPTER 4

PREMATURE RUPTURE OF MEMBRANE (PROM) AND PRETERM LABOR

DEFINATIONS

Preterm rupture of membrane: is spontaneous rupture of membrane occurring before 37th week.

Premature rupture of membrane (PROM): is spontaneous rupture of membrane occurring before onset of labor.

Preterm premature rupture of membrane (PPROM): is if both occur together i.e. if spontaneous rupture of fetal membrane occurs before 37 completed weeks and before the onset of labor.

Prolonged rupture of membrane: is any rupture of membrane for greater than 8 hours. It becomes a risk for chorionamnionitis when it is longer than 18 hours.

Latency Period: is the period between rupture of membrane and onset of labor.

PRETERM LABOR/BIRTH

Classification of the time of labor onset or delivery

	Very early preterm	28-32 ⁺⁶
	Early preterm	33-33 ⁺⁶ weeks
Preterm	Late preterm (accounts for ≥70% of all preterm births)	34-36 ⁺⁶ weeks
	Early term	37-38 ⁺⁶ weeks
	Full term	39-40 ⁺⁶ weeks
Term	Late term	41-41 ⁺⁶ weeks
Post-term	Post-term	>42 completed weeks

Preterm birth:

- Describes neonates who are born early i.e. born before term (before 37 full weeks), but after fetal viability (after 28 full weeks).
- It is with respect to gestational age, but not with respect to size, neonates can be born before term and be small for gestational age, appropriate for gestational age or large for gestational age.
- It should be clearly distinguished from the concept of prematurity. Prematurity is incomplete development of various organ systems at birth.

ETIOPATHOGENESIS AND RISK FACTORS

The four primary processes in PATHOGENESIS of preterm labor are:-

1. Premature activation of the maternal or fetal hypothalamic-pituitary-adrenal axis
2. Inflammation or infection
3. Decidual hemorrhage
4. Pathological uterine distention

Etiologies of preterm births include:-

- Spontaneous unexplained preterm labor with intact membranes
 - Can be due to multifetal pregnancy, intrauterine infection, bleeding, placental infarction, premature cervical dilation, cervical insufficiency, hydramnios, uterine fundal abnormalities and fetal anomalies.
- Idiopathic PPROM
- Delivery for maternal or fetal indication
- Twins and higher-order multifetal births

Risk factors of preterm labor/birth include:-

- **Prior preterm birth:** is the most important risk factor
 - It increases risk by threefold greater when compared with women whose first neonate was born at term.
 - The risk of recurrent preterm birth is influenced by three factors:
 - frequency of prior preterm deliveries,
 - severity as measure by gestational age, and
 - the order in which the prior preterm delivery occurred (consecutively? Or every other pregnancy..)
- **Infection:**
 - chorioamnionitis is the most common associated condition in our setup
- **Pregnancy factors:**
 - Threatened abortion in early pregnancy is associated with later adverse outcomes.
 - Both light and heavy bleeding are associated with subsequent preterm labor, placental abruption and pregnancy loss before 24 weeks.
 - Birth defects may also predispose to preterm birth.
- **Lifestyle factors:**
 - Cigarette smoking, illicit drug use
 - Inadequate maternal weight gain and underweight , young or advanced maternal age, poverty, short stature, vitamin C deficiency.
 - Psychological factors, like depression,
- **Genetic factors:**
 - Recurrent, familial and racial nature of preterm birth suggests that genetics may play a causal role.

- **Interval between pregnancies:**
 - Intervals <18 months and >59 months were associated with risks for both preterm and small-for-gestational age newborns.
- **Uterine condition:** Like:-
 - müllerian malformation
 - cervical insufficiency
 - uterine over distention
- **Obstetric conditions:**
 - Preeclampsia, eclampsia, placenta Previa, fetal growth restriction
- **Other medical conditions:**
 - Chronic hypertension, DM, renal disease

DIAGNOSIS:

History

- Patient may complain:-
 - vaginal bleeding or bloody show
 - pelvic pressure, menstrual-like cramps & lower back pain
 - increased vaginal discharge
 - Gush of fluid → rupture of membrane

Physical examination

- Uterine contraction which is regular, >2 per 30 minutes, dilatation and effacement of cervix with at least 1 cm change or well effaced and dilated (at least 2cm) on admission
- Sterile speculum examination is essential to assess fetal and cervical status.

Early differentiation between true and false labor is difficult especially before demonstrable cervical effacement and dilation.

Uterine activity alone can be misleading because of Braxton Hicks Contractions (irregular, non-rhythmical contraction). Therefore, preterm labor is defined as regular contractions before 37 weeks that are associated with cervical change.

Investigation

- If there is vaginal bleeding present, an ultrasound must be performed to rule out placenta Previa before digital examination is performed.
- Urine specimen is sent for culture and fetal heart rate monitoring is done.

PREMATURE RUPTURE OF MEMBRANE (PROM)

PPROM:

- What is PPRM?
- It is responsible for 25% - 33% of all of preterm births each year.
- The risk factors for PPRM are similar to those for preterm labor. And the pathogenesis is similar with PROM the only difference is that it occurs before term (preterm).

PROM:

- Affects approximately 10.7% of all pregnancies
- About 94% of cases occur at term and 5% preterm.
- It is associated with considerable maternal infection and perinatal morbidity and mortality due to sepsis and prematurity.

Etiopathogenesis and Risk factors

- Most PROM cases occur due to subclinical chorioamnionitis resulting from ascending infection from lower genital tract like STIs.
 - Genital infections produce phospholipases which stimulate production of prostaglandins which further stimulate uterine contraction and subsequent ROM.
- The pathogenesis of PROM is poorly understood.
 - But increased apoptosis or necroptosis of membrane cellular components and greater levels of specific proteases in membranes and amniotic fluid are related to PROM.

Risk factors for prom

MATERNAL	FETAL
➤ Subclinical chorioamnionitis	➤ Polyhydramnios (uterine over distention)
➤ Overt chorioamnionitis	➤ Malpresentation
➤ Past history of PROM	➤ Multiple pregnancy
➤ Prior history of spontaneous preterm delivery	IATROGENIC
➤ Collagen synthesis defect	➤ Amniocentesis
➤ Cervical incompetence	➤ External cephalic version
➤ Vaginal bleeding (2 nd and 3 rd trimester bleeding)	➤ Percutaneous umbilical blood sampling
➤ Cervical conization	
➤ Cigarette smoking	➤ Abdominal trauma
➤ Low body mass index and nutritional deficiency	➤ Idiopathic (but most cases are often suspected to be due to subclinical chorioamnionitis)
➤ Emergency cerclage	➤ Low socioeconomic status
	➤ Pulmonary disease (chronic cough)
	➤ Straining (constipation)
	➤ Heavy physical exercise

COMPLICATIONS

Maternal

- Infectious complications: Chorioamnionitis, puerperal endomyometritis, sepsis. Risk of infection increases with prolonged PROM
- Operative deliveries: due to failed induction
- Prolonged hospitalization and financial implication
- Preterm labor

Perinatal

- Prematurity
- Fetal and neonatal sepsis
- Oligohydramnios with cord compression and fetal asphyxia
- Cord prolapse

DIAGNOSIS AND INVESTIGATIONS

- The diagnosis of PROM is made by:-
 - obtaining a history of leakage of vaginal fluid,
 - pooling on speculum examination, and
 - positive Nitrazine and fern test
 - If these tests are equivocal, an ultrasound can be performed to examine the level of amniotic fluid.
 - If the diagnosis is still unconfirmed, an amniocentesis dye test can be performed.
- A sterile speculum examination
 - is performed to evaluate the fetal membrane status and to inspect the cervix
 - this examination is a key to differentiating PROM from hydrorrhea gravidarum, vaginitis, increased vaginal secretions and urinary incontinence

- The patient's cervix should also be visually inspected to determine the degree of dilatation and effacement and the presence of cord prolapse.
- Membrane rupture is confirmed by visualization of amniotic fluid in the posterior fornix or by passing of amniotic fluid from the cervical canal.

➤ PROM can be confirmed by the following tests and examinations

➤ Pooling:

- Is the collection of amniotic fluid in the posterior fornix

➤ Nitrazine test:

- This test is based on the pH difference between the vagina and AF (normally vagina pH is 4.5 to 6.0 and the pH of amniotic fluid is 7.1 to 7.3).
- Nitrazine test is a sterile cotton tipped swab that is used to collect fluid from the posterior fornix and apply it to Nitrazine (phenolphthazine) paper.
- In the presence of amniotic fluid, the Nitrazine paper turns **blue**, demonstrating an alkaline pH (7.1-7.3). False positive Nitrazine tests result from semen, alkaline antiseptics, bacterial vaginosis and blood.

➤ Ferning test:

- Fluid from the posterior fornix is placed on a slide and allowed to air-dry.
- Amniotic fluid will form a fern-like pattern of crystallization.
 - Cervical mucus can cause ferning, but it is usually patchy and less extensive than that with AF.

- Observing loss of fluid from the cervical os when patient coughs or performs a Valsalva maneuver during speculum examination
- If no free fluid is found, a dry pad should be placed under the patient's perineum and observed for leakage
- If the diagnosis has not been confirmed by all the above methods, perform:
 - Ultrasound examination
 - Oligohydramnios?
 - Amniocentesis and inject a dilute solution of indigo carmine dye
 - Inject the dye after taking amniotic fluid for pulmonary maturity testing, analysis for evidence of subacute intra-amniotic infection and possible culture and sensitivity testing.
 - After 15-30 minutes, examination of the patient's perineal pad will reveal blue dye if the membranes are ruptured.
 - This is also known as the tampon test because the dye is usually identified by its absorption into a tampon.

DIFFERENTIAL DIAGNOSIS

- Urinary incontinence
- Leucorrhea gravidarum
- Vaginal discharge (excessive)
- Perspiration
- Ruptured cyst (like in the vagina)

MANAGEMENT

- Management of PROM Management depends on: Gestational age, duration of rupture of fetal membranes, fetal condition (dead, fetal distress, congenital malformations), presence of infection, labor and previous cesarean scar, and other obstetric indications.

1. Gestational age greater than 34 weeks

- a. Rupture of fetal membranes greater than 8 hours and no previous c/s:
 - Start Ampicillin 2gm IV QID until delivery
 - Start induction with oxytocin if no labor
 - Caesarean delivery is indicated in malpresentation
- b. Rupture of fetal membranes greater than 8 hours and previous c/s:
 - Prophylactic antibiotics (eg. Ampicillin 2gm iv stat)
 - Immediate cesarean delivery
- c. Rupture of fetal membranes less than 8 hours and no previous c/s: -
 - Follow fetal and maternal condition for spontaneous onset of labor for total of 8 hours duration and then start induction if labor does not start –
 - Caesarean delivery is indicated immediately in mal presentations
- d. Rupture of fetal membrane less than 8 hours and previous c/s:
 - Depends on mother's preference whether she wants observation for spontaneous onset of labor for 8 hours or immediate delivery by cesarean.

2. Gestational age between 28- 34 weeks and alive fetus:

- a. Rupture of fetal membranes in absence of infection:
 - Ampicillin 2gm IV QID for 48 hours then amoxicillin 500 mg PO TID for 7-10 days.
 - Erythromycin 500 mg IV QID for 48 hours then 500 mg PO QID for 7-10 days.
 - Start dexamethasone 6 mg IM BID for four doses or Betamethasone 12 mg IM daily for two doses.
 - Follow till 34-37 weeks of GA or till an indication for delivery comes into picture during follow up.
- b. Rupture of fetal membranes in presence of infection and no previous c/s:
 - Start Ampicillin 2gm iv QID + Gentamycin 80 mg IV TID (Ceftriaxone 1 gm IV BID alone)
 - Start induction with oxytocin if no labor
 - Caesarean delivery is indicated in malpresentations
- c. Rupture of membrane with fetal death or severely malformed fetus: -
 - Deliver immediately with induction if there is no previous c/s or by cesarean if there is previous c/s.

Generally indications for pregnancy termination in PROM

- Term PROM
- Chorioamnionitis (regardless of GA)
- Labor
- Placental abruption with significant vaginal bleeding
- IUFD
- NRFHRP
- Congenital anomalies of fetus incompatible to life
- Abnormal fetal surveillance
- Active labor with advanced cervical dilation
- Fetal malpresentation with increased risk of cord prolapse

Components of conservative management:

- Bed rest as long as there is leakage of liquor with restriction of efforts that increase intra-abdominal pressure
- Temperature is recorded every 4- 6 hours
- Observation for malaise, abdominal pain, uterine tenderness and smell of liquor on sterile vulval pads
- Leucocyte count and C-reactive protein may be done every other day
- Prophylactic antibiotics be given as in the above
- Tocolytic drugs are given if uterine activity starts
- Corticosteroid therapy is given for gestations before 34 weeks.
- Treatment with antibiotics can potentially treat or prevent ascending infection, prevent chorioamnionitis, reduce neonatal sepsis, and prolong the latency period.

Management of PROM with viral infection (Herpes genitalis and HIV)

- Route of delivery is abdominal by c/d if duration of rupture of fetal membranes is less than 4 hours and active herpes genitalis is present.

SAMPLE HISTORY

C/c: Gush of fluid of 4hour duration

HPP

This is a 25years old G2 P1 (alive) woman who had her LNMP on 10/05/11 EC with an EDD of 15/2/12 EC and GA of 37⁺¹ (on 30/01/12 EC). Menses was regular and it came every 28-30 days, lasting for 4 days and there was no associated clot and discomfort. She never used contraception.

The pregnancy was first confirmed when she went to a local health center for missing her menses for two weeks and got suspicious of being pregnant. And after urine sample was taken she was told she was pregnant. She had 6 ANC follow ups at a local hospital. Her 1st ANC visit was on her second month of pregnancy. Complete history was taken and physical examination was done. Urine sample, blood sample was taken and U/S (ultrasound) was done. She remembers her blood type is B⁺ (we ask if she knows her blood type because if she is RH negative we have to make sure she took/takes anti-D), but she does not remember her other results. She was given an injection on her left arm (we can ask if she knows what the injection was for- TT (tetanus toxoid) vaccine) and she was given red tablet to take one tablet per day (iron supplementation).

And she was told everything was on good status. Her 2nd ANC follow up was at her third month of pregnancy. Complete physical examination was done and she was given another injection on her arm (second dose of TT vaccine). Her iron supplement was continued and she was told everything was good and that there was no problem. Her 3rd, 4th, 5th and 6th were at her 4th, 5th, 6th and 7th months of pregnancy. Routine history taking and complete physical examination was done and it was uneventful. On her 5th visit she was advised on birth. And U/S was done on her 6th visit.

She doesn't remember when she started to feel fetal movement, but fetal movement has not decreased since first felt. She had an increase in appetite during the pregnancy. She increased her meals from 3 times per day to 5 times per day.

Her staple food is injera made of 'tef' and 'shiro wot' and 'denech wot'. She eats vegetables and fruits. She occasionally eats meat. She claims she gained around 5kg since she changed her diet.

The pregnancy was wanted, planned and supported.

4 hours prior to admission she felt a sudden onset of leakage of gush of fluid while she was washing her hands and it soaked her clothing. Its consistency is water like. The fluid was clear watery and it was odorless, and there was no associated pushing down pain. Associated to this she had back pain. 1 hour prior to admission while she was on the way to the hospital she started to have pushing down pain.

Otherwise: -

Risk factors

She has no history of fever, chills

She has no history of foul smelling vaginal discharge (besides showing sign of infection, large amount of vaginal discharge can be mistaken for leakage of liquor)

She has no prior history if PROM

She has no self or family history of spontaneous preterm delivery

She has no history of vaginal bleeding during pregnancy

She has no history of smoking (or alcohol consumption)

She has no history of trauma to the abdomen

She has no history of chronic cough or straining during pregnancy

She denies and serious stress (stress incontinence)

(Danger signs)

She has no history of blurring of vision

She has no history of epigastric pain or right upper quadrant pain

She has no history of abnormal body movement or loss of consciousness

She has no history of headache

She has no history of nausea or excessive vomiting

She has no history of swelling of the face and hand (swelling of independent areas of the body)

She has no history of flank pain

She has no history of cough or shortness of breath

Differential diagnosis

She has no frequency, urgency (urinary incontinence)

Others

She has no history of blood transfusion

She has no personal or family history of HTN or DM

Her sero-status for RVI is negative

(Then state her economic status)

PHYSICAL EXAMINATION

Vital sign: All, patient may be febrile (?)

HEENT: Conjunctiva

Abdomen: Check for uterine tenderness, uterine size (if fundal height less than that of expected for gestational age, it indicate oligohydramnios)

Pelvic examination:

- External genital examination: may show ongoing AF flow
- Speculum examination: the most important examination in PROM (*see the diagnosis section above*)
- Once membrane rupture has been confirmed, avoid digital vaginal examination until labor or induction of labor (avoid in PPRM given the risk of infection).

INVESTIGATION

- Investigations (Tests) that confirm diagnosis
 - *See above in the diagnosis section*
- Other investigation
 - CBC with differential
 - Hct and H
 - Blood type and RH
 - Ultrasound for fetal size and amniotic fluid index
 - In preterm urinalysis, culture and sensitivity testing done by collecting urine by catheterization
 - If between 32 and 34 weeks, amniotic fluid specimen sent for fetal lung maturity test
 - Amniocentesis in all women with PPROM before 34 weeks to test for evidence of intra-amniotic infection
 - High vaginal swab for culture
 - Biophysical profile

CHAPTER 5

MULTIFETAL GESTATION

DEFINITION AND INCIDENCE

Multifetal gestation (MG): is when more than one fetus simultaneously develops in the uterus. It could be:

- Two- twins, commonest
- Three- Triplet
- Four-Quadruplets
- Five- Quintuplet, etc...

MG result from:-

- two or more fertilization events, or
- a single fertilization followed by a splitting of the zygote, or
- a combination of both

INCIDENCE

- The overall multifetal birth rate was 34.5 per 1000, with twins representing nearly 97 percent of these births in western countries
- The frequency of monozygotic twin births is relatively constant worldwide, and approximately one set per 250 births (4-5% of 1000 pregnancies). It is largely independent of race, heredity, age, and parity.
- Incidence of multiple pregnancies is approximated using:

Helen's Formula → $1: 80^{n-1}$

- Twins $1:80$
- Triplets $1: 80^2 = 1:6400$
- Quadruplets (etc.) $1:80^3 = 1:512,000$

TWIN PREGNANCY

- It could be monozygotic (identical/uniovular) or dizygotic (fraternal/biovular)
- Dizygotic is common, (2/3rd) and monozygotic-1/3rd

Monozygotic twins

- Result from division of a single fertilized ovum
- Normally they are always of same sex
 - Rarely they can be discordant for phenotypic sex, one with 45XO chromosome (Turners syndrome) and the other with normal 46XY chromosome
- They share:-
 - Same physical characteristics; color of skin, hair and eye
 - Same body fluid
 - Same genetic features; blood type and histocompatibility genes
- They are often mirror images of one another
 - Sometimes identical twins can be paradoxically antithesis of identical.
 - Earliest split may be associated with simultaneous chromosomal error, resulting in heterokaryotypic monozygotes, for example, one with down syndrome (Trisomy 21) the other normal
- Although they are similar in a lot of ways, they have different fingerprints.

Genesis of Monozygotic twins

- Genesis of monozygotic twin is poorly understood, but it is assumed to be from:-
 1. Delay in the timing of normal developmental events.
 2. Delayed ovum transport (pregnancies conceived in close temporal proximity, progestational agents & COC pills delay tubal motility→ monozygotic twinning)
 3. Minor trauma to the blastocyst during assisted reproductive technology (ART)
- The division of one fertilized zygote into two does not necessarily result in equal sharing of protoplasmic material.
 - Because of this the process of monozygotic twinning is in a sense a teratogenic event, and monozygotic twins have an increased incidence of often discordant malformations
- About a third as often, twins arise from a single fertilized ovum that subsequently divides into two similar structures, each with the potential for developing into a separate individual

Zygosity and Chorionicity in MZ twins

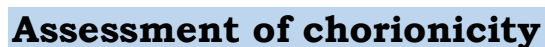
Zygosity: is genetic make-up of twin pregnancy.

- Normally monozygotic twins have same genetic makeup.

Chorionictiy: is the membrane composition, it is determined by mechanism of fertilization and in monozygotic twins by timing of embryo division

The table below shows the variation in fetal membranes and placentation in time correlated genesis of MZ twins

- The percentage distribution of placental variation is shown below.



- Prepared by Jimma University Medical Students of 2008 E.C. Batch**

- Identification of two separate placentas is a highly reliable indicator of dichorionic twins. This indicator is generally only useful in early pregnancy since separate placentas often appear fused later in gestation
- The presence/absence of the inter-twin membrane should be determined and its characteristics assessed early in pregnancy.

- **Monochorionic/monoamniotic;(MCMA)**

- The intertwine membrane is absent

- **Dichorionic/diamniotic;(DCDA)**

- An intertwin membrane with the "*twin peak*" or "*lambda*" sign indicates dichorionic twins.
 - The twin peak or lambda sign refers to a triangular projection of tissue that extends between layers of the intertwin membrane from a fused dichorionic placenta.
 - *It is best seen at 10 to 14 weeks*, becomes less prominent after 20 weeks of gestation, and may disappear.
 - An additional clue that twins are dichorionic is that the intertwin membrane is thicker with dichorionic than monochorionic twins since **the DCDA membrane consists of four layers** (i.e. two layers of both amnion and chorion) whereas the intertwin membrane in a MCDA pregnancy only consists of two layers of amnion.

- **Monochorionic/diamniotic;(MCDA)**

- An intertwin membrane with the "*T*" sign indicates a monochorionic/diamniotic placenta. This sign refers to the appearance of the thin intertwin membrane composed of two amnions as it takes off from the placenta at a 90 degree angle.

- After the first trimester, identification of fetuses of different sex is a highly reliable means of confirming a dichorionic pregnancy.

Dizygotic twins

- Result from separately fertilized ova
- They:-
 - bear resemblance of a sibling
 - may or may not have same blood type
 - can have different sex, but in about 75% of cases they have same sex
- Dizygotic twins are not in a strict sense true twins because they result from the maturation and fertilization of two ova during a single ovulatory cycle

Risk factors for dizygotic twins

- **Use of fertility stimulating drugs or artificial reproductive technology (ART) -**
 - Dizygotic twins are more common in pregnancies conceived with in vitro fertilization (IVF) than in naturally conceived pregnancies (≥95 percent versus 70 percent) since double embryo transfer is commonly performed as part of IVF.
 - Clomiphene citrate is associated with 5-10% increase risk of DZ twin
- **Maternal age-**
 - The rate of natural twinning peaks at age 37 years, when maximal
 - FSH stimulation increases the rate of multiple follicles developing. The fall in incidence thereafter probably reflects physiological follicle depletion.

- **Race/geographic area -**
 - Significant ethnic/racial variations in the prevalence of naturally conceived dizygotic twins occur worldwide.
 - In one report:
 - 1.3/1000 births in Japan,
 - 8/1000 births in United States and Europe,
 - 50/1000 births in Nigeria, were DZ twins
- **Parity** – Increasing parity correlates with an increased likelihood of dizygotic twin birth.
- **Pregnancy soon after cessation of long term oral contraception**
 - Due to **high rebound gonadotropin** secretion
- **Family history** –
 - Dizygotic twinning appears to have a genetic component that is expressed in women but can be inherited from either parent.
- **Maternal weight and height** –
 - Obese (body mass index [BMI] ≥ 30 kg/m²) and tall women (≥ 164 cm) are at greater risk for dizygotic twin birth than underweight (BMI < 20 kg/m²) and short women (< 155 cm).
- **Diet** - some studies have reported that folic acid supplementation increased the rate of twinning.

Zygoty and Chorionicity in DZ twins

- Dizygotic or "fraternal" twins occur from ovulation and fertilization of two oocytes, which results in dichorionic/diamniotic placentation and two separate placentas

SEX RATIOS IN MG

- In humans, as the number of fetuses per pregnancy rises, the percentage of male conceptuses declines.
- Percentage of Male fetus in
 - singleton pregnancy- 51.6%
 - twins, it was 50.9%
 - triplets, 49.5% and
 - quadruplets, 46.5%
- This female predominance was explained by two explanations.
 - First, beginning in utero and extending throughout the life cycle mortality rates are lower in females.
 - Second, female zygotes have a greater tendency to divide.

PHYSIOLOGICAL CHANGES IN TWIN

- Increased weight gain-For normal BMI (increased by 16.8-24.5 Kg)
- Increased cardiac output
- Plasma volume increased by 500ml from singleton
- Increased GFR, Tidal volume & fetoprotein
- Increase BP at least 15 mm Hg in 95 percent of women
- The uterus and its non-fetal contents may achieve a volume of 10 L or more and weigh in excess of 20 pounds!

DIAGNOSIS OF MG

HISTORY

- Pregnancy heavier(bigger abdominal girth) than previous pregnancies
- Personal or family history of twins

- Early onset preeclampsia
- Pregnancy following assisted reproductive technology
- Excessive weight gain
- Exaggerated minor ailments,
 - Earlier and more severe pressure in the pelvis results in, nausea, back pain, constipation, abdominal distention, varicosities hemorrhoids
 - The hormonal change associated with pregnancy which is more severe in MG is also responsible for the ailments

PHYSICAL EXAMINATION

- Barrel- shaped “large” abdomen
- Excessive weight gain not associated with edema or obesity
- Obstetric palpation revealing:-
 - Outline or ballottement of more than one fetus
 - Big for date uterus
 - More than two poles
 - Multiple small parts
- FHR heard by two people at different areas with rate difference of at least 10 bpm (with different rate to the maternal pulse).
- Palpation of 1 or more fetus after delivery of one neonate

INVESTIGATIONS

- **Ultrasound:**
 - Diagnosis of MG,
 - Determination of:-
 - Chorionicity
 - Gestational age
 - Viability,
 - Fetal anomalies
 - Presentation, etc...

➤ **Biochemical:**

- Serum hcG, MSAFP & unconjugated estriol are almost doubled.

➤ **Radiography:** rarely done these days

COMPLICATIONS OF MULTIFETAL PREGNANCY

- MG is associated with higher rates of almost every potential complication of pregnancy, with the exceptions of **post-term pregnancy and macrosomia**.
- The most serious risk is **spontaneous preterm delivery**, which plays a major role in the increased perinatal mortality and **short-term and long-term** morbidity observed in these infants.
- The complications are classified in to maternal and fetal.

Maternal complication

- Hyperemesis
- Abortion
- Maternal anemia
- PIH(PE)
- APH
- Dysfunctional labor
- Malpresentation
- PPH
- Postpartum Depression, etc...

Fetal complication

- Fetal-fetal hemorrhage
- ↑Perinatal mortality(4X,12X,26X–twin,triplet, quadruplet)
- Low birth weight
- Malformations
- Discordant
- Cord accident
- Polyhydramnios

Unique complications of MZ twins

- Cord entanglement
- Conjoined Twins
- Vascular Anastomosis
- Discordant twin
- Locked twins

Cord entanglement:

- Cord entanglement occurs in most, if not all, monoamniotic twin pregnancies.
- Loose cord entanglements probably begin in the first trimester, and have the potential to tighten at any time.
- Intermittent occlusion of umbilical blood vessels may be associated with neurologic morbidity; significant prolonged occlusion can be lethal.

Conjoined twins

Incidence

- Conjoined twins are a rare type of monoamniotic twins, estimated to occur in 1.5 per 100,000 births worldwide.
- Females are affected more often than males.

Types

- When twins are conjoined, the fusion occurs between same body parts. Conjoined twins are classified as:

Types of conjoined twins	Fused part
Cephalopagus	Head
Thoracopagus	Chest
Omphalopagus	Abdomen
Ischiopagus	Caudal
Pygopagus	Sacrum

Prenatal diagnosis

- The diagnosis should be suspected in 1st trimester MA twin pregnancies when the embryonic/fetal poles are closely associated and do not change in position with respect to each other.
- Their findings, which are not all specific to conjoined twins, include:-
 - fetal hyperextension,
 - increased nuchal translucency or cystic hygroma,
 - no sign of separate movement of the twins,
 - juxtaposed embryos with a single midline cardiac motion,
 - fewer limbs than expected,
 - a single umbilical cord with more than three vessels,
 - both heads or breeches consistently at the same level to each other
- Color Doppler, fetal echocardiography, and three-dimensional ultrasound examination can confirm the diagnosis and clarify anatomy, which is critical for assessing prognosis and pre- and postnatal decision-making.
- Congenital anomalies are always present in conjoined twins. The prognosis is poor because these anomalies often preclude survival of one or both twins, even if surgical separation is performed.

Vascular anastomosis between fetuses

- Nearly 100 % of monochorionic twin placentas have vascular anastomosis.

- Most of these vascular communications are hemodynamically balanced and of little fetal consequence.
- The two patterns of hemodynamically significant anastomotic circulations include acardiac twinning and the twin-to-twin transfusion syndrome

Acardiac twin

Pathogenesis

- Large artery-to-artery placental shunts in the embryo, often also accompanied by a vein-to-vein shunt, result in the TRAP sequence.
 - The perfusion pressure of the donor twin overpowers that in the recipient twin, who thus receives reverse blood flow from its twin sibling.
 - The "used" arterial blood reaching the recipient twin preferentially goes to the iliac vessels and thus perfumes only the lower part of the body, leading to disruption or deterioration of growth and development of the upper body.
 - In the TRAP sequence, there is usually a normally formed donor twin who has features of heart failure as well as a recipient twin who lacks a heart (acardius) and various other structures like:-
 - Failure of Head development
 - ➔ **acardius acephalus**
 - Partially developed head with identifiable limbs ➔ **acardius myelacephalus**; and
 - failure of any recognizable structure to form
 - ➔ **acardius amorphous**
- Without treatment, the donor or "pump" twin has been reported to die in 50 to 75 percent of cases.

Twin-to-twin transfusion syndrome (TTTS)

- TTTS results from imbalances in fetoplacental blood flow in the shared placental circulation
- It is a potentially lethal disorder that develops in 10 to 15 percent of monochorionic twins.
- Is characterized by oligohydramnios (including anhydramnios) in one amniotic sac and polyhydramnios in the other sac.

Cerebral palsy, microcephaly, porencephaly, and multicystic encephalomalacia are serious complications associated with vascular anastomoses in twin gestations.

➤ Outcomes of TTTS**○ Donor twin**

- small, pale, dehydrated (IUGR)
- oligohydramnios (due to oliguria)
- die from anemic heart failure

✓ Recipient twin

- plethoric,
- edematous,
- hypertensive, ascites,
- kernicterus (need amniocentesis for bilirubin),
- hepatomegaly,
- polyhydramnios (due to polyuria),
- die from congestive heart failure, and jaundice

➤ Diagnosis

✓ In utero

- Two ultrasound evidences:
 - ✓ 1st – MCDA pregnancy is identified
 - ✓ 2nd - Hydramnios (SDP >8 cm) in one sac and oligohydramnios defined by SDP <2 cm in the other twin is found
- Although growth discordance or growth restriction may be found with TTTS, these per se are not considered diagnostic criteria.

✓ postnatal

- is made based on weight discordancy between twins of 15 or 20 percent and a hemoglobin level difference of 5 g/dL or greater, with the smaller twin being anemic

➤ Staging

TTTS is typically classified by the Quintero (1999) staging system :-

- **Stage I**—discordant amniotic fluid volumes as described in the earlier paragraph, but urine is still visible sonographically within the bladder of the donor twin
- **Stage II**—criteria of stage I, but urine is not visible within the donor bladder
- **Stage III**—criteria of stage II and abnormal Doppler studies of the umbilical artery, ductus venosus, or umbilical vein
- **Stage IV**—ascites or frank hydrops in either twin
- **Stage V**—demise of either fetus

➤ Management

- Several therapies are currently used for twin-to-twin transfusion, including
 - amnioreduction,
 - septostomy,
 - laser ablation of vascular anastomoses, and
 - selective feticide

Discordant twin

- Restricted growth of one twin fetus usually develops late in the second and early third trimester and is often asymmetrical.
- The cause of birth weight inequality in twin fetuses is often unclear
- In monochorionic twins, discordancy is usually attributed to placental vascular anastomosis
- Dizygotic fetuses may have different genetic growth potential

Locked twin

- Occurred only once in 817 twin gestations.
- For twins to lock, the first fetus breech & second cephalic. With descent of the breech, the chin of first fetus locks between the neck and chin of second, cephalic fetus. Cesarean delivery is recommended when the potential for locking is identified

MANAGEMENT IN MG

1. Antenatal management

- Diet: addition 300kcal /day
- Rest
- Supplementary iron & folate
- Frequent antenatal visits
- Fetal surveillance every 3-4 weeks
- Admission not mandatory
- Tocolytics, prophylactic cerclage & steroids to decrease preterm labor are not indicated

2. Management during labor

- Open iv line for all mother with twin gestation
- Place of delivery in a hospital
- First stage same as singleton
- Experts: obstetrician/ anesthesiologist
- Liberal episiotomy
- Avoid general anesthesia
- Avoid uterotonics after 1st baby
- Induction & augmentation are contraindicated

Mode of delivery

- Mode of delivery depends on obstetric factors, presentation of 1st baby, chorionicity & animosity
 - **Vaginal delivery if no indication for CD**
 - **Cesarean delivery:** Indications:-
 - 1st twin non vertex,
 - Twins with complications: IUGR, conjoined, Monoamniotic twins,
 - Placenta previa,
 - severe preeclampsia,
 - previous C/D,
 - contracted pelvis,
 - post-term,
 - abnormal uterine contraction

Delivery of second twins

- Immediately after delivery of first fetus assess the lie, presentation & FHB of second fetus.
- Vaginal: longitudinal lie
- Indications of urgent delivery of second twin:
 - Severe intrapartum vaginal bleeding
 - Cord prolapse of second baby
 - 1st delivery under GA
 - Occurrence of fetal distress
 - Inadvertent use of Ergometrine after 1st baby

CHAPTER 6

MALPRESENTATION

OVERVIEW

Types of pelvic shapes

- **Gynecoid pelvis:** Classic female pelvis (50% of women)
- **Android Pelvis:** Typical male pelvis (25% of women)
- **Anthropoid pelvis;** predisposes to occiput posterior
- **Platypelloid pelvis** (rare); predisposes to transverse lie hence shoulder presentation

• Gynecoid (50%) • Anthropoid (25%) • Android (20%) • Platypelloid (5%)

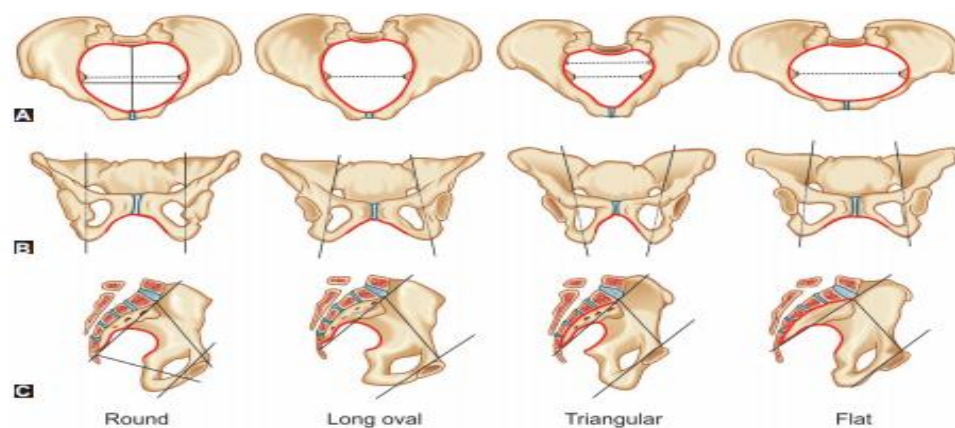


Figure 1. Anatomical features of parent pelvic types: (A) Inlet; (B) Cavity; (C) Outlet

• Fetal lie

The fetal lie indicates the orientation of the fetal spine relative to the spine of the mother. The normal fetal lie is longitudinal and by itself does not indicate whether the pre-presentation is cephalic or breech.

• Fetal presentation

Position of fetus overlying the pelvic inlet

- **Fetal position**

Is the relationship of a definite fetal part to maternal bony pelvis. It's different in early and late labor.

- In early labor; Left occipitotransverse
- At delivery; Occipitoanterior are normal findings

- **Fetal attitude**

It's the degree of extension and flexion of fetal head. Can be classified as:

- Flexed: Vertex; most common, chin is pressed against the chest.
- Military; head is straight
- Extended; Brow (increased extension) and Face (complete extension)

- **Fetal station**

Is the degree of descent of the presenting part through the birth canal

- It's expressed in centimeter above or below the maternal ischial spine. If at the level of the spines it is at "0 (zero)" station, if it passed it by 2cm it is at "+2" station

DEFINATION

Malpresentation is any presentation other than a vertical orientation, or lie, and a cephalic presentation, with the flexed fetal vertex presenting to the pelvis.

INCIDENCE AND RISK FACTORS

Malpresentation is seen in up to **3% to 5%** of singleton gestations at term, **an abnormal lie, presentation, or flexed attitude**

Factors associated with malpresentation include:

- 1) Diminished vertical polarity of the uterine cavity
- 2) Increased or decreased fetal mobility,
- 3) Obstructed pelvic inlet,
- 4) Fetal malformation, and
- 5) Prematurity.

Includes: - Breech, Face, Brow, Compound and Shoulder presentations

BREECH PRESENTATION

- The most common malpresentation and the infant presenting occupy a longitudinal axis with the cephalic pole in the uterine fundus.

INCIDENCE

- It occurs in 3% to 4% of labors overall, although it is found in 7% of pregnancies at 32 weeks and in 25% of pregnancies of less than 28 weeks' duration.

CLASSIFICATION

Based on their varying relations between the lower extremities and buttocks, breech presentation can be classified as Frank, Complete and Incomplete breech.

Types of breech presentation

Frank Breech	Complete Breech	Incomplete (Footling) Breech
Lower extremities are flexed at the hips and extended at the knees	Both hips are flexed, and one or both knees are also flexed	Both hips & knees are partially flexed or knees may even be extended
presenting part consists of the two buttocks and external genitalia only	presenting part consists of two buttocks, external genitalia and two feet	Presenting part consists of one or both feet (single/double footling breech)
Incidence ; Common 60-70% (commonly present in primigravida*; about 70%)	Incidence; Less common (10%) occurs mainly in multigravida → 60%	Incidence is about 25%
Risk of cord prolapse; 0.5-1%	Risk of cord prolapse; 5%	Risk of cord prolapse; 15%
Associations with prematurity; 38%	Associations with prematurity; 12%	Associations with prematurity; 50%

** The increased prevalence in primigravida is due to a tight abdominal wall, good uterine tone and early engagement of breech*

Risk of labor abnormalities:

- Incomplete (footling) breech > Complete breech > Frank breech



Figure 2. A. Frank Breech B. Complete Breech C. Incomplete (Footling) breech

ETIOLOGY AND RISK FACTORS

The following are the known factors responsible for breech presentation. In a significant number of cases, the cause remains obscure.

- **Prematurity:** It is the commonest cause of breech presentation.
- **Factors preventing spontaneous version:**
 - a) Breech with extended legs,
 - b) Twins,
 - c) Oligohydramnios,
 - d) Congenital malformation of the uterus such as septate or bicornuate uterus,
 - e) Short cord, relative or absolute,
 - f) Intrauterine death of the fetus.
- **Favorable adaptation:**
 - a) Hydrocephalus—big head can be well accommodated in the wide fundus,
 - b) Placenta previa,
 - c) Contracted pelvis,

- d) Cornufofundal attachment of the placenta—minimizes the space of the fundus where the smaller head can be placed comfortably.
- **Undue mobility of the fetus:**
 - a) Hydramnios
 - b) Multipara with lax abdominal wall.
- **Fetal abnormality:** Trisomies 13, 18, 21, anencephaly and myotonic dystrophy due to alteration of fetal muscular tone and mobility.

DIAGNOSIS

The diagnosis of breech presentation may be made by abdominal obstetric palpation or vaginal examination and confirmed by ultrasound.

PHYSICAL EXAMINATION:

➤ **Leopold's maneuver**

- **First maneuver**, the hard, ballotable, round fetal head occupies the fundus.
- **Second maneuver**, identifies the smooth surface (back) to be on one side of the abdomen and the small irregular parts (extremities) on the other.
- **Third maneuver**, if not engaged, the softer breech is movable above the pelvic inlet.
- After engagement, the fourth maneuver shows the breech to be beneath the symphysis.

The accuracy of this palpation varies. Thus, with suspected breech presentation or any presentation other than cephalic—sonographic evaluation is indicated.

➤ **Vaginal examination**

- With a frank breech, no feet are appreciated, but the fetal ischial tuberosities, sacrum, and anus are usually palpable. After further fetal descent, the external genitalia may also be distinguished.

When labor is prolonged, the fetal buttocks may become markedly swollen, rendering digital differentiation of a face and breech difficult. In some cases, the anus may be mistaken for the mouth and the ischial tuberosities for the malar eminences. With careful examination, however, the finger encounters muscular resistance with the anus, whereas the hard, less yielding jaws are felt through the mouth. The finger, upon removal from the anus, may be stained with meconium. The mouth and malar eminences form a triangular shape, whereas the ischial tuberosities and anus lie in a straight line.

With a complete breech, the feet may be felt alongside the buttocks. In footling presentations, one or both feet are inferior to the buttocks.

Although physical examination is very important Ultrasonography is most informative in the assessment of breach presentation.

- It confirms the clinical diagnosis— especially in primigravida with engaged frank breech or with tense abdominal wall and irritable uterus.
- It can detect fetal congenital abnormality and also congenital anomalies of the uterus.
- Type of breech (complete or incomplete).
- It measures biparietal diameter, gestational age and approximate weight of the fetus.
- It also localizes the placenta.
- Assessment of liquor volume (important for ECV).
- Attitude of the head—flexion or hyperextension (important for decision making at the time of delivery).

The point of designation in a breech labor is the fetal sacrum.

COMPLICATIONS OF BREECH DELIVERY

Maternal risk/complications	Fetal risk/complications
Operative delivery	High PMR* 2-4 fold increased
Prolonged labor	Intracranial hemorrhage
	Asphyxia
	Injuries

**Perinatal mortality rate*

MANAGEMENT

ANTENATAL MANAGEMENT

Identification of complicating factors associated with breech and External Cephalic Version (ECV) can be done if not contraindicated. And formulation of the line of management should be done, if version fails or contraindicated.

External Cephalic Version (ECV)

- ECV should be carried out in an area that has ready access to a facility equipped to perform emergency cesarean delivery (ACOG, 2016a).
- Because of the risk for surgical intervention, intravenous access is obtained, and patients abstain from eating for 6 or more hours.
- Sonographic examination is performed to confirm nonvertex presentation, document amniotic fluid volume adequacy, exclude obvious fetal anomalies if not done previously, and identify placental location and fetal spine orientation.

The success rate of version is about 60%. Successful version reduces the risk of cesarean delivery significantly.

ECV is considered from 36 weeks onwards. While version in the early weeks is easy but chance of reversion is more. Late version may be difficult because of increasing size of the fetus and diminishing volume of liquor amnii. However, the use of uterine relaxant (tocolysis) has made the version at later weeks less difficult.

Contraindications of ECV

- Antepartum hemorrhage (placenta previa or abruption); risk of placental separation
- Fetal causes—hyperextension of the head, large fetus (>3.5 kg), congenital abnormalities (major), dead fetus, fetal compromise (IUGR)
- Multiple pregnancy
- Ruptured membranes—with drainage of liquor
- Known congenital malformation of the uterus
- Abnormal cardiotocography
- Contracted pelvis
- Previous cesarean delivery—risk of scar rupture
- Obstetric complications: Severe pre-eclampsia, obesity, elderly primigravida, bad obstetric history (BOH)
- Rhesus isoimmunization

Breech with extended legs is not a contraindication for version

Success and dangers of ECV

Successful version is likely in cases of:	Dangers of version:
Complete breech	Premature onset of labor
Non-engaged breech	Premature rupture of membranes
Sacroanterior position (fetal back anterior)	Placental separation and bleeding
Adequate liquor	Entanglement of the cord round the fetal part or formation of a true knot leading to impaired circulation Increased chance of fetomaternal bleed Amniotic fluid embolism
Non-obese patient	

MANAGEMENT AT TERM/LABOR

FIRST STAGE:

The management protocol is similar to that mentioned in normal labor. The following are the important considerations. Spontaneous onset labor increases the chance of successful vaginal delivery.

- Vaginal examination is indicated
 - (a) at the onset of labor for pelvic assessment,
 - (b) Soon after rupture of the membranes to exclude cord prolapse.
- An intravenous line is sited with Ringer's solution, oral intake is avoided, blood is sent for group and cross matching (considering the chance of CS).
- Adequate analgesia is given, epidural is preferred.
- Fetal status and progress of labor are monitored.
- Oxytocin infusion may be used for augmentation of labor.

INDICATIONS OF CESAREAN DELIVERY (CD):

- Weight : ≥ 3500 or < 1800 & ≥ 1000 gm.
- Hyperextended fetal head
- Contracted pelvis
- Footling breech
- Abnormal fetal wellbeing tests
- Cord presentation/prolapse
- Presence of any risk factors – • Post term; previous CS; APH; DM; pre eclampsia...

SECOND STAGE:

There are three methods of vaginal breech delivery:

- **Spontaneous** (10%): Expulsion of the fetus occurs with very little assistance. This is not preferred.

- **Assisted breech:** The delivery of the fetus is by assistance from the beginning to the end. This method should be employed in all cases (see below).
- **Breech extraction** (partial or total): When part or the entire body of the fetus is extracted by the obstetrician. It is rarely done these days as it produces trauma to the fetus and the mother. Indications are:
 - (a) Delivery of the second twin after IPV (Internal Podalic Version),
 - (b) Cord prolapse,
 - (c) Extended legs arrested at the cavity or at the outlet.

FACE PRESENTATION

- Face is a rare variety of cephalic presentation where the presenting part is the face. The attitude of the fetus shows complete flexion of the limbs with extension of the spine. There is complete extension of the head so that the occiput is in contact with the back.

The fetal chin (mentum) is chosen as the point of designation during vaginal examination.

INCIDENCE

The reported incidence of face presentation ranges from 0.14% to 0.54% and averages about 0.2%, or 1 in 500 live births overall.

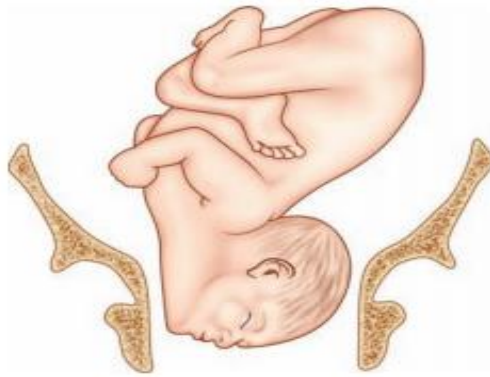


Figure 3. Face presentation

ETIOLOGY OF FACE PRESENTATION

The cause of extreme extension of the head is not clear in all the cases. The following are the factors which are often associated.

Maternal:

1. Multiparity with pendulous abdomen,
2. Lateral obliquity of the uterus especially, if it is directed to the side towards which the occiput lies,
3. Contracted pelvis is associated in about 40% cases. Flat pelvis favors face presentation,
4. Pelvic tumors.

Fetal:

1. Congenital malformations (15%)
 - (a) The commonest one is anencephaly. The almost non-existent neck with absence of the cranium makes it easy to feel the facial structure even with semi-extended head,
 - (b) Congenital goiter—prevalent in endemic areas,
 - (c) Dolichocephalic head with long anteroposterior diameter,
 - (d) Congenital branchocoele.
2. Twist of the cord several turns round the neck.
3. Increased tone of the extensor group of neck muscles

DIAGNOSIS

Antenatal diagnosis is rarely made. Diagnosis is made only during labor but in about half, the detection is made at the time of delivery. It is more often discovered by vaginal examination.

PHYSICAL EXAMINATION:

Second Leopold's Maneuver, if mentoanterior:

- Fetal limbs are felt anteriorly.
- Back is on the flank and is difficult to palpate.
- The chest is thrown anteriorly against the uterine wall and is often mistaken for back

Third Leopold's Maneuver, if mentoanterior:

- Head seems big and is not engaged.
- Cephalic prominence is to the side towards which back lies
- Groove between the head and back is not so prominent

FHS is distinctly audible anteriorly through the chest wall of the fetus towards the side of limbs.

Vaginal examination

The diagnostic features are palpating the mouth with hard alveolar margins, nose, malar eminences, supraorbital ridges and the mentum.

Sonography/Radiography: This should be done to confirm the diagnosis, to exclude bony congenital malformation of the fetus and to note the size of the baby.

MANAGEMENT

VAGINAL DELIVERY

- **MENTOANTERIOR**

FIRST STAGE: In uncomplicated cases, a wait and watch policy is adopted. Labor is conducted in the usual procedure and the special instructions, as laid down in occipitoposterior positions, are to be followed.

SECOND STAGE: One should wait for spontaneous delivery to occur. Perineum should be protected with liberal mediolateral episiotomy. In case of delay, forceps delivery is done.

• MENTOPOSTERIOR

FIRST STAGE: In uncomplicated cases, vaginal delivery is allowed with strict vigilance hoping for spontaneous anterior rotation of the chin.

SECOND STAGE:

1. If anterior rotation of the chin occurs, spontaneous or forceps delivery with episiotomy is all that is needed.
2. In incomplete or malrotation: Early decision for the method of delivery is to be taken soon after full dilatation of the cervix. The following methods may be employed to expedite the delivery.
 - Cesarean section is the preferred method and is commonly done these days.
 - Manual rotation of the chin anteriorly followed by immediate forceps extraction is rarely done these days. The principles and the methods are similar to those employed in unrotated occipitoposterior position.

BROW PRESENTATION

- Brow is the rarest variety of cephalic presentation where the presenting part is the brow and the attitude of the head is short of that degree of extension necessary to produce face presentation, i.e. the head lies in between full flexion and full extension.

INCIDENCE

The reported incidence of brow presentation varies widely, from 1 in 670 to 1 in 3433, averaging about 1 in 1500 deliveries.

Brow presentation is detected more often in early labor before flexion occurs to a normal attitude. Less frequently, further extension results in a face presentation.



Figure 4. Brow presentation

ETIOLOGY

The causes of persistent brow are more or less the same as those of face presentation. The position is commonly unstable and converts to either vertex or face presentation.

DIAGNOSIS

Antenatal diagnosis is rarely made. The findings are more or less like those of face presentation.

PHYSICAL EXAMINATION

Leopold's maneuver:

The cephalic prominence and the groove between it and the back are less prominent. The head feels very big and is nonengaged.

Vaginal examination

The position is to be confirmed on vaginal examination by palpating supraorbital ridges and anterior fontanelle.

If the anterior fontanelle is on mother's left, with the sagittal suture in transverse pelvic diameter, it is left frontum transverse position. In late labor, the landmarks may be obscured by caput formation.

Sonography:

Is confirmatory and also helps in excluding bony congenital malformation of the fetus.

MANAGEMENT

During pregnancy:

- If the presentation is diagnosed during pregnancy and there are no other contraindications for vaginal delivery, nothing is to be done. Contracted pelvis and congenital malformation of the fetus are to be excluded. Spontaneous correction into face is likely to occur.

Elective cesarean section:

- Cases with persistent brow presentation are delivered by elective cesarean section.

During labor:

1. In uncomplicated cases, if spontaneous correction to either vertex or face fails to occur early in labor, cesarean section is the best method of treatment.
2. Manual Correction to face with full dilatation of cervix is seldom practiced nowadays.
3. Craniotomy—if the labor becomes obstructed and the baby is dead, craniotomy is done. Rupture of the uterus should be excluded.

COMPOUND PRESENTATION

Whenever an extremity, most commonly an upper extremity, is found prolapsed beside the main presenting fetal part, the situation is referred to as a compound presentation.

INCIDENCE

- The reported incidence ranges from 1 in 377 to 1 in 1213 deliveries. The combination of an upper extremity and the vertex is the most common.

ETIOLOGY

Conditions preventing engagement of the head can result in slipping of either upper or lower limbs by the side of the head.

- Prematurity (commonest), contracted pelvis, pelvic tumours, multiple pregnancy, macerated fetus, high head with premature or early rupture of the membranes and hydramnios are the known etiological factors.

DIAGNOSIS

The diagnosis is not difficult when the cervical os is sufficiently dilated to feel the limb by the side of the presenting part, especially after rupture of the membranes. Premature or early rupture of the membranes occurs in about one-third of the cases.

Cord prolapse is to be excluded because of its frequent association; 10–15%.

MANAGEMENT

Factors to be considered are:-

1. stage of labor,
2. maturity of the fetus,
3. singleton or twins,
4. pelvic adequacy and
5. Associated cord prolapse.



Figure 5. Compound presentation

The fetal risks in compound presentation are birth trauma and cord prolapse.

Indication of cesarean section:

- Mature singleton fetus associated with contracted pelvis or cord prolapse with the fetus alive should be safely delivered by caesarean section.

Expectant Management:

- In otherwise uncomplicated cases (vertex/hand), an attitude of wait and watch policy is preferable.
- The labor process needs to be monitored very carefully (preferably by electronic fetal monitoring).
- Elevation of the prolapsed limb with descent of the presenting part usually takes place spontaneously. Slight elevation of the prolapsed limb during uterine contraction is a favorable sign. Temptation to replace the limbs early is not only unnecessary but carries increased maternal and fetal risks.

SHOULDER PRESENTATION (TRANSVERSE LIE)

- When the long axis of the fetus lies perpendicularly to the maternal spine or centralized uterine axis, it is called transverse lie. But more commonly, the fetal axis is placed oblique to the maternal spine and is then called oblique lie.

- In either of the conditions, the shoulder usually presents over the cervical opening during labor and as such both are collectively called shoulder presentations.

INCIDENCE

- The incidence is about 1 in 200 births. It is common in premature and macerated fetuses, 5 times more common in multiparae than primigravidae. Transverse lie in twin pregnancy is found in 40% of cases.

ETIOLOGY

The causes are

1. Multiparity — lax and pendulous abdomen, imperfect uterine tone and extreme uterine obliquity are the responsible factors.
2. Prematurity — center of the gravity lies almost in the middle of the body.
3. Twins — it is more common for the second baby than the first one to be in transverse position.
4. Hydramnios
5. Contracted pelvis
6. Placenta praevia
7. Pelvic tumors
8. Congenital malformation of the uterus—arcuate or subseptate and
9. Intrauterine death

DIAGNOSIS

Abdominal examination

Leopold's Manuever

- The fundal height is less than the period of amenorrhea.
- Fundal grip—Fetal pole (breech or head) is not palpable.

- Lateral grip—
 - (a) Soft, broad and irregular breech is felt to one side of the midline and smooth, hard and globular head is felt on the other side. The head is usually placed at a lower level on one iliac fossa.
 - (b) The back is felt anteriorly across the long axis in dorso-anterior or the irregular small parts are felt anteriorly in dorso-posterior.
- Pelvic grip— the lower pole of the uterus is found empty. This, however, is evident only during pregnancy but during labor, it may be occupied by the shoulder.

Vaginal examination

- During pregnancy; the presenting part is so high that it cannot be identified properly but one can feel some soft parts.
- During labor; Elongated bag of the membranes can be felt if it does not rupture prematurely. The shoulder is identified by palpating the following parts—acromion process, the scapula, the clavicle and axilla.

MANAGEMENT

ANTENATAL:

External cephalic version should be done in all cases beyond 35 weeks provided there is no contraindication as mentioned in breech presentation. If the lie fails to stabilize even at 36th week, the case is to be managed as outlined in unstable lie.

If version fails or is contraindicated:

- The patient is to be admitted at 37th week, because risk of early rupture of the membranes and cord prolapse is very much there. Elective cesarean section is the preferred method of delivery.

- Vaginal delivery may be allowed in a dead or congenitally malformed (small size) fetus. The labor may be allowed to continue under supervision till full dilatation of the cervix, when the baby can be delivered by internal version.

DURING LABOR:

The principles in management are as outlined below:

➤ **EARLY LABOR:**

- External cephalic version: provided there is good amount of liquor amnii and there is no contraindication.
 - External cephalic version should be tried in all cases.
- Cesarean delivery is the preferred method of delivery if version fails or is contraindicated.
 - Difficulties are faced during cesarean section as the lower uterine segment is poorly developed. However, the fetus can be manipulated to a polar (cephalic/breech) presentation before entering the uterus and a low transverse incision may be made. Otherwise lower segment vertical incision may be made.

➤ **LATE LABOR:**

- **Baby alive** — there is hardly any scope of external version in late labor because of invariable rupture of the membranes and drainage of liquor.
 - If the baby is mature and the fetal condition is good, it is preferable to do cesarean section in all cases.
 - **Internal version**— in a singleton fetus, the risk of internal version is high. Not only it might inflict injury to the uterus (rupture uterus) but also the fetal mortality is increased to the extent of about 50%.

✓ In modern obstetric practice, internal version is not recommended except in the case of second twin.

- **Baby dead** — cesarean section even in such cases is much safer in the hands of those who are not conversant with destructive operations.
 - If the obstetrician is conversant with destructive operation, decapitation or evisceration is to be done. Following destructive operation, the uterine cavity is to be explored to exclude rupture of the uterus. Internal version should not be done.

SECTION TWO

GYNECOLOGY

CHAPTER 7

ABNORMAL UTERINE BLEEDING (AUB)

DEFINITION AND TERMINOLOGIES

Abnormal uterine bleeding (AUB) is any uterine bleeding which deviates from the normal and may present with different patterns.

- The normal menstrual cycle consists of cyclic bleeding approximately every 28 days plus minus 7 days each lasting 3-8 days, 5 on average and with about 10-80ml of blood loss per cycle, with an average of 50ml loss.

There are several terms used to describe different patterns of AUB:-

1. **Menorrhagia (heavy menstrual bleeding (HMB)):** - defined as cyclic bleeding at normal interval, the bleeding is either excessive in amount (>80ml) or duration (>7 days) or both. The term menotaxis is often used to denote prolonged bleeding (duration).
2. **Metrorrhagia (intramenstrual bleeding):** - irregular acyclic bleeding from the uterus or bleeding that occurs between regular cycles. The amount of bleeding is variable.
3. **Menometrorrhagia:** - the term applied when the bleeding is irregular and excessive that the menses cannot be identified. It is a problem in both cycle length and amount.
4. **Polymenorrhea:** - it is a regular menstrual bleeding which occurs too frequently, i.e. every 21 days or less.
5. **Hypomenorrhea:** - regular menstrual bleeding with unusually light flow. Lasts for less than 2 days.
6. **Oligomenorrhea:** - regular menstrual cycle that occurs more than 35 days apart and remains constant in that frequency.

7. **Post coital bleeding:** - bleeding after or during sexual intercourse.
8. **Withdrawal bleeding:** - predictable bleeding resulting from an abrupt decline in progesterone levels.
- **Postmenopausal bleeding:** menopause is marked by 12 months of amenorrhea after the final menstrual period. Postmenopausal bleeding is any vaginal bleeding that occurs more than 12 months after the last menstrual period.

Assessing heavy menstrual bleeding (HMB) in a clinical setting is difficult, because patient's perception of blood loss and objective measurement often fail to correlate.

Objective methods of assessing blood loss

- **Hallberg and associates** described extracting hemoglobin from sanitary napkins using sodium hydroxide. And it is measured spectrophotometrically.
- **Hemoglobin and hematocrit evaluation** can be done.
 - Hemoglobin concentration below 12g/dL increases the chance of identifying women with HMB. A normal level, however, does not exclude HMB.
- **Estimating the number and type of pads or tampons** used during menses. There is a positive correlation between objective HMB and passing clots more than 1 inch in diameter and changing pads more frequently than every 3 hours.
- This is done using pictorial blood assessment chart (PBAC). With a scoring sheet, patients are asked to record daily number of sanitary products as scores of 1 point for each lightly stained tampon, 5 if moderately saturated, and 10 if completely soaked. Pads are similarly given ascending scores of 1, 5, and 20 respectively. Small clots score 1 point, whereas large clots score 5. Points are then tallied for each day. Totals more than 100 points per menstrual cycle correlate with greater than 80mL objective blood loss.

Pads	Points per each	Tampons	Points per each
	1		1
	5		5
	20		10

Large clots	5
Small clots	1

FIGURE 8-1 Scoring for the pictorial bleeding assessment chart. Patients are counseled to evaluate the degree of saturation for each sanitary product used during menstruation. The total number of points are tallied for each menses. Point totals greater than 100 indicate menorrhagia.

- **Menstrual calendars** are also use by asking the patient to record dates and blood flow quality throughout the month. These aids diagnosis and to document improvement during medical treatment.

INCIDENCE AND ETIOLOGY

- AUB occurs in 10-30% of reproductive age group women and 50% of perimenopausal women.

The etiologies include anatomic change, hormonal dysfunction, infection, system disease, medications and pregnancy complications.

Age related distribution of Etiologies of AUB

Although it may affect females of all ages, age and reproductive status are the most important factors affecting incidence and etiologies of AUB. The common causes of AUB in each age groups include:-

➤ **Prior to menarche:**

- The vagina rather than the uterus is more frequently the source of bleeding.
- **Vulvovaginitis** is often the cause, but other causes can be **dermatologic conditions, neoplasms, trauma by accident, abuse, or foreign body**.
- Urethra bleeding may also originate from urethral prolapse or infection.
- True uterine bleeding usually results from increased estrogen levels as a result of:
 - Precocious puberty
 - Accidental exogenous ingestion
 - Ovarian neoplasm

➤ **In Adolescence(1st decade after menarche):**

- Anovulation and coagulation defects are common causes in this age group.
 - Anovulation results from **immature** Hypothalamic-pituitary-ovarian **(HPO) axis** and leads to amenorrhea alternating with polymenorrhea.
- Pregnancy, STIs and sexual abuse are also considered.
- Benign or malignant neoplastic growths are less frequent.

➤ **Following adolescence (20-40yrs of age):**

- Bleeding related to early and late complications of pregnancy is common in this age group.
- STIs, leiomyomas and endometrial polyps are also common.
- Since HPO axis matures, **anovulatory uterine bleeding is encountered less often**.

➤ **Perimenopause:**

- As with perimenarchal age group anovulatory uterine bleeding from HPO axis dysfunction is common.

- The incidence of bleeding related to pregnancy and STIs declines.
- Risk of benign and malignant neoplastic growth increases.

➤ **After menopause:**

- Bleeding can result from:
 - Benign conditions like endometrial or vaginal atrophy, endometrial polyps, endometrial hyperplasia or atrophic vaginitis.
 - Malignant neoplasm like:-
 - **Endometrial carcinoma or estrogen-producing ovarian carcinoma.**
 - Ulcerative vulvar, vaginal or cervical neoplasms
 - Rarely, serosanguinous discharge from fallopian tube cancer may be a cause.

The new FIGO classification system known by the acronym PALM-COEIN, classifies etiologies AUB as:-

- PALM represents the structural cause of AUB including **P**olyp, **A**denomyosis, **L**eiomyoma and **M**alignancy and neoplasia
- COEIN represents the nonstructural causes including **C**oagulopathy, **O**vulatory disorder, **E**ndometrial, **I**atrogenic and **N**ot yet identified.

- *Previously a state of abnormal uterine bleeding that occurs in the absence of any systemic medical illness or pelvic pathology, i.e. no pathogenic cause identified, was used to be referred to as a **dysfunctional uterine bleeding (DUB)**. It was a diagnosis of exclusion and was thought to attribute to 50% of all AUB. But we do not use this term anymore. Coagulopathy, endometrial dysfunction and ovulatory disorders replace the collection of disorders previously encompassed by the term DUB.*

COMMON DIFFERENTIAL DIAGNOSIS

- Pregnancy (first rule out pregnancy in women of reproductive age)
- Incomplete abortion
- Ectopic pregnancy
- GTD
- Myoma
- Adenomyosis
- Endometrial polyps
- Endometrial hyperplasia
- Endometrial cancer
- Cervical cancer
- Sex cord stromal tumors (ovarian tumor)
- Infections- chronic endometritis
- Systemic abnormality – coagulopathy, hepatic and chronic renal failure
- Thyroid disease (Hypothyroidism)
- Leech infestation

Ectopic pregnancy (EP)

- EP is when the blastocyst implants anywhere other than the endometrial lining of the uterine cavity. The commonest site is fallopian tube 95-96% (11% fimbrial, 70% ampullary, 12% isthmic, 2-3% interstitial and cornual), then ovarian 3%, abdominal 1%, cervical <1% and cesarean scar <1%.

Risk factors:-

- tubal pathology and prior tubal surgery (to restore tubal patency or tubal sterilization)
- prior ectopic pregnancies
- smoking more than one pack cigarette per day
- pelvic inflammatory disease (PID)
- prior abortion and recurrent miscarriage

- age ≥ 40 years and assisted reproductive technology (ART)
- prior IUD use

Clinical manifestation:

- The classic symptom triad of EP is amenorrhea followed by vaginal bleeding and ipsilateral abdominal pain.
- Other symptoms include pregnancy discomfort such as breast tenderness, nausea, and urinary frequency. Vertigo and syncope may arise from hemorrhagic hypovolemia.

Physical examination:

- Speculum and bimanual examination may reveal an adnexal mass that is often tender, a uterus that is small for gestational age and bleeding from the cervix.
- Patients with ruptured EP may be hypotensive, tachycardic and unresponsive.

Adenomyosis

- It is the extension of endometrial tissue (glands and stroma) into the uterine myometrium leading to abnormal bleeding and pain. These rests may be scattered throughout the myometrium (diffuse adenomyosis) or maybe form a localized nodular collection (focal adenomyosis).
- Diagnosis is usually based on the histologic findings in surgical specimens. On gross examination the uterus is globally enlarged, but rarely exceeds a 12week pregnancy. Adenomyosis, endometriosis, and uterine fibroids (myoma) frequently coexist.

Risk factors:

- Parity and age (40s and 50s)
- Use of selective estrogen-receptor modulator like tamoxifen.

Clinical manifestation:

- Approximately one third of women have symptoms.
- Symptomatic adenomyosis occurs most often in parous women between age 35 and 50.
- Most common symptoms are heavy menstrual bleeding (HMB) and dysmenorrhea. There may also be complaint of dyspareunia (10%).

Physical examination:

- Pelvic examination may reveal a diffusely enlarged globular uterus.
- The uterus is usually less than 14cm. The consistency of the uterus is typically softer and boggy than the firm, rubbery uterus containing fibroids. It should have normal motility and no associated adnexal pathology.

Endometrial polyps

- A polyp is a mass of tissue that develops on the inside wall of a hollow organ. Endometrial polyps are localized benign overgrowths of endometrial gland and stroma over a vascular core.

Risk factors:

- increasing age (commonly 40-50 years old),
- obesity
- tamoxifen use
- **Use of oral contraceptive pills appear to be protective.**

Clinical manifestation:

- Most commonly present with abnormal vaginal bleeding, heavy cyclic or intermenstrual bleeding. Bleeding may stem from surface epithelium breaks associated with chronic inflammation and vascular fragility or from apical ischemic tissue necrosis.

Endometrial hyperplasia

- It is the abnormal proliferation of both the glandular and stromal elements of the endometrium. If left untreated, it can progress to endometrial carcinoma and can also coexist alongside endometrial carcinoma.
- Types include simple hyperplasia, complex hyperplasia, atypical simple hyperplasia and atypical complex hyperplasia.
- Patients at risk for endometrial hyperplasia, like those at risk for endometrial carcinoma, are at risk due to unopposed estrogen exposure.

Risk factors:

- can be memorized with the mnemonic '**ENDOMETRIUM**'
 - **E**xcess exogenous estrogen use without progesterone
 - **N**ulliparity
 - **D**iabetes mellitus
 - **O**besity
 - **M**enstrual irregularity
 - **E**levated blood pressure
 - **T**amoxifen use
 - **R**ectal cancer (personal history of hereditary nonpolyposis colorectal cancer)
 - **I**nfertility history
 - **U**nopposed estrogen
 - **M**enopause late (>age 55).

Clinical manifestation:

- Typically present with long periods of oligomenorrhea or amenorrhea followed by irregular or excessive uterine bleeding.

- Uterine bleeding in a postmenopausal woman should raise suspicion of endometrial hyperplasia or carcinoma until proven otherwise.

Physical examination:

- Occasionally the uterus will be enlarged from endometrial hyperplasia. This is attributed to both the increase in the mass of the endometrium and to the growth of the myometrium in response to continuous estrogen stimulation.
Usually the pelvic examination is unremarkable.
- Patients may also have stigmata associated with chronic anovulation such as abdominal obesity, acanthosis, acne or hirsutism.

Endometrial cancer

- It is the fourth most common cancer in American women, exceeded only by cancer of the breast, bowel and lung. Patients usually seek medical attention early due to vaginal bleeding and endometrial biopsy leads quickly to diagnosis.
- The primary treatment is hysterectomy with bilateral salpingo-oophorectomy (BSO) and staging lymphadenectomy for most women. Most are diagnosed with stage I disease.
- Endometrial adenocarcinomas are categorized based on histology as type I (80%) which occurs in women with a history of chronic estrogen exposure unopposed by progestin (also known as estrogen dependent neoplasm) and type II (20%) which is an estrogen-independent neoplasm.

Risk factors:

- Obesity
- Polycystic ovarian syndrome,
- Long term high dose unopposed menopausal estrogens,
- Early age of menarche,

- Late age of natural menopause,
- Infertility
- Nulliparity
- Menstrual irregularities
- Older age
- Tamoxifen use
- Diabetes mellitus and chronic hypertension,
- Cancer of the breast, ovary or colon
- Family history of endometrial cancer.
- Endometrial hyperplasia is another risk factor.
- **Smoking cigarette is protective of endometrial cancer.**

Clinical manifestations:

- 80-90% of women with endometrial cancer have either postmenopausal bleeding or some form of abnormal vaginal bleeding (menorrhagia, postcoital spotting or intermenstrual bleeding).
- 10% of women may also present with a nonbloody vaginal discharge.
- Pelvic pain, pelvic mass and weight loss are seen in women who present with more advanced disease.

Physical examination:

- May reveal obesity, acanthosis, nigricans, hypertension or stigmata of diabetes.
- Look for signs of metastatic disease, including pleural effusion, ascites, hepatosplenomegaly, general lymphadenopathy, and abdominal masses.
- Typically have a normal pelvic examination.
- In more advanced stages of the disease, the cervical os may be patulous, and the cervix may be firm and expanded. The uterus may be of normal size or enlarged. The adnexa should be examined for evidence of extrauterine metastasis and/or coexistent ovarian carcinoma.

Chronic endometritis (infection)

- Is an infection of the uterine endometrium; is the infection invades into the myometrium, it is known as endomyometritis. Underlying infection is often due to bacterial vaginosis, Mycoplasma species, Neisseria gonorrhea and Chlamydia trachomatis.

Risk factors

- retained products of conception
- sexually transmitted infections (STIs)
- intrauterine foreign bodies or growths
- Instrumentation of the intrauterine cavity.
 - ❖ It is seen most commonly after CD, but also after vaginal deliveries and surgical pregnancy terminations.

Clinical manifestation:

- Chronic irregular bleeding, discharge, pelvic pain and fever.

Physical examination:

- Bimanual examination revealing uterine tenderness. Vital sign-febrile

Coagulopathy

- Coagulopathies are infrequent causes of gynecologic bleeding. However, in women with HMB and normal anatomy, the incidence is significantly higher.
- Most frequently identified coagulopathies include von Willebrand disease, thrombocytopenia and platelet dysfunction.

Clinical manifestation

- Easy bruising, menorrhagia, excessive bleeding after dental extractions, bleeding complications with surgery or obstetric delivery, recurrent hemorrhagic ovarian cysts, epistaxis, history of spontaneous bleeding, and gastrointestinal bleeding or a family history of bleeding disorders.

Hepatic and chronic renal failure

- Severe renal dysfunction is often accompanied by endocrine disturbance that leads to hypoestrogenism and amenorrhea or to normal estrogen levels but anovulation.
NB, bleeding may worsen the chronic anemia already associated with renal failure.
- Combined oral contraceptive pills (COCs) may be contraindicated with severe hypertension, which commonly complicates renal disease.
- Liver dysfunction depending on its severity can lead to menstrual abnormalities.
 - The underlying mechanism for bleeding is not clear, but as in renal failure, hypothalamus-pituitary-ovary (HPO) axis dysfunction is suggested.
 - Hemostatic dysfunction may also contribute to bleeding. Most coagulation proteins and most of their inhibitors are synthesized in the liver.
 - Thrombocytopenia is common in women with portal hypertension and splenomegaly.

Thyroid disease

Both hyperthyroidism and hypothyroidism can cause menstrual disturbances ranging from amenorrhea to HMB.

- Mostly menstrual abnormalities precede other clinical findings of thyroid disease therefore in most women with chronic AUB, measurement of serum thyroid-stimulating hormone (TSH) level is recommended.
- In hyperthyroidism, hypomenorrhea and oligomenorrhea are more frequent complaints
- In hypothyroidism, women commonly present with anovulation, amenorrhea and anovulatory AUB.

Clinical manifestations

Symptoms:

- Tiredness, weakness, dry skin, feeling cold, hair loss, difficulty concentrating and poor memory, weight gain with poor appetite, dyspnea, hoarse voice, menorrhagia (later oligomenorrhea or amenorrhea).

Signs:

- Dry coarse skin, cool peripheral extremities, puffy face, hands and feet (myxedema), diffuse alopecia (baldness), bradycardia.

Leech infestation

- Leeches are blood sucking water (aquatic) worms and are parasitic to man and other animals. They are usually taken into human body when using unfiltered or contaminated water to bathe, drink or swim.
- Leeches possess different chemicals such as proteolytic inhibitors which plays a role in the pathogenesis of leech infestation, causing continuous bleeding from site of attachment.

Risk factor: use of river water for deep douching.

Clinical manifestation: itching, bleeding and if it is severe it may result in anemia.

Prepared by Jimma University Medical Students of 2008 E.C. Batch

PATIENT EVALUATION

The main goal of evaluation of a patient presented with AUB is:

- Exclusion of pregnancy and malignancy and
- Identification of the underlying pathology

First confirm that the bleeding is through the vagina and not from the urethra or the rectum.

HISTORY

➤ Thorough menstrual history

- Age at menarche
- Date of last menstrual period
- Timing and amount of blood
- Birth control method (contraception history) (IUD can be associated with AUB)

➤ History of current bleeding

- Timing of bleeding (if during sexual intercourse, intermenstrual...)
- Quantity of bleeding (amount) (excessive bleeding is assessed by number of pads used, passage of clots (size and number) and duration of bleeding).
- Tissue passage (r/o abortion)
- Any passage of vesicles (r/o GTD)
- Association with sexual intercourse (may indicate cervical or vaginal etiology)

➤ Associated symptoms

- fever (r/o infection),
- fatigue, dizziness and sense of rotation (anemia due to increased blood loss),
- pain (dysmenorrhea often accompanies AUB caused by infection, structural abnormality, pregnancy complication),

- bulk symptoms (due to abdominal mass when considering pregnancy and tumor)
- **Assess risk factors**
- **History of use of medication**
 - NSAIDs
 - Anticoagulants
 - Oral contraception
 - HRT
 - Corticosteroids
 - Antidepressants and antipsychotics

PHYSICAL EXAMINATION

G/A: well looking, acute sick looking (in cases like EP), or chronically sick looking (in cases like ovarian neoplasms)

V/S:

- Tachycardia & tachypnea (? Severe anemia)
- Febrile (?Infection)
- Hypotension (? Massive blood loss)

HEENT: pale conjunctiva (signs of anemia)

LGS: Thyroid enlargement

Abdomen:

- abdominal swelling,
- tenderness with palpation

Pelvic examination: thorough pelvic examination is important, including taking sample for Pap smear.

I/S:

- skin pigmentation, ecchymosis, purpura
- Dry/sweaty and cold/hot skin (thyroid disorders)
- palmar pallor (sign of anemia)
- hair distribution (hirsutism)

INVESTIGATION

- **Pregnancy tests** (beta-hCG) (for all in reproductive age group)
- **Complete blood count (CBC)** (assess the presence of anemia, infections and coagulopathy)
- Thyroid stimulating hormone levels (**TSH**)
- **Ultrasonography**
 - **Transvaginal sonography (TVS)**
 - Is chosen by many as a 1st line tool to assess AUB over endometrial biopsy (EMB), because it:
 - Allows assessment of both the endometrium and myometrium
 - Offers greater patient comfort
 - Allows suitable detection of post-menopausal endometrial hyperplasia
 - **Saline infusion sonography (SIS) (Sonohysterography)**
 - Is done by installing saline into the uterine cavity during TVS
 - It permits superior detection of intracavitary lesions
 - It can be used for sonography-guided Pipelle EMB.
 - Limitations: (see Williams gynecology 3rd Ed)
- **Endometrial biopsy –**
 - To rule out malignancies
 - Indications for EMB in a woman with AUB
 - Age >45 years (ACOG, 2012), but the JUSH guideline says age >35yrs.
 - The ACOG suggest EMB in those younger than 45 years with a history of
 - unopposed estrogen exposure such as seen in obesity or polycystic ovarian syndrome (PCOS)
 - failed medical management
 - persistent AUB

- **Hysteroscopy** – involves direct visualization of the endometrial cavity. Usually performed with Dilation and curettage (D&C). Particularly useful when polyp or submucosal fibroid is suspected, because these lesions can be confirmed and removed under direct visualization.
- **Cervical cytology**
- **Coagulation profile-** if indicated

CHAPTER 8

ABDOMINOPELVIC MASS (APM)

WHAT IS ABDOMINOPELVIC MASS?

It is abnormal Abdominal growth/mass/swelling that took its origin down from pelvic.

PATIENT APPROACH

HISTORY:

Detailed and Comprehensive Hx is important

- **Age-** very important in narrowing Ddx
- **Elaboration of the c/c (swelling)**
 - Duration, onset and location,
 - progression- rapid growth is consistent with malignancy
- **Associated sx** - elaborate them accordingly,
 - Pelvic/abdominal pain, low back pain-eg. Inflammatory or invasive conditions
 - Vaginal bleeding- eg. Myoma, Ectopic pregnancy..
 - Vaginal discharge- eg. FT cancer, TOA...
 - Fever- eg. TOA, Pyometra...
 - Urinary sx- urgency, incontinence, retention...
 - GI sx- constipation, bloating, early satiety- eg. Ovarian masses
 - Fatigue, significant weight loss (may indicate malignancy)
- **Risk factors (RF)**
- **Family hx and previous similar self complaint**
- **Reproductive status-** ex. infertility can be RF (eg. low malignant potential ovarian tumors) or complication of some APM (myoma, endometrioma, hydrosalpinx).
- **Menstrual and contraception hx**
- **Prior hx of PID**
- **Prior hx of any gynecological surgery,** risk for ectopic Px, textiloma

PHYSICAL EXAMINATION

Thorough P/E is important

- **General:-** wastage from cancer
- **Vital Signs:-** including BMI (obesity is RF for some APM)
- **LGS:-** important in assessing metastasis (LNs, Breast)

✎ Hereditary ovarian cancer may occur synchronously with Breast cancer and/or the later may metastasize to ovary

- **HEENT:-** Anemia (Pale conjunctiva)-of chronic disease in malignancies, from AUB 2^o APM
- **R/S:**
 - Pleural effusion 2^o to meig's syndrome (Ovarian fibroma) or pseudomeigs syndrome (eg. mature teratoma, stroma ovarii, Myoma, Benign FT)
 - Metastasis to lung (eg. Choriocarcinoma, CRC, bladder cancer)

✎ Findings may include:- decreased tactile fremitus, Dullness, decreased air entry, Localized BBS on upper border of effusion

➤ Abdomen:

- **Inspection**-shape of abdomen, location of swelling, distended vein, any skin color change, any previous surgical scar.
- **Palpation**- superficial and deep
 - ✓ **Size**- in weeks of pregnant uterus size. (...a X weeks gravid uterus sized APM...)
 - 12 weeks at symphysis pubis
 - 20 weeks at umbilicus
 - 38 weeks at xiphisternum

- ✓ **Origin**- APM arising from the pelvis or an abdominal mass? It can be differentiated by identifying if one can go below the mass in to the pelvic cavity or not.

➤ Lower border of AMP is unreachable. i.e. one cannot advance fingers between the mass and pubic symphysis

- ✓ **Site**-Location in the Abdomen
- ✓ **Shape**- globular, irregular
- ✓ **Consistency**- soft or cystic, firm or hard
- ✓ **Surface contour**-smooth, or nodular
- ✓ **Border**-regular or irregular
- ✓ **Mobility**- fixation may indicate adhesions or malignancy

➤ a fixed mass that is hard, nodular with irregular borders indicate malignancy.

- ✓ **Tenderness** - indicate inflammatory process or torsion
- ✓ **Surface Temperature** -comparable or not with surrounding area.

✎ Ex. There is a 14 wks. gravid uterus sized APM which occupied lower Abdomen, mostly the left side. The mass is hard, smooth, immobile, non-tender and globular/irregular in shape with irregular border and comparable surface Temperature with surrounding.

- **Percussion**

- Shifting dullness and fluid thrill to detect ascites
- Differentiation of a large ovarian tumor versus ascites

- ✎ Large ovarian tumor has central dullness with tympanicity at the flanks as opposed to ascites with central tympanicity

➤ Pelvic Examination

Complete (both abnormal and normal) finding should be reported for every Gynecologic case.

1. Examination of external genitalia- Inspection and palpation

- ✓ Discharge or bleeding from the introitus – should be noted.
- ✓ Hymen
 - Unruptured - septate, annular
 - Imperforate
 - ✚ All can result in Hemato/Pyometra

2. Speculum examination

- ✓ Look for Cervix- scarring from previous procedures or infection and/or cervical mass may interfere with menstrual outflow and end up with hemato/pyometra
- ✓ Submucous Myoma may deliver through cervical canal

3. Digital vaginal examination (PV)

- ✓ Appreciate Vaginal wall, esp. Bulging in posterior fornix(Cul-de-sac) (eg. In ovarian cancer metastasis)
- ✓ Transverse Vaginal septa- hemato/pyometra
- ✓ Cervical Excitation (motion tenderness)- PID

4. Bimanual pelvic examination

- ✓ Help to differentiate whether origin of APM is uterus or adnexa (uterine origin mass move with cervical motion while that of adnexal will not)

5. Rectovaginal Examination

- ✓ Appreciate the rectal wall and pouch of Douglas (for nodularity of Cul-de-sac in case of metastasis and endometriosis)
- ✓ Inspect for blood on examining finger for possibility of Colorectal cancer (CRC)

➤ I/S &MSS:-

- Lower extremities edema may result as a complication of compressive APM (when it is large enough to compress large Pelvic Vessels)

INVESTIGATIONS (Ix's)

➤ Laboratory Ix's

- **Pregnancy test** - with Urine or Serum β -hCG should be performed in any reproductive age group women with pelvic mass
- **CBC**- Anemia, leukocytosis(TOA)
- **Serum Biomarkers for malignancy**- their utility is limited esp. in reproductive age group women because of low specificity

- ✎ Mainly useful for postoperative follow-up of the patient (assessing the degree of response to Therapies)

➤ Imaging

- **Ultrasonography(U/S)**- TVS and/or Abdominal U/S is the best and 1st line imaging modality for evaluation of pelvic mass

- **MRI &/or CT-** for further evaluation (Anatomical details), staging malignancy and planning surgery

✎ Other Imaging modalities- depending on patient's presentation or primary image findings. Ex. Hysteroscopy (if bleeding), HSG(Infertility), Cystoscopy/urodynamic study (significant urinary symptoms)

➤ **Pathological study**

✎ definitive Dx of type of pelvic mass can be made only with histopathologic evaluation of tissue sample

MANAGEMENT

Will be discussed under each case

DIFFERENTIAL DIAGNOSIS OF APM

- As the female pelvis is an anatomic region which is a quite complex and contains organ of different system, Causes of APM can be Gynecologic or non-gynecologic.

Gynecological masses:

- **Ovary:**
- Benign and malignant tumors
 - Organic and Functional cysts
 - Endometrium (Endometriosis to Ovary)
 - Metastasis to Ovary (Breast, GI...)
- **Fallopian Tube:**
- TOA
 - Ectopic pregnancy (EP)

- Hydrosalpinx
- Para-ovarian/tubal cysts
- FT neoplasm
- **Uterus:**
 - Fibroids/Myoma,
 - Sarcoma,
 - Fibroma
 - Hemato/pyometra
 - Adenomyosis

Non-gynecologic masses:

- **GI system:**
 - Appendicular mass (Abscess, mucocele)
 - Diverticular abscess
 - Mesenteric cyst
 - Colorectal Cancer (esp. left side)
 - IBD (Crohn's disease)
 - Intestinal tuberculosis
- **Urinary tract:**
 - Pelvic kidney
 - Bladder tumors,
 - full bladder
 - Urachus Cyst
- **Miscellaneous:**
 - LAP's (eg.mesenteric LAP)
 - Peritoneal carcinomatosis
 - Pelvic Musculoskeletal tumors, infections
 - Previous Surgery complications
 - Foreign bodies(Texitiloma)

Depending on Age and Reproductive status of the women different types of pelvic mass may be more likely than other

➤ Infants and Adolescents:

- Ovarian tumor (germ cell ca, mature cystic teratoma)
- Follicular cyst and other functional cysts
- Pregnancy and its complications
- Hematoma- 2^o to imperforated hymen
- PID and its complications
- Endometrioma
- Appendicular Abscess

✎ **NB**, risk of malignancy is higher in prepubertal than in adolescents

➤ Premenopausal (reproductive age):

- Functional cysts- follicular, corpus luteum
- Pregnancy related- Pregnancy, EP, theca lutein cyst
- Inflammatory-
 - ✓ PID related-TOA, Hydrosalpinx
 - ✓ Appendicular/diverticular Abscess
- Ovarian tumors- benign>>malignant
 - ✓ Endometrioma
- Leiomyoma (uterine fibroid)
- Adenomyosis
- Para ovarian/tubal cyst

➤ Postmenopausal:

- Ovarian cancer (1^o and metastatic)
- Fallopian tube cancer
- Sarcoma of uterus

DISCUSSION ON SOME DDX OF APM

The most common causes of APM in our setup (ward admission) - Ovarian Tumors and Myoma- will be discussed in detail under separate chapter.

1. Functional ovarian cysts

Follicular cyst:

- is the most common type of ovarian cyst
- In menstruating women, a follicle containing the ovum (unfertilized egg) will rupture during ovulation. If this does not occur (failure in ovulation), most likely due to disturbances in the release of the pituitary gonadotropins, the fluid of the incompletely developed follicle is not reabsorbed, producing an enlarged follicular cyst.

Corpus luteum cysts:

- appear after ovulation
- following normal ovulation, the granulosa cells lining the follicle become luteinized. In the stage of vascularization, blood accumulates in the central cavity, producing the corpus hemorrhagicum. Resorption of the blood then results in a corpus luteum, which is **defined as a cyst when it grows larger than 3 cm.**

Theca lutein cysts:

- Occur within the thecal layer of cells surrounding developing oocytes
- Under the influence of **excessive hCG** (in case of GTD, clomiphene therapy and rarely normal pregnancy), thecal cells may proliferate and become cystic. This is usually bilateral

Presentation of functional cysts

- Dull aching pain within the abdomen or pelvis,
- AUB, menstrual irregularity and Dysmenorrhea.
- Fullness, heaviness, pressure, swelling, or bloating in the abdomen.
- pressure symptoms- urinary frequency, constipation
- Nausea or vomiting or weight gain

Complications

- Rupture of ovarian cysts
- Adnexal torsion

2. Ectopic pregnancy (EP)

It is an early complication of pregnancy in which the embryo attaches outside the uterus. Most EP (>95%) are tubal pregnancies. It can also occur in the cervix, ovaries, or within the abdomen.

Risk factors-

- PID,
- use of IUD (failed IUD),
- previous exposure to DES,
- intrauterine surgery (e.g. D&C),
- smoking, previous EP,
- endometriosis,
- tubal surgery, and tubal ligation.

In up to one half cases, the RF cannot be identified

Presentation-

Hx: -

- vaginal bleeding,
- acute lower abdominal pain,
- pelvic pain,
- nausea, vomiting and diarrhea
- patient may be asymptomatic (10%)

P/E: -

- adnexal mass,
- tender cervix,
- adnexal tenderness

Ix: -

- serum β -Hcg (increased), TVS

Complications-

Rupture of an EP leads to

- abdominal distension,
- tenderness,
- peritonism and
- hypovolemic shock

3. PID related TOA & Hydrosalpinx**Tubo-ovarian Abscess (TOA)**

- It is an inflammatory mass involving the FT, ovary and, occasionally, other adjacent pelvic organs.
- Is one of the late complications of PID.
- Most commonly in reproductive age women

Presentation:**Hx:-**

- Acute lower Abdominal/Pelvic pain,
- Fever, Chills,
- Purulent Vaginal discharge,
- Abdominal swelling,
- hx of prior STD

P/E:-

- Abdominal mass,
- pelvic tenderness (lower abdomen)
- Cervical motion tenderness (CMT)

Ix's:-

- CBC (Leukocytosis, elevated ESR),
- U/S (complex mass that mimic malignancy)

Complications: -

- Sepsis if abscess ruptured- life threatening

Hydrosalpinx

- Is a distally (at fimbriated end) blocked FT filled with serous or clear fluid. It is usually bilateral
- Cause can be PID (major cause), endometriosis, surgery, tubal TB, cancer of FT & Ovary

Presentation-

- Commonly Infertility, recurrent lower Abdominal or pelvic pain, prior hx of PID, Pelvic mass

4. Adenomyosis

Is characterized by uterine enlargement caused by ectopic rest of endometrial tissue, both glands and stroma, located deep within myometrium

- ★ **Both**-ectopic tissue should be both glands and stroma
- ★ **Deep**- superficial invasion of myometrium by endometrium is normal

Can be classified into two

1. **Diffuse type** -ectopic tissue rests scattered and the uterus becomes bulky and heavier.
2. **Focal type (Adenomyoma)**-localized, nodular collection of ectopic tissues

Risk factors

- Parity-90% of cases occur in parous women
- Uterine surgery
- Age-nearly 80% occur in 40s and 50s
- Tamoxifen

Presentation:

- Mostly asymptomatic,
- if symptomatic-HMB, dysmenorrhea, dyspareunia, chronic pelvic pain and bladder irritation

Diagnosis

TVS:-sonographic finding of diffuse Adenomyosis includes

- a globular enlarged uterus
- anterior/posterior wall thickness asymmetry
- myometrial hypoechoic cysts
- Myometrial texture heterogeneity
- Diffuse myometrial echogenicity
- Ill-defined endometrial echo
- Striated projection extending from the endometrium to myometrium (sign of endometrial invasion to the myometria)

MRI:-provides better diagnostic capability due to the increased soft tissue differentiation and when coexisting myoma distort anatomy

✎ Exact diagnosis of adenomyosis only possible in hysterectomy specimen.

5. Hematometra/pyometra

- collection or retention of blood (or Pus-if blood is infected) in the uterus
- develops when the Uterus becomes distended with blood 2^o to menstrual outflow obstruction from blockage or atresia of the lower reproductive tract—the Ux, Cx or Vx
- most commonly caused by congenital abnormalities, including imperforate hymen, transverse vaginal septum or vaginal hypoplasia.
- Other causes are acquired, such as cervical stenosis, intrauterine adhesions, endometrial Carcinoma, and Cervical Carcinoma.

Risk factors

- uterine surgery such as endometrial ablation
- cervical Surgery or procedures
- female genital mutilation(FGM)
- Abortion
- childbirth

Presentation

- cyclic, cramping pain in the midline of the pelvis or lower abdomen and Low back pain
- urinary frequency or retention and constipation
- dysmenorrhea (pain during menstruation)
- amenorrhea (lack of menstruation)
- postmenopausal women are more likely to be asymptomatic.
- Fever and leukocytosis (pyometra)
- May develop low blood pressure.
- firm and enlarged Ux which may become tender

Diagnosis

- often based purely on the pt's Hx of amenorrhea and cyclic abdominal pain + palpable pelvic mass
- confirmed by ultrasound

6. Para ovarian/tubal cysts

- are epithelium-lined fluid-filled cysts in the adnexa adjacent to the FT and ovary.
- originate from the mesothelium and are presumed to be remnants of the Müllerian duct and Wolffian duct
- Eg. Hydatid cysts of Morgagni, or Morgagni's cysts, are common and appear as pedunculated, often tiny, frequently multiple cysts connected to the fimbriae of the FT. They thus appear to be a specific variant of paratubal cysts

Presentation

- Mostly small and asymptomatic
- Pressure sx
- Pain in the pelvis
- Infertility

SAMPLE HISTORY: for major cases (myoma and ovarian masses) is included in the respective portions of the topics

CHAPTER 9

LEIOMYOMAS

DEFINITION AND EPIDEMIOLOGY

- Leiomyomas, (also referred to as fibroids or simply myomas) are benign monoclonal tumors arising from the smooth muscle cells of the myometrium.
- They are the most common pelvic tumor in women and they are more commonly multiple.

Epidemiology

- The incidence of myoma ranges from 20-25%, but is as high as 70-80% in studies using histologic or sonographic examination
- It is responsible for 27 percent of inpatient gynecologic admission and one-third of all hysterectomies performed are for uterine fibroids
- Typically occur in women of childbearing age.
 - The prevalence is highest between 35-40 years.
 - Leiomyomas have not been described in prepubertal girls, but they are occasionally noted in adolescents.
 - Most, but not all, women have shrinkage of leiomyomas after menopause.
- African American women are more likely to:
 - be younger at the time of diagnosis
 - have larger fibroids and a greater number of fibroids
 - have heavier bleeding, and more severe anemia

FACTORS ASSOCIATED WITH LEIOMYOMA

Factors that increase incidences

- **Race:** the incidence is 2x greater in black women than in white women.
 - Differences in genetic factors, diet, lifestyle, psychosocial stress, and environmental exposures contribute this disparity.
- **Early menarche:** (<10 years old)
 - is associated with increase of estradiol to post-pubertal levels which can plausibly lead to increased fibroid growth
- **Reproductive and endocrine factors:**
 - Leiomyoma parallels the ontogeny and life cycle changes of the reproductive hormones estrogen and progesterone.
- **Prenatal exposure to diethylstilbestrol**
- **Obesity:**
 - production of more estrogens from increased conversion of androgens to estrogen in adipose tissue by aromatase
- **Diet:**
 - Significant consumption of beef and other reds meats or ham is associated with an increased relative risk of fibroids.
- **Alcohol:**
 - Consumption of alcohol, especially beer.
- **Genetics:**
 - Studies imply a familial predisposition to leiomyoma in some women.

Factors that decrease incidences

- **Parity:**
- **Hormonal contraception:**
 - Long-acting progestin-only contraceptives (eg, depot medroxyprogesterone) appear to protect against development of leiomyomas
- **Smoking:**
 - Decreases the risk of fibroid developments possibly through the inhibition of aromatase
- **Diet:**
 - Consumption of green vegetables and fruit (especially citrus fruit), dietary vitamin A from animal sources may also be associated with decreased fibroid risk.

PATHOPHYSIOLOGY

- The cause of uterine leiomyomas is unclear.
- Fibroids are benign **monoclonal tumors**, with each tumor resulting from proliferation of a single smooth muscle cell.
- Genetic predisposition, steroid hormone factors, growth factors, and angiogenesis may all play a role in the formation and growth of uterine fibroids.
- Fibroids are hormonally responsive to both estrogen and progesterone but the relationship is complex.
 - Evidence for the relationship include:
 - Myomas contain estrogen & progesterone receptors in higher concentration than surrounding myometrium
 - Myomas may increase in size with estrogen therapy & in pregnancy
 - They are not detectable before puberty
 - During menopause, the tumors usually stop growing and may atrophy in response to naturally lower endogenous estrogen levels.

- Progesterone increase mitotic activity & reduce apoptosis
- There may be genetic predisposition
 - mutation in chromosome 6,7,12, and 14 are associated with the rate and direction of tumors growth

CLASSIFICATION

Uterine fibroids are classified by:

- Simply their location in the uterus
 - Submucous leiomyoma
 - Intramural or interstitial
 - Sub serous or sub peritoneal
 - Parasitic
 - Intra-ligamentary
 - Cervical
- The International Federation of Gynecology and Obstetrics (FIGO), as follows
 - Submucosal myomas (FIGO type 0, 1, 2)
 - protrude into the uterine cavity
 - Intramural myomas (FIGO type 3, 4, 5)
 - are located within the uterine wall
 - they may enlarge sufficiently to distort the uterine cavity or serosal surface
 - Subserosal myomas (FIGO type 6, 7)
 - They may have a broad or pedunculated base and may be intraligamentary (i.e., extending between the folds of the broad ligament).
 - Cervical myomas (FIGO type 8) – are located in the cervix rather than the uterine corpus.

Leiomyoma subclassification system



SM - Submucosal	0	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
O - Other	3	Contacts endometrium; 100% intramural
	4	Intramural
	5	Subserosal ≥50% intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
	8	Other (specify e.g. cervical, parasitic)
Hybrid leiomyomas (impact both endometrium and serosa)		
		Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below
		2-5 Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities, respectively.

Figure 1: FIGO Classification of myoma

SECONDARY CHANGES IN MYOMA

Benign Degeneration

➤ Atrophic:

- Signs and symptoms regress or disappear as tumor size decreases at menopause or after pregnancy.

➤ Hyaline:

- Yellow, soft, and often gelatinous areas. These tumors are usually asymptomatic.

➤ Cystic:

- Liquefaction follows extreme hyalinization, and physical stress may cause sudden evacuation of fluid contents into the uterus, the peritoneal cavity, or the retroperitoneal space.

➤ **Calcific (Calcareous):**

- Sub serous leiomyoma are most commonly affected by circulatory deprivation, which causes precipitation of calcium carbonate and phosphate within the tumor.

➤ **Septic:**

- Circulatory inadequacy may cause necrosis of the central portion of the tumor followed by infection and result acute pain, tenderness, and Fever.

➤ **Carneous (Red)**

- Venous thrombosis and congestion with interstitial hemorrhage are responsible for the color.
- Discrepancy between growth of myoma & blood supply results in aseptic degeneration & infarction
- The process is usually accompanied by pain but is self-limited.
- Most common during pregnancy,

➤ **Myxomatous (Fatty):**

- uncommon and asymptomatic, it follows hyaline and cystic degeneration.

➤ **Metastasizing Leiomyomata**

- Rarely, myomas spread beyond the uterus to distant locations such as the Peritoneum (Leiomyomatosis peritonealis disseminate/LPD) distant vasculature, and lung.
- They are often asymptomatic.
- Most women with these tumors have undergone a prior dilatation and curettage (D&C), myomectomy, or hysterectomy, suggesting the possibility of surgically induced vascular spread of leiomyoma cells.

Carcinomatous changes

- Very rare; mostly leiomyosarcomadenovo.

CLINICAL FEATURES

- The majority of myomas are small and asymptomatic
- The symptoms are related to the number, size, and location of the tumors.

Symptoms are classified into three categories:

- Abnormal uterine bleeding (AUB)
- Bulk-related symptoms, such as pelvic pressure and pain
- Reproductive dysfunction (i.e., infertility or obstetric complications)
- AUB:- in 30% of women
 - Heavy or prolonged menstrual bleeding —the most common fibroid symptom.
 - Intermenstrual bleeding and postmenopausal bleeding should prompt investigation to exclude endometrial pathology.
 - The presence and degree of uterine bleeding is determined, largely by the location of the fibroid (size is of secondary importance.)
 - **Submucosal myomas** that protrude into the uterine cavity (eg, types 0 and 1) are most frequently related to significant heavy menstrual bleeding than women with myomas in other locations (34 versus 25 percent).
 - The mechanism of bleeding are:
 - Interruption of the blood supply to the endometrium
 - Distortion and congestion of the surrounding vessels, particularly the veins
 - Ulceration of the overlying endometrium
 - increased surface area

- Alteration of normal myometrial contractile function in the small artery and arteriolar blood supply underlying the endometrium.
- Inability of the overlying endometrium to respond to the normal estrogen/progesterone menstrual phases, which contribute to efficient sloughing of the endometrium.
- Pressure necrosis of the overlying endometrial bed, which exposes vascular surfaces that bleed in excess of that normally found with endometrial sloughing.

➤ Bulk-related symptoms

- Irregularly shaped and enlarged myomatous uterus exerts pressure on the surrounding structures, resulting in:-
 - pelvic pressure or pain: it is likely to be chronic, intermittent, dull pressure or pain
 - Pain result from degeneration associated with
 - ✓ vascular occlusion
 - ✓ infection
 - ✓ torsion of a large pedunculated tumor
 - ✓ myometrial contractions to expel a subserous myoma from the uterine cavity
 - Urinary tract or bowel symptom
 - ✓ Urinary symptoms –frequency, difficulty emptying the bladder, or, rarely, complete urinary obstruction. It may also result in hydronephrosis
 - ✓ Bowel symptoms –constipation.
 - Venous compression — Very large uteri may compress the vena cava and lead to an increase in thromboembolic risk

- Painful menses —in many women appears to be correlated with heavy menstrual flow and/or passage of clots.
- Painful intercourse — anterior or fundal fibroids are the most likely to be associated with deep pain with intercourse.
- Fibroid degeneration or torsion — fibroids cause acute pain from breaking down of the fibroid tissue.

➤ Reproductive dysfunction

- Leiomyomas account for 1 to 3 % of infertility
- Fibroids, particularly those that impinge upon the endometrium, may affect fertility by:-
 - interfering with implantation over the myoma site
 - rapidly distending the uterus in early pregnancy,
 - impairing uterine contractility
- The location of a fibroid, and not its size, is the key factor regarding fertility
 - Leiomyomata with a submucosal or intracavitary component were associated with lower pregnancy rates
 - ✓ the likely mechanism is inhibition to normal implantation
 - In contrast, subserosal fibroids do not impact fertility.
 - The role of intramural fibroids in infertility is controversial
- Fibroid near a fallopian tube ostium or near the cervix may impede fertilization.
- Spontaneous Abortion; both uterine leiomyoma and spontaneous miscarriage are common, and an association between these has not been shown convincingly.

➤ Prolapsed fibroid

- Infrequently, a sub mucosal leiomyoma will prolapse through the cervix and present with a mass, bleeding, and possible ulceration or infection.

➤ Endocrine effects

- Rare symptoms of fibroid tumors where fibroids can secrete ectopic hormones include:
 - Polycythemia: from autonomous production of erythropoietin
 - Hypercalcemia: from autonomous production of parathyroid hormone-related protein
 - Hyperprolactinemia

The Mnemonic: **“FIBROIDS”** can be used to recall clinical symptoms of uterine leiomyomas

- **F:** Frequency and retention of urine, hydronephrosis
- **I:** Iron deficiency anemia
- **B:** Bleeding abnormalities (menorrhagia, metrorrhagia, menometrorrhagia, postcoital spotting), bloating
- **R:** Reproductive difficulties (dysfunctional labor, premature labor/delivery, fetal malpresentation, increased need for cesarean delivery)
- **O:** Obstipation and rectal pressure
- **I:** Infertility (failed implantation, spontaneous abortion)
- **D:** Dysmenorrhea, dyspareunia
- **S:** Symptomless (most common)

COMPLICATIONS

- Anemia
- Urinary or bowel obstruction from large or parasitic myomas
- Malignant transformation is rare

- Red degeneration
- Pregnancy associated complications (see below)
- Surgical complications especially ureteric injury or ligation in cervical myomas.

MYOMAS AND PREGNANCY

➤ Myoma in pregnancy: Incidence: Around 0.1 – 3.9%

Influence of pregnancy on myoma:

- 1/3 of the myoma increases in size,
- 1/3 remain same and
- 1/3 decreases in size
 - When an increase has been reported, most of the growth takes place in the early part of pregnancy, after which they remain static or decrease.
- Red degeneration

Influence of myoma on pregnancy:

- Early pregnancy bleeding and abortion
- Preterm labor
- Placental abruption: placentation over a fibroid appears to be a consistently strong risk factor for abruption.
- IUGR
- Fetal compression syndromes: Dolicocephally, head molding, asymmetric ventricles.
- Incarceration of the uterus:
 - When trapped within the pelvis with further uterine enlargement occurring by sacculation.
 - Present with abdominal pain and urinary retention.
- At delivery:
 - Malpresentation, obstructed labor,
 - postpartum hemorrhage
 - post-myomectomy uterine rupture

DIFFERENTIAL DIAGNOSIS

Patient with myoma can present usually with AUB (more commonly) or abdominal mass

For mass	For AUB
Pregnancy	Endometrial hyperplasia
Ovarian Ca	Endometrial or tubal Ca
Tubo-ovarian abscess	Uterine sarcoma
Endometriosis	Endometrial polyps
Adenomyosis	Adenomyosis
Myometrial hypertrophy	DUB
Endometrial Ca....	Endometriosis...

MANAGEMENT

- Choice of treatment depends on:
 - Symptoms
 - Age of patient
 - Parity
 - Presence of pregnancy
 - Plan for future fertility
 - General health of the patient
 - Location of the myoma

- General treatment include:-

- Treatment of anemia
- Analgesia
- Observation

Observation:

- Asymptomatic leiomyomas usually can be observed and surveyed during annual pelvic examination
- Exceptions:
 - Fibroids growing rapidly
 - If they are pedunculated and prone to torsion
 - If they are likely to complicate future pregnancy
 - If there is suspicion of malignancy

➤ Drug therapy:

- Advantage:
 - Reduces / relieves symptoms
 - Correct preoperative anemia
 - Option for a women at late menopausal transition
- Disadvantage:
 - Recurrence of fibroids after stopping treatment

Indications for medical management of uterine leiomyoma

Agent	NSAIDs	COCs	DMPA	LNG-IUS	GnRH Agonist
Symptom					
Dysmenorrhea	+	+	+	+	+
Menorrhagia	-	+	+	+	+
Dyspareunia	-	-	-	-	+
Pelvic pressure	-	-	-	-	+
Infertility	-	-	-	-	+

GnRH agonist

- Is used for 3 – 6 months
- Control bleeding and improve preoperative HCT
- Is temporarily used till surgery is planned
- Is used if menopause is anticipated

- Shrinks myomas (40 – 60%) to allow vaginal hysterectomy and technically easier surgery with diminished blood loss.

Mechanism of action (MOA)

- There are two suggested MOA of GnRH agonists

a) Effect on HPO axis

- GnRH agonists stimulate receptors on pituitary gonadotropes → supraphysiological release of LH and FSH (called Flare and typically last 1 week)
- However, with their long-term action GnRH agonists downregulate receptors in gonadotropes → creates desensitization to further GnRH stimulation → decreased gonadotropin secretion
 - This leads to suppression of estrogen and progesterone levels 1 to 2 weeks after initial GnRH agonist administration

b) Direct effect on leiomyoma

- leiomyomas themselves may contain GnRH receptors, and agonists may directly decrease leiomyoma size

- GnRH agonists suppress leiomyoma cell proliferation and induce cell apoptosis by the fourth week of GnRH agonist therapy.

Side effects of GnRH agonists

- Occur in up to 95 percent of women
- They result from the profound drop in serum estrogen levels
- It includes vasomotor symptoms, libido changes, vaginal epithelium dryness, accompanying dyspareunia, and loss in trabecular bone (6 months use will result in 6% trabecular bone loss)

- <10% of patients terminate treatment secondary to side effects
- To obviate the side effects:-
 - These agents alone are not recommended for longer than 6-months' use
 - Or add-back therapy is added

Add back therapy

- Typically begun 1 to 3 months following GnRH agonist initiation
- Includes: estrogen combined with a progestin or selective estrogen-receptor modulator (SERMs)
- Advantages of SERMs include the ability to begin them concurrently with GnRH agonist treatment without negating the agonist effects of leiomyoma shrinkage.

LNG-IUS:

- Advantage:
 - Reduces menorrhagia
 - Avoids surgery
 - Prevents pregnancy
- Disadvantage:-
 - No improvement of bulk symptoms
 - May lose string as uterus enlarges

Androgens:

- Danazole:-
 - Reduces endogenous production of ovarian estrogens

➤ Surgical Management

- It is the mainstay of treatment in myomas
- It should be timed closely to planned pregnancy, if possible, to limit the risk of tumor recurrence
- Indications for emergency surgery are presence of complications:
 - Infected myoma
 - Acute torsion
 - Intestinal obstruction
- It includes:-
 - Hysterectomy
 - Myomectomy
 - Myolysis.

Hysterectomy

- In symptomatic women who have completed child bearing
- Can be performed
 - vaginally,
 - abdominally, or
 - laparoscopically
- Conserve ovaries unless there is indication to remove them
- Advantage:-
 - Eliminates symptoms & recurrence
 - The only definitive treatment
 - Malignancy can be ruled out
- Disadvantage:-
 - Preclude future fertility
 - Surgical complications

Myomectomy

- Methods
 - Laparoscopic in subserous& intramural myomas
 - Hysteroscopic in submucous myomas
- Advantage:
 - Fertility is preserved(since uterus will not be removed) or enhanced
- Disadvantage:
 - Hemorrhage during surgery requiring blood transfusion
 - Persistence of menstrual symptoms
 - Recurrence of fibroids: 50–60% recurrence risk with 25 % requiring surgery
 - Adhesion formation
 - ✓ subsequent subfertility
 - ✓ difficulty of subsequent myomectomy

When to conceive after myomectomy?

- After 3 – 6 months
- If pregnancy occurs following myomectomy, recurrence rates are diminished as pregnancy has protective effect on myoma growth

Myomectomy during pregnancy

- Generally avoid myomectomy in pregnancy
- Indications for myomectomy during pregnancy
 - Intractable pain
 - to gain access to fetus
 - facilitate uterine repair at cesarean delivery

➤ Other managements

- Endometrial Ablation
- Uterine Artery Embolization (UAE)
- Magnetic Resonance Imaging-Guided Focused Ultrasound (MRgFUS)

SAMPLE HISTORY

Chief complaint: Abdominal swelling of 6 months duration.

HPI:

This is a 32 years, Para 4(no abortion) mother, whose LMP was two weeks ago. She was relatively healthy 6 months back at w/c time she started to experience gradual onset of lower abdominal swelling w/c was initially small and she noticed it first while she was taking shower but later increased gradually to attain current size w/c is around mid-abdomen. Associated with the swelling she also developed mild lower abdominal pain of the same duration w/c is dull, intermittent, nonradiating with no known aggravating or relieving factors identified.

Her menses starts at age of 14 years. It comes every 28 day, last for 3 to 5 days and she use 1to 2 pads per day. It is dark red, non-clotting type and has no associated pain. But since 2 months back her menses become heavy and she started to use 4 to 5 pads per day and lasts for 9 to 11 days. It becomes bright red, clotting and painful.

Otherwise:

She has no history of cigarette smoking alcohol intake

She has no history of previous self or family history of similar illness in the families

She has no history of use of any contraceptive or other medications

She has no history of gynecologic surgeries and procedures

She has no history of constipation, diarrhea or blood in stool

She has no history of urgency, frequency or pain during urination

She has no history of pain during sexual intercourse or any bulging of swelling through vagina

She has no history of easy fatigability, weight loss or loss of appetite

She has no history of cough or shortness of breath

She has no history of blurring of vision, vertigo or light-headedness

She has no history of fever, malaise or rigor

She has no history of itching, burning sensation around genitalia or foul smelling vaginal discharge

She has no history of nausea, vomiting and absence of menstruation

She has no history of Orthopnea, PND or lower extremity swelling

She has no history of RUQ pain or yellowish discoloration of eye

She has no history of flank pain or decreased urine output

She has no history of personal or family history of DM, HTN, asthma, TB or renal disease

She is seronegative for RVI

Her usual diet is injera made of teff with shirowot made of Atter & she gets 3 times per day sometimes she gets meat, fruits & vegetables.

She was 18 years old during her marriage and first coitus; she is sexually active

Physical examination

G/A: well looking

V/S: (all normal), look for any distressing signs (in case of complications)

HEENT: Pink connective and non-icteric sclera

Abdomen

➤ Inspection:

- Abdomen is asymmetrically distended, more on the left side of lower quadrant.
- Flanks are not full.
- No striae gravidarum, linea nigra, scar
- Inverted Umbilicus
- no distended veins, no visible peristaltic movement, or pulsations
- hernia sites are free

➤ Superficial Palpation:

- there is no superficial tenderness or mass

➤ Deep palpation:

- There is 24 weeks sized mobile mass, that has irregular surface, tender, firm in consistency whose upper border is defined but lower border can't be reached (hand cannot pass below mass into pelvic inlet).

➤ Percussion: No shifting dullness or fluid thrill

➤ Auscultation: Bowel sounds well heard no bruits over the mass.

Pelvic Examination

- Bimanual pelvic examination:
 - Irregular enlarged with well-defined border firm in consistency mobile and tender mass on upper part of uterus.

Assessment: *Abdominopelvic mass secondary to symptomatic myoma*

Investigations

- CBC➔
 - r/o anemia/polycythemia, infection, thrombocytopenia (important for surgical patient)
- Blood group & Rh (for all surgical patients)
- Pregnancy test
- Ultrasound:
 - it is used to determine size, location, consistency, number of mass and hydro ureter & hydro nephrosis
- RFT (BUN & Serum creatinine)
- TFT(TSH, for surgical patient)
- Hystroscopy
- KUB or IVU (if urinary symptoms are there)
- Endometrial biopsy or D&C
 - is essential in the evaluation of abnormal bleeding to exclude endometrial Ca

CHAPTER 10

OVARIAN TUMORS

EPIDEMIOLOGY

- A woman's risk at birth of having ovarian cancer sometime in her life is 1% to 1.5%, and that of dying from ovarian cancer is almost 0.5%
- Each year, more than 225,000 women are diagnosed, and 140,000 women die from this disease worldwide.
- Ovarian cancer is the fifth most common cause of death from malignancy in women.

ETIOLOGY AND RISK FACTORS

Family history of breast or ovarian cancer is the most important identifiable risk factor

- Approximately 10% of patients have an inherited genetic predisposition.

Most risks in the other 90% of cases are related to a pattern of uninterrupted ovulatory cycles during the reproductive years

Uninterrupted ovulatory cycles during the reproductive years and repeated stimulation of the ovarian surface epithelium is hypothesized to lead to malignant transformation.

RISK FACTORS

- **Nulliparity** (associated with long periods of repetitive ovulation, and patients without children have double the risk)
- **Infertility** (One theory suggests that pregnancy may induce premalignant ovarian cell shedding)
- **Early menarche**
- **Late menopause**

➤ **White race**

NB, ovarian tumors are one of the few gynecologic abnormalities that are common in the white population (POP too)

➤ **Increasing age** (allows accumulation of random genetic alterations within the ovarian surface epithelium)

NB, increasing age is risk only up to mid-70s, and the risk decreases beyond 80yrs.

➤ **Residence in North America and Northern Europe** (developing countries and Japan have the lowest rates, regional dietary habits may be partly responsible)

➤ **Family history**

- Of ovarian cancer in first-degree relative (mother, daughter, or sister) triples a woman's life time risk, the risk further increase if the number of affected family members increase
- Of Lynch syndrome (hereditary nonpolyposis colorectal cancer, (HNPCC))

Although this syndrome is highly associated with life time risk of colon cancer (85 percent), it also increase risk of gynecologic malignancies like, ovarian cancer (10 to 12%) and endometrial cancer (40 to 60%)

➤ **Personal history of breast cancer**

➤ **Ethnic background** (European Jewish, Icelandic, Hungarian)

➤ **Postmenopausal hormone therapy**

➤ **Pelvic inflammatory disease**

➤ **Use of coffee, tobacco, alcohol & dietary fat**

Hereditary Ovarian Cancer

More than 90 percent of inherited ovarian cancers result from germline mutations in the BRCA1 or BRCA2 genes. Patients with a proven mutation have a dramatically elevated risk of developing ovarian cancer (39 to 46 percent). *BRCA2* is located on chromosome 13q12 and in general is less likely to lead to ovarian cancer (12 to 20 percent).

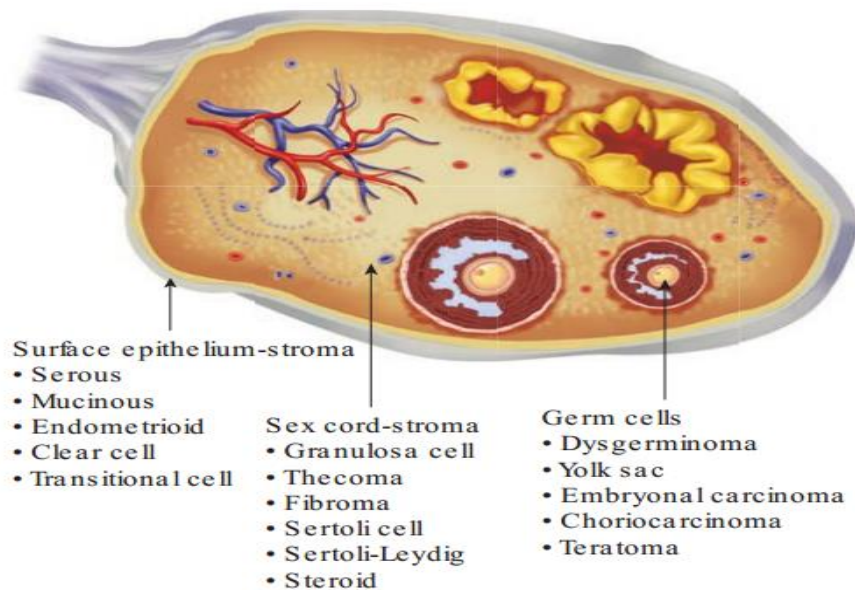
PROTECTIVE FACTORS

- **Parity** (having at least one child is protective of the disease, with a risk reduction of 0.3 to 0.4%)
- **Breast feeding** (perhaps by prolonging amenorrhea)
- **Long-term (5 year) combination oral contraceptive use** (reduces the risk by 50%. The duration of protection lasts up to 25 years after the last use)
- **Prophylactic salpingo-oophorectomy** (reduces, but does not eliminate the risk because the entire peritoneum is still going to be at risk)
- **Tubal ligation** and **hysterectomy**, (theoretically, any gynecologic procedure that precludes irritants from reaching the ovaries via ascension from the lower genital tract might plausibly exert a similar protective effect)
- **consumption of foods low in fat but high in fiber, carotene, and vitamins appears protective**

CLASSIFICATION OF OVARIAN TUMORS(OVARIAN MASSES)

- Based on clinical behaviors:
 1. Benign
 2. Borderline (low malignant potential)
 3. Malignant

- Based on morphologic characteristics:
 1. Cystic
 2. Solid
 3. Mixed
- Based on histological features (cell origin)
 1. Epithelial ovarian tumors
 2. Germ cell tumors of the ovary
 3. Sex-cord stromal tumors



BENIGN OVARIAN MASSES

➤ Functional Cysts

- Follicular Cyst
- Corpus Luteum (Granulosa Lutein) Cysts
- Theca Lutein Cysts
- Hyperthecosis
- Polycystic Ovarian Syndrome (Stein-Leventhal Syndrome)
- Luteoma of Pregnancy
- *Endometriomas, (is not a functional cyst, but it is one of the common ovarian cyst)*

➤ Epithelial Tumors

- Serous Tumors
- Mucinous Tumors
- Endometrioid Lesions
- Clear Cell (Mesonephroid) Tumors
- Transitional Cell (Brenner) Tumors

➤ Sex Cord-Stromal Tumors

- Thecoma
- Fibroma
- Hilus Cell Tumors

➤ Germ Cell Tumors

- ❖ MATURE Teratomas(*dermoid cysts*)

CLINICAL FEATURE OF BENIGN TUMORS

- Commonly seen in late child bearing age groups and most are asymptomatic
- Dermoid cyst & mucinous cystadenomas are common in reproductive age group
- Dermoid cyst & serious cystadenomas are common during pregnancy
- If symptomatic-
 - Swelling (distention),
 - Heaviness
 - Dull aching lower abdominal pain, are seen
- Signs are usually unaffected, but if there is any, it include:-
 - Cachexia (in mucinous cystadenoma)
 - Pitting edema (from compression of draining lymphatic vessels and veins from the lower limb)
 - Mass (cystic/ solid, mobile (from side to side but not from above to downwards), usually smooth surface, non-tender)
 - Positive fluid thrill

- ❖ Presence of an abdominopelvic mass (Ovarian fibroma), ascites (fluid thrill), right pleural effusion (reduce tactile fremitus & chest expansion dullness in percussion) is indicative of Meig's syndrome.

DIFFERENTIAL DIAGNOSIS FOR BENIGN OVARIAN MASSES

- Full bladder
- Fibroid
- Functional cyst
- Encysted peritonitis
- Pregnancy with or without fibroid
- Ascites
- Mesenteric cyst
- Para-ovarian cyst
- Textiloma (can be due to a forgotten gauze)

COMPLICATIONS OF BENIGN OVARIAN TUMORS

- 1) Torsion of the pedicle
- 2) Intracystic hemorrhage
- 3) Infection
- 4) Rupture
- 5) Pseudomyxoma peritonei
- 6) malignancy

BORDERLINE OVARIAN MASSES

- 10 to 15 percent of epithelial ovarian cancers have histologic and biologic features that are intermediate between clearly benign cysts and frankly invasive carcinomas. They are termed as *low malignant-potential (LMP) tumors or borderline tumors*.

Although LMP tumors may develop at any age, on average patients are in their mid-40s, which is 15 years younger than women with invasive ovarian carcinoma.

Histologically, LMP tumors are distinguished from benign cysts by having at least two of the following:-

- nuclear atypia
- epithelial stratification
- microscopic papillary projections
- cellular pleomorphism or
- mitotic activity

Unlike invasive carcinomas, LMP tumors lack stromal invasion, LMP tumors lack stromal invasion. However, up to 10 percent of LMP tumors will exhibit areas of *microinvasion*, defined as *foci*, measuring < 3 mm in diameter and forming < 5 percent of the tumor.

CLINICAL MANIFESTATION

- Ovarian LMP tumors present similar to other adnexal masses
(see manifestation of benign masses above)

MALIGNANT OVARIAN MASSES

Include:-

1. Epithelial ovarian cancer
2. Germ cell tumors
3. Sex-cord stromal tumors

EPITHELIAL OVARIAN CANCER (EOC)

Approximately **90%** of ovarian cancers are derived from tissues that come from the coelomic epithelium or mesothelium.

PATHOGENESIS

There are three distinct tumorigenic pathways:-

- Most carcinomas appear to originate **de novo from ovarian surface epithelial cells** that are sequestered in cortical inclusion cysts (CICs) within the ovarian stroma.
 - The replicative stress and DNA damage transforms the entrapped surface epithelial cells within CICs into any of the histologic ovarian cancer variants
- At least 10 percent of epithelial ovarian carcinomas, invariably high-grade serous tumors, result from **an inherited predisposition**.
 - Women born with a BRCA gene mutation require only one “hit” to the other normal copy (allele) to “knock out” the BRCA tumor-suppressor gene product. BRCA-related serous cancers appear to have a unique molecular pathogenesis, requiring p53 inactivation to progress.
- **Accumulation of genetic alterations** that leads to malignant transformation. As such, mutation the ras family of oncogenes (K-ras, H-ras, and N-ras) are implicated in carcinogenesis by their inhibition of cellular apoptosis and promotion of cellular proliferation

HISTOPATHOLOGY AND PATTERN OF SPREAD

Histologic Type	Cellular Type
<i>I. Serous</i>	<i>Endosalpingeal</i>
<i>II. Mucinous</i>	<i>Endocervical</i>
<i>III. Endometrioid</i>	<i>Endometrial</i>
<i>IV. Clear-cell “mesonephroid”</i>	<i>Mullerian</i>
<i>V. Brenner</i>	<i>Transitional</i>
<i>VI. Mixed epithelial</i>	<i>Mixed</i>
<i>VII. Undifferentiated</i>	<i>Anaplastic</i>
<i>VIII. Unclassified</i>	<i>Mesothelioma,</i>

GRADING

Ovarian tumors are classified as:

- grade 1 (well-differentiated)
- grade 2 (moderately differentiated)
- grade 3 (poorly differentiated) lesions

Patterns of Spread

- **Transcoelomic:** The most common and earliest mode of dissemination of ovarian epithelial cancer is by exfoliation of cells that implant along the surfaces of the peritoneal cavity. The cells tend to follow the circulatory path of the peritoneal fluid, to dependent areas
- **Lymphatic:** to the pelvic and para-aortic lymph nodes is common, particularly in advanced-stage disease
- **Hematogenous:** at the time of diagnosis is uncommon

CLINICAL MANIFESTATIONS OF EOC

- More than 80% of epithelial ovarian cancers are found in postmenopausal women. The peak incidence of invasive epithelial ovarian cancer is at 56 to 60 years of age
- The age-specific incidence of ovarian epithelial cancer rises precipitously from 20 to 80 years of age and subsequently declines. Less than 1% of epithelial ovarian cancers occur before the age of 21 years, two thirds of ovarian malignancies in such patients being germ cell tumors
- About 30% of ovarian neoplasms in postmenopausal women are malignant, whereas only about 7% of ovarian epithelial tumors in premenopausal patients are frankly malignant

Symptoms:

The majority of women with epithelial ovarian cancer have vague and nonspecific symptoms:

In early-stage disease,

- Irregular menses if she is premenopausal.
- If a pelvic mass is compressing the bladder or rectum, she may report, urinary frequency or constipation
- Occasionally, she may perceive
 - ✓ lower abdominal distention,
 - ✓ pressure, or pain, such as dyspareunia.
- Acute symptoms, such as pain secondary to rupture or torsion, are unusual

In advanced-stage disease,

- Patients most often have symptoms related to the presence of ascites, omental metastases, or bowel metastases, include:-
 - ✓ abdominal distention
 - ✓ bloating, constipation, nausea, anorexia, or early satiety
- Premenopausal women may report irregular or heavy menses, whereas vaginal bleeding may occur in postmenopausal women

Signs:

- The most important sign of epithelial ovarian cancer is the presence of a pelvic mass on physical examination.
 - A solid, irregular, fixed pelvic mass is highly suggestive of an ovarian malignancy. If an upper abdominal mass or ascites is also present, the diagnosis of ovarian cancer is almost certain.
- In patients who are at least 1 year past menopause, the ovaries should have become atrophic and not palpable. It has been proposed that any palpable pelvic mass in these patients should be considered potentially malignant, a situation that has been referred to as the postmenopausal palpable ovary syndrome.

DIAGNOSIS

➤ **Hx and P/E**

➤ **Investigations**

Laboratory Tests

- **CBC:** Of affected women, 20 to 25 percent will present with thrombocytosis (platelet count $> 400 \times 10^9/L$). Malignant ovarian cells releasing cytokines are believed to increase platelet production rates
- **serum electrolytes:** Hyponatremia, typically ranging between 125 and 130 mEq/L
- **serum tumor marker:**
 - CA125 levels are elevated, an elevated value (false-positive) may be associated with various common benign indications such as PID, endometriosis, leiomyomas, pregnancy, and even menstruation
 - the human epididymal protein 4 (HE4) tumor marker
 - OVA1 is another biomarker blood test panel: women with an identified ovarian mass when surgery is planned Ware Scores ≥ 5.0 in premenopausal and scores ≥ 4.4 in postmenopausal women suggest a need or gynecologic oncologist consultation
 - cancer antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA): when a mucinous ovarian tumor is identified

Imaging

- **Transvaginal sonography:** In general, malignant tumors are multiloculated, solid or echogenic, and large (> 5 cm), and they have thick septa with areas of nodularity. Other features may include papillary projections or neovascularization demonstrated by adding color Doppler. Ascites, if present, is easily detected.

- **Radiographic tests (CXR):** detect pulmonary effusions or infrequently, pulmonary metastases.
- **Barium enema:** helpful in excluding diverticular disease or colon cancer or in identifying ovarian cancer involvement of the rectosigmoid.
- **Computed tomography (CT):** scanning has a primary role in treatment planning or women with advanced ovarian cancer. Preoperatively, implants in the liver, retroperitoneum, omentum, or other intraabdominal site are detected to thereby guide surgical cytoreduction or demonstrate obviously unresectable disease
- **Magnetic resonance (MR) imaging**
- **Bone scan**
- **Positron emission tomography (PET)**

Paracentesis

- This procedure is typically avoided diagnostically as cytologic results are usually nonspecific and abdominal wall metastases may form at the needle entry site

DIFFERENTIAL DIAGNOSIS FOR EOC

- Benign ovarian neoplasms
- Functional cysts of the ovaries.
- Pelvic inflammatory disease (TOA?),
- Endometriosis
- Uterine leiomyomata
- Nongynecologic causes of a pelvic tumor, such as an
 - ✓ Inflammatory or neoplastic colonic masses
 - ✓ A pelvic kidney

STAGING OF EOC

Steps in surgical staging of EOC

- *A midline or paramedian abdominal incision is recommended to allow adequate access to the upper abdomen*
- *Any free fluid, especially in the pelvic cul-de-sac, should be submitted for cytologic evaluation*
- *If no free fluid is present, peritoneal washings should be performed by instilling and recovering 50 to 100 mL of saline from the pelvic cul-de-sac, each paracolic gutter, and beneath each hemidiaphragm.*
- *A systematic exploration of all the intra-abdominal surfaces and viscera is performed, proceeding in a clockwise fashion from the cecum cephalad, The small intestine and its mesentery from the Treitz ligament to the cecum should be inspected*
- *Any suspicious areas or adhesions on the peritoneal surfaces should be biopsied. If there is no evidence of disease, multiple intraperitoneal biopsies should be performed.*
- *The diaphragm should be sampled either by biopsy or by scraping with a tongue depressor and obtaining a sample for cytologic assessment*
- *The omentum should be resected from the transverse colon, a procedure called an infracolic omentectomy*
- *The retroperitoneal spaces should be explored to evaluate the pelvic and paraaortic lymph nodes.*

STAGES

FIGO Staging of Carcinoma of the Ovary, Fallopian Tube, and Primary Peritoneal Carcinoma Stage Characteristics

I= Tumor confined to ovaries (or to fallopian tubes)

- IA, Tumor limited to 1 ovary (or 1 tube); capsule intact, no tumor on surface, negative washings
- IB, Tumor involves both ovaries (or both tubes), otherwise like IA
- IC1, Tumor limited to 1 or both ovaries (or tubes), with surgical spill
- IC2, Tumor limited to 1 or both ovaries (or tubes), with capsule rupture before surgery or tumor on ovarian surface
- IC3, Tumor limited to 1 or both ovaries (or tubes), with malignant cells in ascites or peritoneal washings

II= Tumor involves 1 or both ovaries (or 1 or both tubes) a with pelvic extension (below the pelvic brim) or primary peritoneal cancer

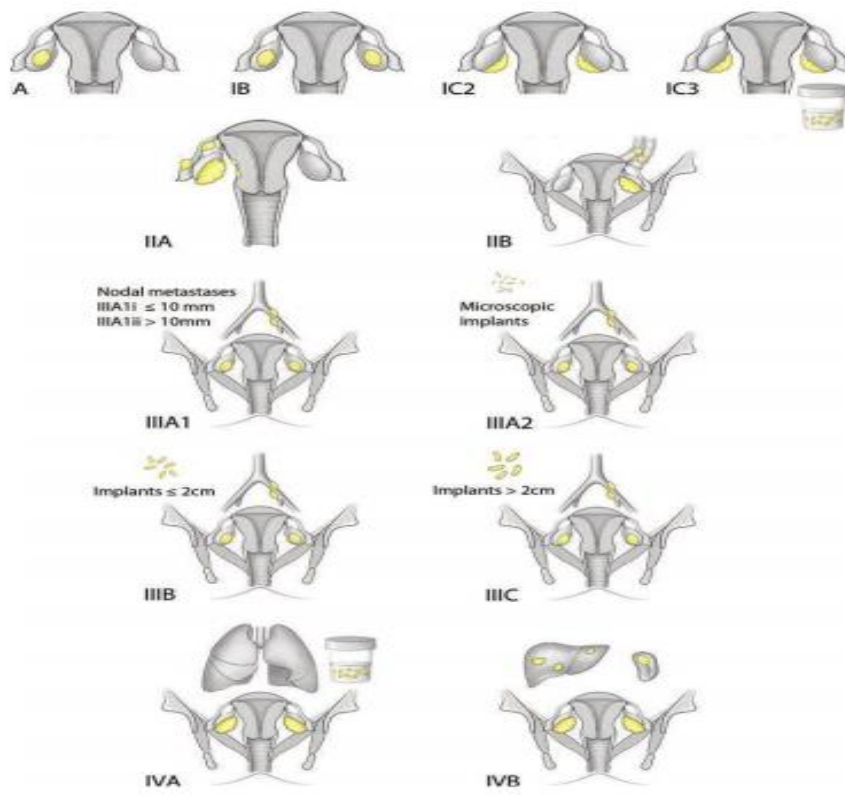
- IIA Extension and/or implants on uterus and/or fallopian tubes (and/or ovaries)
- IIB Extension to other pelvic intraperitoneal tissues

III= Tumor involves 1 or both ovaries (or 1 or both tubes) a with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to retroperitoneal lymph nodes

- IIIA1 Positive retroperitoneal lymph nodes only (i) Metastasis $\leq$ 10 mm (ii) Metastasis $>$ 10 mm
- IIIA2 Microscopic, extrapelvic (above the brim) peritoneal involvement $\pm$ positive retroperitoneal nodes
- IIIB Macroscopic, extrapelvic, peritoneal metastasis $\leq$ 2 cm $\pm$ positive retroperitoneal nodes. Includes extension to capsule of liver/spleen
- IIIC Macroscopic, extrapelvic, peritoneal metastasis $>$ 2 cm $\pm$ positive retroperitoneal nodes. Includes extension to capsule of liver/spleen

IV= Distant metastasis excluding peritoneal metastasis

- IVA Pleural effusion with positive cytology
- IVB Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)



MANAGEMENT PRINCIPLE

Early stage (stage I-II)

- **Low risk** (Stage IA or IB, grade 1 and 2)
 - Surgery: Total abdominal hysterectomy (TAH) & bilateral salpingo-oophorectomy (BSO)
 - Adjuvant chemotherapy not recommended.

- **High-risk**

Includes: stage IA or IB, grade 3; Stage IC (tumor on external surface, ruptured capsule, ascites or positive peritoneal washing); clear cell histology and all stage II

- Surgery: TAH, BSO & surgical staging
- Chemotherapy: adjuvant chemo is recommended.
 - Regimens: carboplatin (AUC=7.5) and paclitaxel (175/m²) chemotherapy for 3-6 cycles.

Advanced-stage Epithelial Ovarian Cancer (stage III-IV)

- Surgery:
 - Primary cytoreductive surgery (debulking)
 - Includes: - TAH, BSO, complete omentectomy, and resection of any metastases from peritoneal surface or intestine.
 - The goal is residual lesion < 1.5 cm
 - Secondary cytoreductive surgery
 - Considered after completion of first line chemotherapy,
- Chemotherapy.
 - Neoadjuvant chemotherapy (debulking chemotherapy)
 - May be considered for sub-optimally staged (resected) stage III & IV.
 - 2-3 cycles may be helpful in patients with massive ascites and pleural effusion

Prognostic Factors

- **Pathologic Factors**

- High grade tumors and those with extensive invasion have poor prognosis
- Clear cell carcinomas are associated with a prognosis worse than that of other histologic types

➤ **Biologic Factors: FIGO stage and ploidy**

- Low-stage cancers tend to be diploid and high-stage tumors tend to be aneuploid.

Patients with diploid tumors have a significantly longer median survival than those with aneuploid tumors. 30% of epithelial ovarian tumors expressed HER-2/*neu* oncogene and that this group had a poorer prognosis. The most commonly expressed tumor suppressor gene in ovarian cancer is *p53*

➤ **Clinical Factors:**

- In addition to stage, the extent of residual disease after primary surgery, the volume of ascites, patient age, and performance status are all independent prognostic variables.

Ovarian cancers that undergo intraoperative rupture or spillage do not worsen prognosis, whereas tumors found to have already ruptured preoperatively do have a poorer prognosis.

For early stage disease, poor prognostic variables were tumor grade, capsular penetration, surface excrescences, and malignant ascites, but not iatrogenic rupture

MALIGNANT OVARIAN GERMCELL TUMORS

- Germ cell tumors arise from the ovary's germinal elements and make up one third of all ovarian neoplasms.

Three features distinguish malignant germ cell tumors from epithelial ovarian cancers.

- typically present at a younger age, usually in their teens or early 20s
- most have stage I disease at diagnosis
- prognosis is excellent—even for those with advanced disease—due to exquisite tumor chemosensitivity

HISTOPATHOLOGY**Modified WHO Classification of Ovarian Germ Cell Tumors**
Germ cell tumors**Germ cell tumors**

- Dysgerminoma
- Yolk sac tumor (endodermal sinus tumor)
- Embryonal carcinoma
- Nongestational choriocarcinoma
- Mature teratoma
 - ✓ Solid
 - ✓ Cystic(dermoid cyst)
- Immature teratoma
- Mixed germ cell tumor

Monodermal teratoma and highly specialized types arising from a mature cystic teratoma

- Thyroid tumors (struma ovarii: benign or malignant)
- Carcinoids
- Neuroectodermal tumors
- Carcinomas (squamous cell or adeno-)
- Sebaceous tumors

DIAGNOSIS**Hx:**

- Subacute abdominal pain in 85% of patients and reflects rapid growth of a large, unilateral tumor undergoing capsular distention, hemorrhage, or necrosis
- Severe acute abdominal pain. In 10 percent of cases, secondary to cyst rupture, torsion, or intraperitoneal hemorrhage
- Abdominal distention In more advanced disease, ascites may develop and cause it
- Heavy or irregular menses Because of the hormonal changes that frequently accompany these tumors

P/E:

- A palpable mass on pelvic examination is the most common, premenarchal patients may require examination under anesthesia(EUA) to adequately assess a suspected adnexal tumor. The remainder of the physical examination searches for signs of ascites, pleural effusion, and organomegaly

Investigations**Laboratory Testing**

- Serum Tumor Markers in Malignant Ovarian Germ Cell Tumors

Histology	AFP	hCG
Dysgerminoma	—	±
Yolk sac tumor	+	—
Immature teratoma	±	—
Choriocarcinoma	—	+
Embryonal carcinoma	+	+
Mixed germ cell tumor	±	±
Polyembryoma	±	±

AFP = alpha-fetoprotein; hCG = human chorionic gonadotropin.

Placental alkaline phosphatase (PLAP), lactate dehydrogenase (LDH) α1-Antitrypsin (AAT) can, are rarely be detected in association with germ cell tumors.

Imaging

- same as for EOC

MANAGEMENT

❖ **Surgery:**

- Fertility preserving surgery is generally possible
- The minimal surgery is unilateral oophorectomy and surgical staging

❖ **Chemotherapy:**

- Is regarded as treatment of choice to preserve fertility as it occurs in young ladies.

❖ **Adjuvant chemotherapy**

- Completely resected Stage I-III: Stage I, II, or III (endodermal sinus tumors, mixed cell tumors, embryonal carcinomas, choriocarcinomas, and immature teratoma) need adjuvant chemotherapy.

❖ **Radiotherapy**

- Sensitive but rarely used as primary therapy of germ cell cancers

OVARIAN SEX CORD-STROMAL TUMORS (SCST)

- SCST are neoplasms that originate from the ovarian matrix. Cells within this matrix have the potential for hormone production. As a result, individuals with these tumors typically present with signs and symptoms of estrogen or androgen excess.

The overall prognosis of ovarian SCSTs is excellent—primarily due to early-stage disease at diagnosis and curative surgery.

EPIDEMIOLOGY

- SCSTs account for 3% to 5% of ovarian malignancies. These tumors are more than twice as likely to develop in black women. In contrast with (EOC) or (GCT), ovarian SCSTs typically affect women of all ages.

- There are no proven risk factors for SCSTs. However, obesity as a hyperestrogenic state was independently associated, whereas parity, smoking, and oral contraceptive use were protective.
- The etiology of SCSTs is largely unknown. However, a single, recurrent *FOXL2* gene mutation (402C> G) is present in virtually all adult-type granulosa cell tumors.

CLASSIFICATION

Modified WHO Classification of Ovarian Sex Cord-Stromal Tumors

Pure stromal tumors

- Fibroma/fibrosarcoma
- Thecoma
- Sclerosing stromal tumor
- Leydig cell tumor
- Steroid cell tumor

Pure sex cord tumors

- Granulosa cell tumor
- Adult type
- Juvenile type
- Sertoli cell tumor
- Sex cord tumor with annular tubules

Mixed sex cord stromal tumors

- Sertoli-Leydig cell tumors
- Sex cord-stromal tumors, NOS

DIAGNOSIS**Hx**

- Isosexual precocious puberty is the presenting sign in more than 80 percent of prepubertal girls ultimately diagnosed with an ovarian SCST.
- Adolescents often report secondary amenorrhea. Abdominal pain and distention are other common complaints in this age group
- In adult women, heavy, irregular bleeding and postmenopausal bleeding are the most frequent symptoms.
- mild hirsutism that rapidly progresses to frank virilization should prompt evaluation to exclude these tumors.
- The classic presentation is a postmenopausal woman with rapidly evolving stigmata of androgen excess and a complex adnexal mass.

P/E:

- Abdominal tenderness or a palpable mass

Investigations**Laboratory Testing:**

- Elevated circulating levels of testosterone or androstenedione or both are strongly suggestive of an ovarian SCST in a woman with signs and symptoms of virilization.

Clinical hyperandrogenism is more likely to be idiopathic or related to polycystic ovarian syndrome, but serum testosterone levels > 150 g/dL or dehydroepiandrosterone sulfate (DHEAS) levels > 8000 g/L strongly suggest the possibility of an androgen-secreting tumor.

Imaging

- CT, MRI, U/S

MANAGEMENT

- Surgery:
 - ✓ Fertility preserving surgery is possible
 - ✓ Unilateral salpingo-oophorectomy and surgical staging for young ladies, however total abdominal hysterectomy and bilateral salpingo-oophorectomy for older ones
- Chemotherapy:
 - ✓ No recommendation of chemotherapy
- Radiotherapy
 - ✓ Usually for recurrence only

OVARIAN CANCER DURING PREGNANCY

- Adnexal masses occurs in 0.2-2% during pregnancy and 5% are malignant
- Found in 1% of 20,000 deliveries, 75% are early stage. Most are unilateral and virilization sometimes occur

Relative frequencies by histologic types

Histologic types	Frequency (%)
EOC	40
Germ cell tumors	30
SCST	17
Others	13

Diagnosis

- ✓ First trimester is the best time
- ✓ Based on clinical and ultrasound

Management

- Surgery
 - ✓ The optimum time for surgery is 16-18 weeks of gestational age
 - ✓ Symptomatic, complex and solid ovarian tumors should be operated immediately
 - ✓ Never perform TAH & BSO on the basis of frozen section diagnosis, discuss options with the patient
 - ✓ If Malignant or metastatic treat as non-pregnant or one can omit hysterectomy Progesterone replacement if before 10 weeks of gestation and pregnancy to continue
- Adjuvant chemotherapy

Prognosis

- Pregnancy doesn't worsen ovarian cancer, 5 year survival rate is 72-90%

SAMPLE HISTORY

Chief complaint: Abdominal swelling of 8 month duration

HPI

This is a 59 years old nulliparous woman who has been amenorrheic for the past 7 years. She was relatively healthy till 8 month back at which time she started to experience abdominal swelling, w/c was initial in lower abdomen, but increase in size gradually to attain its current size within 5months. She also has lower abdominal pain for past 5mo w/c is non-radiating, intermittent and aching type, w/c has no any alleviating or exacerbating factors, the pain increase in severity recently and has been preventing her from doing her routine activities. Associated to this she has history of bloating, nausea, anorexia, early satiety, constipation, urinary frequency and urgency (11 times per day) and unquantified but significant weight loss of the same duration.

She started seeing her menses at age of 12, it used to come every 4wk and lasted 5 days, it did not show difference in amount month to month, and it was not associated with any lower abdominal discomfort. She stops seeing menses at age of 52. Her mother died of ovarian cancer 7 years back. She usually eat injera made of teff and shiro made ater with meat, she takes coffee 3x/day, and around 5 bottles of beer every weekend.

Otherwise she has no Hx of:

- ✓ Oral contraceptive use and Postmenopausal hormone therapy
- ✓ Gynecologic surgery and radiation to pelvic
- ✓ Talc exposure
- ✓ Breast mass
- ✓ Vaginal bleeding
- ✓ Yellowish discoloration of eyes and contact with yelloished discolored eye(chronic liver disease)

- ✓ Blood in stool(colonic cancer)
- ✓ Cough and SOB(plural effusion)
- ✓ Contact with chronicle coughing person(pelvic TB)
- ✓ Multiple sexual partner, vaginal discharge or itching sensation(PID, TOA)

Gynecologic history and Past obstetric history: add to HPI if any pertinent Hx.

Physical examination:

- Do full examination
- Refer the Approach to APM for characterization of findings in abdominal and pelvic examination

Assessment: APM secondary to r/o ovarian tumor

Investigation:

- CBC→
 - r/o anemia(of chronic disease), infection, thrombocytopenia (important for surgical patient)
- Blood group & Rh (for all surgical patients)
- Ultrasound:
 - it is used to determine size, location, consistency, number of mass and hydro ureter & hydro nephrosis
- RFT (BUN & Serum creatinine) and TFT(TSH, for surgical patient)
- CXR
 - for all surgical patients above 60yrs old
- ECG
 - for all surgical patients above
-

CHAPTER 11

GESTATIONAL TROPHOBLASTIC DISEASE

Gestational trophoblastic disease (GTD)

- Refers to a spectrum of interrelated but histologically distinct tumors originating from abnormal proliferation of trophoblast of the placenta.

Gestational trophoblastic neoplasia (GTN)

- Refers to the subset of GTD that develops malignant sequelae. These tumors require formal staging and typically respond favorably to chemotherapy.
- GTNs are among the rare human tumors that can be cured even in the presence of widespread dissemination.

EPIDEMIOLOGY AND RISK FACTORS

- Estimates of the incidence of GTD vary dramatically in different regions of the world.
 - For example, in Japan it is 2 per 1,000 pregnancies, which is about threefold higher than the incidence in Europe or North America (about 0.6 to 1.1 per 1,000 pregnancies) .
- This variation in incidence result from differences between reporting population-based versus hospital based data.
- In Ethiopia from various hospital based studies the magnitude is 1.8-3 per 1000 deliveries.
- From a thorough pathologic review, the incidence of partial mole is reported to be higher than complete mole which is:-
 - Complete mole- 1 per 1,945 deliveries
 - Partial mole- 1 per 695 deliveries

RISK FACTORS

- The main risk factors for hydatidiform mole are extremes of maternal age and a history of previous mole.
- Other risk factors include:-
 - **Prior molar pregnancy:** -10x increased risk after
 - After 1 → 1%,
 - After 2 → 23%
 - So for a women with prior history of molar pregnancy , ultrasound examination first trimester is a must
 - **Extreme maternal age (<15 and >35years):** -
 - 2x for > 35, 7.5X for > 40 years, 45 years -1% , 50 years – 17%.
 - B/C ova from older women may be more susceptible to abnormal fertilization.
 - This is much greater for complete mole than partial mole.
 - **Prior unsuccessful pregnancies:** -
 - spontaneous abortion => 2x increased risk of GTD
 - **Combination oral contraceptive pills use:** -
 - doubles the risk
 - **Blood type AB, A, and B impregnated by BG- O**
 - Those with blood group AB tend to have worse prognosis
 - **Vitamin A deficiency and low dietary intake of carotene**
 - are associated only with an increased risk of complete moles
 - **Higher educational levels, smoking,**
 - **Irregular menstrual cycles,**
 - **Obstetric histories in which only male infants are among the prior live births**
 - are linked with partial moles

CLASSIFICATION

Table 1

Modified WHO Classification of GTD

Molar pregnancies

Hydatidiform mole

Complete

Partial

Invasive mole

Trophoblastic tumors

Choriocarcinoma

Placental site trophoblastic tumor

Epithelioid trophoblastic tumor

PATHOGENESIS

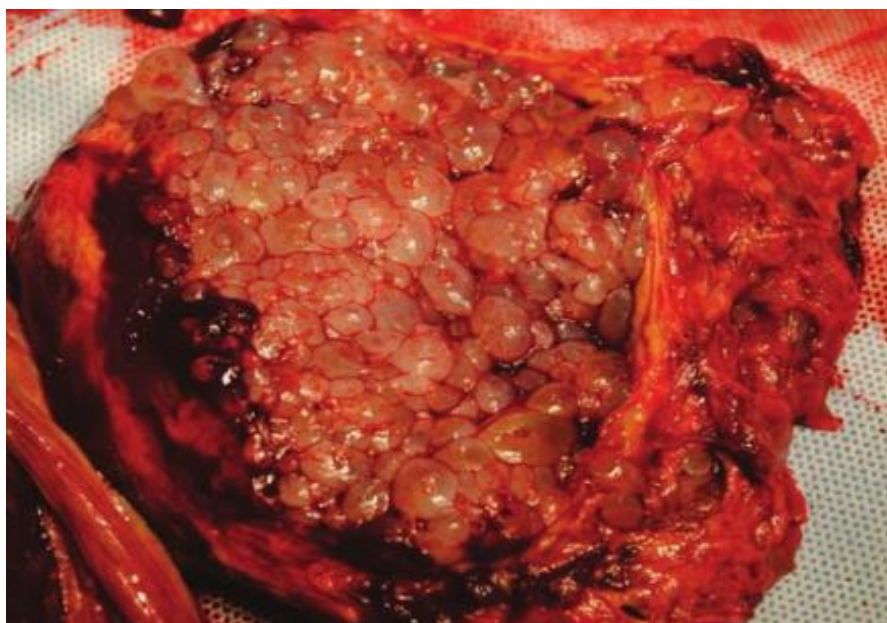
- Two forms moles exist: Complete and partial moles which are different in karyotype, in histologic features, and clinical presentation.

Cytogenetic studies demonstrate that:-

A complete mole:-

- Are usually euploid paternal in origin, and sex chromatin positive- 46 XX (90%) or 46 XY (10%)
- It develops when an empty ovum with an absent or inactivated nucleus is fertilized by a haploid sperm that duplicates its own chromosomes or by two haploid sperm

Although nuclear DNA is entirely paternal, mitochondrial DNA remains maternal in origin.



Photography of complete mole

A partial mole:-

- Is triploid-69 XXY (70%), 69 XXX (27%), or 69 XYY (3%).
- It arises when an ovum with active nucleus is fertilized by a duplicated or two haploid sperm.

Table 2 Comparison Between Complete And Partial Mole

Feature	Complete Mole	Partial Mole
Karyotype	46,XX or 46,XY	69,XXX or 69,XXY
Pathology		
Fetus/embryo	Absent	Present
Villous edema	Diffuse	Focal
Trophoblastic proliferation	Can be marked	Focal and minimal
p57Kip2 immunostaining	Negative	Positive
Clinical presentation		
Typical diagnosis	Molar gestation	Missed abortion
Postmolar malignant sequelae	15%	4–6%

CLINICAL FEATURES

- Patients with complete molar pregnancy are increasingly being diagnosed earlier in pregnancy and treated before they develop the classic clinical signs and symptoms.
- This may be because of changes in clinical practice, such as the frequent use of serum hCG measurement and vaginal US in early pregnancy in women with vaginal staining and even asymptomatic women.

Symptoms

- **Vaginal bleeding:**
 - The most common symptom causing patient to seek treatment in 97% previously, but currently 84 % of patients.
 - It results from separation of the molar villi from underlying decidua.
 - It usually is associated with passage of grape like vesicles.
- **Pelvic pressure or pain:**
 - due to enlarged uterus 28% or cystic ovaries
- **Nausea and vomiting:**
 - which is excessive and requires medical attention (HEG due to excessively elevated β -hCG), currently 8%
- **Chest pain and dyspnea:**
 - B/c of trophoblastic embolization in 2 % of patients (this is one of the feared fatal complication of GTD)
- **Heat and cold intolerance, palpitation, sweating:**
 - B/c of hyperthyroidism which was observed in 7% of patients with complete molar gestation as a result of thyrotrophic effect of hCG, currently rare

- **Headache, blurring of vision, ABM, and epigastric pain:**
 - early onset pre-eclampsia previously 27%, currently 1 in 74
- **Cramping lower abdominal pain:**
 - b/c of uterine contraction to evacuate its content
- **Absent fetal kick:**
 - **NB**, 100% of pregnant ladies feels fetal quickening by 24 weeks of gestational age, if not it needs to be evaluated

Signs

- Acute sick looking: bleeding, in respiratory distress, in pain
- Tachycardia, tachypnea, elevated BP (pre-eclampsia) or decreased BP (heavy bleeding)
- Pale conjunctiva, icteric sclera, dry tongue and buccal mucosa
- Thyroid swelling
- IC/SC retraction, crackles, decreased air entry
- Active precordium, S-3 gallop, systolic murmur- high output heart failure 2ndry to anemia
- Soft abdomen (duffy abdomen), no palpable fetal parts, uterine size greater than gestational age (positive discrepancy by > 2 weeks), negative fetal heart sound.
- Adnexal mass
- Warm moist skin, tremor

Patients with **partial hydatidiform** mole usually do not have the dramatic clinical features characteristic of complete molar pregnancy.

In general, these patients have the signs and symptoms of incomplete or missed abortion, and partial mole can be diagnosed after histologic review of the tissue obtained by curettage.

NATURAL HISTORY OF GTD

Complete mole

- Complete moles have a potential for local invasion and dissemination.
 - After molar evacuation, local uterine invasion occurs in 15% of patients, and metastasis occurs in 4%.
- Risk factors for developing post molar tumor are:
 - hCG level >.100,000 mIU/mL
 - Excessive uterine enlargement > 14 weeks
 - Theca lutein cysts 6 cm in diameter
- Older patients are also at increased risk of developing postmolar GTT
- Persistent tumor, usually nonmetastatic, develops in approximately 2% to 4% of patients with a partial mole, and chemotherapy is required to achieve remission

COMPLICATIONS

- **Hyper emesis gravidarum (HEG):** in 8% of patients
- **Pre-eclampsia before 20 weeks of GA:**
 - it was observed in 27% of patients with a complete hydatidiform mole
- **Hyperthyroidism:** in 7% of patients with a complete molar gestation.
 - Anesthesia or surgery may precipitate thyroid storm.
 - Thus, if hyperthyroidism is suspected before the induction of anesthesia for molar evacuation, β -adrenergic blocking agents should be administered.
 - Thyroid storm may be manifested by hyperthermia, delirium, convulsions, tachyarrhythmia, high-output heart failure, or cardiovascular collapse.

➤ **Theca leutin cyst:**

- Prominent theca lutein ovarian cysts (6 cm in diameter) develop in about one half of patients with a complete mole.
- After molar evacuation, theca lutein cysts normally regress spontaneously within 2 to 4 months. If it is bilateral it is sign of poor prognosis.

➤ **Anemia:** Because of heavy bleeding. Currently in 5%

➤ **Trophoblastic embolization:** in 2% of patients

➤ **Local invasion and dissemination**

INVESTIGATION

1. Pelvic Ultrasonography:-

- Ultrasonography is a reliable and sensitive technique for the diagnosis of complete molar pregnancy. Its sensitivity is 70 to 90 %

Sonographic features suggestive of a complete mole include:

- Absence of an embryo or fetus
- Absence of amniotic fluid
- Central heterogeneous mass with numerous discrete anechoic spaces- this has classically been described as a “**snowstorm or swiss chess pattern**”
- Ovarian theca lutein cysts

Sonographic features suggestive of a partial mole include

- Placenta with one or more abnormal findings: enlarged, cystic spaces and increased echogenicity of chorionic villi
- Increased transverse diameter of gestational sac- due to embryopathy of tripoidy
- Amniotic fluid is present, but the volume is reduced
- Theca lutein cysts are usually absent

On ultrasound a partial mole is diagnosed as missed or incomplete abortion in 15 to 60 % of cases

2. CBC: Anemia

3. hCG:

- Sometimes urine hCG is negative because of excessively elevated hCG level.
 - This is because of both the capture and tracer antibodies used in immunoradiometric assays become saturated, preventing the binding of the two to create sandwich.
 - So after we have collected urine specimen we have to dilute it with normal saline in 1 to 9 ratio.
- This false negative test is called **hook effect**.
- The minimum hCG level for a positive test
 - **For Urine pregnancy test**
 - ✓ Qualitative test: 20 to 50 milli-int. units/mL, depending on test
 - **Serum pregnancy test**
 - ✓ Qualitative test: 5 to 10 milli-int. units/mL, depending on test
 - ✓ Quantitative test: 1 to 2 milli-int. units/mL for an ultrasensitive test

▪ Causes for false positive and false negative urine hCG test

Causes of a false-negative test	1. Performed too soon after conception; hCG concentration is below threshold for a positive test 2. The hCG isoform measured is different from the hCG isoform in the sample (pertains mostly to urine tests) 3. Hook effect due to extremely high hCG concentration (>500,000 milli-int. units/mL, these levels are most commonly seen in gestational trophoblastic neoplasia)
Causes of a false-positive test	1. Recent first-trimester pregnancy loss (induced or spontaneous) in which hCG levels, though declining, are still elevated 2. Pregnancy loss very soon after implantation ("biochemical pregnancy") 3. hCG secretion from a tumor 4. Pituitary hCG secretion 5. Interference from human antibodies against animal antibodies or heterophilic antibodies (serum test positive but urine hCG will be negative) 6. Patient has received a medication containing hCG or certain antibodies

hCG: human chorionic gonadotropin.

4. Blood group and Rh

5. Chest x-ray for those with pulmonary symptoms

6. Histopathologic examination: Two specimens

- One specimen from the content of the uterus, to confirm GTD and determine whether it is complete or partial mole
- Another specimen from the uterine wall to know whether it is invasive or not.

7. Metastatic workup: RFT, LFT, TSH, serum electrolyte, chest X-ray, CT/MRI

TREATMENT OF BENIGN GTD

After the patient's condition has been stabilized, a decision must be made concerning the most appropriate method.

➤ Suction Curettage

- Preferred method for who desire fertility & involves the following steps:
- Oxytocin infusion be setup / made ready before induction of anesthesia.
- Cervical dilatation
- Suction curettage/electrical is preferred.

For uterine size < 14 weeks, it is better to put one hand on fundus and massage the uterus.

➤ Sharp Curettage

- To remove any residual molar tissue
- Send it separately for histopathology.

➤ Anti-D immune globulin

- for Rh negative give at the time of evacuation

➤ Prophylactic Chemotherapy

- For high-risk is recommended (one of the following required):
 - hCG level >100,000 mIU/mL
 - Excessive uterine enlargement (> 14-16 weeks)
 - Theca lutein cysts ≥ 6 cm in diameter
 - Poor compliance for follow up.

➤ Hysterectomy

- For patients who doesn't need their fertility. Need follow-up like other patients.
- Benefits of hysterectomy for GTD patients
 - No risk of postmolar malignancy
 - No risk of endometrial cancer

Follow-up

- Patient needs follow up by β -hCG weekly until levels are normal for three consecutive weeks, then monthly until normal for 6 months because there is risk of postmolar malignancy.
- Effective contraception during the entire follow-up is mandatory.
 - Because of the potential risk of uterine perforation, intrauterine devices should not be inserted until the patient achieves a normal hCG level.
 - Estrogen-progestin contraceptives are preferred because of their lower failure rate and relatively low incidence of irregular bleeding, since this symptom may raise concern about recurrence.
- When follow-up is difficult as per protocol:
 - Patient can be appointed at 3 months (average time when hCG expected to be normal).
- Counsel patient on symptoms of persistence

GESTATIONAL TROPHOBLASTIC NEOPLASIA

- This term primarily encompasses pathologic entities that are characterized by aggressive invasion of the endometrium and myometrium by trophoblast cells.

Histologic categories include

- **Common tumors:** the invasive mole and gestational choriocarcinoma
- **Rare tumors** placental-site trophoblastic tumor and epithelioid trophoblastic tumor
- Most cases follow a hydatidiform mole. Rarely, GTN develops after a term a live birth, miscarriage, or termination.

Non metastatic Disease

- Locally invasive GTT develops in about 15% of patients after evacuation of a complete mole and infrequently after other gestations.
- These patients usually present with the following symptoms:
 - Irregular vaginal bleeding
 - Theca lutein cysts
 - Uterine subinvolution or asymmetric enlargement
 - Persistently elevated serum hCG levels.
- The trophoblastic tumor may perforate the myometrium, causing intraperitoneal bleeding, or erode into uterine vessels, causing vaginal hemorrhage.
- Bulky, necrotic tumor may involve the uterine wall and serve as a nidus for infection. Patients with uterine sepsis may have a purulent vaginal discharge and acute pelvic pain.

- After molar evacuation, persistent GTT may exhibit the histologic features of either hydatidiform mole or choriocarcinoma.
- After a nonmolar pregnancy, however, persistent GTT always has the histologic pattern of choriocarcinoma.
 - Histologically, choriocarcinoma is characterized by sheets of anaplastic syncytiotrophoblast and cytotrophoblast without chorionic villi.

Placental-site Trophoblastic Tumor

- Placental-site trophoblastic tumor is an uncommon but important variant of choriocarcinoma that consists predominantly of intermediate trophoblast.
- Relative to their mass, these tumors produce small amounts of hCG and human placental lactogen (hPL), and they tend to remain confined to the uterus, metastasizing late in their course.
- In contrast to other trophoblastic tumors, placental-site tumors are relatively insensitive to chemotherapy.

Metastatic disease

- Metastatic GTT occurs in about 4% of patients after evacuation of a complete mole, but it is seen more often when GTT develops after nonmolar pregnancies.
- Metastasis is usually associated with choriocarcinoma, which has a tendency toward early vascular invasion with widespread dissemination.
- Because trophoblastic tumors often are perfused by fragile vessels, they are frequently hemorrhagic.
- Symptoms of metastases may result from spontaneous bleeding at metastatic foci.

- The most common sites of metastases are lung (80%), vagina (30%), pelvis (20%), liver (10%), and brain (10%).

Pulmonary

- At the time of diagnosis, lung involvement is visible by chest radiography in 80% of patients with metastatic GTT.
- Patients with pulmonary metastasis may have chest pain, cough, hemoptysis, dyspnea, or an asymptomatic lesion visible by chest radiography.

GTT may produce four principal pulmonary patterns:

- An alveolar or “snowstorm” pattern
 - Discrete rounded densities: cannon ball appearance
 - Pleural effusion
 - An embolic pattern caused by pulmonary arterial occlusion
- Because respiratory symptoms and radiographic findings may be dramatic, the patient may be thought to have a primary pulmonary disease.
 - Pulmonary hypertension may develop in patients with GTT secondary to pulmonary arterial occlusion by trophoblastic emboli.
 - The development of early respiratory failure requiring intubation is associated with a poor clinical outcome.

Vaginal

- Vaginal metastases occur in 30% of the patients with metastatic tumor. These lesions are usually highly vascular and may bleed vigorously when biopsied.

Hepatic

- Liver metastases occur in 10% of patients with disseminated trophoblastic tumor.
- Hepatic involvement is encountered almost exclusively when there is a protracted delay in diagnosis and the patient has an extensive tumor burden.
- Epigastric or right upper quadrant pain may develop if metastases stretch the hepatic capsule.
- Hepatic lesions may be hemorrhagic, causing hepatic rupture and exsanguinating intraperitoneal bleeding.

Central Nervous System

- Metastatic trophoblastic disease involves the brain in 10% of patients.
- Cerebral involvement is generally seen in patients with advanced disease;
 - Virtually all patients with brain metastasis have concurrent pulmonary or vaginal involvement or both.
- Because cerebral lesions may hemorrhage spontaneously, patients may develop acute focal neurologic deficits.

DIAGNOSTIC EVALUATION

- All patients with persistent GTT should undergo a careful pretreatment evaluation, including the following:
 - Measurement of the serum hCG value.
 - Hepatic, thyroid, and renal function tests
 - Determination of baseline peripheral white blood cell and platelet count

FIGO Criteria for Gestational Trophoblastic Neoplasia Diagnosis

β -hCG level plateau persists in four measurements during a period of 3 weeks or longer (days 1, 7, 14, and 21)

β -hCG level rise in 3 weekly consecutive measurements or longer, over a period of 2 weeks or more (days 1, 7, and 14)

β -hCG level remains elevated for 6 months or more

Histologic diagnosis of choriocarcinoma

➤ **The metastatic workup should include the following:**

- Chest radiograph or computed tomography (CT) scans
 - Ultrasonography or CT scan of the abdomen and pelvic CT
 - Magnetic resonance imaging (MRI) scans of the head
- In patients with choriocarcinoma or metastatic disease, hCG levels may be measured in the cerebrospinal fluid (CSF) to exclude cerebral involvement if the results of CT scanning of the brain are normal.
- The ratio of plasma-to-CSF hCG tends to be lower than 60 in the presence of cerebral metastases.

STAGING

- An anatomic staging system for GTT has been adopted by the International Federation of Gynecology and Obstetrics

Stage I: Patients have persistently elevated hCG levels and tumor confined to the uterine corpus.

Stage II: Patients have metastases to the vagina and pelvis both.

Stage III: Patients have pulmonary metastases with or without uterine, vaginal, or pelvic involvement.

Stage IV: Patients have advanced disease and involvement of the brain, liver, kidneys, or gastrointestinal tract. These patients are in the highest risk category because they are most likely to be resistant to chemotherapy.

MANAGEMENT

Depends on:

- WHO's PSI
- Disease stage
- Previous chemotherapy

Modified WHO Prognostic Scoring System as Adapted by FIGO

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

- When the prognostic score is higher than 7, the patient is categorized as high risk and requires intensive combination chemotherapy to achieve remission.
- Malignant GTD is curable in 85 – 100% as they are Chemo sensitive.

Risk stratification: Approximately 80% are low risk group

Low risk	High risk
Stage I and low risk stage II & III	Stage IV & high risk stage II & III
Needs single agent chemoRx	Combination chemoRx

Low risk

- ***Hysterectomy plus single agent chemotherapy:*** If no need of fertility
- ***Chemotherapy alone***
 - Commonly used agents → Methotrexate (M), Actinomycin-D (A)
 - Alternatives → Etoposide (E) & 5-Flourouracil (5-FU).
- ***Refractory to single agent chemotherapy***
 - MAC regimen:
 - MTX (methotrexate) 1mg/kg/d IM on day 1,3,5,7 & leucovorin 0.1mg/kg/d IM on day 2,4,6,8.
 - Actinomycin 12mcg/kg/d IV for 5 ds. Cyclophosphamide 3mg/kg/d for 5 ds Cycles repeated Q 21ds. If resistant to this regimen EMA/CO used.

High risk: stage II, III & stage IV

- EMA/CO - preferred initial regimen.
 - Etoposide 100mg/m² iv/30' on day 1&2.
 - MTX 100mg/m² IV push followed by 200mg/m² iv/12hrs on day 1.
 - Acatinomycin 0.5 mg IV bolus on day 1&2.
 - Leucovorin 15 mg Q 12hrs for 4-doses
 - Cyclophosphamide 600mg IV on day 8.
 - Oncovin 1mg/m² IV on day 8.

- Repeated every 2wks until remission (normal serum hCG over 3 consecutive wks & negative radiographic evident disease). Complete remission rate 78%.

Other regimens:

- EMA as effective as EMA/CO
- EMA/EP: given if relapse occur after EMA/CO and if refractory to MAC or EMA.
- PVB/PEB: if resistant to EMA/CO or EMA/EP and it is less toxic than EMA/EP

In patient with metastatic disease Hysterectomy may be required:-

- ✎ To control uterine hemorrhage and sepsis
- ✎ To reduce the trophoblastic tumor burden and there by limit the need for multiple course s of chemotherapy

Duration of therapy

- After normal hCG levels are attained, at least two additional courses of chemotherapy are administered to reduce the risk of relapse.

Monitoring during & after chemotherapy

- Stage I-III
 - Weekly serum hCG until 3- consecutive normal, monthly until 12 consecutive normal.
- Stage IV:
 - Weekly serum hCG until 3 consecutive normal, monthly until normal for consecutive 24 months.
- CBC, organ function tests based on clinical condition of the patient, U/S, chest X-ray, Serum electrolytes are done

Effective contraception should be used during serum hCG follow-up

SAMPLE HISTORY

ID: 42 years old

C/C: Vaginal bleeding of 2 days duration

HPI:

This is a gravida 4 para III (all alive and males) mother whose LNMP was 25/04/11 E.C which makes her EDD on 29/01/11E.C, and gestational age 25 weeks. The cycle was regular coming every 4 weeks and she has never used contraception for 8 month before her LMNP. She suspected she was pregnant after she missed one menstrual cycle. Then diagnosis of pregnancy was confirmed by urine pregnancy test. She has one ANC contact at local health center. It was on 5th month of amenorrhea. Detailed history was taken and general physical examination and laboratory tests were done. She gave blood and urine sample. She was given TT vaccination and she was told everything was normal and that she should continue her follow up every 4 weeks.

She doesn't felt any fetal quickening still now.

Currently she is presented with vaginal bleeding of 2 days duration which is associated with passage of grape like vesicles. The bleeding is bright red and non-clotting. It soaked 2-3 pads completely per day and her underwear is also soaked. But not associated with coitus or deep washing. In association to this she is also complaining cramp lower abdominal pain which does not radiate to another site and no aggravating or relieving factors noticed by the patient. The pain is severe enough to prevent her from her daily activities. She also complains rapid and excessive enlargement of her abdomen compared to her prior pregnancies. She has also history of excessive sweating which wets her night clothes and palpitation of the same duration. She complains tinnitus and vertigo of 1 day's duration. For all this complaint she was taken to local health center where they referred her directly to our hospital for better investigation and treatment.

Otherwise

- She has no cough chest pain or shortness of breath
- She has no excessive form of nausea and vomiting than her prior pregnancy
- She has no history of headache, vision disturbances,
- She has no history of epigastric pain or yellowish discoloration of skin.
- She has no history of abnormal body movement or loss of consciousness
- She has no history of smoking, menstrual irregularities.
- She has no previous history of similar complaint
- She has no history vaginal discharge or fever.
- She has no history of trauma to abdomen and genital area
- She has no history of bleeding from other sites
- She has no history of river water contact
- Her serostatus for RVI is negative
- She has completed her family size

She eat 4 meals per day (injera, fruits, meat, vegetables and cereals)as the pre pregnancy time. The pregnancy was unplanned, but wanted and supported.

Ass't: R/o GTD + completed family size

NB: mentioning the completeness of the family size is important for the management purposes, for example, if she has completed her family size hysterectomy is the best treatment option.

DDX for GTD includes

- Abortion (incomplete, missed)
- Cervicitis
- Cervical cancer
- Ectopic pregnancy
- Vaginitis
- Trauma
- Ectropion

CHAPTER 12

CERVICAL NEOPLASIA

CERVICAL INTRAEPITHELIAL NEOPLASM

CIN, formerly called *dysplasia*, means disordered growth and development of the epithelial lining of the cervix

Classification of CIN

- Based on degree of dysplasia CIN is classified in to four:-
 - **CIN I** (Mild dysplasia), is defined as disordered growth of the lower third of the epithelial lining.
 - **CIN II** (moderate dysplasia), abnormal maturation of the lower two-thirds of the epithelial lining
 - **CIN III** (Severe dysplasia), encompasses more than two thirds of the epithelial thickness.
 - **Carcinoma in situ (CIS)** representing full-thickness dysmaturity.
- According to the Bethesda system which based on cytologic smear, it is classified in to:-
 - Atypical Squamous cells of Undetermined Significance (ASCUS)
 - Atypical Squamous cells where high-grade lesions must be excluded (ASC-H).
 - Low-grade squamous intraepithelial lesion (LSIL) encompasses cytologic changes consistent with koilocytic atypia or CIN I
 - High-grade squamous intraepithelial lesion (HSIL) denotes the cytologic findings corresponding to CIN II and CIN III

Risk factors of CIN

- Similar with risk factor of cervical Ca (see below)

CIN and Human papilloma Virus (HPV)

- Analyses of cervical neoplasia lesions show the presence of HPV in more than *80% of all CIN* lesions and in *99.7% of all invasive cervical cancers*.
 - Based on their malignant potential, HPV subtypes are categorized into
 - **Low-risk** (HPV types 6, 11, 42, 43, and 44) are associated with condylomata accuminata and low-grade lesions (CIN I) and;
 - **High-risk** (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) are associated with invasive cancer in addition to CIN II and CIN III.
- The 2 most common high-risk HPV types are HPV-16, and HPV-18.
- Once the epithelium is acutely infected with HPV, 1 of 3 clinical scenarios ensues:
 - 1) Asymptomatic latent infection
 - 2) Active infection in which HPV undergoes vegetative replication but not integration into the genome (eg, leading to condyloma or CIN I).
 - 3) Neoplastic transformation following integration of oncogenic HPV DNA into the human genome

Outcomes of HPV infection:

- Resolution in more than 90% of immunocompetent women spontaneously over a 2-year period.
- Only approximately 5% will have cytologically detectable CIN.

This suggests that infection with HPV alone is insufficient for the development of CIN or cervical cancer and underscores the importance of other cofactors, such as cigarette smoking or immunosuppression

Diagnosis

- There are usually no symptoms or signs of CIN, and the diagnosis is most often based on biopsy findings following an abnormal routine cervical cytology smear.
- On cytologic examination, the dysplastic cell is characterized by:-
 - Anaplasia, an increased nuclear-to-cytoplasmic ratio (ie, the nucleus is larger),
 - Hyperchromatism with changes in the nuclear chromatin
 - Multinucleation, and abnormalities in differentiation.

Screening for CIN & Cervical Cancer

It is critical that women, whether vaccinated for HPV or not, follow current cervical cancer screening guidelines.

The screening modalities include:-

➤ Cervical cytology screening (Pap smears)

- The *American Cancer Society (ACS) updated recommendations* of 2002 states that screening with conventional Pap testing should occur every year. If liquid-based cytology is being used, screening can be extended to every 2 years
- Screening **begins** at age 21; or within 3 years of the onset of sexual activity
- Recommended every 3 years for women 21–29 years of age.
- Women age 30 or older should be screened with cytology and HPV co-testing every 5 years or cytology alone every 3 years.
- Screening should be **discontinued** in women older than 65 years with negative consecutive screening in the preceding 10 years.

- Cytology testing should be discontinued in women who have had a total hysterectomy and do not have a prior history of CIN 2/3 or worse
- **Screening in special circumstances**
 - Women who are HIV positive should be screened twice in the first year after diagnosis and annually thereafter.(Based on 2009 ACOG guidelines,)
 - Immunosuppressed women(other than those with HIV) or those who had in utero DES exposure should be screened annually.
- If both (cytology and HPV co-testing) results are negative, combined screening should not be repeated for 5 years.
- If cytology and HPV testing are positive, triaging to colposcopy is as outlined earlier.
- If cytology is normal, but HPV test is positive, repeat cytology and HPV testing in 6–12 months is recommended.

➤ **Repeat cervical cytology,**

- The cervical cytology smear should be repeated every 6 months until there are 2 consecutive normal smears

➤ **HPV testing**

- Primary screening modality in combination with cervical smear testing or alone.
- HPV testing as primary screening modality should be used only for women >30 years
- Two types of HPV tests are available for the screening
 - Hybrid capture 2
 - Cervista HPV HR test, also referred as “cervista HPV 16 &18” or HPV genotyping identifies 14 high risk serotypes.
- Positive test implies significant high risk of development of CIN 3 or cervical cancer.

➤ **Visual Inspection with Acetic Acid (VIA)**

- Also called cervicoscopy, consists of naked-eye visualization of the uterine cervix after the application of 3% to 5% acetic acid then cervix is illuminated with a light source.
- Acetic acid dehydrates cells so that squamous cells with relatively large or dense nuclei (eg. metaplastic cells, dysplastic cells, cells infected with HPV) reflect light and therefore appear white.
- Blood vessels and columnar cells are not affected by acetic acid, but become easier to visualize against the white background

➤ **Visual Inspection with Lugol Iodine Schiller test.**

- Lugol's solution is an aqueous iodine preparation.
- Normal mature squamous epithelium of the cervix contains glycogen, which combines with iodine to produce a *deep mahogany-brown color*.
- **Non staining**, therefore, indicates abnormal squamous (or columnar) epithelium or immature metaplastic epithelium, and constitutes a positive Schiller test.

➤ **Colposcopic examination.**

- The colposcope is an instrument that uses illuminated low-power magnification (5–15×) to inspect the cervix.
- After the application of 3–5% **aqueous acetic acid** solution abnormalities in the appearance of the epithelium and its capillary blood supply can be identified by colposcopy

Indications for colposcopy are:

1. Abnormal cervical cytology smear or HPV testing;
2. Clinically abnormal or suspicious-looking cervix;
3. Unexplained intermenstrual or post coital bleeding;
4. Vulvar or vaginal neoplasia; or
5. History of in utero DES exposure

Normal finding from colposcopy

- **The original squamous epithelium**, which extends from the mucocutaneous vulvovaginal junction to the original squamocolumnar junction.
- **The columnar epithelium of the endocervical canal**
- **The transformation zone**
 - The original SCJ is the junction between the stratified squamous epithelium of the vagina and ectocervix, and the columnar epithelium of the endocervical canal.
 - In 2/3 of female infants, this original SCJ is located on the ectocervix, in close to a 1/3 in the endocervical canal, and in a very small subset out in the vaginal fornices
 - During a woman's life cycle the squamocolumnar junction "migrates". Following menarche, the SCJ is generally found on the ectocervix, with further eversion during pregnancy. In the postmenopausal patient, the SCJ is frequently within the endocervical canal
 - If the new SCJ is visualized in its entirety, the colposcopic examination is called satisfactory; if it cannot be fully visualized, the examination is called unsatisfactory.

Abnormal findings indicative of dysplasia and CIN are those of:

- **Leukoplakia or hyperkeratosis**
 - An area of white, thickened epithelium that is appreciated prior to the application of acetic acid and may indicate underlying neoplasia.
- **Acetowhite epithelium**,
 - Which is epithelium that stains white after the application of acetic acid

- **Mosaicism or punctation**

- Reflecting abnormal vascular patterns of the surface capillaries.
- As general rule, capillary thickness and intercapillary distances correlate with the severity of the lesion and thus tend to be larger and coarser in higher -grade lesions.

- **Atypical vessels with bizarre capillaries**

- With so-called corkscrew, comma shaped, or spaghetti-like configurations suggest early stromal invasion.

➤ **Diagnostic conization**

- Indications:-
 - If colposcopy is unsatisfactory.
 - If the lesion extends into the cervical canal beyond the view afforded by the colposcope
 - If there is a significant discrepancy between the histologic and the cytologic examination,
 - If adenocarcinoma in situ is suspected,
 - If micro invasive carcinoma is suspected

PREVENTION

➤ **Behavioral**

- Sexual abstinence,
- delaying coitarche, and
- limiting the number of sexual partners are some of behavioral modification.
- Condoms do not cover all potentially HPV-infected anogenital skin. Therefore, condoms may not be completely protective.

➤ **HPV Vaccination**

- Advisory Committee on Immunization Practices (ACIP) recommends that all girls 11–12 years of age should be routinely offered HPV vaccination,

- As well as girls and women age 13–26 who have not yet been vaccinated
- They also recommend for boys too and vaccination is possible as early as 9 years. In case you got someone who want to be vaccinated after 15 still you can give 3 shots over six months.

The vaccines are:

- **Cervarix (HPV2)** is a bivalent vaccine against HPVs 16 and 18.
- **Gardasil (HPV4)** is a quadrivalent vaccine against HPV types 6, 11, 16, and 18.
- **Gardasil 9 (HPV9)**, a nonavalent vaccine, which protects against all HPV types in HPV4 plus types 31, 33, 45, 52, and 58.
- They are administered in three intramuscular doses during a 6-month period; the second dose is given 1 to 2 months after the first dose, and the third 6 months after the first dose.
- The recent CDC guideline recommend as only two dose (first dose-11-12 years, second dose after 6months of the first dose) is enough for those 9-15 years. If age is 15 and greater 3doses within six months is recommended.
- Vaccination can be given during lactation but is avoided during pregnancy.

Outcome of CIN

	CIN I	CIN II	CIN III
Regression to normal	60%	40%	30%
Persistence	30%	35%	48%
Progression to CIN III	10%	20%	-
Progression to cancer	<1%	5%	30-40%

CERVICAL CANCER

- Worldwide, cervical cancer is common, and it ranks fourth among all malignancies for women after breast, colorectal, and lung cancer (WHO 2012). From this developing countries contribute **85 percent**.
- Is the *second most common* cause of cancer-related morbidity and mortality among women in developing countries. The median age at diagnosis is **49 years**.

Risk factors

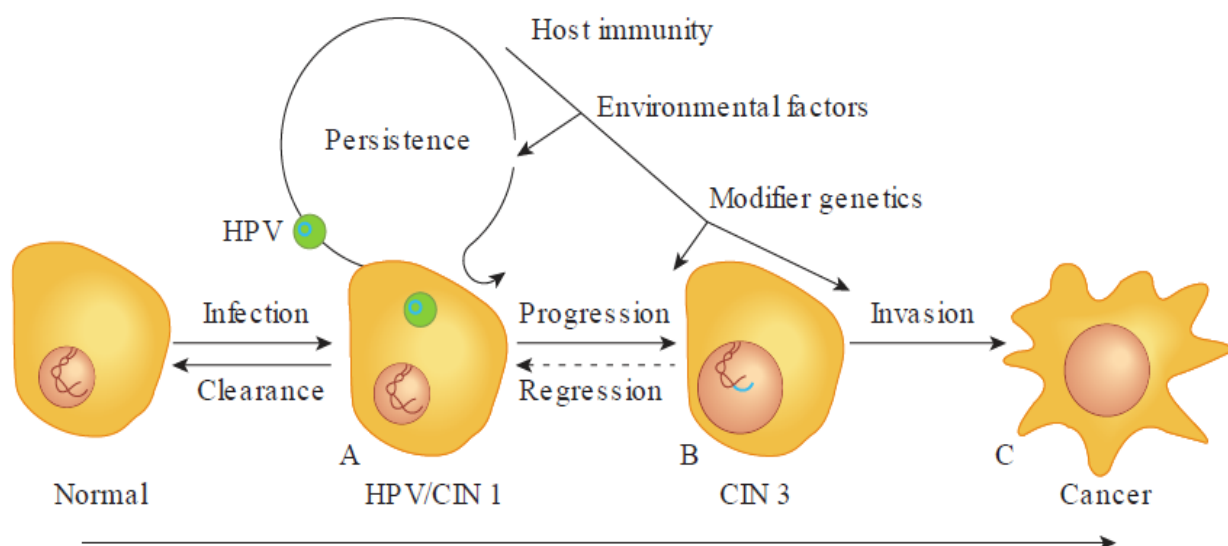
- **Cigarette smoking:**
 - Both active and passive smoking increases cervical cancer.
 - Among HPV-infected women, current and former smokers have a two- to threefold increased incidence
 - plausible explanations about how smoking might cause cervical cancer
 - One is that smoking inhibits the immune response to HPV.
 - second is that carcinogenic HPV-infected cells are exposed to smoking carcinogens that cause DNA damage while HPV oncoproteins block apoptosis and cell cycle arrest.
- **High parity:**
 - Those with one or two full term pregnancy have a twofold risk when compared with nulliparous.
 - If she had seven pregnancies fourfold risk.
- **Long-term combination oral contraceptive.**
 - Increase risk by four fold if she is HPV positive.
- **Young age at first intercourse (<20years)**

- **Multiple sexual partner.**
 - Having more than six lifetime sexual partners)
- **Immunosuppression.**
 - *Cervical cancer is one of AIDS defining illness*
- **Race:** black and Hispanic has highest incidence.

Tumor genesis

- In general, progression from dysplasia to invasive cancer requires several years, although times can vary widely.
- HPV is the primary etiologic agent associated with cervical cancer. HPV 16 is more commonly associated with squamous cell carcinoma of the cervix, whereas HPV 18 is a risk factor for cervical adenocarcinoma
- The E6 and E7 oncoproteins produced interfere with and accelerate degradation of p53 and pRb which are key tumor suppressor proteins produced by the host. This is central to host cell immortalization and transformation

Molecular pathways of cervical CA



Patterns of spread

- Direct invasion into the cervical stroma and local invasion
 - To urethra then blockage frequently develops, resulting in hydronephrosis,
 - The bladder may be invaded by direct tumor extension through the vesicouterine ligaments
 - The rectum is invaded less often because it is separated from cervix by the posterior cul-de-sac
- Lymphatic metastasis:
 - The cervix has a rich network of lymphatic's, which follow the course of the uterine artery
 - These channels drain principally into the paracervical and parametrial lymph nodes → obturator lymph nodes → the internal, external, common iliac lymph nodes, and ultimately the paraaortic lymph nodes.
 - Drainage from the posterior cervix course drains to the rectal lymph nodes.

Lymphovascular space involvement is when the tumor invades deeper into the stroma and enters blood capillaries and lymphatic channels.

Distant metastasis results from hematogenous dissemination, and the **lungs, ovaries, liver, and bone** are the most frequently affected.

Histologic types

- The two most common histologic subtypes of cervical cancer are **squamous cell** (70%) and **adenocarcinoma** (25%).
 - **Squamous cell subtypes:** Keratinizing, Non keratinizing and Papillary
 - **Adenocarcinoma subtypes:** Mucinous, Endometrioid, Serous, Clear cell and Mesonephric.
 - **Mixed cervical carcinoma**
 - **Neuroendocrine cervical tumor**
 - **Others:** Sarcoma, Lymphoma, Melanoma

Clinical manifestation

Symptoms

- Abnormal vaginal bleeding is the most common symptom and may take the form of a blood-stained leukorrheal discharge, scant spotting, or frank bleeding.
- A history of postcoital post douching bleeding may be elicited on specific questioning
- Pelvic pain, radiating to the hip or thigh, is a manifestation of advanced disease.
- Incontinence sign of fistula formation.
- Acute blood loss and anemia may occur in a bulky or ulcerating stage I lesion.

Physical Examination

- Most women with this cancer have normal general physical examination findings.
- With speculum examination lesions may be an exophytic or endophytic growth; a polypoid mass, papillary tissue, or barrel-shaped cervix; a cervical ulceration or granular mass; or necrotic tissue.
- A watery, purulent, or bloody discharge can also be seen

- During bimanual examination, enlarged uterus resulting from tumor invasion and growth. Alternatively, **hematometra or pyometra** may expand the endometrial cavity following obstruction.
- The size of the cervix and the tumor measured in cm (a normal cervix is 4×5 cm in size)
- Extend into the vagina, and disease extent can be appreciated during anterior vaginal wall palpation or during rectovaginal examination.
- During digital rectal examination, parametrial, uterosacral, and pelvic sidewall involvement can be appreciated.
- Involved tissues feel thick irregular, firm, and less mobile
- A fixed mass indicates that tumor has probably extended to the pelvic sidewalls.
- With advancing disease, enlarged supraclavicular or inguinal lymphadenopathy suggest lymphatic tumor spread
- Lower extremity edema and low back pain, often radiating down the posterior leg, may, reflect compression of the sciatic nerve root, lymphatics, or veins.

Investigations

- When obvious tumor growth is present, a cervical biopsy is usually sufficient for diagnosis.
- If gross disease is not present, a colposcopic examination with cervical biopsies and endocervical curettage is warranted
- If the diagnosis cannot be established conclusively with colposcopy and directed biopsies, cervical conization may be necessary.

Investigations/procedures Used During Cervical Cancer Evaluation

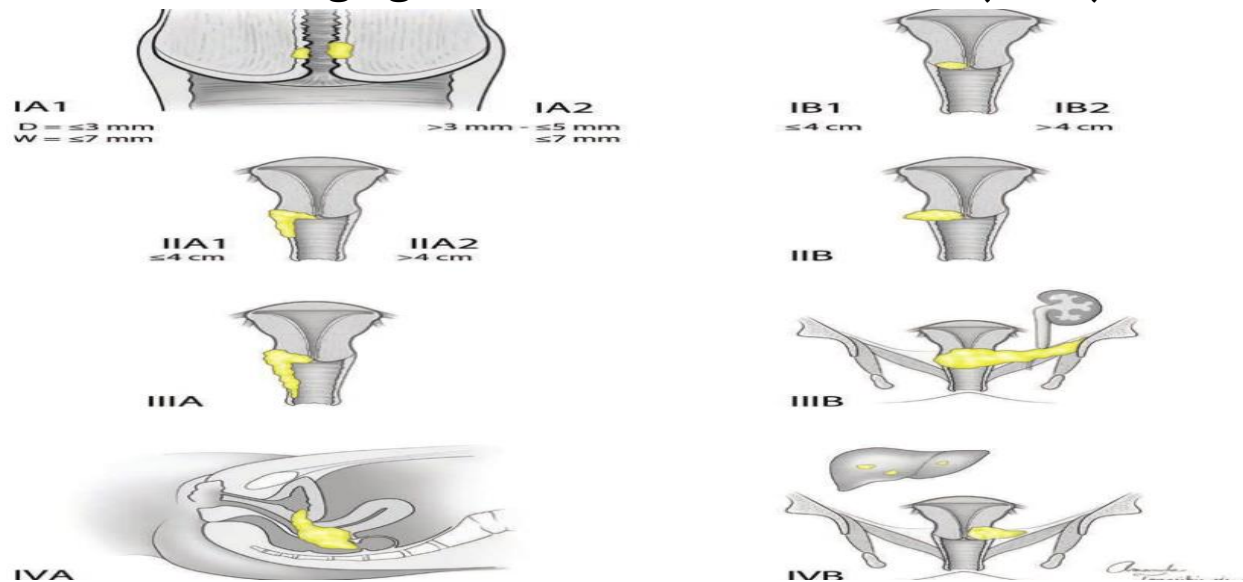
	Investigations	To Identify:
Laboratory	CBC	Anemia
	Urinalysis	Hematuria
	Chemistry profile	Electrolyte abnormality
	Liver function	Liver metastasis
	Creatinine/BUN	Renal impairment or obstruction
Radiologic	Chest radiograph	Lung metastasis
	Intravenous pyelogram	Hydronephrosis
	Nodal or CT scan(abdominopelvic)	distant organ metastasis
	MR imaging	Local parametrial invasion
Procedural	Cystoscopy	Bladder tumor invasion
	Proctoscopy	Rectal tumor invasion
	EUA	Extent of pelvic tumor spread

Staging

Cervical cancers are staged **clinically**.

- Allowable components of staging include
 - cold-knife conization,
 - pelvic examination under anesthesia,
 - cystoscopy,
 - proctoscopy,
 - chest radiograph, and intravenous pyelogram

FIGO staging of cancer of the cervix uteri (2018)



Stage	Characteristics
0	Carcinoma in situ, cervical intraepithelial lesion (CIN) 3
I	Carcinoma is strictly confined to cervix (extension to corpus should be disregarded)
IA	Microscopic lesion, invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm
IA1	Measured invasion of stroma no greater than 3 mm in depth and no wider than 7 mm
IA2	Measured invasion of stroma greater than 3 mm and no greater than 5 mm in depth and no wider than 7 mm
IB	Clinical lesions confined to the cervix or preclinical lesions greater than IA
IB1	Clinical lesions no greater than 4 cm in size
IB2	Clinical lesions greater than 4 cm in size
II	Carcinoma extends beyond cervix but has not extended to pelvic wall; it involves vagina, but not as far as the lower third
IIA	No obvious parametrial invasion
IIA1	Clinical lesions no greater than 4 cm in size
IIA2	Clinical lesions greater than 4 cm in size
IIB	Obvious parametrial involvement
III	Carcinoma has extended to the pelvic wall; on rectal examination there is no cancer-free space between tumor and pelvic wall; tumor involves lower third of vagina; all cases with hydronephrosis or nonfunctioning kidney should be included, unless they are known to be due to another cause
IIIA	No extension to pelvic wall, but involvement of lower third of vagina
IIIB	Extension to pelvic wall, or hydronephrosis or nonfunctioning kidney due to tumor
IV	Carcinoma has extended beyond true pelvis or has clinically involved mucosa of bladder or rectum
IVA	Spread of growth to adjacent pelvic organs
IVB	Spread to distant organs

General Treatment for Primary Invasive Cervical Carcinoma

Cancer Stage	Treatment
IA1	Simple hysterectomy preferred if childbearing completed or Cervical conization
IA1(with LVSI)	Modified radical hysterectomy and pelvic lymphadenectomyor Radical trachelectomy and pelvic lymphadenectomy for selected patients desiring fertility
IA2	Radical hysterectomy and pelvic lymphadenectomyor Radical trachelectomy and pelvic lymphadenectomy for selected patients desiring fertility
IB1c Some IB2 IIA1	Radical hysterectomy and pelvic lymphadenectomy or radical trachelectomy and pelvic lymphadenectomy for selected patients desiring fertility or Chemoradiation
Bulky IB2 IIA2	Chemoradiation
IIB to IVA	Chemoradiation Or Rarely, pelvic exenteration
IVB	Palliative chemotherapy and/or Palliative radiotherapy or Supportive care (hospice)

Sample history

Chief complaint: *vaginal bleeding of three month duration.*

HPI:

This is a 40years old Para 7(all lived) 0 abortion mother whose LMNP was two week back. She was relatively healthy three month back at which time she start to experience vaginal bleeding of which was initially bright red scanty bleeding and has relationship with her menses. The bleeding was exacerbated after sexual intercourse and post douching and has no known relieving factor.

She also experience watery discharge which increase in amount and sometimes become blood stained. She also has intermittent moderate dull aching lower abdominal pain for the last two month which radiate to her thigh and has no known relieving and exacerbating factor. She also has loss of appetite significant but unqualified weight loss vertigo and tinnitus since the last one month.

Her menses started when she was 13 years old and come every 24 days. It stays for 3-4 days she uses 2 pads for it. The bleeding was black and non clotting.

She was married when she was 16years old and she claimed to be virgin before her marriage.

She used OCP for the last four year after delivery of her last baby.

Other wise

She has no history of cigarettes smoking.

She has no history of foul smelling vaginal discharge, genital ulcer or treatment for STD

She has no history of multiple sexual partner.

She has no history of urinary incontinence, frequency, urgency or dysuria.

She has no history of cough shortness of breath chest pain or blood stained sputum.

She has no history of RUQ pain, yellowish discoloration of eye and bleeding from other site.

She has no history of bone pain or fracture.

She has no history of pelvic trauma.

Physical examination

G/A: *chronically sick looking, Look wasted and in pain*

Vital sing: *No vital sign derangement*

HEENT: *pale conjunctiva non icteric sclera.*

LGS: *no significant lymphadenopathy*

No respiratory and cardiac finding

Abdomen: *flat abdomen that moves with respiration, No scar
No distended vein.*

On palpation: there is no palpable mass and organomegaly

On percussion there is no sign of fluid collection

MSS: *no lower extremity edema.*

Genitourinary system: *no costovertebral angle tenderness. The kidneys are not palpable.*

Pelvic examination:

External genitalia examination: Inverted triangle type of pubic hair pattern. No discoloration of skin around vulva, no swelling, ulcer or discharge

Speculum examination: there is cervical ulceration and necrotic tissue are visible, Bloody discharge is also visible from cervix

Digital vaginal examination: there is irregular firm lesion on cervix which measures around 4 cm. cervix is mobile not attached to adjacent structure. No involvement of vagina.

Bimanual examination: the uterus is normal size and position

Digital rectal examination: no parametrial uteresacral and pelvic side wall involvement.

CHAPTER 13

ABORTION

DEFINITION AND TERMINOLOGY

Abortion is defined as the spontaneous or induced termination of pregnancy before fetal viability.

- Viability lies between the lines that separate abortion from preterm birth. It is defined by pregnancy duration and fetal weight for statistical and legal purpose.
 - Both CDC and WHO define abortion as pregnancy termination before 20weeks of gestation or with fetus born weighing <500g.
 - In Ethiopia and the UK the age of viability is 28weeks of gestation.
- The term *miscarriage* is usually for spontaneous abortion.
- The use of transvaginal sonography and precise measurement of serum hCG concentrations are used to identify extremely early pregnancies and makes it possible to distinguish between a chemical and a clinical pregnancy.
 - Abortion of such early pregnancies is termed as *early pregnancy loss or early pregnancy failure or wastage*.

INCIDENCE

- Although the true incidence of spontaneous abortion is unknown, approximately 15% of clinically evident pregnancies and up to 50% of chemically evident pregnancies end in spontaneous abortion.

CLASSIFICATION

Based on:-

- Mechanism/onset
 - Spontaneous (see further clinical classification below)
 - Induced
- Gestational age at onset
 - Early(<12wks) or first trimester
 - Late(>12wks) or midtrimester
- Place of abortion
 - Safe(health facility)
 - Unsafe abortion,
- Presence or absence of infection
 - Septic
 - Aseptic

SPONTANEOUS FIRST TRIMESTER ABORTION

- More than 80% of spontaneous abortion occurs within the 1st 12 weeks of gestation.

Pathogenesis

- In 1st trimester losses, death of the embryo or fetus nearly always precedes spontaneous expulsion which → hemorrhage in to the decidua basalis → necrosis of adjacent tissue that stimulate uterine contraction and expulsion. Thus the key to determining the cause of early miscarriage is to ascertain the cause of fetal death.
- In contradistinction, in later pregnancy losses, the fetus usually does not die before expulsion, and thus other explanations are sought.

Etiologies and Risk factors

Fetal factors

▪ Chromosomal abnormalities

Approximately half of first-trimester miscarriages are anembryonic, that is, with no identifiable embryonic elements.

The remaining (embryonic miscarriages), can be further grouped as either, those with normal chromosome (euploid abortions, in 45-55%) or those with chromosomal anomalies (aneuploid abortions)

Chromosomal abnormalities	Percentage
Aneuploidy	
Autosomal trisomy	22-32
Monosomy X (45,X)	5-20
Triploidy	6-8
Tetraploidy	2-4
Double or triple trisomy	0.7-2
Structural anomaly	2

Almost 95 percent of chromosomal abnormalities in aneuploid fetuses are caused by maternal gametogenesis errors. Chromosomal abnormality decrease with advancing GA (55%, 35%, & 5% in 1st, 2nd and 3rd trimester abortuses/stillbirth respectively).

Aneuploid Abortion

- 50% of embryonic abortions are aneuploid
- Monosomy X or Turner's syndrome is the single most common aneuploidy, comprising approximately 18% of these gestations.
- As a group, the autosomal trisomies account for more than half of aneuploid losses, with trisomy 13, 16, 18, 21, and 22 being the most common. Autosomal trisomies have been noted for every chromosome except chromosome number 1.

- Most trisomic pregnancies end in miscarriage. The exceptions are trisomy 21, 18, and 13, which have survival to birth rates of 22%, 5%, and 3%, respectively.
- Polyploidy, usually in the form of triploidy, is found in approximately 20% of all miscarriages. Polyploid conceptions typically result in an anembryonic gestation.(C)
- About 75% of aneuploid fetuses aborted before 8 week.

Chromosomal structural abnormalities infrequently cause abortion.

Maternal factors

- **Age:** the rate of clinical miscarriages is almost doubled when either parent is older than 40yrs. The incidence of euploid abortions increases dramatically after maternal age exceeds 35 yrs.
- **Infections:** systemic or local (GU) infections can cause pregnancy loss. Such infections include; Chlamydia trachomatis (in 4% of abortuses), Polymicrobial infections from periodontal disease, HIV and Bacterial vaginosis (2nd trimester)
- **Medical disorders:** like DM, thyroid disorders (especially severe iodine deficiency), celiac disease, inflammatory bowel disease and SLE
- **Uterine and cervical factors:** Congenital uterine anomalies, such as unicornuate, bicornuate, or septate uterus; asherman's syndrome and cervical insufficiency.
- **Medications and toxic factors:** IUDs, antineoplastic drugs, anesthetic gases, alcohol, nicotine, or cocaine, lead, ethylene oxide, and formaldehyde.
- **Radiotherapy:** exposure to >5rads of radiation in abdominopelvic radiotherapy may later be at increased risk for miscarriage.
- **Surgical procedures:** like early removal of the corpus luteum or the ovaries,

- **Trauma:** direct abdominal trauma, amniocentesis or chorionic villus sampling. Generally trauma seldom cause miscarriage
- **Nutrition:** both extremes of malnutrition (severe dietary deficiency and morbid obesity) are associated with miscarriage.
- **Social and behavioral factor:** substance abuse
- **Occupational factor:** exposure to toxic chemicals.

Paternal factors

- Chromosomal abnormalities in sperm and increasing paternal age had an increased abortion risk

Clinical classification of spontaneous abortion

▪ Threatened abortion

- The clinical diagnosis of threatened abortion is presumed when bloody vaginal discharge or bleeding appears thru a closed cervical Os during the 1st 28weeks. Bleeding is by far the most predictive risk factor for pregnancy loss.
- Approximately 25% of pregnancies experience 1st trimester bleeding. Bleeding must be differentiated from an implantation bleeding
- With miscarriage bleeding usually begins 1st and crampy lower abdominal pain follows hours to days later. The combination of bleeding and pain predicts a poor prognosis or pregnancy continuation.
- About 43% of these cases will subsequently miscarry. Even if miscarriage does not occur, these pregnancies are associated with high risk of late adverse maternal and perinatal outcomes.
- The primary goal in evaluating a woman with early pregnancy bleeding is prompt diagnosis of an ectopic pregnancy. Serial quantitative serum β -hCG levels, progesterone levels, and transvaginal sonography, alone

or in combination, can help ascertain if the fetus is alive and if it is within the uterus.

▪ **Inevitable abortion**

- Is characterized by bleeding with cervical dilation, often with back or abdominal pain
- gross rupture of the membranes along with cervical dilatation is nearly always followed by either uterine contractions or infection, which is inevitably followed by abortion
- the products of conception have not passed from the uterine cavity

▪ **Incomplete abortion**

- Incomplete abortion is defined as the passage of some but not all of the products of conception from the uterine cavity
- Before ten weeks of gestation, the placenta and fetus are generally passed together, but after this time, they are passed separately.
- Bleeding and cramping usually continue until all products of conception have been expelled
- There is dilation of the cervical Os

▪ **Complete abortion**

- All of the products of conception have passed from the uterine cavity and the cervix is closed.
- A history of heavy bleeding, cramping, and passage of tissue or a fetus is common

▪ **Missed abortion**

- Is defined as a pregnancy that has been retained within the uterus after embryonic or fetal demise.
- Cramping or bleeding may be present, but often there are no symptoms.

- The cervix is closed, and the products of conception remain in situ.
- It may be complicated by bleeding disorders and infection

▪ **Recurrent abortion**

- Is defined as 3 or more consecutive spontaneous abortions
- Approximately 1 percent of fertile couples have recurrent miscarriages; most of these are embryonic or early losses.
- The risk of spontaneous abortion is at least doubled in women experiencing recurrent pregnancy loss.
- Possible causes:
 - ✓ Parental chromosomal abnormalities
 - ✓ Immunologic factors (esp, antiphospholipid antibody syndrome)
 - ✓ Anatomic factors
 - bicornuate uterus, is the most common uterine anomaly (39%) and has 40-70% pregnancy loss rate
 - septate or unicornuate uterus, seen is 14-24% of uterine anomalies and has 34-88% pregnancy loss rate
 - uterine leiomyoma
 - ✓ Endocrinologic abnormalities
 - Progesterone deficiency caused by luteal phase defect (LPD), which is associated with inadequate endometrial development at implantation.
 - Thyroid disorders
 - ✓ Microbiologic (TORCH), and thrombophilic abnormalities. (See details on Current 11th ed).
 - ✓ NB. Approximately 50% have no definitive cause

- The prognosis after repeated losses is good, with most couples having an approximately 60% chance of a viable pregnancy.

▪ **Septic abortion**

- Usually occur in induced abortions that occur in an illegal setups, especially in developing countries.
- Infection usually begins as endometritis involving the endometrium and any retained products of conception.
- The 2 most common causes of septic abortion are retained products of conception and bacteria that have been introduced into the uterus via ascending infection.
- These patients present with fevers, chills, abdominal pain, vaginal bleeding, and malodorous vaginal discharge.
- Without treatment, endometritis may spread beyond the uterus, leading to peritonitis, bacteremia, and sepsis. Particularly worrisome are severe necrotizing infections and toxic shock syndrome caused by *S pyogenes*.

SPONTANEOUS MIDTRIMESTER ABORTION

- The timespan that defines a midtrimester fetal loss extends from the end of the first trimester until the fetus weighs ≥ 500 g or gestational age reaches 20 weeks (28weeks).
- Incidence and Etiology
 - Abortion becomes much less common by the end of the first trimester, overall, spontaneous loss in the second trimester is estimated at 1.5 to 3 percent, and after 16 weeks, it is only 1 percent.
 - First-trimester bleeding doubles the incidence of second-trimester loss
 - Risk factors for second-trimester abortion include race, ethnicity, prior poor obstetrical outcomes, and extremes of maternal age.

- Some causes include;
 - ✓ Fetal anomalies; Chromosomal or Structural
 - ✓ Uterine defects; Congenital, Leiomyomas and Incompetent cervix
 - ✓ Placental causes; Abruption, previa, Defective spiral artery transformation and Chorioamnionitis
 - ✓ Maternal disorders; Autoimmune, Infections and Metabolic

INDUCED ABORTION

- Is surgical or medical termination of a live fetus that has not reached viability
- It can be classified in to two, (1) indicated or therapeutic and (2) elective or voluntary.
- Indications:
 - Maternal health problems like:-
 - persistent cardiac decompensation
 - pulmonary arterial hypertension
 - advanced hypertensive vascular disease
 - diabetes with end-stage organ failure
 - malignancies
 - maternal mental illness
 - rape or incest
 - significant fetal anatomic, metabolic, or mental deformity
 - Age of woman less than 18 years
 - Extreme poverty

Complication of abortion

- Hemorrhage, shock, anemia
- Infection
- Intrauterine synechiae (Asherman's syndrome)
- Perforation of the uterus

- Injury to bowel and bladder
- Fistula formation
- Rh isoimmunization
- Tetanus
- Ectopic pregnancy in later life
- Renal failure
- Death
- Psychological trauma - depression

APPROACH

HISTORY

- Age
- LNMP, hx of amenorrhea and symptoms of pregnancy like morning sickness(nausea and vomiting)
- Vaginal bleeding, assess onset, consistency(any embryonic/fetal(solid) part
- Cramping(lower abdominal pain), assess onset in relation to vaginal bleeding
- Fever or chills, in case of septic abortion
- Risk factors
- Symptoms of anemia
- Sexual assault hx, in case of induce abortion
- **DDx**
 - ✓ ectopic pregnancy in intact tube
 - ✓ cervical polyps
 - ✓ vaginitis
 - ✓ cervical carcinoma
 - ✓ gestational trophoblastic disease
 - ✓ trauma
 - ✓ foreign body

PHYSICAL EXAMINATION

- **G/A:** well looking, distress or lethargic (from severe anemia or septic shock)
- **V/S:**
 - ✓ Tachycardia, tachypnea or hypotensive (from blood loss)
 - ✓ Febrile, in case of septic abortion
- **HEENT:** pale conjunctiva?
- **Abdominal examination:**
 - ✓ Inspect the skin changes associated with pregnancy
 - ✓ Severe unilateral tenderness in lower abdomen may indicate ectopic pregnancy
 - ✓ Determine uterine size: especially in case of midtrimester it is important to determine size of the uterus, if it is less than the appropriately determined GA, it may indicate incomplete or complete loss of product of conception
 - ✓ Listen to FHT
- **Pelvic examination**
 - ✓ See if there is ongoing blood loss, or passage of amniotic fluid
 - ✓ Check the cervix (open or closed)

INVESTIGATIONS

- **CBC:** anemia? Or infection?
- **Blood type and Rh**
- **Serial serum β -hCG:**
 - Falling or abnormally rising serum levels of β -hCG are diagnostic of an abnormal pregnancy, either a failed intrauterine gestation or an ectopic pregnancy.
- **Ultrasound:**
 - ✓ Transvaginal ultrasound allows us to visualize gestational sac (GS) as early as 4–5 weeks of gestation.
 - ✓ At 5–6 weeks' gestation, a yolk sac will be present. In general, a GS with a mean sac diameter (MSD) of ≥ 8 mm should contain a yolk sac. Similarly, a GS with an MSD of > 16 mm should also contain an embryo.

- ✓ Pregnancies with a large GS and no embryo are typically anembryonic gestations and are managed in a similar manner as a missed abortion
- ✓ Fetal heart motion is expected in embryos with a crown to rump length of >5 mm or at 6–7 weeks' gestation.
- ✓ If a repeat ultrasound in 1 week does not show embryonic cardiac activity, the diagnosis of embryonic demise is made.
- **Urinalysis: to identify cause**
- **Endocervical cultures**
- **Blood cultures: in septic abortion**

MANAGEMENT

- **Threatened abortion:**
 - There is no effective therapy for threatened intrauterine pregnancy other than pelvic rest.
- **Inevitable abortion:**
 - Awaiting spontaneous expulsion
 - Oxytocin use or Suction curettage or evacuation and curettage depending on the gestational age
 - Rh D Ig for Rh negative
- **Incomplete abortion:**
 - Uterus should be evacuated either by suction curettage or E&C as quickly as possible depending on GA (suction being the recommended method for GA up to 12 weeks)
 - Rh Ig for Rh negative
 - Prophylactic antibiotics – doxycycline 200 mg stat dose or 100mg BID for three days
- **Missed abortion**
 - Immediate evacuation of the uterus is preferred treatment, but treatment choice between expectant management and immediate evacuation should depend on the woman's informed decision

- Expectant management is possible for three weeks with assessment of coagulation profile every week
- Risk of DIC is very low before 15 weeks of GA
- Nearly in 80% of cases spontaneous expulsion during expectant management can occur in three weeks' time.
- If immediate evacuation is decided, one has to use protocol for induced abortion

➤ **Septic abortion:**

- Add broad spectrum antibiotics

➤ **Induced abortion**

- ✓ *Medical or Surgical. See technique and procedure in GYNEOLOGY MANAGEMENT GUIDELINE IN JUSH*

Components of Post abortion care (PAC)

- Emergency treatment of incomplete abortion and potentially life threatening complications
- Post-abortion family planning counseling and services
- Links between post-abortion emergency services and the reproductive health care system.
- Community service provider partnership
- Counseling

CHAPTER 14

PELVIC ORGAN PROLAPSE

POP is a bulge or protrusion of pelvic organs and their associated vaginal segments into or through the vagina. In the United States, it is the **third** most common indication for hysterectomy

- A woman has an estimated lifetime risk of 12% to undergo surgery for prolapse or incontinence.
- **50%** of women older than age 50 have some degree of pelvic organ prolapse, but fewer than 20% seek treatment.
- This may be due to a number of reasons, including lack of symptoms, embarrassment, or misperceptions about available treatment options.

PATHOPHYSIOLOGY

- Pelvic organ support is maintained by complex interactions among the:-
 - pelvic floor muscles
 - pelvic floor connective tissue, and
 - vaginal wall
- Pelvic organ prolapse results from attenuation of this supportive structures, whether by actual tears or “breaks” or by neuromuscular dysfunction or both.

Factors believed to be involved in pelvic organ support failure:

- Genetic predisposition,
- Loss of pelvic floor striated muscle support,
 - The **levator ani muscle** muscles comprised of three regions *iliococcygeal*, *pubococcygeus* and *puborectalis* muscle

- When the levator ani muscle has normal tone and the vagina has adequate depth, the *upper vagina lies nearly horizontal in the standing female*.
 - When the levator ani muscle loses tone, the vagina drops from a horizontal to a *semivertical position*.
 - This widens or opens the genital hiatus and predisposes pelvic viscera to prolapse.
- Vaginal wall weakness, and loss of connective attachments

Vagina has three levels of support, as described by DeLancey

- **Level I Support:** consists of the *cardinal and uterosacral ligaments*
- The uterosacral ligaments are posterior fibers that attach to the presacral region at the level of S2 through S4.
 - Defects in this support complex may lead to *apical prolapse*.
- **Level II Support:** These are the connective tissue attachments of the lateral vagina anteriorly to the arcus tendineus fascia pelvis and posteriorly to the arcus tendineus rectovaginalis.
- Detachment of this connective tissue from the arcus tendineus fascia pelvis leads to lateral or paravaginal anterior vaginal wall prolapse.
- **Level III Support:** The perineal body, superficial and deep perineal muscles.
- Damage to level III support contributes to anterior and posterior vaginal wall prolapse,

Supports of the uterus

- **Upper tier**
- Endopelvic fascia covering the uterus
 - Round ligament
 - Broad ligament

It is the weakest of the uterus and it maintain the uterus in anteverted position

➤ **Middle tier**

- Condensations of endopelvic fascia
 - Cardinal / Transverse cervical/ Mackenrodt's ligament
 - Utero sacral ligament
 - Pubocervical ligament
 - Pubourethral ligament

The strongest support of the uterus

➤ **Inferior/ Lower tier**

- Pelvic diaphragm: Levator ani muscle
- Perineal body: Fibro muscular condensation between the vagina & the rectum

RISK FACTORS

Risk Factors Associated with Pelvic Organ Prolapse

Pregnancy

Vaginal childbirth

Menopause

Aging

Hypoestrogenism

Chronically increased intraabdominal pressure

Chronic obstructive pulmonary disease (COPD)

Constipation

Obesity

Pelvic floor trauma

Cigarette smoking

Genetic factors

Race(highest risk in white women)

Connective tissue disorders

Spina bifida

- Vaginal childbirth is the most frequently cited risk factor. The risk of POP increased **1.2 times** with each vaginal delivery.
- In women age 20 to 59 years, the incidence of POP roughly doubled with each decade.
- Black women more commonly have a *narrow pubic arch and an android or anthropoid pelvis*. These shapes are protective against POP compared with the *gynecoid* pelvis typical of most white women.
- Being overweight (BMI 25–30 kg/m²) was associated with an increased risk of 31 to 39%, and obesity (BMI >30 kg/m²) with an increased risk of 40 to 75%.

DESCRIPTION AND CLASSIFICATION

Pelvic organ prolapse includes:-

Anterior compartment defects

- Urethrocele
- Cystocele

Apical defects

- Uterine prolapse
- Vaginal vault prolapse(Post hysterectomy)

Posterior compartment defects

- Enterocele
- Rectocele

- **Cystocele** is a herniation of the urinary bladder through the anterior vaginal wall.
- **Uterocele** is generally the result of poor cardinal or uterosacral ligament apical support, which allows downward protrusion of the cervix and uterus toward the introitus.
- **Procidentia**, which involves prolapse of the uterus and vagina, and total vaginal vault prolapse, which can occur after hysterectomy, represent eversion of the entire vagina.

- **Rectocele** is a protrusion of the rectum into the vaginal lumen
- **Enterocoele** is a herniation of the peritoneum and small bowel and is the only true hernia among the pelvic support disorders.

POP GRADING/QUANTIFICATION SYSTEM

POP-Q system

- This system contains a series of site specific measurements each measured relative to the hymen which is an anatomic landmark.
- With the hymenal plane defined as zero, Points proximal to the hymen are described with a negative number. Positions distal to the hymen are noted using a positive number
- There are nine points; all except TVL, are measured during patient Valsalva and should reflect maximum protrusion.

Possible Ranges of the Six Sites specific Pelvic Organ Prolapse.

Points	Description	Range
Aa	Anterior wall 3 cm from hymen	-3 cm to +3 cm
Bb	Most dependent portion of rest of anterior wall	-3 cm to +TVL
C	Cervix or vaginal cuff	±TVL
D	Posterior fornix (if no prior hysterectomy)	±TVL or omitted
Ap	Posterior wall 3 cm from hymen	-3 cm to +3 cm
Bp	Bp Most dependent portion of rest of posterior wall	-3 cm to +TVL

- **The total vaginal length (TVL)** is the greatest depth of the vagina in centimeters when point C or D is reduced to its fullest position.
- **Genital Hiatus and Perineal Body.**
 - The genital hiatus is measured from the middle of the external urethral meatus to the midline of the posterior hymenal ring.
 - The perineal body is measured from the posterior margin of the genital hiatus to the mid anal opening.

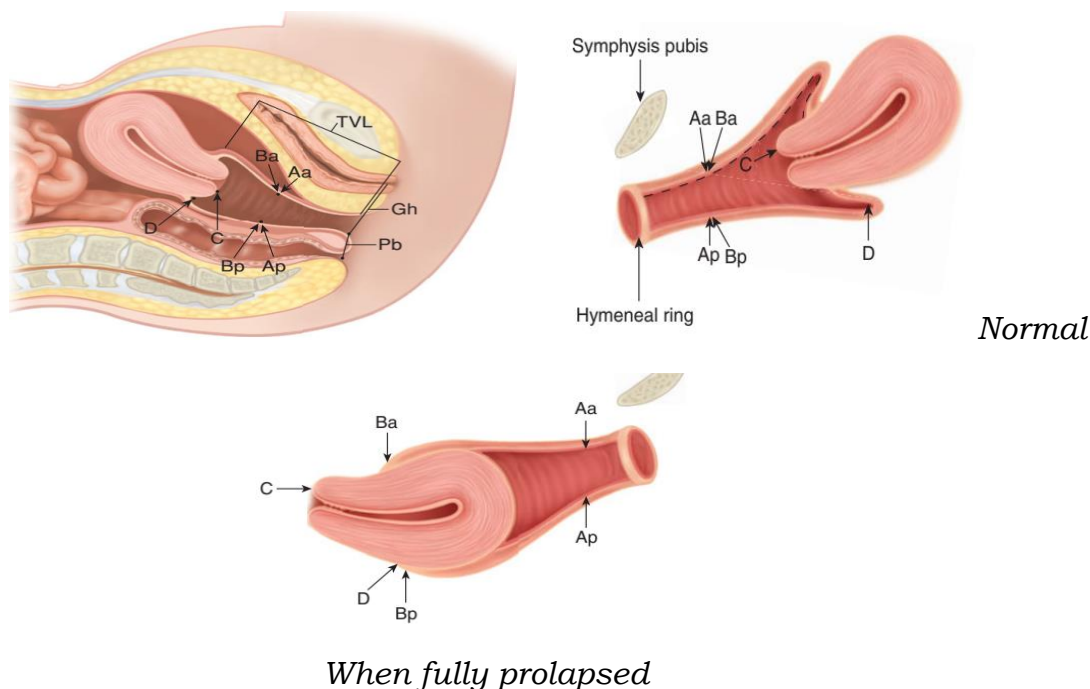


FIGURE 1: The anatomic landmarks used during pelvic organ prolapse quantification (POP-Q)

The POP-Q staging system of pelvic organ support

Stage 0	No prolapse is demonstrated. Points Aa, Ap, Ba, and Bp are all at -3cm, and either point C or D is between -TVL cm and (TVL-2) cm
Stage I	The criteria for stage 0 are not met, but the most distal portion of the prolapse is >1 cm above the level of the hymen (i.e., its quantitation value is < -1 cm)
Stage II	The most distal portion of the prolapse is ≤1 cm proximal to or distal to the plane of the hymen (i.e. its quantitation value is ≥ -1 cm but ≤ +1cm)
Stage III	The most distal portion of the prolapse is > 1 cm below the plane of the hymen but protrudes no further than 2 cm less than the total vaginal length in centimeters (i.e., its quantitation value is > +1 cm. But < [TVL-2] cm).
Stage IV	Essentially, complete eversion of the total length of the lower genital tract is demonstrated. The distal portion of the prolapse protrudes to at least (TVL-2) cm (i.e., its quantitation value is ≥ +[TVL-2] cm).

BADEN-WALKER HALFWAY SYSTEM

- This descriptive tool is also used to classify prolapse during physical examination and is in **widespread clinical use**.

Grade 0	Normal position for each respective site
Grade 1	Descent halfway to the hymen
Grade 2	Descent to the hymen
Grade 3	Descent halfway past the hymen
Grade 4	Maximum possible descent for each site

CLINICAL MANIFESTATIONS OF POP

SYMPTOMS

➤ **Bulge symptoms**

- Sensation of vaginal bulging or protrusion
- Seeing or feeling a vaginal or perineal bulge
- Pelvic or vaginal pressure
- Heaviness in pelvis or vagina

➤ **Urinary Symptoms**

- Stress urinary and urge incontinence (SUI), urinary frequency, urinary retention, recurrent urinary tract infection, or Manual reduction of prolapse to start or complete voiding.

➤ **Bowel symptoms**

- Incontinence, feeling of incomplete emptying, constipation, urgency, digital evacuation to complete defecation.

➤ **Sexual symptoms and pain**

- Dyspareunia, decreased lubrication, decreased sensation, decreased arousal or orgasm.

Pelvic and Back Pain

PHYSICAL EXAMINATION

PELVIC EXAMINATION

- The vulva and perineum are examined for signs of vulvar or vaginal atrophy, lesions, or other abnormalities.
- **Sacral reflexes** is using a cotton swab.
 - *The **bulbocavernosus reflex***: is elicited by tapping or stroking lateral to the clitoris and observing contraction of the bulbocavernosus muscle bilaterally.
 - ***Anal wink reflex***: for evaluation of anal sphincter innervation is completed by stroking lateral to the anus and observing a reflexive contraction of the anus.
 - ❖ *Intact reflexes suggest normal sacral pathways.*
- Examination of prolapsed organ begins by asking a woman to attempt Valsalva maneuver prior to placing a speculum in the vagina.
- If unable to adequately complete a Valsalva maneuver; are asked to *cough*. If the full extent of prolapse cannot be demonstrated, a woman should be examined in a *standing position*.

During this assessment try to answer three questions:

- (1) Does the protrusion come beyond the hymen?
- (2) What is the presenting part of the prolapse (anterior, posterior, or apical)?
- (3) Does the genital hiatus significantly widen with increased intraabdominal pressure?

- The use of a **Graves speculum** or Baden retractor can help to evaluate the apical compartment of the vagina.
- The anterior and posterior compartments are best examined with the use of a **univalve or Sims' speculum**.
- **Rectovaginal examination** may be useful in evaluating the posterior compartment to distinguish a posterior vaginal wall defect.

- A clinician's index finger is placed in the rectum and thumb on the posterior vaginal wall.
 - Small bowel may be palpated between the rectum and vagina, confirming enterocele.
 - Enterocele can only definitively be *diagnosed by observing small bowel peristalsis* behind the vaginal wall.
- **Bimanual examination** is performed to identify other pelvic pathology and a stress test for associated stress incontinence.
- If the **POP-Q examination** is performed, the genital hiatus (Gh) and perineal body (Pb) are measured during Valsalva maneuver.
- The total vaginal length (TVL) is then measured by placing a marked ring forceps, or a ruler, at the vaginal apex and noting the distance to the hymen.
- A bivalve speculum is then inserted to the vaginal apex. It displaces the anterior and posterior vaginal walls, and points C and D are then measured with Valsalva.
- A univalve speculum is then used to displace the posterior vaginal wall and allow for visualization of the anterior wall and measurement of points Aa and Ba;
- Then the speculum is rotated 180 degrees to displace the anterior wall and allow examination of the posterior wall and Points Ap and Bp are measured.

MANAGEMENT PRINCIPLE

➤ **Non-surgical measures:**

Considered in women with:-

- Mild to moderate prolapse (stage I & II)
- Those who desire preservation of future childbearing
- Those who do not desire surgical intervention.

Includes;-

1. Pelvic Floor Muscle Exercises
 - Referred to as Kegel exercises. Aimed to tighten and strengthen the pubococcygeus muscles.
2. Estrogen; in postmenopausal women, local estrogen therapy.
3. Weight reduction in obese patients
4. Modification of life style (avoid heavy exercise, other habits)

➤ **Surgical measures:**

- Anterior colporrhaphy for anterior prolapse
- Posterior vaginal defect repair: Colpoperineorrhaphy and Posterior colporrhaphy
- Apical Vaginal Repair: Vaginal hysterectomy with culdoplasty; Vaginal hysterectomy with sacrospinous fixation

SAMPLE HISTORY

Chief complaint: Mass protruding per vagina of 2 years and 2 month duration.

HPI

This is a 55 years old para 8,abortion 0 patient who has been amenorrhic for the last 6 years; was relatively healthy until she presented with protruding mass of 2 years, which begins to get worse since 6 months back. The mass protrudes out up on standing, coughing and lifting heavy objects and returns on attaining supine position. The mass was soft and she was able to push back the mass manually. It is painless and not associated with abnormal bleeding or foul smelling discharge. She also complains of dragging type of lower abdominal pain which doesn't radiate and get exacerbated when she stands and strains while relieved upon rest. For this reason she went to a local health center and was referred to Jimma medical center.

She also has frequent urination, urgency, leakage of urine while coughing or sneezing and a burning sensation during urination. Due to urinary frequency, she was forced to reduce her water intake during work.

Her first delivery was 35years back and her last was 10 years back. All of her children were born through spontaneous vaginal delivery at her house attended by traditional birth attendants. Labor, lasted less than 6 hours in all cases. All her children are alive and healthy. None of her pregnancies had antepartum or post-partum complications.

She works in a factory as a daily laborer(animal food product factory). The job requires heavy lifting and lots of strenuous activities.

Prepared by Jimma University Medical Students of 2008 E.C. Batch

Otherwise:-

She has no history of vaginal bleeding or discharge,
She has no history of reddish discoloration of urine.
She has no history of abdominal swelling or distention.
She has no history of chronic cough,
She has no previous history of constipation.
She has no history of trauma to the pelvis or gynecological surgery
She has no history of similar illness in the family.
She has no personal and family history of chronic illness like DM, hypertension or asthma.
She has no color change to the mass or ulceration.
She has no history of urinary retention, change in bowel habits.
She is not sexually active currently.
She came to this hospital by walking.

Pertinent physical examination:

General appearance: Stable, comfortable, well-nourished and cooperative during physical examination.

Vital sign: BP=130/80 mm Hg from right arm, supine position.

PR=88 beats/min from radial artery.

RR=18 breaths/min

T^o=36.0°C from axilla

Weight: 83kg height: 160cm

BMI: 32.4kg/m²

Pelvic examination

Examination of external genitalia: atrophic vulva, inverted triangle like hair distribution. Type I clitoridectomy, No ulcers, discolorations, pruritus or warts.

Digital vaginal examination: a soft, non-tender and reducible mass felt bulging from the anterior vaginal wall.

After straining a mass protruding per vagina is seen half way past the hymen. By Baden-Walker Half Way system = stage three pelvic organ prolapse.

No cervical motion tenderness.

Recto vaginal examination: no peristalsis felt behind the vaginal wall

Assessment:

Differential Diagnosis

- Tumors of the urethra and bladder
- Urethral diverticulum
- Skene's and Bartholin's glands cysts or abscesses.
- Soft tumors (lipoma, leiomyoma, sarcoma)
- Cervical/endometrial tumors (pedunculated myoma or endometrial polyps); if prolapsed through a dilated cervix.
- Elongated cervix

Investigations

- Hematocrit, Blood group & Rh, U/A
- RFT
- U/S for residual volume, kidneys, abdominal masses.
- Intravenous pyelogram (IVP)

Management

(See above)

CHAPTER 15

PELVIC PAIN

HISTORY

Detail elaboration of the pain. We can use the mnemonic “OLD CAARTS” to remember the contents we need to include.

- **O** => onset
 - Sudden, indicate rupture of a cyst, an ectopic pregnancy, obstruction or perforation of a hollow viscus
 - Gradual, indicate a progressive or chronic condition
- **L** => location, (on history it is better to say lower abdominal pain)
 - Unilateral, usually indicate adnexal pathology in that side and a localized etiology
 - Bilateral,
 - Midline (diffuse or generalized), indicates a visceral pain from distention, stretching or spasm of abdominal organs (which have their origin from the embryological hind gut, like the colon or intraperitoneal portions of the genitourinary tract)
- **D** => duration, (see the detail below)
 - Acute or Chronic
- **C** => character
 - Intermittent, usually associated with contraction of the bowel or the uterus
 - Continuous,
 - Sharp, kind of stabbing, indicate a localized cause,
 - Dull ache, diffuse pain from the viscera
 - Cramp, associated with contraction of a hollow viscus, like intestine or uterus in attempt to relive an obstruction

- **A** => alleviating or aggravating factors
 - Pain aggravated with motion may indicate peritonitis (from rupture of a cyst or appendix)
 - Pain relived with acquiring certain position may indicate obstruction of a vicious organ, as in renal colic. Is the pain relived by any medications?
- **A** => associated symptoms, (this should be included after completion of the pain description)
 - vaginal bleeding or discharge, amenorrhea, infertility.... => gynecologic pathology
 - dysuria, hematuria, frequency, or urgency.... => urinary pathology
 - diarrhea, constipation, or gastrointestinal bleeding.... => gastrointestinal (GI) disease.
 - vomiting
 - In the acute surgical abdomen, if vomiting occurs, it usually *follows as a response to pain* and results from vagal stimulation.
 - This vomiting is typically severe and develops *without nausea*. For example, *vomiting has been found in approximately 75 percent of adnexal torsion cases*
 - if *vomiting is noted prior to the onset of pain*, a surgical abdomen is less likely
 - Fever, chills ... indicate an acute inflammatory/infectious condition
- **R** => radiation, to
 - The shoulder, indicate hemoperitoneum, may be from ruptured ectopic pregnancy
 - The groin, from the costovertebral angle, indicate ureteral colic
- **T** => timing/ temporal

- What time of day (relation to menstrual cycle and activities of daily living)?
- Pelvic can occur associated with
 - Menses=> dysmenorrhea
 - Sexual intercourse=> dyspareunia
 - Urination=> dysuria
 - Defecation=> dyschezia
- **S** => severity
 - Has the patient stopped daily activity b/c of the symptom? Or lost normal sleep?
 - Does simple rest relieve the pain?
 - Is the pain associated any indicators systemic autonomic response like, diaphoresis, vomiting?

See P/E and Investigations under each differentials

CLASSIFICATION

- Acute pelvic pain
- Cyclic pelvic pain
- Chronic pelvic pain

Comparison between Acute Vs Chronic pelvic pain

	Acute pelvic pain	Chronic pelvic pain
Duration	Less than 7 days	Greater than 6 months
Onset	Rapid	Gradual
Type	Inflammatory	Neuropathic
Etiology	Infection, ischemia, or chemical irritation	Often it is obscure.

Association	Often associated with ➤ profound autonomic reflex responses, such as nausea, emesis, diaphoresis, and apprehension, ➤ unstable vital signs and obvious abnormalities on physical examination and laboratory assessment	➤ obvious autonomic reflex responses are not present ➤ is characterized by neurological, psychological, and behavioral alterations, like anxiety and depression ➤ vital sign derangements and obvious anatomic abnormalities may not be there
Treatment	Is directed against the underlying condition	If focused on treating the pain symptoms

ACUTE PELVIC PAIN

- Acute pain is intense and characterized by sudden onset, sharp rise, and short course.
- It can be a somatic or visceral pain
 - **Somatic pain** arises from the parietal peritoneum, muscle, subcutaneous tissue or the skin. it is typically sharp and localized. it is often unilateral

- **Visceral pain** arises from the visceral peritoneum or the viscera.
 - The viscera are relatively insensitive to pain.
 - The first perception of visceral pain is a vague, deep, poorly localizable sensation associated with autonomic reflex responses; however, once the pain becomes localized, the pain is called referred pain.
 - Referred pain is well localized and superficial. It is appreciated within the nerve distribution or dermatome of the spinal cord segment innervating the involved viscus
 - The pain is often diffuse and dull ache, but it can be localized to the midline

DIFFERENTIAL DIAGNOSIS OF ACUTE PELVIC PAIN

Gynecologic Disease or Dysfunction
Complication of pregnancy
Ectopic pregnancy
Abortion, threatened or incomplete
Acute infections
Endometritis
Pelvic inflammatory disease (acute PID) or salpingo-oophoritis
Tubo-ovarian abscess
Adnexal disorders
Hemorrhagic functional ovarian cyst
Torsion of adnexa
Rupture of functional, neoplastic, or inflammatory ovarian cyst
Prolapsing leiomyoma

Gastrointestinal

Gastroenteritis

Appendicitis

Bowel obstruction

Diverticulitis

Irritable bowel syndrome

Genitourinary

Cystitis

Pyelonephritis

Ureteral lithiasis

Musculoskeletal

Abdominal wall hematoma

Hernia

Ectopic pregnancy

- An ectopic pregnancy is defined as implantation of the fetus in a site other than the uterine cavity. The fallopian tube is the most common site of implantation (~95%)
- Implantation of the fetus in the fallopian tube produces pain only with acute dilation of the tube. If tubal rupture occurs, localized abdominal pain tends to be temporarily relieved and is replaced by generalized pelvic and abdominal pain as the hemoperitoneum develops.
- *A period of amenorrhea followed by bleeding and pain compose the classic triad of symptoms.*
- *A mass in the cul-de-sac may produce an urge to defecate*

Torsion of Adnexa

- Torsion (twisting) of the vascular pedicle of an ovary, fallopian tube, paratubal cyst, or rarely just a fallopian tube results in ischemia and rapid onset of acute pelvic pain.
- A benign cystic teratoma is the most common neoplasm to undergo torsion.
- Ovarian carcinoma and inflammatory masses are rarely affected by torsion (because of adhesions). *It is also unusual for a normal tube and ovary to torque*, although a polycystic ovary can undergo torsion
- *The pain of torsion can be severe and constant or, if the torsion is partial and intermittently untwists, it could be intermittent.*
- *The onset of the torsion and the symptoms of abdominal pain frequently coincide with lifting, exercise, or intercourse.*
- *Autonomic reflex responses are usually present (e.g., nausea, emesis, apprehension).*

Leaking or Ruptured Ovarian Cyst

- Functional cysts (e.g., follicle, corpus luteum) are the most common ovarian cysts and rupture more readily than do benign or malignant neoplasms.
- A hemorrhagic corpus luteum cyst can develop in the luteal phase of the menstrual cycle. Rupture of this cyst can produce either a small amount of intraperitoneal bleeding or frank hemorrhage resulting in significant blood loss and hemoperitoneum.
- Nonmalignant neoplasms, most commonly cystic teratomas (dermoid cysts) or cystadenomas, as well as inflammatory ovarian masses, such as endometriomas, can also leak or rupture.
- A corpus luteum cyst is the most common cyst to rupture and lead to hemoperitoneum.

- *Symptoms of a ruptured corpus luteum cyst are similar to those of a ruptured ectopic pregnancy.*
- *The onset of pain is usually sudden and is associated with increasing generalized abdominal pain and occasionally dizziness or syncope if a hemoperitoneum develops.*

Uterine Leiomyomas

- Leiomyomas are uterine smooth muscle tumors (see the myoma section).
- Discomfort may be present when myomas are intramural, fundal, or encroaching on adjacent bladder, rectum, or supporting ligaments of the uterus.
- Although rare, fibroids are more likely to cause *dyspareunia and noncyclic pelvic pain*
- Acute pelvic pain can develop if the myoma undergoes degeneration or torsion. Degeneration of myomas occur secondary to loss of blood supply, usually attributable to rapid growth associated with pregnancy.
- A pedunculated subserosal leiomyoma can undergo torsion ischemic necrosis; when this situation occurs, it is associated with *pain similar to that of adnexal torsion.*
- When a submucous leiomyoma becomes pedunculated, the uterus contracts force-fully as if to expel a foreign body, and the resulting pain is similar to that of labor. *The cramping pain is usually associated with hemorrhage.*

Pelvic inflammatory disease (PID) (see below)

Appendicitis

- Is most common intestinal source of acute pelvic pain in women

- The symptoms and signs of appendicitis can be similar to those of PID.
- *The first symptom of appendicitis is typically diffuse abdominal pain, especially periumbilical pain, followed by anorexia, nausea, and vomiting. Within a matter of hours, the pain generally shifts to the right lower quadrant. Fever, chills, emesis, and obstipation may ensue.* However, this classic symptom pattern is often absent.

Acute Diverticulitis

- Acute diverticulitis is a condition in which there is inflammation of a diverticulum or outpouching of the wall of the colon, usually involving the sigmoid colon.
- Diverticulitis typically affects postmenopausal women but can occur in women in their 30s and 40s.
- The severe, left lower quadrant pain of diverticulitis can occur following a long history of symptoms of irritable bowel (bloating, constipation, and diarrhea), although diverticulosis usually is asymptomatic. Diverticulitis is less likely to lead to perforation and peritonitis than is appendicitis. Fever, chills, and constipation typically are present, but anorexia and vomiting are uncommon.

Intestinal Obstruction

- The most common causes of intestinal obstruction in women are postsurgical adhesions, hernia formation, inflammatory bowel disease, and carcinoma of the bowel or ovary.
- Intestinal obstruction is heralded by the onset of colicky abdominal pain followed by abdominal distention, vomiting, constipation, and obstipation.
- Higher and more acute obstruction results in early vomiting, whereas colonic obstruction presents with a greater degree of abdominal distention and obstipation.

- Vomiting first consists of gastric contents, followed by bile, then material with feculent odor, depending on the level of obstruction.

Ureteral colic

- Ureteral colic is a cramping lower abdominal pain that is due to ureteral lithiasis is caused by a sudden increase in intraluminal pressure and associated inflammation.
- The pain of lithiasis is typically severe and crampy; it can radiate from the costovertebral angle to the groin. Hematuria is often present

UTI

- Urinary tract infections producing acute pain include cystitis and pyelonephritis. The most common microbes causing urinary tract infections are *E. coli* followed by *Proteus*, *Klebsiella*, and *Pseudomonas*.
- Cystitis is associated with dull suprapubic pain, urinary frequency, urgency, dysuria, and occasionally hematuria. Because urethritis can occur secondary to chlamydia or gonorrhea and has similar symptoms, these infections must be ruled out if appropriate.
- Pyelonephritis is associated with flank and costovertebral angle pain, although lateralizing lower abdominal pain occasionally is present.
- On physical examination there is pain with firm pressure over the costovertebral angle in the case of lithiasis or pyelonephritis. Peritoneal signs are absent. Suprapubic tenderness may accompany cystitis.

PELVIC INFLAMMATORY DISEASE (PID)

- Pelvic inflammatory disease (PID) comprises a spectrum of inflammatory disorders of the upper female genital tract (above the internal Os), including any combination of endometritis, salpingitis, tubo-ovarian abscess, and pelvic peritonitis.
- Involvement the fallopian tube in PID is of special importance because of subsequent complication (infertility).

Etiology and Risk factors

- Pelvic inflammatory disease is commonly caused by *N. gonorrhea*, *C. trachomatis*, and *T. vaginalis*, although the infection is usually polymicrobial.
- Upper genital tract infections are usually caused by bacteria that ascend from the lower reproductive tract.

Risk Factors for PID

- Douching
- Single status
- Substance abuse
- Multiple sexual partners
- Lower socioeconomic status
- Recent new sexual partner(s)
- Younger age (10 to 19 years)
- Other sexually transmitted infections
- Sexual partner with urethritis or gonorrhea
- Previous diagnosis of pelvic inflammatory disease
- Endocervical testing positive for *N. gonorrhea* or *C. trachomatis*
- Not using mechanical and/or chemical contraceptive barriers

Classification of PID

- Pelvic inflammatory disease can be segregated into “silent” PID and PID. The latter can be further subdivided into acute and chronic.

Silent PID

- Silent PID is thought to follow multiple or continuous low-grade infection in asymptomatic women.
- Is not a clinical diagnosis. Rather, it is an ultimate diagnosis given to women with tubal-factor infertility who lack a history compatible with upper tract infection.
- Many of these patients have antibodies to C trachomatis and/or N gonorrhea.
- At laparoscopy or laparotomy,
 - affected women may have evidence of prior tubal infection such as adhesions, but for the most part, the fallopian tubes are grossly normal or they may have hydrosalpinx
 - fine adhesions between the liver capsule and anterior abdominal wall may also reflect prior silent disease

Acute PID

- Acute gonococcal PID is manifested by the acute onset of pelvic pain that increases with movement, fever, purulent vaginal discharge, and sometimes nausea and vomiting.
- The pain is often associated with a menstrual period.
- Chlamydial salpingo-oophoritis is associated with more insidious symptoms.

On physical examination:

- Direct and rebound abdominal tenderness with palpation are usually notable

- The most important signs of acute salpingo-oophoritis are cervical motion tenderness and bilateral adnexal tenderness.
- Lack of a discrete mass or masses differentiates acute salpingo-oophoritis from tubo-ovarian abscess or torsion.

The most recent diagnostic criteria presented by the CDC (2015) are for sexually active women at risk for STDs who have pelvic or lower abdominal pain and in whom other etiologies are excluded or unlikely.

- PID is diagnosed if uterine tenderness, adnexal tenderness, or cervical motion tenderness is present. One or more of the following enhances diagnostic specificity:
 - 1) Oral temperature > 38.3°C (101.6°F)
 - 2) Mucopurulent cervical discharge or cervical reliability
 - 3) Abundant WBCs on saline microscopy of cervical secretions
 - 4) Elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
 - 5) Presence of cervical N gonorrhea or C trachomatis

Thus, a diagnosis of PID is one typically based on clinical findings.

Tubo-ovarian Abscess (TOA)

- TOA, a sequela of acute salpingitis, are usually bilateral, but unilateral abscess formation can occur.
- The symptoms and signs are similar to those of acute salpingitis, although pain and fever have often been present for longer than 1 week before presentation to the emergency room.
- A ruptured tubo-ovarian abscess is a life-threatening surgical emergency because gram-negative endotoxic shock can develop rapidly.

- Tubo-ovarian abscesses can be palpated on bimanual examination as very firm, exquisitely tender, bilateral fixed masses. The abscesses can be palpated in the pelvic cul-de-sac.

Based on the antecedent event, PID can also be classified as:

- Post-partum
- Post abortal
- Post-operative
- Post IUCD/Instrumental
- Post STD
- Post TB

PHYSICAL EXAMINATION FOR ACUTE PELVIC PAIN

G/A: Acutely sick looking, patient lying still (peritonitis) or restless (cramping)

V/S: tachycardia & tachypnea (severe pain), pyrexia (infection/inflammation) or hypotension (from hypovolemia)

Abdominal examination:

- Inspection:
 - Distended abdomen:- bowel obstruction, torsion or hemoperitoneum
 - Abdomen doesn't move with respiration:- peritonitis
 - Scar:- bowel obstruction, ectopic pregnancy
 - Hernia sites
- Palpation
 - Generalized abdominal rigidity with significant tenderness and rebound tenderness => peritoneal irritation (in most of the cases)
 - Tenderness limited to the lower abdomen
- Percussion
 - Hypertympanic=> bowel obstruction

- Dullness=> blood or cystic fluid in the peritoneum
- Auscultation
 - Hyperactive bowel sound=> early stage of bowel obstruction
 - Absent bowel sound=>

Pelvic examination

- Check the introitus and urethral orifice for discharge or bleeding
- Cervical motion tenderness, can be seen with PID, appendicitis, diverticulitis, and intraabdominal bleeding
- Uterine enlargement, in case of leiomyomas, pregnancy, and adenomyosis
- A tender adnexal mass may reflect ectopic pregnancy, tubo-ovarian abscess, or ovarian cyst with torsion, hemorrhage, or rupture
- ✚ Rectal examination can add information regarding the source and size of pelvic masses and the possibility of colorectal pathologies.

INVESTIGATION

- **Urine or serum β -human chorionic gonadotropin (hCG)** testing is recommended in those of reproductive age without prior hysterectomy.
- **Complete blood count (CBC)** can identify hemorrhage, both uterine and intraabdominal, and can assess the possibility of infection.
- **Urinalysis**, to evaluate possible urolithiasis or UTI
- ESR & CRP, shows an inflammatory state
- **Microscopic evaluation and culture** of vaginal discharge
- **Sonography (ultrasound)**, transabdominal or transvaginal

Is very important to assess most of pelvic pathologies and identify fluid in the abdomen.

- **Computed tomography (CT scan)**, has superior performance in identifying GI and urinary tract causes of acute pelvic and lower abdominal pain
- **Magnetic resonance imaging (MRI)**, if initial sonography is non-diagnostic
- **Plain abdominal x-ray**, (plain= no contrast) for bowel obstruction
- **Intravenous pyelography (IVP)**, for ureteral colic
- **Laparoscopy**, for both diagnostic and management purpose
Operative laparoscopy is the primary treatment of suspected appendicitis, adnexal torsion, ectopic pregnancy, and ruptured ovarian cyst associated with ongoing symptomatic hemorrhage.
- **Culdocentesis**, in evaluation of suspected ruptured cyst

CYCLIC PELVIC PAIN

Cyclic pain refers to pain that occurs with a definite association to the menstrual cycle.

Dysmenorrhea or painful menstruation, is the most common cyclic pain phenomenon, affecting as many as 50% of menstruating women. It is classified as primary and secondary dysmenorrhea.

	Primary dysmenorrhea	Secondary dysmenorrhea
Underlying pelvic pathology	Absent	Present
Onset in relation to menarche	Within 1 to 2 years of menarche	Years after menarche
Onset in relation to menses and duration	Begins a few hours before or just after the onset of a menstrual	Begins 1-2wks before menstrual flow and persists until a few

	period and may last 48 to 72 hours	days after the cessation of bleeding
Mechanism	Increased endometrial prostaglandin production → higher uterine tone with high-amplitude contractions causing dysmenorrhea.	Diverse and not fully elucidated, although most involve either excess prostaglandin production or hypertonic uterine contractions secondary to cervical obstruction, intrauterine mass, or the presence of a foreign body
Pain relief with treatment	NSAIDs are effective	NSAIDs and hormonal contraceptives are less likely to provide relief

Primary dysmenorrhea affects younger women but may persist into the 40s. The pain is similar to labor, with suprapubic cramping, and maybe accompanied by lumbosacral backache.

On examination, except suprapubic & uterine tenderness on bimanual palpation, there is no abnormal finding.

The most common cause of secondary dysmenorrhea is endometriosis, followed by adenomyosis and intrauterine device.

CHRONIC PELVIC PAIN

- Chronic pelvic pain remains an inclusive, general diagnosis.
- Various forms of chronic pelvic pain affect 12% to 20% of women in the United States.
- Patients with chronic pelvic pain are frequently anxious and depressed. Their marital, social, and occupational lives are usually been disrupted.

- These patients have often had poor treatment outcomes and may have undergone multiple unsuccessful surgical procedures for pain.
 - About 12% to 19% of hysterectomies are performed for pelvic pain.
- Approximately 60% to 80% of patients undergoing laparoscopy for chronic pelvic pain have no intraperitoneal pathology, nor do they have tissue distortion that correlates with the pain.
- Nongynecologic causes of pain, such as irritable bowel syndrome, interstitial cystitis, abdominal wall or pelvic floor myofascial syndrome, or neuropathy, are frequently overlooked but common causes of chronic pelvic pain.
- In addition to detail on the pain, history of any musculoskeletal trauma, surgical procedure (including cesarean delivery) and medical interventions done for similar or other complaint are very important.
- Current and past psychological history including psychosocial factors; history of past (or current) physical, sexual, or emotional abuse; history of psychiatric hospitalization; suicide attempts; and chemical dependency need to be included.

Physical examination should focus on abdomen and the musculoskeletal system.

Abdomen

- Inspect for scars (esp. Surgical→adhesion) and hernia
- Demonstrate Carnett test, which is an evaluation of the abdomen with muscles tensed (head raised off the table or with straight leg raising) to differentiate abdominal wall and visceral sources of pain. Abdominal wall pain is augmented

- and visceral pain is diminished with these maneuvers
- Perform superficial and deep palpation
 - Increased bowel sound may indicate irritable or inflammatory bowel disease.

Differential Diagnosis of Chronic Pelvic Pain

Gynecologic	Genitourinary
Non-cyclic	Recurrent or relapsing cystourethritis
Adhesions	Urethral syndrome
Endometriosis	Interstitial cystitis
Salpingo-oophoritis	Ureteral diverticuli or polyps
Retained ovary syndrome	Carcinoma of the bladder
Pelvic congestion	Ureteral obstruction
Ovarian neoplasms	Pelvic kidney
	Neurologic
Cyclic	Nerve entrapment syndrome, neuroma, or other neuropathies
Primary dysmenorrhea	Trigger points
Mittelschmerz	Musculoskeletal
Secondary dysmenorrhea	Low-back-pain syndrome
Endometriosis	Congenital anomalies
	Scoliosis and kyphosis
Asherman's syndrome	Spondylolysis
Endometrial polyps	Spondylolisthesis
Uterine leiomyomata	Spinal injuries
Adenomyosis	Inflammation
Pelvic congestion syndrome	Tumors
Atypical cyclic	Osteoporosis
Endometriosis	Degenerative changes
Adenomyosis	Coccydynia
Ovarian remnant syndrome	Myofascial syndrome
Chronic functional cysts	Hernia

Gastrointestinal	Systemic
Irritable bowel syndrome	Fibromyalgia
Ulcerative colitis	Acute intermittent porphyria
Crohn's disease	Abdominal migraine
Carcinoma	Connective tissue disease including systemic lupus erythematosus
Infection	Lymphoma

ENDOMETRIOSIS

- Endometriosis is defined as the presence of endometrial glands and stroma outside the uterine cavity.
- The annual incidence of surgically diagnosed endometriosis is 1.6 per 1000 women aged 15-49yrs. the prevalence in different in asymptomatic women (6-11%), in patient with infertility (20-50%) and in patient with pelvic pain (40-50%, in Novak's gynecology 14th ed this figure is 15-40%).

Risk factors for endometriosis

- Nulliparity
- Early menarche/late menopause
- Short menstrual cycles
- Prolonged menses
- Müllerian anomalies (increase ectopic implantation of endometrial tissue)

Endometriosis is an estrogen dependent disorder, any factor that increase estrogen exposure increases the risk. It is rarely seen in postmenopausal women and nonexistent in pre-pubertal girls.

The definitive cause of endometriosis remains unknown, but different theories have been suggested:

- Retrograde menstruation through the fallopian tubes (the more favored one)
- The stem cell theory
- Aberrant lymphatic and vascular spread of endometrial tissue
- Coelomic metaplasia theory

Endometriosis may develop anywhere within the pelvis and on other extrapelvic peritoneal surfaces. Most commonly, it develops in the dependent areas of the pelvis like

- the anterior and posterior cul-de-sacs,
- other pelvic peritoneum,
- the ovary, and
- uterosacral ligaments are frequently involved.

Additionally, the rectovaginal septum, ureter, and bladder and rarely, pericardium, surgical scars, and pleura may be affected. One pathologic review revealed that endometriosis has been identified on all organs except the spleen.

Implants may be:-

- superficial or
- deep infiltrating endometriosis (DIE), that is, infiltrative forms that involve vital structures such as bowel, bladder, and ureters.
 - Some definitions of DIE also quantify invasion as > 5 mm

Ovarian endometriomas

- are frequent manifestations of endometriosis
- these smooth-walled, dark-brown ovarian cysts are filled with a chocolate-appearing fluid and may be unilocular or, when larger, multilocular

- their pathogenesis is unclear, yet three theories include invagination of ovarian cortex implants, coelomic metaplasia, and secondary involvement of functional ovarian cysts by endometrial implants located on the ovarian surface

Endometriosis produces a low-grade inflammatory reaction; over time this results in adhesions between confluent pelvic organs. However, the cause of the pain is not well established.

Classification

- The American Society for Reproductive Medicine allows endometriosis to be quantified and classified in to four stages.
- With this, endometriosis on the peritoneum, ovaries, fallopian tubes, and cul-de-sac is scored at surgery.
- At these sites, points are assigned for:-
 - disease surface area,
 - degree of invasion,
 - morphology, and extent of associated adhesions
- Also, endometriotic lesions are morphologically categorized as white, red, or black.
- In this system, endometriosis is classified as
 - stage I (minimal, score 1-5),
 - stage II (mild, score 6-15),
 - stage III (moderate, score 16-40), and
 - stage IV (severe, score >40)

NB, there is poor correlation with stage of disease and pain & infertility

Clinical manifestation

Pain:

- Is the most common symptom.
- Endometriosis associated chronic pelvic pain (dysmenorrhea, dyspareunia and non-cyclic pain) is common.
- Less often dyschezia, dysuria and abdominal wall pain are seen. *(dysmenorrhea, dyspareunia, dyschezia and dysuria are sometimes can be remembered as 4Ds of endometriosis)*
- Vaginal, uterosacral ligament and rectovaginal septum endometrioses are associated with deep dyspareunia.
- Dyspareunia
 - may be caused by
 - ✓ pressure on inflamed tissues and neural invasion,
 - ✓ stretching and tearing during intercourse of pelvic structures bound by adhesions.
 - Endometriosis associated dyspareunia is suspected if pain develops after years of pain free intercourse.
- Dysuria and dyschezia are associated with DIE to the respective organs

Infertility:

- Endometriosis is seen in 20-30% of patients with subfertility.
- Adhesion, which is associated with impairment of normal oocyte pick-up and transport by the fallopian tube, is the main cause of infertility.
- Subtle defects like perturbations in follicle development, ovulation, sperm function, embryo quality and development, and implantation are also possible causes

Other symptoms depend on the system/site involved.

- Rectosigmoid lesions → dyschezia, constipation diarrhea and cyclic hematochezia
- Urinary tract lesion → dysuria, hematuria, suprapubic pain and frequency
- Abdominal wall lesions → abdominal pain
- Thoracic lesions → cyclic chest pain, hemoptysis and pneumothorax associated with menses, which are sometimes refereed as *catemenial*.

Physical examination

- Often no abnormal findings are seen in physical examination.
- Most common finding is tenderness when palpating the posterior fornix.
- Other frequent findings:
 - localized tenderness in the pouch of Douglas or uterosacral ligaments,
 - palpable tender nodules in the posterior cul-de-sac, uterosacral ligaments, or rectovaginal septum,
 - thickening and induration of uterosacral ligaments,
 - pain with uterine movement,
 - tender enlarged adnexal masses and
 - fixation of adnexa or uterus in a retroverted position.

Diagnosis

- Endometriosis is a surgical diagnosis based on identification of characteristic lesions.
- Laparoscopy is the gold standard investigation.
- Histologic and imaging studies are also required for definitive diagnosis. Although nonspecific CA125 is elevated in endometriosis.

Management

Management depends on age, symptoms, stage, and the need for fertility. It includes:

1. Expectant Management
2. Medical treatment
3. Hormonal treatment
4. Surgical treatment
5. Combination Medical and surgical treatment

ADHESIONS

- Adhesions noted at the time of laparoscopy are often in the same general region of the abdomen as the source of the pelvic pain; however, neither the specific location nor density of the adhesions correlates consistently with the presence of pain symptoms.

Symptoms

- Noncyclic abdominal pain, sometimes increased with intercourse or activity, is a common source of pain in women with adhesions, but there is no symptom pattern specific for adhesions.
- Chronic pelvic pain developing from adhesions is thought to result from restriction of bowel mobility and distention. Furthermore, dense adhesions involving bowel can cause partial or complete bowel obstruction.

Signs

- The abdominal wall must be carefully evaluated for myofascial or neurological sources of pain.
- Most women with adhesions have had a prior surgical procedure with possible injury to abdominal wall structures that may be the cause of pain.
- Decreased mobility of pelvic organs or adnexal enlargement can often be detected in patients with adhesions.

CHAPTER 16

GENITOURINARY FISTULA (GUF)

A genitourinary fistula is defined as an abnormal communication between the urinary (ureters, bladder, urethra) and the genital (uterus, cervix, vagina) systems.

Incidence

- The true incidence of genitourinary fistula is unknown and varies according to whether the etiology is obstetric or gynecologic.
- In Asia and Africa, up to 100,000 new cases of obstetric genitourinary fistula are added each year to the estimated pool of 2 million women with unrepaired fistulas.
- For industrialized countries, most fistulas occur iatrogenically from pelvic surgery, and the generally accepted incidence derives from data on surgeries to correct these fistulas.
- Of genitourinary fistulas, the vesicovaginal fistula is most common.

CLASSIFICATION

Many classification systems exist for genitourinary fistula:

Classification of Genitourinary Fistula Based on Anatomic Communication

- Communication between the urinary tract and vagina:-
 - Ureterovaginal
 - Vesicovaginal
 - Urethrovaginal

➤ Communication between the cervix and the urinary tract

- Ureterocervical
- Vesicocervical
- Urethrocerical

➤ Communication between the uterus and the urinary tract

- Ureterouterine
- Vesicouterine

Vesicovaginal fistulas can also be classified by their size and location in the vagina.

- *high vaginal*, when found proximally in the vagina
- *low vaginal*, when noted distally; or
- *midvaginal*, when identified centrally

Others classify vesicovaginal fistula based on the complexity and extent of involvement

✓ Simple

- Size $\leq$ 3 cm
- Located near the cuff (supratrigonal)
- No prior radiation or malignancy
- Normal vaginal length

✓ Complicated

- Prior radiation therapy
- Pelvic malignancy present
- Vaginal length shortened
- Size $>$ 3 cm
- Located distant from cuff or has trigonal involvement

In one obstetric classification system, high-risk vesicovaginal fistulas are described by their size ($>$ 4 to 5 cm in diameter); involvement of urethra, ureter(s), or rectum; juxtacervical location with an inability to visualize the superior edge; and reformation following a failed repair.

A surgical classification to objectively evaluate obstetric urinary fistula repair has also been introduced:-

- ✓ **Type I fistulas** are those that do not involve the urethral closure mechanism,
- ✓ **Type II fistulas**, type II fistulas are divided into: (A) without or (B) with subtotal or total urethra involvement. type IIB fistulas are further subdivided as: (a) without or (b) with a circumferential configuration around the urethra. and
- ✓ **Type III fistulas** involve the ureter and include other exceptional fistulas.

To aid objective comparison of surgical outcomes, a more comprehensive and standardized classification system has been developed

- It integrates fistula distance from the external urethral meatus, fistula size, degree of surrounding tissue fibrosis, and extent of vaginal length reduction
- This new classification divides genitourinary fistulas into four main types, depending on the distance of the fistula's distal edge from the external urinary meatus.
 - **Type 1:** Distal edge of fistula > 3.5 cm from external urinary meatus
 - **Type 2:** Distal edge of fistula 2.5–3.5 cm from external urinary meatus
 - **Type 3:** Distal edge of fistula 1.5 to < 2.5 cm from external urinary meatus
 - **Type 4:** Distal edge of fistula < 1.5 cm from external urinary meats

These four types are further sub-classified by the size of the fistula, extent of associated scarring, vaginal length, or special considerations.

- By the size of the fistula
 - a) Size < 1.5 cm, in the largest diameter
 - b) Size 1.5–3 cm, in the largest diameter
 - c) Size > 3 cm, in the largest diameter
- By the extent of scarring/fibrosis
 - i. None or only mild fibrosis (around fistula and/or vagina) and/or vaginal length > 6 cm, normal capacity
 - ii. Moderate or severe fibrosis (around fistula and/or vagina) and/or reduced vaginal length and/or capacity
 - iii. Special consideration, e.g., postradiation, ureteric involvement, circumferential fistula, or previous repair

ETIOLOGY AND RISK FACTOR

- Congenital genitourinary fistulas are rare, but if found, are commonly associated with other renal or urogenital abnormalities.
- Acquired and typically result from either obstetric trauma or pelvic surgery.
 - Obstetric Trauma: In developing countries, more than 70 percent of genitourinary fistulas arise from obstetric trauma, specifically from prolonged or obstructed labor or complicated cesarean delivery.
- Factors associated with fistula formation in developing countries
 - Both childbearing at a young age
 - Female genital mutilation, may significantly narrow the vaginal introitus and obstruct labor
 - Prolonged obstructed labor or
 - Anatomic malpresentation of the presenting fetal part

These factors can cause pressure and ischemic necrosis of the anterior vaginal wall and bladder, subsequently resulting in fistula formation.

- Instrumental delivery used to deliver stillborn infants or perform abortion, may damage the vagina
- Malnutrition and limited health care in many of these countries can further diminish wound healing.

Fistula in developed countries

- Obstetric procedures or deliveries are unusual causes of fistula in developed countries.
- Iatrogenic injury during pelvic surgery is responsible for 90 percent of vesicovaginal fistulas in these nations.
- The accepted incidence of fistula formation after pelvic surgery is 0.1 to 2 percent. In industrialized countries, hysterectomy is the most common surgical precursor to vesicovaginal fistula, accounting for approximately 75 percent of fistula cases.
- Other Causes include:-
 - radiation therapy (6%),
 - malignancy (1.8%),
 - trauma (4%),
 - foreign bodies, i
 - infections, pelvic inflammation, and
 - inflammatory bowel disease.
 - Other rare causes of fistula formation include infections such as lymphogranuloma venereum, urinary tuberculosis, pelvic inflammation, and syphilis; inflammatory bowel disease; and autoimmune disease.
 - Additionally, conditions that interfere with healing such as poorly controlled diabetes mellitus, smoking, local infection, peripheral vascular disease, and chronic corticosteroid use are potential risks.

SYMPTOMS

- Classically presents with unexplained continuous urinary leakage from the vagina after a recent operation.
- Other less specific symptoms of genitourinary fistula include fever, pain, ileus, and bladder irritability.

DIAGNOSIS

- A thorough history and physical examination identifies most cases of vesicovaginal fistula.
- Visual assistance with an endoscopic lens and translucent vaginal speculum can sometimes help identify a vaginal-apex fistula, which can be more difficult to detect.

Investigations

- Measurement of the vaginal fluid's creatinine content can sometimes be used to confirm its origin.
 - Although creatinine levels in urine vary, with mean levels reaching 113.5 mg/dL, a value > 17 mg/dL is consistent with urine.
 - In contrast, fluid with a concentration < 5 mg/dL is highly unlikely to be human urine.
- Retrograde bladder instillation of visually distinct solutions such as sterile milk or dilute methylene blue or indigo carmine can often indicate a fistula and aid in its localization.
- A **three-swab test**, commonly known as the “tampon test” is recommended
 - Two to four pieces of gauze sequentially packed into the vaginal canal.
 - A diluted solution of methylene blue or indigo carmine is instilled into the bladder using a transurethral catheter.

- After 15 to 30 minutes of routine activity, the gauze is removed serially from the vagina, and each is inspected for dye.
- The specific gauze colored with dye suggests the fistula location-a proximal or high location in the vagina or the innermost gauze and a low or distal fistula or the outermost.

- **Cystourethroscopy** is another valuable diagnostic tool and vaginoscopy.
- **CT-scanning**
- **Intravenous pyelography (IVP)**
 - can adequately confirm integrity of the upper collecting system and exclude ureteral involvement in a fistula
- **Voiding cystourethrography (VCUG)**
 - can help confirm the presence, location, and number of fistulous tracts
- **Transabdominal sonography**

TREATMENT

Conservative Treatment

- Approximately 12 percent of women treated by sustained catheterization alone had fistulas that healed spontaneously.
- Fibrin sealant also colloquially called fibrin glue can be used

Surgical Treatment:

- Fundamentals of genitourinary fistula repair include accurate fistula delineation; adequate assessment of surrounding tissue vascularity; timely repair; multilayer, tension- free, and watertight defect closure; and postoperative bladder drainage.

Timing of Repair

- One principle of fistula repair dictates that, a repair be performed in non-infected and non-inflamed tissues.
- Early surgical intervention of uncomplicated fistulas within the first 24 to 48 hours following the inciting surgery.
- In instances of extensive and severe inflammation, we recommend delaying operative repair or 6 weeks until the inflammation subsides.

Route of Surgical Repair

- Vaginal: Latzko technique, classical technique
- Abdominal (Transperitoneal): This approach is used or situations in which the fistula:
 - 1) is located proximally in a narrow vagina,
 - 2) lies close to the ureteral orifices
 - 3) is complicated by a concomitant ureteric fistula
 - 4) persists after prior repair attempts,
 - 5) is large or complex in configuration, or
 - 6) requires an abdominal interposition graft, described in the next section

Sample history

C/c: Involuntary Leakage of urine of 05 months duration

HPI:

This is a 52 years old para 6(all alive) lady who has been amenohric for the past 3 years, she was relatively health 5mo ago at w/c time she started to experience involuntary leakage of urine, w/c started 2 weeks after delivering her last child by C/S(b/c it comes in upside down) after a lobur of 2 days and is continues and small in amount and not associated with cough, since than she has no sexual contact and not participating in any social gathering.

Otherwise she has on Hx of

- vaginal discharge and itching sensation
- fever, pain,
- radiation therapy,
- malignancy ,
- trauma ,
- foreign bodies

Don't forget obstetrics and gynecological Hx

See physical examination and investigation above

REFERENCE

1. **Williams Obstetrics, 24th edition and 25th edition**
2. **Gabbe Obstetrics, Normal and Problem Pregnancies, 7th edition**
3. **Current Diagnosis and Treatment, Obstetrics And Gynecology, 11th Edition**
4. **DC Dutta's Textbook Of Obstetrics 7th Edition**
5. **Jimma University Specialized Hospital Obstetrics and Gynecology Management Guideline, 2010G.C**
6. **Williams gynecology, 3rd edition**
7. **Berek and Novak's Gynecology, 14th edition**
8. **Up-to date 2018**

PROM Chart

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