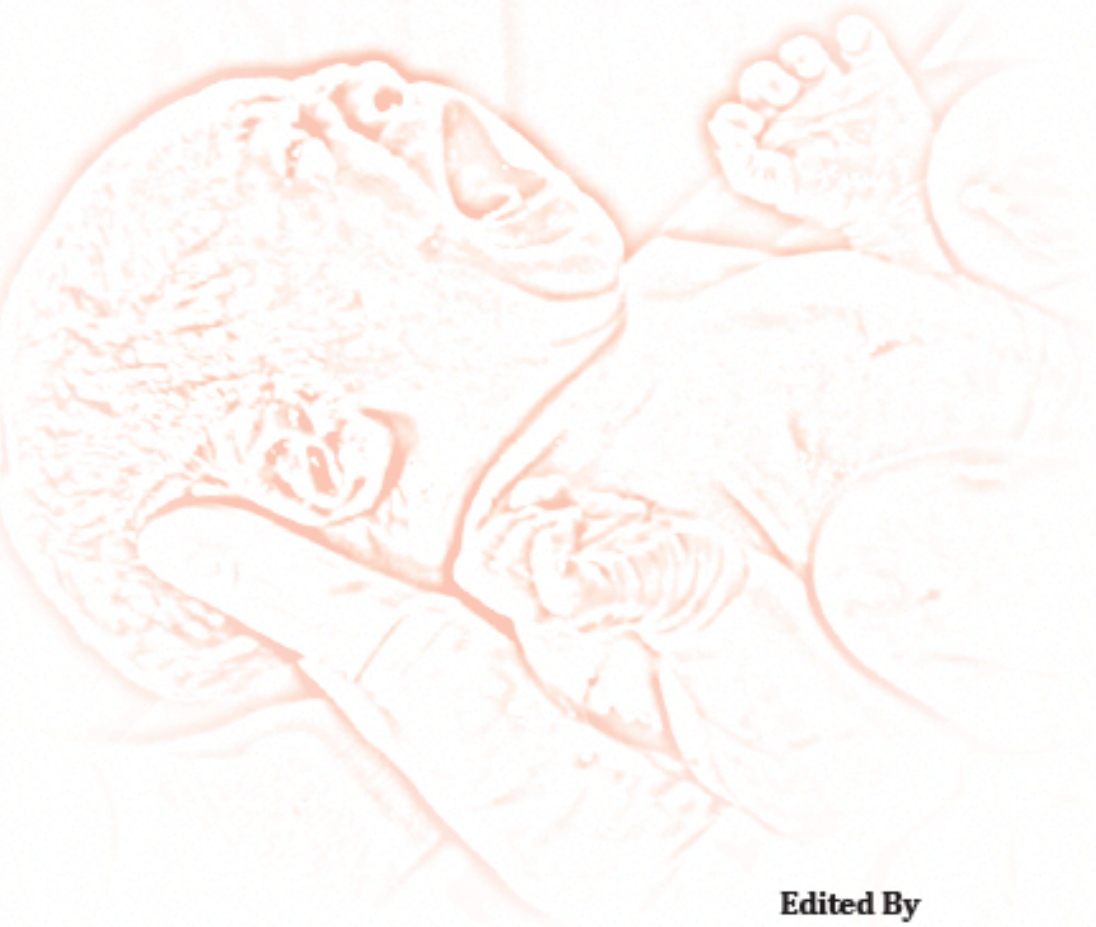
OBSTETRICS



Edited By
Hassan A Nasrat

The Text Book for Undergraduates

The Book and the Author

This book is written with the students in mind. It does not only addresses what a medical student should know for his/her examination but also what they need to know in their clinical practice as graduate doctors or even a residents in Obstetrics and Gynecology program.

Each chapter begins with a paragraph that describes the core objective of the subject, followed by highlight box of the "learning objectives" to be achieved.

The book is easy to read, direct to the point and taking care of ethical and legal issues relevant to our community.

The author has more than 35 years of experience in setting up curricula, teaching and examinations of both under and postgraduate students. He is former Chairman of the Department of Obstetrics and Gynecology, Member of the Scientific Council and the Examination Committee for Obstetrics and Gynecology of the Saudi Commission for Health Specialty, and Chairman of the Reference Committee of the Royal College of Obstetrics and Gynecology in Saudi Arabia. He is Director of the Fetal Medicine Unit and Chairman of the Unit of Bioethics at the Faculty of Medicine, King Abdul-Aziz University.

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Chapter 1

Anatomy of the Female Pelvis

Dr Sama Nazer

By the end of this chapter you should be able to:

- Describe the female pelvis:
  - Boundaries of inlet, cavity, outlet and dimensions of normal pelvis.
- Describe the components of the pelvic floor:
  - Muscles and ligaments of the pelvic floor and its attachments
  - Compartments of the pelvic floor
- Describe the anatomical landmarks of female perineum:
  - The contents and boundaries of the urogenital and anal triangle and its relevant clinical significance
  - Nerve supply of the perineum.
- Describe the relevant of gross and histological anatomy of the uterus:
  - The upper and lower segment.
  - The layers of the uterus.
- Describe the vascular supply of the pelvis:
  - Uterine, vaginal and perineal vascular supply.
- Describe the Innervation of the pelvis:

Anatomy of the Pelvis: (Figure 1-1)

The bony pelvis is a basin shaped ring formed by four bones: two hip bones (consisting of the ilium, ischium, and pubis) and the sacrum and coccyx. The ileopectineal line divides the pelvis into the false pelvis above and the true pelvis below the line and the pelvic cavity in-between. The normal female pelvis is described as "gynecoid" to be differentiated from the male "android pelvis".

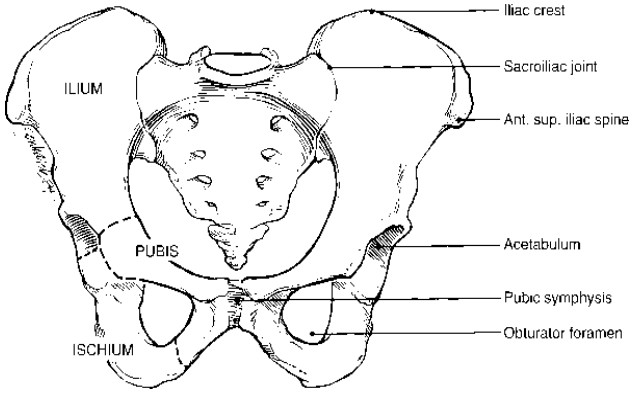

Figure 1-1: Frontal superior view of a "Gyncoid" female pelvis. The plane of the pelvic brim faces forward and forms an angle of about 60 degrees to the horizontal. The features that most clearly distinguish the female from the male "Android" pelvis include a wider subpubic angle, wider sciatic notch, and greater distance from pubic symphysis and anterior edge of the acetabulum.

The pelvic inlet "pelvic brim: (Figure 1-2) The boundaries of the inelt are posteriorly the sacral promontory, laterally the ileopectineal line, and anteriorly the superior aspect of the pubic symphysis. The most important diameters of the pelvic inlet are:

1. The antero-posterior (AP) diameter from the upper border of the symphysis pubis to the sacral promontory (11-12 cm).
2. The transverse diameter is the widest part of the brim (13 cm). Engagement of the fetal head usually occurs through the transverse diameter.

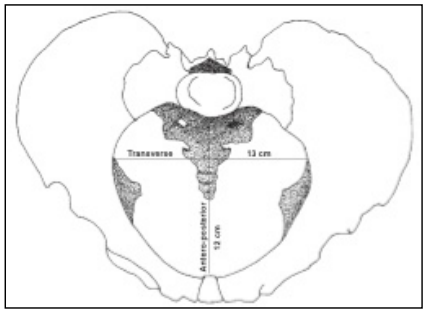

Figure 1-2: The pelvic Inlet "Brim"

The pelvic cavity is the curved canal between inlet and outlet. In the normal female pelvis the cavity is circular in shape and curves forwards. All its diameters measure approximately 12 cm.

The pelvic outlet (Figure 1-3) is diamond-shaped and bounded posteriorly by the caudal sacrum and coccyx, laterally by the ischial tuberosities and sacrotuberous ligaments, and anteriorly by the inferior aspect of the pubic symphysis and ischiopubic rami. Anteriorly the two pubic bones make the pubic arch, which in the normal female pelvis forms an angle not less than 90°. A narrow angle will force the fetal head at delivery posteriorly and thus increase the risk of perineal tear.

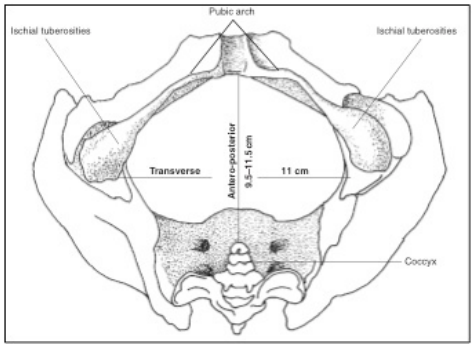

Figure 1-3: The pelvic oulet

The most important diameters of the pelvic outlet are:

1. The transverse diameter is measured between the two-ischial spines and is normally 10.5–11 cm.

2. The antero-posterior diameter is measured from the apex of the pubic arch to the sacro-coccygeal joint and is normally approximately 13 cm. During birth, the coccyx bends backwards to increase the diameter of the pelvic outlet.

Pelvic ligaments: (Figure 1-4)

The major two pelvic ligaments are the sacrospinous and sacrotuberous ligaments. During pregnancy temporary changes takes place in the ligaments that permit both movements and enlargements of the pelvic cavity, which are important changes during parturition.

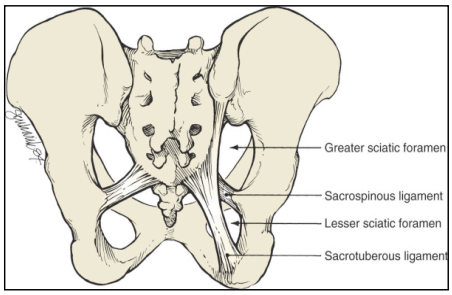

Figure 1-4: The major pelvic ligaments

The ligaments create the greater and lesser sciatic foramen.

The greater sciatic foramen allows for the exit of major neurovascular structures, such as the sciatic nerve, the nerve to the quadratis femoris, and the major vasculature to the gluteum and posterior thigh.

The pudendal neurovascular bundle exits out of the greater sciatic foramen and reenters the pelvis through the lesser sciatic foramen. This is the site for administration of pudenal block for local anesthesia.

Pelvic Diaphragm and Ligaments: (Figure 1-5)

The pelvic diaphragm or pelvic floor consists of number of muscles and ligaments. The two main muscles are the levator ani muscle group and the coccygeus muscles.

The levator ani: is composed of three muscles: Pubococcygeus, puborectalis, and iliococcygeus. These muscles extend from the lateral pelvic walls downward and medially to fuse with each other posteriorly. The levator hiatus lies anteriorly and accommodates the urethra, vagina, and anus.

The coccygeus is a triangular muscle that occupies the area between the ischial spine and the coccyx. It arises from the ischial spine and inserts onto the sacrum and coccyx.

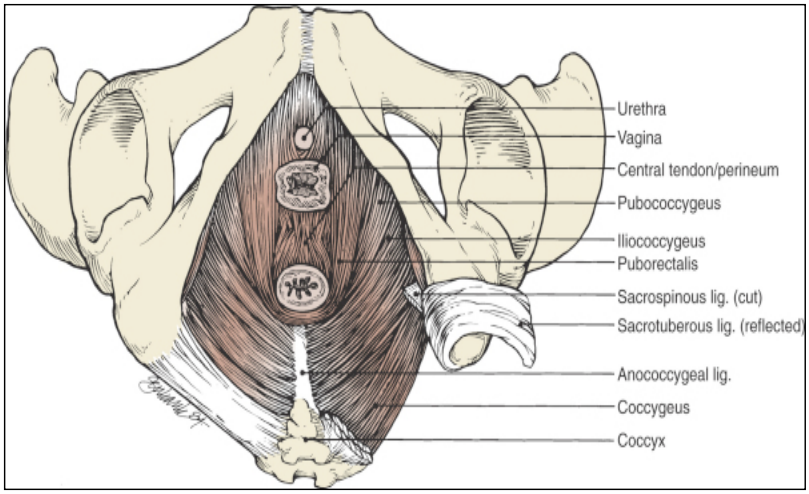

Figure 1-5: Inferior view of muscles of the pelvic diaphragm.

The Perineum: (Figure 1-6)

The perineum anatomically is divided into two distinct parts (or triangles), an anterior or urogenital triangle and a posterior or anal triangle. The midline attachment forms a fibromuscular mass called the perineal body. The perineal body is an important structure between the anal canal and the vagina.

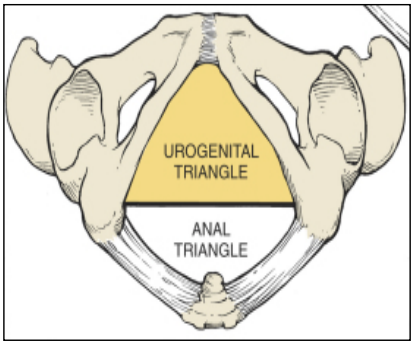

Figure1-6: the anatomical triangles of the outlet

- The urogenital triangle is further subdivided into superficial and deep perineal spaces by a fibromuscular septum called the urogenital diaphragm.

The superficial perineal Space: (Figure 1-7) space is bounded by three sets of muscles, the ischiocavernosus, bulbocavernosus (the sphincter of the vagina), and superficial transverse perinei. It also includes the Bartholin's glands and the vestibular bulbs. The superficial perineal muscles of the urogenital triangle and the muscles of the anal triangle all converge in the midline.

The deep perineal space contains the deep transverse perineal muscles and the sphincter urethra.

- The anal triangle: (Figure 1-8) The anal triangle is the area of the perineum behind an imaginary line that extends between the ischial tuberosities. It is traversed by the terminal portion of the anal canal with its surrounding external sphincter muscle. On both sides of the anal canal are the ischiorectal fossae, which are potential cone shaped spaces, filled with fat. It lies between the skin and levator ani on each side of the anal canal. Together the two fossae make a horse shoe shape; since they connect posteriorly with each other, anteriorly they are separated by the perineal body.

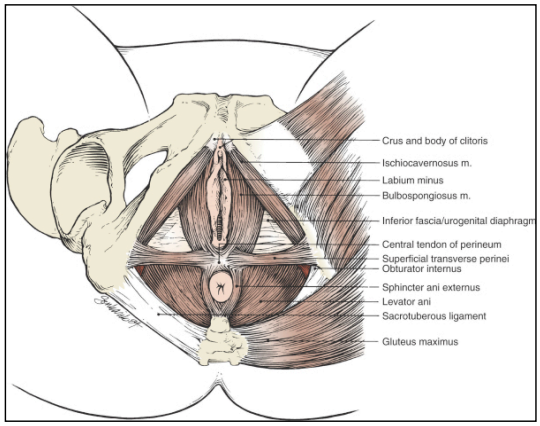

Figure 1-7: the Muscles of the superficial perineal space, as viewed from below. During episiotomy it is important to recognize superficial transverse perinei muscle in order to ensure proper cooptation

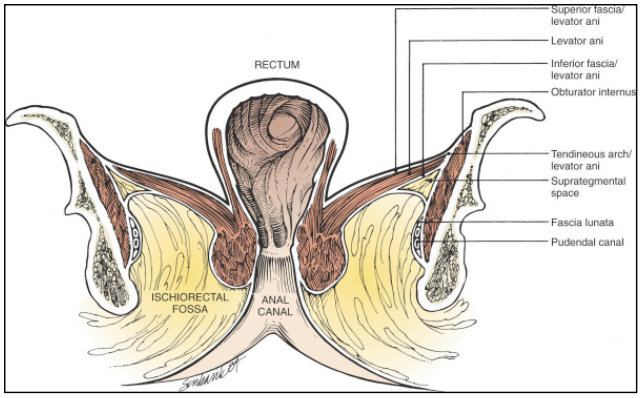

Figure 1-8: The ischiorectal fossa surrounds the rectum and vagina and forms most of the potential space within the posterior triangle of the perineum.

The potential space of the fossae allows distention of the rectum during defecation and the vaginal wall during second stage of labor. It is also a potential space for huge (up to one liter) hematoma collection and abscess formation.

The obturator nerve and internal pudendal vessels run alongside the lateral wall of the ischiorectal fossa in the pudendal or Alcock's canal. This canal is formed from the splitting of the fascia on the lateral wall of the ischiorectal fossa together with the obturator fascia itself.

The external anal sphincter: (Figure 1-9)
The voluntary muscle which is responsible for fecal continence is located within the anal triangle. Its total length is about 2 cm, and it is composed of three components; the subcutaneous, superficial and deep components. The superficial and deep components running on top of each other originate posteriorly from the coccyx and are inserted anteriorly into the perineal body. In between, they diverge to surround the anal canal. The third component, the subcutaneous part, surrounds the anal canal and runs circumferentially around it.

Tear of external anal sphincter is not uncommon during delivery particularly operative one and should be carefully repaired. Failure to recognize tears of the external sphincter or inappropriate repair can precipitate anal incontinence.

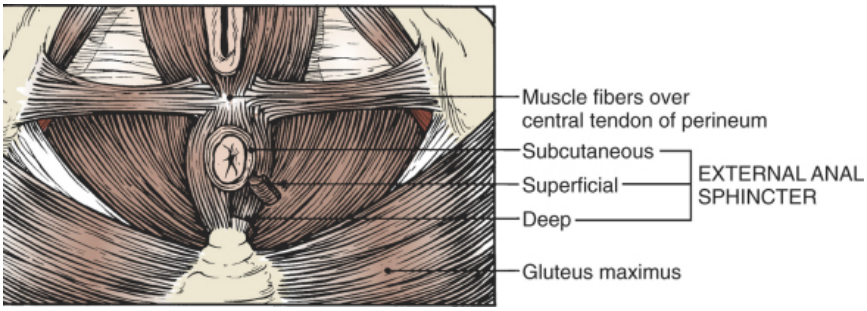

Figure 1-9: The three muscles layers of the external sphincter. Midline or mediolateral episiotomy may damage this sphincter; proper reapproximation is essential for fecal continence.

Nerve supply of the perineum: (Figure 1-10)

The major nerves supplying the skin of the perineum are:
The pudendal nerve (S2-4) carrying both motor fibers to the perineal pelvic floor muscles and sensory fibers to most of the perineal skin, vulva and clitoris. It terminates as the dorsal nerve of the clitoris.
Coccygeal and last sacral nerves (S4, 5): supply skin posterior to the anus and over the. tip of the coccyx.

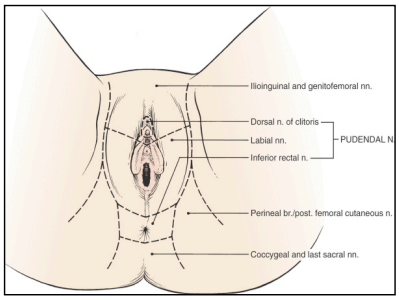

Figure 1-10: nerve supply of the perineum

Perineal branch of posterior femoral cutaneous nerve: supply skin lateral to the anus and the most posterior and lateral portions of the labia majora.
Ilioinguinal nerve (L1) and genitofemoral nerve (L1, 2): These nerves descend from the anterior abdominal wall to supply the skin of the mons pubis and most of the anterior portion of the labia majora (except the clitoris).

The Uterus: (Figure1-11)

The uterus located centrally in the female pelvis between the bladder and the rectum, attached to the lateral sidewall of the pelvis by the broad ligaments. In 75% the uterus is in the anteverted, anteflexed position. On rare occasion a retro-verted gravid uterus may get entrapped within the pelvis and beneath the sacral promontory, giving rise to anterior sacculatoin of the uterus. Clinically this presents with acute retention of urine.

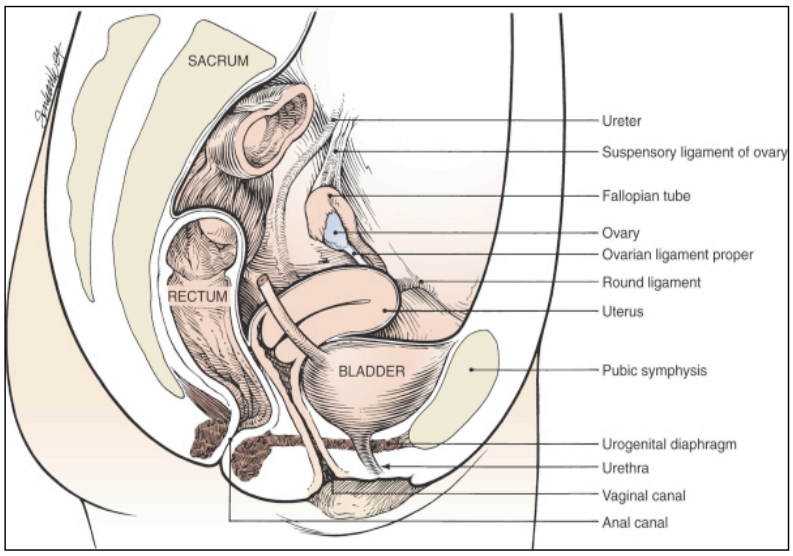

Figure 1-11: Sagittal section of the pelvis. The internal organs of the pelvis are supported by the levator ani. The uterus in 75% of cases is in the anteverted, anteflexed position. The ureter crosses the lateral aspect of the uterus at the level of the internal os on its way to the bladder. The actual position of the ovary and fimbriated end of the tube is variable

The uterus has two main parts: the body and the cervix. The body forms the upper two thirds of the uterus.

- The body of the uterus: is formed of three major parts:

- The fundus is the dome of the uterus above the level of the tubal ostia.
- The body is the part of the uterus that lies below the entrance of the oviducts into the uterus.
- The Isthmus is the short constricted area that marks the junction of the uterine body with the cervix. The isthmus becomes thinner and distends during pregnancy to form the lower uterine segment (Figure 1-13)
- Note that the peritoneal reflection of the bladder occurs at the level of the uterine isthmus.

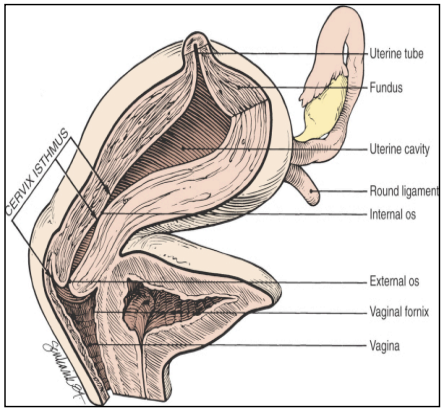

Figure 1-12: Anatomic regions of the uterus, lateral view.

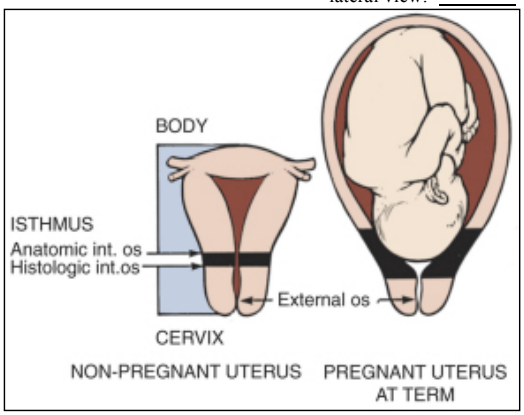

Figure 1-13: The hormonal changes of pregnancy cause the development of the lower uterine segment from the vestigial uterine isthmus

The body of the uterus has three layers: the endometrium, the myometrium and the perimetrium.

The endometrium: is the innermost layer and this is where the fertilized ovum embeds. During pregnancy and childbirth, the endometrium is referred to as the decidua.

The myometrium has longitudinal, circular and oblique muscle fibres and is very expansile. The oblique muscle fibres run “criss-cross” and compress the blood vessels when the uterus is well contracted. It is found mostly in the upper segment of the uterus, where the placenta normally embeds. The richness in muscle finbers and its criss-corss arrangment is important to ensure proper hemostasis following

placental delivery. In contrast to that is the lower uterine segment which is poor in muscle fibers and rich in fibrous tissues. This explains why bleeding in the third stage is more difficult to control if the placenta is implanted in the lower uterine segment as in cases of placenta praevia.
The perimetrium is a layer of peritoneum that covers the uterus except at the sides where it extends to form the broad ligaments. Significant bleeding and hematoma can extend within the layers of the broad ligament into the extra peritoneal space with serious consequences.

The Cervix: It is a tubular structure consists predominantly of collagenous connective tissue and mucopolysaccaride ground substance that pierces the anterior wall of the vagina. It communicates with the uterine cavity through the internal os and with the vaginal canal through the external os.
The endocervical canal is fusiform in shape, about 2.5 to 3 cm in length. It is lined by a single layer of specialized columnar epithelium and secretes mucus to facilitate sperm transport. During pregnancy the glands secretion forms a plug of mucus which helps protect against infection. This plug of mucous comes away stained with some blood just before labour commences. Many women refer to this as the "show".

Vascular Supply of the Pelvis: (Figure 1-14)

The vascular supply of the pelvis and internal pelvic organs are derived from three major sources: The internal iliac, middle sacral, and superior rectal (hemorrhoidal) arteries.
Common iliac arteries:
Originate from the bifurcation of the aorta at the level of the fourth lumber vertebra. Each common iliac artery is approximately 5 cm in length before it divides into the external and internal (hypogastric) arteries.

The hypogastric arteries:
They arise approximately at the level of the lumbosacral joint. They are short vessels (3-4 cm in length) running downwards in the pelvis anteriorly to (crossing) the hypogastric veins and posteriorly to the ureter. Each artery divides into an anterior and posterior division (trunk).

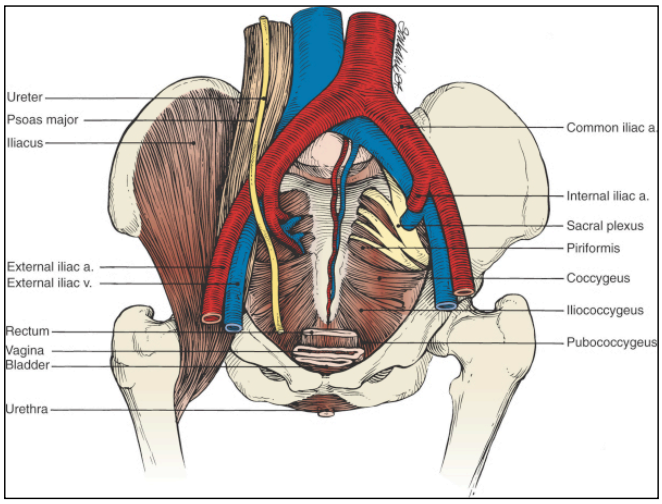

Figure 1-14: The major vascular blood supply of the pelvis. Note the proximity of the ureter to the internal iliac (hypogastric). Ligation of the hypogastric artery may thus jeopardize the ureter unless care is taken. Ligation of the internal iliac artery is one of the measure used in intractable PPH before resorting to hysterectomy.

The uterine artery: (Figure1-15) Arises from the anterior division of the hypogastric artery and runs medially towards the isthmus of the uterus. At the base of the broad ligament it makes an abrupt turn towards the internal cervical os. At this point, the uterine artery crosses over the ureter and reaches the lateral side of the uterus, where it divides into large ascending and smaller descending branches. The ascending branch runs in the broad ligament to finally anastomose with the ovarian artery in the mesovarium.

Throughout its course it gives off 'arcuate' branches to supply the myometrium and unite with the arcuate branches from the opposite side. For this reason, longitudinal incision in the middle of the uterus produces less bleeding than a transverse one. These series of arcuate arteries develop radial branches that supply the myometrium and the basalis layer of the endometrium. They then give rise to the spiral arteries of the functional layer of the endometrium. The descending branches of the uterine artery produce branches that supply the cervix and the vagina and anastomose with the vessel from the other side. Because both the uterine and ovarian arteries provide the blood supply of the uterus therefore in intractable post partum hemorrhage, bilateral hypogastric arteries ligation may not be enough to stop the bleeding.

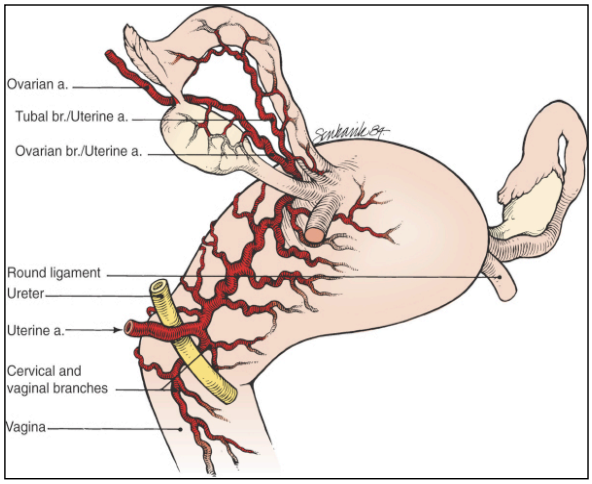

Figure 1-15: The vasculature supply to the major pelvic organs is derived from the internal iliac (uterine) artery and the ovarian artery. Note the anastomotic plexuses of vessels along the lateral aspect of the uterus at the region of the cornu. Descending branches from the uterine artery supply the cervix and vagina.

Blood supply of the vaginal: (Figure 1-16)
The vagina receives its blood supply from the anterior division of the internal iliac artery and/or from the uterine artery. The vagina becomes very vascular during pregnancy.

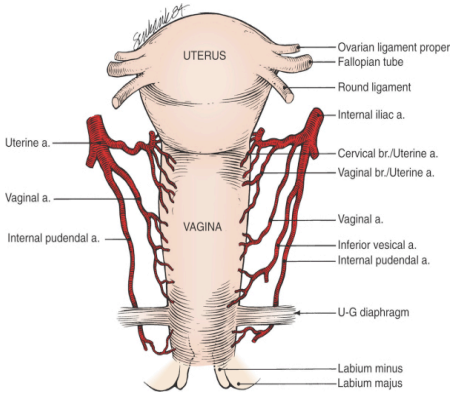

Figure 1-16: the vagina derives its blood supply from two major sources: the uterine and pudendal arteries.

Vessels and nerves of the deep perineal space: (Figure 1-17) The vasculature and innervation to the deep perineal space enters the anterior triangle from superior to inferior, in contrast to the superficial perineal space vessels and nerves. The Internal Pudendal artery which is the terminal branch of the hypogastric artery supplies branches to the rectum, labia, clitoris and perineum.

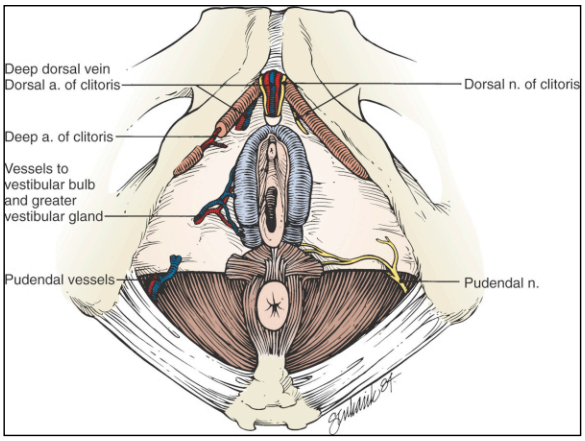

Figure 1-17: Vessels and nerves of the deep perineal space. Note that the blood supply and innervation to the vestibular bulb and greater vestibular gland (Bartholin's gland) are derived from the deep perineal vessels and nerves

Innervations of the Pelvis: (Figure 1-18)

Afferent Sensory fibers from the uterus accompany the sympathetic nerves that enter the nerve roots of the spinal cord at T11 and T12. Hence referred uterine pain is often felt in the lower abdomen.

Afferent sensory fibers from the cervix and upper end of the vagina enter the spinal cord in nerve roots of S2, S3 and S4. Hence referred pain from cervical inflammation is characterized as low back pain in the lumbosacral region.

The lower end of the vagina is innervated by the pudendal nerve. The exact line of demarcation between these two distributions is ill defined.

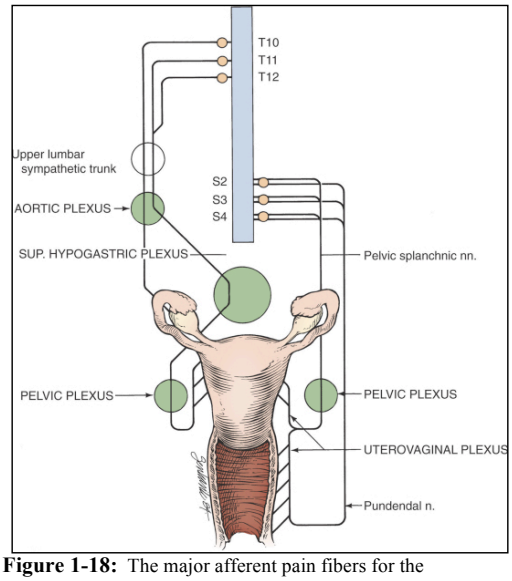

Figure 1-18: The major afferent pain fibers for the uterus, tubes, and ovaries enter the cord at T10, T11, and T12. The afferent innervation of the vagina and external genitalia enter at S2, S3, and S4

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Chapter 2

Approach to the Obstetric Patient

Professor Tarik Zamzami

By the end of this chapter you should be able to:

- Take systematic history of obstetric patient.
- **Identify risk factors:** in each of the history sections and its potential impact on current pregnancy.
- **Perform general examination:** of obstetric patient.
- **Perform obstetric examination:** in the different trimesters of pregnancy.
- Perform the Leopold's maneuvers in the third trimester and realized the objective of each one.
- **Define each of the following terminology**: Fetal Lie, Presentation, and attitude, cephalic engagement, position, and attitude.

Obstetric History

Pregnancy is usually a happy occasion; therefore a pregnant woman is not a "patient" in the real sense. However once a woman gets pregnant she is becomes exposed to potential risks than non-pregnant woman. She is also often has concerns and worries about her fetus and herself that need to be addressed and alleviated. Therefore the approach when taking history and performing examination of a pregnant woman should differ in several respects from doing the same in other circumstance.

The objectives of obstetric history are:

- To identify potential risk factors, and accordingly plan the level of antenatal care for the woman during the pregnancy.
- Patient education regarding the various aspects related to pregnancy and childbirth.
- Addressing any special concerns that the patient might have.

Elements of obstetric history:

Personal Data:

- This should include name**,** age, occupation and marital status (married, divorced, widow, and duration of same.)

Possible factors of concern:

- Risk of trisomy related to older women
- Age related disorders such as high blood pressure, diabetes etc.
- History of infertility:
- Some occupations may impose risks.

History of present pregnancy:

- First day of the last menstrual period.
- Enquire about any specific complaints or relevant problems.

Whilst it is essential to listen to all complaints described by the patient, it is equally important to be able to differentiate between a clinically significant problem and a non-significant complaint that requires reassurance or simply symptomatic treatment.

Weeks of gestation (EDD) are calculated using the **Naegele's Rule** is a standard way of calculating the due date for a pregnancy. The rule estimates the expected date of delivery (EDD) by adding one year, subtracting three months, and adding seven days to the first day of a woman's last menstrual period (LMP). The result is approximately 280 days (40 weeks) from the LMP.
- Date of the first day of last menstrual period, followed by use of the modified rule of Nägele by adding nine months and seven days.

Example; First day of last menstrual period was January 10th
EDD(using rule of Nägele) will be October 17th.

It is important to note the following:
Nägele's rule is dependant on the following factors;

1. The woman is certain of her LMP .
   (as few as 30% are certain)
2. Her menstrual cycles are normal, and occurring every 28 days.
3. Menstrual flow in last period was normal, and like all previous periods.
   (Some women are already pregnant, but experience slight bleeding around the expected date of their period, and mistakenly consider it a period)
4. Use of contraceptive pills, either immediately or shortly before last menstrual period.
   (Some women may develop post-pill amenorrhea before they conceive, leading to a false prolongation of gestational period)

Previous obstetric history:

A detailed history of past obstetric performance should be obtained under the following headings:

- Dates of deliveries, or miscarriages.
- Location of each delivery or miscarriage,(home or hospital).
- Duration of each pregnancy, noting any significant complications such as hypertension or diabetes…etc.
- Type of labor (spontaneous or induced)If induced, for what reason?
- Type of delivery; was it vaginal or by caesarean section? For operative delivery try to establish reason for operative intervention and whether there were complications or not.
- Puerperium complications: a helpful question is to ask about blood transfusions, and time of discharge from hospital.
- Outcome; Sex and birth weight of fetus, feeding method and any complications such as congenital anomalies or admission to neonatal unit. An ideal question to ask is if the mother heard her baby cry immediately after birth, and if the baby was discharged home with her.
- Miscarriage? Was surgical evacuation performed?

Menstrual History:

The importance of obtaining an accurate menstrual history is to obtain the date of first day of the last normal menstrual period (LMP). This should be verified in the present obstetric history. Menstrual pattern prior to the LMP is not significant in obstetric cases.

Contraceptive History:
Type, when started and duration of previously used contraceptive methods, particularly in relation to the current pregnancy (a pill period would make the date of the LMP unreliable). Enquiry should be made if there were any complications, e.g. thromboembolic complications with hormonal contraceptive pills, or pregnancy whilst intrauterine contraceptive device in situ.

Medical History:
- Current significant medical illness e.g. hypertension, diabetes…etc.
- Long term use of medications e.g. steroids, thyroid replacement…etc.
- Any known allergies.

Surgical History:
All details of previous surgery, including date, type …etc., and any relevant complications including anesthesia related complications, should be recorded.

Social History:
It is important to record all relevant social data including;
- Educational background and occupation. (Some occupations may impose a hazard to the conceptus).
- Habits including smoking, drug abuse, alcohol intake.
- Occupation of husband and evaluation of socio-economic status.

Obstetric Examination:

At the time of the first antenatal visit, a full general and obstetric examination should be performed. The objective of this examination is to establish a baseline data. Additionally, it is not uncommon that some disorders are accidentally discovered for the first time during pregnancy e.g. cardiac disease.

During examination, a courteous and professional approach should be followed. The examination table should be in a position that maximizes patient privacy. The woman should be made comfortable, covered with a sheet or blanket, exposing only the part of the body to be examined. A chaperone nurse should be present at all times.

General Examination:

- Vital signs; Blood pressure, pulse and temperature should be obtained. A baseline record of weight and height is recorded.

In pregnancy measurement of blood pressure should be performed with the patient sitting, or in a semi recumbent position. The sphygmomanometer is placed at the cardiac level. In the supine position, blood pressure tends to be lower due to supine hypotensive syndrome.

General impression; Signs of anemia, body build, with signs of poor nutrition or obesity noted and recorded.

Mouth should be examined for signs of gum disease, or tooth decay. If necessary a referral to a dentist should be made.

Neck examination for signs of goiter or abnormal swelling.

Chest examination, heart and lungs. Diastolic murmur may be present in as many as 80% of pregnant women. This is usually due to hyperdynamic circulation in pregnancy, rather than manifestation of cardiac disease.

Examination of the lower limbs: for oedema and varicose veins.

Internal pelvic examination; Unless there is an indication such as symptoms of vaginitis, or other specific complaints, internal pelvic examination is NOT a standard step of normal obstetric examination.

Abdominal obstetric examination:

The approach and objectives of abdominal obstetric examination differ according to gestational age. In early pregnancy where the uterus is mostly a pelvic organ abdominal examination follows that same principles and have the same objectives as in non-pregnant women. While in late in pregnancy particularly in the second half of the third trimester obstetric examination follows standard steps or maneuvers called "Leopold's Maneuvers". Its final objectives are to determine the lie and presentation, whether the presenting part is engaged or not and whether the size of the fetus (or gestational age) is compatible with the menstrual age or not.

Inspection; for abdominal contour, movements of abdominal wall, distribution of abdominal hair, scar of previous cesarean section or other surgery should be noted and recorded. Other abnormalities such as divarication of the recti muscle, or noticeable hernias should be recorded. Symmetry of uterine distension becomes an important observation in the third trimester, as asymmetry could suggest abnormal fetal lie.

Palpation:

In the first trimester, the uterus is usually not palpable abdominally until 12-14 weeks. Exceptions to this occur in extremely slim women with an anteverted uterus. Therefore, a standard superficial and deep abdominal palpation should be performed until then. Once the uterus is enlarged enough to be an obvious abdominal organ (usually after 18 or 20 weeks) the standard technique of palpation for organomegaly (liver and spleen) is not as reliable as in non pregnant state and certainly not be performed in the third trimester.

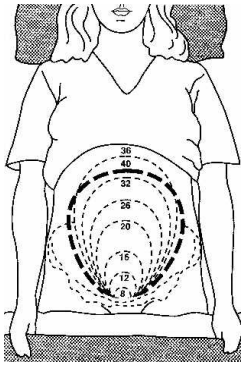
In the second trimester until almost the 28^{th} week, the objective of abdominal examination is to define the fundal height. This is usually done in relation to specific land marks (Figure 1-2) *at the umbilicus the uterine fundus corresponds to about 20 weeks, midway between the symphysis pubis and the umbilicus, corresponds to about 16 weeks, four fingers above the umbilicus is approximately 27 weeks.*

To elicit the fetal heart is a routine part of the examination, and one that usually adds to the contentment of the woman, (lowering any level of anxiety). Using an electronic Doppler device, the fetal heart can be detected by 11 to 12 weeks of gestation.

In the third trimester, and as the woman approaches term, it becomes increasingly important to screen for fetal growth. Equally important, is to define fetal lie, presentation, engagement…etc.

Clinically the examination includes:

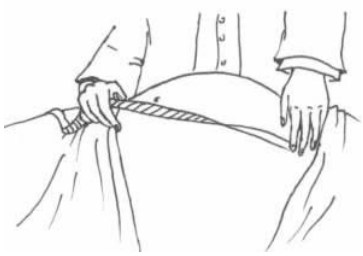
- Fundal level; estimated by placing the ulnar border of the straightened hand, at the highest point of the uterus, and comparing this with acceptable levels for different periods of gestation **(Figure 2-1).**



(Figure 2-1) The xiphisternum being a reference point for full term pregnancy, the umbilicus for 20 weeks gestation. Between the umbilicus and xiphisternum the area is divided into 4-5 equal divisions (each is approximately 2-3 finger breadths, each representing a period of 4 weeks.). Note that at full term (40 weeks) if the head becomes engaged the fundal drop, a symptom known as "lightening" which what the patient feels.

- Symphysis fundal height measurement:

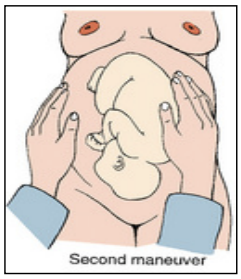
Because estimation of gestational week and/or fetal growth by clinical palpation for fundal level was found to be inaccurate and liable to subjective variation between different examiners, the method of symphysis fundal measurement was introduced. With the patient lying supine and comfortable, abdominal palpation is performed to identify the fundal level. A non-stretchable tape measure is used with the centimeters on the underside to reduce bias. The distance from the top of the fundus to the top of the symphysis pubis is measured (Figure 1-2). This technique has its value as cheap, simple screening method of fetal growth abnormalities after 24-26 weeks of gestation.



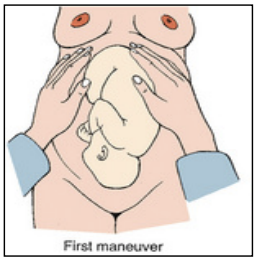
(Figure 2-2) Symphysis fundal height measurement. Although more reproducible than clinical palpation but factors such as hydramnios, multiple gestation and obesity will affect its accuracy.

Leopold's Maneuvers: The standard obstetric palpations performed in the third trimester. Comprised of five maneuvers, each with a specific objective as follows;

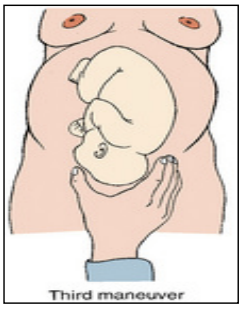
1. The Fundal palpation (grip): The objective is to define the part of the fetus occupying the uterine fundus, whether head or breech. The procedure is performed while facing the head of the patient. The hands of the examiner are placed on the sides of the uterine fundus, following its contour. The head is hard, smooth, rounded, and ballot (ballottement means the head can bounce backwards and forward between the examiners hands). The breech is softer, less defined in shape, and does not ballot.



2. Lateral Palpation (umbilical grip): Its primary objective is to define the fetal lie. A secondary objective, to define the fetal back. Whilst in the same position, the hands of the examiner are moved down to the level of the umbilicus. With gentle pressure and dipping movements, the lie can be ascertained. In most cases the continuous resistance of the back can be felt on one side with the fetal limbs felt as mobile irregularities on the other side. The procedure is made easier, if alternate hands are used to steady the trunk, and push it towards the opposite examining hand. If the fetus is in a posterior position (occipitoposterior) the limbs will be felt on both sides of the midline, or clearly felt to one side.



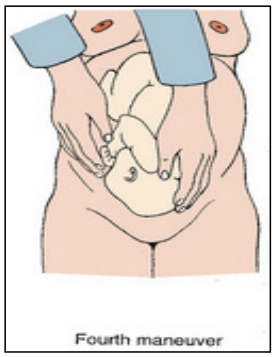
3. Pelvic Palpation (first pelvic grip): Its objectives are to determine the presenting fetal pole, and in the case of cephalic presentation, the degree of flexion, and engagement. The fingers of one hand are well spread, and placed in the suprapubic skin fold which runs out to each iliac fossa. Findings are mainly derived from the thumb and middle finger, which move in a coordinated scanning fashion.



The degree of flexion is determined from the relative level of the occiput and sinciput.

The degree of head descent is determined from the amount of presenting part which is out of the pelvis. It is common to use a numerical system to describe the degree of head descent. The range is from 5/5 to 0/5 for a head that is just sitting on the pelvic brim to a deeply engaged head (hardly palpable abdominally).

4. Deep pelvic palpation (second pelvic grip): To determine the degree of head flexion. Not a routine step, but may be applied if the presenting part is not easily palpable by the first pelvic grip, as in late pregnancy or in labor. It also provides additional information regarding cephalopelvic relationship. The examiner turns to face the patient's feet. The hands are placed over the sides of the lower uterus. In cephalic presentation, the two prominences of the head are located and an estimate is made of attitude, by comparing the relative heights of sinciput and occiput. In a well-flexed head the sinciput will be 2-4 cm higher than the occiput.


Fourth maneuver

Auscultation of the fetal heart sounds: The site for best detection of fetal heart depends on the period of gestation, the presentation and the position of the fetus. Therefore in later pregnancy, the point of maximum detection of the fetal heart could assist in determining the fetal position. An example of this is in the third trimester with cephalic presentation, if the fetus head in the left occipito-transverse position, the fetal heart sounds are best heard below the umbilicus and to the left, over the anterior shoulder of the fetus being the nearest point to the fetal heart. In breech presentation, it is located above the umbilicus, and in direct occipito-posterior position it is best heard below the umbilicus in the midline.

Definitions:

Fetal presentation is a term that describes the first part of the fetus, which presents at the cervix **Fetal Lie**: Is the relation of the longitudinal axis of the fetus to the longitudinal axis of the uterus. The fetal lie can be longitudinal, oblique or transverse.

Head Engagement: It is defined as passage of the largest diameters of the fetal head through the pelvic brim. In a well-flexed head with "*vertex presentation" the biparietal and suboccipitobregmatic diameters* are the largest diameter. Engagement of the head in the pelvis is a reassuring sign that there is no major cephalopelvic disproportion.

Clinically the diagnosis of engagement is made when only 2/5 of the head is palpable by the first pelvic grip, and the occiput is not felt abdominally.

For women in labor the diagnosis of engagement is made by vaginal examination when the presenting part descends to the level of the ischial spine.

In primigravidas, because of the abdominal muscle are still strong, it facilitate descent of the fetal head towards the pelvic brim and it gets engaged usually during the last one or two weeks of pregnancy.

Determination of the fetal presentation, lie and engagement are important in the last few weeks of pregnancy as the patient approach term.

Fetal position: The relationship of a nominated site of the presenting part to a denominating location on the maternal pelvis. In cephalic presentation the nominated site is the occiput (e.g. left occiput anterior LOA). In breech presentation the nominated site is the sacrum (e.g. right sacrum anterior RSA) (see chapter 10 "malposition and malpresentation). The importance of examining for fetal position is during labor when it can be assessed during vaginal examination.

Attitude: Refers to the position of the head with regard to the fetal spine (i.e. the degree of flexion and/or extension of the fetal head). Flexion is important to facilitate engagement of the head in the maternal pelvis. In a well-flexed head the engaging diameter is the smallest diameter, which is suboccipito-bregmateic diameter (9.5 cms)

References and further readings:

- Reproductive health indicators-guidelines for their generation, interpretation and analysis for global monitoring WHO. Department of Reproductive Health and Research. *Reproductive health indicators—guidelines for their generation, interpretation and analysis for global monitoring*. Geneva, World Health Organization, 2006.

Chapter 3

Placental and Fetal Physiology

Dr Sara Ghazali

During prenatal life, the fetus goes through phases of growth, organ differentiation and maturation. At all times it depends on the placenta for gaseous exchange (lung functions), nutrients supply (gastrointestinal function), and excretion of metabolic waste products (kidneys function). In addition the placenta produces important peptide and steroid hormones which plays crucial function in the establishment, maintenance of pregnancy.

The normal environment of the fetus is the amniotic fluid. Those unique features are the subject of 'fetal physiology" which will be addressed in this chapter.

By the end of this chapter you should be able to:

- List the functions of the placenta: Nutrient transfer, gaseous exchange and hormonal production.
- Define the placental barrier and its component.
- Describe the different mechanisms of placental transfer for nutrients.
- Describe the mechanism of "O2 and CO2" exchange The fetal O dissociation curve and Boher effect
- Describe the difference between fetal and adult circulation.
- List the changes the take place in the fetal circulation at birth.
- Describe the phases of fetal lung maturation
- List the tests used in assessment of fetal lung maturity.
- Describe the stages of hemoglobin maturation and relation to Hemoglobinopathies.

Amniotic fluid as the normal fetal physiological environment and its circulation.

- The fetal vs. adult circulation and the changes from fetal to adult circulation at birth.

Differences between adult and fetal hemoglobin

Physiology of the placenta

The placenta is the interface between the mother and the fetus. It performs several critical functions including gaseous exchange (respiratory function), nutritional supply (gastrointestinal function) and eliminate fetal waste products (renal functions). In addition it produces important peptide and

steroid hormones that have crucial roles in the establishment and maintenance of pregnancy.
The processes of placentation, anatomic and histologic aspects of the placenta are discussed in Chapter ----- of the Gynecology volume of this book. This section focuses on placental function and physiology.

From the physiological point of view, the functions of the placenta can be considered under two main headings: 1) Endocrine functions and 2) Transfer functions.

1) Placenta Endocrine Functions:

The hormones produced by the placenta are: 1) Peptide hormones and 2) Steroid hormones. Figure 3-1 shows the main hormones produced by the placenta and their principle functions. Collectively those hormones are responsible for modulating the maternal physiological system to adapt the growing fetus demands, stabilization of the pregnancy and initiation of labor.
The most important hormones are:

- Human chorionic gonadotropin"hCG": Its primary function is to maintain the endocrine activity of the corpus luteum (i.e. the synthesis of progesterone during the early stages of pregnancy. It can be detected in maternal serum as early as day 8 after conception. The level of hCG rise throughout the early stages of pregnancy and reach their maximum level at week 8 of gestation. By week 13, the level drops dramatically and reaches a low steady state. By this time the placenta produces enough progesterone to support the pregnancy.
- Human placental lactogen "hPL": The principal function of hPL is to increase the supply of glucose to the fetus by decreasing maternal stores of fatty acids. It does this by altering maternal secretion of insulin.
- Progesterone: Progesterone is necessary for the maintenance of a quiescent, non-contractile uterus. The hormone has anti-inflammatory and immunosuppressive functions, which protect the conceptus from immunological rejection by the mother.
- Estrogens: The placenta alone is not capable of estrogen production as it cannot hydroxylate C21 steroids at the 17 position. Therefore the placenta receive dehydroepiandrosterone sulfate (DHEAS), the substrate

for estrone and estradiol, and 16-hydroxy-DHEAS, the substrate for estriol primarily from the fetal adrenal.

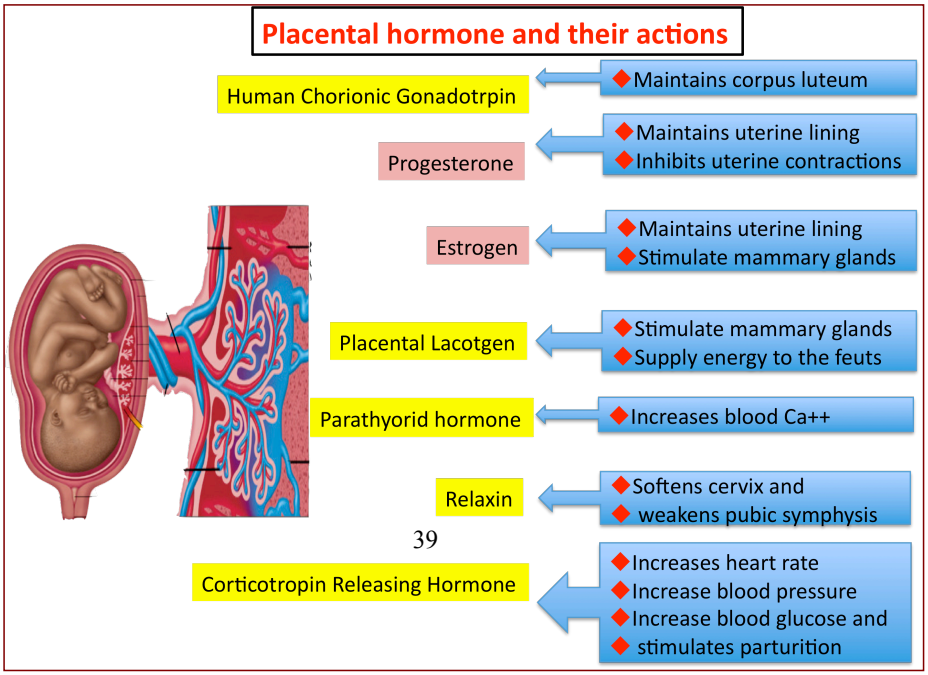
- Corticotropin releasing hormone "CRH": This hormone plays a role in both term and preterm birth since it enhances prostaglandin production by amnion, chorion, and decidua. CRH can also directly augment myometrial activation.

In normal pregnancy the CRH level raises throughout gestation but its free level do not increase because of parallel increase in CRH binding protein (CRHBP) secreted by liver.

At or near term the concentration of CRHBP begins to decrease, so that the level of unbound CRH begins to rise. The rise in CRH stimulates placental prostaglandin production and enhances both fetal and adrenal cortisol synthesis (through the stimulation of the maternal and fetal HPA). Since cortisol has stimulatory effect on placental CRH expression, a positive feed back loop is created where both cortisol and prostaglandins further stimulate CRH release from the placenta. Thus it may be postulated that the placental CRH determines the length of gestation ("placental clock").

If those sequences of events as outlined above occur too early in gestation, PTL and PTB may result. This may be triggered by a rise in adrenal cortisol production, which may occur in association fetal and/or maternal stress.

Figure 3-1: placental hormones and their actions



2. Placental transfer function:

Placental substance Transfer:

The transfer of any substances across the placenta from the intervillous space (maternal blood), to the fetal capillary blood or visa versa, has to traverse the 'placental barrier' i.e the cellular structures that separate the two spaces (**Figure 3-1**). As pregnancy progresses the placental barrier that separates fetal from maternal circulation becomes very thin.

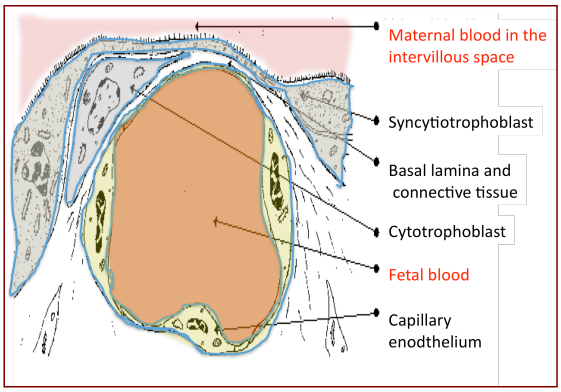


Figure 3-2: The placental barrier. Cross section of a Chorion chorion villous. During the 1st trimester, the villi have a nearly complete cytotrophoblast layer underneath the syncytiotrophoblast layer. Later on, it becomes discontinuous. By the end of the pregnancy, the minimal materno-fetal diffusion distance is about 4 µm.

Mechanisms of placental transfer:

- The main mechanisms of substances transfer across the placental barrier are:
  - Passive diffusion.
  - Facilitated diffusion.
  - Active transport.

  Other mechanisms include:
  - Endocytosis (invagination of the cell membrane to form an intracellular vesicle containing extracellular fluids)
  - Exocytosis (release of the vesicle to the extracellular space).

- The rate of placental transfer is influenced by a number of factors which include:

1. The concentration gradient of the free fraction, as opposed to the protein bound fraction of the substance in the maternal circulation relative to the fetal circulation.
2. The rate of maternal blood flow through the intervillous space.
3. The molecular weight of the substances. Most substances < 500 d MW, diffuse readily across the placenta. Some substances of high molecular weight, such as immunoglobulin G (MW about 160,000), do cross the placenta by way of a specific trophoblast receptor mediated mechanisms.

4. The lipid solubility of the substances. Lipophilic (highly lipid soluble) substances diffuse readily across the trophoblastic membrane, compared to lipid insoluble 'hydrophilic' substances.

SUBSTANCE	TRANSFER MECHANISM	COMMENTS
Glucose	Facilitate diffusion	Glucose is the primary substrate for fetal oxidative metabolism. Various mechanisms of transport have been observed. Although fetal glucose increases as maternal glucose rises, the relation is not absolutely linear.
Amino acids	Active transport	The fetus is dependent on placental transfer of amino acids for protein synthesis for fetal growth. Amino acid concentration in the fetal umbilical cord is higher than in maternal blood, i.e. transport is against a concentration gradient. Individual amino acids may be transported by single or multiple transport proteins.
Lipids	Different mechanisms	Fatty acids are essential for fetal development, both as an energy source and also as a precursor for several important bioactive compounds, such as prostaglandins and thromboxane. Essential fatty acids are transferred more efficiently than non essential ones.
Calcium	Active transport	Level is higher in fetal than maternal blood.
Iron, IgG, Cholesterol / others	e.g. Receptor mediated Endocytosis / Exocytosis	
Respiratory Gases (O2 and CO2)	Simple diffusion or flow limited mechanism. Both oxygen and carbon dioxide are lipophilic molecules	The placental membranes are highly permeable to O2 and CO2. 'Flow-limited,' means that blood flow is the limiting step for exchange of the respiratory gases across this tissue. The partial pressure and the difference between maternal and fetal hemoglobin affinity for O2 are two important factors that determine rate of exchange.

Table 3-1: some substances and its transfer mechanism

Placental Transfer of Respiratory Gases (O2 and CO2):

The exchange of gases across the placenta, fetal O2 uptake and CO2 excretion, are primarily controlled by two variables:
1) Blood flow in the placental and umbilical vessels.
2) The carrying capacities of maternal and fetal blood for O2 and CO2.

- Placental Blood Flow: The uterine blood flow increases as pregnancy progresses. At term it comprises of about 10 % to 15% of the total maternal cardiac output, (approximately 750 ml/min). Of this, about 90% goes to the placenta and the remainder to the myometrium and endometrium.

- O2 Carrying capacity of maternal and fetal blood:

The fetus has several mechanisms that ensure adequate O2 uptake by the fetal red blood cells, while at the same time maintain low venous PO_2 pressure (PO_2 is about 28 mmHg) those mechanisms include:

- A higher concentration of fetal hemoglobin (about 18 g/dl at term), which has higher affinity for O_2 than adult hemoglobin.
- O_2 dissociation curve of fetal hemoglobin is shifted to the left, compared to the adult hemoglobin. This is due to a higher affinity of the fetal hemoglobin (HBF) for O_2 than adult hemoglobin HBA. This results in fetal hemoglobin acquiring larger amounts of oxygen (% of O_2 saturation) at standard conditions of PC O_2, PH and temperature (Figure 3-2).

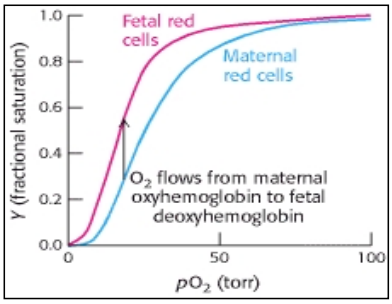


Figure 3-3: Fetal O_2 dissociation curve shifted to the left compared the adult

- Double Bohr effect:

  The release of fetal metabolites (CO_2 and fixed acids) into the maternal blood, results in a fall in the pH of maternal blood, and a rise in the fetal blood pH. Thus, the fetal red blood cells affinity for oxygen uptake increases, while at the same time the maternal red blood cells affinity for oxygen decreases (a Double Bohr effect) (Figure 3-3)

Amniotic Fluid

The amniotic fluid is the normal environment for the fetus. Its volume increases in parallel with fetal growth. At 12 weeks the amniotic fluid volume is approximately 50 ml, reaching 1000 ml at term. It then declines to about 500 ml by 42 weeks.

Origin of amniotic fluid:

The source(s) of amniotic fluid change throughout pregnancy as follows:

- First trimester: the amniotic fluid is mostly formed of transudate of fetal plasma through the highly permeable fetal surface (skin) prior to keratinization. It is very similar in composition to the fetal extracellular fluid. Further contribution to the amniotic fluid comes from transudation of maternal plasma across the chorioamniotic membrane.
- Second and third trimester: The fetal skin mature and is no longer permeable to fetal plasma. At the same time fetal organ maturation progresses. Gradually the fetal urine and lung liquids become the major sources of amniotic fluid. The contribution of the

kidneys and lungs to amniotic fluid increases as pregnancy progresses. At term, fetal urine production ranges between 400 to 1200 ml/day, while the fluid produced by the lungs is about 400 ml/day.

Circulation of amniotic fluid:

The amniotic fluid volume is maintained within a "normal" range due to balance between production (by fetal lung liquid and urine) and reabsorption (through fetal swallowing and to a minimal extent, through flow across the amniotic and/or chorionic membrane to the fetal circulation or maternal uterus).

Functions of amniotic fluid:

- Mechanical protection "cushioned effect" to the fetus and umbilical cord.
- Provide the environment required for fetal musculoskeletal development and movement. (Loss of amniotic fluid, particularly early in gestation is complicated by serious fetal musculoskeletal deformities.)
- Promotion of normal growth and maturation of the fetal lungs and fetal gastrointestinal tract. Fetal breathing movements in utero are essential for pulmonary maturation. Loss of this movement (e.g. due to loss of amniotic fluid early in pregnancy) is associated with lung hypoplasia at birth, which is incompatible with life.
- Antibacterial activity: amniotic fluid inhibits the growth of potentially pathogenic bacteria.
- Maintenance of fetal temperature.

Abnormalities of Amniotic Fluid

Oligohydramnios*: is a condition of decrease in amniotic fluid. Occur in association with conditions such as placental insufficiency, due to decrease in fetal urine output. Fetal anomalies such as fetal renal agenesis or obstructive fetal uropathy.*

Polyhydramnios*: abnormal increase in amniotic fluid may occur due to excessive production e.g. neural tube defect or diminished intake e.g. Fetal GIT obstruction.*

Fetal Circulation

There are crucial differences between fetal and adult circulation. In adults, the circulation is a single closed circuit ,starting with venous blood returning to the right heart, lungs, left heart, and then to the systemic circulation and back to the right heart. Contrary to that, in the fetus there are two parallel circulations **(Figure 3-4)**:

- The left heart pumps well oxygenated blood to the brain and the upper body.
- Whereas the right heart pumps less oxygenated blood to the lower body.

• The blood supply to the brain and upper body:

- Well-oxygenated blood (80% O_2 saturated) coming from the placenta via the **umbilical veins**. It enters the portal system where it supplies branches to the liver, but the majority of the blood bypasses the liver into the **ductus venosus,** which join the **inferior vena cava** to reach the **right atrium**.

- In the right atrium, the well-oxygenated blood (from the ductus venosus flow) splits on the free edge of the inter-atrial septum to be preferentially directed into the left atrium across the foramen ovale.

- From the left atrium it passes to the left ventricle, into the ascending aorta, on to the arteries going to the brain and upper body. This ensures that the brain receives well-oxygenated blood.

• The blood supply to lower body:

- The remaining blood in the right atrium is formed of a less oxygenated stream of blood from the inferior vena cava, which had not passed to the left atrium via the foramen ovale, mixed with unsaturated blood returning via the superior vena cava (25%), is directed into the right ventricle.

- From the right ventricle, the blood passes into the pulmonary artery. However, because of high pressure in the collapsed lung vessels, most of the blood is directed through the **ductus arteriosus** to the descending aorta. Thus, during fetal life, only 5-10 % of the cardiac output goes to the lungs.

- The descending aorta supplies branches to the lower body. However, the major portion of blood is drained along the umbilical arteries, which arise at the iliac arteries (at the bifurcation of the abdominal aorta) to be carried back to the placenta for oxygenation.

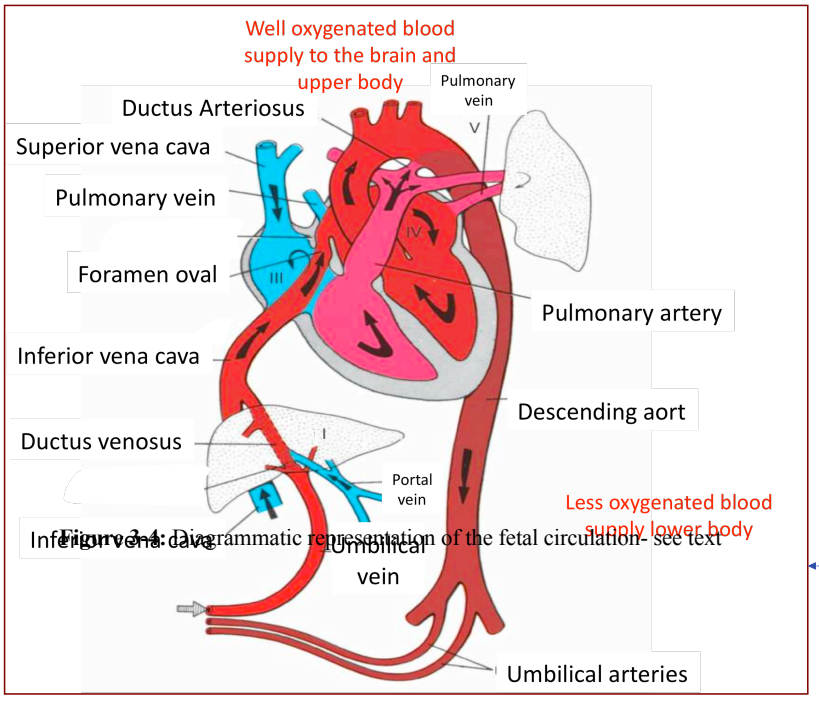


Figure 3-4: Diagrammatic representation of the fetal circulation- see text

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Circulatory changes at birth:

The changes from fetal to adult circulation that occur after birth are secondary to the occlusion of the placental circulation and opening of the pulmonary vessels.

The sequences of changes are as follows:

1. Occlusion of the placental circulation leads to immediate fall in blood pressure in the inferior vena cava and the right atrium.

2. Expansion of the lungs leads to opening of pulmonary vessels and great reduction of resistance to blood flow to the lungs. Thus, the pulmonary circulation is established which result in:

- A rise in the left atrial pressure due to the increase in the arterial blood returning to the left atrium via the pulmonary veins.
- At the same time the right atrial pressure has already fallen.

3. Closure of the foramen ovale: occurs secondary to change in pressures in the two atria..

4.Closure of the ductus arteriosus: Rise of oxygen tension in the blood stimulates release of prostaglandin which contraction of smooth muscles in the wall of the ductus arteriosus. Normally it becomes functionally closed after 10-15 hours.

In this way two parallel fetal circulations become one single closed adult circulation.

Hemoglobin Synthesis and Maturation

Hemoglobin is a tetrameric protein composed of two polypeptide chains (globin) with a heme molecule attached to each chain. The main function of hemoglobin is oxygen pick-up and delivery to tissue.

In humans, there are six distinct species of normal hemoglobin:

- Three appear only during embryonic development: Hb Gower-1, Hb Portland, and Hb Gower-2
- Three are expressed during fetal and adult life, in variable proportion: Hb F, HbA2, and HbA. Following the embryonic phase, fetal hemoglobin (HbF)—composed of two alpha and two gamma globins chains (α_2/γ_2), predominates and remains the dominant hemoglobin during in utero life. **HbF has higher oxygen affinity than adult hemoglobin and allows transport of oxygen to peripheral tissues in "hypoxemic" fetal environment.**
- In the third trimester, the β− and δ-globin genes become active so that there is gradual increase in the amount of adult hemoglobins HbA (α_2/β_2) and HbA_2 (α_2/δ_2). The proportion of adult hemoglobin increases from 0% at 26 weeks gestation to about 30% at term.

- Because of the long life span of circulating red cells, HbF is slowly replaced by HbA. Infants generally do not become dependent on HbA synthesis until 4 to 6 month of age. One clinical consequence of this is that disorders of α-globin synthesis may manifest in utero or at birth, while disorders of β-globin synthesis tends to manifest clinically after 6 months of age.

The synthesis of globins is controlled by genes that reside on chromosomes 11 and 16 (**Figure 3-5**). The sequence of synthesis is controlled by activation and deactivation of the different globin gene during different phases of embryonic and fetal development.

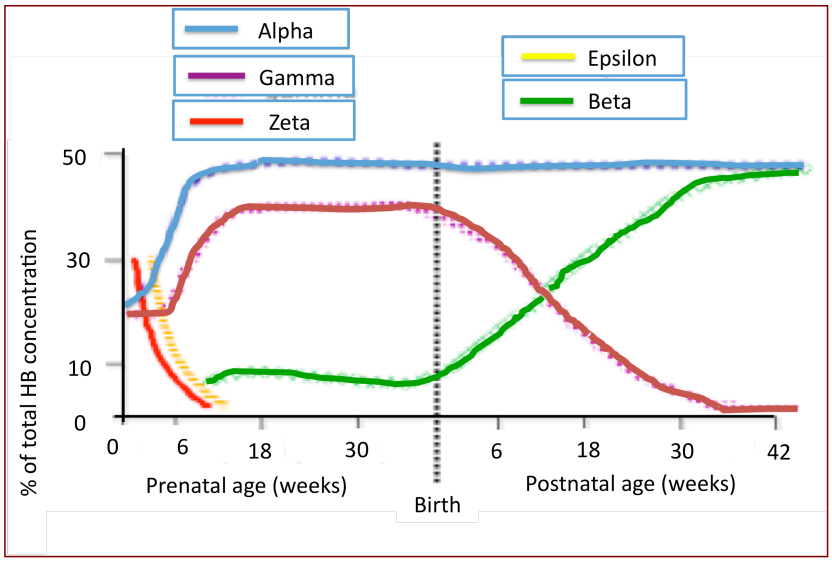

Figure 3-5: The sequence of hemoglobin synthesis from embryonic to adult post natal hemoglobin

Fetal lung
Development and maturation

Prenatal lung development takes place through mainly three stages: pseudoglandular, canaliclular and saccular stages. However lung development continues for few months after the baby is born. During these stages, cells differentiate into individual structures within the lungs, and the bronchial airways are formed.

- The pseudoglandular stage: (5-16 weeks) During this time, the conducting airways are formed inside a gland-like structure. Tall columnar epithelium cells grow to make the inside lining of primitive airways. Tubular branching continues to develop throughout this stage. At approximately two months all of the bronchi segments are present.
- The canalicular stage: (17-24 weeks) involve development and multiplication of the terminal respiratory bronchioles, the alveolar capillaries for gas exchange, and the surrounding lung muscles. In this stage also the differentiation of type I and type II alveolar cells begins.
- The saccular and alveolar stages: (24 weeks continue to term and past-term) during this stage true alveoli starts to appear. The bronchiole formations that appeared in the previous stage begin to grow.

A fourth developmental stage, called the alveolar period, occurs after the fetus is born and will continue into the fourth year of childhood (Figure 3-7)

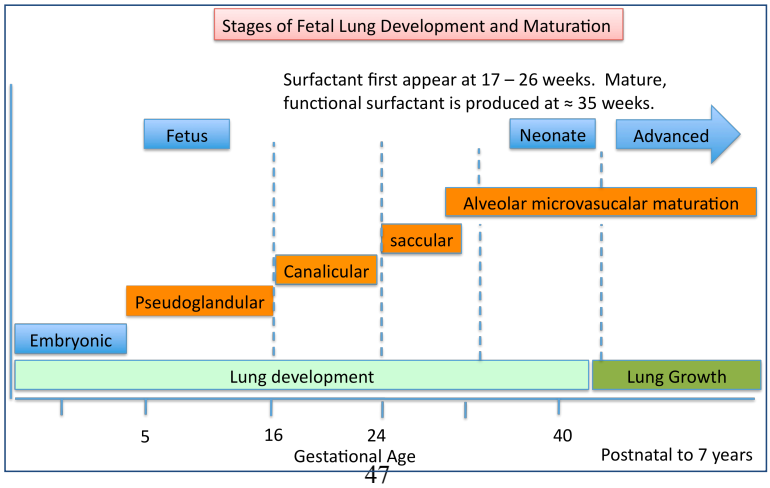

Figure 3-6:: Shows stages of fetal lung development

Physiology of fetal lung maturation:

In utero, the lungs of the fetus are filled with lung fluid. With the first breath, the newborn must eliminate the fluid present in the lungs and maintain a level of lung expansion that allows exchange of gases. The distending pressure of an alveolus (pressure required to keep the lung open) depend on 1) the *surface tension* of the fluid within the alveolus (The cohesion force produced by the molecules of fluid present within the alveoli) and 2) the radius of the alveoli itself.

During fetal maturation the lungs produce a complex compound within the alveoli called *surfactant.* Its main function is to disrupt the cohesion force produced by the molecules of fluid thus reduces the surface tension of the liquid within the lung.

The pulmonary alveoli of premature fetuses have high surface tension because inadequate production of lung surfactant. This increases the newborn's work of breathing, and result in respiratory distress and sometimes-overt respiratory failure.
. It is therefore important to establish the level of pulmonary maturity in the fetus when planning for preterm delivery.

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Other important functions or surfactant include; enhancing capillary circulation, allowing for normal ventilation / perfusion ratios, protecting alveolar tissues from barotrauma, stabilizing alveoli, and aiding evacuation of fetal fluid.

Surfactant is produced by *alveolar type II pneumocytes*, which first appear in the 17 – 26 weeks of gestation. The major components of surfactant include *phosphatidylcholine* (PC) and *phosphatidylglycerol* (PG). Mature, functional surfactant is produced at approximately 35 weeks gestation.

Assessment of fetal lung maturity:

There are a number of laboratory tests that can be performed to assess fetal lung maturation and predict the risk of Respiratory Distress Syndrome (RDS). Generally, these tests require a sample of amniotic fluid. In women with intact membranes, amniotic fluid is obtained by amniocentesis but if the membranes are ruptured; a syringe can be used to aspirate amniotic fluid pooled in the posterior vaginal fornix. The most commonly employed tests are:

- **L/S Ratio (Lecithin/Sphingomyelin Ratio)**

It requires an amniotic fluid sample (acquired by amniocentesis) to quantify the ratio of lecithin and sphingomyelin present. The risk of development of RDS is exceedingly low when the lecithin/sphingomyelin ratio is greater than 2.0. A ratio of less than 1:1 indicates immaturity and a high risk for developing of Respiratory Distress Syndrome (RDS). A ratio between 1 and 2 RDS is less helpful in predicting when RDS may develop.
The test has the disadvantages of being technically difficult to perform, the amniotic fluid sample should be kept on ice or refrigerated if transport to a laboratory, it takes several hours to perform and the result is affected by blood and meconium. Therefore it cannot be performed on vaginal pooled sample.

- **Phosphatidylglycerol (PG) level**

PG is a minor constituent of surfactant. It begins to increase in amniotic fluid after 35 weeks, several weeks after the rise in lecithin PG enhances the spread of phospholipids on the alveoli and its presence indicates an advanced state of fetal lung development and function. The test result is usually qualitatively reported as 'PG present' or 'PG absent'.
An advantage of this test is that usually it is not affected by the presence of blood or meconium. While a disadvantage of the test is that if the test is negative, especially before 36 weeks of gestation, it is less predictive of the occurrence of respiratory distress.

- **Foam Stability Index (FSI)**

The FSI is a predictor of fetal lung maturity based upon the ability of surfactant to generate a stable foam in the presence of ethanol. Ethanol is added to a sample of amniotic fluid. The mixture is then shaken and will demonstrate generation of a stable ring of foam if surfactant is present. The foam stability index (FSI) is calculated by utilizing serial dilutions of ethanol to quantitate the amount of surfactant present
In this test the presence of blood or meconium interferes with results of the FSI.

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Chapter 4

Maternal Physiological adaptation to pregnancy
Professor Tarik Zamzami

Pregnancy imposes major physiological demands on almost every system in the mother. In response, the maternal body adapt in a way that maintain normal maternal function while at same time fulfill the fetal demands. Some of the adaptive changes may be considered as pathological by the non pregnant standard. Therefore knowledge of the normal maternal physiology is essential in order to correctly interpret results of investigations, clinical changes, and avoid unnecessary diagnostic or therapeutic intervention.

An important feature of almost all the maternal physiological adaptive changes in pregnancy, such as the increase in cardiac output, is that it occurs in anticipation. In other wards most of it takes place at an early stage of pregnancy prior to any actual fetal demands. This chapter reviews the important aspects of maternal physiological changes in pregnancy and highlights its clinical implication on function and potential adverse effects on the mother.

By the end of this chapter you should be able to:

- **Describe** the water and electrolyte changes in pregnancy
- **Describe** the maternal cardiovascular changes during pregnancy
- **Describe** the Respiratory system changes during pregnancy
- **Describe** the hematological chagnes during pregnancy
- **Describe** the changes in the urinary system during pregnancy
- **Describe** the Musculoskeletal system changes in pregnancy
- **Describe** the changes in the endocrine system in pregnancy
- **Describe** the changes in the Breast and preparation for lactaion

Water and Electrolyte Metabolism

Water Metabolism:

Pregnancy induces a state of chronic volume overload (hypervolemia) due to active sodium and water retention. By the end of pregnancy the total body water increase by an average of 6 to 8 L. As a result the plasma osmolality falls by about 10 moms/kg below

the non pregnant level. This change in normal plasma osmolality is brought about and maintained by resetting of the osmoregulation mechanism which normally depends on the threshold of thirst and the threshold for vasopressin hormone (antidiuretic hormone) secretion. In normal pregnancy the threshold for thirst is lowered and the threshold for vasopressin secretion is raised.

However because resetting of the threshold of drinking precedes changes in osmotic threshold for vasopressin secretion, pregnant woman develop a transient state of polyuria and polydipsia between 5 and 8 weeks gestation.

The increase in total body water is responsible for several changes reflected in:

1. Increase maternal weight gain.
2. Hemodilution of pregnancy (causes physiologic anemia)
3. Elevation in maternal cardiac output.

Sodium and electrolytes metabolism:

During pregnancy approximately about 900 mEq of sodium and 300 mEq of potassium are retained. Despite that, the serum concentrations of these electrolytes decrease in pregnancy compared to its level in the non pregnant state.
The mechanisms responsible for this change include:

- *Increase renal tubular reabsorption of sodium* (in the face of increase glomerular filtration rate).
- *Increase in the activity of the Renin-Angiotensin-Aldosterone System:* Renin, produced by the maternal kidney and the uteroplacental unit, increases by 5 to 10 folds, the renin substrate (angiotensinogen), produced by both maternal and fetal liver increases four to five folds, and plasma aldosterone level reaches to approximately two folds higher than its non pregnant level during the third trimester of pregnancy.
- *Atrial Natriuretic Peptide*:
  This is a group of biologically active peptides synthesized and secreted by the atrial myocytes. It plays a major role in the regulation of extracellular fluid volume. It has the following actions: diuretic, a natriuretic, and a vasorelaxing action in addition of being antagonist to rennin angiotensin system (decrease renin secretion).
  However there is still uncertainties to its exact level in normal and abnormal pregnancy, while some authors have reported higher plasma level of ANP others have reported no changes.

Cardiovascular System

From the early weeks after conception the cardiovascular system undergoes remarkable changes that involve both its anatomical and functional aspects. The aim of those changes is to secure the requirements of the growing fetus while maintaining the integrity of the maternal cardiovascular function. It is important to understand those changes as it may mimic some pathological conditions.

The Heart: Both physical and functional changes take place:

Physical changes: As the diaphragm becomes progressively elevated the heart is displaced to the left and upwards, while at the same time it is slightly rotated on its long axis. This causes lateral displacement of the cardiac apex and increase in the size of the cardiac silhouette on radiography giving a false impression of cardiomegaly.

Since pregnancy is a hyperdynamic state the following alterations may normally be detected on cardiac auscultation:

- An exaggerated splitting of the first heart sound with increased loudness of both components and a loud easily heard third heart sound.
- Different heart murmurs can be heard; 80-90% of women may have systolic murmur, 20% diastolic murmur and continuous murmur arising from the breast vasculature in 10%.

Functional changes:

Cardiac output "CO":

The CO begins to rise from as early as 5 weeks, until it reaches about 40% above non-pregnant value somewhere between 25 to 30 weeks. The increase in the CO is due to increase in both the cardiac stroke volume (SV) and the heart rate. The contribution of the increase in heart rate (by about 10 bpm) seems to be more significant in early pregnancy than the increase in the SV and vise versa in the late weeks of gestation. The increase in the stroke volume is due to increase in blood volume (by about 30-50%) and decrease in peripheral vascular resistance. In twin pregnancy the increase in the CO is about 15% above that of singleton pregnancies.

The CO in pregnancy is influenced by maternal position. Being lowest in the supine position, due to decrease in the venous return, and highest in the right and left lateral position.

In late pregnancy the inferior vena cava is completely occluded in the supine position with the venous return from the lower extremities occurring through the dilated paravertebral collateral circulation. *This explain the development of the "supine hypotensive syndrome" experienced by some 5-10% of women which is feeling of dizziness, lightheadedness, nausea and even syncope if the women remain in the supine position for some time.*

Arterial Blood Pressure:

The arterial blood pressure (BP) is the product of cardiac output and systemic vascular resistance (SVR) (BP=CO×SVR). However despite the large increase in the CO, in pregnancy the maternal BP decrease. This is due to decrease in the SVR. The decrease in arterial BP occurs from as early as 8 weeks of gestation, affects the diastolic more than the systolic pressure. It reaches a nadir at midpregnancy and return to almost non pregnant level by term.

In clinical practice two important factors influence the actual reading of BP those are:

- Posture: the BP is lowest in the supine position. Therefore for pregnant women the BP should be measure while they are sitting or in the recumbent posture
- The Korotkoff 5th sound (the BP when the sound disappears) should be used as opposed to Korotkoff 4 (when there is muffing of the sound). The latter is identified in only about 50% of women).

Systemic Vascular Resistance:

The systemic vasculare resistance (SVR) decreases in pregnancy. This change is due primary to the relaxing effect of the elevated progesterone level on the smooth muscle walls of the vascular bed. Other substances which might contribute to the decrease in the SVR are prostaglandin, nitric oxide, or ANP.

The venous Blood pressure: in the upper arms the venous pressure remains almost unchanged. However in the femoral veins the pressure rises steadily from 8 cm H_2O early in pregnancy to 24 cm H_2O at tem. This is primarily induced by pressure effect of the enlarged uterus on the pelvic veins and inferior vena cave. The same mechanism is also responsible for impairment in the venous blood return from the lower limbs.

Clinically these changes contribute to development of dependent edema, increased predisposition for varicose veins of the lower limbs, vulva, hemorrhoids and increased risk of deep vein thrombosis.

Hemodynamic parameters	Changes during normal pregnancy	Changes during labor and Delivery	Changes in the postpartum
Blood volume	+ 40-50%	+	_
Heart Rate	+ 10 -15 beats/min	+ Additional 50%	_
Cardiac output	+ 30- 15% above baseline	+	_
Blood Pressure	- 10mmHg	+	_
Stroke volume	+ First and second trimester and decline in third trimester	+ 300-500ml/contractions	_
Systemic vascular resistance	_	+	_

Table 4-1: summary of hemodynamic changes in pregnancy

The Respiratory System

In pregnancy the total body O2 consumption increases by about 15% to 20%. The uterus and its contents account approximately half of this while the remainder by the increase in the workload of other maternal body systems. In order to meet the increased demands the respiratory system (together with the cardiovascular system) undergoes mechanical changes which are reflected on the lung volume and pulmonary function:

Mechanical changes: The configuration of the chest changes so that the subcostal angle widened from 68 degrees to 103 degrees, the transverse diameter of the chest expands by 2 cm, and the chest circumference expands by 5 to 7 cm.

Lung volume and pulmonary function:

Women in pregnancy are in a state of chronic hyperventilation, which is due to progesterone effect. This results in 30-40 % increase in minute ventilation (Minute ventilation = Tidal volume × Respiratory rate). However the respiratory rate does not change (Figure 4-2).

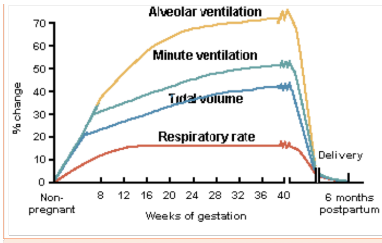

Figure 4-2: shows the percentage in changes parameters of lung function during pregnancy

Gas Exchange:

Hyperventilation results in a decrease in $PaCO_2$ (arterial) from normal level of 37-40 mmHg to 27- 32 mmHg inducing a state of respiratory alkalosis. This change facilitates the transfer of CO_2 from the fetus to the mother. The kidneys compensate for this effect by increase in excretion of bicarbonate, which help maintain the pH between 7.4 and 7.45 and lower serum bicarbonate levels to 18 to 21 mEq/l.

Early in pregnancy the arterial oxygen (Pa O_2) increases (106 to 108 mmHg) as the PaCO2 decreases. By the third trimester a slight decrease occur in the PaO2 (101 to 104) as a result of elevation of the diaphragm. Also the arterial oxygen (Pa O_2) increases (from 106 to 108 mmHg) as the $PaCO_2$ decreases.

Hematological Changes

Plasma volume and Red Blood Cell Mass:

The total blood volume begins to increase from as early as the first trimester to reach a value about 40 to 50% above the prepregnancy level at or very near term.

Both elements the plasma and erythrocytes contribute to this increase. However there are differences in the pattern and the degree of increase. The plasma volume increases by an average 30-40 % starting from as early as 6 weeks reaching a plateau by about 30-34 weeks.

While the increase in the red blood cell mass begins at around 10 weeks and reaches about 18% (with iron supplementation it reaches about 30%).

- Without iron supplementation the RBC mass shows about 18% increase vs. 30% with iron supplementation.
- **"Physiological anemia"** results from the discrepancy between the in increase in plasma volume (40%) and RBC mass volume (18%).

The white blood cells (WBC):

The WBC count increases in pregnancy, mainly due to increase in the number of granulocytes. It may further increase during labour. It returns to non-pregnant value during pregnancy.

Iron Metabolism in Pregnancy:

During gestation the total iron requirements is about 1000 mg. It is distributed as follow:

- 500 mg for the increase in maternal RBC mass.
- 300 mg for the fetus and placenta.
- 200 mg to compensate for the normal obligatory daily maternal iron loss.

Iron is actively transported to the fetus even in cases of severe maternal iron deficiency. Therefore there is no correlation between maternal and fetal hemoglobin concentration.

The need for routine maternal iron supplementation has been a subject of debate. However studies have shown that the large proportion of women is deficient in iron store. Thus iron supplementation is often needed in pregnancy but rarely before 20 weeks. The recommended prophylactic dose is 30 mg of elemental iron per day. The therapeutic dose for treatment of anemia is about of 300 mg of ferrous sulphate daily.

Platelets:

Most studies points to some decline in platelet counts during pregnancy, possibly caused by destruction. The counts return to normal values by 1 to 2 weeks postpartum.

"gestational thrombocytopenia" with a drop in the platelets count between 70,000 and 150,000/mm3 may be observed in approximately 8% of gravid women. This thought to be an exaggeration of the normal process of platelets destruction, with no complications.

Coagulation system:

Pregnancy is a state of hypercoagulability, thus pregnant

women run a higher risk of developing thromboembolic diseases.
This is due to exaggeration of all the risk factors (Virchow's triad) for thrombosis.

- Venous stasis (particularly in the pelvic and lower limbs veins).
- Increase liability to of vessel wall injury (especially after operative delivery)
- Changes in the coagulation cascade and the fibrinolytic system that favor coagulation (see below).

This state of hypercoagulability is an adaptive mechanism that provides some defense against peripartum hemorrhage.

- The coagulation cascade: Almost all procoagulant factors shows marked increase including factors I (fibrinogen 50% increase), VII, VIII, IX and X.

- The fibrinolytic system: In addition to increase in coagulability pregnancy causes a decrease in the level of available circulating plasminogen activator, the natural inhibitor of coagulation. Some natural coagulation inhibitors such as free protein S shows decreases from early pregnancy.

The Urinary System

Anatomic Changes:

- The kidneys: As a result of the increased renal vasculature, interstitial volume and size of urinary dead space (the renal pelvis, calyces and ureters) the kidneys enlarge in size and weight. The pelvicaliceal system on the right enlarge more than the left.

- The ureters: Begins to show dilatation and elongation from the second trimester (before any mechanical pressor), a result from the smooth muscle relaxing effect of progesterone. Further dilatation and tortuosity occurs by the middle of the second trimester due to the additional mechanical compression of the ureter at the pelvic brim by the enlarging uterus and also by the ovarian vein complex. Those changes, ureteric dilatation, tortuosity and apparent kinking are normal in pregnancy and resolve approximately 6 weeks postpartum.

- Bladder and Urethra: From about 12 weeks onwards the bladder trigone is elevated and the bladder wall shows increased vascular tortuosity (increased incidence of

Clinical implications of anatomic changes in the urinary system:

- *The uretero calyceal dilatation increases the risk of ascending pyelonephritis in patients with asymptomatic bacteruria.*
- *The uretero calyceal dilatation makes interpretation of urinary system imaging more difficult*
- *Bladder changes increases risk of urinary incontienece*

microhematuria). There is actual increase in the intravesical pressure but also there is compensatory increase in intraurethral pressure.

Functional Changes:

The Effective Renal plasma flow (ERPF): increases early in the first trimester until it reaches to about 75% over non-pregnant levels at term. This increase is established around end of first trimester (average 16 weeks gestation) and maintained until about 34 weeks until there is a drop of about 25% which is not due to posture.
The Glomerular filtration rate (GFR) begins to increases by 5-6 weeks, by the end of the first trimester it is 50% higher than in non pregnant level. This rise is maintained throughout pregnancy despite the decrease in ERPF which take place in late pregnancy.
The filtration fraction: because the ERPF increases more than the GFR early in pregnancy, the filtration fraction falls from non pregnant levels until the late third trimester. At that time because of the decline in ERPF, the filtration fraction returns to non pregnant values of 20 to 21 percent.

Clinical Consequences of renal functional changes:

- Reduction in maternal plasma levels of creatinine, blood urea nitrogen (BUN) and uric acid: these changes occur as a result of increase in the GFR. However in late pregnancy the uric acid level returns to its normal non pregnant values because of increased renal tubular reabsorption.
- Nocturia: reversal of the usual non pregnant diurnal pattern of urinary flow i.e. nocturia is common in pregnancy because the water retained during day time tends to be excreted by night when the mother in the lateral recumbent position. Furthermore the urine is more diluted but that does not signify failure of kidneys to concentrate urine.
- Renal Tubular Function/Excretion of Nutrients:
- Glucose: In pregnancy glucosuria does not necessary indicate hyperglycemia i.e. it is not correlated with the blood glucose level. Furthermore it is intermittent and does not depend on the stage of pregnancy. The causes of glucosuria in pregnancy are: (1) increased GFR (since glucose is freely filtered by the glomeruli) which result in at least 50% increase in the glucose load to the proximal tubules. (2) Impaired proximal tubular reabsorptive capacity of glucose. However women with repeated glycosuria should still be screened for diabetes mellitus.
- Proteinuria: This is not a feature of normal pregnancy. The mean 24 hours urine protein loss during pregnancy is 116.9 mg, and the upper 95% confidence limit is up to 260 mg. Loss of more that 300 mg of protein/24hours is abnormal.
- Potassium: In pregnancy the kidney has more ability to conserve potassium, probably a progesterone mediated effect. Thus despite increased level of aldosterone production (which normally enhances urinary potassium excretion) pregnant women retain about 350 mmol of potassium (mostly in the fetus and

placenta). But the mean potassium concentration in the maternal blood is just slightly below non pregnant levels.

- Loss of other nutrients: Aminoaciduria (increase excretion of amino acids), increased amount of calcium and water soluble vitamins are lost in urine at higher rate than in non pregnant state.

- Pregnancy induces a state of compensatory respiratory alkalosis: with chronic loss of bicarbonate. This reduction in the renal buffering capacity predisposes pregnant women to severe metabolic acidosis (either ketoacidosis or lactic acidosis).

Alimentary Tract

Appetite: The recommended dietary allowance (RDA) demands an additional 300 kcal/day; however energy requirement varies according to an individual and population needs. At the same time the appetite increases during pregnancy by about 200 kcal/day.

Mouth: The PH and production of saliva is probably not changed in pregnancy. Ptyalism is a rare condition due to inability of nauseated women to swallow the normal amount of saliva, rather than excessive production.
Teeth: There is no evidence that pregnancy increases risk of dental caries.
The gums (gingivitis): The gums swell and may bleed easily which give rise to what is called "gingivitis of pregnancy". Tumorous gingivitis (epulis gravidarum or pyogenic granulomas) is a rare complication. It appears as violaceous pedunculated lesions consists of granulation tissues and inflammatory infiltrate. It might need surgical excision but normally disappear 1 to 2 months after delivery.

Stomach:
The tone and motility of the stomach decrease during pregnancy. This is probably an effect of increased progesterone production. Nevertheless the evidences for delayed stomach emptying during pregnancy are inconclusive.
However during labour the gastric emptying time is typically delayed which is subscribed to the pain and stress of labour. *This can pose serious risk of regurgitation and aspiration of either food laden or highly acidic gastric contents especially during anesthesia.*

Gastroesophageal reflux (heartburn): Reflux of the stomach acidic secretion in the lower esophagus is common. It is caused by esophageal dysmotility and a decrease in the tone of the gastroesophageal sphincter in addition to gastric compression from the enlarged uterus.

Intestine:

Perturbations in the motility of the small intestines and colon are common in pregnancy. It results in increase incidence of constipation. These effects are probably progesterone mediated.

Gallbladder:
There is impairment of gallbladder contraction, reflected in increase in its volume (both fasting and residual) and it prolongs its emptying time. These changes are thought to be progesterone mediated effects.
Also the composition of the bile changes with increase in biliary cholesterol saturation and decrease in chenodeoxycholic acid. Those two changes explain the increased prevalence of cholesterol stones particularly in parous women.

Liver:

Many clinical and laboratory sings that is usually associated with liver disease are observed in pregnancy.

- Spider angiomas and palmer erythema are common and caused by elevated estrogen levels.
- The serum albumin and total protein levels fall progressively during gestation despite an overall increase in total body protein. This apparent effect occurs as a result of hemodilution.
- Total serum alkaline phosphatase rises up to two to four times the non pregnant level. Most of this rise produced by increased placental production of the heat stable isoenzyme. No other liver function tests show specific change in pregnancy.

There is increase in many of the serum proteins produced by the liver such as fibrinogen, ceruloplasmin and transferring and the binding proteins for corticosteroids, sex steroids, thyroid hormones and vitamin D.

Nausea and Vomiting of Pregnancy:

Nausea and vomiting "morning sickness" complicate 70% of pregnancies. The onset is typically around 4-8 weeks with spontaneous improvements by 14-16 weeks. The condition seldom leads to weight loss, ketonemia, or electrolyte disturbance.
The causes are not known. Relaxation of the smooth muscle of the stomach has been implicated as a possible factor. Elevated level of HCG has traditionally been implicated. However the correlation between maternal HCG and the degree of nausea and vomiting is week.

Hyperemesis gravidarum: A vicious form of nausea and vomiting associated with weight loss, ketonemia, electrolyte imbalance and dehydration. It often persists throughout

pregnancy. Other diseases such as pancreatitis, hepatitis or thyroid diseases should be excluded. Treatment often requires hospital admission, intravenous fluid and electrolyte replacement and antiemetic therapy.

The Skeleton

Calcium Homeostasis: Pregnancy induces profound stress on calcium homeostasis and metabolism due to:
(1) increased fetal demands, where calcium is actively transported across the placenta
(2) a decrease in calcium concentration attributed to hemodilution
(3) increased renal calcium loss. The fetus at term accumulate around 21 g (range 13-33 g) of calcium throughout pregnancy, 80% of this amount is acquired during the third trimester.

In pregnancy the maternal serum ionized calcium (50% of the total calcium) level remains unchanged despite a decline in the total calcium level which is attributed to a decrease in the albumin bound fraction of calcium. Maternal serum phosphate level is unchanged.

The maintenance of the normal maternal calcium level is achieved through several changes in the mechanisms responsible of calcium and phosphorus homeostasis. These changes include:
(1) increase production of parathyroid hormone which stimulate bone resorption, intestinal absorption and kidney reabsorption of calcium to increase extracellular fluid calcium and decrease phosphate.
(2) Increase in calcitonin secretion which opposes the action of parathyroid hormone to protect skeletal calcification.
(3) Increased level of 1, 25 dihydroxyvitamin D_3 as a result of increased production by the kidneys and the fetoplacental unit which appear to be independent of PTH control. 1, 25 dihydroxyvitamin D_3 stimulate resorption of calcium from bone and absorption from the intestine.

Skeletal bone and postural changes:
In pregnancy there is a progressive increase in anterior convexity of the lumber spine (lordosis). The aim of this postural adaptation is to keep the women center of gravity on her legs as the uterus enlarges. Not uncommonly these results in low back pain which is a common complain during pregnancy.

The ligaments of the pubis symphysis, sacroiliac joint and sacrococcygeal loosen in pregnancy as a result of the hormone relaxin. Exaggeration of this effect might sometimes cause marked widening of the pubic symphysis from 3-4 mm to 7.7-7.9 mm. This causes pain over the symphysis that may be radiating to the inner thigh with

standing, and result in a maternal sensation of snapping or movement of the bones with walking.

Endocrine changes

The Thyroid:

Women in pregnancy remain euthyroid despite changes in the morphology (slight enlargement), histology (increase thyroid vasculature and some degree of follicular hyperplasia) and laboratory indices. The progressive increase in the maternal basal metabolic rate by as much as 25% is attributed to fetal metabolic activity rather than solely to increased maternal oxygen consumption.

In pregnancy the changes in the thyroid, function and morphology in order to maintain maternal euthyroid state are attributed to:
(1) Decrease in serum iodine level due to increase renal loss of iodine, and iodine transfer to the fetus particularly in the latter half of pregnancy.
(2) Increase in the thyroid binding globulin, which raise the total thyroxine (T4) and triiodothyronine (T3) levels while the free fraction remains almost the same and
(3) Thyroid stimulating factors of placental origin mainly the HCG. The exact role of the thyrotropic effect of HCG is still not clear. It could explain an initial rise in thyroid hormones in the early weeks of gestation.

Therefore clinically the free T4 and T3 index is an appropriate measure of thyroid function, with the same normal range as in the non pregnant state. Also thyroid stimulating hormone "TSH", apart from a slight decrease in early pregnancy which coincide with a rise in T3 remain within normal values for non pregnant women

The relation of maternal thyroid function to fetal development:

There is a complex though indirect relation of the maternal thyroid physiology and the fetal thyroid function. It is known that the thyroid stimulating hormone (TSH) does not cross the placenta while the thyrotropin releasing hormone TRH can cross the placenta.
The T4 crosses the placenta. However a large proportion of maternal T4 is broken down prior to transfer to the fetus by the deiodinase activity of the placenta. The small amount of maternal T4 that reaches the fetus seems to be critical for its normal neurological development particularly before the 10^{th} week of gestation. After this age the fetal thyroid becomes autonomous.

Hypothyroid women and those living in iodine deficient areas is associated with neonatal hypothyroidism and defects in long term neurological function and mental retardation or

endemic cretinism. Also maternal hypothyroidism is associated with slightly lower IQ scores in children at ages of 7 to 9.

In pregnancy the WHO has recommended that iodine intake should be increased from 100 to 150 µg/ day to 200 µg/ day.

Adrenal Gland:

Pregnancy is associated with marked changes in the adrenocortical function with increased levels of aldosterone, deoxycorticosterone (DOC), corticosteroid binding globulin (CBG), cortisol and free cortisol. The diurnal variation in cortisol levels is maintained during pregnancy.

- Cortisol: The elevation of cortisol level (free cortisol level doubled from the first to the third trimester) is the result of several mechanisms. It is partly mediated by marked rise in corticotropin releasing hormone (CRH) produced by the placenta and fetal membranes and released into the maternal circulation. Other causes include decrease in the renal clearance and possibly resetting of the hypothalamic pituitary sensitivity to cortisol feed back on ACTH production.

- The mineralocorticoids aldosterone and DOC both shows increase. The rise in DOC is probably produced by the fetoplacental unit hence the loss of response to ACTH stimulation or dexamethasone suppression tests.

- Androstenedione and Testosterone: The maternal levels of these androgens are increased during pregnancy. However both are almost completely converted to estradiol by the placenta, which increase their clearance rate. The source of these androgens is unknown but it is likely originates in the ovary.

Pituitary Gland:

The pituitary gland enlarges (its mean weight increases by 136% at term) in pregnancy mainly because of proliferation of prolactin producing cells in the anterior pituitary. Enlargement of a preexisting macroadenoma (10 mm or greater) is likely in pregnancy.
The enlargement of the pituitary makes it susceptible to alteration in blood supply and increases risk of postpartum infarction (Sheehan's syndrome) should a large maternal blood loss occur.

- Serum prolactin level rises from as early as 5 to 8 weeks gestation to be about 10 times higher at term. Its function is to prepare the breast for lactation. Paradoxically after delivery there is a decrease in prolactin concentration even in

women who breast feed. During early lactation there are pulsatile bursts of prolactin secretion apparently in response to suckling.

- Maternal LH and FSH decrease to very low level as a result of the feedback inhibition of the elevated level of estrogen and progesterone.
- Maternal growth hormone level also suppressed because of the negative feed back effect of placental growth hormone variant.

Pancreases and Fuel metabolism:

Glucose:

Pregnancy induces significant changes in glucose metabolism. The two important facts are:

The fetus is primarily dependent on maternal glucose for its fuel requirements that increases gradually as pregnancy progresses.

Glucose is transported across the placenta by an energy independent facilitated transport mechanism.

In order to ensure adequate supply of glucose to the fetus the placental produce hormones with anti-insulin effect namely human placental lactogen (hPL) in addition the placental steroid hormones. The function of these hormones in the maternal body is to work at cellular level to antagonize the function of insulin and prevent the utilization of glucose by the maternal tissue thus sparing it for the fetus.

Unless the maternal pancreas can response to this challenge-provoked by the anti-insulin hormones by producing increasing amount of insulin a state of maternal hyperglycemia known as "gestational diabetes" occurs.

Healthy pregnant women normally shows high level of plasma insulin in order to maintain their euglycemic state. Also normally the - the β-cells (insulin producing cells) in the islands of Langerhans of the maternal Pancrease undergo hyperplasia and hypertrophy.

The overall results are that normal pregnancy is characterized by fasting hypoglycemia, postprandial hyperglycemia and hyperinsulinemia.

In early pregnancy The maternal blood glucose level decreases by about 10% due to increased insulin release. This result in increase in lipogenesis and storage of fat, apparently in preparation for rise in energy needs later in gestation.

As pregnancy advances, there is increase in the level of anti-insulin placental hormones mainly human placental lactogen as well as other hormones such as estrogen, progesterone and cortisol.

There is also increasing fetal demand that is estimated at approximately 6.0 mg/kg/min by the third trimester. These two factors again induce characteristic changes in the fasting and fed state.

In maternal fasting (starvation) state there is more rapid conversion from predominantly carbohydrate to predominantly fat utilization. The later (i.e. lipolysis) generate glycerol, fatty acids and ketones for gluconeogenesis and fuel metabolism (exaggerated starvation ketosis) and preserve the utilization of glucose and amino acids for the maternal CNS.
In summary the starvation state in late pregnancy is characterized by maternal hypoglycemia, hypoinsulinemia, hyperlipidemia, and hyperketonemia.
In maternal fed state, there is hyperglycemia, hyperinsulinemia, hyperlipidemia and reduced tissue sensitivity to insulin.

The Breast

During pregnancy the breasts are being prepared for lactation. Growth of the ductal and alveolar elements, rather than fat, is the main reason for the observed breast enlargement during pregnancy. Ductal growth is dependent on estrogen while alveolar growth is dependent on progesterone.
The nipple becomes more mobile and mobile and the areolas enlarge and are more deeply pigmented. Montgomery glands are small elevations appear in the areola which are hypertrophied sebaceous glands.

The physiology of lactation:

- Duringpregnancythebreastsarepreparedforla ctation.Growthoftheductaland alveolar elements, rather than fat, is the main reason for the observed breast enlargement during pregnancy.
- Ductal growth is dependent on estrogen, while alveolar growth is dependent on progesterone.
- Thedevelopmentofthebreastduringpregnan cy:occursintwodistinctphases,with characteristic early and late stages. In the trimester "phase" ductular sprouting predominates, while in the second trimester lobular formation exceeds ductal sprouting.
- Breast growth is stimulated by increasing prolactin secretion throughout pregnancy, but lactation does not occur during pregnancy due to the inhibitory effect of progesterone produced by the placenta.
- Initiation of lactation: Is due primarily to the rapid decline in the level of placental progesterone. Pharmacologic levels of estrogen (estrogen from

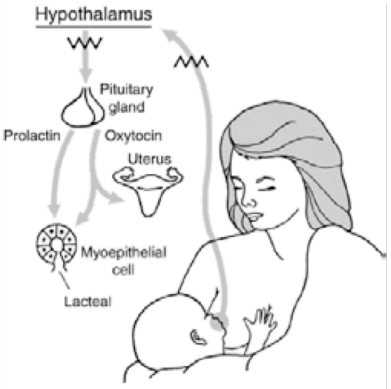

Figure 3-3: mechanism of milk secretion "The sucking reflex"

exogenous sources vs. endogenous sources as in contraceptive pilles) also block prolactin activity.

- Threetofourdaysinthepostpartumperiod after the steroid hormones is cleared from maternal circulation milk secretion begins.

Milk secretion and ejection: "the sucking " Suckling stimulates an hypothalamic release of prolactin and oxytocin. Placationis important for the initiation of milk production as well as the maintenance of milk
production.
Oxytocinactonthemyoepithelialcellsurroundingthealveoliandforcesthemilkinto the ducts from the alveolar lumens.
The optimal quantity and quality of breast milk are also dependent on other factors, such as the availability of thyroid hormone, insulin and insulin-like growth factors, cortisol, and the intake of nutrients and . However continuation of milk production is primarily regulated by the emptying of the breast.

Skin Changes

Pigmentation: Hyperpigmentation occurs in approximately 90% of pregnancies may be generalized or localized to areas of increased melanocyte density.
It may be generalized or localized to areas such as the areola, umbilicus, vulva and perianal skin. The linea Alba become darker and known the linea nigra. Nevi become more pigmented.
The face develops what is known as melasma or chloasma which is a well defined hyperpigmented centrofacial patches. Those changes may be induced by the rise in melanocyte stimulating hormone. Estrogen and progesterone are reported to have some melanocyte stimulating effect.

Hair Growth: Mild degree of hirsutism is common. It is probably due to placental androgen production as well as elevated level of cortisol.

Striae Distensae: Striae begin to appear in the late second trimester in up to 90% of cases. It is thin atrophic pink or purple linear bands found on the abdomen, breast, and thighs. It results from two factors; Stretching and tearing of the collagen matrix of the dermis induced by adrenocorticosteroid and estrogen. After delivery they partly atrophy and acquire a silvery white color.
•scular changes: Occur as a result of proliferation of blood vessels and congestion induced by high estrogen level. It appears in the form of mottling of skin, scattered petechiae, spider angioma, palmar erythema and sometimes vasomotor instability.

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Chapter 5

Evidence Based Medicine

Dr Sameera Al Basri

By the end of this chapter you should be able to:
Define the term "Evidence Based Medicine"
List the standard five steps for application EBM in clinical practice
Describe the Sources and Levels of evidence:
Realize the importance of applying "Evidence Based Medicine" in clinical practice
Realize that: The practice of EBM is a life long learning processes

Definition: The most common definition of EBM is taken from Dr. David Sackett who defined EBM as "**the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient**". It simply means integrating individual clinical expertise with the best available external clinical evidence from systematic research.

It should be emphasized that the presence of evidence, by itself, does not make a clinical decision. Scientific evidences should be integrated with both "clinical experience" and "patient expectation".

The practice of EBM is usually triggered by the patient encounters or clinical presentation, which generate questions about the effects of different therapeutic intervention, the utility of diagnostic tests, the prognosis of diseases, or the etiology of disorders (*e.g. typical example is gestational diabetes where there is need for evidence as regards what diagnostic test, the exact etiology, the value of therapy and the short and long term prognosis*)

How does the concept of evidence-based medicine evolved?

Practicing medicine based on evidence is not a new concept. Perhaps throughout the history of medicine no one argued against scientific evidence. However for long time the source of evidence used to be one's own experience, which meant, "experience rather than evidence based medicine". This however is not adequate to ensure that the patient is getting

the best care because "personal experience" is usually based on limited number of cases and often biased by the clinician own views.

More recently the concept of EVB evolved and became possible because of:

- A rapidly increasing understanding of how to conduct, understand and analyze valid clinical research particularly randomized controlled trials "RCT"
- The ability to access vast and growing volume of those trials through the WWW.
- The ability to distinguish credible from trivial or misleading research results.
- The ability to construct guidelines based on rigorous criteria for level of evidences to guide clinical decisions which is far beyond what one can gain from self limited experience.

Steps in Practicing Evidence-Based Medicine

The practice of EBM can be summarized in 5 steps Table 5-1.

The Question	1. Construct a well build clinical question derived from the case i.e. Clinical problem
The resource	2. Select the appropriate resource(s) and conduct a search
The evaluation	3. Appraise that evidence for its validity (closeness to the truth) and applicability (usefulness in clinical practice)
The patient	4. Return to the patient–integrate that evidence with clinical expertise, patient preference and apply it to practice
Self -evaluation	5. Evaluate your performance with this patient

Table 5-1: Steps in practice of EVM

- **Step 1:** Construct a valid "question":

The first step is to convert the need for information into a well-built and answerable question. This is usually initiated through a patient encounter that generates questions about diagnosis, therapy, prognosis or potential harm of therapy or etiology of the disease Table 5-2.

Diagnosis	**How to select and interpret diagnostic tests**
Therapy	**How to select treatment that does more good than harm and that are worth the efforts and costs**
Prognosis	**How to estimate the patient's likely clinical course over time and anticipate likely complications of disease**
Harm/Etiology	**How to identify causes for disease (including iatrogenic forms)**

Table 5-2: Patient encounter usually generate multiple questions

e.g. patient with recurrent pregnancy wastage: how to select diagnostic tests, what therapy, how to estimate the prognosis and clinical course and what is the cause of the problem and potential effect of medication.

Formulating a "valid" answerable question require training and adoption of evidence based approach to clinical problems. To begin with the question should be relevant to the population of interest "e.g. pregnant women", it should also define exactly the intervention required *"e.g. administration of aspirin or placing cervical cerclage suture"*. The clinician should then seek comparison between the intervention and other measures or placebo and compare the outcome in each case. Seeking a comparison will leads to the next step i.e. locating the best evidence.

The four letters "PICO" that helps to create a valid clinical quesion
- **P**atient/population: e.g. Pregnant women
- **I**ntervention: e.g. Aspirin for primary prevention
- **C**omparison: e.g. with Placebo
- **O**utcome: prevention of PET

- **Step 2: Locate the Best Evidence**

Not very long ago the only sources of evidences were ones own personal or colleagues experience, textbooks and specialized periodicals. They all have limitations.

In the present age of electronic media, information and experience from all over the world are available for search and evaluation. This however creates new challenges: **First**: "Knowledge

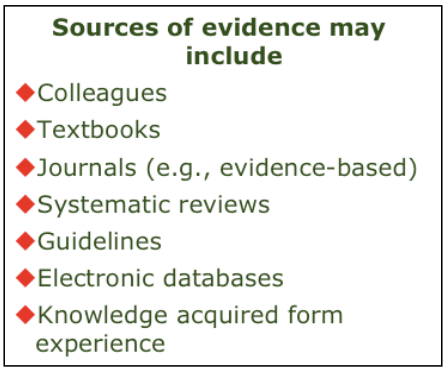

Figure 5-1: Sources of evidences

management skill" or how to find the best available answers to specific questions amidst the huge volume of available information?

Second: to evaluate the level of strength of evidence of the different constructed studies.

Levels strength of evidence:

Evidence for interventions commonly begins with observational studies, including unblinded case series, case-control studies, and cohort studies. It then culminates into the interventional randomized controlled trials (Figure 5-2).

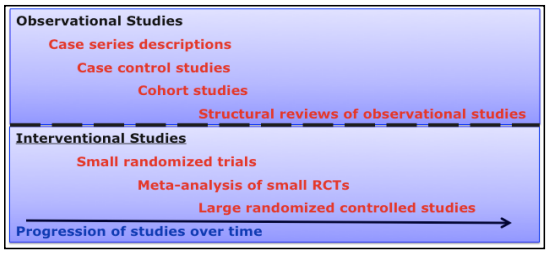

Figure 5-2: Common progression of research in building the strength of evidence. RCTs, randomized, controlled trials.

- **Case series:**

Case series are simply report of a series of patients with an outcome of interest e.g. birth outcome of in obese women. No control group is involved therefore they have no statistical validity

- **Case-Control Studies:** are studies in which patients who already have a specific condition are compared with people who do not. Case controlled studies are retrospective they often rely on medical records and patient recall for data collection (e.g. Birth weight in relation to smoking). They are relatively inexpensive and rapid studies to complete. The association between exposure and outcome is commonly summarized by a statistical measure called an *odds ratio*.

An odds ratio is an estimation of the true relative risk for the outcome in question.

- **Cohort Studies**

Cohort studies are typically prospective and often the next step in building the strength of evidence regarding an association between an exposure and an outcome.

Cohort studies take a large population and follow patients who have a specific condition or receive a particular treatment over time and compare them with a group that has not been affected by the condition or the treatment being studied.

They are generally more expensive in term of cost and take longer to complete than case-control studies. However, they provide a more accurate estimate of the relative risk (e.g. in case of women who take folic acid) and those who do not.

In a cohort study of "folic acid" and "spina bifida", a researcher would identify a group of women taking "folic acid" and a similar group of women who have chosen not to take "folic acid", and the researcher would then follow them over time and count the number of "spina bifida" events. Because outcome events may be uncommon in each group and may take many months to occur, cohort studies often require large numbers of participants and long follow-up periods to show significant differences between groups.

The Odds and Odds ratio (OR)

The Odds: The probability that an event will occur expressed as a proportion of the probability that the event will not occur i.e. the ratio of events to non events e.g. if the event rate of a disease is 0.2 (20%) and its non-event is 80% then its odds are 20/80 = ¼ =0.25.

Odds ratio (OR): measure treatment effectiveness. It is the odds of an event happening in group receiving intervention expressed as a proportion of the odds of the event happening in the control group.

OR < 1.0 indicate protection from outcome
OR > 1.0 indicate risk of outcome
OR = 1.0 indicate no association to outcome
i.e. the further away the value is from 1.0 the stronger the relationship and vies versa

The primary statistical measure from a cohort study is *relative risk*. This is a ratio of the rate of "spina bifida" events among women who choose to take "folic acid" divided by the rate among women who choose not to take "folic acid".

The Relative Risk

The number of times more likely (RR >1) or less likely (RR<1) an event is to happen in one group compared with another. It is the ratio of absolute risk (AR) for each group i.e. the absolute risk in the intervention group divided by the AR in the control group.

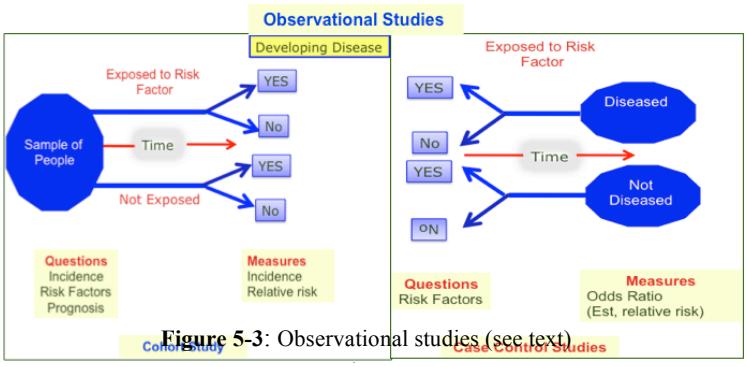

Figure 5-3: Observational studies (see text)

- **Randomized-controlled studies "RCTs":**

In RCTs, study participants are randomly allocated to two or more groups and then assigned to receive an intervention (e.g. Folic acid, or HRT, or certain procedures as elective cesarean section for breech…etc) or to receive no active treatment or intervention or to continue with their usual care.

RCTs greatly add to the confidence in the measured results because the structure of a RCT helps to eliminate many of the inherent biases in observational studies (Figure 5-4)

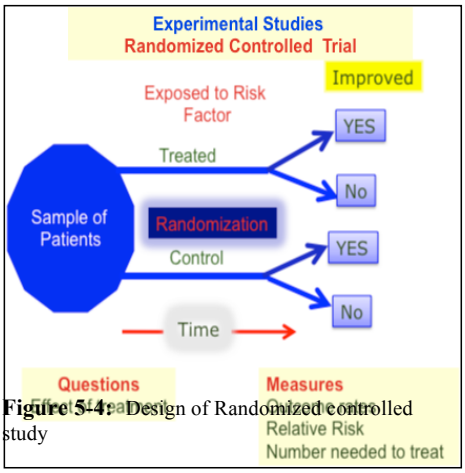

Figure 5-4: Design of Randomized controlled study

However RCT cannot be applied in all situations. For example, although a "cohort study" ranked lower than a "RCT", it may provide the highest level of evidence (excluding systematic reviews) for some aspects of patient care (e.g., validity of diagnostic tests, assessing prognosis). Also in some situations randomized controlled clinical trials cannot be performed due to ethical concerns (e.g., study of harmful interventions or exposures).

<u>Systematic review of randomized studies</u>:

The randomized trial (especially the systematic review of randomized trials) has become the "gold standard" for judging whether or not a particular treatment is beneficial.

- **<u>Systematic reviews:</u>**

It usually focuses on a clinical topic and answers a specific question. It involves conducting an extensive literature search to identify all studies with sound methodology. The studies are reviewed, assessed, and the results summarized according to predetermined criteria of the review question. It provides **qualitative** information from the reviewed studies. It may or may not involve meta-analysis.

- **<u>Meta-analysis:</u>**

It is a type of systematic review that uses rigorous statistical methods to **quantitatively** summaries or synthesis the results of multiple RCS. It allows increased statistical power to determine the weight of evidence from a series of similar studies. Some clinicians put Meta-analysis at the top of the "Evidence Pyramid" because part of the methodology includes critical appraisal of the selected RCTs for analysis (Figuer5-3)

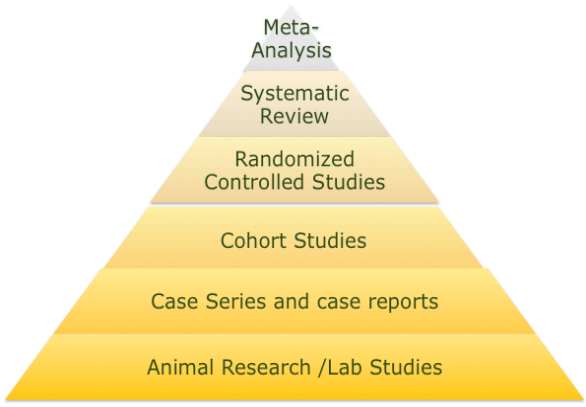

Figure 5-5: the "evidence pyramid". Information usually starts in laboratory then the human testing may begin with volunteers, RCT test the effectiveness and efficacy of a drug or therapy. A Meta-analysis will thoroughly examine a number of valid studies

- **Step 3: Critically Appraise the Evidence**

The third step in the process of practicing evidence-based medicine is to critically appraise the evidence.

This requires examination of the details of the study in term of its objectives, methodology, analysis of results …etc. The important questions to be answered in this respect are:

- The Validity: Can I trust this information? e.g. are the study methods sounds.
- Clinical importance: Are the valid results of the study important? e.g. what is the magnitude of the treatment effect.
- Applicability: Can the result be applied to my patients?

e.g. Is my patients so different from those in the study that its results cannot apply?

Guidelines: **G**uidelines, sat by international bodies are based on reviewing the contents of dozens of journals, and evaluating each article or review. Good guidelines are evidence-based guidelines since it describe the strength of the evidence and categorize it according to its level of strength (Table 5-1).

Level Evidence	
I	Blinded randomized controlled trails
II-1	Controlled trials without randomization
II-2	Well-designed cohort and case control studies
II-3	Cross sectional studies, studies with external control groups
III	Case series evidence-derived from report of an expert committee, which itself used a scientific approach

Table 5-1: Level of Evidence based on its sources

- **Step 4: Integrate Findings With Clinical Expertise and Patient Needs**

In clinical practice evidences obtained from research may not apply exactly to all individuals, or to a particular clinical problem. Therefore, the it must be evaluated for its specific context, and integrated with clinical expertise as well as the preferences and values of each patient.

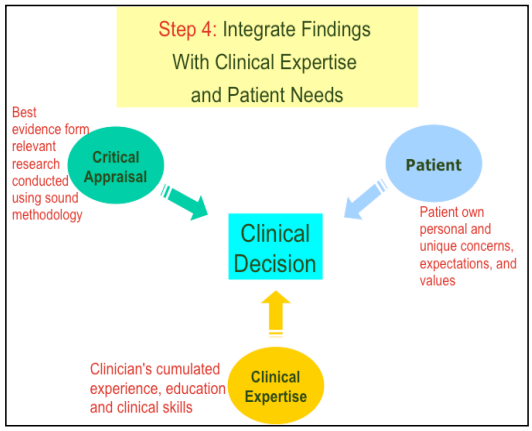

Figure 5-6: Applying EBM

In applying evidence based medicine clinical decision for individual patient should integrate the clinical expertise (clinician's cumulated experience, education, and clinical skills), patient values (preferences, concerns, and expectations), and the best evidence (found in clinically-relevant research that has been conducted using sound methodology) into the decision-making process for patient care.

➢ **Step 5: Evaluate Performance and Seek Ways to Improve**

The fifth step in practicing evidence-based medicine is often overlooked. This is self-evaluation, which allows physicians to identify areas that need improvement and reinforces strengths.

Asking the right questions, tracking down solid evidence, ensuring that evidence is applicable to a particular patient, and doing this on an everyday basis.

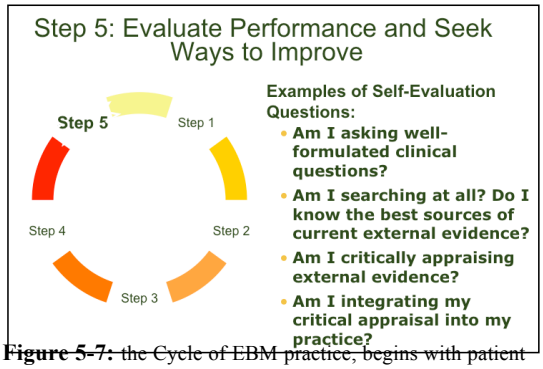

Figure 5-7: the Cycle of EBM practice, begins with patient encounter and end with results of (effect) of intervention on patient encounter

Lifelong learning model

It is obvious that evidence-based medicine requires new skills including efficient use of the internet search engines for literature searching, and the application of formal rules of evidence in evaluating clinical literatures.

It is a process of lifelong, self-directed, problem-based learning in which caring for one's own patients creates the need for clinically important information about diagnosis, prognosis, therapy and other clinical and health care issues.

Resource	Internet Address
ACP Journal Club	www.acpjc.org
Cochrane Library	www.update-software.com
UpToDate	www.uptodate.com
PubMED	www.ncbi.nlm.nih.gov/PubMed
eMedicine	www.emedicine.com
Clinical practice guidelines	www.guidelines.gov
MD Consult	www.mdconsult.com
EBMR[1] Reviews (OVID)	www.ovid.com/site/catalog

Some selected resources for EBM

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Chapter 6

Preconception and Prenatal Care

Dear Dr Sara Ghazali

By the end of this chapter you should be able to:

Preconception care:
- **Define** preconception care: Its objectives and components.
- **Advice** women on immunization strategy and principle of immunization in pregnancy

List the objectives of prenatal care:
- **Discuss** the measures of antenatal care in each trimesters of pregnancy
- **Discuss** the importance of the first antenatal visit (booking visit)
- **Discuss** the potential concerns of antenatal care for pregnant women in "Ramadam"

Preconception Care

Preconception Care is considered an essential part of primary and preventive care. It refers to interventions that aim to identify and modify medical, behavioral, and social risks to a woman's health or pregnancy outcome through prevention and management.

Although preconception and antenatal care are now considered a continuous process that have the same objective, in real life few proportion of women present specifically for preconception advice and counseling. Therefore it is the responsibility of health care provider to identify and utilize opportunities for preconception counseling that often occur during many other health care encounters such as; premarital examination and testing, contraception counseling, evaluation for vaginal infection, after a negative pregnancy test, or at anytime a woman of childbearing age presents for a periodic health examination

Objective of preconception care: The objective of preconception care is to optimize the health of the woman before pregnancy' in order to ensure a healthy pregnancy and a healthy baby. To achieve this goal the following measures are adopted:

- History: Once the patient attends for preconception care, a full personal and family history should be taken.

- Examination: This visit provides a good opportunity for general and local pelvic examination including Pap smear.

- Intervention measures: The measures provided in the pre-conception clinic can be discussed under three headings, namely *health behavior modifications, preconception counseling*, and *effective intervention measures*.

I. Health behavior modification:

Pregnancy, as well as planning for pregnancy is an optimum opportunity for behavior modifications such as:

- General advice should be given regarding the importance of healthy behavior e.g. women who smoke or drink should be advised against such habits .
- Diet and weight adjustment: being over and underweight are recognized risk factors for adverse pregnancy outcomes. For example obesity is associated with increased risk of gestational diabetes (GD), while underweight is a risk factor for low birth weight and preterm labor.

II. Preconception counseling.

The three components of preconception counseling are:

- Identification of risks relevant to pregnancy: e.g. medical, genetic disorders.
- Patient education regarding pregnancy risks, management options, and reproductive alternatives
- Initiation of interventions, when possible, to provide optimum pregnancy outcome

Medical conditions: Women with pre-existing medical conditions should be carefully counseled to maximize pre-pregnancy health prior to conception.

Diabetes mellitus is by far one of the most commonly encountered conditions where pre conceptional intervention is critical. The incidence of congenital anomalies is directly related to the degree of glycemic control at the time of conception and period of organogenesis. Women on oral hypoglycemic drugs should be advised to change to insulin for their diabetes control.

Other maternal conditions which benefit significantly from preconception interventions include; epilepsy, hypertension, asthma, thromboembolic disease, autoimmune conditions, thyroid disorders, renal disease and cardiac disease. Most women with these conditions will benefit from preconception referral to a maternal-fetal-medicine specialist for in depth discussion of the impact of pregnancy on her health and the likelihood of neonatal complications.

Genetic counseling: Patients with a specific indication for genetic testing such as maternal age greater than 35, family history of a genetic disease, or history of a previously affected pregnancy should be referred for genetic counseling. Also, screening for heterozygote status such as thalassemia and sickle cell disease should be offered for at risk groups. Several other conditions may need to be screened for in specific ethnic groups, such as Tay-Sachs screening in Ashkenazi Jewish population.
Positive cases need referral to specialist in fetomaternal medicine for further tests including screening of the husband and counseling regarding risk for offspring, the available reproductive options e.g. preimplantation genetic testing (PGD), and prenatal diagnosis.

III. Effective intervention measures:

The measures that have been found to be effective include:

- Folic acid supplementation:

Peri-conceptional supplementation with folic acid can reduce the risk of neural tube defects by more than two thirds. Neural tube closure occurs during the first four weeks of gestation, very often before pregnancy is diagnosed. Therefore, the recommended dose of folic acid supplementation of 0.4–0.8 mg/day should be commenced at least one month prior to conception and continued throughout the first trimester. In some situations a higher dose of folic acid (4 mg/day) is recommend such as in women with a prior history of neural tube defect, and epileptic women on medications.

- Immunizations:

Immunization programs are among the most cost-beneficial health interventions. All women of childbearing age should be questioned as to their immunization status (or probably exposure) and advised on immunization strategy. This can significantly reduce the occurrence of preventable diseases, benefiting not

Guidelines for vaccination of women in Childbearing age

1. All women of childbearing age should be evaluated for the possibility of pregnancy before immunization. (III-A)

2. In general, live and/or live-attenuated virus vaccines are contraindicated during pregnancy, as there is a, largely theoretical, risk to the fetus. (II-3)

3. However women who have inadvertently received immunization with live or live-attenuated vaccines during pregnancy should not be counseled to terminate the pregnancy because of a teratogenic risk. (II-2)

4. Non-pregnant women immunized with a live or live-attenuated vaccine should be counselled to delay pregnancy for at least four weeks. (III)

5. Inactivated viral vaccines, bacterial vaccines, and toxoids are considered safe in pregnancy. (II-1)

6. Women who are breastfeeding can still be immunized (passive-active immunization, live or killed vaccines). (II-1)

SOGC clinical practice guidline: J Obstet Gynecology Can 2008;30(12):1149–1154

only the patient and her infant but also the rest of the population. In general the principle of the benefit vs. risk of vaccination (for both mother and fetus) is the guideline for advice on immunization. See the pink box for general guidelines of the principle of vaccination of women of childbearing age and table (6-1) for commonly used vaccines.

Vaccine	Indications in pregnancy	Comments
Live		
Measles	Contraindicated	No known fetal effects, but theoretical increased risk of preterm labour and low birthweight with live vaccine
Rubella	Contraindicated	
Varicella	Contraindicated	
Poliomyelitis Sabin/Salk	To be considered in high-risk situations (inactivated preparation)	No known fetal effects
Influenza	indicated in pregnancy, primarily for protection at > 20 weeks when risk is greatest	Influenza may be associated with greater morbidity in pregnancy, so immunization recommended
Rabies	No indication of fetal anomalies-	Risks from inadequate treatment significant
Non Live		
Hepatitis A	Low theoretical risk	Appropriate in the presence of medical indication
Hepatitis B	No apparent fetal risk	Vaccine recommended for pregnant women at risk
Pneumococcus	Indicated in high-risk patients	no adverse effects reported; high-risk patients should therefore be vaccinated
Meningococcus	Safe and efficacious in pregnancy	vaccinated as per general guidelines for non-pregnant patients
Diphtheria/tetanus	No evidence of teratogenicity	Susceptible women to be vaccinated as per general guidelines for non-pregnant patients
HPV vaccine	Are manufactured using recombinant technology. Although there is no evidence of teratogenicity it is not recommended for use during pregnancy. If a woman becomes pregnant part way through the vaccine series, it is recommended that the rest of the series be deferred until after pregnancy.	

Prenatal Care

The overall goal of prenatal care is *'to maintain the mother's well-being throughout the pregnancy and achieve a healthy outcome for herself and her infant*'. Several components are described achieve this goal. It may summarized in the following items:

1. Early, accurate estimation of gestational age
2. Identification of patients at risk for complications (for the mother and/or the fetus)
3. Ongoing evaluation of the health status of both mother and fetus

Table 6-1: common vaccination in pregnancy.

4. Anticipation of problems and intervention, if possible, to prevent or minimize morbidity
5. Patient education and communication

The first and second items are usually obtained in the first prenatal visit, whereas the fifth item is an ongoing process throughout pregnancy.

First Prenatal Visit 'booking visit':
This is the most important visit that determines the level of care and follow up during the remaining period of pregnancy. The overall objectives of this visit are:

- To confirm the pregnancy, and accurately determine gestational age and due date. If the date of the last menstrual period cannot be relied upon, an ultrasound scan should be ordered. Similarly, ultrasound scan is ordered if there is any suspicion that the pregnancy may be ectopic (see chapter 29 for ultrasound in pregnancy).
- To identify risk factors and accordingly plan the level of care and follow up for the remaining of the pregnancy. In some cases arrangement for combined care may be needed e.g. cardiologist, endocrinologist…etc.
- Providing therapeutic interventions known to be beneficial such as folic acid and iron supplementation. Other vitamin and calcium supplementation needs to be determined on an individual basis.

In this visit the following procedures should be performed:

- Full history and examination: (see chapter on approach to obstetric patient).

- Screening tests: According to the WHO (World health organization) and other international bodies there are a number of tests proven to be effective and should be performed for all women. Those tests are:

    - Hemoglobin and hematocrit determination.
    - ABO and Rh blood group and screening for irregular antibodies.
    - Screening for Rubella immune status by testing for IgG antibody.
    - Screening for hepatitis B surface antigen (mainly in areas with high prevalence)
    - Screening for Syphilis by VDRL (Venereal Research Laboratory) test.

- Midstream urine sample for asymptomatic bacteruria

Screening for Toxoplasmosis is currently not recommended as a routine screening test.

Other specific screening tests:

In certain areas or population, screening for other diseases or disorders may be necessary e.g. HIV and Chlamydia screening is recommended by the ACOG. However, this is currently not routinely performed in Saudi Arabia since the prevalence of these diseases is believed to be low. Similarly, in certain areas it is important to screen for hemoglobinopathies as in the Eastern region of Saudi Arabia where the prevalence of hemoglobin disorders is rather high.

- Ultrasound scan: Although it is widely used, ultrasound fetal scanning is not a routine test unless there is doubt about the gestational age or suspicion of ectopic pregnancy.
- Screening for genetic diseases: Routine screening for genetic diseases is a well-established practice of antenatal care in many of the Western countries. All pregnant women are offered screening tests for genetic disorders, namely neural tube defects and Down syndrome (see chapter on prenatal diagnosis). This practice requires not only resources but also general consensus among the society (both medical care providers and patients) to encourage or approve routine screening for fetal anomalies, which is not yet established in most of the developing countries.
- Patient education specific to pregnancy: Patient education is an on going process throughout the period of antenatal care. The emphasis of discussion and education may change according to the stage of pregnancy.

  In the first trimester women particularly primigravidas are educated, about many aspects of pregnancy e.g. normal symptoms of pregnancy, nutrition and weight gain, fetal movements…etc.

  Later in pregnancy, discussion should include symptoms and plans for labor, the postpartum period and baby care and, discussion on family planning options.

The education program should also include information about emergencies during pregnancy and how to deal with them.

At the end of the first visit, arrangements are made for follow up visit to check the results of the investigations and plan subsequent visits. The majority of patients belong to the *no more than average risk* 'low risk group' and subsequent follow up can continue along a standard protocol, ideally undertaken by a trained midwife or specialist.

A proportion of cases, because of present or past history, will need special care and more frequent visits. They will need to be followed up by a consultant specialist or in a combined care clinic (e.g. diabetic or cardiac cases...).

Follow-up visits:

There is no agreement on the optimum number of antenatal visits during pregnancy. Traditionally, prenatal follow up visits are arranged every four weeks until 28 weeks, then every two weeks until 36 weeks and weekly thereafter. However there is no scientific evidence that support such scheme of care for better or optimum outcome. Moreover studies have shown that the frequency of antenatal visits may be reduced without compromising the objectives of prenatal care.
Fewer visits does not only have the advantages of saving resources but also allows more opportunity to care for a larger number of the women. It has also become clear that the efficacy of prenatal care does not depend on the "number" of visits but rather on the following two factors:
(1) Objective of the visit: The objective of antenatal care is greatly related to the pregnancy trimester (see table 6-2 for summary of objectives of visits in first, second and third trimester).
(2) The quality of care: provided by the health care provider.

The following routine procedures are performed at each visit:

- Measurement of blood pressure; and weight of the patient.
- Urine strip test for proteinuria (qualitative test) and glycosuria.

- Enquiry about any health matters related to the patient. Also time should be allowed for addressing any queries or questions that the woman might have.

Screening for gestational diabetes (GDM); screening for glucose intolerance should be performed between 24 and 28 weeks (see chapter on DM and pregnancy). Also repeat CBC for anemia should be performed at 24 and 34 weeks.

- Abdominal obstetric examination: The objectives and techniques of abdominal obstetric examination vary according to the pregnancy trimester and weeks of gestation (see chapter on obstetric examination).

Visit Week	Intervention
First Visit	Confirm pregnancy, gestational age, EDD (full history, examination and investigations) Education
Second Visit: 12 to 14 weeks	Review results and accordingly plan level and subsequent visits Counseling on Screening for Genetic anomalies (11-14 wks scan for NT and biochemical screening tests (if available and agreeable)
20-28 Weeks	Screening for fetal anomalies 18 weeks Fetal echocardiography 20-22 weeks (if available and agreeable) Education and address of any questions Early diagnosis and treatment of anemia and PET Screening for gestational diabetes 24-28 weeks
28-34 weeks	Fetal growth (screening for FGR) and fetal wellbeing Administration of anti D prophylaxis (For Rh negative patients who are not sensitized)
36 -40 weeks	Determination of fetal lie, fetal growth, wellbeing Discuss plan for delivery Education on symptoms of labor, options for analgesia and anesthesia in labor, where to go when labor starts Contraception options

The table 6-2: summarizes the timing and objectives of antenatal visits in relation to the weeks of gestation (trimesters) in low risk cases. The plan for follow up for cases with specific maternal risks e.g. cardiac, diabetic cases or obstetric factors such as growth restriction or multiple pregnancy, require a different approach for follow up, depending on the nature of the problem and severity of the disorder. Screening for genetic Down syndrome and fetal anomalies is becoming an important element in prenatal care, but requires resources and general consensus among both the society and the health care providers.

Antenatal care for Fasting women in Ramadan

Ramadan is one of the pillars of Islam; all sane adults' persons are obliged to fast the month of Ramadan. From the physical point of view fasting of Ramadan entails abstinence from food, drink and sexual marital relation from sunrise to sunset for the whole lunar month of Ramadan.
However in relation to pregnancy and lactation there are exemptions from fasting this include:

- If a pregnant woman either unable to fast or if medically instructed not to fast because of fear for her health or the heath of her unborn baby.
- The same principle applies for lactating women.

In such cases the woman has to make up for the broken days by fasting after Ramadan.

Pregnancy and fasting:
The majority of pregnant Muslim women chose to fast in Ramadan sharing the family and the whole Muslim community rather than having to compensate for the broken days of fasting at a latter date.
The overwhelming evidence from clinical experience and the studies that has been conducted, though small in number, in attempt to examine the safety of Ramadan fasting in pregnancy have concluded that:

- There is no difference between the birth weights and Apgar score of babies of women who fasted, and the babies of women who did not fast.
- Some studies have shown that some women who fast during pregnancy may go on to have lower-birth weight babies. However, these result came from a study of women who were more likely to have poor diets or too little food.
- Fasting by a pregnant woman does not seem to affect the potential IQ of her baby.
- Women do experience changes in the chemical balance of their blood while fasting. But the changes do not appear to be harmful to either the women or their babies, and do not affect the babies' birth weights.

In conclusion in the majority of cases there are usually no contraindications against fasting of healthy pregnant women in Ramadan as long as she can

tolerate it and there is no strong medical reason against fasting e.g. diabetics on insulin, cases with FGR or other disorder.

The obstetrician has dual responsibilities; on one hand not to deprive the woman form having to fulfill one of the most important duties she has to observe as a Muslim on the other hand taking care of the patient and her unborn baby's health.

Advice for Fasting in pregnancy:

The following advice should be offered for pregnant women who wishes to fast:

- The woman should be advised to have a variety of healthy food and plenty to drink at Iftar, the pre-dawn meal, and Suhoor, the meal taken at dusk.
- The type of food chosen is better to be of the kind that allow slow release of energy e.g. complex carbohydrates, such as whole grains and seeds, and high-fiber foods, such as pulses, vegetables and dried fruits. This will help to avoid constipation. Food that raises blood sugar quickly should be avoided
- Plenty of fluid (on average two liters of water) should be taken over the night (during the permissible period). Caffeinated drinks should be avoided since caffeine is diuretic and enhance dehydration.
- The patient should avoid stressful and strenuous situations. Fasting women seem to already have higher levels of the stress hormone cortisol, in their blood than women who are not fasting.
- Patient should ensure adequate rest and sleep time.

Other issues related to pregnancy and fasting:

- **Vaginal examinations for a fasting woman:** The general consensus is that vaginal examination is not allowed in the fasting state. It is best to perform the vaginal examination after the fast is broken (after *iftār*). If the patient is so "ill" that she must have an immediate vaginal examination then she should not be fasting in the first instance.

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Chapter 7
Ant-partum Fetal Evaluation

Dr Nabeel Bondagji

Fetuses exposed to chronic hypoxia regardless of the primary cause; respond with sequences of compensatory changes. The ability to monitor those changes, which include biological functions such fetal heart rate, fetal breathing and movements, form the bases of prenatal fetal surveillance. Several methods have been developed for fetal monitoring only few are based on scientific evidence from randomized trials. Hence understanding the pathophysiology of intrauterine asphyxia as well as an awareness of the capabilities and limitations of available antepartum fetal assessment tools to diagnose intrauterine fetal asphyxia is crucial for its appropriate utilization.

By the end of this chapter you should be able to :

- Discusses the objectives
- List indications of prenatal fetal monitoring
- Discusses the fetal response to hypoxia (patho-physiology of fetal response to hypoxia): The compensation and decomposition of the fetus to hypoxia.
- List the methods of fetal monitoring:
    - Fetal Movements count:
    - Fetal Heart Monitoring (Non-Stress Test):
    - Biophysical Profile (BPP):
    - Contraction Stress Test:
    - Viboracustic Stimulation:
    - Doppler Blood Flow:
- For Each method you should be able to describe : The principle, technique and interpretation.

Objectives and indications of prenatal fetal monitoring:

Prenatal fetal surveillance is now a standard element of prenatal care. Its primary goal is to recognize fetuses in whom timely intervention will prevent death. A secondary goal is to avoid fetal neurologic injury from prolonged exposure to intrauterine hypoxia.

Simple methods of monitoring such as "fetal movement count" may be applied and taught to almost all pregnant women (see later). But more specific measures of fetal monitoring should be offered to fetuses at risk of chronic hypoxia (Table 7-1). The type and frequency of monitoring depends on several factors including current indication, previous obstetric history and results of monitoring.

1.	**Patients at high risk of uteroplacental insufficiency e.g.:**
	- Prolonged pregnancy. - Hypertension - Diabetes - Previous stillbirth - Suspected FGR - Multiple pregnancy - Advanced maternal age - Antiphospholipid syndrome
2.	When other tests suggest fetal compromise e.g.:
	- Suspected FGR (on clinical examination) - Decreased fetal movements - Oligohydramnios

Table 7-1: Indications for Antepartum Fetal Monitoring

Neurological Maturation of Fetal function and Patho-physiology of fetal Adaptation to Hypoxia:

- Neurological maturation of fetal biological function:

The development and maturation of the neurological control of the fetus biological functions such as tone, movements, breathing and cardiac functions occur gradually as pregnancy progress.

- The fetal tone and movements: are the earliest of such changes; both are controlled by cerebral centers. The center for muscle tone develops around 7.5 -8.5 weeks and for fetal movements develops around 9 weeks.
- The breathing movements: are controlled by the breathing center in brain stem. Breathing movements start to appear from early second trimester. Fetal breathing is established by around 20th
- Cardiovascular functional maturation evolves with maturation of the autonomic nervous system, the sympathetic and parasympathetic nervous system that control the cardiac function. Other factors that modulate the cardiac function include: baro and chemoreceptors at the carotid as well as hormones such as adrenal hormones.

Effect of gestational age on FHR

The parasympathetic nervous system has a slowing effect on the FHR and the heart rate variability. the which increase as the gestational age advances. Sympathetic stimulation results in release of norepinephrine, which accelerates the FHR and improves inotropy. As an example the fetal heart is much faster in early pregnancy compared to its rate in the third trimester. By 28 weeks the parasympathetic nervous system is consistently developed

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- Patho-physiology of fetal compensation to hypoxia:

Fetal hypoxia, regardless of the cause, triggers several compensatory mechanisms. These mechanisms include:

1) A decrease in heart rate (Bradycardia) and variability (beat to beat variation).
2) A reduction in oxygen consumption by cessation of nonessential functions such as gross body movements.

3) Redistribution of cardiac output to preferentially perfuse the more vital organs, such as the heart, brain, and adrenal glands.

4) A switch to anaerobic cellular metabolism, which precipitate metabolic acidosis.

The degree to which these mechanisms are effective in preventing asphyxia and its adverse consequences depends on the underlying health of the fetus and the placenta as well as the duration, frequency, and intensity of the hypoxemic event(s).

If hypoxia is prolonged enough, the fetus starts to decompensate i.*e. loses the ability to protect its vital organs*. Eventually, there is a decrease in cardiac output. This, in turn, leads to marked hypotension and a subsequent further decrease in blood flow to the heart and the brain.

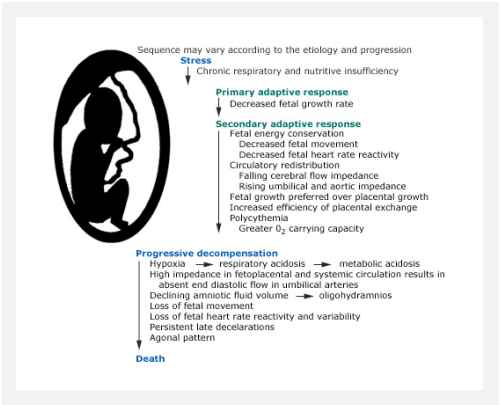


Figure 7-1: Sequence of fetal hypoxia

Prolonged asphyxia with metabolic acidosis leads to cellular death, tissue damage, multiple system failure, and,

ultimately, fetal death.

Interpretation of Fetal monitoring:

The general principle in interpretation of any of the methods of fetal monitoring should take in consideration: gestational age, maternal conditions (including medications E.g. administration of steroid for fetal lung maturity is associated with reduced BPP for period up to 3 days), and fetal condition (e.g. growth restriction, anemia, arrhythmia).

Usually more than one method should be used because of the limited sensitivity of most of them. Depending on the results of the tests, gestational age, and overall clinical situation, delivery may be warranted if the risks of continuing the pregnancy outweigh the benefits.

Methods of fetal surveillance during pregnancy:

I. Maternal Assessment of Fetal Activity (Fetal Movement Count Chart):

Maternal monitoring of fetal movement is the simplest method of monitoring of fetal wellbeing. It has the advantage of not only being of low cost but also can be offered to almost all pregnant women.

Principle:

The presence of normal fetal movement is a sign of functional integrity of fetal neuro-regulatory systems. In the presence of mild hypoxemia, the fetus compensate by decreased frequency and strength of movements. Hence decreased fetal movement "DFM" has been considered a warning sign for further fetal evaluation.

The Technique: A special chart called "kick Chart" is used by the mother to record her baby's movement over a period of time. If the fetus moves less than certain number of movements the mother is asked to report to the clinic. However the criteria or number of fetal movements "FMs"

that reliably distinguishes a healthy fetus from a fetus at risk has not been determined. The following three criteria are the most commonly used for reassurance of fetal wellbeing and any one of them may be used:

- Perception of at least 10 FMs during 12 hours of normal maternal activity
- Perception of least 10 FMs over two hours when the mother is at rest and focused on counting "Cardiff Count-to-Ten chart"
- Perception of at least 4 FMs in one hour when the mother is at rest and focused on counting.

DD of decreased movements "DFM": Infrequent fetal movement does not necessarily mean the fetus is compromised or even inactive. Transient decrease in fetal activity can be due to fetal sleep states, maternal drug use (e.g. sedatives), or maternal smoking. Also the fetus may be active but its movements are not adequately perceived by the mother such in: early gestational age, decreased/increased amniotic fluid volume, maternal position (sitting or standing versus lying), fetal position (anterior position of the fetal spine), obesity, anterior placenta, and maternal physical activity (or just being mentally distracted).

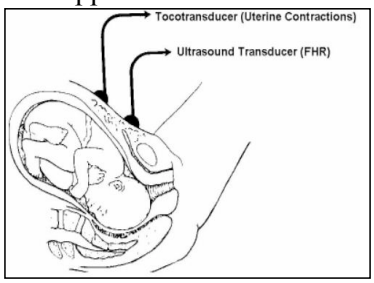
II. Electronic Fetal Heart Rate Monitoring:

Principle: Monitoring of fetal heart activities is indirect way for assessment of fetal oxygen status. Fetal hypoxia affects the cardiac control centers, and result in diminished heart activities "rate, variability and reactivates" through the autonomic nervous system.

In respond to Hypoxia:
- Chemoreceptors: signal to first increase HR and variability and then, if persists or worsens, constrict peripheral arterial beds, resulting in systemic hypertension and redirecting blood flow for vital organs (brain, heart and adrenal) .- Baroreceptors: send signals to the brainstem that leads to stimulation of the vagus nerve and consequent slowing of the fetal heart

The technique: Electronic fetal heart monitoring depends on recording fetal heart activities in response to uterine contractions and or fetal movments.

To do this, two abdominal transducers are used, a Doppler ultrasound transducer that transmits electronic signals of the FH activities and a tocotransducer "tocodynamometer" to detect uterine contractions.



Fetal movements are usually recorded by the patient using an event marker or noted by the staff performing the test.

The typical fetal monitor strip consists of two rows

of graphs; the upper graph displays the fetal heart activities (rate, variability, and response to uterine contractions or fetal movements) and the lower graph displays the uterine contractions (in mm of Hg).
There are two types antenatal fetal heart rate monitoring: **(1)** The Non Stress Test "NST" and **(2)** The Contraction Stress Test "CST" or sometimes called oxytocin stress test.
Non-stress test "NST": The NST is the most commonly used cardiotocographic method of antepartum fetal assessment. It is noninvasive (unlike the CST) and there are no direct maternal or fetal risks, and virtually no contraindication for it.

Interpretation: the results of a NST is interpreted as either reassuring or non reassuring based on criteria related to the rate of the fetal heart, its variability "beat to beat variation" and response to uterine contractions and/or fetal movements:

- **Reassuring patterns "Reactive test":** To be labeled as reactive the following criteria should be fulfilled over 20 minutes of fetal monitoring: A basal fetal heart rate within normal (110-160 bpm), normal range of variability (5-25 beats), and at least two accelerations of the fetal heart rate of approximately 15 bpm amplitude and for 15 seconds' duration. If these criterions are not met the test may be extended for further 20 minutes.
- **Non –reassuring pattern "Non-reactive test":** The test is labeled as non reactive if after 40 minutes the criteria for reactivity are not met. A non reactive test may be associated with adverse fetal or neonatal outcomes.
  In some cases if the test is non-**reactive**, acoustic stimulation may be used to apply a sound stimulus for 1 to 2 seconds (see vibroacoustic stimulation).

The severity and nature of non-reactivity varies depends on the element(s) being affected (heart rate, variability, or response of fetal heart to the stress

of uterine contractions) and its severity (see tables 7-2 and 7-3 for interpretation of fetal heart tracing).

Criteria for reactive
(Reassuring Fetal heart tracing test)

1) Heart Rate: 110 – 160 bpm

2) Positive acceleration (> 15 beat and 15 second duration) that coincide with contractions and or fetal movements

3) Beat to beat variability of between 5-15 beats

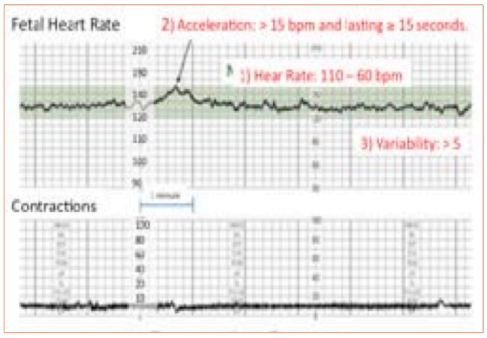


Figure 7-2: Criteria for reassuring fetal heart rate

In relation to NST it should be noticed that:

- Interpretation of the CTG results should take in consideration the gestational age because the response of the fetal heart depends on maturation of the fetal autonomic nervous system. Therefore the ability of the fetus to accelerate its heart rate is gestational age-dependent. For example from 24 to 28 weeks gestation no more that 50% of NSTs will be reactive, while from 28 to 32 weeks of gestation 85% of NSTs are reactive.
- The presence of a reassuring pattern indicates that there is no fetal hypoxemia only at the time of testing.

The frequency of doing the test is based on clinical judgment and the indication for testing. It may be performed at daily to weekly intervals as long as the indication for testing persists.

- Differential diagnosis of Non Reactive Test:

- Causes other than fetal hypoxia should be considered such as:
  Benign and temporary non-reassuring test due to fetal immaturity, maternal smoking, or fetal sleep. , or maternal smoking. In some cases if the test is non-reactive a sleeping fetus may be exposed to acoustic stimulation to apply a sound stimulus for 1 to 2 seconds (see vibroacoustic stimulation).
- Fetal neurological or cardiac anomalies and sepsis.
- Maternal ingestion of drugs with cardiac effects.

The Contraction Stress Test "CST":

Principle: uterine contractions cause reduction in blood flow to the intervillous space and transient state of hypoxia. A fetus with inadequate placental reserve (i.e. uteroplacental insufficiency) would demonstrate late decelerations in response to the transient hypoxia of uterine contractions.

The Technique: The CST is ideally conducted in the labor and delivery suite or in an adjacent area. After baseline fetal heart monitoring uterine contractions are induced using oxytocin infusion or nipple stimulation technique. The aim is to induce at least three contractions within 10 minutes.

Contraindications to the test include; patients at high risk for premature labor, placenta previa and a previous classic cesarean section or uterine surgery.

Interpretation of the Contraction Stress Test: the results of CST are interpreted as negative if no deceleration occurred during the period of the test. A negative test result is associated with good fetal outcome and allow prolongation of pregnancy. A positive test, the occurrence of late deceleration or suspicious test indicate that the fetus is at risk and require further action depending on other risk factors and gestational age.

III. **Vibroacoustic stimulation (VAS)**

Principle: It depends on stimulation of the fetus by an artificial burst of noise produced by a hand-held battery-powered artificial larynx. It generates

sound pressure levels measured at 1 m in air of 82 dB with a frequency of 80 Hz and a harmonic of 20 to 9,000 Hz.
The goal is to alter the fetal behavioral state, wake a sleeping fetus, and provoke accelerations in the heart rate thus shorten the length of the NST. Whether it is the acoustic or vibratory component of this stimulus that alters fetal state is unclear.

IV. **Fetal Biophysical Profile "BPP":**
Fetal biophysical profile is based on the use of real-time ultrasonography to perform an in utero physical examination and evaluate dynamic functions reflecting the integrity of the fetal CNS (i.e. oxygenation)
Principle: the physical activities that reflect the biological integrity of the fetal central nervous system include five parameters. Four are based on ultrasound studies include: Fetal breathing movements (FBM), fetal body movement, fetal tone, and amniotic fluid volume and the fifth is the result of NST.
It is important to realize the following:

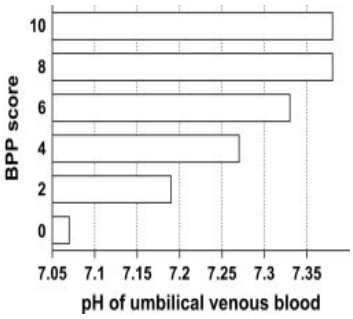
- The presence of all the parameters is sign of healthy and well-oxygenated system. Generally as the number of absent parameter increases, the likelihood of fetal compromise (hypoxia) increases.
- It was also noted that in hypoxic fetus, those fetal biophysical activities that appear earliest in fetal development are the last to disappear (i.e. An alteration in fetal heart rate is the earliest sign of fetal compromise while loss of fetal tone is the last to disappear).
- FBM, fetal body movement, and fetal tone: reflect the function of the fetal CNS at the time of the examination or short-term hypoxia.
- Diminished Amniotic fluid volume "oligohydramnios" reflects long-term fetal hypoxia since it results from diminished fetal urine output. This takes place secondary to compensatory redistribution of fetal circulation.

The Technique: Ultrasound examination is used to study the 4 parameters of the BPP i.e. amniotic fluid assessment, fetal breathing movements, fetal

gross body movements, and fetal tone. The examination is usually carried out over 30 minutes. Real-time ultrasound is used to document the fluid assessment and movement variables, and a 30-minute time period is allowed if needed to visualize fetal behavior.–

Interpretation of the BPP "The Fetal BPP Score"

Each of the five parameters of the BPP is awarded 2 points. The highest score a fetus can receive is 10, if all parameters are satisfactory, and the lowest score is 0. The lower the score the higher the risk of fetal compromise, fetal hypoxia and acidosis (Figure 7-3). Based on studies of correlation between BPP and umbilical venous-blood pH values the following recommendation have been suggested:



- A score of 8 or more is interpreted as normal with a very little risk of fetal death within 1 week (estimated as <1 in a 1,000).

- A score of 6 out of 10 may reflect lack of fetal well being, especially if there is oligohydramnios. A repeat test should be undertaken within same is indicated soon or delivery if the fetus is at term.
- A score of 4 out of 10 should raise serious concern of fetal compromise, with a high risk of fetal death, such that delivery would be indicated in most situations.
- A score of 0 to 2 out of 10 is an emergency and delivery should occur depending on the clinical circumstance.

However like all tests for fetal wellbeing the interpretation of the BPP is influenced by the gestational age, non hypoxic causes of low score such as maternal hypoglycemia (e.g. Fasting in the month of Ramadan) and drugs or

sedative that the mother might be receiving all are factors that can reduce fetal activity.

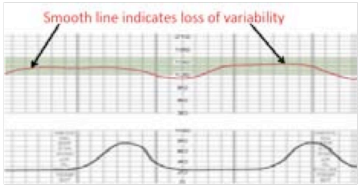
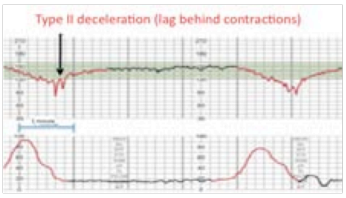
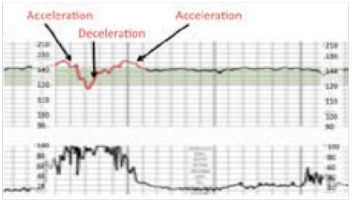
Variability fluctuation in FHR base line between 5 to 25 bpm. **Significance**: A constant variation from the baseline (variability) reflects a healthy nervous system, chemoreceptors, baroreceptors and cardiac responsiveness **Loss of variability reflects loss of autonomic modulation and control of the heart.**	
Early deceleration (Type I) is a decrease in the FHR in associated with a uterine contraction, and recover with the recovery of the contraction. **Significance: It indicates head compression but not placental insufficiency**. Usually seen in the second stage of labor.	
Late deceleration (Type II) The onset, nadir, and recovery of the deceleration occur after the beginning, peak, and ending of the contraction, respectively. **It indicates hypoxia and suppression of the central control of cardiac function.** **Combination of deceleration with bradycardia and or loss of variability signify serious hypoxia.**	
Variable Deceleration An abrupt decrease in the FHR of ≥ 15 bpm lasting ≥15 seconds. Its onset, depth and duration vary with successive contractions. **Often occur with cord compression as in oligohydramnios.** **If prolonged it could reflect fetal hypozia**	

Table 7-3: Illustration of different types of fetal heart rate abnormality, its pathogenesis and significance. The combination of more than one abnormality indicates more serious fetal hypoxia.

The Modified BPP: Because FHR accelerations are one of the last of biophysical variables to develop, therefore if the NST is reactive, then the other variables should be present. Also adequate amniotic fluid usually indicates that the fetus is not suffering from chronic placental insufficiency. Based on these two principles a modified BPP test has been suggested which consists of a NST and an assessment of the amniotic fluid index (AFI).
The modified BPP is considered normal if the fluid volume is adequate (AFI greater than 5 cm) with a reactive NST. The AFI is obtained from the sum of the four largest vertical pockets of amniotic fluid noted in each quadrant of the uterus, measured in centimeters.
The modified BPP has the advantages that it takes less time to accomplish and is less subject to interobserver variability. Furthermore, it has been found to be a good predictor of pregnancy outcome.

V. **Doppler Ultrasound:**

Principle: Doppler ultrasound is a noninvasive assessment of the blood flow in the fetal, maternal, and placental circulations. Various blood vessels have been investigated using Doppler velocimetry, including the maternal uterine artery, fetal middle cerebral artery, and fetal ductus venosus

In normal pregnancy the placental vascular resistance decreases as the pregnancy progresses, hence the umbilical blood flow increases. But in cases with placental insufficiency e.g. pre-eclampsia, or FGR (fetal growth restriction) this pattern is reversed as the resistance of the placental blood flow increases. In such cases the Doppler blood flow study shows decreased blood flow especially during diastole.
The fetus would also try to compensate by compensate by shunting most of the blood flow to the brain, heart, and adrenal glands at the expense of the placenta and peripheral circulation, a phenomena known as " brain-sparing

reflex". Therefore the Doppler blood flow study of cerebral vessels would show increase in blood flow in the fetal cerebral circulation.

The technique: Doppler hemodynamic blood flow study is based on directing beam of ultrasound waves with a particular frequency on to the desired blood vessel. The beam returns with different frequency proportional to the speed and direction of flow of the blood cells in the studied vessel. The difference between the frequency of the emitted beam and the frequency of the returned beam is known as the "Doppler shift". The difference "i.e. the Doppler shift" is an audible frequency that reflects the blood flow velocity, and can be recorded and displayed electronically.
Blood flow within any vessel may be affected by several factors such as vessel diameter (e.g. increased forward resistance in umbilical arteries in cases of increased resistance of placental blood flow), the viscosity of the blood within the vessel, or poor cardiac function leading to diminished backward pump pressure.

Interpretation of Doppler Ultrasound: The main application of Doppler flow velocity measurements has been in pregnancies at risk of FGR due to placental insufficiency. For example in studying umbilical artery blood flow, an increased difference between the peak blood flow during systole and during diastole reflect increased placenta resistance. In severe cases there may be no flow during diastole or worst a reversal of blood flow during the diastolic phase of the cardiac cycle. Many indices have been devised to evaluate blood flow but a commonly used one is peak systolic-flow velocity over peak diastolic flow velocity in a cardiac cycle. Figure (Figures 7-3) shows the pattern of umbilical artery flow in normal and abnormal cases.

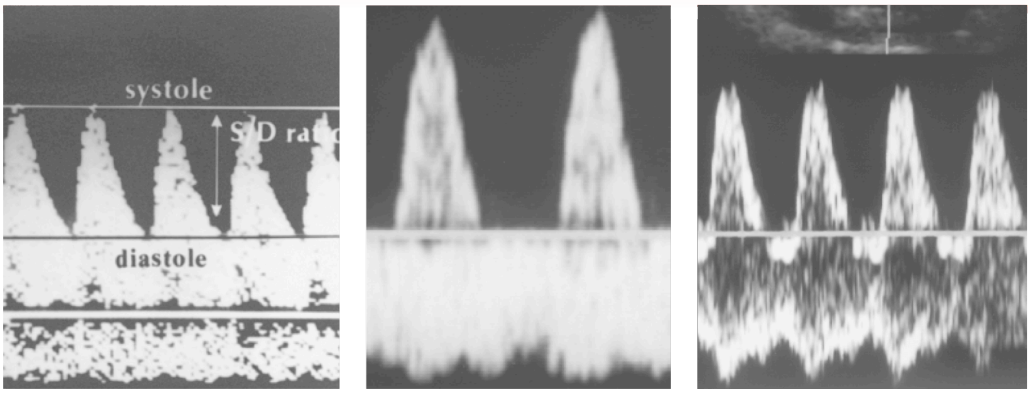


Figure: 7-3 shows umbilical arterial waveforms. Normal blood flow (a), Absent end diastolic blood flow (b), Reversal blood flow (c). Absence of end-diastolic velocities is associated with an increase in perinatal morbidity and mortality.

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Chapter 8

Normal Labor and its Mechanism

Dr Wafa Fageeh

Successful labor and delivery depends on complex interaction between three major elements; uterine contractions (***the force***), the birth canal (***the Passage***) and the fetus (***the passenger***). Coordinated uterine contractions (the force) initiate the changes in the birth canal (the passage) mainly cervical effacement and dilation. Once the birth canal is fully dilated the fetus (passenger) negotiate its way through it to the outside world by adopting series of "cardinal" movements.

Although labor is a continuous process, it is usually considered as three distinct stages. The **first stage** is concerned primarily with cervical effacement and dilatation, while in the **second stage** the fetal head "or the presenting part" descend through the birth canal until the fetus is completely delivered. In the **third stage** the delivery of the placenta and membrane takes place.

By the end of this chapter you should be able to:

- **Define** normal labor
- **Describe the mechanism of labor**: the role of each of the three variables and their interaction in labor;
    - The Force: the role of coordinated uterine contractions
    - The Passage: The soft and hard passage, cervical effacement and dilatation
    - The Passenger: the fetal cardinal movements
- **Describe the stages and phases of labor** and the characteristic features of each one.

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What is labor:

Labor is the chain of physiologic events that leads to the delivery of the fetus to the outside world. Labour may occur **preterm** (or prematuere) (< 37

weeks, 259 days), at **term** (37 weeks to ≤42 weeks) or **post-term** (>42 weeks 294 days). It can also be spontaneous or induced.

Mechanism of Labor:

Successful labor depends on the interaction of three variables:

- The force (uterine contractions).
- The passenger (the fetus).
- The passage (the birth canal).

Uterine contractions (The Force):

Coordinated, regular uterine contractions are the driving force responsible for initiation and completion of successful labor. In the first stage uterine contractions result in cervical dilatation. In the second stage it drives the fetus downwards through the birth canal. While in the third stage it is responsible for separation, and expulsion of the placenta and prevention of atonic postpartum hemorrhage.

Dilatation of the cervix is measured in centimeters. At full dilatation (the end of the first stage) the cervix is said to be 10 cm dilated and the birth canal becomes a continuous uniformed passage.

In the second stage another source of force is added and that is the maternal urge for bearing downwards "pushing". This is an almost involuntary urge occurs as the presenting part (usually the fetal head) is pushed against the pelvic floor in the second stage of labor. *Therefore a woman who is having epidural analgesia usually has prolonged second stage because she either completely or partly looses the urge for straining.*

The exact mechanism responsible for the initiation of the coordinated uterine contractions of labor is not fully understood. However it involves complex biochemical and physiologic maturation that includes full development of the gap junctions between the uterine muscle fibers, and increase in concentration of oxytocin receptors within the uterine muscle fibers above a threshold level. *Therefore induction of labor before term is more likely to fail than induction at term.*

The difference between the histology and physiology of the upper and lower uterine segments is responsible for completion of successful labor. The

upper segment is rich in muscle fibers that actively contract and retract (retraction means the muscle fibers do not go back to its same length after contraction). Whereas the lower segment is rich in fibrous tissue therefore it does not contract but is rather passively pulled up by the actively contracting upper segment. Therefore with repeated contractions and retraction the muscle fibers of the upper segment gradually becomes shorter and thicker while the lower segment become thinner and increase in length inducing shortening of the cervix (effacement) followed by dilatation. At the same time as the room for the fetus in upper segment become smaller it is forced downwards through the birth canal (Figure 8-1)

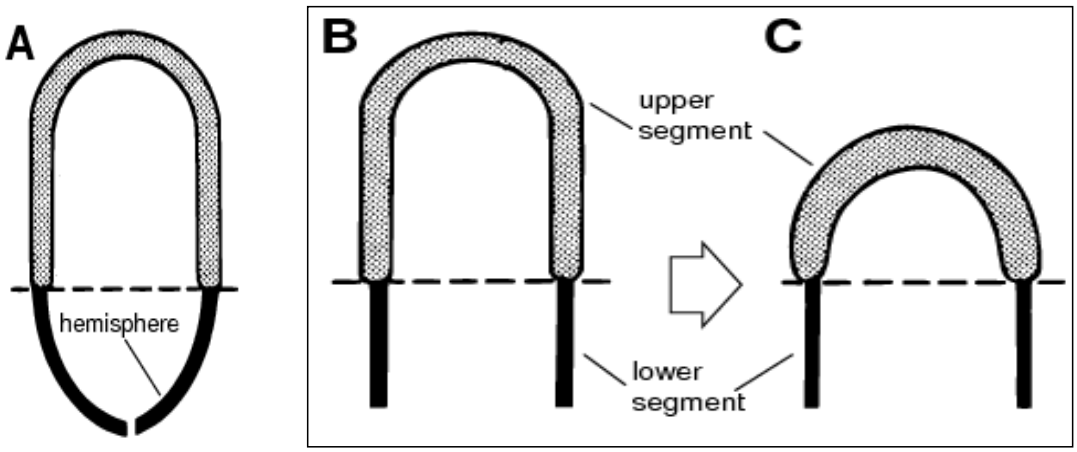

Figure 8-1: "A" at onset of active stage of labor the lower segment is this and the cervix is effaced (thin and short). "B-C" During the active phase of labor with contraction and retraction the upper segment fibers becomes shorter, thicker the results are dilatation of the cervix and descent of the fetus.

The Fetus (The Passenger):

In normal labor as the fetus descends through the birth canal it undergoes series of movements. The aim of those movements is to adapt the fetus smallest head diameters to through the largest pelvic diameters as it passes each strata of the pelvis i.e. inlet, cavity, and outlet. It enters the inlet of the pelvis in the widest transverse diameter,

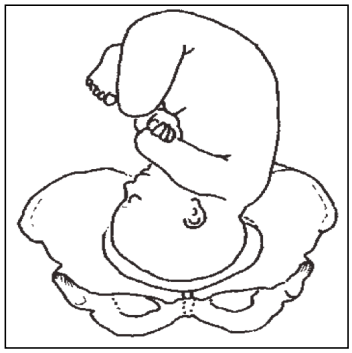

Figure 8-2: A well flexed head engaged in the transverse diameter with the occiput to the left (left occipito-transverse)

(approximately 13 cm) in a flexed attitude, undergoes internal rotation within the pelvic cavity and emerges from the pelvic outlet in the widest diameter, i.e. the antero-posterior diameter (approximately 13 cm). They include five movements: increased flexion and engagement, internal rotation, extension, and external rotation or restitution. The fifth one is the delivery of the shoulders and the body.

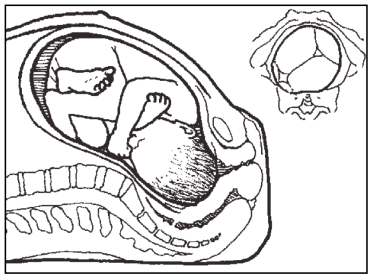

Figure 8-7a:: Flexion, engagement and descent.

- *Increased Flexion and Engagement:* the fetus in-utero is usually in a flexion attitude, but with uterine contraction the flexion increases. The complete flexion attitude of the fetal head ensures that it enters the pelvis with the smallest diameter biparital and suboccipitobregmatic diameter (9.5 cm each) through the largest diameter of the pelvic inlet (the transverse diameter 13cm) (Figures 8-2,3)

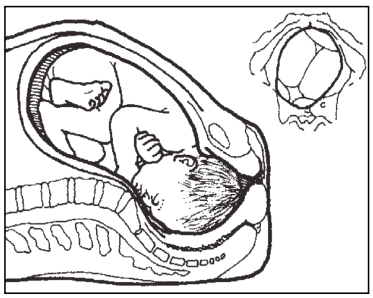

Figure 8-7b: Further descent and internal rotation

- *Internal rotation*: occurs within the true pelvic cavity when the occipital part of the fetal head reaches the pelvic floor approximately at the level of the ischial spines. Internal rotation allows the head to come out through the AP diameter of the pelvic outlet (which is the largest diameter of the outlet 13 cm). In normal labor the occiput rotates anteriorly because the occiput is the first part to reach the pelvic floor if the head is well flexed. In addition the direction of the pelvic floor muscle has downward and forwards slope (*failure or posterior rotation of the occiput causes prolonged or abnormal labor*). Eventually the head presents at pelvic outlet through its widest diameter (anteroposterior diameter) and the occiput slips beneath the sub-pubic arch. Further contractions induce "crowning" of the fetal head. This term means that the widest transverse diameter of the head is born beyond the pelvic floor muscle and occipital part of the head no longer recedes between contractions.

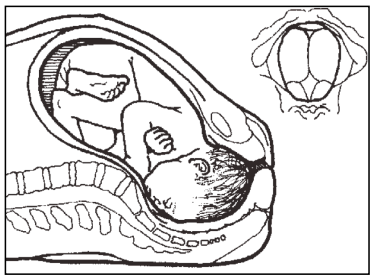

Figure 8-7c: Complete rotation, beginning of extension

- *Extension:* of the fetal head follows crowning. The nape of the neck pivots on the lower border of the symphysis

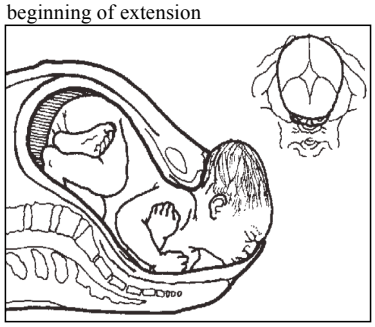

Figure 8-7d: Complete extension and delivery

pubis, while the forehead, face and chin pass over the thinned-out perineum.

- *External rotation* (restitution): a slight untwisting movement known as restitution corrects the twist in the neck of the fetus, which resulted from internal rotation. With this movements the shoulders are now in the antero-posterior diameter of the pelvic outlet. The internal rotation of the shoulders corresponds with the external rotation of the fetal head. If it is a vertex left occiput anterior, the fetal head will turn to the left while in a vertex right occiput anterior position it will turn to the right.
- *Delivery of the shoulders:* After delivery of the head and external rotation, further descent brings the anterior shoulder to the level of the symphysis pubis. The anterior shoulder, now at a lower level than the posterior shoulder, rotates under the symphysis pubis and delivered, after that the posterior shoulder and the rest of the body usually deliver without difficulty.

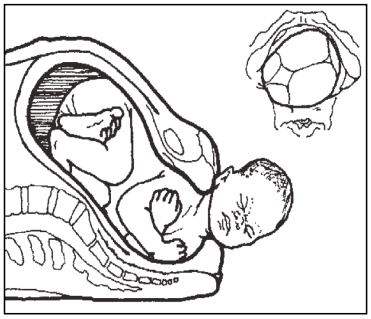

Figure 8-7f: delivery of the anterior shoulder.

Molding of the fetal head:

In addition to increased felxion attitude, further reduction in the fetal head diameters by about 1-2 cm is achieved through a degree of overlapping of the fetal skull bones on each other. This process of shaping of the fetal head to facilitate passing in the birth canal is known as "Molding". *Limited or failure of "molding" occurs in post term pregnancies, as the fetal skull bones become more ossified and less susceptible to sliding and overlapping. Also excessive molding can be dangerous and in the absence of progress of labor it is considered as warning sign of cephalo-plevic disproportion or obstruction of labor.*

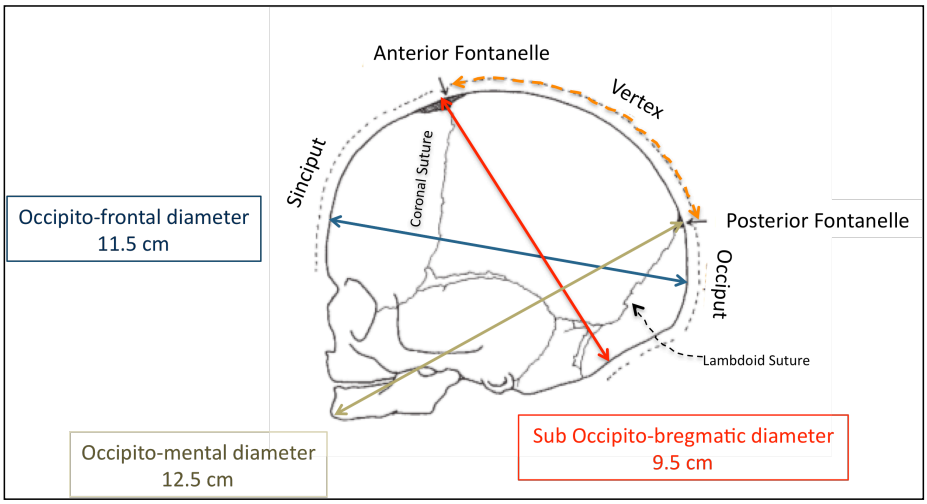

Figure 8-3 shows the diameters of the fetal head at different levels of flexion. In occipito-anterior position with full flexion the engaging diameter is the suboccipitobregmatic diameter (9.5 cm) compared to occipito posterior presentation with deflexed head the engaging diameter is Occipito-frontal diameter (11.5 cm).

The Pelvis (Passage):

The term passage refers to the bony pelvis and the soft tissues of the birth canal (i.e., cervix, vagina, and pelvic floor musculature), they undergo important changes throughout pregnancy and during labor.

- A typical normal female pelvis "*gynecoid pelvis"* allows the delivery of an average sized baby at term (see diameters of pelvis in chapter 1). If the diameters are small or the pelvis is abnormal e.g. Android pelvis, delayed or failure of delivery occurs (Figure 8-4). In addition, at term the pelvic ligaments under the

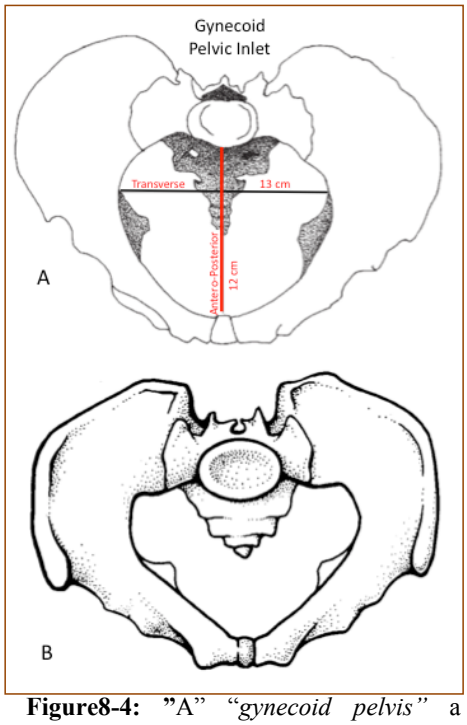

Figure8-4: "A" "*gynecoid pelvis"* a rounded oval pelvis with well-rounded anterior and posterior segments "B" Android pelvis showing wedge-shaped inlet and narrow anterior segment

influence of the hormone "Elastine" already became soft and lax. This allows further stretching and increase in the absolute pelvic diameters during the descent of the fetus. The extent of increase in pelvic dimensions as a result of this process (sometimes known as "pelvic give") cannot be predicted until labor takes place. *Hence the old practice of doing pelvic x ray to assess the pelvic capacity during pregnancy has become almost obsolete because the dynamic interaction between the fetal head (increased flexion and molding on one hand and the "pelvic give" on the other hand) can significantly affect the course of labor and can not be predicted till labor starts*

- During pregnancy the soft tissues of the birth canal (cervix, vagina, and pelvic floor muscle) gradually get softer and more stretchable. As pregnancy approaches term the cervix undergoes process of "ripening" which involve series of biochemical changes that alter its physical properties; elasticity, plasticity, and tensile strength of the cervical tissue. A "ripe" cervix at term facilitate stretching and dilatation in response to uterine contractions. *If ripening of the cervix takes place prematurely it increases risk of preterm labor.*

Stages and phases of Labor:

As mentioned before the process of labor is basically a continuous one. However it is possible to consider the main changes that eventually lead to delivery of the fetus, placenta and membranes over three stages. Each stage has its own distinct features, and potential disorders. Understanding the pattern of each stage, and its "normal" duration is important in order to predict deviation from normal and prevent complications e.g. obstructed labor.

First Stage:

The first stage commences with the onset of labor and ends at full cervical dilatation (10 cm). It is divided into two phases according to the rate of cervical effacement and dilatation (Figure 8-5):

1. Latent phase: the whole mark of this phase is "effacement of the cervix" with little degree of dilatation (2-3 cm). Cervical effacement refers to the process by which a ripe cervix becomes short and thin secondary to uterine contractions. The latent phase begins with the onset of labor until the cervix becomes completely effaced with a dilatation about 3-4 cm.

2. Active phase: the whole mark of this phase is dilatation of the already effaced cervix. The rate of cervical dilatation varies between a primigravid and multigravid women. It ends when the cervix becomes fully dilated (10 cm).

Second Stage:

The second stage of labor begins with full cervical dilatation and end with complete delivery of the fetus. During this stage the fetus descend through the birth canal. To do that the fetus has to adopt series of movements "known as cardinal movements" in order to negotiate the birth canal until it is completely delivered (see above).

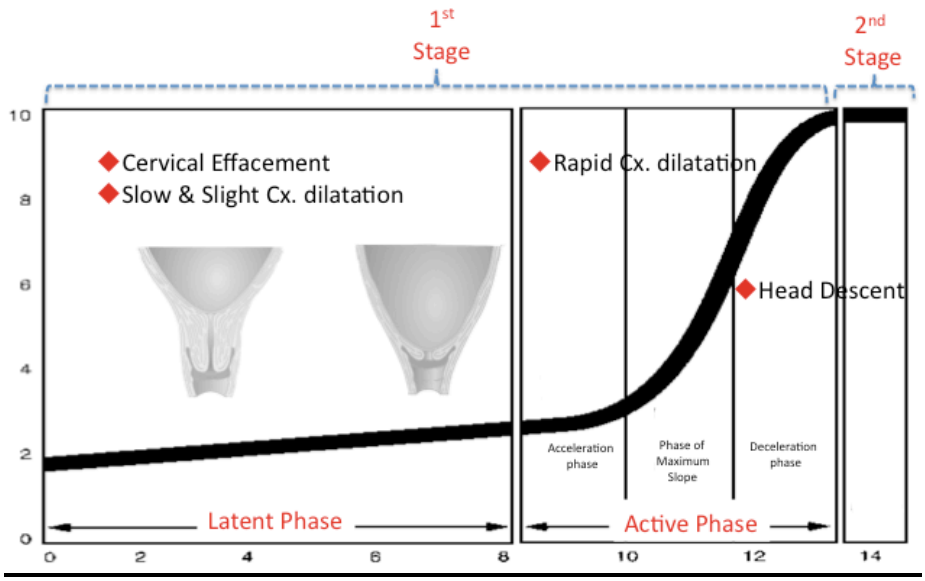

Figure 8-5: Shows Phases of labor. The first stage composed of the Latent and Active phase. The main changes in the latent phase is cervical effacement and slight degree of dilatation. The Active phase is the phase of rapid cervical dilatation

Third Stage:

The third stage of labor begins after delivery of the baby and end with the delivery of the placenta and fetal membranes.

***Mechanisms of Placental delivery**:* the delivery of the placenta involves two steps: separation followed by expulsion of the placenta. *Separation* of the placenta occurs as uterine surface area underneath the placenta diminishes in size secondary to the strong sustained uterine contractions. The placenta is thus separated either from the center or the edge and a retro-placental bleeding occurs. *Expulsion* of the separated placenta occurs due to the combined effects of uterine contractions, the pressure of the accumulating blood retroplacental clot in addition to an increase in maternal intra-abdominal pressure from the maternal pushing effort.

Delay or Failure of placental separation

May be due to abnormal invasion of the placental trophoblast deep into the uterine wall. 3 degrees: **Placneta accreta** Abnormal adherence of the chorionic villi (CV) to the myometrium with partial or complete absence of the decidua basalis and stratum spongiosum.

Placenta increta: penetration of CV into the myometrium.

Placenta percreta: invasion of CV through the myometrium reaching the peritoneal covering

The attending physician can recognize placental separation by the following important signs: (1) a gush of blood, (2) lengthening of the umbilical cord and (3) the uterus becomes firm and globular (Figure 8-4).

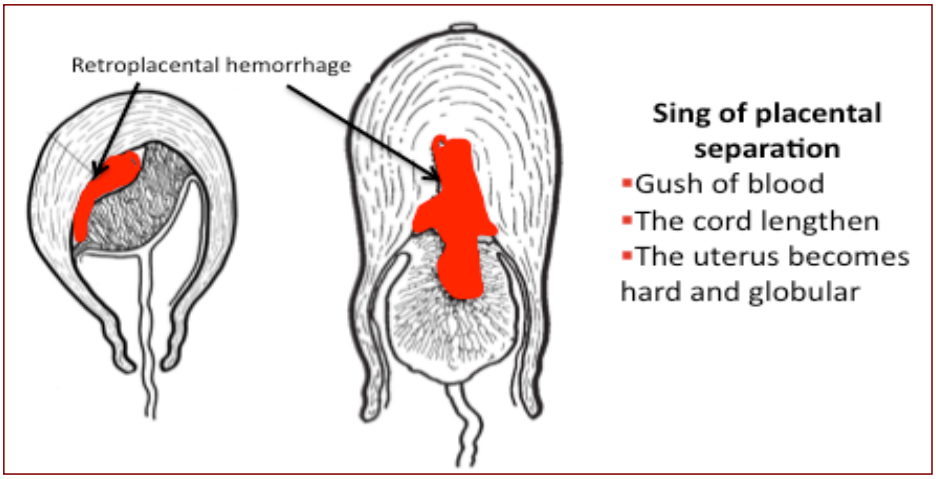

Figure 8-6 Placenta before and after separation with retropalcental clot. Note the 3 signs of placental separation in the diagram on the right.

Duration of the third stage: Normally the placenta is delivered within few minutes after delivery of the fetus. In about 2-3% of cases, the placenta may remain undelivered for more than 30 minutes. If by then the placenta is not

easily delivered the condition is diagnosed as “retained placenta” which require special management (chapter 18 Postpartum Complications)

The pattern and duration of normal labor:

Although labor is a continuous process however the two main variables that determine successful labor namely rate of cervical dilatation and rate of descend of the presenting part (fetal head) tends to follow a set pattern. Friedman and colleagues was the first to study this pattern on hundreds of women and was able to define pattern of labor progress and graphically describe the two variables i.e. cervical dilatation and descent of the fetal head against time factor.

From the original studies of Friedman and others it was obvious that the average duration of labor, and its stages varies between primigravida and multigravida. Table 8-1 shows the approximate mean, upper and lower ranges of “normal” labor in nulliparous and multiparous women. The maximum (slowest) duration of each stage is defined as two standard deviations below the mean. For example, the minimum rate of cervical dilatation of 1.2 cm/h for a nulliparous patient represents two standard deviations below the mean rate of cervical dilatation for nulliparous and not the average rate of cervical dilatation (which is 3 cm/h).

Labor is considered abnormally prolonged if it exceeds the normal upper limits of the normal range.

Parameters	**Nulliparous**		**Multiparous**	
Duration of labor	Mean	Mean +2SD	Mean	Mean +2SD
Total duration of labor (hours)	10.7	25	6.2 h	19.5
First Stage (hours)	9.7	24	8.0	18.0

Second Stage (minutes)	33.0 m	117.0 m	8.5 m	46.5 m
Third stage (minutes)	5 m	30 m	5 m	30 m
Rate of cervical dilatation	Mean	Mean -2SD	Mean	Mean -2SD
Rate of cervical dilatation Cm /hour	3.0	1.2 cm/h	5.7	1.5

Table 8-1: Mean normal duration of labor and the two standard deviation from the mean. Currently the duration of the 2nd stage is based on parity and the presence of regional anesthesia with no

Further studies have led to the formation of the "**Partogram**" (*parto* refers to parturition, *gram* refers to graphic display). The partogram is not only graphic display of the rate of cervical dilation and head descent in relation to time but also all other events related to labor this include: the fetal heart, uterine contractions, maternal vital signs …etc. **Thus a *partogram* is a graphic display for the progress of labor, and all the events related to labor** (*see figure 9-1,* chapter on *management of normal labor*).

In practice, using the partogram, it is possible to plot the rate of cervical dilatation, for any patient in labor, against time. By comparing the rate of cervical dilatation with the normal profile described by Friedman, it is possible to detect *abnormal labor patterns* and identify pregnancies at risk for adverse events.

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Chapter 9

The Management of Normal Labor

Dr Wafa Fageeh

The conclusion of a safe childbirth with the delivery of healthy baby and healthy mother is the overall objective of midwifery.

Prior to discussing the details of management of labor there are important aspects related to the care of laboring women that must be appreciated.

- All labor room staff should have a clear appreciation and understand*ing of the emotional and psychological* needs of a laboring woman and her family.
- The proper management of labor depends on correct diagnosis of onset of "true" labor. This is because once the patient is admitted to the labor room she begins to receive intensive care. While this is important it is also distressing to many women. In addition it consumes huge resources of the labor word where only women in active labor should be managed in this unit. Furthermore an erroneous diagnosis of "true labor" can adversely affect subsequences decisions on the management of labor.

By the end of this chapter you should be able to:

- **Describe** the diagnosis of labor: Symptoms and signs
- **List** the general measures of management of patients admitted to the labor room.
- **Describe management of the first stage**: its objectives including monitoring of both the progress of labor and maternal and fetal wellbeing.
- **Describes management of the second stage**: its objectives including safe delivery of the baby, and protection against laceration of the genital tract.
- **Describe management of the third stage:** its objectives including Prevention of PPH and the different methods of placental delivery.
- **Define** the The fourth stage of labor and its objectives.

Diagnosis of labor:

Labor is one of the few acute emergencies that are often self-diagnosed by the patient. Women usually bring themselves to the hospital or emergency *room with symptoms suggest*ive of labor. The duty of the attending physician is to confirm whether or not the patient is in true labor before admitting deciding to admit her to the labor suite.
The diagnosis of labor depends o*n symptoms and signs:*
1. *Sympt*oms of labor:

- The most important symptom is regular uterine contractions, which increase in frequency and intensity. The way the patient describe this contractions induced pain e.g. in the lower abdomen or back. …etc. is not very relevant.
- Passage of the mucus plug or 'show': which is the mucus that normally, plugs the cervical canal. When it is dislodged, signifying stretching and dilatation of the cervix, it comes out stained with blood, hence the term "show". The bloodstaining comes from torn capillaries and small vessels. Sometimes the bleeding can be heavy to the extent of being confused with other causes of antepartum hemorrhage. However, a history of passage of show is not a prerequisite for the diagnosis of labor.

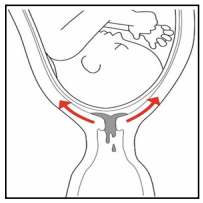

Figure 9-1: passage of the cervical mucus plug with some bleeding "show" signifies beginning of cervical dilatation

Rupture of the fetal membranes with leakage of amniotic fluid is not a symptom of labor. Occasionally, however, a patient may present with symptoms suggestive of rupture of the membranes before the onset of uterine contractions, a condition known as (premature rupture of membranes).

2. Signs of labor:
    - The most important sign are cervical changes in the form of effacement (shortening) and dilatation of the cervix as detected by vaginal examination.

In most cases the diagnosis of labor is easily confirmed or excluded based on symptoms and sings. However, in some cases the diagnosis may not be clear. Such cases may either be reassured and sent home, or admitted to the hospital for observation in the antenatal ward -not in the labor room- to be reassessed after a period of time and a final decision is made.

General measures:
Once the diagnosis of labor is confirmed the patient should be admitted to the labor room where the following general measures are usually undertaken:

- Review of the medical and obstetric history for any risk factors that may require special attention (e.g. diabetes, cardiac diseases…etc).
- Review of the details of the current obstetric history, including gestational age, any risk factors that may have developed or previously unnoticed.
- A quick general examination including recording of vital signs should be performed.
- Abdominal obstetric examination for fetal size, lie, presentation, presence of previous surgical scars and its nature.
- Tests and investigations: The basic tests include recent hemoglobin and blood grouping (ABO and Rh). *For patients who have no antenatal records (un-booked patients) serology tests for Rubella IgG and hepatitis should be*

undertaken. Further tests, such as vaginal swab for group B streptococci or serum for HIV and VDRL tests depends on the local agreed policy.

- Other General Measures: include the following:
  - Empty bowel and bladder: by encouraging patient to go to the toilet or sometimes administering a low rectal enema.
  - Insertion of intravenous cannula: Is usually done at the time of taking blood sample for tests. The cannula is used for administration of fluid, including saline and glucose or any necessary medication such as oxytocin. In addition, securing an open vein is important for all patients in labor.

  - Vaginal examination: to assess the degree of cervical dilatation and effacement, identify the presenting part, its station, position, and finally the adequacy of the pelvis.

  - Recording all relevant data on data on "Partogram": The findings on vaginal examination, including the state of membranes, (ruptured or not) and the color of amniotic fluid should be recorded on the *partogram* (Figure 9-2).

The partogram is a graphic display of the labor progress and its events. It contain the following sections:

- Fetal Monitoring: for recording the fetal heart rate and amniotic fluid color changes.
- The cervicograph: this is the most important section for monitoring the progress of labor as it contains the data on the progress of cervical dilatation and head descent in relation in relation to time.
- Drugs and infusion administration: this section contains data on fluid administered as IV infusion including oxytocin, also data on the strength of uterine contraptions.
- Maternal vital signs section: for recording of maternal blood pressure, pulse rate ant temperature.
- Urine output: to record results of dipstick test of urine for protein and sugar.

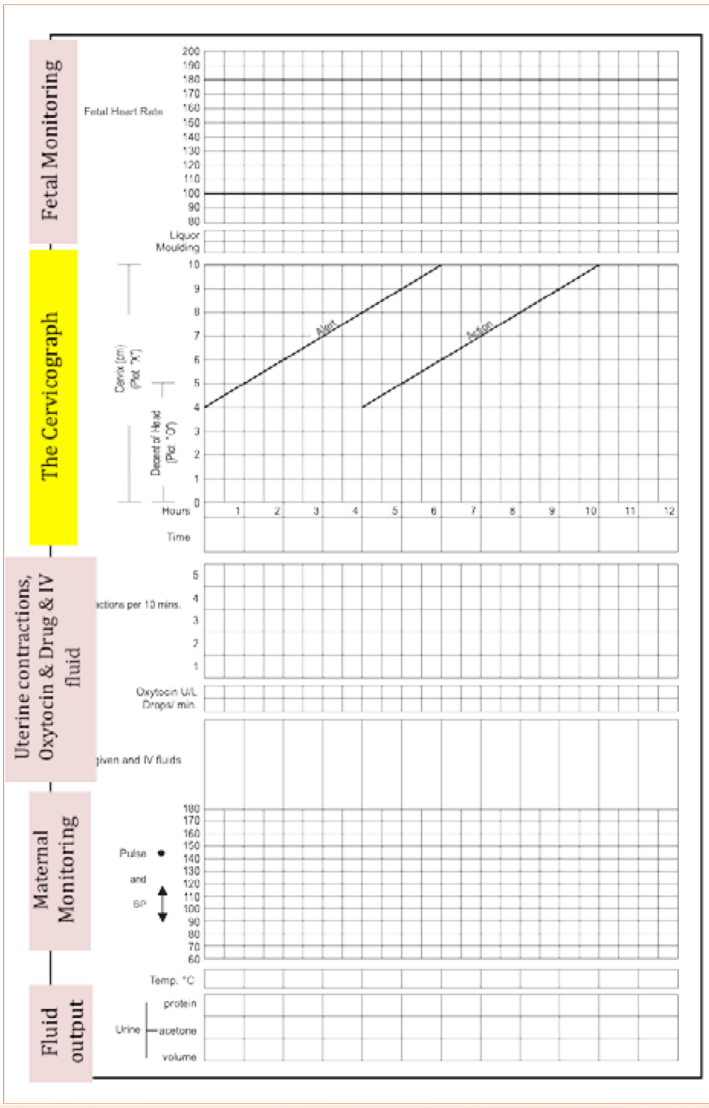

Figure 9-2: The partograph is graphic record of all of the progress and observations made during labor. The most important is the graphic recording of the dilatation of the cervix as assessed by vaginal examination and descent of the fetal head. Note that this particular partogram begins at cervical dilatation of 4 cm, because at less than 4 cm patient is still in the latent phase and should not be in the delivery room. In addition to the progress of labor there are section for recording FHR, amniotic fluid, strength of uterine contractions, drug and fluid administration during labor, maternal vital signs, and urine dipstick test results.

Management of the first stage:

In this stage the objectives of management are: monitoring of the progress of labor, and maternal and fetal wellbeing .

- Monitoring of progress of labor:

This requires repeated vaginal examinations in order to assess the degrees of (1) cervical dilatation and (2) descent of the presenting part (head).

The cervical dilatation is assessed in centimeters (full dilatation is 10 cm). The head descent is also estimated in number of centimeters above or below the ischeal spine which is considered the "0" point.

The frequency of doing vaginal examination depends on the phase of labor, but on average it can be repeated every two hours and the findings should be plotted on the *partogram*.

- Monitoring of maternal well-being:

The maternal wellbeing includes both her psychological state (morale) as well as her physical condition. This require:

- Regular monitoring of vital sings.
- Input and output fluid chart should be observed. No food should be allowed. However the majority of "low risk" cases are allowed to drink some water and other fluids. If it is anticipated that labor will exceed four to six hours, an intravenous infusion of glucose and normal saline should be administered at a rate of one liter per 8 hours.
- Sympathetic and understanding support: This is an essential element in the management of women in labor. Ideally one nurse should be in charge of each patient in labor. All other persons participating in the care of a

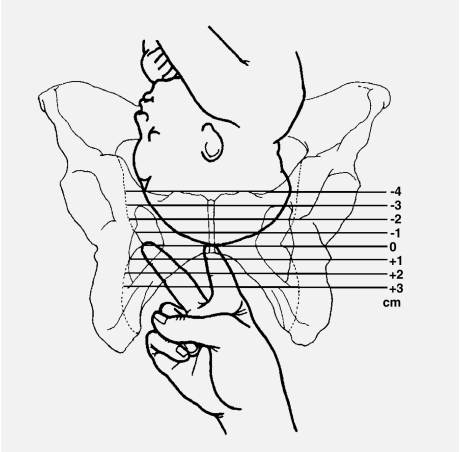

Figure 9-3: Head descent is determined by its relation to the Ischial spines which is considered as the "0" station. Below and above the spines is described as "+" or "-" the ischial spines in centimeters respectively.

laboring woman (e.g. house staff or medical students) should be introduced to her and take permission to do that.
- The patient should be informed of the progress of her labor and counseled regarding any decisions concerning her management such as administration of IV fluid, need for augmentation of labor…etc.
- Adequate analgesia: the details and types of analgesia used are discussed in chapter 13. .

- Monitoring of Fetal-Wellbeing:

Currently electronic fetal monitoring is applied to almost all patients in labor, although there is no strong evidence to support its routine use in low risk cases. However it has important value in high-risk cases (Chapter 11, Intrapartum Fetal Monitoring).

Management of the second stage:

The diagnosis of the second stage of labor is suspected when the mother develop strong urge to "bear down". It is then confirmed by vaginal examination, which should reveal a fully dilated cervix. From that point onward the mother should not be left alone.

The objectives of management of the second stage are: to ensure safe delivery of the baby and prevent laceration of the perineum and the genital tract.

The fetal hear rate should be closely monitored. Type I decelerations i.e. deceleration of the fetal heart rate that coincides with contractions but recovers in between contractions do not indicate fetal hypoxia and is considered normal.

The mother should be instructed on how and when to "bear down" with contractions. She should not exhaust herself by starting to push down too early in the second stage. Pushing should be deferred until the head becomes low enough along the birth canal or almost visible, at the introitus, between contractions.

The duration of the second stage depends on the patient parity but also influenced by several factors such as epidural analgesia, duration of the first stage, maternal size, birth weight, and station at complete dilation (Table 8-1)

	Mean	Mean +2SD
Nulliparas	33.0	117
Mulitparas	8.5	18

Table 8-1: Duration of 2nd Stage in minutes

Preparation for delivery: Once the baby's head descended low enough or becomes visible on the perineum, preparation for delivery should be undertaken. Usually the patient is placed in the lithotomy position, the perineum cleaned with sterile solution, and the legs and the lower abdomen draped with

sterile towels. At this point a local perineal infiltration with local anesthetic (e.g. Zylocain) may be administered in anticipation of the need for episiotomy (Chapter 13)

Delivery of the head: should be allowed to occur slowly and under control to minimize the risk of perineal tears by preventing sudden extension of the head. The patient is asked not to push instead she can make only small expulsive efforts as the head becomes fully crowned. At the same time, the obstetrician places one hand on the vertex to maintain the head in a flexed position, while the other hand eases the perineum over the fetal face.

Episiotomy: episiotomy is performed in order to avoid perineal lacerations during delivery of the head; otherwise episiotomy should NOT be a routine procedure. Other indications for episiotomy are soft tissue dystocia, or when there is the need to facilitate delivery of a possibly compromised fetus e.g. premature fetus (see chapter 19, on operative obstetric procedures).

Once the fetal head is delivered, external rotation (restitution) is allowed to occur. If the cord is around the neck, it should be looped over the head or, if not reducible, a single loop doubly clamped and transected.

Mucus can then be gently suctioned from the fetal mouth, oropharynx, and nares using a bulb syringe.

Delivery of the shoulders: After delivery of the head, a hand is placed on each parietal eminence and the anterior shoulder is delivered with the next contraction, using gentle downward traction towards the mother's sacrum in co-ordination with maternal expulsive efforts.

The posterior shoulder is then delivered by upward traction. These movements should be performed with as little downward or upward force as possible, to avoid perineal injury and/or traction injuries to the brachial plexus. The delivery is then completed, either spontaneously or with a gentle maternal push.

Care of the infant: The infant is wiped dry with a towel while any mucus remaining in the airway is suctioned with bulb syringe. Vigorous suctioning should be avoided, as posterior pharyngeal stimulation can cause a vagal response with fetal bradycardia induced.

Early interaction between the mother and her infant should be encouraged. This is may be accomplished by supporting skin-to-skin contact between the mother and her baby and early initiation of breastfeeding. The infant should be kept warm by wrapping it in a blanket and covering its head with a hat or a portion of its blanket.

Management of the third stage:

The objective of management in the third stage is to ensure safe delivery of the placenta and membranes and prevent postpartum hemorrhage.

There are two approaches for management of the third stage, either passive or active.

- Passive management of the third stage:

The delivery of the placenta is almost allowed to occur spontaneously. The obstetrician only observes for signs of placental separation, before applying any traction on the cord. The passive approach for placental delivery is associated with high rate of postpartum hemorrhage hence active management of third stage is the preferred method.

- Active management of the third stage:

Active management generally consists of three elements:

1. Intramuscular administration of oxytocin or syntometrine (0.5 mg ergotamine+5units oxytocin): This is administered immediately after delivery of the baby or sometimes after delivery of the baby's head and before the delivery of the shoulders.
2. Early cord clamping.
3. Controlled cord traction to facilitate separation and delivery of the placenta: The technique of controlled cord traction, know as *Brandt-Andrews maneuver,* involve holding the clamp on the cord with one hand to maintain sustained downward traction, while the other hand is placed on the suprapubic region of the mother's abdomen to secure the uterine fundus and prevent uterine inversion. Gentle upward and backward pressure may be applied by the suprapubic hand to facilitate separation of the placenta. No cord traction should be exerted if the uterus is not contracted otherwise it increases the risk of uterine inversion.

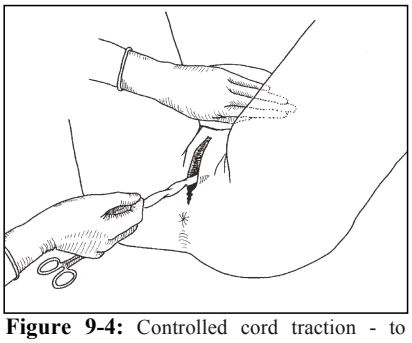

Figure 9-4: Controlled cord traction - to avoid inversion of the uterus, controlled cord traction should never be applied without counter-traction

The placenta, umbilical cord, and fetal membranes should be examined. The fetal side is assessed for any evidence of vessels coursing to the edge of the placenta and into the membranes, suggesting missing placental lobe as in succenturiate placental lobe. The numbers of vessels in the cord are counted.

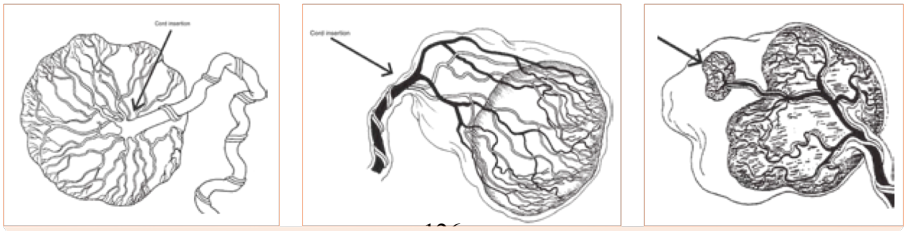

Figure 9-5: "A" Normal placenta, "B" Velamentous insertion of the cord (cord insertion in the membrane", "C" Placenta succenturiata (extra lobe), In "B" there is risk of cord avulsion and "C" risk of retained lobe.

Retained placenta and normal duration of the third stage: "Retained placenta" is the term usually used if the placenta is not delivered after 30 minutes (The World Health Organization defines a retained placenta as one that has not been expelled by 60 minutes after delivery). Such cases require "*manual removal"* under general or epidural anesthesia, which is normally performed in the operating theatre (see chapter 19, on operative obstetric procedures).

After delivery of the placenta and membranes, the obstetrician should examine the genital tract including the vagina and cervix for any lacerations. Episiotomy and/or any lacerations should be carefully sutured under local or regional anesthesia.

The Fourth Stage of labor:

The fourth stage describes the two to three hour's period after delivery during which the patient should remain under close observation in the labor room before she is transferred back to the postnatal ward. During this period there is high risk of postpartum hemorrhage from uterine atony or previously undetected lacerations, retention of urine, vomiting or inhalation of solid products (the risk is higher especially after operative delivery, or in patients under heavy sedation or epidural). If all observations are stable the patient can be safely transferred to the postnatal ward.

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Chapter 10

Fetal Malpresentation and Malposition

Fetal malpresentation and malposition are important causes of labor dystocia (prolonged labor). They should always be searched for if there is slow progress or arrest in the active phase or second stage of labor. Abnormal fetal lie (abnormal fetal axial attitude) such as transverse or oblique lie cannot be delivered vaginally unless it is a very premature or macerated dead fetus.

Some fetal malpresentation such as breech or shoulder presentation should be diagnosed and managed before labor starts. Other cephalic malpresentations such as brow or face are often discovered during the course of labor. Cord presentation and cord prolapse are acute emergencies and require immediate delivery.

By the end of this chapter you should be able to:
Define malposition and malpresentation
Describe the common causesof malposition and malpresentation (fetal, uterine, placental and AF).
Describe the consequences and options of management occipito posterior position being the commonest form of malposition.
Face and Brow (Deflection attitude):
Describe the types of **Cephalic Malpresentation** (Deflection attitude) i.e Faces and Brow presentation. Its causes, diagnosis and management.

- **Breech Presentation**:

Knows the **incidence** of breech throughout pregnancy.
List the types of breech and its relation to outcome and management
Describe the **management** of breech during pregnancy.
Describe the aim, contraindications and potential complications of External cephalic version in the management of breech.
Counse patient regarding the options of breech delivery: CS vs. trial of vaginal delivery.
List the **criteria for trial of vaginal breech delivery**.
List the **maternal and fetal risks** of breech delivery.

- **Cord presentation and Cord prolapse**:

An Over View Of Malpresentation And Malposition:

- **Normal presentation and Normal position:**

Normal presentation: the term "presentation" *refers to the first part of the fetus that presents at the cervix.* .
In "normal" cephalic presentation with a well flexed head the vertex -the area

between the anterior and posterior fontanel- is the leading part that first present to the cervix.

Normal position: the term "Position" *refers to the relationship of a nominated site of the presenting part to a donominating location on the maternal pelvis.* The nominated site of the presenting part is determined during digital vaginal examination by palpating for the landmarks of the presenting part. Figure 10-1, shows the important anatomical landmarks of the fetal head.

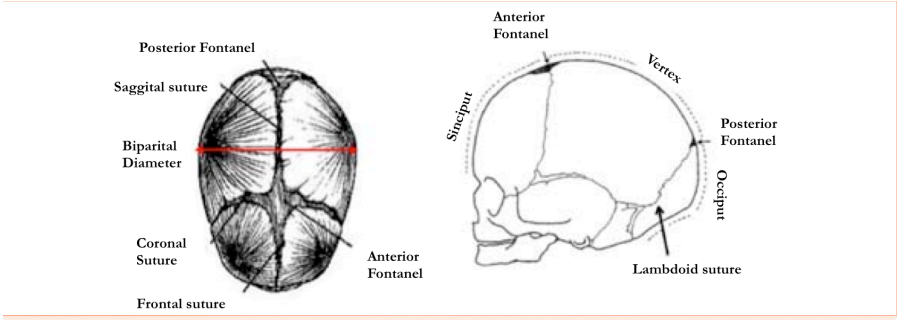

Figure 10-1: the important landmark of the fetal head: the midline suture and the posterior and anterior fontanels

In cephalic vertex presentation the only normal positions are occipito-anterior position, (left occipito anterior "LOA" or right occipito anterior "ROA"), and occipito transverse ("LOT" left or right occipito transverse (LOT and ROT).
In other presentations e.g. breech and face, the position is determined by defining the landmarks of the presenting part (figure 10-2)

Malpresentation: is any presentation other than cephalic presentation with the fetal occiput leading into the pelvis e.g. face, brow, breech or shoulder…etc. are all abnormal presentation "i.e. malpresentation". Sometimes the presentation can be compound, which means the presence of more that one fetal part overlying the pelvic cervical internal os (e.g. head and arm). Rarely the cord may be the presetting part.

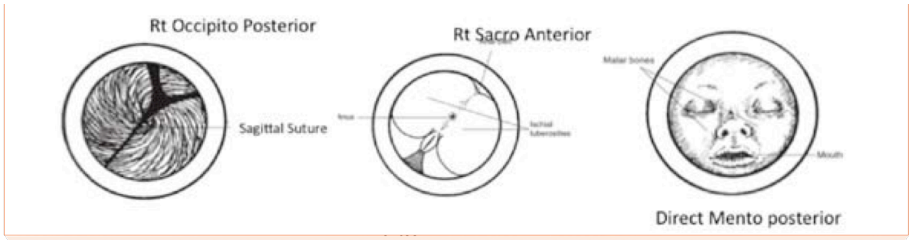

Figure 10-2: diagram for the landmarks and nominated sites in different presentations; the nominated site for cephalic is the occiput, for breech the sacrum and for the face the mentum.

sition: If the fetal occiput is directed posteriorly either direct posterior, to the left or the right plan of the pelvis labor is likely to be prolonged. Therefore occipito posterior position (either direct, right of left occipito posterior "DOP, ROP, LOP") is considered abnormal. Occipito-posterior is the most common malposition and it will be discussed in the next section.

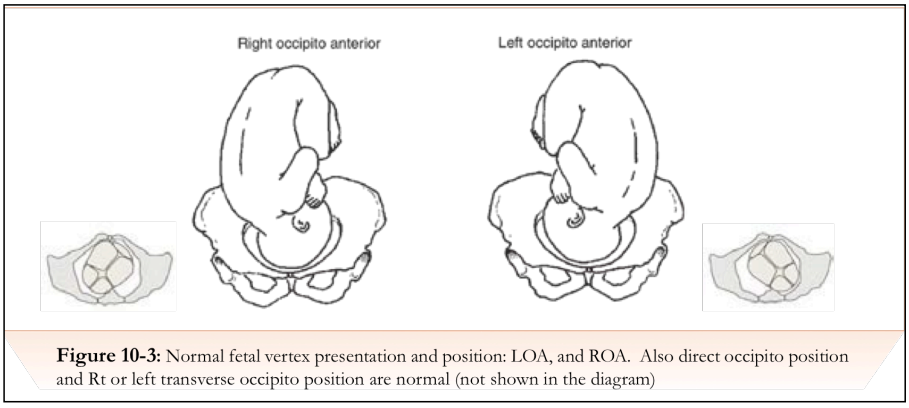

Figure 10-3: Normal fetal vertex presentation and position: LOA, and ROA. Also direct occipito position and Rt or left transverse occipito position are normal (not shown in the diagram)

Causes of Malposition and Malpresentation:

For a normal fetus at or near term, the optimum presentation is cephalic, and the optimum lie is the longitudinal lie with a flexion attitude, in which the head is well flexed on the neck. This is because the *pear* shape of the uterine cavity at term makes it easier for the bulk of fetal breech and flexed legs to be accommodated in the broad uterine fundus and the head in the narrower lower segment.

Any factor(s), which may interfere with this relationship, is likely to predispose to malpresentation and/or malposition. Examples of those factors are:

- Uterine factors: e.g. uterine malformations (e.g. bicornuate uterus) and fibroids.
- Fetal factors: e.g.prematurity, fetal anomalies (e.g. anencephaly or hydrocephalus), multiple gestations.
- Polyhydramnios and oligohydramnios, low-lying placenta or placenta previa.
- Other maternal factors such as grand multiparity due to laxity of the maternal abdominal muscles, contracted pelvis or pelvic tumors that interferes with head engagement.

However, in many instances there is no obvious cause.

An overall approach to management of malpresentation and malposition: Determining fetal presentation is a crucial step in the evaluation of labor. Subsequent management if a malpresentation or malposition is found depend on its the type. In all cases the following points should be examined:

- Exclude potentially dangerous causes such as placenta previa, especially with axial malpresentation such as oblique or transverses lie,
- Exclude major fetal malformation (*the incidence of malformations among breech is approximately 9%).*
- Patient should be delivered in well-equipped hospital with experienced obstetricians and a neonatologist.
- When choosing the mode of delivery careful balance should be made between the benefit and safety to the mother and baby. In modern obstetrics there is no place for heroic procedures that endanger maternal or fetal life.

Malposition: "Occipito Posterior Position"

Occipito posterior position "*Cephalic vertex presentation with the occiput directed backward*" is the most common cephalic malposition. It is encountered in labor in approximately 15-20 % of cases. The diagnosis is made by defining the landmarks of the fetal head during digital vaginal examination (figure 10-4).

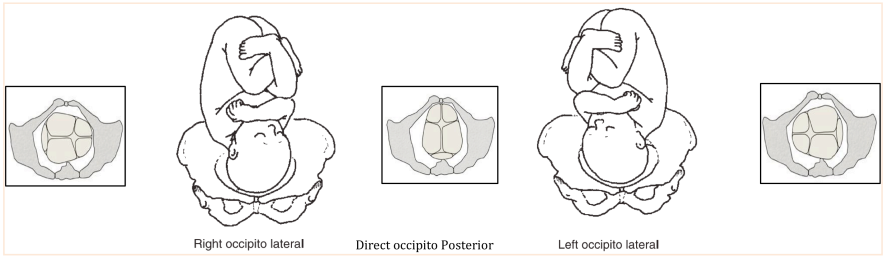

Figure 10-4: Diagram of Occipito posterior

Labor and deliver in OP: In OP position because the fetal head is deflexed, the engaging diameters is the "occipito-frontal diameter which is 11.5 cm. (which is 2

cm > the suboccipito-bregmatic diameter in case of OA position).

The mechanism of labor in OP is the same as in OA but the progress of labor is slower because the fetal head has to go through a longer "internal rotation" to bring the occiput anteriorly underneath the pubic arch.

Morbidity associated with OP: Include all the consequences of prolonged labor such as fetal and maternal distress, increased rate of operative delivery; lower Apgar score at birth, birth trauma, and higher rate of infection.

The management of OP: include maternal support, adequate analgesia (epidural analgesia), close fetal monitoring, and ensuring adequate uterine contractions. The result of labor in OP position is one of the following:

- Full anterior rotation of the occiput and delivery as occipito anterior. This occurs in the majority of cases after slow and prolonged labor.
- Delivery in the occipito posterior position (as face to pubis). This occurs in 5% of cases if the pelvis is large and the fetus is small.
- In the remaining proportion failure of the progress of labor occur due to either failure or arrest of rotation of the fetal head at the pelvic transverse diameter (i.e. deep transverse arrest of the fetal head). Such cases require operative intervention for delivery. The options for operative delivery are one of the following:
    - Manual rotation and delivery.
    - Vacuum extraction delivery or rotation forceps and delivery
    - Cesarean section delivery.

The choice of which option to take is not easy and require careful evaluation of the maternal and fetal condition by a senior obstetrician.

Face and Brow Presentation

Face and brow presentation are abnormalities of the flexion attitude of the fetal head in relation to the neck. A partial deflection may cause brow presentation while extreme degree of deflection (complete extension) results in face presentation. The incidence of face presentation is around 1 in 800 while brow presentation occurs in about 1 in 1500 deliveries.

Etiology: in the majority of times the cause is unknown. Common risk factors include anomalous fetus, particularly anencephaly or an anterior neck mass (fetal

goiter). Multiple nuchal cord loops may also prevent flexion of the head. Abnormal spasm of the fetal neck muscles has been described among causes of deflection attitude of the fetal head. All other factors associated with malpresentation and malposition should also be considered.

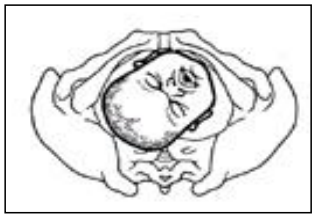

Figure 10-5: Face presentation in mentum anterior the land marks are the orbital ridge, saddle of the nose, mouth, and the chin

Diagnosis:

On abdominal examination the diagnosis may be suspected during Leopold's first and second pelvic palpation if the head is not engaged and felt to be deflexed. However, the diagnosis has to be confirmed during labor either in the first or even the second stage by careful digital vaginal examination and searching for the landmarks for each type of malpresentation: .

In case of face presentation: The landmarks on digital examination are the orbital ridge, saddle of the nose, mouth, and the chin (Figure10-5).
In brow presentation: The landmarks on digital examination are the forehead with the anterior fontanel, saddle of the nose, and orbits. Face presentation is excluded because the mouth and chin are not palpable. A face presentation may be mistaken for a breech since both are comprised of soft tissues with an orifice.

In some cases, it may be necessary to confirm the diagnosis by radiographic studies or ultrasound examination which show a hyperextended fetal neck .

- **Delivery in Face Presentation**: In face presentation the engaging fetal head diameter is the submento-bregmatic diameter (about 10.2 cm.), which can still progress through the pelvis. However the position of the face whether mento-anterior or posterior should be determined because ONLY fetuses in mento-anterior position can deliver vaginally. While it is impossible for fetuses in persistent mentum posterior to have spontaneous vaginal delivery because the head is already in maximum hyperextension (figure 10-6).

However most fetuses in *mentum transverse* and *mentum posterior* positions will spontaneously convert to the mentum anterior position during the course of labor. Therefore when face presentation is diagnosed in the early stages of labor especially in the presence of adequate pelvic dimensions a trial of vaginal deliver may be given with careful monitoring of progress of labor.

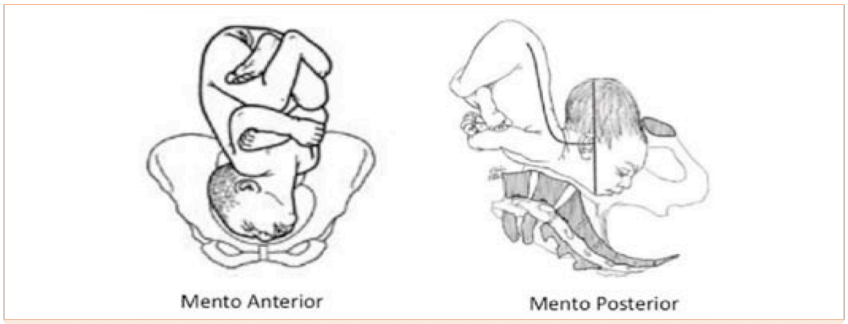

Figure 10-6: In mentum anterior "A" vaginal delivery is possible but in mentum posterior "B" is impossible because of the head is already hyperextended unless rotation to mentum anterior occur.

Mechanism of labor in mentum anterior face presentation:
Mento-anterior position occurs in 60% of cases of face presentation. In such case the mechanism of labor follows the normal sequences as in normal cephalic presentation; engagement, increased extension (instead of flexion as in normal cases) and internal rotation bringing the chin anteriorly. As the face descends onto the perineum, the fetal chin passes under the maternal symphysis pubis, and delivery of the head occurs in flexion with the maternal expulsive forces.
Neonates born in face presentation: neonates who are in face presentation often have significant facial edema and skull molding. The mother should be reassured that this usually resolves within the first 24 to 48 hours of life.

Difficulty in ventilation during resuscitation is not uncommon. It is attributed to tracheal and laryngeal trauma and edema. Therefore, equipment and experienced personnel to perform endotracheal intubation should be readily available at the time of delivery.

- **Delivery in Brow Presentation**:

In brow presentation the engaging fetal head diameter is the mento-occipital (about 13 cm.) diameter which is bigger than any maternal pelvic diameter. Therefore vaginal delivery can not take place and labor would be obstructed unless the fetus is extremely small or if it is a macerated infant, or with an unusually large maternal pelvis.
However, in early labor a brow presentation is often a transient finding . The course of events following an early diagnosis is one of the following :

-In 30% of cases further neck extension occur and the brow is converted into face presentation.
-In 20% of cases further neck flexion results in conversion into vertex presentation.
-50% will persist as brow. *Persistent brow presentation is not compatible with vaginal birth.*

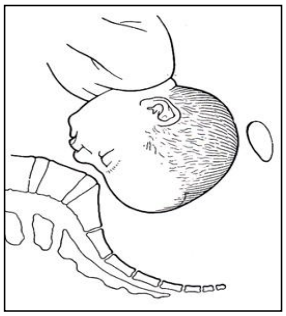

Figure 10-7: Brow presentation

Breech Presentation

Breech Presentation; occurs if a fetus in a longitudinal lie presents with the buttocks or feet closest to the cervix.

Incidence: the incidence of breech presentation correlates negatively with the gestational

Types of breeches
Figures 10-8, describe the types of breech and the approximate frequency of each type.

Gestational Age weeks	Breech %
21-24	33
25-28	28
29-32	14
33-36	9
37-40	7

Table 10-2: the % of breech decreases with gestational age

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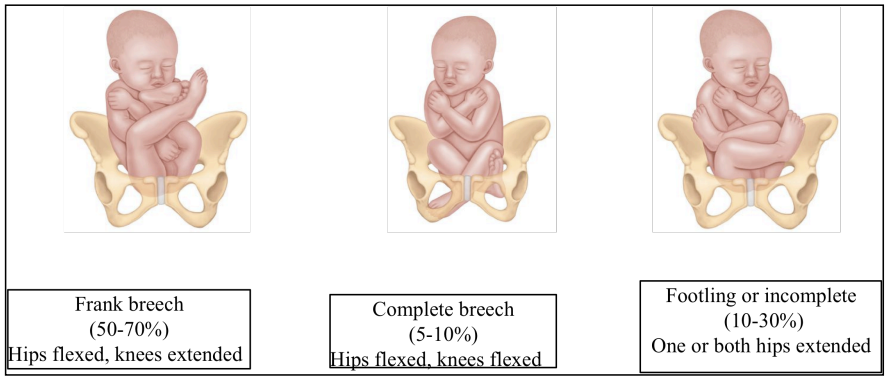

Figure 10-8: Types of breech.

Footling or incomplete breech is associated with the highest risks of fetal morbidity due to high risk of cord prolapse (17%) or descent of fetal limb(s) and body through an incompletely dilated cervix with the risk of retention of the after coming head.

Diagnosis of breech:

Breech presentation is suspected clinically and confirmed by ultrasound examination.

- Clinically the diagnosis of breech can usually be made during the Leopold maneuver if the hard ballottable head is palpated in the fundus and the soft bulky, irregular breech is palpated in the lower uterine pole. In addition, on auscultation the fetal heart sounds are heard above the umbilicus.
- However in some cases (e.g. obese women) the diagnosis can not be confidently made. In such cases an ultrasound examination should be requested in order to confirm the diagnosis.

The role of ultrasound examination goes beyond confirming the diagnosis of breech presentation. It exclude major anomalies, placenta previa and aid in estimating fetal weight and amount of amniotic fluid. These are all important information when deciding on the optimum management breech cases (see later).

In laboring patient digital vaginal examination will also confirms the landmarks of breech, which are the ischial tuberosities, sacrum, and anus. In complete breech the feet may be palpated with the buttocks, and in incomplete breech one or both feet/knees may be palpated.

Management of Breech Presentation:

I. Management during pregnancy: the management of breech starts by attempting to convert the breech into cephalic provided there is no contraindication and the patient accept the procedure known as *External Cephalic Version* or ECV. The objective of ECV is to avoid the potential fetal complications associated with breech delivery (see below for complications of breech delivery) and reduce the risk of cesarean delivery.

If there is contraindication for ECV, or the patient refuses the procedure or if the attempt fails, then the obstetrician has to counsel the patient regarding the options for breech delivery; namely planned elective cesarean section or trial of vaginal breech delivery. The pros and cons for each method should be clearly explained.

- Elective Cesarean Section: The current available evidences show that on the short term delivery of breech babies by cesarean section is associated with significantly less fetal morbidity compared to vaginal breech delivery. This however, has to be balanced against the potential morbidity of surgery and the risks of a cesarean scar on subsequent pregnancies and deliveries, including uterine rupture and placental attachment abnormalities (placenta previa, abruption and accreta).

- Trial of vaginal delivery for breech: Trial of vaginal delivery is also an acceptable option for patients who decline elective cesarean section, provided that the following criteria are fulfilled:

  - Fetal weight less than 3600 g
  - The breech type is either frank or complete breech (incomplete breech or footling breech are associated with high risk of cord prolapse)
  - Well-flexed fetal head as shown by US (hyperextension of the head is a contraindication for vaginal delivery)
  - No other fetal or maternal indication for cesarean section
  - The presence of experienced obstetrician and the facilities to resort to cesarean section at short notice.

External Cephalic Version:

External cephalic version (ECV) is trans-abdominal manual rotation of the fetus into a cephalic presentation. The procedure should not be considered before 36 weeks age of gestation. Before this age spontaneous version to cephalic is probably the more likely course, given the extra few weeks. Moreover even if ECV is successful there is high chance that it reverts back to breech.

The Procedure

- The patient should be prepared for possibly cesarean delivery if for example fetal distress or other complications occur during the procedure. This mean that the patient should sign a consent form, blood should be grouped and screened and the patient fasting for at least 8 hours prior to the procedure. The procedure should be performed in or near by the delivery theatre suite in case an emergency cesarean delivery is required.
- A non-stress test is performed prior to ECV to confirm fetal well-being.

- Ultrasound scan is performed to check fetal presentation, amniotic fluid volume, and to rule out placenta previa.
- ECV is accomplished by gentle manipulation of the fetal head towards the pelvis while the breech is turned up toward the fundus. Forward roll is first attempted then if failed a backward roll tried. Excessive force should not be used at any time, as this may increase the risk of fetal and/or placental trauma.
- Following an ECV attempt, whether successful or not, a non-stress test (biophysical profile if needed) should be repeated prior to discharge of the patient.

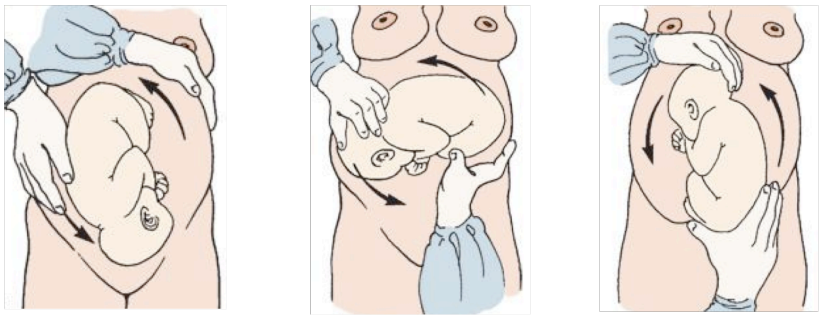

Figure 10-9: External cephalic version

Risks and Complications of ECV:

- Common risks: transient fetal bradycardia (in as many as 40% of cases) is not uncommon. This is most probably due to transient vagal response to head compression with ECV.
- Less common risks of ECV include; precipitation of labor or premature rupture of membranes, abruptio placenta, fetomaternal hemorrhage (0-5%), and cord entanglement (<1.5%).

Contraindications for ECV:

- Absolute contraindications; include multiple gestations, the presence of contraindications to vaginal delivery (e.g. herpes simplex virus infection, placenta previa), nonreassuring fetal heart rate tracing.
- Relative contraindications: poly or oligohydramnios, fetal growth restriction, uterine malformation and major fetal anomaly. A previous cesarean section is also a relative contraindication.

II. Management in labor "Management of vaginal breech delivery":

Management in the first stage: In addition to the standard care of women in labor there are special preparations that should be undertaken with breech delivery:

-All patients should have complete blood count (CBC), blood type and cross match.

-Experienced obstetrician should be present in the delivery suite.

-Anesthetist and preparation for emergency cesarean section should be available if intrapartum complications develop and the patient requires general anesthesia. Epidural anesthesia is preferred as analgesia as it facilitates manipulation during the second stage and if necessary emergency cesarean section may be performed under epidural.

-Pediatrician should always be available at the time of breech delivery.

-Continuous intrapartum fetal monitoring should be applied.

Management in the second stage:

Once the patient is in the second stage and the cervix is fully dilated, preparation for breech delivery should be undertaken. The rule is that breech delivery should NOT be rushed. Therefore the patient should not be placed in the lithotomy position until the breech has descended enough to distend the perineum during and in between contractions.

Vaginal breech delivery may be accomplished in one of three ways:

- Spontaneous breech delivery: No manipulation of the infant is necessary other than simple support of the infant. This occurs predominantly in very preterm, often previable deliveries.
- Assisted breech delivery: This is the most common type of vaginal breech delivery. The infant is allowed to spontaneously deliver up to the umbilicus, then maneuvers are initiated to assist in the delivery of the remainder of the legs, body, arms, and head (see details below)
- Total breech extraction: The fetal feet are grasped, and the entire fetus is extracted. The procedure is associated with birth injury rate up to 25% andmortality rate of approximately 10%. Therefore in current obstetric practice, total breech extraction is abandoned. It is only allowed in cases of a non-cephalic second twin.

Assisted breech delivery:

With the patient placed in the lithotomy position, perineal infiltration and pudendal block should be administered if there is no epidural analgesia (See Chapter 19). Episiotomy may be performed only after the fetal anus has appeared at the vulva.

Delivery of the legs: the mother should be encouraged to push with contractions. In this way the buttocks with the limbs are usually delivered spontaneously in cases of complete breech (flexed knees). No attempt should be made to pull on a foot or leg, even if it is visible and protruding outside the introitus.

In cases of frank breech, gentle traction may be needed, with a finger from each hand placed around the hips of the fetus and into each inguinal region (Figure 10-10)

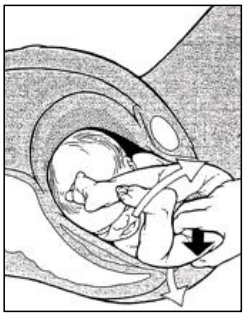

Figure 10-10: delivery of the legs

If spontaneous delivery of the legs does not occur, the *Pinard maneuver* (Figure 10-11) may be applied to facilitate delivery of the legs. The maneuver involves exerting pressure in the popliteal space, to flex the knee then pushing it to the side of the baby so that the foot can be delivered out of the vagina.

Figure 10-11: Pinards Maneuvers

Cord pulsation is checked and a small loop pulled down to prevent traction on the cord

Delivery of the body: The fetal body should be wrapped in dry towel. No traction should be exerted on the infant until the fetal umbilicus is past the perineum. The body is delivered mostly by the maternal expulsive efforts until the scapula and axilla are visible. At this stage it is important to ensure that the fetal back is turned anteriorly, or the fetus may gently be rotated to maintain the back forward.

Delivery of the arms: The arms are delivered following one of three methods:

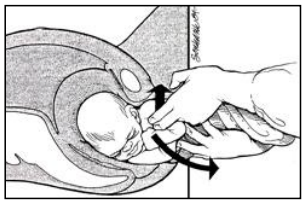

Figure 10-12: Delivery of the anterior arm

- First: In most cases the fetal arms are folded over the chest and its delivery is accomplished by further maternal pushing until the shoulders

present. The fetal trunk is then turned to the anterior-posterior plane and the anterior arm is delivered almost spontaneously then repeating the maneuver in the reverse direction to delivery the posterior arm (figure 10-12).

- Second: If the first method failed to deliver the anterior arm the posterior arm is delivered first by lifting up the baby's legs and trunk over the mother's groin, which enables a finger to reach an elbow joint of the posterior arm, flexing it, and delivering it across the chest.
- Third: With extended or nuchal arms it is necessary to slide two fingers along the humerus until the elbow is reached. The fingers are used to splint the humerus, while the forearm of the fetus is swept across the baby's face and chest out of the vagina.

Delivery of the head:

- Controlled delivery: After deliver of the shoulders the baby's head descend and the hairline of the head starts to appear. If this does not occur, the baby's body is turned to face the floor and suprapubic pressure is used to flex the head and push it down into the pelvis. Once the hairline is visible, the fetus' legs are swung upwards, keeping the vulva completely covered with the operator's other hand. This hand is then opened slowly to allow first the baby's face and then the remainder of the head to deliver. Extreme elevation of the fetal body should be avoided as it may result in hyperextension of the cervical spine and potential neurologic injury.
- Mauriceau Smellie Veit maneuver: In this maneuver the fetal body is allowed to rest on the hand and forearm, while the middle finger of one hand is placed in the mouth, and the second and fourth fingers on the malar eminences of fetal maxilla to promote flexion. The 2 fingers from the other hand are placed on either side of the baby's neck. The shoulders are grasped and downward traction is applied, until the fetal subocciput appears beneath the symphysis pubis. The fetus is subsequently elevated towards the maternal abdomen with delivery of the mouth, nose, brow, and occiput beyond the perineum. An assistant may apply suprapubic pressure during the Mauriceau maneuver to aid in delivery of the head (figure10-13).

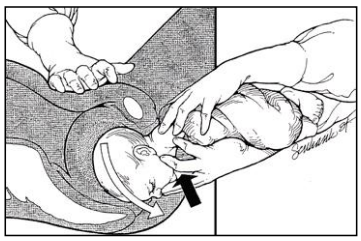

Figure 10-13: Mauriceau Smellie Veit maneuver

- Forceps delivery of the after-coming head: For this method, a long non-rotating forceps such as Neville Barnes or Piper's forceps is used to maintain the head in a flexed position. Other advantages of use of forceps are that it protects the head from sudden decompression / compression and minimize traction on the fetal neck. The forceps are applied while the assistant supports the fetal body in a horizontal plane (figure10-14).

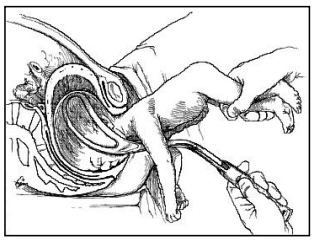

Figure 10-14: Forceps delivery of the after coming head

Difficulties and risks with vaginal breech delivery:

Difficulties may be encountered at all stages of vaginal breech delivery and the obstetrician should be prepared to deal with such acute emergencies. The most common (serious) difficulties are:

- Difficulties with the delivery of the arms: "*Nuchal arms position": refers to* a situation in which one or both arms are wrapped around the back of the neck (occurs in 0-5% of vaginal breech deliveries and in 9% of breech extractions). Nuchal arms position may result in neonatal trauma (including brachial plexus injuries) in 25% of cases.
- Fetal head entrapment: May result from an incompletely dilated cervix. This occurs in 0-8.5% of vaginal breech deliveries. This percentage is higher with preterm fetuses (<32 wk), when the head is larger than the body. The cervix may have to be incised at one or more sites to relieve cervical entrapment (known as Dührssen incisions). However, extension of the incision can occur into the lower segment of the uterus, and the operator must be equipped to deal with this complication. Another difficult maneuver (The Zavanelli maneuver) has been described, which involves replacement of the fetus back into the abdominal cavity, followed by cesarean delivery. While success has been reported with this maneuver, fetal injury and even fetal death have occurred.

Difficulties and risks with Cesarean Section breech delivery:

Currently the weights of evidence are in support for delivery of all breeches at term by elective cesarean section. However, cesarean section for breech delivery still requires skill and experience and is not without risk, particularly for preterm breeches.

-The Maneuvers for delivery of breech by cesarean section are similar to those

for vaginal breech delivery, including the Pinard maneuver, head flexion during traction, rotation and sweeping out of the fetal arms, and the Mauriceau Smellie Veit maneuver.

-The most common difficulty in CS for breech is entrapped head, particularly with premature breech (< 32 weeks). A low vertical uterine incision for preterm breeches prior to 32 weeks' gestation may be safer. The options of management of head entrapment during cesarean section include: extension of the transverse incision vertically upward (T incision). Alternatively, the transverse incision can be extended laterally and upward, taking care to avoid trauma to the uterine arteries. A third option is the use of a short-acting uterine relaxant (e.g., nitroglycerin) in an attempt to facilitate delivery.

Maternal and Fetal risks associated with breech pregnancy:

- Maternal risks: The primary risks for the mother are those risks associated with operative delivery (e.g., wound infection, aspiration, anesthesia risks, and long term risks of uterine scar), especially with emergency delivery.

- Fetal risks: The major risks of breech delivery are fetal. They lead to higher rate of perinatal mortality and morbidity among breech fetuses compared to cephalic ones. The overall perinatal mortality is increased 2- to 4-fold with breech presentation, regardless of the mode of delivery, mostly due to higher incidence of malformations and prematurity.

Fetal morbidity and mortality related to delivery include:

-Intracranial hemorrhage: Could result from either too fast or too slow delivery of the fetal after coming head. With too fast delivery the fetal head is exposed to sudden compression and decompression that may leads to tentorium tears and hemorrhage. While with too slow delivery as with fetal head entrapment there is risk of cord compression and prolonged fetal hypoxia that precipitates intraventricular hemorrhage.

-Skeletal fracture of arms or legs due to rough handling and improper maneuvers.

-Neurological injury due to forceful traction on the fetal spine or hyperextension of the fetal head with resultant spinal cord or plexus injuries.

-Soft tissue injuries such as rupture of spleen, liver, adrenals, and bowel due to applying too much pressure on the fetal abdomen.

-Cord prolapse: Its incidence depends on type of breech presentation. It reach approximately 17%, 5%, and 0.5% in fooling, complete, and frank breech respectively.

Cord presentation and cord prolapse

Definitions: Cord presentation is descent of the umbilical cord through the cervix in the presence of intact membranes. The condition is called "occult" if the prolapse occurred alongside the presenting part and "overt" if it past the presenting part. If the membranes are ruptured the condition is called cord prolapse.

Morbidity and mortality: Cord prolapse is an acute obstetric emergency associated with high risk of fetal morbidity and mortality due to fetal asphyxia. The principal causes of asphyxia are *compression* of the umbilical veins and *vasospasm* of the umbilical arteries, secondary to exposure to vaginal fluids and/or air.

Risk factors for cord prolapse: Prematurity and congenital malformation are important risk factors and account for the majority of adverse outcomes associated with cord prolapse.

Other risk factors include abnormal fetal lie such as transverse, oblique or unstable lie, abnormal presentation (e.g. breech especially footling), premature rupture of members with non-engaged head and polyhydramnios.

Prevention: Although cord prolapse can occur in the absence of risk factors, prophylactic measures should be taken in certain situations with recognized association with cord prolapse such as:

- -Women with transverse or unstable lie who should be offered elective admission to hospital at 37+6 weeks of gestation, or earlier if there are signs of labor or suspicion of ruptured membranes.
- -Women in labor with sings of fetal bradycardia or variable fetal heart rate decelerations who should receive prompt vaginal examination.
- -Careful examination of the cord should be performed at every vaginal examination and after spontaneous rupture of membranes in labor.
- -Artificial rupture of membranes should be avoided whenever possible if the presenting part is unengaged and mobile. If it is necessary to rupture the membranes in such circumstances, this should be performed in operating theatre with preparation ready for cesarean section. The fluid should be released slowly under control "controlled amniotomy".

-In all cases before rupture of the membranes, careful examination should be undertaken to exclude cord presentation, particularly the occult type. In such cases cesarean section is the optimum mode of delivery.

Management:
Cord prolapse is an acute emergency and the fetal mortality and morbidity is directly related to the period of fetal exposure to hypoxia and asphyxia. Therefore, all obstetric units should have clear guidelines and protocols on how to deal with cord prolapse.

- If cord prolapse is diagnosed before full cervical dilatation:

The patient should immediately be prepared for cesarean section provided cord pulsations are present, if not then fetal viability should quickly be documented. The following steps should be undertaken:

1.Assistance should be immediately summoned.
2.Venous access should be obtained.
3.Consent taken (verbal consent will be adequate)
4.Preparations made for immediate delivery in theatre.

Meantime **while those steps are being undertaken**, the following measures should be applied to reduce or prevent cord pressure and vasospasm.

-If the cord loops are lying outside the vagina, it should be minimally handled and if possible covered and replaced in the vagina with surgical packs soaked in warm saline.
-Elevation of the presenting part to relieve pressure on the umbilical cord and prevent mechanical vascular occlusion. This can be done manually by inserting two gloved fingers in the vagina and pushing the presenting part upwards to prevent cord compression. Alternatively, especially if the decision-to-delivery interval is likely to be prolonged (e.g. if it involves ambulance transfer) elevation of the presenting part can be accomplished through bladder filling with about 500-700 mL saline through a Foley's catheter.
-Cord compression can further be reduced by the mother adopting the knee–chest position or head-down tilt (preferably in left-lateral position).
-Tocolysis can be considered if the delivery is likely to be delayed.

- If prolapse of the cord occurs at full cervical dilatation and imminent vaginal birth:

In most cases, operative vaginal birth can be attempted, with a method that depend on the presentation:

- In cephalic presentation; forceps or ventouse delivery especially in parous women is often successful.
- Breech extraction; can be performed in some situations e.g. after internal podalic version for the second twin, or in singleton breech babies when the presenting part is distending the perineum.

The newborn: a neonatologist should attend all deliveries with cord prolapse since live born neonates after cord prolapse are at significant risk of low Apgar scores (AS <7, 21% at one minute and 7% at five minutes).

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Chapter 11

Intrapartum Fetal Monitroing

Dr Nabeel Bondagji

During labor the fetus is exposed to severe stressful challenges induced by repeated uterine contractions. A healthy fetus has adequate placenta reserve and is able to tolerate those "transient hypoxic" events. Assessment of the fetal wellbeing during labor is based on monitoring the fetal heart activity, which assume to reflect the fetal cardiac and medullary response to hypoxia, acidemia and change in blood volume. A typical reassuring pattern of FHR response usually indicates a healthy outcome. However a non-reassuring pattern does not always indicate fetal hypoxia or acidosis. Further tests such as fetal stimulation, Fetal ECG, and fetal scalp blood sampling are often used to evaluate the significance of non-reassuring FHR response before embarking on operative delivery.

By the end of this chapter you should be able to:

List the objective and rationale of FHR monitoring in labor:

- Prevent fetal death and avoid fetal neurologic injury

Define the effectiveness of intrapartum fetal heart rate monitoring:

List the indications of fetal heart monitoring:

Describe the methods of fetal heart rate monitoring:

- External Continuous cardiotocography (CTG) or continuous electronic FHR monitoring:
- Intermittent auscultation.
- Fetal electrocardiogram "internal monitoring of FHR"

Interpret the criteria for reassuring and non-reassuring FHR

Describe the place and utilization of the other methods for evaluation of the non-reassuring FH pattern:

- Fetal Stimulation techniques and its value:
- Fetal ECG "STAN":
- Fetal scalp blood sampling:

Outline the management of non-reassuring FHR abnormalities

⇒Objective of FHR monitoring in labor:

The rationale of monitoring the fetal heart activity during labor is based on the principle that cardiac activities are indirect marker of medullary responses to blood volume changes, acidemia, and hypoxemia.

The objectives of FHR monitoring are:

- First: to prevent fetal death through identify hypoxemic and acidotic fetuses and thus intervene at appropriate time.
- Second: to avoid fetal neurologic injury at the long term.

⇒**Effectiveness of Intrapartum FHR monitoring "the evidence":**

Unfortunately there are no evidences that the objectives of fetal monitoring have been fulfilled at least in low risk cases. Analysis of data from randomized studies comparing electronic fetal monitoring vs. intermittent auscultation in low risk cases have revealed important facts:

- The intrapartum fetal death rate is approximately 0.5 per 1000 births with either approach
- Apgar scores and neonatal intensive care unit admission rates are similar for both modalities
- Neither approach reduces the risk of long-term neurologic impairment or cerebral palsy.

Furthermore in low risk cases continuous electronic FHR monitoring may have additional disadvantage that it could lead to leads to higher operative delivery rates.

The message from those facts is that it is crucially important for those dealing with laboring women to be aware of the limitation FHR monitoring in labor and be familiar with proper interpretation and management of cases with non-reassuring FHR pattern.

⇒**Indications of fetal heart monitoring:**

Based on the available evidence the guidelines for indications of FHR monitoring differs between high risk and low risk pregnancies as follow:

- High-risk pregnancies (e.g. preeclampsia, suspected growth restriction, type 1 diabetes mellitus) should be monitored continuously during labor.
- Low risk and uncomplicated cases: either electronic FHR monitoring or intermittent auscultation is acceptable.

⇒ **Methods of fetal heart rate monitoring:**

I. External Continuous cardiotocography (CTG) or continuous electronic FHR monitoring: In this method a Doppler ultrasound device is belted to the maternal abdomen throughout labor.

The device is connected to an electronic monitor, which continuously plots the FHR on a paper strip, while a pressure transducer simultaneously monitors the frequency, timing, and duration of uterine contractions.

II. Intermittent auscultation: in this method a Doppler device is used to determine the FHR over one to two minutes at intervals of 5 to 30 minutes, depending upon the stage of labor. This method does not provide any information about FHR variability, the shape of FHR decelerations, or uterine contractions.

III. Internal electronic FH monitoring "Fetal electrocardiogram": Internal measurement of FHR is an invasive procedure; thus, its use is restricted to the intrapartum period. A bipolar spiral electrode is inserted transcervically to penetrate the fetal scalp and a second reference electrode is placed upon the maternal thigh to eliminate electrical interference. The internal electrode detects the fetal electrocardiogram (ECG) and calculates the FHR based upon the interval between R waves. This signal is very clear and provides accurate measurement of beat-to-beat variability. Artifact is kept to a minimum, and there is little need for autocorrelation (Figure 11-1).

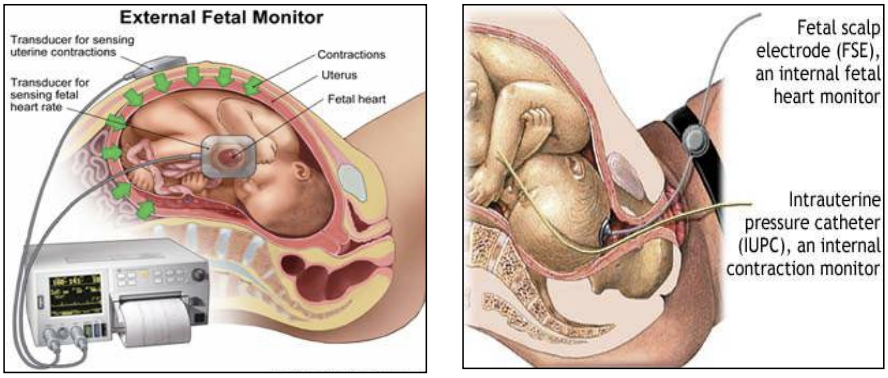

Figure 11-1: Diagram of external monitor (left), internal monitoring (right). In this illustration an intrauterine catheter is inserted to monitor the intrauterine pressure

External monitoring is usually as reliable as internal monitoring and is the preferred approach since it is noninvasive. However internal monitoring should be used when the externally derived tracing is difficult to interpret because of technically poor tracing quality. This occurs in various situations, such as when the fetus or mother is frequently changing position and sometimes in multiple fetus gestations.

The parameters that are normally examined in electronic fetal heart monitoring include the FHR base line, variability, acceleration and deceleration. Table 11-1 describes the definitions for the different parameters.

Variability
Fluctuations in baseline that are irregular in amplitude and frequency **Absent** = amplitude undetectable **Minimal** = amplitude 0 to 5 bpm **Moderate** = amplitude 6 to 25 bpm **Marked** = amplitude over 25 bpm Measured in a 10-minute window. The amplitude is measured peak to trough. There is no distinction between shortterm and longterm variability.
Baseline rate
Bradycardia = below 110 bpm **Normal** = 110 to 160 bpm **Tachycardia** = over 160 bpm The baseline rate is the mean bpm (rounded to 0 or 5) over a 10 minute interval, excluding periodic changes, periods of marked variability, and segments that differ by more than 25 bpm. The baseline must be identifiable for 2 minutes during the interval (but not necessarily a contiguous 2 minutes), otherwise it is considered indeterminate.
Acceleration
An abrupt increase in the FHR. Before 32 weeks, accelerations should last ≥10 sec and peak ≥10 bpm above baseline. As of 32 weeks, accelerations should last ≥15 sec and peak ≥15 bpm above baseline. A prolonged acceleration is ≥2 minutes but less than 10 minutes. An acceleration of 10 minutes or more is considered a change in baseline.
Late deceleration
A gradual decreases and returns to baseline of the FHR a uterine contraction. The deceleration is delayed in timing, with the nadir of the deceleration occurring after the peak of the contraction. The onset, nadir, and recovery usually occur after the onset, peak, and termination of a contraction
Early deceleration
A gradual decrease and return to baseline of the FHR associated with a uterine contraction. The nadir of the FHR and the peak of the contraction occur at the same time. The deceleration's onset, nadir, and termination are usually coincident with the onset, peak, and termination of the contraction.

Variable deceleration
An abrupt decrease in FHR below the baseline. The decrease is ≥15 bpm, lasting ≥15 secs and <2 minutes from onset to return to baseline. The onset, depth, and duration of variable decelerations commonly vary with successive uterine contractions.
Prolonged deceleration
A decrease in FHR below the baseline of 15 bpm or more, lasting at least 2 minutes but <10 minutes from onset to return to baseline. A prolonged deceleration of 10 minutes or more is considered a change in baseline.
Variability
An abrupt decrease in FHR below the baseline. The decrease is ≥15 bpm, lasting ≥15 secs and <2 minutes from onset to return to baseline. The onset, depth, and duration of variable decelerations commonly vary with successive uterine contractions.
Prolonged deceleration
A decrease in FHR below the baseline of 15 bpm or more, lasting at least 2 minutes but <10 minutes from onset to return to baseline. A prolonged deceleration of 10 minutes or more is considered a change in baseline.

Figure 11-1: Development Workshop Report on Electronic Fetal Monitoring: Update on Definitions, Interpretation, and Research Guidelines. Obstet Gynecol 2008; 112:661.

⇒<u>Interpretation of FHR</u>:

The results of FHR tracing is generally interpreted as reassuring, non-reassuring or undetermined patterns.

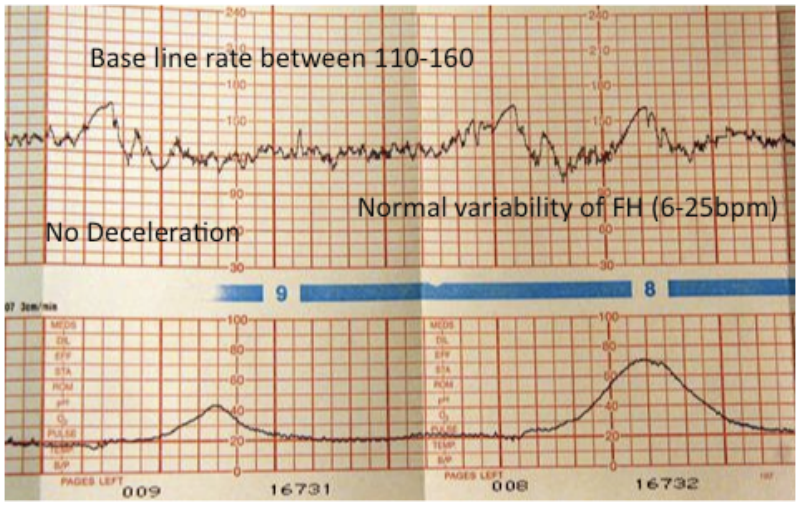

Figure 11-2: Reactive "Reassuring FH pattern"

- Reassuring patterns: Indicates that there is minimal likelihood of acidemia at the time of testing. It is not predictive of future status, as tracing patterns can change. A reassuring fetal heart rate pattern should have all of the following components:
  - A baseline fetal heart rate of 110 to 160 bpm
  - Absence of late or variable FHR decelerations
  - Moderate FHR variability (6 to 25 bpm) (figure 2A-B)

- Non-reassuring patterns: A nonreassuring tracings (category III) are associated with abnormal fetal acid-base status at the time of observation. It includes absent or minimal variability with deceleration or bradycardia and sinusiodal pattern. These patterns require prompt evaluation and intervention because fetal or neonatal death or damage may occur if the pattern does not resolve over an hour or more.

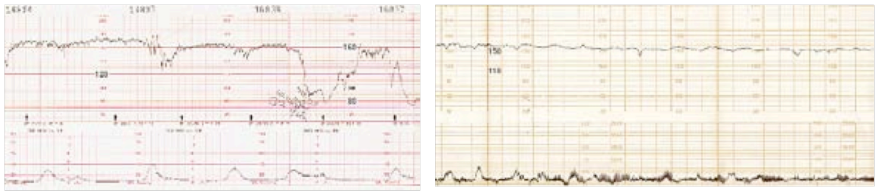

Figure 11-3: Non-reactive FHR pattern (left) and Type II delayed deceleration (Right)

- Indeterminate patterns: FHR patterns that are neither reassuring nor nonreassuring and are considered indeterminate. The fetus may not be acidotic; however, continuation or worsening of the clinical situation may result in fetal acidosis. Therefore, continued surveillance and evaluation of these patients is indicated. Table 11-2 describe the three patterns , outline characteristics and management.

Reassuring pattern of FH "Category I" Criteria are predictive of normal fetal acid-base balance at the time of observation.	
All the criteria must be present. Tracings meeting these	➢ Baseline rate: 110-160 beats per minute (bpm)
	➢ Moderate baseline FHR variability
	➢ No late or variable decelerations
	➢ Early decelerations may be present or absent
	➢ Accelerations may be present or absent
Non Reassuring pattern of FH "Category III" Criteria predictive of abnormal fetal acid-base status at the time of observation.	
Prompt evaluation and intervention is indicated it include: • Supplemental oxygen • Change in position. • Treatment of hypotension. • Discontinuation of any uterotonic drugs being administered.	(1) Absent baseline FHR variability and any of the following: • Recurrent late decelerations • Recurrent variable decelerations • Bradycardia
	(2) Sinusoidal pattern
Un-determined pattern of FH "Category II" Not predictive of abnormal fetal acid-base status, but require continued surveillance and evaluation. The guidelines do not offer specific recommendations for evaluation of these fetuses, but it seems reasonable to employ other diagnostic measures, such as sonography, scalp stimulation, and scalp blood sampling	
• Require continued surveillance • Intervention as before may be needed • Other diagnostic measures, such as sonography, scalp stimulation, and scalp blood sampling if the pattern persist	The FHR tracing does not meet criteria for either category I or III and is considered indeterminate

Table 11-2: Management approach to FHR patterns. Form From Macones, GA, Hankins, GD, Spong, CY, et al. The 2008 National Institute of Child Health and Human Development Workshop Report on Electronic Fetal Monitoring: Update on Definitions, Interpretation, and Research Guidelines. Obstet Gynecol 2008; 112:661.

⇒**<u>Further evaluation of the non-reassuring FH pattern</u>:**

In some cases (e.g. persistent undetermined FH pattern) it is appropriate to apply other method to distinguish between the fetus with a nonreassuring FHR tracing that is hypoxemic, but well compensated, from one who is acidotic and at risk for neurologic impairment or death and thus require immediate delivery.

In such cases one of the following methods can be applied:

1. Eliciting FHR response to stimulation: In this method stimulation of the fetus is applied on its vertex by prodding it with the examining finger or an instrument, such as an Allis clamp, during vaginal examination, or externally by Viboracoustic stimulation. If FHR acceleration (rise of ≥15 bpm above baseline lasting for ≥15 seconds) is elicited it indicates absence of acidosis (i.e. fetal pH greater than 7.20) .
2. The STAN fetal heart monitor: In this technique the fetal electrocardiogram (ECG) is monitored during labor via a spiral electrode attached to the fetal scalp. The principle of this method depends on the fact that fetal hypoxemia can result in elevation or depressions of the ST segment. Using special software, it is possible to automatically identify and analyzes changes in the T wave and the ST segment of the fetal ECG. While this method proved to have reasonable sensitivity in distinguishing the acidotic and at risk fetuses its application and utilization require special training.
3. Fetal scalp blood sampling: Fetal scalp blood sampling for measurement of either fetal blood PH or Fetal lactate concentration (a major determinant of fetal blood ph). Both require the same equipment and techniques for obtaining the fetal scalp blood sampling. A scalp pH value of <7.20 has traditionally been used to represent the critical value for identifying fetal acidosis.

   Draw back of FBS include the technical skill required, cost, need for continuous availability of standardized equipment and trained personnel, in addition to the discomfort experienced by the patient.

⇒**Management of Fetal heart rate patterns:**

The management of abnormal fetal heart rate pattern should take in consideration the whole clinical picture including pregnancy complications, gestational age, and maternal disorders that are known to affect pregnancy such as diabetes.

Figure 11-2 summaries the approach to the management of abnormal or non-reassuring FH pattern based on the category of the FH pattern.

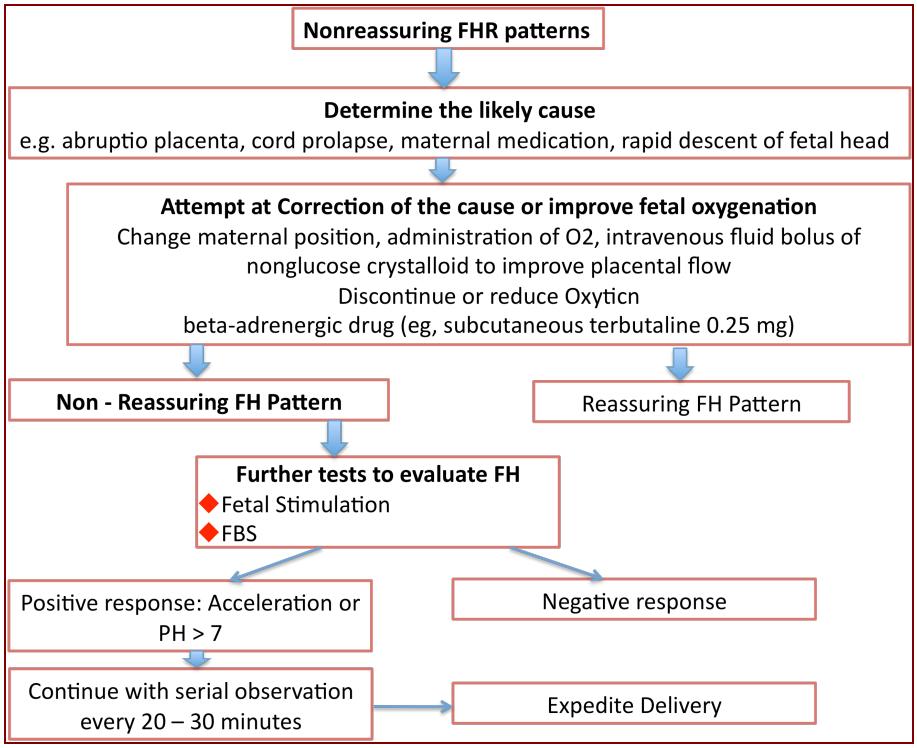

Figure 11-2: Management algorithm of abnormal fetal heart rate pattern

References and Further Readings:

- Alfirevic, Z, Devane, D, Gyte, G. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. Cochrane Database Syst Rev 2006; 3:CD006066.

- ACOG Practice Bulletin No. 106: Intrapartum Fetal Heart Rate Monitoring: Nomenclature, Interpretation, and General Management Principles. Obstet Gynecol 2009; 114:192.

Chapter 12

Induction of labor

Dr **Nora Sahly**

In an ideal world, a pregnancy should end at term by spontaneous onset of labor and a vaginal delivery. Sometimes however, pregnancy continues beyond term (> 42 weeks) or the delivery needs to be undertaken before term either because of maternal or fetal indications,. In either case delivery can be achieved either through elective cesarean section or by *'induction of labor'*. Therefore induction of labor should be viewed as a therapeutic intervention to initiate uterine contractions with the objective of achieving vaginal delivery. As such induction of labor should only be undertaken, when there are good enough indications that outweigh any its potential risks and/or consequence .

By the end of this chapter you should be able to able to:

- **Describe the physiological background related to maintenance of pregnancy**: Specific features of the uterus and the cervix.
- **Define Cervical ripening:** Definition of *ripe* or favorable and *unripe* or unfavorable cervix
- **Describe** the methods for assessment of cervical ripening "the Bishop Score" ultrasound …etc.
- **Define Induction of labor as a therapeutic intervention**:
- **List the** indication and contraindications for induction of labor
- **List the Methods of induction of labor:** ARM, Oxytocin, Prostaglandin.
- **Describe** the advantages, indications and risks of each method.
- **Describe the approach and management of patients for induction of labor.**
- **List the potential complications** of induction of labor and how to avoid/treat.

Physiological background:

In normal pregnancy there is a dynamic balance between the factors responsible for uterine quiescence and those responsible for uterine contractility. There is also a balance between the factors that keep the cervix closed and firm and the factors that soften the cervix and allow dilatation in response to uterine contraction. Understanding the mechanisms that control this balance is required for a rational approach to induction of labor as well as for treatment of preterm birth.

The uterus: The smooth muscle fibers of the uterus, like all smooth and striated muscle fibers are rich in the contractile protein actomyosin. It is thus capable of contraction throughout pregnancy. However, normally the uterus remains in a quiescent state until labor begins. Several systemic, as well as local uterine factors are responsible for this

state of "uterine quiescence". These factors include: a higher balance of progesterone to estrogen hormones, low prostaglandins activity, uterine insensitivity to oxytocin, and lack of the gap junction between uterine muscle fibers which are essential for coordinated synchronized contractions.

The cervix: Throughout pregnancy the cervix must remain firm and closed, with very little change until labor begin. The histology of the cervix is well prepared for such function. It is mainly formed of connective tissue rich in collagen fibers. The smooth muscle component of the cervix is no more than 10% to 15%, its distribution tapers off along the cervix constituting 25, 16, and 6% in the upper, middle and lower segment of the cervix respectively (figure 12-1).

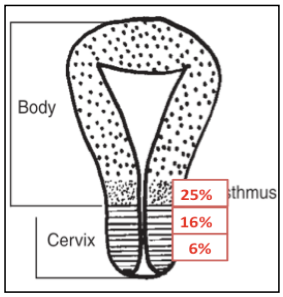

Figure 12-1 shows the distribution of muscle fibers along the cervix.

Cervical ripening:

Is a complex process that involves a series of anatomical and physiological changes in the properties of the cervix. It eventually change it from a firm, long structure into a soft and short one that permits cervical dilatation concurrent with uterine contractions.

Cervical ripening occurs secondary to alterations at the molecular and biochemical levels within the cellular and non cellurlar cervical tissue matrix. Normally the process of cervical repining begins days or weeks before the onset of labor.

The factors responsible for initiation of the ripening process are not fully understood. Change in the estrogen to progesterone ratio has been suggested. Estrogen can promote cervical ripening by up regulating collagenase, whereas progesterone withdrawal or the use of progesterone antagonist accelerates the ripening process.

Prostaglandins also play an important role in cervical ripening. They increase collagen degradation, cause dilation of small vessels in the cervix, increase hyaluronic acid, increase in chemotaxis for leukocytes (which causes increased collagen degradation) and increased stimulation of interleukin (IL)-8 release.

Research in this area is important for finding better measures for induction of labor, better treatment for preterm labor and pathological conditions such as cervical incompetence.

Assessment of cervical ripening:

In clinical practice, the most common method of assessment of cervical ripening is by vaginal examination for physical characteristics, namely; consistency of cervical tissue, length of the cervix, its dilatation and position. The first person to put those

characteristics into quantitative objective scoring method was *Bishop in 1946.* The original Bishop score has been modified to make it simplified; table 12-1 shows the FIVE characteristics that are currently used to assess the condition of the cervix, favorable or unfavorable, before attempting induction of labor.

Point value	**0**	**1**	**2**
Dilatation (cm)	<1.5	1.5 – 3.0	> 3.0
% Effacement	Un effaced	Intermediate	Effaced
Cervical length	≥ 1.5	1.5 – 0.5	≤ 0
Station	-2	-1	-1/0
Consistency	Firm	Medium	Soft
Position	Posterior	Middle	Anterior

Table12-1: The Burnett Scoring System (or Modified Bishop score) (1966)

Other methods for assessment of cervical ripening have also been tried e.g. measurement of cervical length by transvaginal ultrasound but have not offered advantages over the simple method of *Bishop Score.*

Induction of labor:

It is defined as a ***therapeutic intervention that aims to initiate uterine*** **contractions,** ***with an objective of achieving vaginal delivery***. Therefore, induction of labor, as any other therapeutic intervention should have clear indications that outweigh any potential complications.

Indications and contraindications for induction of labor:

Since induction of labor is viewed as a therapeutic intervention, several factors have be considered before contemplating induction of labor these include: gestational age, fetal lung maturity, severity of the clinical condition, and cervical status.

The final decision should be made after reviewing the following two criteria:

1. The continuing the pregnancy is believed to be associated with greater maternal or fetal risks than the risks associated with induction of labor.
2. There is no contraindication to vaginal birth

Examples of indications of induction of labor include common medical and obstetrical conditions for which induction may be indicated include postterm pregnancy, prelabor (premature) rupture of membranes, intrauterine fetal growth restriction, and preeclampsia/eclampsia.

Contraindicating for induction of labor:

There are few situations when induction of labor is considered either relatively or absolutely contraindicated (Table 12-2).

Placenta or vasa previa
Abnormal fetal lie
Cord presentation
Presenting part above pelvic inlet
Prior classical uterine incision
Prior myomectomy or uterine unification surgery
Active genital herpes infection
Pelvic structural abnormalities
Invasive cervical carcinoma

Table 12-2: contraindication for induction of labor.

Methods of ripening the cervix and induction of labor:

Before deciding on induction of labor, the clinician in charge should review the following:

- The indication(s) for induction: this should be strong enough to justify the intervention, including the risk that induction might fail and end in cesarean delivery.
- The condition of the cervix: whether the cervix is favorable or unfavorable. In patients with favorable cervix (Bishop Score > 6), induction of labor carries no more risk than that of spontaneous labor. On the other hand, in patients with an unfavorable cervix, an initial cervical ripening is required. This means a prolonged period of hospitalization, more "stress" and increased rate of failed induction among this group of patients.

Methods of induction of labor "IOL":

In modern obstetrics, the commonly used methods of IOL include one or more of the following three methods:

1) Amniotomy.
2) Oxytocin.
3) Prostaglandin compounds PGE_2 and F_2-α and prostaglandin analogue, particularly Misoprostol

Other methods for induction/ripening of the cervix that have been described but not very commonly used, include; mechanical methods for cervical ripening, membrane stripping, antiprogesterone, and relaxin hormone.

Amniotomy for induction of labor:

Amniotomy or "artificial rupture of membranes "ARM" is rarely used alone to induce labor. More frequently, amniotomy is undertaken in combination with other uterotonic

agents such as, oxytocin or prostaglandin. Amniotomy may also be performed to accelerate an already established labor.

Advantage of Amniotomy

1. Induce or accelerate uterine contractions through an increase in the release of local secretion of endogenous prostaglandin, either directly from the chorion-amnion cell damage that ensues, or indirectly "mechanically" due to the increased force of pressure of the head on cervix.
2. Enhanced response to oxytocin.
3. Permits better monitoring of fetal status since it permit application of internal scalp electrode for electronic fetal monitoring, in addition it reveals the color of the amniotic fluid if it is clear or stained with meconium.
4. Allows placement of intrauterine catheter for monitoring of uterine contractions.

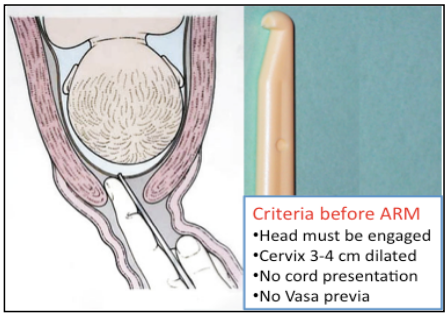

Figure 12-1: diagram showing the technique of ARM. Also the amnio-hook, a tool often used for the procedure. Some basic criteria should be fulfilled before ARM in order to avoid its potential complications (see text)

Method: the forewater is ruptured using either a toothed forceps or more commonly, a special instrument designed for that purpose (e.g. amnio-hook). Rarely the hindwater is targeted for ARM using special catheter for the that purpose.

Potential complications of amniotomy;

- Cord prolapse: if the presenting part is high or not engaged or in cases of hydramnios.
- Infection: The risk increases if the interval from amniotomy to delivery is unduly prolonged especially if the patient is subjected to frequent vaginal examination. *Amniotomy is contraindicated in patients with known HIV, or active herpes virus infections.*
- Abruptio placenta: may occur as a result of sudden release of intraamniotic pressure in cases of polyhydramnios.
- Fetal hemorrhage: may occur in the rare cases of velamentous cord insertion, if fetal vessels are running in the membranes (vasa previa).

Those complications are very rare and can be avoided by careful selection of cases before performing amniotomy.

Oxytocin: Oxytocin, together with vasopressin (the antidiuretic hormone), are the two hypothalamic neurohormones released by the posterior lobe of the pituitary gland. Both are peptide hormones that contain nine amino acids. They are synthesized in separate cells in the supraoptic and paraventricular nuclei of the hypothalamus. They are transported down the axons and stored in secretory granules in nerve terminals in the

posterior pituitary. Normally, oxytocin is released in a pulsatile fashion in response to stimulation of mechanoreceptors in the uterus and vagina during parturition. The nipple also sends nervous impulses to the hypothalamus upon suckling, leading to contraction of the myoepithelial cells and expulsion of milk under positive feedback control.

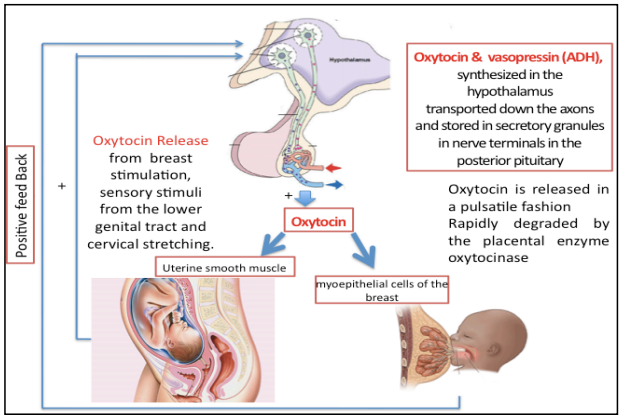

Figure 12-2: Schematic presentation of Oxytocin secretion and its primary actions. Oxytocin and ADH have very close molecular similarity. This accounts for the small ant diuretic and vasoactive activity produced by oxytocin

Effects of oxytocin: The two major targets for oxytocin are the myoepithelial cells of the breast, which surround the alveoli of the mammary gland, and the smooth muscle cells of the uterus. It produces:

- Milk ejection effect.
- Stimulates periodic contraction of uterine smooth muscle cells through two mechanism; a) Direct interaction with myometrial receptors and b) Indirectly by stimulation of the release of prostaglandin E2 and F_2-α in fetal membrane through activation of phospholipase C.

In normal pregnancy, both the concentration and distribution of oxytocin receptors change over the weeks of gestation. By about 13 to 17 weeks, the concentration of oxytocin receptors is about six times higher than the non-pregnant level, and at the end of pregnancy it is about 80 folds higher, reaching maximum level at the onset of labor whether full term or preterm.

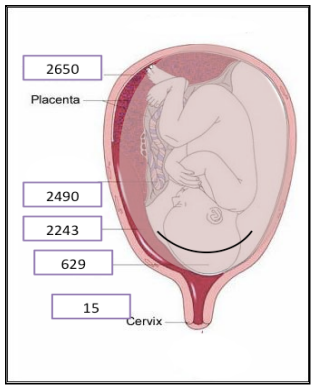

Figure 12-2 shows the distribution of Oxytocin receptors in the uterus and the cervix

Also, the distribution of oxytocin receptors within the uterus occurs in such a way that it is highest around the uterine fundus and tapers off to become very low in the cervical tissue (Figures 12-2).

The clinical implication is that the uterus is insensitive to the uterotonic effect of oxytocin until substantial oxytocin receptor concentrations are induced. Also, because receptors are spare in the human cervix, oxytocin alone has no direct effect on cervical ripening.

Preparation and routes of administration:
The commercially available synthetic oxytocin (Pitocin, Syntocinon) is available in injectable form (10 units /ml) that can be given intravenously and intramuscularly or as a nasal spray (40 units /ml).
However, for the purpose of induction of labor with a viable fetus, the only acceptable route of administration of Syntocinon is by continuous intravenous infusion. This permits constant blood levels and tight titration of uterine activity to the infused oxytocin concentration.
A number of protocols have been described (*Tables* 12-3) with various starting infusion rates, intervals for incremental increases, magnitude of interval increase, and maximum rate.
The principle is that the dose and infusion rate should be titrated to the uterine response and fetal condition. The objective is to achieve uterine contractions every 2-3 minutes, lasting 60-90 seconds, with an intensity of 150 to 350 Montevideo units (i.e., the peak strength of contractions in mmHg measured by an internal monitor multiplied by their frequency per 10 minutes).

Regimen	Initial Dose (Mu/min)	Incremental increase, mU/min	Dosage interval (minutes)
Low Dose	0.5 to 1	1	30 to 40
Alternative low - dose	1 or 2	2	15
High-Dose	6	6 maximum 40 mU	15
Alternative High-Dose	2	4 Maximum: 32 mU	15

Table 12-3: The table shows different regiments for starting oxytocin infusions. No evidences that one regiment better than the other. Factors such as condition of the cervix, body surface area, gestational age can affect the regiment and dose of oxytocin.

Prostaglandin (Dinoprostone) PGE_2

Prostaglandins are 20 carbon prostanoic acid derivatives. Four basic groups of Prostaglandins exist (A, B, E, and F). Each of these is further subdivided into 1 or 2,

depending on the number of saturated bonds between the carbon atoms, and alpha or beta, depending on their spatial arrangements. Prostaglandins is present in almost all body tissues. The highest concentration is thought to be in the prostate hence its name (seminal prostaglandin comes from the seminal vesicles). Prostaglandins play a major role in normal parturition, particularly in cervical ripening and the final pathway of uterine contraction.

Only the E_1, E_2 and F_2 components are of obstetric interest. Prostaglandins are produced in the placenta and fetal membranes. Many factors affect the production of prostaglandins. Prostaglandin levels are increased before and during the onset of labor.

Prostaglandins in cervical ripening and induction of labor:

PGE_2 are effective when given orally, intravenously, intravaginally, and intracervically. However, side effects of prostaglandin such as diarrhea, vomiting and pyrexia are more pronounced with the oral and intravenous route. Currently, the *intracervical or intravaginal routes are the commonly used ones.*

Dose of PGE_2: The currently available formulas are prostaglandin gel (Dinoprostone) 1 or 2 mg and prostaglandin tablets 3 mg. More recently, controlled release prostaglandin system has been introduced to the market (Figure 12-3).

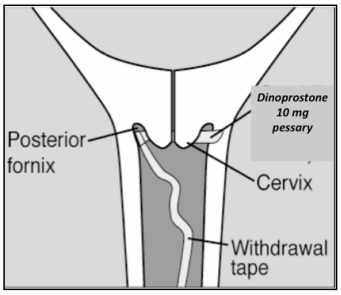

Figure 12-3: Dinorprostone (PGE)

Prostaglandin is commonly used for cervical ripening, but there is no such dose for ripening and dose for induction. Therefore any patient who starts with the intention of cervical ripening is potentially in labor.

Most of the guidelines agree that the manufacturer recommendations should be followed regarding the dose and frequency of prostaglandin administration. It is customary that primigravidas with unfavorable cervix can receive 2 mg PGE_2 gel while multi gravidas receive 1 mg as initial dose. The dose is repeated not less than every 6 hours unless there are uterine contractions.

The number of doses that can be given should also be sought. However, in principle if there is no response after a reasonable attempt, then failure of induction should be pronounced and the indication for delivery should be revised. If delivery is judged to be mandatory a cesarean section has to be undertaken.

Misoprostol:

This is a prostaglandin E_1 analogue that has the advantages over Dinoprostone of not only being less expensive but also stable in room temperature, whereas Dinoprostone requires refrigeration to prolong its half life. Misoprostol is marketed for prevention and treatment of gastric and duodenal ulcers. Despite its effectiveness in inducing labor the drug has not yet been approved for that purpose by major administrative bodies.

The drug may be given vaginally or orally, but the appropriate dose for either route is not yet determined. However, if given vaginally for cervical ripening, it is *recommended* that the lower dose of 25 µg every 4 to 6 hours should be used. Many authorities still do not approve the use of Misoprostol for labor induction with a live fetus except within a setting of clinical trails.

Other methods primarily used for cervical ripening:

Prostaglandin agents are currently the agents most commonly used for cervical ripening. Other methods of cervical ripening/induction shown to be effective in individual trials include mechanical methods such as Foley's catheter and laminaria tents, relaxin, antiprogestins, membranes stripping/sweeping.

Patient Pre-induction preparation and Management:

Once a decision for induction is made, it is the responsibility of the obstetrician to explain to the patient the reason for this decision and what to expect when labor is induced. The medical and obstetric history should be reviewed. Contraindication for induction should be sought and ruled out. The following points should specifically be assessed:

1) The readiness of the cervix (Bishop Score): is the cervix favorable or unfavorable (*recent* Bishop Score assessment)?
2) Gestational age and fetal pulmonary maturity: is there a need to test for fetal lung maturity?
3) The presumed ability of the fetus to tolerate labor: e.g. cases of severe FGR may not tolerate vaginal delivery and will have a better outcome by cesarean section.
4) The stability of the maternal condition: e.g. cardiac cases may not tolerate prolonged labor.

- Each obstetric unit should have its own policy for fetal monitoring. The principle is that all induced patients should be managed in the labor room with continuous monitoring for uterine contractions and fetal heart.
- Labor data, including cervical dilatation, should be plotted on partogram, as in patient with spontaneous labor. However, induced patients are expected to have longer periods of latent and active phases of labor, which should be acceptable as long as fetal and maternal conditions permit.

Low risk patients with unripe cervix may not necessarily require labor room management, but continuous monitoring of fetal heart should be commenced as soon as there are uterine contractions.

Untoward effects and complications of induction of labor:

Complications or untoward effects of induction of labor may be attributed to:

1. Prolonged labor and its physical and psychological consequences; prolonged labor means prolonged maternal distress, repeated vaginal examination, fetal and maternal monitoring. All that can adversely affect the mother morale and increase her requirements for analgesics and sedatives.
2. Increased rate of fetal distress: likely to occur secondary to uterine hyperstimulation, but can also be related to the primary indication for induction.
3. Increased rate of instrumental delivery: maternal exhaustion after a prolonged labor may be partially responsible for the increased need for instrumental delivery among induced labors.
4. Uterine hyperstimulation and fetal distress: care should be taken not to over stimulate the uterus. In most cases when the active phase of labor begins the oxytocin infusion can be decreased or sometimes discontinued.

Uterine hyperstimulation is defined as contractions frequency more often than every 2 minutes or contraction duration longer than 90 seconds with or without fetal heart rate changes.
Management of uterine hyperstimulation: In the event of hyperstimulation the oxytocin infusion should immediately be decreased or discontinued until the uterus relaxes. If uterine hyperstimulation persists and or/fetal heart rate abnormality continues despite discontinuation of oxytocin infusion, intrauterine fetal resuscitation should be initiated. This includes; oxygen administration, positioning the mother on her left side, intravenous fluid (if not contraindicated). Tocolytic such as intravenous Terbutaline 0.125 mg may be used. In some cases, an emergency cesarean section has to be undertaken due to persistent fetal distress.

5. Uterine rupture; cases of uterine rupture among induced patients have been recorded more often in grand multiparous especially in the presence of malpresentation or uterine overdistension, or patients with previous cesarean section scar.

6. Specific complications related to the agent used for induction:

Prostaglandins: particularly if given orally cause nausea, vomiting, diarrhea and pyrexia.
Oxytocin: may be associated with the following side effects:

a) Direct vascular and smooth muscle relaxation, hence the association of prolonged oxytocin administration with postpartum hemorrhage. Bolus dose of intravenous administration of oxytocin may result in hypotension, reduced coronary perfusion and cardiac arrest. These effects are most pronounced in the patient under anesthesia

b) Antidiuretic effect: Although the antidiuretic effect of oxytocin is approximately 1% that of vasopressin, the use of large doses or in the presence of excessive intravenous fluid administration can result in water intoxication.

c) Neonatal hyperbilirubinemia and jaundice have also been associated with the use of oxytocin, more commonly with preterm fetuses.

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Chapter 13

Management of Pain in Labor and Delivery

Dr Nora Sahly

The pain experienced during labor and delivery is probably the most severe physiologically based pain. Nevertheless it is the obstetrician duty to undertake all possible safe measures to relief the severity of this pain. Severe labor pain, that is not properly managed can be detrimental to the maternal and fetal wellbeing and contribute to the labor dystocia and failure of normal delivery. The management of labor pain should begin during pregnancy with appropriate preparation and education of expectant mothers as to what they expect to experience and what they supposed to do throughout the different stages of labor. They should also be assured about the measures available for help in pain relief. Finally the woman choice should be respected, even if she chose no intervention and wishes to practice self-control of pain.

By the end of this chapter you should be able to:

Describe the pathway of labor pain in each of the:

- **First stage**: visceral pain fibers through T10, T11, T12, and L1
- **Second stage:** additional Somatic pain fibers (S2, S3, and S4)

List the Adverse consequences of labor pain: on the mother, the fetus and progress of labor,

Outline the approach to management of labor pain:

- The alternative medicine approach:
- The conventional medicine approach:

List the systemic approach to management of pain in labor

The intravenous, intramuscular, or inhalation routes.

Describe the Regional approaches (neuraxial analgesia), indication, target nerves, and place of application each one:

- Epidurals, Spinals, Combined spinal-epidurals (CSE).
- Local injection as pudendal and paracervical nerve block.

Describe the following points regarding Regional techniques (epidural, spinal):

- The advantages of epidural and spinal anesthesia:
- Drugs used for epidural and spinal techniques:
- Epidural Vs. Spinal "intrathecal" routes (Figure 13-3):
- Techniques of administering epidural anesthesia
- Contraindications to spinal and epidural anesthesia:
- Complications of spinal and epidural anesthesia:
- Effect of neuraxial analgesia on the progress and outcome of labor:

⇒**Pathway of Labor pain:**

- **First stage**: In this stage the pain is mainly visceral produced by distention of uterine and cervical mechanoreceptors and ischemia of uterine and cervical tissues. The pain signal enters the spinal cord after traversing the T10, T11, T12, and L1 white rami communicants.
  The pain is usually described as cramp-like pain. It may also be referred to other areas than the uterus such as the abdominal wall, lumbosacral region, iliac crests, gluteal areas, and thighs.
  As the patient approach the second stage she starts to experience the additional somatic elements of pain.
- **Second stage:** During this stage the pain is a combination of visceral pain from uterine contractions and cervical stretching in addition to the somatic pain produced by stretching of the vagina, pelvic ligaments and pressure on pelvic floor. The pain signals from these areas are transmitted to the spinal cord via three sacral nerves (S2, S3, and S4), which comprise the pudendal nerve.
  At this stage patients experience rectal pressure and an urge to "bear down" as the presenting part descends into the pelvic outlet.

⇒**Adverse consequences of labor pain:** The pain of labor produces not only emotional distress and suffering but also pathophysiological changes that can be detrimental to the maternal and fetal wellbeing which include:

- Increased oxygen consumption
- Hyperventilation that can lead to hypocapnia and respiratory alkalosis which can affect maternal-fetal oxygen handling.
- Decreased placental perfusion: an adverse effect of stress hormones (cortisol and epinephrine) on the placental blood flow.
- Gastric inhibition and increased gastric acidity.
- Increased rate of lipolysis
- Increased peripheral vascular resistance, cardiac output, blood pressure
- Incoordinate uterine activity which can lead to labor dystocia

In addition to those short term complications, a women who is left to suffer from labor pain without proper management are more prone to long term psychological complications in the form of postpartum depression and posttraumatic stress disorder.

In some cases the trauma of labor pain may be so severe that it puts the woman off the idea of ever getting pregnant. Sometimes this may be a major cause of marital and family problems.

Approach to management of labor pain:

Labor pain, as any other acute pain, has two components: a sensory or physical components, and affective components due to interpretation of the pain stimuli through a wide variety of other factors emotional, social, cultural and cognitive variables unique to the individual (Figure 13-1)

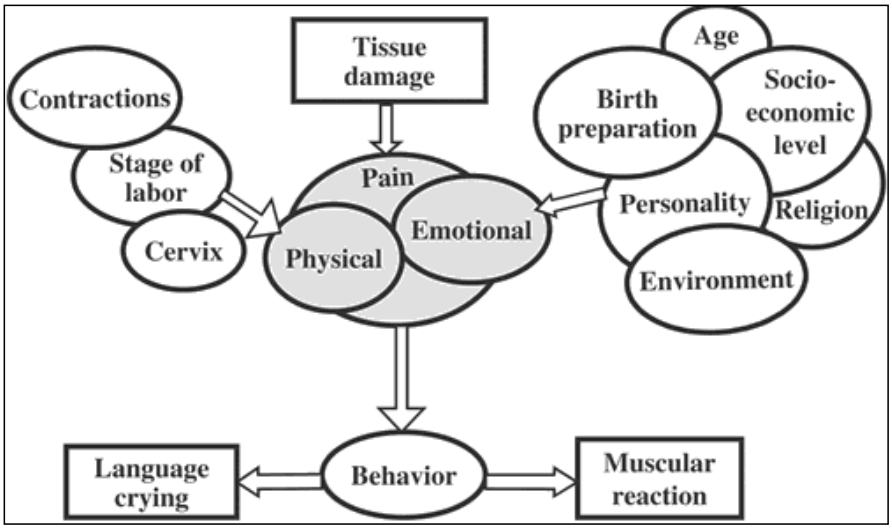

Figure 13-1: the factors that interact to determine the expression of physical pain

In general there are two approaches to the management of pain:

- Using alternative medicine approach: It deals mainly with emotional components of pain.
- Using the conventional medicine approach: deals mainly with physical components of pain.

Ideally the approach to the management of pain should address both components. Therefore women and husbands should be encouraged to attend prenatal classes for relaxation, breathing exercise and to learn about the process of labor and what they should expect.

I. Alternative approach to the management of labor pain:

Complementary and alternative methods applicable to labor pain can be divided into:

- Mind-body interventions: e.g. psychoprophylactic methods: based on removing fear from labor "fearless instead of painless labor". Therefore women preferably with their husbands are encouraged to attend prenatal classes for relaxation, breathing exercise and to learn about the process of labor e.g. the stages of labor and how to behave and cope with each stage.
- Alternative system of medical practice: e.g. Acupuncture technique.
- Alternative medicine: include herbal and aromatherapy.

In term of evidence based evaluation none of those methods are effective in relieving labor pain. They may however have benefit during the early phase of cervical dilatation. However when women enter the active phase of dilatation or during the delivery itself, there is usually a need for additional conventional analgesics.

II. Conventional approach to the management of labor pain:

1. Systemic approach with pharmacologic agents: either parenteral or inhalation.
2. Regional techniques (neuraxial (i.e. local anesthetics placed around the nerves of the central nervous system):

⇒ Systemic approach to management of pain in labor:

The systemic routes are useful for patients who prefer less invasive techniques, or in whom regional techniques are contraindicated, or not available.

Systemic administration of pharmacologic agents for management of pain can be through either intravenous, intramuscular, or inhalation routes.

- The most popular systemic agents are shown in table 13-1. it include: Opioids (e.g. morphine, fentanyl, meperidine) or
- Mixed opioid agonists-antagonists (e.g. pentazocine).
- Non-opioid agents are promethazine, Pentobarbital, and Diazepam. The antihistamines e.g. promethazine are often administered in combination with an opioid to potentiate analgesia and decrease side effects, such as nausea and vomiting.
- Inhalation agents: The most common inhalation is "Entonox" which contain oxygen and nitrous oxide in equal mix of 50% each. The patient self-administrates the anesthetic gas using a hand-held face mask. The safety of this technique is due to the fact that the parturient will be unable to hold the mask if she becomes too drowsy, and thus will cease to inhale the anesthetic.

	Dose	Onset	Duration	Comments
Opioid				
Meperidine	25-50 mg IV	5 min IV	2-3 hr	Active metabolite is normeperidine a potent respiratory depressant;neonatal effect most likely if delivery occurs between 1 and 4 hr after administration
	50 -100 mg IM	40 min IM		
Morphine	2-5 mg IV	3-5 min IV	3-4 hr	Infrequent use during labor; greater respiratory depression in neonate than meperidine
	5-10 mg IM	20 -40 min IM		
Fentanyl	25-50 mcg IV	1-3 min IV	30-60 min IV	Short-acting, potent respiratory depressant; best used by PCA
	100 mcg IM	7-10 min IM	1-2 hr IM	
Mixed opioid agonists-antagonists				
Pentazocine (Talwin)	20-40 mg IV/IM	2-3 min IV	2-3 hr	Agonist/antagonist; ceiling of respiratory depression; dysphoria
		5-20 min IM		
Non-opioid				
Promethazine (Phenergan)	25-75 mg IV/IM	10-20 min	3-4 hr	Commonly used with opioids to mitigate nausea & vomiting; may produce hypotension
Pentobarbital	100-200 mg	30-60 min	3-6 hr	Hypnotic; used only in early

(Nembutal)	PO/IM			or prodromal labor
Diazepam (Valium)	2-5 mg IV	5 min	1-2 hr IV	Sedation and anxiolysis for vaginal delivery; potent amnestic; rapid onset/offset; prolonged half-life; used for eclamptic seizures
	10 mg IM	3-4 hr IM		

Table 13-1: Common Systemic analgesics used in labor

⇒**Regional approach or techniques (neuraxial analgesia):** It include:

- Epidurals.
- Spinals.
- Combined spinal-epidurals (CSE).
- Local injection as pudendal and paracervical nerve block, which are usually performed for specific indications. Those two methods have the advantages that it is performed by the obstetrical provider, easy to learn and have low rate of complications. The drugs used for local injection anesthesia are shown in table 13-2.
- Lumber sympathetic block: it is not commonly used. It relieves pain in the first stage labor (not in the second stage) by interrupting visceral afferents from the uterus and cervix, which join the sympathetic chain at L2 and L3. Requires two injections, does not provide analgesia for the second stage of labor.

Agent	Onset in minutes	Duration	Maximum dose (mg/kg)
Bupivacaine	5 (0.25%)	120-240	2
Lidocaine	<2	30-60	5
Chloroprocaine	6-12 (1, 2 percent)	30-60	10

Table 13-2: drugs used for local injection anesthesia

Pudendal block (Figure 13-1):

- **Indications:** the primary indications are to alleviate pain induced by minor surgical procedures (e.g. episiotomy) or intervention involving the perineum such as applying low forceps and sometimes-ventous delivery. Sometimes it may be applied to alleviate pain induced by vaginal and perineal distension during the second stage of labor. It may also be the preferred method in cases with contraindications for

epidural (e.g. patient with a bleeding diathesis) or as a supplement for epidural labor analgesia, which occasionally may have some sacral sparing.

- **The target:** the sensory and motor fibers of the pudendal nerve (sacral nerve roots 2,3, and 4) as it crosses around the ischial spine. At this site about 10 cc of 1% lidocaine is injected (Figure 13-2).
- **Complications:** are rare and include:
  - Hematoma formation from breaking of a blood vessel.
  - Infection at the site of injection.
  - Ischial region paresthesias or sacral neuropathy may be experienced on the first few days after delivery.
  - Systemic toxicity from inadvertent intravascular administration.

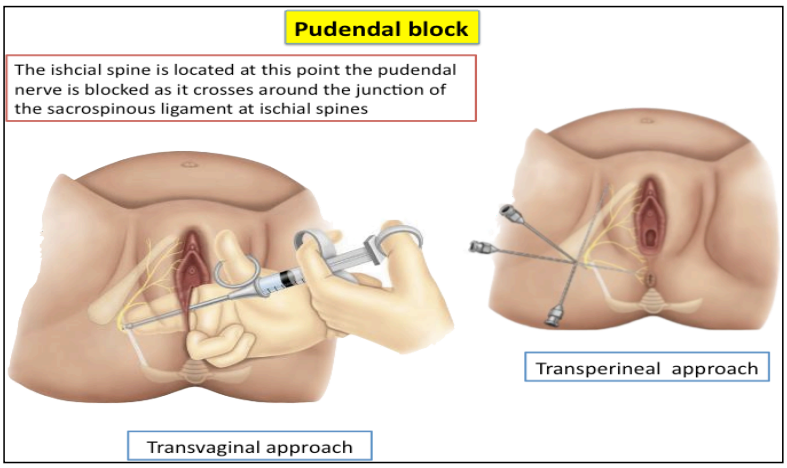

Figure 13-2: Pudenda block

Paracervical block (Figure 13-2):

- **Indications:** This approach is today rarely used in Obstetric. More commonly it is used to provide analgesia during Gynecological procedures such as termination of early pregnancy or missed abortion by dilation and aspiration.
- **The target:** It interrupts the visceral sensory fibers of the lower uterus, cervix, and upper vagina (T10-L1) as they pass through the uterovaginal plexus (Frankenhauser's plexus) on each side of the

cervix, but does not affect the motor pathways. Therefore, the patient can ambulate during labor.

- **Complications:** It is now rarely used because alternative methods are already available in addition to its potential side effects which include:
  - Post-block fetal bradycardia: typically occurs 2 to 10 minutes after infiltration. It is usually transient, but can last as long as 40 minutes.
  - Systemic toxicity after intravascular administration: causing excessive sedation, generalized convulsions, and cardiovascular collapse.
  - Lower extremity paresthesias have been reported in up to 7 percent of cases
  - Vaginal/broad ligament hematoma or infection in 0.4 percent of cases. Allergic reactions are rare with local anesthetics.

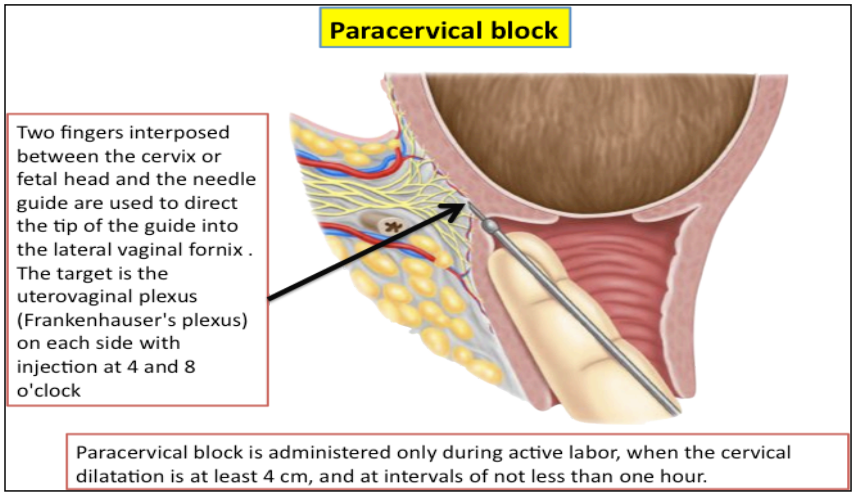

Figure 13-3: Paracervical block

Regional Techniques (Epidural, Spinal):

Epidural and spinal (intrathecal) techniques are the most effective means of providing pain relief in labor.

Advantages of epidural and spinal anesthesia:

In comparison to systemic agents, regional analgesia has the following advantages:

- Provide effective pain relief (for 90-95% of women).
- Provide pain relief for operative procedures such as forceps, episiotomy repair, or even cesarean section.
- Mothers can remain cooperative, clear-headed, think and converse normally. They are also able to rest; even sleep for few hours while the cervix continues to dilate. This is particularly important if prolonged labor is anticipated as with primigravidas or in occipito-posterior position.
- Systemic side effects of narcotics are reduced since it is given via the epidural route rather than I.V..
- Lower the blood pressure: While the "hypotension" induced may causes some problems (see later) but it becomes useful and effective in the management of hypertensive women e.g. with pre-eclampsia.

Drugs used for epidural and spinal techniques: The various classes of analgesics used for epidural and spinal block include local anesthetics, opoids, adrenerginc agents and cholinergic agents (table 13-3).

Agents	Action
Local anesthetics	Inhibit neural conduction by reversibly blocking conductance in axonal sodium channels
Opioids	Reversibly binding to opioid receptors in the dorsal horn of the spinal cord
Alpha-2 adrenergic agents	Interact with alpha-2 adrenergic receptors in the spinal cord
Cholinergic agonists	Increases the concentration of acetylcholine proximate to muscarinic and nicotinic receptors in the superficial layers of the dorsal horn of the spinal cord.

Table 13-3: Drugs used in regional spinal and epidural analgesia and its mechanism of action

Epidural Vs. Spinal "intrathecal" routes (Figure 13-4):

- The onset of action: in the epidural the onset of action is delayed compared to the spinal approach. This is because with epidural the administered analgesic drugs must first diffuse through the dura to gain access to the intrathecal space, while in spinal the drugs are deposited directly into the cerebrospinal fluid (CSF).

- The dose of the drugs used: The dose of analgesics required for spinal anesthesia low. This almost eliminates the risk of systemic drug toxicity. Whereas with the epidural route a higher dose of drugs is required because only a fraction of the injected dose crosses the dura into the CSF and much of the drug given via the epidural route is absorbed via the epidural veins and distributed systemically

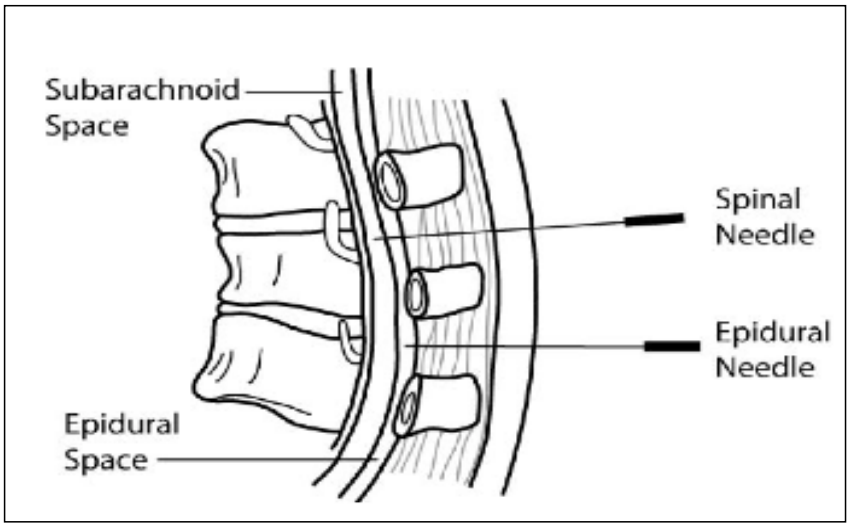

Figure 13-4:In spinal the needle pierce the dura which is not the case in epidural

Techniques of administering epidural anesthesia (Figure 13-5**):**

Cather and needle insertion: For epidural catheterization, the tip of a specialized needle (e.g. 17 or 18 gauge) is positioned within the epidural space. A thin catheter (e.g. 19 or 20 gauge) is then threaded through the needle, and the needle is withdrawn. The catheter is secured to the skin of the patient's back with an adhesive dressing. The catheter may be used to administer additional doses of analgesics on an intermittent and/or continuous basis throughout labor and delivery. In addition, the epidural catheter may be utilized to administer a more concentrated dose of local

anesthetic for instrumental or cesarean delivery. The catheter may also be left in situ postpartum and used to manage pain after delivery.

Maintenance of epidural analgesia: Once the catheter in place the analgesia may be maintained either by intermittent bolus injections, or continuous epidural infusion using a special infusion pump or PCA "Patient-controlled epidural analgesia". In the later case the patient herself is taught to administer a dose of analgesic drug depends on her perception of pain.

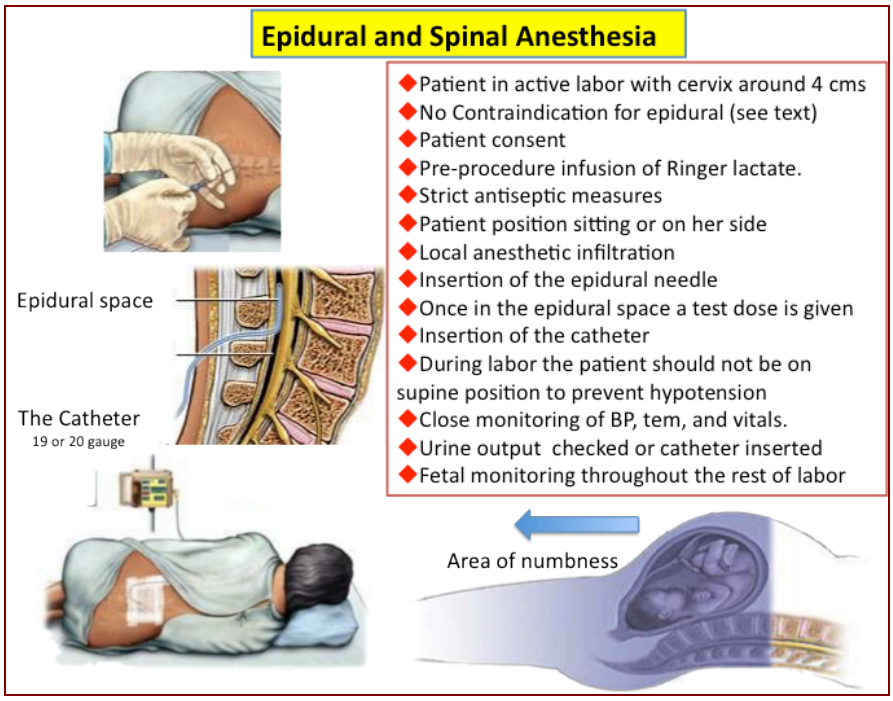

Figure 13-5: Epidural and spinal techniques

Contraindications to spinal and epidural anesthesia:

Absolute

- Patient refusal

- Coagulopathy.
- Patient on therapeutic anticoagulation.
- Skin infection at injection site.
- Raised intracranial pressure.
- Hypovolaemia.

Relative

- Uncooperative patients
- Pre-existing neurological disorders:
- Fixed cardiac output states. E.g. aortic stenosis, hypertrophic obstructive cardiomyopathy (HOCM), mitral stenosis and complete heart block. Patients with these cardiovascular abnormalities are unable to increase their cardiac output in response to the peripheral vasodilatation caused by epidural blockade, and may develop profound circulatory collapse which is very difficult to treat.
- Anatomical abnormalities of vertebral column
- Patients on prophylactic low dose heparin

Complications of spinal and epidural anesthesia:

- **Hypotension:** Hypotension is a common side effect of local anesthetics administered into the neuraxis. It is due to blockage of sympathetic nerves with subsequent dilation of the vascular beds particularly of the lower half of the body and decrease of the venous return.

The hypotension is considered clinically significant if associated with maternal symptoms such as lightheadedness, nausea and/or deterioration of the fetal heart rate, a sign of compromised utero-placental perfusion. Alternatively if the systolic blood pressure drop <100 mm Hg or display a decrease of 25 percent below the preblock reading.

Complications of epidural

Immediate

- Hypotension
- Local anesthetic-induced convulsions*
- Local anesthetic-induced cardiac arrest*

Delayed

- Urinary Retention
- Postdural puncture headache
- Transient backache
- Epidural abscess or meningitis*
- Permanent neurologic deficit

* Very rare

Symptomatic hypotension should be anticipated and prevented. This can be

achieved by loading the patient circulation by intravenous infusion of an isotonic electrolyte solution (e.g., lactated Ringer's solution, 500 to 1,000 mL) prior to the procedure in addition to close monitoring of the blood pressure during initiation of the procedure.

Hypotension during epidural analgesia is treated with additional intravenous boluses of crystalloid solution and/or administration of small intravenous doses of a vasopressor (e.g., ephedrine, in a dosage of 5 to 10 mg).

- **Post dural puncture headache (post-spinal headache)**: often results from unintentional dural puncture with a 16- or 18-gauge epidural needle. This result in leakage of CSF through a dural rent, traction on cranial structures, and cerebral vasodilation, which causes a typical positional headache i.e. headache that is worsened by sitting or standing and relieved by lying down. This complication is now infrequent with the use of fine pencil-point spinal needle and if occurs it usually resolves spontaneously.
  The definitive treatment for persistent postdural puncture headache is an autologous epidural blood patch (i.e., sterile injection of 15 to 20 mL of the patient's fresh blood into the epidural space, preferably at the site of the dural puncture).
- **Failed block**: A failed neuraxial block is defined as inadequate analgesia/anesthesia following an epidural or spinal.
- **Pruritus**: is a common side effect of neuraxial opioid administration. It is more likely to occur after intrathecal rather than epidural techniques. The etiology of neuraxial opioid-induced pruritus is unclear.
- **Nausea and Vomiting**: epidural and spinal local anesthetic may precipitate nausea and vomiting by decreasing blood pressure.
- **Shivering**: Postpartum shivering is not uncommon after normal labor. But the shivering related to neuraxial anesthesia is explained in part, by sympathetic block induced vasodilation, with redistribution of heat from the core to the periphery.

➢ Rare but life-threatening complications:

- **Systemic toxicity**: Systemic toxicity from local anesthetics is related to high plasma drug concentrations. Is more common after epidural than after spinal administration because of the high dose of drug with epidural.

The most common etiology is accidental injection of local anesthetic into a blood vessel. It manifest as CNS toxicity: tinnitus, disorientation, and (ultimately) seizures. Also Cardiovascular toxicity: hypotension, dysrhythmias, and cardiac arrest. It can be avoided by administration of initial small test dose before the full dose is administered.

- **High spinal**: A high spinal refers to more cephalad progression of the level of anesthesia than planned when the neuraxial block was administered. Consequences of high spinal can be very serious if it is not recognized and appropriately managed. It may include:
  - Massive sympathectomy that results in hypotension.
  - Block of the cardiac accelerator fibers (T1 to T4), which inhibits compensatory tachycardia.
  - Hypoperfusion of the brainstem causing respiratory depression and nausea.
  - Dyspnea resulting from anesthesia of the chest.
  - Complete diaphragmatic paralysis if the C3 to C5 roots are blocked.
  - Aspiration of gastric contents due to loss of consciousness and compromise of airway reflexes.

One cause of high spinal is accidental intrathecal injection of a local anesthetic dose intended for the epidural space.

- **Respiratory depression**: due to cephalad spread of opioids to brainstem respiratory centers after neuraxial block is a rare complication in laboring patients. Factors that increase the likelihood of respiratory depression include a large opioid dose, poor opioid lipid solubility (e.g., morphine), and concomitant use of additional sedatives and opioids by other routes.
- **Spinal epidural hematoma**:

Spinal hematoma can occur in any patient, but is more likely in patients with disorders of coagulation and in those receiving anticoagulants. .

- Delayed complications include:

- **Backache**: Some studies have shown increase rate of residual backache among women who had epidural analgesia. More recent studies have confirmed that there is no correlation between epidural labor analgesia and an increased incidence of long-term backache.
- **Urinary retention**: Women who receive neuraxial anesthetic may not be able to sense when their bladder is full and may not be able to void spontaneously. Catheterization is indicated in these women.

- **Infection:** resulting in epidural abscess or meningitis are uncommon complications of neuraxial block.
- **Maternal temperature elevation:**

A rather frequent occurrence following epidural analgesia, its etiology is not clear,

Effect of neuraxial analgesia on the progress and outcome of labor: neuraxial analgesia tends to slow labor and been associated with increased rates of instrumental and cesarean delivery. This however is disputed and most probably the rate of instrumental delivery is not increased provided the obstetrician is aware that it is normal to have a prolonged second stage in patients having neuraxial analgesia. In such cases as long as the fetal condition stable is stable the standard time limit for the stages of labor should not be applied.

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Chapter 14

The Neonate

The transition from the intrauterine to the extrauterine life involves major physiological changes on part of the newborn. In the majority of times the fetus adapt to those changes with no untoward effect. However in some at risk cases particularly in preterm infants the fetus may be subjected to serious traumatic events either physical or metabolic, before or during birth that could have serious consequences. Asphyxia and intracranial hemorrhage are particular risks that threaten the short and long term outcome of preterm infants.

Obstetrician, for both medical and medico legal reasons needs to be aware of risk factors of fetal asphyxia, causes, and prognosis of such adverse events in addition they should be skilled in the principle of neonatal resuscitation.

By the end of this chapter you should be able to:

- **Birth Asphyxia**
  - **Define** Birth Asphyxia:
  - **Describe** Fetal response to asphyxia:
  - **List** causes of Birth asphyxia:
  - **List** the sequelae of fetal asphyxia:
  - **Define** Cerebral palsy
  - **List** the criteria for diagnosis of CP related to birth asphyxia:
- **Intraventricular "IVH" and Periventricular hemorrhage**
  - **Describe** the pathophysiology of PVH/IVH:
  - **List** the grades of PVH-IVH and prognosis:
- **Assessment and Care of the Newborn**
  - **List** the routine care required of the newborn
  - **Memories** the The Apgar Score
  - **Lists** the risk factors for infants at risk for resuscitation
  - **Describe** the the principle of resuscitation of the newborn

Birth Asphyxia

Definition:

Fetal asphyxia may be defined as "a process of progressive hypoxaemia and hypercapnia with a significant metabolic academia" A fetal blood ph of < 7.0 and base deficit of > 12 mmol/l have been suggested as a cut off point for defining pathological fetal academia.

Its incidence varies between 1 and 5% depending on the gestational age and the criteria used for its diagnosis. It is probably much higher in preterm infants.

Fetal response to asphyxia:

> Fetal asphyxia is a metabolic disorder that results from progressive hypoxemia and hypercapnia with a significant metabolic academia. While healthy fetuses can tolerate transient hypoxia, in vulnerable fetuses (e.g. FGR, and preterm ones) asphyxia can be detrimental to them.

It is well recognized that fetuses and newborns have natural tolerance to a significant degree of hypoxia. This ability depends on:

1. Intact chemo and barorecptor's mechanism: therefore in response to hypoxia there is increase in sympathetic discharge and release of noradrenalin in order to secure redistribution of blood flow to cardiac, cerebral and adrenals while diminish flow to the skin, skeletal muscle, liver, kidney and intestine.
2. Utilization of the alternative pathway of anaerobic glycolysis: this require adequate glycogen store. However the glycogen reserve, particularly of the heart is quickly exhausted and produces a state of metabolic acidosis.

Clinically the newborn appears cyanosed (due to vasoconstriction of peripheral circulation) and apnoeic. There is however some muscle tone and heart beat > 100 beat/m. (a state known as Primary Apnea or the old asphyxia livida). Further hypoxia causes hypoxic depression of the myocardium and progressive failure of blood perfusion of critical organs.

Clinically hypotension and bradycardia occur and the color becomes pale (a state known as Terminal Apnea or the old asphyxia pallida).

Causes of Birth asphyxia:

A transient degree of hypoxia is needed for stimulation of the fetal respiratory center. In fact in normal delivery there are two sources which stimulate the respiratory center of healthy fetus: **(1)** changes in blood gases (rising CO2, fall in blood O2 and pH) and **(2)** sensory stimuli brought about by thermal (change in skin temperature) and tactile stimulation.

Furthermore a healthy fetus can tolerate short lasting degree of hypoxia or asphyxia that may occur as a result of airway obstruction with mucus or amniotic fluid, or fetal CNS depression secondary to maternal administration of sedatives or anesthetics.

However if the fetus is already compromised or the hypoxic episode is severe and/or prolonged a state of asphyxia will develop with dire consequences.

The underlying causes of asphyxia are usually described in relation to the timing factor as follow.

- **Antenatal**: if it occurs before the onset of labor. This includes any condition associated with uteroplacental insufficiency and fetal growth restriction e.g. PET.
- **Intrapartum**: It includes causes of acute interruption of umbilical blood flow such as with cord prolapse, premature placental separation or ruptured vasa previa. Also prolonged hypoxic labor with recurrent intermittent episodes of hypoxia.
- **Postnatal**: if it occurs after the birth has been completed. It include delay or failure in the execution of proper resuscitation e.g. due to faulty equipments, or certain fetal congenital abnormalities such as diaphragmatic hernia.

The term **perinatal asphyxia** is used when the timing is uncertain.

Sequelae of fetal asphyxia:

Fetal asphyxia can have a wide spread organ injury (Table 14 -1). If the infant survives the immediate insult, the major concern is permanent central

System	*Manifestations*
Central Nervous System	Cerebral edema, seizures, and hemorrhage
Cardiac	Papillary muscle necrosis, transient tricuspid insufficiency, cardiogenic shock
Pulmonary	Aspiration syndromes (meconium, clear fluid), acquired surfactant deficiency, persistent fetal circulation
Renal	Acute tubular necrosis
Adrenal	Hemorrhage with adrenal insufficiency
Hepatic	Enzyme elevations, liver failure
Gastrointestinal	Necrotizing enterocolitis
Metabolic	Hypoglycemia, hypocalcemia
Hematologic	Clotting disturbances

Table 14-1: Acute Sequelae of Asphyxia

nervous system damage. Of the important and most serious long term sequelae are the condition known as cerebral palsy "CP". The latter condition deserves special consideration not only because of its clinical significance but also because importance of defining the extend of its relation to birth asphyxia.

Cerebral palsy and fetal asphyxia:

CP is defined as "a disorder of posture or movement which is persistent but not necessary unchanging, and caused by non-progressive lesion of the brain, acquired at time of rapid brain development". It may, but not always be accompanied by other neurological impairments such as mental retardation, cortical vision defects or epilepsy. Of the several verities of CP only the spastic quadriplegic and, less commonly, the dyskinetic varieties are the ones associated with acute hypoxic intrapartum events

The incidence of CP has been variably reported between 2-4 cases per 1000 births. This is due to variation in definition and ascertainments of cases.

What is the relation between intrapartum hypoxia and CP?

The relationship between intrapartum hypoxia and later development of CP has important medical and legal aspects. Recent research strongly suggests that the large majority of the neurological pathologies causing cerebral palsy occur as a result of multifactorial and mostly unpreventable reasons during either fetal development (prenatal causes) or the neonatal period (postnatal causes) and not necessary acute intrapartum hypoxia (Table 14-2). The fact is that no more than 8-10 % of cases of cerebral palsy may be associated with birth asphyxia.

Umbilical arterial base deficit less than 12 mmol/l or pH greater than 7.00
Infants with major or multiple congenital or metabolic abnormalities
Central nervous system or systemic infection
Early imaging evidence of longstanding neurological abnormalities for example, ventriculomegaly, porencephaly, multicystic encephalomalacia
Infants with signs of intrauterine growth restriction
Reduced fetal heart rate variability from the onset of labor
Microcephaly at birth (head circumference < third of the percentile)
Major antenatal placental abruption
Extensive chorioamnionitis
Congenital coagulation disorders in the child
Presence of other major antenatal risk factors for cerebral palsy for example, preterm birth at less than 34 weeks' gestation, multiple pregnancy, or autoimmune disease
Presence of major postnatal risk factors for cerebral palsy for example, postnatal encephalitis, prolonged hypotension, or hypoxia due to severe respiratory disease
A sibling with cerebral palsy, especially of the same type

Table 14-2: The presence of any those factors suggest a cause of cerebral palsy other than acute intrapartum hypoxia (*Bakketeig, BMJ 1999)*.

Because of the ability of healthy fetus to tolerance a wide margin of hypoxia and asphyxia, the majorities of newborns who are asphyxiated at birth even to a severe degree go on to develop normally. This however does not mean that beyond a certain degree of hypoxia particularly if combined with ischemia and diminished cerebral perfusion the fetal compensatory mechanisms would be overwhelmed and is not restored even if the perfusion pressure is raised.

However for unhealthy fetuses that is compromised by intrauterine growth restriction due to placental insufficiency may not be able to withstand even the normal hypoxic episodes associated with recurring uterine contractions of normal labor.
Those babies are already affected by chronic hypoxia and may well have sustained some form of damage. Animal studies have shown that induced, prolonged placental insufficiency in the last third of gestation resulting in persistent moderate fetal hypoxemia disrupts myelination and the growth of the cerebellum. Moreover, in mid-gestation, an episode of 12 hours' hypoxemia is enough to cause damage to white matter and neuronal death in the hippocampus, cerebral cortex, and cerebellum.

Prediction of CP and "Neonatal Encephalopathy": The ability to predict which fetuses are likely to develop long term CNS disability has both medical as well medico legal importance The currently available tests for antenatal assessment of fetal wellbeing as well as intrapartum fetal monitoring tests were shown in several studies to be inadequate as predictors of long term CNS disability. Even after birth most infants with low Apgar score proved to be normal at follow up examination.

"**Neonatal Encephalopathy**" is a combination of features that include difficulty with initiating and maintaining respiration, depression of tone and reflexes, altered level of consciousness, and often seizures during the first week after birth. The development of this condition was shown to be a reliable indicator of later neurological abnormalities. This however can only be applied to term babies since in preterm ones similar clinical signs could occur because of prematurity rather than encephalopathy.

Criteria for diagnosis of CP related to birth asphyxia: It is obvious that for medicolegal purpose cases of CP that may be attributed to birth asphyxia should be based on strict and reliable criteria. In table 14-3, are the criteria that have been agreed upon by several international bodies as essential for defining features of intrapartum hypoxia that may be related to later development of CP (Table 4-3).

Essential criteria
1 Evidence of a metabolic acidosis in intrapartum fetal, umbilical arterial cord, or very early neonatal blood samples (pH <7.00 and base deficit ≥ 12 mmol/l)
2 Early onset of severe or moderate neonatal encephalopathy in infants of ≥ 34 weeks' gestation
3 Cerebral palsy of the spastic quadriplegic or dyskinetic type
Criteria that together suggest intrapartum timing but by themselves are non-specific
4 A sentinel (signal) hypoxic event occurring immediately before or during labor
5 A sudden, rapid, and sustained deterioration of the fetal heart rate pattern usually after the hypoxic sentinel event where the pattern was previously normal
6 Apgar scores of 0-6 for longer than 5 minutes
7 Early evidence of multisystem involvement
8 Early imaging evidence of acute cerebral abnormality

Table 14-3 *the template of evidence required to suggest the occurrence of damaging intrapartum hypoxia sufficient to cause permanent neurological impairment.* Subsequently, the determination whether the hypoxia was acute or chronic require that all the criteria from 4 to 8 should be preset

Intraventricular "IVH" and Periventricular hemorrhage "PVH"

IV and PVH are mostly related to prematurity; nevertheless it still can occur in term fetuses especially in association with trauma and asphyxia.

Pathophysiology of PVH/IVH: The site of PVH /IVH is the subependymal layer within the wall of the lateral ventricles (Figure 1).

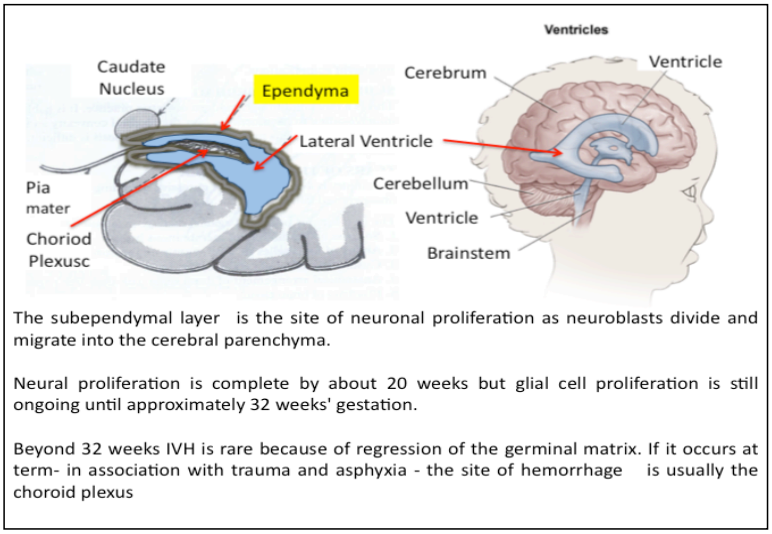

Figure 14-1: The ependymal and subependymal layer within the wall of the lateral ventricles

- A rich network of primitive and fragile single cell-thick matrix capillaries furnishes the blood supply of these metabolically active differentiating cells.
- The blood flow and pressure within these capillaries is regulated by an auto regulatory mechanism that protects such fragile plexus from direct transmission of systemic arterial and/or venous pressure.
- A number of obstetrical or pediatric circumstances can result in significant hypoxia and hypercapnia, both causes profound increase in cerebral blood flow, and could disrupt this mechanism (Table 14-4).
- Thus a state of pressure passive cerebral flow results with the consequent rupture of the fragile capillaries.
- This is more likely to occur in fetuses already under stress (e.g. hypoxic IUGR fetuses) with impaired cerebral autoregulation.

Pathogenesis of IVH

It is primarily associated with prematurity.

It occurs secondary to direct transmission of systemic pressure of blood into the fragile capillary network of the subependymal layer within the wall of the lateral ventricles.

Beyond 32 weeks IVH is rare because of regression of the germinal matrix.

Obstetrical	Pediatrics
Prematurity	Immaturity
Hypoxia in labor	Hypoxia and hypercapnia arising from IRDS
Chronic hypoxia in pregnancy	Coagulation defects
Birth Trauma	

Table 14-4: Some of the causes of IVH and PVH

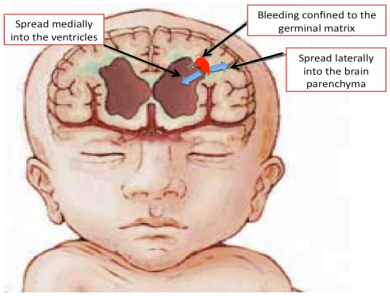

Figure 14-2: Case of intraventriculr hemorrhage, the ventricles are already distended. Bleeding may remains confined in the germinal matrix or progress into the brain parenchyma or medially into the ventricular cavity.

Grades of PVH-IVH:

Intraventricular "IVH" and Periventricular hemorrhage has been graded into four grades of severity. This grading is useful for prognostic reasons when counseling parents and caregivers (Table 14-5). Grades I and II are most common ones. Grade I may be silent and discovered during routine

imagining. Routine ultrasound examination has shown that IVH and PVH occur in about 40% of premature infants (< 1500 g).

Grade	Radiological Appearance – Site of Hemorrhage	Prognosis
Grade I	Subependymal region and or germinal / matrix	Generally good
Grade II	Subependymal hemorrhage with minimal filling (10-40%) of lateral ventricles with no or little ventricular enlargement	Good long term prognosis
Grade III	Subependymal hemorrhage with significant filling of lateral ventricles (>50%) with significant ventricular enlargement	Less favorable prognosis
GradeIV	Intraparenchymal venous hemorrhage	Unfavorable

Table 14-5: Grades of IVH according to imagining examination

The major sequelae of PVH-IVH relate to the destruction of cerebral parenchyma and the development of post-hemorrhagic hydrocephalus. Also following parenchymal hemorrhages, necrotic areas form cysts that can become contiguous with the ventricles (porencephalic cysts).

Cerebral palsy is the primary neurological disorder observed after PVH-IVH. In general the outcome shows inverse relationship with the extent of hemorrhage. Both mortality and morbidity are higher in infants suffering large bleeds, with mortality rates of 50% to 65% and morbidity of 65 to 100 % having been reported for severe bleeds. However with better obstetric and neonatal care, which aims mainly for the prevention of both perinatal and postnatal hypoxia and acidosis, the outcome even in severe cases can be improved.

Assessment and Care of the Newborn

Most infants successfully transfer from intrauterine to extrauterine life without any special assistance. However, about 10 percent of newborns will need some intervention, and 1 percent will require extensive resuscitative measures at birth.

Routine care of the newborn:

After delivery, immediate neonatal care includes drying the infant, clearing the airway of secretions, and providing warmth. Evaluation is generally

based upon the assignment of an Apgar score at one and five minutes of age. The Apgar score include the following sings and each is given values of 0, 1, or 2 and added to compute the total score out of 10.

- Heart rate
- Respiratory effort
- Muscle tone
- Reflex irritability
- Color

About 90 percent of all neonates have Apgar scores of 7 to 10, and generally require no further intervention apart from routine level 1 newborn nursery care.

Infants with lower scores may require further evaluation and intervention including one percent of all neonates who require extensive resuscitative measures at birth

Infants at risk of resuscitation:

One or more of the following risk factors can identify infants who are more likely to require resuscitation:

- Fetal risk factors: Prematurity, postmaturity, congenital anomalies, or multiple gestations. Preterm are special risk group and if possible should be transferred to tertiary care unit before delivery.
- Antepartum risk factors: Placental anomalies (e.g. placenta previa), or presence of either oligohydramnios or polyhydramnios
- Delivery risk factors: Transverse lie or breech presentation, chorioamnionitis, foul-smelling or meconium-stained amniotic fluid, antenatal asphyxia with abnormal fetal heart rate pattern, maternal administration of a narcotic within four hours of birth, or delivery that requires instrumentation (e.g. forceps, vacuum, or cesarean delivery)

However because in the majority of neonates resuscitation is not anticipated it is recommended that all delivery room personnel should have adequate training in neonatal resuscitation including endotracheal intubation and administration of medications. In addition the equipment needed for resuscitation should be available at every delivery area and routinely checked to ensure the equipment is functioning properly (Figure 14-3).

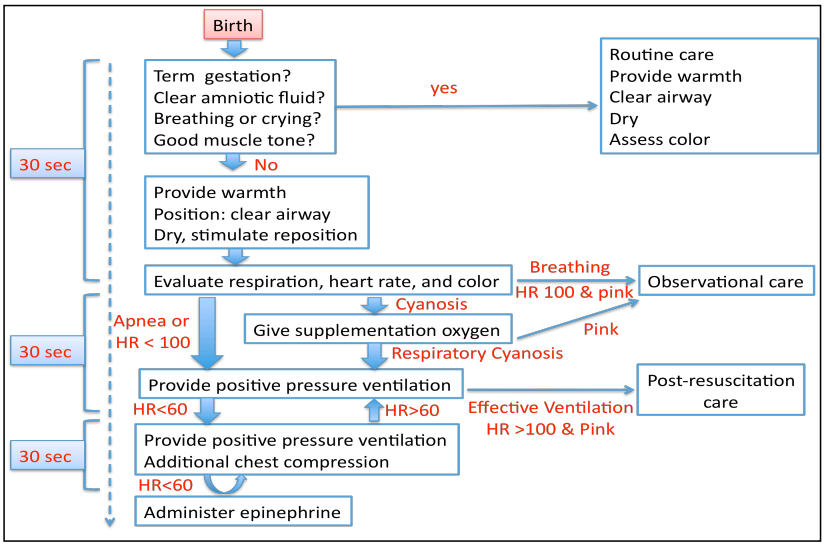

Figure 14-3-: Algorithm for neonatal resuscitation. The American Heart Association, American Academy of Pediatrics, and International Liaison Committee on Resuscitation (ILCOR) guidelines for neonatal resuscitation be followed when providing resuscitation to newborn infants (algorithm 1).

In difficult cases such as extremely premature or malformed infants or in cases that does not show positive respond from resuscitation the parents should be counseled as to the prognosis and benefits of initiation and/or maintenance of resuscitation efforts.

References and Further reading:

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The Normal Puerperium

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As in prenatal and natal care, in "postnatal care" the duty of the medical care provider is to ensure the normal return of the mother's body to the pre-pregnancy normal physiology and to prevent, detect and treat any complications.

By the end of this chapter you should be able to:

- **Define** the puerperium
- **Describe** the physiological changes in each of:
  - **The CVS**
  - **Blood coagulation**
  - **The genital tract: the perineum, uterine involution**
- **Define** the postpartum blues and psychological changes.
- **Describe** the approach for postnatal care: examination, tests, contraception and follow up care.
- **Define** the rules for praying and fasting for postnatal women

Definition: The postpartum period or puerperium is the time during which the mother's altered anatomy, physiology, and biochemistry returns to the non-pregnant state. While its beginning is well defined by the end of the delivery its end is ill defined. Traditionally it is is considered completed by the end of the 6 to 8 weeks of delivery.

Vital sings, Blood and Fluid Changes:

- The cardiac output remains elevated for at least 48 hours postpartum. Most likely this is due to increase in the cardiac stroke volume from increased venous return. Thus the pulse rate remain elevated and drops to normal within the first 24 hours. The temperature may show slight elevation since low-grade fever is not uncommon especially after vaginal birth. There is usually no significant change in the blood pressure nevertheless it should be regularly monitored. An abnormal rise in blood pressur could be a signs of postpartum pre-eclampsia.

- Normally, during the first few postpartum days, hemoglobin concentration and hematocrit fluctuate moderately. The hematocrit rises secondary to diuresis and diminished blood volume. Marked leukocytosis occurs, the leukocyte count sometimes reaches 30,000/L.
- Pregnancy-induced changes in the blood coagulation factors persist for variable periods during the puerperium. Elevation of plasma fibrinogen is maintained at least through the first week.
- Weight Loss: In addition to the loss of about 5 to 6 kg due to uterine evacuation (fetal, placental and amniotic fluid) and blood loss, there is usually a further fluid loss of 2 to 3 kg through diuresis.

The Genital tract and the Breasts:

Uterine involution: begins immediately after delivery of the placenta. Clinically the uterine fundus is located near the umbilicus within 24 hours after delivery, midway between the symphysis pubis and umbilicus within one week postpartum, and is not palpable abdominally by two weeks postpartum. It reaches its normal non-pregnant size by six to eight weeks postpartum. Contractions of the involuting uterus are often painful and may require analgesics. This is more so in multiparous women, and increases with lactation due to secretion of the hormone oxytocin.

The lochia: Is the term that describe the decidual tissue slough together with erythrocytes, epithelial cells and bacteria that are discharged out of the uterus during the few days after delivery. It begins as a rather heavy blood stained loss t for several hours which rapidly diminish in amount and change in character to become reddish brown discharge that lasts for the first three or four days postpartum (lochia rubra). During the next five to 10 days, the lochia becomes more serous and pinkish brown and decreases in amount (lochia serosa). Finally by the 7^{th} to 10^{th} day the lochia decreases in amount and becomes pale yellow-white in color (lochia alba).

However the amount of flow and color of the lochia vary considerably. Fifteen percent of women continue to have lochia 6 weeks or more postpartum.

It is not uncommon that some women experience increase in the amount of

vaginal bleeding about one or two weeks after delivery secondary to the sloughing of the eschar on the placental site. This is the classic time for delayed postpartum hemorrhages to occur

The breasts: After delivery the breasts begins to secrete colostrum, a deep lemon-yellow colored liquid which is already formed in the breasts, but released by the newborn suckling of the breasts. The process of lactation begins as an endocrine process and switches to an autocrine process one. The removal of milk from the breast stimulates more milk production. Over the first five to seven days the colostrum matures to proper milk that contains all necessary nutrients in the neonatal period. However the breast milk continues to change throughout the period of breastfeeding to meet the changing demands of the baby.

The postpartum blues: It is not uncommon for mothers to exhibit some changes in ther moods in the first few days after delivery. Commonly known as "postpartum blues" which is a self-limiting condition. Numbers of factors may be responsible for these changes including worries, deprivation of sleep, exhaustion and others. Symptoms of postpartum blues are mild depressive , tearfulness (often for no discernible reason), anxiety, irritability, mood lability, increased sensitivity and fatigue. The blues typically peak 4 to 5 days after delivery, can last hours to days, and usually resolve by the 10^{th} postnatal day.

Approach to postpartum care:

As described before the postpartum period is a the perido during which the maternal body systems returns to its normal physiological and anatomical shape. It is should also be a happy and enjoyable time with the arrival of a new family member. The health care provider should appreciate this aspect, when dealing with normal cases. **His/her duty is simply to monitor the "normal" changes of the puerperium and ensure that the mother does not develop any of the puerperal complications.**

- General measures: After normal delivery postpartum recovery is usually rapid. Full ambulation is encouraged as soon as possible and regular diet may be offered as soon as the patient requests food. Showers are encouraged, but vaginal douching is prohibited during the early postpartum period.

- Examination: During the first hour after delivery, blood pressure and pulse should be taken every 15 minutes, or more frequently if indicated. The amount of vaginal bleeding is monitored, and the uterine fundus should be palpated to ensure that it is well contracted.

Subsequently routine observation of vital sings, general wellbeing to ensure that the patient is regaining her normal physiological function and not experiencing excessive bleeding can be applied

- Perineal care: An ice bag applied to the perineum help to reduce edema and discomfort during the first several hours after episiotomy repair. This is becomes more important if there is perineal tear or excessive edema. After about 24 hours moist heat as provided with warm sitz baths can be used to reduce local discomfort. The patient should be instructed to cleanse the vulva from anterior to posterior (vulva toward anus).

Analgesic drugs may be offered for pain as necessary but with some care as to the dose, and type of drug in nursing mothers, because most drugs are secreted in breast milk.

- Bladder care: The puerperal bladder has an increased capacity and decreased senstivity to to increase in intravesical pressure. Over-distention, incomplete emptying, and excessive residual urine are common.

Regional anesthesia (spinal or epidural) delays ambulation and also can delay spontaneous urination. Catheterization is recommended if significant urine output is not achieved by 12 hours and a distended bladder is palapable .

Hemorrhoids: not uncommon compalin and should be managed by maintaining appropriate diet, if necessary local medications, good bowel function and and warm sitz baths.

- Routine tests and investigations:

Before discharge from hospital the following investigations should be checked and undertaken if it has not been undertaken before.

- A hemoglobin test:
- Serum IgG for Rubella antibodies: Seronegative women should be immunized against rubella before discharge.
- Serum hepatitis B antibodies should be checked. If the results are positive the newborn should receive vaccination and anti-hepatitis immunoglobulin.
- Women who has Rh-negative blood, not sensitized, and has an infant with Rh-positive blood, should be given Rho(D) immune globulin 300 µg within 72 hours of delivery to prevent sensitization.

- Breast Care:

Breast-feeding is generally encouraged, except in very few occasions if there are contraindications.

Advice on breast-feeding should be given including nipple care, cases with inverted or retracted nipples...etc (see chapter maternal physiology).

If the mother is not going to breast-feed, lactation can be suppressed by firmly supporting the breasts, because gravity stimulates the let-down reflex and encourages milk flow and some restriction of oral fluid intake for few days should also help in reducing milk formation within 3 to 5 days.

- Contraception:

The issue of contraception and family planning should have been discussed in the prenatal clinic. However before the patient is discharged from hospital she should be advised as to the different choices of contraception.

In mothers who are not breast-feeding, ovulation begins after 6 to 8 weeks. But ovulation and conception as early as 2 weeks postpartum has been recorded. In breast-feeding mothers ovulation tends to be delayed up to 10 to 12 weeks postpartum. The frequency of breast-feeding, the duration of feeds, and the proportions of supplemental feeds influence the period of of anovulation.

- Nutrition, supplementation and postnatal exercise:

Advice on nutrition and requirements for vitamin and calcium supplementation should be discussed with the mother before discharge.

Postnatal aerobic exercise and perineal muscle exercise should be part of the routine discussion and should best be provided in reading leaflets before discharge.

Discharge and postnatal follow up:
The time of discharge varies according to hospital policy. If a patient has adequate support at home (i.e., help with housekeeping and meal preparation), there is little value in an extended hospital stay, provided the mother is adequately educated about infant care and feeding and in the identification of serious signs in either the infant or herself.
Physical activity, including walking up and down stairs, lifting moderately heavy objects, riding in a car, and performing muscle-toning exercises, can be resumed without delay if the delivery has been uncomplicated.
Sexual activity may be resumed when the perineum is comfortable and when bleeding has diminished. The desire and willingness to resume sexual activity in the puerperium varies greatly among women, depending on many physical and psychological factors. tturn of libido.
Follow up appointment are usually arranged after six weeks. Special cases e.g. diabetic patients, hypertensive… may require early appointment.
At the 6-week visit questions regarding depression, energy, sexuality, contraception, and future pregnancies should be addressed

Prayer and Fasting In the Puerperium:
A woman bleeding after child delivery is, like the menstruating woman, in a state of *nifās* and is not allowed to fast. However the maximum

period allowed for post-natal bleeding that prevent fasting ranges between 40 to 60 days. At the end of this period the patient is considered as Mustah□ādha (menstrual dysfunction bleeding rather than puerperal bleeding) which means that she must clean herself by taking *ghusl (washing)* and must perform *s□alāh (prayer)* and keep fast.

Occasionally a woman may have a shorter puerperium than the maximum allowed (for example if she had hysterectomy). She then must fast after taking *ghusl* once the bleeding stops. If she bleeds again she abstain from observing those religious duties until the bleeding subside.

Chapter 16

Abnormal labor and Shoulder Dystocia

Difficult labor can be a very damaging experience. Not only because of the increased rate of maternal and fetal morbidity - sometimes even mortality- but also the experience of a traumatic delivery can be devastating often with an adverse impact on the whole family.

Therefore the primary duty of the medical staff who looks after laboring women is to ensure that their labor is progressing normally and delivery is accomplished with no or minimal degree of morbidity to the mother and her newborn. A delay in the diagnosis of abnormal labor increases the rate of both short and long term maternal and fetal morbidity and if neglected may well bring mortality.

By the end of this chapter you should be able to:

- **Define:** the terms: labor Dystocia, Prolonged and Obstructed labor
- **Recognize** the potential complications of abnormal or prolonged labor.
- **List the principle causes of abnormal labor:** the Force, the Passage and the Passenger (CPD)
- List the **risk factors of abnormal labor:**
- Describe the types of **of abnormal labor and the role of the** "Partogram" in its early diagnosis.
- **Describe the types of abnormal labor in each of the first and second stages and the options of management:**
  - **First Stage abnormalities:**
    - Latent phase disorder: Prolonged latent phase
    - Active phase disorder: slow or arrest of dilatation of cervix in the active phase.
  - **Second stage abnormalities:**
    - Failure or arrest of head descends in the second stage.

    Possible causes and management in each case
  - **List** the causes of obstructed labor:
  - **Describe** the symptoms and for the diagnosis of obstructed labor.
  - **Describe** the risk factors, clinical features for ruptured uterus
  - **Describe** the principle of management of rupture uterus
  - **Shoulder dystocia:** Anticipation, principle of management

- **<u>Dystocia of labor</u>:** means abnormal or difficult labor. Sometime the term is used to describe a prolonged or slow progressing labor. But it can also

occur as an acute complication during labor e.g. shoulder dystocia (see below)

- **Prolonged labor:** This is a retrospective diagnosis in which the duration of labor from onset of regular, rhythmical painful contractions accompanied by cervical dilation is longer than 24 hours (table 16-1). The term dystocia of labor is also used to describe prolonged labor which often a difficult one.

- **Obstructed labor**: This term is used to describe failure of descent of the fetal presenting part into the pelvis despite adequate strong uterine contractions. Obstruction of labor may be due to an insurmountable barrier that prevent the descent of the presenting part descent or abnormality of the presenting part itself (e.g. hydrocephalus or shoulder presentation). Obstruction usually occurs at the pelvic brim, but occasionally it may occur in the cavity or at the outlet of the pelvis.

Parameters	**Nulliparous**		**Multiparous**	
	Mean	Mean+2SD	Mean	Mean+2SD
Total duration of labor (hours)	10.7	25	6.2 h	19.5
First Stage (hours)	9.7	24	8.0	18.0
Latent phase (hours)	6.4	20	4.8 h	13.6
Second Stage (minutes	33.0 m	117.0 m	8.5 m	46.5 m
Rate of cervical dilatation andMean -2 SD “Cm /hour:	3.0 cm/h	1.2 cm/h	5.7 cm	1.5 cm

Table 16-1: Mean and SD for labor and cervical dilatation.

Complications of prolonged labor and/or labor dystocia:

Prolonged labor is associated with increased rates of maternal and fetal distress, operative delivery and infection (both to the mother and baby) due to operative intervention and repeated vaginal examination. In addition it increases the rate of both physical and psychological complications in the postpartum period.

On the long term the memories of a traumatic and/or prolonged labor may put the woman off getting pregnant again which can be responsible for adverse family and marital relationship.

Causes of abnormal labor (dystocia):

Abnormal labor could be due to defect in one or more of the three elements of labor:

- Powers: poor or uncoordinated (dysfunctional) uterine action
- Passenger: fetal head too large or the position of the head is abnormal (e.g. occipito-posterior)
- Passage: Contracted pelvis or obstruction by pelvic deformity or tumor.

However there is often interaction between the three elements. For example a mild degree of cephalo-pelvic disproportion (CPD) may be the underlying cause of unfavorable fetal head position as "OP". Also in-coordinate or dysfunctional uterine contractions may be secondary to cephalo-pelvic disproportion.

Risk Factors of abnormal labor (dystocia):

Patients at increased risk of developing labor dystocia may exhibit one or more of the following risk factors:

- Maternal factors: short stature, history of pelvic trauma or diseases, previous difficult vaginal delivery and cesarean section.
- Fetal factors: fetal macrosomia especially in diabetic women, fetus in occipito-posterior position, non engaged head in a primigravida, or fetal brow presentation.

Classification of Abnormal Labor:

⇒Prolonged latent phase: The latent phase is said to be prolonged when it lasts longer than 20 hours in a primipara or 14 hours in a multipara (>the mean+2SD).

⇒Abnormalities in the active Phase: There are two types of abnormalities in the active phase:

- Prolonged or protracted active phase: occurs if the rate of cervical dilation is less than the 5th percentile of the normal rate for primipara

and multipara. This mean less than 2 cm/hour for primiparous women and 1.5 cm/hour for multiparous women (table 5-1). The diagnosis is usually suspected after repeated vaginal examination.
This is usually due to inefficient uterine action (the power), which could be primary or secondary to mild undetected CPD.

- Arrest of active phase of labor (secondary arrest of labor): this diagnosis is made if there is cessation of cervical dilation for 2 hours following previously normal rate of cervical dilation. This can be a serious sing and often indicate significant CPD.

⇒Abnormalities in the second stage: Abnormalities in the second stage also include protracted or arrested descent of the fetal head:

- Arrest of descent (failure of descent): is said to occur if there is no change in the fetal head station despite adequate uterine contractions and maternal pushing force.

- A protracted descent: is defined by a rate of head descent less than 1 cm/hour in primiparas and less than 2 cm/hour in multiparas. This diagnosis should prompt an evaluation for cephalo-pelvic disproportion, fetal macrosomia, dysfunctional uterine contractions or a mother who is unable to push properly.

In modern obstetrics units the use of partogram to follow the progress of labor facilitate early diagnosis of abnormal progress in labor from normal pattern of progress (Figure 5-1).

Management of Abnormal Labor:

Management of Labor Dystocia in the latent phase**:** A prolonged latent phase causes exhaustion due to lack of sleep, dehydration and psychological stress. In some cases it is not uncommon the diagnosis of labor was wrongly made. There are a number options for management of protracted (prolonged) latent phase:

• Therapeutic rest: Is usually the primarily option. It can be accomplished using strong sedatives as morphine (Subcutaneous morphine 0.15 mg/kg) or pethidine so that the woman can sleep. A proportion of women will wake up and have already entered the active phase of labor,

while some will go out of labor, which indicates that they were never in true labor.

• Oxytocin and or amniotomy: to accelerate the latent phase. This may be undertaken if there is a strong indication for delivery and the diagnosis of true labor is confirmed. In some cases cervical ripening with prostaglandin E2, or misoprostol may be used to shorten the latent phase.

Management of Labor Dystocia in the Active phase:

Management of protracted Active Phase: the causes of protracted active phase include fetal malposition (e.g. occiput posterior) causing relative cephalopelvic disproportion (CPD), hypotonic uterine contractions, and anesthesia. After evaluation of maternal and fetal condition and exclusion of major CPD the management options are:

- Enhancement of uterine contractions by amniotomy with or without administration of syntocinon infusion.
- Allow further observations for the progress of labor with careful monitoring (continuation of trial of labor) provided the uterine contractions are adequate.
- Cesarean section delivery: If there is major CPD or none of the above options are valid.

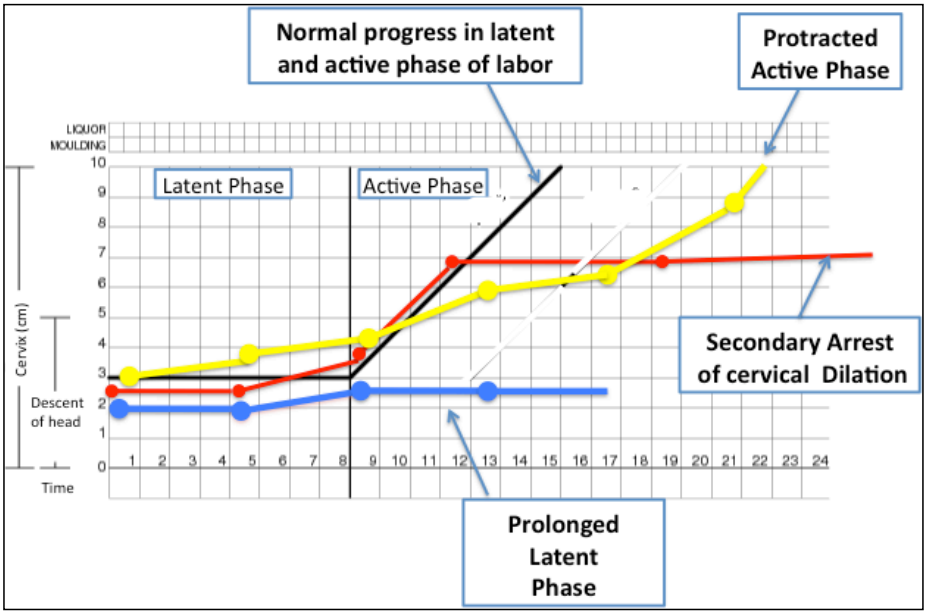


Figure 16-1: The central part of the partogram showing the graphic recording of the dilatation of the cervix as assessed by vaginal examination. The diagram shows different types of labor abnormalities (see text for causes and management)

Management of secondary arrest in the active phase: secondary arrest of cervical dilation is usually more serious. This abnormality is often a sign of significant CPD. In majority of time and after careful evaluation delivery have to be accomplished by cesarean section.

Abnormalities of the Second Stage of Labor:

- A protracted descent: Factors that can cause protracted descent of the fetal head include: Maternal exhaustion, full bladder, ineffective maternal pushing effort, conduction anesthesia, perineal resistance and cephalopelvic disproportion.
- Arrest of descent (failure of descent): This diagnosis is serious and should prompt careful search for significant cephalopelvic disproportion,.

The management of second stage abnormalities require evaluation and management by an experienced obstetrician. The options include either allowing more time with encouragement of patient to push, operative vaginal delivery either forceps or ventouse, or cesarean section delivery.

In all cases of abnormal labor the following elements are important for successful of management:

- Maintaining communication with the patient to explain the extent of difficulty and the plan of management.
- Appropriate analgesia should be administered. In cases of trial of labor epidural analgesia is the ideal.
- Ensure adequate hydration and maintain an empty bladder (catheterisation may be necessary).
- Maintain monitoring of fetal wellbeing.

Stage of Labor	Type of abnormal labor	Examples of Causes	Option of Management
First stage	Prolonged Latent Phase	▪ False labor	▪ Rest and Sedation ▪ Induction of labor if there is strong indication for delivery (e.g. post-term pregnancy)
	Protracted Active Phase (slow dilatation)	➢ Inefficient contractions. ➢ CPD	ARM ± Oxytocin Oxytocin Allow more time for labor
	Arrest of Cervical Dilatation	➢ CPD either absolute or relative (e.g. OP position) ➢ Incoordinate contractions	-Exclude CPD -Stimulation of contractions -Follow up in 1-2 hours if FH are stable -Emergency CS
Second Stage	Arrest of descent of the fetal head	- Macrosomia - Brow Presentation - Hydrocephalus	•CS delivery
	○ A protracted descent of the fetal head	-Small pelvis -Macrosomia -Occipito- posterior	- Require very careful re-evaluation to exclude major CPD before attempting operative vagina delivery. - Emergency Cesarean section
In all cases the obstetrician should ensure Adequate hydration, Analgesia and Communication with the patient			

Table 16-2: Summary of the types of labor abnormalities, its possible causes and principle of management.

Obstructed labor:

Labor is said to be obstructed if despite regular uterine contractions the fetal presenting part does not/or can not descent into the birth canal.

- In some situation obstruction of labor is anticipated as in cases with major cephalopelvic disproportion (too large fetus or too small pelvis or both), hydrocephalic fetus, transverse lie…etc. In such cases vaginal birth should not be allowed to take place and delivery is accomplished by elective cesarean section.
- Historically the term-obstructed labor refers to neglected prolonged labor labor. The mother is often is a state of septicemia, with signs of

impending uterine rupture or even already ruptured uterus. The fetus is often dead.

In modern obstetrics practice obstructed labor should not be allowed to occur. Since with the use of partogram and proper intrapartum care early diagnosis of protracted labor and timely intervention should prevent the development of labor obstruction with its adverse effects on the mother and fetus.

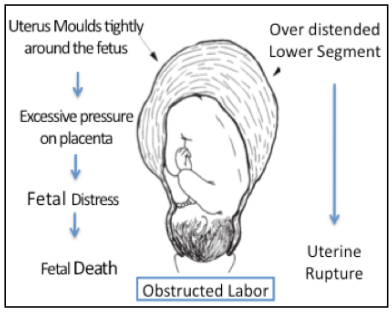


Figure 16-2: Bandl's ring is a depression at junction of the grossly thickened, retracted upper uterine segment with the distended, thinned lower uterine segment.

Unfortunately however cases with the full-blown picture of obstructed labor still occurs. This condition constitute and obstetric emergency and require experienced obstetric care for both its diagnosis and management.

Diagnosis of obstructed labor:

General feature of obstructed labor:

- The mother and fetus are in severe distress. The mother has been in labor for many hours and usually days with very little progress. in obstructed labor with maternal shock (from rupture uterus) and fetal death (from asphyxia).
  - General features: Fever, dehydration and ketoacidosis. Abdominal pain which may be continuous
  - Feature of shock due to uterine rupture and/or sepsis: rapid, weak pulse (100 per minute or more), diminished urinary output, cold clammy skin, pallor, low blood pressure (systolic less than 90 mmHg), rapid respiratory rate (30 per minute or more), anxiousness, confusion, or unconsciousness.

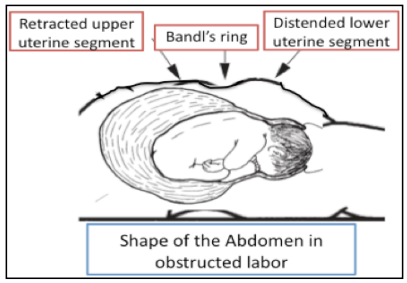


Figure 16-3: Fetal and maternal complications of obstructed labor

Abdominal examination:

- The widest diameter of the fetal head can be felt above the pelvic brim

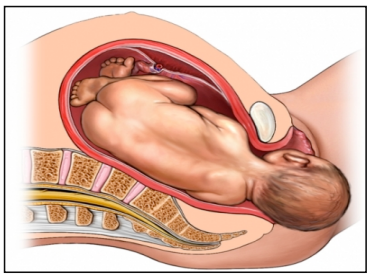
because it is unable to descend.

- In severe cases the fetus is already dead as a result of anoxia.
- The uterus is tonic, difficult to palpate, hard and very tender. A depression called " the Bandl's ring" may be visible and/or palpable abdominally. It is the area of junction between the upper and the distended lower uterine segments indicating obstructed labor (figure 5-2).
- On vaginal examination: a large caput succedaneum is usually felt with severe degree of fetal skull bones molding.

Vaginal examination:

The signs of obstruction, which varies in severity include:

- Foul-smelling meconium draining
- Catheterization will produce concentrated urine which may contain meconium or blood
- Oedema of the vulva, and the cervix (if it is not fully dilated). The vagina is hot and dry because of dehydration especially if the woman has been pushing for a long time
- The fetal head is impacted in the pelvis, has large caput succedaneum and excessively moulded skull bones. Malposition or malpresentation e.g. shoulder, brow or posterior face presentation, may be recognized.



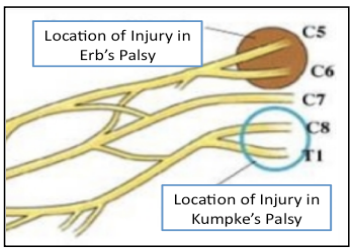


Figure 16-4: The anterior shoulder is impacted behind the pubic bone. Lower picture shows the nerve roots stretched. Fundal pressure cause more impaction.

Uterine rupture: Signs and symptoms of uterine rupture:

- Shock.
- Abdominal distension with free fluid.
- On palpation the abdomen is tender and uterus display abnormal uterine contour
- The fetal parts may be easily palpable and non-engaged.

- Absent fetal movements and fetal heart sounds.

Diagnosis could be more difficult if rupture is incomplete or the tear is small. In such cases the symptoms may initially be very slight, even labor may continue. However uterine rupture may be suspected if the fetus suddenly becomes distressed and the mother's pulse starts rising.

Shoulder Dystocia

Shoulder dystocia: refers to difficult delivery due to shoulder impaction. It is the result of impaction of the anterior shoulder against the pubic symphysis after the delivery of the head.

Frequency: The incidence of this condition varies widely between 0.3% to 1% but rises to 5 to 7% with macrosomic fetuses (birth weight greater than 4500 gm).

The variation in the incidence of shoulder dystocia is due to inconsistency in the diagnosis. Classically the diagnosis is confirmed when standard delivery maneuvers (downward traction) fail to deliver the fetus, and the head to body delivery interval is prolonged ≥ 60 seconds. However the diagnosis is sometimes made if there is difficulty or delay in the delivery of the shoulder of < 30 seconds.

Fetal Perinatal morbidity and mortality: Shoulder dystocia is an obstetric emergency that is associated with serious complications such as:

-Brachial plexus injury is the major risk. It commonly manifests as Erb's palsy due to injury of the fifth and sixth cervical roots. Also Kumpke palsy which involves the lower trunk lesions from nerve roots C7, C8 and T1. Fortunately, most cases are transient, with full recovery in 90 to 95 percent of infants

-Fracture of the clavicle

-Prolonged fetal hypoxia can result in severe neurologic damage and even death.

Fetal morbidity is not always immediately apparent. Some neuropsychiatric dysfunction appears on follow up at 5- to 10 years.

Maternal complications are mainly soft tissue lacerations as a consequence of attempt to deliver the baby e.g. extension of an episiotomy to a fourth-

degree laceration, with disruption of the anal sphincter and rectal mucosa. Other serious complications include hemorrhage secondary to uterine atony, vaginal lacerations, and (rarely) uterine rupture.

Risk factors of shoulder dystocia: It is important to identify women at risk of having shoulder dystocia in order to be prepared for its management:

-Fetal Macarosomia: especially if associated with gestational diabetes and or prolonged pregnancy "post term pregnancy"
-Maternal obesity.
-Previous birth of an infant weighing more than 4,000 g,
-Diabetes mellitus.
-Prolonged second stage of labor
-Instrumental midpelvic delivery.
-Previous shoulder dystocia**.**

Management:

Shoulder dystocia is one of the serious acute obstetric emergencies. It should be anticipated in patients with any one or more of the above risk factors. However in about 50% of the times there are warning sings. Therefore every obstetric unit should have clear protocol on how to deal with shoulder dystocia.

Once shoulder dystocia is diagnosed, a sequence of maneuvers can be used to disimpact the shoulder.

- A senior obstetrician, anesthetist, and pediatrician should immediately be notified. At least two experienced assistants are required to be present.

Throughout all the maneuvers excessive traction on the fetal head should be avoided because it may stretch the brachial plexus causing further damage. Also pushing on the uterine fundus and or maternal expulsive effort should be temporarily stopped.

The following maneuvers are applied in sequence:

⇒ Mild downward traction on the fetal head: The woman's legs are maximally flexed on her abdomen and the maternal buttocks are repositioned downward at the edge of the bed. Gentle downward traction on the fetal head is applied with the aim to deliver the impacted anterior shoulder.

⇒ McRoberts maneuver (Figure 16-5) :

The mother's thighs are flexed onto her abdomen. This increases the inlet diameter as a result of straightening of the lumbosacral lordosis, and removes the sacral prominence as a possible obstruction to delivery (Figure 16-5).

At the same time the accoucheur applies gentle traction to the fetal head.

This maneuver is successful in more than 40 % of cases (over 50 % when combined with supra- pubic pressure).

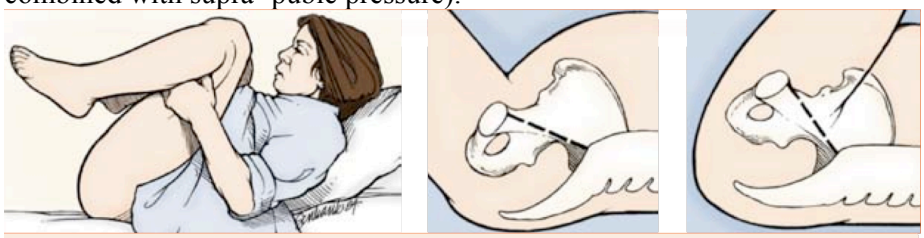


Figure 16-5: McRoberts maneuver, straightens the lumbosacral lordosis, and removes the sacral prominence as a possible obstruction to delivery

⇒ Supra-pubic pressure (Rubin 1):

Pressure is applied to disimpact the shoulder with the fist or heel of the hand just above the symphysis in the midline. The aim is to push the anterior shoulder to an oblique angle under the symphysis (Figure 16-6)

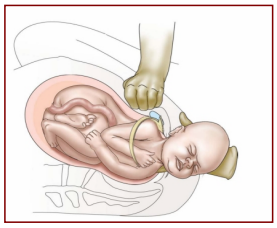


Figure 16-6: Supra-pubic pressure (Rubin 1)

⇒ Rotation of the anterior shoulder (Rubin11 manoevre): The accoucheur inserts the fingers of one hand into the vagina and applies pressure behind the back of the anterior shoulder so that the anterior shoulder is displaced towards the fetal chest.

The aim is to bring the shoulder in the oblique diameter to facilitate delivery. McRoberts maneuver is also applied throughout the procedure (Figure 16-7)

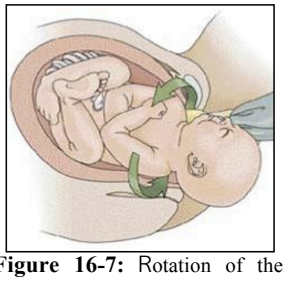


Figure 16-7: Rotation of the anterior shoulder (Rubin11

⇒ Wood's screw maneuver:

The fingers of the hand are inserted behind the posterior shoulder. The aim is to rotated the shoulder 180° forward towards the fetal chest wall (Figure 16-8)

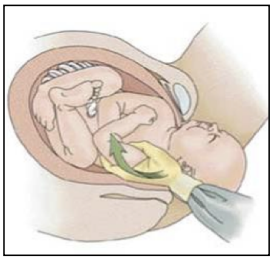


Figure 16-8: Wood's screw maneuver

⇒ Delivery of the posterior arm: The posterior arm is delivered by grasping it along the forearm and sweeping it across the chest and out the vagina. Once the posterior arm is out, the anterior shoulder can usually be displaced downward, or the baby can then be rotated, allowing completion of the delivery (Figure 16-9)

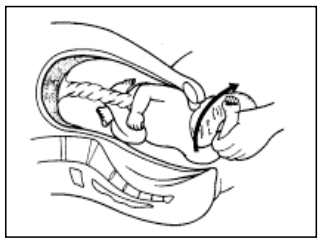


Figure 16-9: Delivery of the posterior arm

⇒ Rotation onto the four:

All fours position (rotating the pregnant woman onto her hands and knees) increases the pelvic diameters allowing better access to the posterior shoulder. This procedure can not be performed with obese patient or if under epidural analgesia.

⇒ Additional maneuvers:

- *Zavanelli manoeuvre:*

This maneuvers involves replacement of the head back into the vagina and proceed to caesarean section

- *Cleidotomy (fracture of fetal clavicle):*

Deliberate fracture of the clavicle is possible and will facilitate delivery by diminishing the rigidity and size of the shoulder girdle. The fracture is usually performed by pressure exerted in a direction away from the lung to avoid puncture.

- *Symphysiotomy:*

Only to be considered by those with experience with this procedure.

Precipitous Labor

Precipitous labor refers to delivery of the infant in less than 3 hours. Precipitous labor and delivery alone is not usually associated with significant maternal and infant morbidity or mortality. However too short labors can endanger the fetus if it happened with out adequate preparation to take care of the newborn. In addition it is often associated with placental abruption or uterine tachysystole both of which are associated with maternal and fetal risks.

Chapter 17

Bleeding in Pregnancy

(Dr Anas Marzouki)

Bleeding during pregnancy is a common occurrence that is very alarming to patients and often present as acute obstetric emergency. The causes, management and prognosis of bleeding in the first half of gestation are rather different from bleeding in the second half. The approach to management begins by evaluation of the patient hemodynamic condition. Based on the clinical presentation a provisional diagnosis can usually be reached which then may have to be confirmed by appropriate investigations mainly ultrasonography.

By the end of this chapter you should be able to:
List the causes and DD of bleeding in early gestation < 20 weeks:
- Implantation bleeding
- Miscarriage
- Ectopic pregnancy
- Molar pregnancy
- Local lesions

List the causes and DD of bleeding in the second half of gestation > 20 weeks
Define what is antepartum hemorrhage
List the causes and DD of antepartum hemorrahge
Describe the types of placenta previa
Describe the different clinical presenation of patients with placenta previa
Outline the management of placenta previa
Define abruptio placena
Describe the types of abruptio placneta
Outline the management of each type of abruptio placenta
Describe the approach to the management of patient with bleeding in the third trimester of pregnancy

Bleeding in the first half of gestation (< 20 weeks)

It is estimated that approximately 20-40% of pregnant women experience vaginal bleeding in the first trimester. It may be any combination of light or

heavy, intermittent or constant, painless or painful. The four major causes of bleeding in early pregnancy are:

1. Ectopic pregnancy: is the least common but the most serious cause therefore it usually the first diagnosis to be excluded.
2. Miscarriage often the threatened type.
3. Implantation bleeding: this condition refers to the slight bleeding, usually in the form of spotting for one or two days anywhere from 6-12 days after conception. (some women may later mistake it as their the last period)
4. Local lesions i.e. cervical, vaginal, or uterine pathology (e.g. polyps, inflammation)

Approach to diagnosis and management:

- Evaluation of bleeding: The general condition of the patient and the vital signs should first be evaluated. Heavy bleeding, with impending shock require basic "ABC" resuscitative measures. If there is associated pain, its site, radiation and severity should be determined.
- History of risk factors for ectopic and/or miscarriage: enquiry should be made for relevant risk factors such as use of intrauterine device, previous ectopic or pelvic surgery. Also history of previous miscarriage or systemic diseases such as diabetes or thrombophilia.
- Physical examination:
  - **General examination**: for general wellbeing and hemodynamic parameters.
  - **Local examination**: should be started by standard abdominal examination looking for signs of tenderness and guarding, which indicate peritoneal irritation (e.g. from ruptured ectopic pregnancy). The uterine fundus may be palpable if the pregnancy is more than 12 weeks (before that the uterus is a pelvic organ). The fetal heartbeat can be checked using handheld Doppler device. If detected it is reassuring of intrauterine pregnancy but its absence does not confirm fetal demise or absence of pregnancy.
  - **Vaginal examination**: begins with inspection for any bleeding. A vaginal speculum is then inserted; any blood clots and tissue are removed and send for pathology. Speculum examination may reveal a source of bleeding that is not related to pregnancy; in such cases, further evaluation

depends upon the nature of the abnormality e.g. laceration, polyp, wart, neoplasm ...etc

The cervix should be noted for signs of dilatation. In some cases products of conception tissues may be seen protruding through the cervix, which can often cause severe pain and neurogenic type of shock. Gentle attempts to remove these tissues relieve the neurogeneic relief of pain.

- **Manual digital examination** is then performed to evaluate the uterine size, adnexal fullness, cervical motion tenderness. Palpation for adnexal masses and/or tenderness should be very carefully undertaken otherwise it may disturb (rupture) an already intact ectopic pregnancy. At the same time a negative bimanual vaginal examination does not exclude the presence of a small-undisturbed ectopic pregnancy.

➢ Investigations:

- Transvaginal ultrasound is the gold standard in the evaluation of bleeding in early pregnancy (first trimester). It can define pregnancy location, viability, number embryos or fetuses. In addition to cervical length and subchorionic hematoma. It can also show adnexal signs suggestive of ectopic pregnancy (e.g. fetal pulsation at ectopic site, adnexal masses or collection).

An empty uterus after 5.5 or 6 weeks amenorrhaea should raise the possibility of ectopic pregnancy. In such cases the findings should be correlated with serum human chorionic gonadotrophin "hCG" concentration. The absence of an intrauterine pregnancy on transvaginal ultrasound examination when the serum hCG concentration is greater than 1000 to 2000 IU/L strongly suggests ectopic pregnancy even in the absence of adnexal mass. If there is doubt about the diagnosis because of low serum hCG level and non-conclusive ultrasound examination repeat serial measurements of serum hCG is indicated.

- Serial measurements of hCG: is indicated in the first six weeks of pregnancy if ultrasonography is non-diagnostic i.e. the site and viability of the pregnancy are not revealed. The results of serial hCG measurements will be one of the following:

- A falling beta-hCG concentration: Indicate a falling pregnancy, which could be either a nonviable intrauterine pregnancy or involuting ectopic pregnancy.

- Appropriately rising hCG levels (either double or 66% increase in 48 hours): This is usually consistent with a viable intrauterine pregnancy. However some ectopic pregnancies also display this pattern.
- Plateaued or slow increase in hCG level: Usually suggest an ectopic pregnancy.
  - Other investigations: Include CBC, blood group and Rh factor. Patients who are Rh(D) negative are given anti-D immunoglobulin to protect against Rh(D) isoimmunization, unless the vaginal bleeding is clearly due to a nonplacental, nonfetal source, such as a vaginal laceration.

The management:

- Miscarriage: the management of miscarriage depends on its type whether threatened, inevitable or incomplete (see chapter…)
- Ectopic pregnancy: can be managed medically or surgically depends on the site, size and B-hCG level and facilities available.

These two topics (miscarriage and ectopic pregnancy are further discussed in the Gynecological volume of this book)

Bleeding after 20 weeks gestation
Antepartum hemorrhage

Definition and Incidence: The term antepartum hemorrhage "APH" refers to uterine bleeding after 20 weeks of gestation and before expulsion of the fetus and is not related to labor or delivery. It complicates about 3% of pregnancies.

Causes of APH: The major causes are:

- Placenta previa (20 percent)
- Abruptio placenta (30 percent)
- The remaining proportion include APH of undetermined origin. This is often attributed to marginal separation of the placenta. In reality it is a kind of mild grade abruptio placena (grade I abruptio placenta). Other less common but important causes are: uterine rupture and bleeding from Vasa previa.

Placenta Previa

⇨**Definition:** Placenta previa refers to placenta, which is implanted, either partly or wholly, in the lower uterine segment.

⇨**Incidence:** The diagnosis of palacenta previa is often based on ultrasound examination. Therefore its frequency is influenced by the week of gestation an ultrasound is made. The earlier the examination the higher is the incidence of placenta previa. For example at 20 weeks the incidence of placenta previa around 5-6 % while at term it is only 0.5%.

This discrepancy is due to phenomena known as "placental migration". The placenta does not actually migrate but its relative relation to the internal os changes as the lower segment grows from 0.5 cm at 20 weeks to about 5 cm at term. Thus a placenta which appears low and close to the internal os in early pregnancy is in fact still within the upper uterine segment since the lower uterine segment has not yet developed.

⇨**Grades of Placenta Previa**:

Depending upon the relation of the placenta to the internal cervical os, four grades of placenta previa have been defined (Figure 17-1):

- Grade I: Low-lying placenta: this term sometimes used in the second trimester to describe an "apparent" placenta previa. While in the third trimester it describe placental edge that lies within 2 to 3 cm of the internal os. Low lying placentas are also associated with an increased risk of bleeding, and possibly other adverse perinatal outcomes.
- Grade II: Placenta previa marginalis: The placenta is adjacent to the internal os, but does not cover it.
- Grade III: Partial placenta previa: The placental edge partially covers the internal cervical os, which must be partly dilated for this to occur
- Grade IV: complete placenta previa: The placenta completely covers the internal os i.e. the internal os is approximately equidistant from the anterior and posterior placental edges.

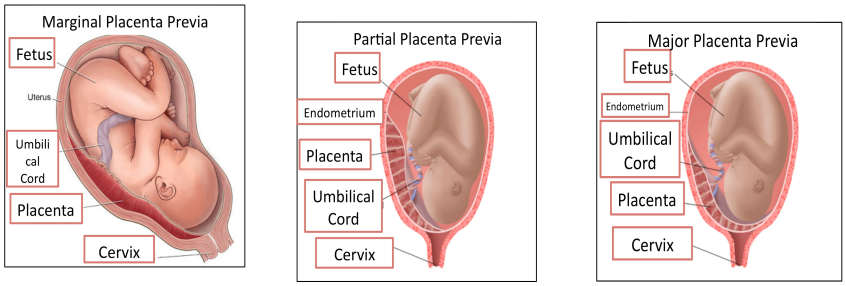


Figure 17-1: Placenta previa, according to the relation to the cervical internal os from left to right: marginal, partial and complete or major PP

⇨Risk factors for placenta previa:

- Increasing number of prior caesarean deliveries (the incidence of placenta previa rises up to 10 percent after four or more CS)
- Increasing parity (the incidence of placenta previa is 0.2 percent in nulliparas versus up to 5 percent in grand multiparas)
- Increasing maternal age (incidence is 0.03 percent in nulliparous women aged 20 to 29 years versus 0.25 percent in nulliparous women ≥40 years of age)
- Multiple gestation (3.9 and 2.8 previas per 1000 live twin and singleton births, respectively)

⇨Pathogenesis of bleeding in placenta previa:

Bleeding in placenta previa is mainly from sinuses in the placental bed that gets exposed due to separation of the placenta secondary to contractions of the upper segment. This means that most of the bleeding is maternal in origin. Placental separation can also be triggered by coitus or manual vaginal examination.

⇨Clinical presentation:

The characteristic clinical presentations of placenta previa include one of the following:

- The typical presentation is by painless vaginal bleeding after 20 weeks of gestation; this occurs in 70 to 80 percent of patients. Characteristically the bleeding is causeless, painless and recurrent.

- In about 10 to 20 percent of cases the women present with uterine contractions associated with bleeding.
- In the remaining proportion, around 10 percent are incidentally detected by ultrasound examination and remain asymptomatic.

⇨**Management of Placenta previa**: the management of palcenta previa depends on the gestational age, and the clinical presentation (Figure 17-2):

➢**Asymptomatic placenta previa**: This entity include cases of placenta previa discovered during a routine ultrasound examination with no history of bleeding depends primarily on the gestational age.

- If the diagnosis is made after 37 weeks the best option would be planned delivery by elective cesarean section. Rarely vaginal deliver may be allowed under close observation (see below).

If the diagnosis is made before 37 weeks the management include:

- Patients with Grade IV place previa are advised to stay in hospital until approximately 37 weeks for delivery by elective cesarean section.
- Patients with less advanced degree of palcenta previa especially if remote from term (e.g. < 30 weeks) may be allowed home provided they understand the implication and have readily access to medical care if they bleed. Mean time they should be advised against exercise, physical activity and coitus. The patient should be instructed to seek immediate medical attention if contractions or vaginal bleeding occur.
- Sonographic re-assessment to determine changes placental location: this is especially important if the diagnosis is made before 28 weeks of gestation since there is chance for "placental migration". Sonographic examination is repeated at approximately 3-4 weeks interval to re-evaluate the location of the placenta.
- In all cases vaginal digital examination should be avoided.

➢**Acute care of symptomatic "bleeding" placenta previa:**

Patient presenting with active bleeding from placenta previa constitute one of the serious obstetrical emergency. The final decision depends on the severity of bleeding and the gestational age.

The following management should be immediately instituted:

- Admission to the labor and delivery unit: Resuscitation measures should be immediately initiated as required (see approach to management of

bleeding in the third trimester below). Subsequent management takes one of the following routes:

- Immediate delivery by cesarean section (active management) or conservative "expectant" management:

o **Active management "immediate delivery by cesarean section":** is indicated in the following situations:

1. If the bleeding is heavy and/or does not stop.
2. If the pregnancy is already beyond 37 weeks with minimal risk of fetal prematurity.

o **Conservative "expectant management":** If the bleeding stop and the pregnancy is less than 37 weeks expectant management can be applied. The elements of expectant management include:

1. Hospitalization: Patient is advised to remain in hospital because the frequency and severity of recurrent bleeding episodes are unpredictable. Hospitalization enables prompt access to transfusion therapy and emergency caesarean delivery if needed. While in hospital cross matched blood should be reserved and kept ready if needed. However in selected cases home management may be acceptable under certain condition.
2. Correction of anemia: this require iron supplementation and in some cases blood transfusion (packed cells).
3. Antenatal corticosteroids: for patients between 24 and 34 weeks of gestation to enhance fetal pulmonary maturity.
4. Rh(D) immune globulin: Rh(D)-negative women should receive Rh(D)-immune globulin with the initial bleeding episode.
5. Fetal surveillance: especially if there is signs of fetal growth restriction.

Criteria of home management

- The patient is able to reach the hospital at any time within very short period (approximately 20 minutes).
- Have an adult companion available 24 hours a day who can immediately transport the woman to the hospital.
- Be reliable and able to maintain bed rest at home, and understand the risks entailed by outpatient management

Termination of expectant management: expectant management should be terminated if there is any of the following: recurrent active bleeding, signs of fetal distress, and spontaneous onset of labor or when the pregnancy reaches 37 weeks.

⇨**Delivery of patient with placenta previa:**

In the majority of cases planned delivery is undertaken at 37 weeks by elective caesarean section.

- Cesarean section in placenta previa: Two to four units of red blood cells should be available for the delivery. Appropriate surgical instruments for performance of a cesarean hysterectomy should also be available since there is at least a 5 to 10 percent risk of placenta accreta. The risk is higher in cases of anterior placenta previa and prior cesarean delivery. Efforts should be made to avoid cutting through the placenta in order to reduce fetal blood loss. The infant should be delivered rapidly and the cord promptly clamped

- Trail of vaginal delivery in placenta previa: In few cases of low lying placenta i.e. more than 20 mm from the internal os, vaginal delivery may be allowed under close observation provided there are no other contraindications to vaginal birth

If there is doubt about the level of the lower placental edge especially in asymptomatic woman a "**double set-up examination**" can be performed. In this technique sterile vaginal digital examination is undertaken in the operating theatre while all preparation are ready for immediate cesarean section. If the examination reveals a low-lying placenta and/or bleeding occurs an immediate cesarean section is undertaken. Alternatively if no placenta tissues are felt beyond the fetal head this indicates a low grade of placenta previa. In such cases vaginal delivery may be allowed under close observation.

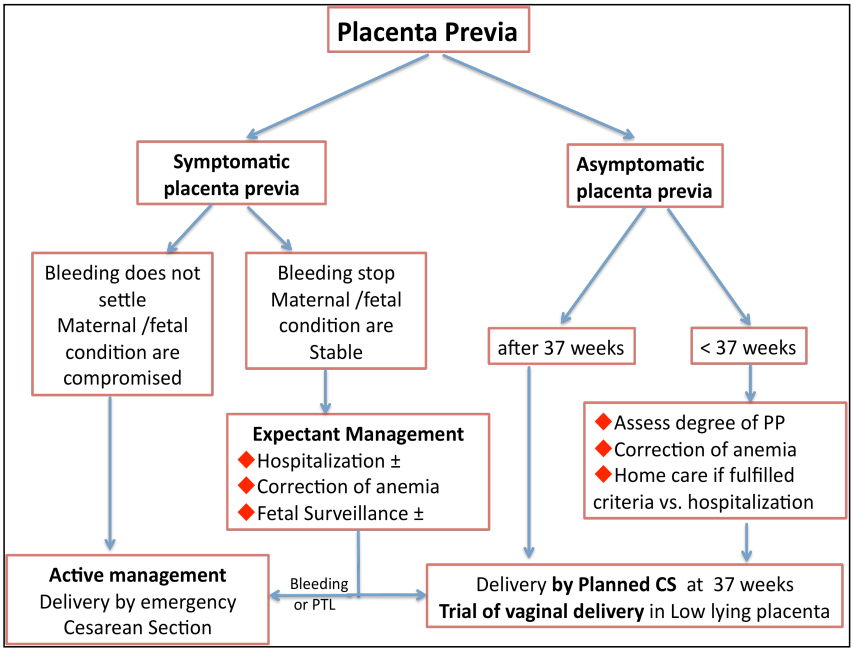


Figure 17-2: Algorithm of management of placenta previa

Outcome of placenta previa:

- Hemorrhage: Placenta previa is not only a recognized cause of antepartum hemorrhage but also for intrapartum, and postpartum hemorrhage. Postpartum hemorrhage is caused by inadequate hemostatic mechanism of the lower segment due to its deficiency in muscle fibers.
- Maternal mortality: about 1%, which is high, compared to normal cases. It can even be higher in developing countries.
- Neonatal morbidity and mortality: The principal cause of neonatal morbidity and mortality is preterm delivery. There is a correlation

between the gestational age at onset of vaginal bleeding and the probability of preterm delivery (i.e. earlier bleeding is associated with a higher risk of prematurity).

Placenta Abruption

⇨**Definition:** Abruptio placenta is defined as decidual hemorrhage leading to the premature separation of the placenta prior to delivery of the fetus.

⇨**Incidence:** Abruptio placenta complicate approximately less than 1% of pregnancies (about 0.8 %). However severe abruption that results in stillbirth occurs in about 1 in 830 deliveries (1.2 per 1000 births).

Risk Factor	Strength	RR/OR
Acute Etiology		
Abdominal trauma/Accidents	+++	5.0 -10.0
Cocaine or other drug abuse	+++	5.0 -10
Polyhydramnios	++	2.0-3.0
Obstetrical/Medical risk factors		
Chronic Hypertension	++	1.8-5.1
PET/pregnancy induced hypertension	++	0.4-4.5
Eclampsia	+++	3.0-5.5
PROM	++	1.8-5.1
Chorioamnionitis		2.0-2.5
Thrombophilia		
Previous ischemic placental disease		
PET	++	1.5
Fetal growth restriction/Small for gestation age infant	++	1.4
Previous abruption	++++	8.0-12.0
Socio demographic/behavioral		
Maternal age	+	1.1-1.3
Parity	+	1.1-1.6
Smoking during pregnancy	++	1.4-2.5

⇨**Risk factors of Abruption placenta:** In most cases abruptio placenta occur with no warning signs. However there are some disorders, that are associated with increased risk of abruption. These include hypertension, pre-eclampsia, previous history of abruption in addition to other risk factors (table 17-1)

⇨**Pathogenesis of Placental abruption:** The immediate cause of the premature placental separation is rupture of maternal vessels in the decidua basalis, where it interfaces with the anchoring villi in the placenta. The exact cause is unknown, however it is possible that there is some degree of vasculopathy (intrinsic abnormalities of the vessels) that leads to its rupture.

In some cases the separation of the placenta from the uterine wall can be the result of a mechanical force (e.g. blunt trauma to the abdomen or rapid uterine decompression as sudden release of hydramnios)

- Sequel of decidual hemorrhage: Decidual hemorrhage and retroplacental accumulation of blood splits the decidua, separate a thin layer of decidua with its placental attachment from the uterus which trigger a cascade of events including: reduced maternal-fetal oxygen and nutrient exchange, increased myometrial contractility due to release of prostaglandin, and risk of membrane rupture.

  The resultant hematom may be small and self-limited, or may continue to dissect through the placental-decidual interface, leading to complete or near complete placental separation.

  Some times it dissects within the uterine muscle wall, leading to ischemia of the uterine muscle fibers. During cesarean section the ischemic uterine muscle fibers appears black, fails to contract a condition known as "Couvelaire uterus ". A "Couvelaire uterus" may fails to contract and requires hysterectomy.

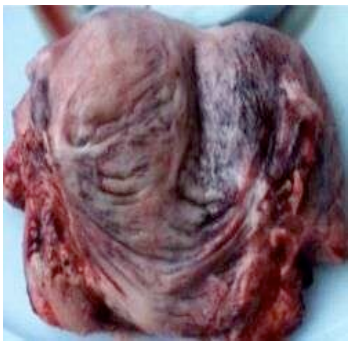


Figure 17-3: Couvelaire uterus

- Systemic consequences of severe placental abruption: The growing retroplacental hematoma under pressure squeezes a great deal of tissue thromboplastin into the circulation over a brief period of time. This generate massive amount of thrombin, resulting in acute disseminated intravascular coagulation (DIC). The clinical consequence is profound systemic bleeding diathesis, due to widespread intravascular fibrin deposition. This result in tissue ischemic injury and development of microangiopathic hemolytic anemia.

⇨Clinical manifestations:

The clinical manifestations of placental abruption depend on variety of factors, including whether the hemorrhage is (1) acute or chronic, (2) concealed or revealed, and (3) mild or severe.

The amount of vaginal bleeding correlates poorly with the degree of placental separation and does not serve as a useful marker of impending fetal risk.

- **Acute revealed placental abruption:** Clinically the patient presents with vaginal bleeding, abdominal and/or back pain, and high frequency, low amplitude uterine contractions. The uterus is usually rigid and tender. The condition of the fetus depends on the degree of placental separation. However there are usually sings of fetal heart distress or may be absent if the fetus is already dead (Figure 17-4).
- **Concealed abruption placenta:** "Concealed" hemorrhage occurs in as many as 10 to 20 percent of abruptions. In these cases, all (complete) or most (incomplete) of the blood is trapped between the fetal membranes and decidua, rather than escaping through the cervix and vagina. The patient clinical picture and fetal condition depends on the degree of placental separation and amount of concealed hemorrhage. In severe degree of completely concealed abruptio placenta the patient is in a state of shock that is out of proportion to the revealed blood loss. The shock in such cases is due to both blood loss and the severe neurogenic shock induced by the enlarging retroplacental hemorrhage. Not uncommonly patient with concealed abruption placenta presents with clinical picture of preterm labor, and no or minimal vaginal bleeding.

It is important that any patient in the second or third trimester who presents with even small amounts of vaginal bleeding, abdominal pain and uterine contractions receive prompt close maternal and fetal evaluation for placental abruption.

- **Chronic abruption**: In those cases patients' presents with relatively light, chronic and recurrent bleeding. Although clinically those patients are stable, the uterus is usually soft and the fetal heart is stable but the recurrence of the bleeding may lead to the development of placental insufficiency with the consequence of fetal growth restriction, oligohydramnios, increase risk of preterm birth and premature rupture of membranes.

  Pathologically, in chronic abruption the placental separation occurs at the periphery of the placenta and is caused by low pressure venous hemorrhage (marginal placental separation)

Presentation in severe placental abruption: In the presence of a severe abruption (≥50 percent placental separation) whether revealed or concealed, both fetal and maternal lives are at risk. There is high risk of acute

disseminated intravascular coagulation (DIC), renal, hepatic and lung damage.

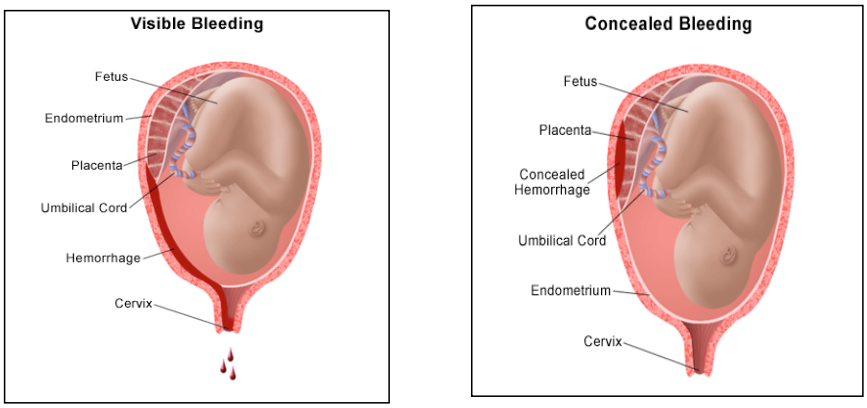


Figure 17-4: Abruptio placenta

⇨**Diagnosis of Placenta Abruption:** The diagnosis of abruption placenta is mainly a clinical diagnosis. The diagnosis of placental abruption should be considered in pregnant women who present with one or more of the following: vaginal bleeding, abdominal pain, preterm labor, or trauma.

- History: may elicit one or more of the risk factors such as hypertension, previous abruption, recent trauma (e.g. a fall or a care accidents)
- Symptoms: the patient will often complain of pain (the severity varies depending on the type and degree of placenta abruption). The pain is almost continuous due to persistent uterine contractions induced by the large amount of local prostaglandin released from the ruptured decidual layer at the site of abruptio.
- Signs: On abdominal obstetric examination the uterus is tender to touch and hard to feel. The fetal presentation is usually normal but the fetal parts are difficult to palpate. The fetal heart is either absent (intrauterine fetal death) or shows features of fetal distress.

➢ Investigations: Ultrasound has low sensitivity for detecting abruption however the presence of sonographic features of abruption has a very high positive predictive value. An important benefit of ultrasound in cases of APH is to exclude placenta previa.

Remember the diagnosis of placenta previa is clinical diagnosis
No time should be wasted awaiting ultrasound

⇨ **Management of Placental abruption:**

Abruptio placenta is an acute obstetric emergency. Patients suspected to have a placental abruption should undergo a rapid initial hemodynamic evaluation.

Subsequent management depends upon the severity of the abruption, the gestational age, and maternal and fetal status (Figure 17-5)

➢ Evaluation of maternal hemodynamic status: should immediately begin (see approach to bleeding in pregnancy below). Two wide-bore intravenous lines (needle gauge 16) should be inserted to secure intravenous access.

- In severe cases, a Foley catheter should be inserted to monitor maternal urine output hourly. The urine output should be maintained at above 30 ml/hour.
- Blood sample is withdrawn for complete blood count, blood type and Rh, coagulation studies (platelets count, fibrinogen level, fibrinogen degradation products, PT and PTT) and cross matching. A low fibrinogen level is the most sensitive indicator of coagulopathy related to abruption
- The extent of blood loss should be evaluated carefully. Blood loss is frequently underestimated since the bleeding may be largely concealed, and the actual loss may be far in excess of what is observed.

Subsequent management depends primarily on whether the fetus is alive or dead, gestational age and maternal status.

It is important to remember that when there is partial placental separation, total abruption may occur suddenly and without warning. Thus, the fetus should be continuously monitored, and preparation should be ready in case urgent operative delivery is required.

➢ **Lives fetus at or near term (>34 weeks):** In this case the delivery should be immediately undertaken. This is usually accomplished by membrane rupture with or without oxytocin administration. The uterus usually contracts vigorously and results in rapid delivery. However cesarean delivery is indicated if the fetal heart

tracing is non-reassuring, there is ongoing major blood loss or other serious maternal complications, or if vaginal delivery is contraindicated.

- **Lives fetus remote from term (< 34 weeks):** In such cases delivery may be delayed provided the fetal well-being are reassuring and there is no evidence of maternal coagulopathy, hypotension, or ongoing major blood loss.
  - Patient should be hospitalized at least for few days after the bleeding subsides and hematological parameters are normal.
  - Fetal assessment with a non-stress test or biophysical profile is performed at least weekly. In addition to serial sonographic estimation of fetal growth since these fetuses are at risk of developing growth restriction.
  - Delivery should be considered by 37 to 38 weeks because of the increased risk of stillbirth.
- **If the fetus is already dead**: When fetal death has occurred, the mode of delivery should be vaginal unless urgent delivery is needed to enable stabilization of the mother or there are obstetrical contraindications to vaginal birth (e.g. previous classical hysterotomy).

Cesarean section in abruptio placenta:

Cesarean section in placenta abruption carries high risk of increased blood loss due to 1) coagulopathy and 2) failure of uterine contraction in cases of severe abruption with extravasation of blood into the myometrium (Couvelaire uterus).

If a cesarean section has to be performed urgently, blood, fresh frozen plasma, platelets, and cryoprecipitate should be available in the operating room and should be administered if there is any evidence of impaired coagulation (e.g. persistent bleeding without clotting from incision and needle sites). In these cases, fresh frozen plasma and cryoprecipitate should be given immediately, without waiting for the results of coagulation studies.

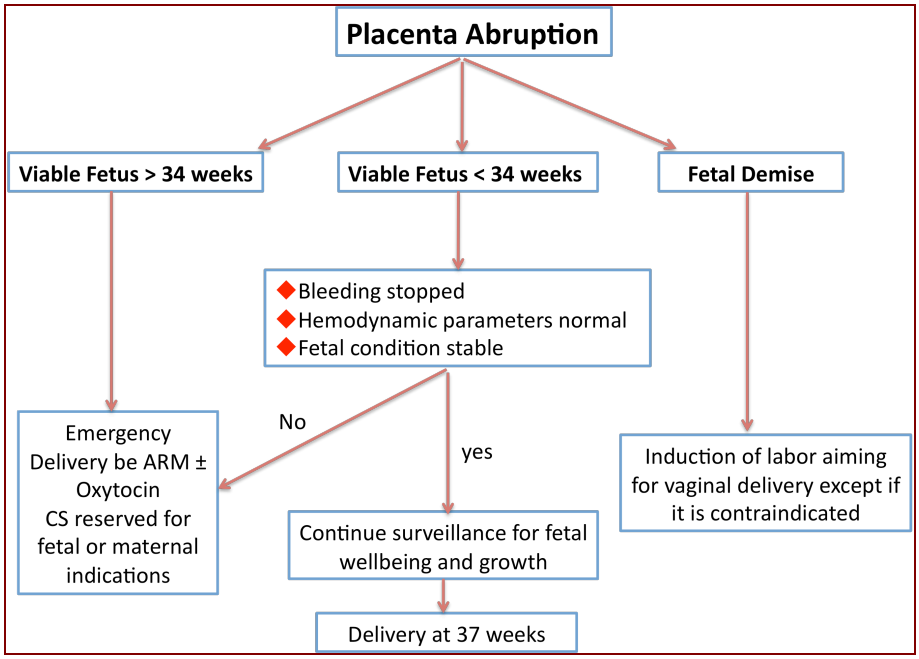


Figure 17-5: Algorithm of management of placenta Abruption

⇨Outcome of Placental abruption:

Pregnancy outcome after placental abruption depends primarily on the degree of placental separation and the gestational age at which the abruption occurs.

➢Maternal mortality and morbidity:

Severe placental abruption carries a significant risk of maternal complications, including hemorrhage, renal failure, hysterectomy, and, rarely, maternal death.

➢Fetal risk: With mild separation, there may be no significant adverse effects. As the degree of placental separation increases, the risks of preterm birth, intrauterine growth restriction, and fetal or neonatal death increases.

Approach to the management of patients with vaginal bleeding in third trimester

Antepartum haemorrhage is an acute emergency. The objectives of management are to stabilise the mother hemodynamic condition, identify the cause of bleeding, evaluate the fetal condition and accordingly apply the appropriate treatment plan. For that purpose a prompt systematic approach should be adopted.

It should be realised that because of the increased blood volume in pregnancy (>= 50% above non pregnant level) pregnant women are able to tolerate a relatively large volume of blood loss before showing clinical signs of shock.

Therefore pregnant women may go through early phase of compensation before the condition deteriorates into secondary hemorrhagic shock. Table 17-2 describe the clinical signs at the two phases of primary and secondary shock. Clinician should be aware of those signs and interfere early to prevent the development of secondary shock with its irreversible consequences.

Important points

- Pregnant women may remain hemodynamically stable until about 25% of their blood volume (approximately 1500 ml) is lost.
- If adequate treatment is not provided rapid decompansation will follow.
- Investigations including hematocrit test are often deceiving.
- Clinical evaluation should be the primary guide to manage a patient with haemorrhage.

Clinical signs	Primary shock		Secondary shock
	Early	**Late**	
Maternal state	Alert and anxious	Confused	Coma
General Appearance	Normal and Worm	Pale and cold	Cyanotic and cold
Blood pressure	Slightly hypotensive	Moderately hypotensive	Markedly hypotensive
Respiratory system	Slightly tachypnea	Tachypnea	Tachypnea and cyanosis
Urinary output	30 to 60 ml/h 0.5 to 1.0 ml/Kg/h	< 30 ml/h < 0.5 mL/Kg/h	Anuria
Effect of volume challenge on:			
Blood pressure	Increased	Slightly increased	No response
Urinary output	Increased	Slightly increased	No response

Table 17-2: Clinical Picture in hemorrhagic shock and expected response to volume replacement. From the American College of Obstetrician and Gynaecologists. Washington, DC: ACOG Educational Bulletin no. 235, April 1997.

Patient evaluation:

- General evaluation for the patient hemodynamic status should be the first step If judged to be unstable (table 17-2) the standard ABCs of resuscitation should be implemented. "A" ensures clear airway, and breathing "B".
- Secure adequate circulation "C" through insertion of two large bore intravenous catheters and infusion of crystalloid fluid replacement should be started.
- At same time blood should be withdrawn for haemoglobin, hematocrit, blood group (including Rh grouping), coagulation studies and cross matching.

Fetal evaluation:

- The gestational age should be verified and accordingly fetal electronic monitoring should be started.

Identification of the cause of bleeding:

- Once the condition is stabilized further actions aims to identify the cause of bleeding based on brief "targeted" history and examination. The cardinal clinical features, which differentiate between the two major causes of antepartum hemorrhage: "placenta previa" and "placental abruption" are described in table 17-3.

  No digital vaginal examination should be performed before excluding the diagnosis of placenta previa by ultrasound examination.
- If placenta previa and placental abruption are excluded, search for local cause should be made by speculum examination followed by digital vaginal examination. Sometimes the bleeding may be due to "**heavy show**" from cervical stretching and effacement, which precede onset of preterm labor.
- Some cases will be labelled as "**antepartum haemorrhage of undetermined cause**" which most probably due to marginal placental separation. Those cases require hospitalisation and observation for few

days after the bleeding settle. Further follow up will depends on gestational age and fetal and maternal condition.

- Further management: Further management of acute antepartum haemorrhage depends on the cause and severity of bleeding, the gestational age as well as other factors (e.g. fetal conditions such as fetal distress or known anomalies and maternal factors such as chronic maternal illness or known diseases that might favour termination of pregnancy). (see specific management of placenta previa and placental abruption above)

	Placenta Previa	***Abruptio Placeenta***
History:	Positive history of "threatened bleeding"	No history of prior bleeding
Symptoms	bleeding is painless except in some cases if there are uterine contractions or PTL	usually associated with severe pain
Signs	Sings proportional to the amount of blood lost	Sings of hemodynamic instability are out of proportion to the amount of blood loss Because bleeding is concealed in addition to the nuerogenic shock
The fetus	Abnormal fetal lie or non-engagement of the presenting part. The fetal heart sounds are usually heard	Fetal heart are non-reassuring or absent. The presenting part is difficult to feel and is deeply engaged
The uterus	The uterus is soft and lax unless there is PTL	Hard, tonic and tender uterus
Ultrasound examination	Confirm the diagnosis of placenta previa	Exclude placenta previa and may show signs of abruption

Table 17-3: Clinical features the differentiate placenta pevia from abruptio placenta

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Chapter 18

Postpartum Complications

Dr Anas Marzouki - Dr Ahmed Merstani

The postpartum period should be an enjoyable, uneventful period. The objective of medical care during this period is to detect and treat any deviation from normal as early as possible. Some complications can be very acute such as postpartum hemorrhage; others can be less drastic but have serious long-term consequences if not promptly treated such as endometritis and psychological disorders. This chapter addresses the most common puerperal complications.

By the end of this chapter you should be able to:

- **Define** the different type of postpartum hemorrhage.
- **List** the causes of each type of postpartum hemorrhage.
- **Outline** the principle of management of primary post partum hemorrhage:
- **Describe** causes and management delayed post partum hemorrhage
- **Define** post partum pyrexia and puerperal fever (endometritis)
- **List** the causes and outline management of puerperal pyrexia
- **Describe** the tissues involved in each of the different degrees of Perineal laceration
- **List the different types of post partum psychological disorders**
- **Describe** the risk factors and clinical presentation and management of venous thromboembolism
- **Describe** the causes of mastitis and principle management .

I. Postpartum hemorrhage "PPH"

Postpartum hemorrhage (PPH) is one of the most serious obstetrical emergencies. It can follow vaginal or cesarean delivery. It is a major cause of maternal morbidity such as shock, renal failure, acute respiratory distress syndrome, coagulopathy, and Sheehan's syndrome (i.e., postpartum hypopituitarism). It is also one of the major causes of maternal mortality particularly in developing and low-income countries.

There are two types of postpartum hemorrhage:

- Early or primary PPH if it occurs within 24 hours of delivery.
- Late or secondary PPH if it occurs 24 hours after delivery up to six

weeks postpartum.

Definition and Incidence: Postpartum hemorrhage is defined as bleeding from the genital tract during or after the third stage of labor of more than 500 ml after vaginal delivery and more than 1000 ml with cesarean section delivery. The estimation is subjective and often liable to underestimation. An alternative definition for PPH that depends on the clinical condition of the patient is "excessive bleeding that makes the patient symptomatic (e.g. lightheadedness, vertigo, syncope) and/or results in signs of hypovolemia (e.g. hypotension, tachycardia, or oliguria).
The incidence of PPH after vaginal delivery ranges between 2 to 4 %. While cesarean delivery is associated with approximately 6 % incidence of PPH. Delayed or secondary postpartum hemorrhage occurs in 1-2% of patients.

Causes of PPH:

- **Uterine atony: (**i.e. lack of effective contraction of the uterus after delivery), is responsible for at least 80 percent of cases of PPH.
  Risk factors for uterine atony include:
  - Uterine Overdistension (e.g. in multiple gestation, polyhydramnios, macrosomia)
  - Uterine infection (chorioamnionitis even subclinical)
  - "Uterine fatigue" after a prolonged labor, common in induced labor
  - Uterine inversion
  - Retained placenta (either a normally attached placenta or placenta accreta).
- **Trauma:** Trauma-related bleeding can be due to lacerations (perineal, vaginal, cervical, uterine), incisions (hysterotomy, episiotomy), or uterine rupture. Lacerations are more common after instrumental delivery.
- **Coagulation defects:** usually acquired and less commonly congenital bleeding diatheses. Acquired causes of coagulation disorder include severe preeclampsia, HELLP syndrome, abruptio placentae, fetal demise, amniotic fluid embolism, and sepsis. Also severe hemorrhage itself may induce a vicious cylce of consumptive coagulopathy.
-

Mangement of Primary PPH:

Once a diagnosis of post partum hemorrhage is made, the management should be prompt and along an organized plan. The objectives are: First to maintain the patient hemodynamic stability and second to identify the cause and stop the bleeding.

⇒The first objective is achieved by applying ABC principles:

A: ensure patent Air Way
B: ensure breathing
C: ensure adequate circulation. Two wide bore (gauge 16) intravenous cannulae should be inserted. At the same time blood is withdrawn for hemoglobin measurements, cross matching of four units of blood, and coagulation profiles study.
Crystalloid solutions (e.g. Saline) should be started immediately until the cross-matched blood arrives.

⇒The second objective i.e. to identify the cause of PPH and stop the bleeding: depends on the circumstances e.g. if bleeding occurs as a result of obvious trauma during cesarean section or operative vagina delivery. However in clinical practice in 80% of cases uterine atony is the cause of PPH.

- **Uterine Atony:** The diagnosis of uterine atony can be confirmed by abdominal palpation if the uterus is found to be atonic and flaccid (or may not be palpable); with no other obvious cause(s) of bleeding. Once the diagnosis is made the management of uterine atony should follow the following sequence of steps:

- External massage of the uterus: should be performed, as the first step and the bladder must be emptied by catheterization.
- Utertonic agents: Oxytocin is the first line and should be used in all cases. In some cases additional agents has to be used (table 5-1).
- Uterine tamponade: It includes measures such as bimanual compression, intrauterine packing. Special uterine tamponade catheters has also been designed for this purpose (e.g. Bakri uterine catheter) (Figures 5-1 and 2)

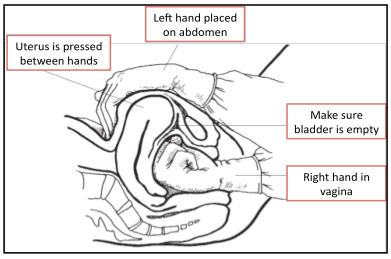

Figure 18-1: Internal bimanual compression of the uterus

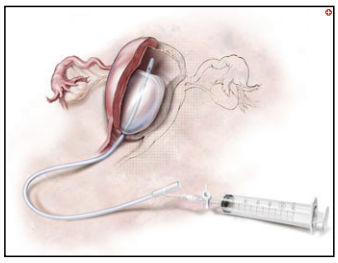

Figure 18-2: Bakri uterine catheter

- Selective arterial embolisation: should be considered in hemodynamically stable patient and if the facilities are available. The technique involves pelvic angiography to visualize the bleeding vessels and placement of Gelfoam (gelatin) pledgets into the vessels for occlusion
- Surgical measures: if the above measures are not successful laparotomy should be performed. The options available include:
    - Haemostatic arterial ligation: several measures have been described. The goal of arterial ligation is to decrease uterine perfusion and subsequent bleeding. Arterial ligation to ensure hemostasis should include the ascending uterine arteries, the utero-ovarian arteries, the infundibulopelvic ligament vessels. Another measure is bilateral hypogastric arteries ligation.
    - Uterine suturing techniques: the principle is to replace multiple haemostatic compression sutures around the uterus e.g. the B-Lynch compression suture (Figure 5-3)

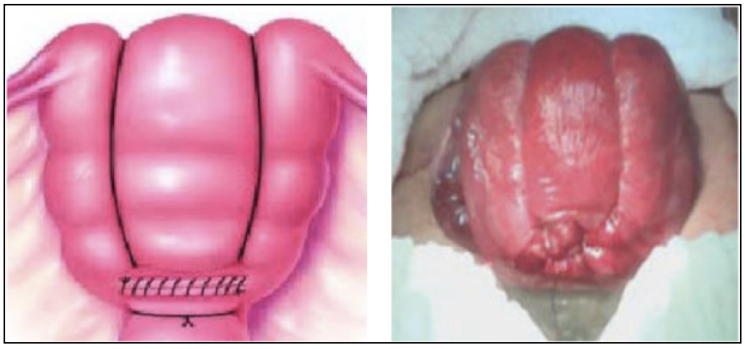

Figure 18-3: On the left side is a diagram of B-Lynch suture in which a large absorbable suture is anchored within the uterine myometrium both anteriorly and posteriorly and passed in a continuous fashion around the external surface of the uterus. When the suture is tied, uterine compression occurs. On the left is the suture as it appear after been tied.

    - Hysterectomy: if the above measures failed hysterectomy should be undertaken with out undue delay.

Pharmacological agents used in PPH	
Oxytocin	40 units in 1 liter of normal saline intravenously or 10 units intramuscularly
Methergine	0.2 mg intramuscularly (including directly into the myometrium) (never intravenously) if no hypertension
Carboprost (15 methyl-PGF2alpha)	250 mcg intramuscularly (including directly into the myometrium) every 15 to 90 minutes, as needed, to a total cumulative dose of 2 mg (8 doses)
Misoprostol (PGE1)	800 or 1000 mcg rectally; 200 mcg orally plus 400 mcg sublingually ; and 200 mcg orally plus 400 mcg sublingually plus 400 mcg rectally
Dinoprostone (PGE2)	20 mg vaginal or rectal suppository, which can be repeated in two hours
Recombinant human Factor VIIa	Lower doses (10-20 mcg/kg) administered IV

Table 18-1: Pharmacological drugs used in PPH

- **Traumatic post partum hemorrhage:** Traumatic lacerations of the genital tract are the second most common cause of PPH and can occur with both vaginal and cesarean deliveries.

Diagnosis: Should be suspected in cases of PPH and/or hemodynamic instability in the presence of an adequately contracted uterus. The bleeding may be revealed or masked (concealed) e.g. as in broad ligament or retroperitoneal haematoma. In the later circumstances the primary presenting symptoms are those of hemodynamic instability and may be pain due to the expanding hematoma.

Sites: Lacerations could affect any part of the genital tract: **the lower genital** tract (perineum , vulva, vagina, and cervix) or **upper genital tract** (uterus). Upper genital tract lacerations are typically associated with broad ligament and retroperitoneal hematomas (Figure 5-4)

Risk factors: for genital tract lacerations include operative vaginal delivery, fetal malpresentation, fetal macrosomia, precipitous delivery, prior cerclage placement, trial of labor after cesarean section or hystrotomy scar espicallay if the pervious section was a classical or upper segment one.

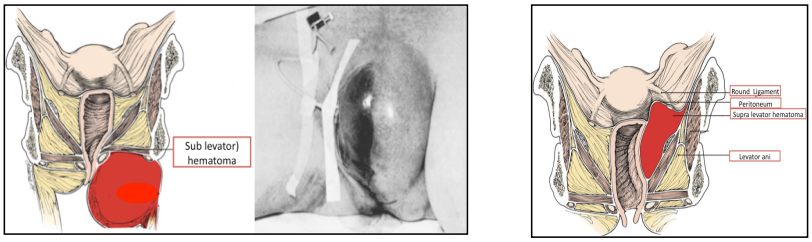

Figure 18-4: on the left a sub-levator ani perineal hematoma causing severe pain and shock. On the Right a supra-levator hematoma causing shock but concealed hemorrhage and minimal or no pain as it spread within the layers of the broad ligament and retroperitoneal space

Treatment: **the** genital tract should be examined systematically **under adequate general or epidural anesthesia** and adequate lighting conditions. Cervical tears should be repaired with absorbable sutures. Care should be taken not to miss the apex of the tear (Figure 5-5).

In some cases lapartomy has to be performed in order to reach the site of tears as in cases of uterine lacerations or rupture. The management depends upon the severity and location of the laceration. The objective is to stop the bleeding and repair the lacerations. In some cases of uterine rupture hysterectomy may have to be undertaken.

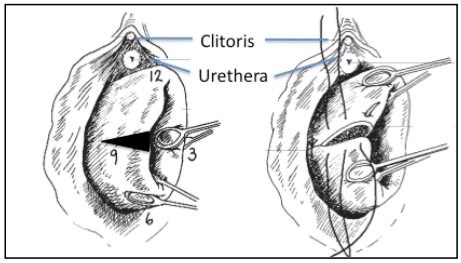

Figure 18-5: careful examination under good light and anesthesia revealed cervical tear at 9^{o}clock. Good exposure is necessary to start repair from the apex of the tear

Uterine Rupture

There are two types of uterine ruptures:

- Complete uterine rupture refers to the "complete" nonsurgical disruption of all uterine layers (endometrium, myometrium, and serosa).
- Incomplete uterine rupture or "uterine dehiscence" is often used to describe the cases with small rupture, which may have minimal bleeding and insignificant maternal-fetal consequences.

Incidence and Risk Factors

The overall incidence of uterine rupture is 1 in 2,000 deliveries. The risk of uterine rupture increases in patients with prior uterine incisions as follow:

- With prior transverse lower segment uterine incisions the risk of scar rupture/dehiscence is 0.2- to 1.5 percent with
- With prior classical or T-shaped incision respectively the risk is 4-9 percent.

Clinical Manifestations and Diagnosis

Uterine rupture is suspected clinically but confirmed surgically at laparotomy. A high index of suspicion is required in order to diagnose uterine rupture at early stage before the patient becomes hemodynamically unstable. During labor the sings and symptoms of uterine rupture include both fetal and maternal clinical manifestations:

- A non-reassuring fetal heart rate pattern is the most common fetal finding, including variable and late decelerations, followed by bradycardia. In late cases the fetal lie and station becomes abnormal.
- Maternal manifestations: Persistent tachycardia, constant abdominal pain, uterine tenderness, a change in uterine shape, cessation of contractions, hematuria (if extension into the bladder has occurred), blood loss per vagina of variable amount, and finally signs of hemodynamic instability.

Management

Surgical exploration should immediately be performed. At laparotomy the site of rupture should be assessed to determine if it could be repaired. Repair of the rupture is carried out in multiple layers with absorbable suture. Hysterectomy should be reserved for cases in which the defect is large and difficult to close or when the mother is hemodynamically unstable.

Uterine Inversion

Uterine inversion is a rare complication of vaginal delivery (incidence range from 1 in 2000 to 1 in 20,000). It is an obstetric emergency if not promptly recognized and treated, it can lead to severe hemorrhage and shock, resulting in maternal death.

Causes: Uterine inversion has been attributed to excessive cord traction and

fundal pressure on uncontracted uterus especially in the presence of fundal implantation of the placenta. However it can still occur even with spontaneous placental delivery.

Pathology: Uterine inversion is classified according to its severity into:

- Incomplete: the fundus lies within the endometrial cavity
- Complete: the fundus protrudes through the external cervical os.
- Prolapsed: the fundus extends to or through the vaginal introitus.

And may also be classified according to the timing of inversion as:

- **Acute** (within 24 hours of delivery)
- **Subacute** (more than 24 hours postpartum)
- **Chronic** (more than a month postpartum).

The diagnosis of uterine inversion: is based upon clinical findings: (1) direct visualision of the inverted uterus (2) bleeding, which may be severe and result in cardiovascular collapse; and (3) Abdominal palpation which may reveal absence or malposition of the uterine fundu.

Management:

Uterine inversion is an obstetric emergency that require simultaneous actions including:

- The ABC principle for Resuscitative measures, anesthetist, and senior obstetrician should be summoned. At the same time attempts to replace the inverted uterus goes into the following sequences:

1. Immediate replacement of the inverted uterus as soon as it occurs (Figure 5-6).
2. Uterine fundal replacement under anesthesia: if immediate uterine replacement could not be performed a tight lower segment muscular ring will be formed which makes further attempts at replacement more difficult. Forcefutl

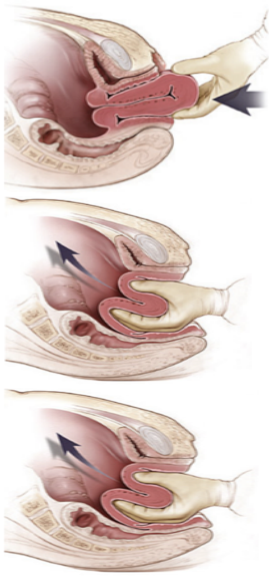

Figure 18-6: manual replacement of acute uterine inversion

attempts should be abandond ans the patient should immediately moved for management in operating theater under anesthesia. Uterine relaxing agents (e.g. Nitroglycerin or anesthetic agent Hallothane) need to be administered and re-attempt at replacement is tried under anesthesia.

3. The Hydrostatic technique: this technique depends on creating a high pressure of water in the vagina to stretches the tight muscular ring and force the inverted fundus back to its normal position. A bag of warmed fluid is hung above the patient and allowed to flow through tubing into the vagina using the physician's hand or a silastic ventouse cup to retain the water in the vagina and generate intravaginal hydrostatic pressure.
4. In difficult cases: laparotomy have to be performed and uterine fundus is located and gentle traction is gradually applied to replace the uterine fundus to its place.

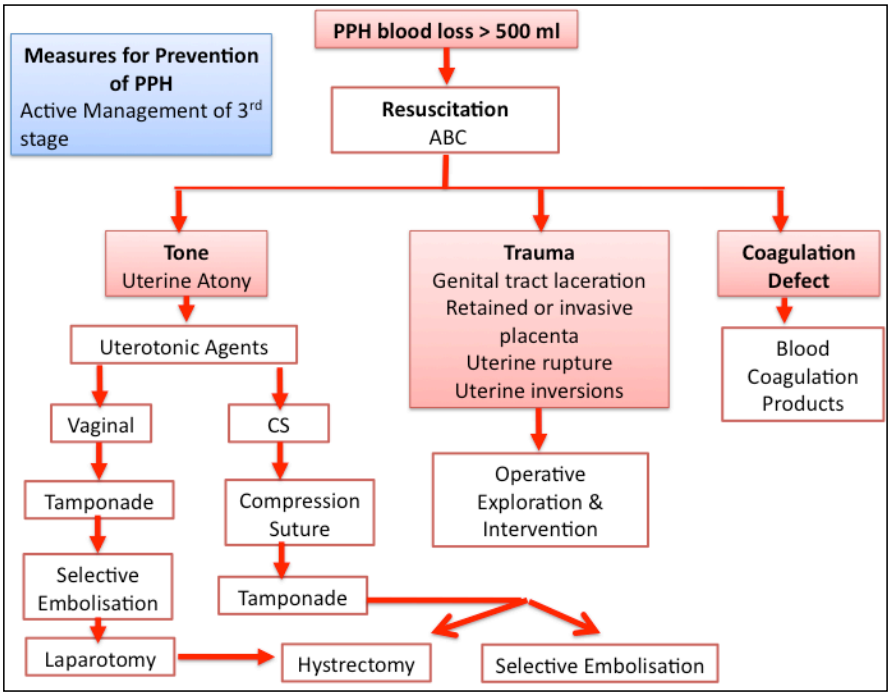

Figure 18-7: Algorithm for managmetn of postpartum hemorrhage.. The first step in management begins with prevention through applying active management of the third stage of labor and be prepared for cases at high risk of PPH

Delayed Postpartum Hemorrhage and Postpartum:

Delayed postpartum hemorrhage is uterine bleeding of sufficient quantity to require medical attention at any time from 24 hours to 6 weeks after delivery. It occurs in 1 to 2 percent of patients.

Causes of secondary postpartum hemorrhage:

- Infection: is the most common cause it usually occurs on top of retained placental tissue.
- Uterine atony as primary cause may be responsible for secondary postpartum hemorrhage in small percentage of cases (2%)
- Hereditary Coagulation disorder: as in von Willebrand's disease which is one of the most common causes of postpartum hemorrhage that

occurs 2 to 5 days after delivery. Von Willebrand's factor increases in pregnancy, and thus excessive bleeding usually does not occur in the first 48 hours after birth. Screening for this condition should be considered in some cases.

Management of secondary postpartum hemorrhage:

- Significant bleeding may require treatment with utertonic agents or curettage. Ultrasound examination should be performed to determine if there is any significant retained intrauterine material.
- If evacuation is necessary it is best performed by "suction evacuation". Curettage should be very carefully performed because over curetting has the risk of uterine perforation and/ or inducing uterine synechia.
- Antibiotics should start before surgery to reduce risk of formation of uterine synechiae.
- Selective arterial embolization: should be tried in cases that do not respond to the previous measures.

Postpartum Infection (Postpartum Pyrexia)

Postpartum febrile morbidity is a rise in temperature of 38.0°C (100.4°F) or higher on any two of the first 10 days after delivery, exclusive of the first 24 hours. Low-grade fever in the first 24 hours is not uncommon and usually resolves spontaneously.
Puerperal sepsis is a term that refers to "any bacterial infection of the genital tract which occurs after the birth of a baby".
Causes:

- Endometritis: is the primary cause of postpartum pyrexia. Occur in about 2 percent of patients after normal delivery and in about 10 to 15 percent after cesarean. The rate goes up to 30% in cases of emergency CS after failure of labor.

However other causes of fever must be excluded:

- Urinary tract infection.
- Upper or lower respiratory infection
- Surgical wound infections.
- Thrombophlebitis

- Mastitis.

Also other disorders not related to pregnancy such as viral infection or appendicitis must be considered.

Post partum Ednometritis:

Definition: Is bacterial infection of the decidua that becomes clinically symptomatic.

Complications: Early diagnosis and treatment is important because of its short and long term complications.

- On the short term if neglected endometritis progress deep into the myometrium (myometritis), the parametrium (parameteritis) and subsequent peritonitis and septicaemia (septic shock). Other complications include pelvic abscess and pelvic thrombophlebitis.

- On the long term it can lead to chronic pelvic inflammatory disease and/or to sterility secondary to damage of the fallopian tubes.

Risk factors of Endometritis:

- Cesarean section especially non-elective operations is the most common risk factors.

- Other risk factors include: premature rupture of the membrane, prolonged labor with repeated vaginal examinations, operative delivery, manual removal of the placenta, and maternal diabetes.

- Women at high risk of upper genital tract infection such as cases with vaginal bacterial vaginosis or colonization with group B streptococcus and cases with diminished immunity e.g. diabetics and HIV infection.

Microbiology:

- It is a polymicrobial infection involving a mixture of two to three aerobes and anaerobes from the genital tract.
- Other rare, but potentially lethal causes of endometritis include:
    - Clostridium sordellii: give a septic shock like syndrome.
    - Streptococcal or staphylococcal toxic shock syndrome: Streptococcal infection should be suspected in patients with early onset, high fever.

Diagnosis:

The symptoms:

- Chills, fever, fatigue and tiredness.
- The lochia becomes heavier, darker in color with offensive smell.

Sings:

- The uterus is tender, softer and sub-involuted (larger in size)

Vaginal examination is not necessary and very painful but if done it can further elicit hotness and severe tenderness on bimanual examination or cervical movements.

The severity of the symptoms and signs depend on the extend of the condition.

Investigations: the diagnosis and treatment is usually based on clinical symptoms and signs. However the following investigations may be requested.

- CBC for basal hemoglobin level, urinalysis, urine culture, as well as endometrial swab and blood cultures.
- Imaging: ultrasound examination for the pelvis to exclude retained placental tissues.

Treatment: the objectives of treatment are to improve patient general condition and prevent short and long-term complications. **Hence treatment should be initiated as soon as the condition is suspected without awaiting results of bacteriology swabs.**

- General measures: included hydration, antipyrtics and analgesics.
- Treatment of infection: The currently standard regimen is combination of Clindamycin (for anerobes and gram positives) and Gentamyceinn (for gram negative bacteria).
- Surgical evacuation: if retained products of conception are present (e.g., fetal membranes, placental fragments). The procedure should be performed by suction evacuation and if necessary gentle careful uterine curettage.

Response is expected within 24 hours of starting antibiotics. In cases with

delayed or no response other causes of fever should be suspected.

Perineal Laceration

Minor lacerations (first degree) are not uncommon. More major degree of laceration may occur despite careful management of delivery in the second stage of labor especially in primigravidas and if the baby is rather large.

The perineal tears are classified into four degrees depending on its extend (Figure 5-8)

- First degree tears (heal spontaneously without sutures).
- Second degree tears.
- Third degree tears.
- Fourth degree tears (if rectal mucosa is involved).

In all cases careful examination of the genital tract including rectal examination should be undertaken after vaginal delivery. Inappropriate repair of the perineal muscles is important cause of long term morbidity including: dyspareunia, bladder and/or anal incontinence in addition of being a possible cause of prolapse.

Surgical repair can be done under local anesthesia for first or second degree. Third and fourth degree tears require repair under regional (epidural) or general anesthesia with adequate relaxation, lighting conditions and assistance.

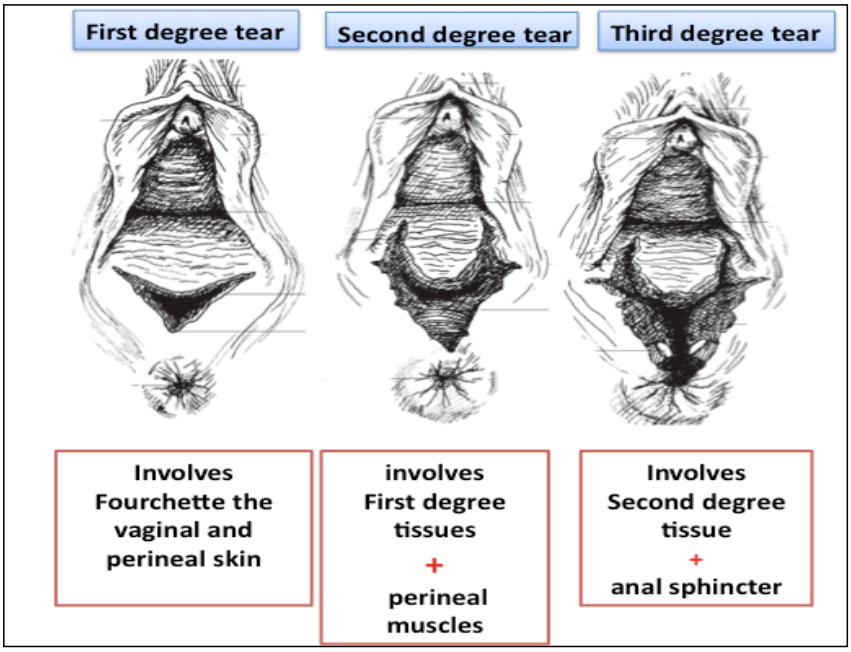

Figure 18-8: Degrees of perineal tears. Sometimes if the rectal mucosa is torn the condition is diagnosed as fourth degree tear.

Post partum Psychological Disorders

Three psychiatric disorders may arise in the postpartum period: postpartum blues, postpartum depression (PPD), and postpartum psychosis.

- Postpartum blues is a transient disorder, lasts hours to weeks and is characterized by bouts of crying and sadness. Approximately 50-70% of women who have given birth develop symptoms of postpartum blues.
- PPD is a more prolonged affective disorder that lasts for weeks to months. It occurs in 10-15% of new mothers. The signs and symptoms do not differ from depression in other settings.
- Postpartum psychosis occurs in the first postpartum year and refers to a group of severe and varied disorders that elicit psychotic symptoms. The incidence of postpartum or puerperal psychosis is 0.14-0.26%.

Morbidity and mortality

Psychiatric disorders can have deleterious effects on the social, cognitive, and emotional development of the newborn. It can also lead to marital difficulties.

Prevention and treatment: Patient at risks should be identified and if necessary referred for psychiatric consultation. The risk factors that should be attended to are patients with underlying depression, a previous history of postpartum depression, and family history of depression.

In the great majority of cases of maternity blues, is self-limited and usually remits after 2 to 3 days, although it sometimes persists for up to 10 days. Depression and psychosis needs specialized psychiatric consultation and management.

Septic Pelvic Thrombophlebitis

Is defined as venous inflammation with thrombus formation in association with fevers unresponsive to antibiotic therapy. It often occurs secondary to clinical or subclinical endometritis.

Risk factors include cesarean birth, prolonged rupture of membranes, and excessive blood loss.

Morbidity and mortality

In its early stages the ovarian veins are often involved with later involvement of the iliofemoral vein. Migration of small septic thrombi into the pulmonary circulation can take place, resulting in effusions, infections, and abscesses. Only rarely is a thrombus large enough to cause death.

Diagnosis:

Clinically the condition should be suspected in patients with enodmetritis who after initial improvement continue to complain of lower abdominal pain, with or without radiation to the flank, groin, or upper abdomen. Other symptoms include nausea, vomiting, and bloating. Frequently, patients continue to have fever despite antibiotics and with no clinically identifiable origin.

Investigations:

- Full work up for fever of fever of unknown origin should be undertaken including: urinalysis, urine culture, and CBC count with differential.
- Imaging: CT scan and MRI are the studies of choice for the diagnosis of septic pelvic thrombophlebitis. These imaging modalities are capable of identifying both ovarian vein and iliofemoral involvement.

Treatment The treatment includes both anticoagulation and antibiotic therapy (most commonly used therapy gentamicin and clindamycin). Long-term anticoagulation is not usually not required.

Mastitis

Mastitis is inflammation of the mammary gland. It is a moderately delayed complication that often develops after the first one or two weeks of delivery. But can occur any time during the period of nursing.

Pathogenesis:

Development of mastitis is predisposed by milk engorgement due to incomplete emptying of the breast and the presence of nipple injury or cracked nipples, which provide access to the skin flora.

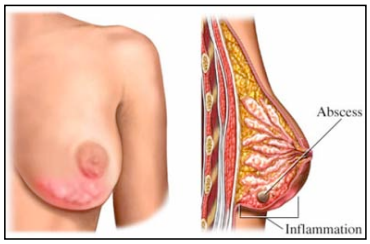

Figure 18-9: Mastitis progressing into abscess

The most common organism is *Staphylococcus aureus*. Other common pathogens include *Staphylococcus epidermidis, S saprophyticus, Streptococcus viridans,* and *E coli.*

Morbidity:

Neglected, resistant, or recurrent infections can lead to the development of an abscess. Abscess development complicates 5-11% of the cases of postpartum mastitis and should be suspected when antibiotic therapy fails (Figure 5-9)

The diagnosis of mastitis is solely based on the clinical picture.

Prevention and Treatment:

Milk stasis should be treated with moist heat, massage, fluids, rest, nursing or manual expression of milk, and analgesics.

- If mastitis develops, it should be promptly treated to prevent development of breast abscess. penicillinase-resistant penicillins and cephalosporins, such as dicloxacillin or cephalexin, are the drugs of choice.

- Resolution usually occurs 48 hours after the onset of antimicrobial therapy.
- Abscess requires surgical drainage.

Chapter 19

Operative Procedures in Obstetrics

Dr Anas Marzouki

The skills of operative obstetric procedures are learned in the obstetric floor. However it is important to be familiar with the indications, benefits and risks including short and long term ones on both the mother and the baby.

By the end of this chapters you should be able to:
Define operative delivery.
List the following aspects regarding The Vaccum extractor and Forceps:
- **Indications:** Maternal and Fetal.
- **Contraindications:**
- **Prerequisite for its use**:
- **Types of forceps delivery**.
- **Risks for Vacuum and forceps:** maternal and fetal
- **Principle of application and use:**

Describe the following aspects regarding Episiotomy:
- Types
- Indications and benefits and risks
- Principle of the technique

Describe types of Cesarean section:
- Categories
- Types and complication of each

Describe the principe of pre and postoperative care

Operative Delivery
Forceps and Vacuum Extraction

Operative vaginal delivery: refers to a delivery in which the operator uses forceps or a vacuum device to assist the mother in accomplishing vaginal delivery.

Indications:

1. Prolonged second stage of labor: The definition of prolonged second of labor varies from nulliparous to multiparous women and whether or not regional anesthesia is used.

- In nulliparous women: prolonged second stage is defined as lack of continuing progress for three hours with regional anesthesia or two hours without anesthesia.
- In multiparous women: prolonged second stage is defined as lack of continuing progress for two hours with regional anesthesia or one hour without anesthesia.

However, these criteria are not absolute especially with the availability of fetal monitoring. A longer duration is accepted provided there is progress in term of head descent, the fetal and maternal condition are stable.

2. Nonreassuring fetal status (fetal distress):
3. Maternal cardiac or neurological disease: Forceps or vacuum can be used to shorten the second stage of labor if the Valsalva maneuver is contraindicated because of maternal cardiovascular or neurologic disease, or if pushing is ineffective because of maternal neurological or muscular disease. Sometimes also with hypertension when prolonged maternal pushing is undesirable.

Prerequisites for operative delivery: Primarily the operator should be experienced in operative vagina delivery procedure. Secondly the following prerequisites should be available prior to application of instruments

- The cervix is fully dilated.
- The membranes are ruptured.
- The head is engaged.
- The position of the fetal head, and any asynclitism shuold be known.
- Clinically there should be no cephalopelvic disproportion
- Adequate maternal analgesia or anesthesia. This is especially important with forceps delivery.
- Maternal bladder should be empty (catheterization may be needed).
- The patient consents to the procedure (The risks and benefits should be clearly explained and all questions answered).
- Finally preparation should be ready for immediate cesarean section if complications arise.

The procedure should be documented in the medical record including patient consent and the indication of the procedure, maternal and fetal assessments.

Contraindications:

Most contraindications to instrumental delivery are related to increased rate of unacceptable fetal risks.

- Fetal prematurity (< 34 weeks) is a relative contraindication particularly for Vacuum extraction because of increased risk of fetal intraventricular hemorrhage.
- Fetal diseases such as: known fetal demineralizing diseases (e.g. osteogenesis imperfecta), fetal bleeding diatheses (e.g. hemophilia, alloimmune thrombocytopenia).
- Other contraindication is unknown fetal head position

Forceps delivery:

Forceps delivery may be classified into three categories:

- **Outlet forceps**: The term describe forceps application with the fetal skull has reached the pelvic floor, the scalp is visible at the introitus without separating the labia, the sagittal suture is in anteroposterior diameter or a right or left occiput anterior or posterior position, rotation does not exceed 45 degrees.
- **Low forceps:** The application of forceps when the leading point of the fetal skull is 2 cm or more beyond the ischial spines, but not on the pelvic floor. Rotation of the head more than 45 degree may be required.
- **Midforceps:** The application of forceps when the head is engaged, but the leading point of the skull is higher than +2 cm station.

High forceps (head above +2 cm) should not be attempted except in very unusual circumstances, such as the sudden onset of severe fetal or maternal compromise, while simultaneously initiating preparations for a cesarean delivery in the event the forceps maneuver is unsuccessful.

Risks and complications:

Operative procedures are associated with increased rate of injuries to both the mother and fetus. Most injuries are mild, short term and resolve spontaneously if diagnosed and treated properly. Occasional it might have long lasting consequences and rarely may be fatal.

- **Maternal:**
  - **Short-term**: maternal risks are more common with forceps delivery particularly high and or rotation forceps. It includes lower genital tract

laceration, hematomas, bladder or urethral injuries. Extension of episiotomy incision, and 3rd or 4th degree laceration.
Additional maternal morbidities include an increased risk of postpartum hemorrhage, especially with extended episiotomy and/or laceration.

- **Long-term:** Long-term maternal sequelae from operative delivery are primarily related to potential disturbances in urinary and anal function, such as urinary incontinence, fecal incontinence, pelvic organ prolapse, and, occasionally, fistula formation.

➢ **Fetal complications**:

- **The short-term complications**:

The short-term complications to the fetus from operative vaginal delivery are usually caused by **head compression** and **traction** on the fetal intracranial structures, face, and scalp. The most serious complication is intracranial hemorrhage. The type and rate of injuries varies between forceps and vacuum extractor.

- **Long-term complications**: Sometimes the acute fetal injuries include intracranial hemorrhage (subdural, subarachnoid, intraventricular and/or intraparenchymal hemorrhage) results in long-term sequelae and neuromuscular injury.

Fetal complications of vacuum-assisted deliveries: Fetal injuries are induced by wrong traction and torsion with the vacuum cup, which can cause:

- Fetal scalp abrasions and lacerations.
- Cephalohematoma and other types of hemorrhage (figure 19-1).
- Intracranial hemorrhage.
- Hyperbilirubinemia, and retinal hemorrhage.

These hemorrhages typically resolve without sequelae within four weeks of birth. Except subgleal hemorrhage (i.e., collection and spread of blood between the aponeurosis covering the scalp and the periosteum) which is associated with mortality as high as 20%

Fetal complications of forceps-assisted deliveries:

The more specific fetal complications of forceps are due to wrong application and/or excessive pressure on the fetal skull, which can cause:

- Skin markings and lacerations, external ocular trauma, subgleal hematomas, hyperbilirubinemia, and retinal hemorrhage.
- Facial palsies, and depressed skull fractures and death.

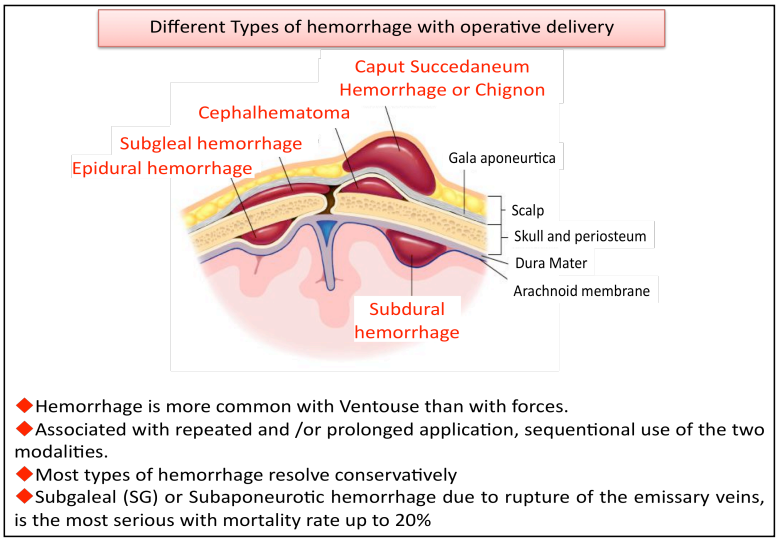

Figure 19-1: Different types of hemorrhage with operative delivery. More with Vacuum Extraction than forceps

Basic components of Forceps: There are hundreds of types of forceps,either short lift out forceps (for outlet procedures) or long traction forceps with or without rotation. The basic components are the same with some differences as follow (figure 19-2) :

- A handle: which varies in length, in lift-out low forceps it is deliberately made short to limit the traction force.
- Blades: which has cephalic and pelvic curves, except with rotation forceps (khielland's forceps), which has very shallow pelvic curve to allow rotation of the head with causing injuries to the maternal tissues.
- Lock: between the two blades, in some forces including rotation forceps the lock is sliding which is helpful when there is asynclitism.

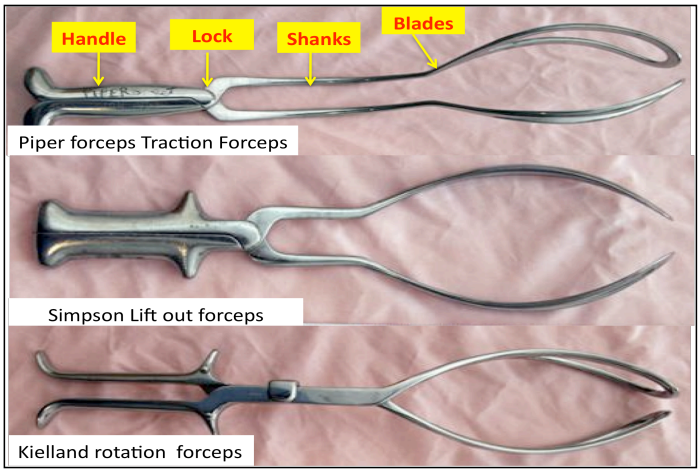

Figure 19-2: examples of traction long forceps (top), short lift out forces (middle) and long traction and rotation forceps. Notice the basic components and the differences in between the three types (see text)

Basic components of Vacuum extractor:

The basic instruments consists of the following parts (Figure 19-3):

- Vacuum Suction pump: The suction can be generated manually or with an electrical suction device.
- Vacuum cups: either soft (pliable) or rigid. Soft cups are made of plastic, silicone, rubber, or polyethylene
- Attachment handle: some type of handle attached to the cup, which is pulled to generate traction.

A suction cup is placed onto the head of the baby and the suction draws the skin from the scalp (produce swelling known as chignon) into the cup. Proper placement is critical to keep the head flexed (Figure 19-3).

Figure 19-3: Ventouse delivery

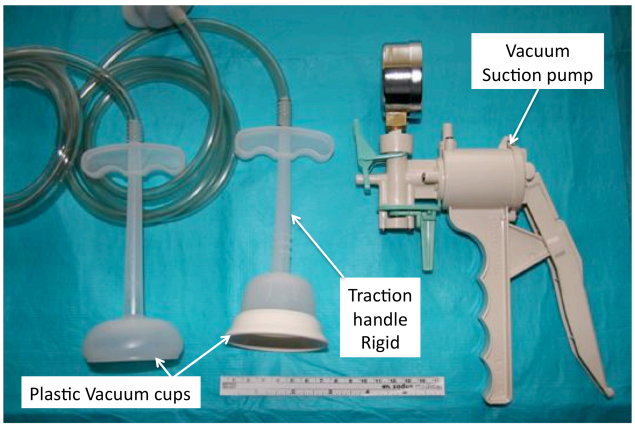

Figure 19-4 Vacuum extractor with manual pump and plastic cup

Principle of operative delivery: The details of the procedures should be read in operative obstetric textbook and learned in the labor floor. However the following are some important principles:

- **Application**: In both instruments proper assessment of the fetal position and station, identify molding, caput, and asynclitism are important before application.
- The vacuum cup should be applied to the flexion point since the location of cup placement is the leading point of the fetal head. Failure to place the cup over the flexion point increase head extension and impedes delivery, rather than assisting it.

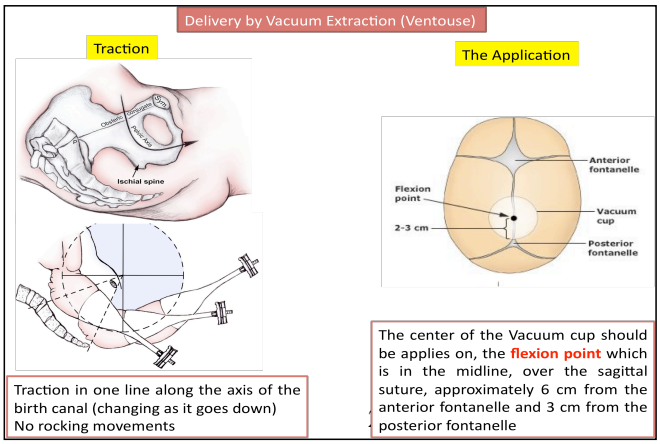

Figure 19-5 The principle of Application and Traction of VE

• **Traction:** Traction with forceps or vacuum should be:

- Steady (not rocking)
- In the line of the birth canal.
- Should be exerted with each contraction and in conjunction with maternal expulsive efforts; the forceps can be relaxed between contractions to reduce fetal cranial compression.
- No more than three tractions should be applied. However this figure may be exceeded if there is noticeable progress. In most cases, progress is noted with the first or second pull and delivery occurs by the third or fourth pull.
- The procedure should be abandoned if descent does not occur with appropriate application and traction.

Multiple attempts at operative vaginal delivery using different instruments (vacuum, different types of forceps) should be avoided except in extreme cases due to the greater potential for maternal and/or fetal injury.

Comparison of Forceps Vs. Vacuum extractor:

The choice of instrument depends on the experience and training of the operator. Other factors include the availability of the instrument and the degree of maternal anesthesia.
In general, vacuum delivery is probably safer than forceps for the mother, while forceps are probably safer than vacuum for the fetus.

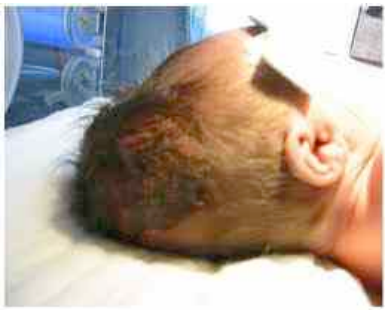

Figure 19-6: Chignon, a temporary swelling induced by the vacuum cup

➢ **Vacuum devices**: are easier to apply, place less force on the fetal head, require less maternal anesthesia, result in less maternal soft tissue trauma, and do not affect the diameter of the fetal head compared

to forceps.

- **Forceps by comparison:** are unlikely to detach from the head, can be used on premature fetuses or for a rotation of the fetal head, result in less cephalohematoma and retinal hemorrhage, and do not aggravate bleeding from scalp lacerations.

Episiotomy

Episiotomy refers to the surgical incision of the female perineum performed at the time of parturition.

Benefits and indications of episiotomy:

- The primary reason to perform an episiotomy is to prevent the occurance of irregular tears of the perineum. The main benefit is that a controlled surgical incision (the episiotomy) is easier to repair and to obtain anatomical cooptation than with spontaneous laceration.
- Secondary benefits are to facilitate delivery, and reduce the time for expulsion of the infant (shorten the second stage).
- Long-term benefit is to reduce the occurrence of pelvic organ prolapse. However, there is an increasing consensus that the procedure is not effective for this purpose.

The rate of episiotomy is getting less as it became evident that there are potential disadvantage to episiotomy, which sometimes outweigh the proposed benefits (see table 19-1) for the risks and benefits of episiotomy).

Episiotomy	
Benefits	Risks
➢ Reduction of third and fourth degree tears ➢ Ease of repair and improved wound healing ➢ Preservation of the muscular and fascial support of the pelvic floor ➢ Reduction of neonatal trauma, such as with the premature infant (soft cranium) or macrosomic infant (shoulder dystocia) ➢ Reduction of dystocia by increasing the diameter of the soft tissue outlet ➢ Expedited delivery of fetuses with non-reassuring fetal heart rate tracings	➢ Extension of the incision, leading to third and fourth degree tears ➢ Unsatisfactory anatomic results (e.g. skin tags, asymmetry, fistula, narrowing of introitus) ➢ Increased blood loss. ➢ Increased postpartum pain. ➢ Higher rates of infection and dehiscence. ➢ Sexual dysfunction. ➢ Possible increased risk of perineal laceration in subsequent deliveries.

Table 19-1: Risks vs. benefits of episiotomy

Therefore episiotomy should not be made routinely but for only recognized indications such as:

1. Fetal distress in the second stage of labor, to speed up the delivery of the baby.
2. Previous (repaired) third or fourth degree tear.
3. If complicated delivery is anticipated e.g. shoulder dystocia, or in breech delivery.
4. Operative delivery such as with forceps or vacuum deliveries.
5. Maternal stress due to exhaustion or heart failure.
6. A very tight perineum that prevents delivery.

The procedure:

- Anesthesia**:** Adequate anesthesia should be available before performing an episiotomy. If there is no regional anesthesia, such as an epidural block, an appropriate local anesthetic should be administered (e.g. pudendal nerve block, local field block).
- **Timing:** Episiotomy should be performed at a peak of uterine contractions and the fetal head is expected to be born within the next three to four contractions. If it is performed too early it result in excessive blood loss. And if it is made too late it becomes difficult to do safely because the baby's head distends the perineum so much and tear of the perineal muscle may already have taken place.

- **Types:**

1. Median episiotomy: The incision beings at the fourchette and extended caudally in the midline. The anatomical structures involved in the incision include the vaginal epithelium, perineal body, and the junction of the perineal body with the bulbocavernosus muscle in the perineum.
2. Mediolateral episiotomy: The incision also begins at the fourchette and cut at an angle (usually to the maternal right for right

The mediolateral episiotomy:
- Associated with more blood loss.
- More difficult to repair.

The median episiotomy:
- Easier to repair
- Yields a better cosmetic result
- Higher rate of third and fourth degree lacerations

handed clinicians), approaching 45 degrees. The anatomical structures incised include the vaginal epithelium, transverse perineal and bulbocavernosus muscles, and perineal skin. If the incision is large, adipose tissue within ischiorectal fossa may be exposed.

3. J incision: The purpose of the "J" incision is to combine the advantages of the median and mediolateral techniques, while avoiding their disadvantages. The incision starts at the fourchette, is initially extended caudally in the midline and then curved laterally at an angle, similar to the letter "J".

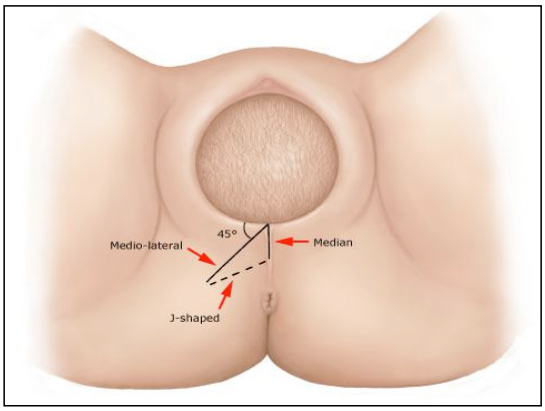

Figure 19-7: the two common types of episiotomies

Complications:

The most common complications of episiotomy are bleeding, infection, and dehiscence.

Local anesthetic:
10 ml of local anesthetic
Protect the baby by two fingers between the baby's head and the perineum.
The needle is inserted at the fourchette through the perineum at a 45° angle

Making the incision:
Two fingers are placed in the vagina between the scissors and baby's head, to prevent accidentally injuring the baby.
The incision should start at the centre of the perineum at a 45° angle. Use sharp blunt ended scissor

Repair:
The vaginal mucosa: 2–0 suturing material with a continuous suture
start about 1 cm above the apex
The perineal muscle by interrupted 2–0 sutures
The skin by interrupted (or subcuticular) 2–0 sutures

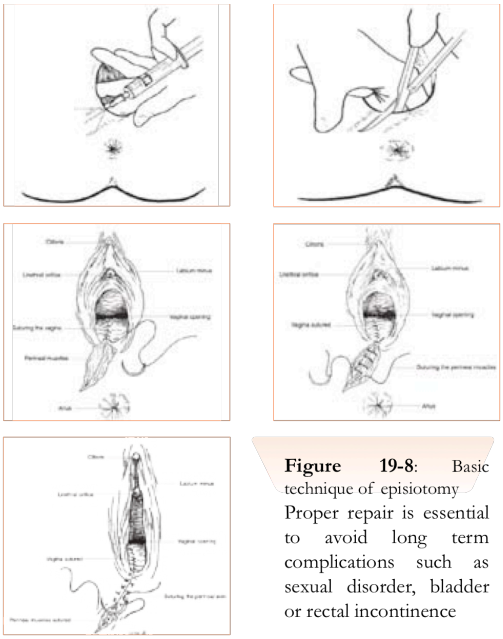

Figure 19-8: Basic technique of episiotomy
Proper repair is essential to avoid long term complications such as sexual disorder, bladder or rectal incontinence

Cesarean Delivery

Cesarean delivery (CD) (also called cesarean section and cesarean birth) refers to the delivery of a baby through surgical incision in the abdomen and uterus.

Types of Cesarean deliveries:
Cesarean sections are categorized as either primary (i.e. first cesarean delivery) or repeat (i.e. after a previous cesarean birth).
Also the operation may be:

- Planned (scheduled CS): When the decision to perform an indicated cesarean delivery is made antepartum (before labor)
- Unplanned (Un-scheduled): when the decision to perform a cesarean delivery does not occur as a consequence of a complication of labor but after the onset of labor.

- Emergency Cesarean section: refers to unplanned operation that is performed as a consequence of complication of labor e.g. acute fetal distress, abruptio placenta…. etc.
  In general the maternal and fetal complications rate is higher with unplanned cesarean sections.

Indications of Cesarean Section:

Cesarean delivery is performed either for maternal or fetal indications if it is felt that abdominal delivery is likely to provide better outcome to either the mother or the fetus or both.

- The four most common indications for cesarean deliveries:
  - Failure to progress during labor
  - Previous hysterotomy (usually related to previous cesarean delivery, but also related to myomectomy or other uterine surgery)
  - Non-reassuring fetal status
  - Fetal malpresentation (breech and other malpresentation)
- Additional, less common indications for cesarean delivery include:
  - Abnormal placentation (e.g. placenta previa, vasa previa, placenta accreta)
  - Maternal infection (e.g. herpes simplex or human immunodeficiency virus)
  - Multiple gestation
  - Fetal bleeding diathesis
  - Mechanical obstruction to vaginal birth (e.g. large leiomyoma or condyloma acuminata, severely displaced pelvic fracture, macrosomia, fetal anomalies such as severe hydrocephalus)
- Other indications include women who have undergone repair of a rectovaginal fistula or pelvic organ prolapse.
- Occasionally it is performed for fetal conditions such as extremely or very low birth weight (<1000 g and ≤1500 g, respectively), or certain congenital anomalies (e.g. open neural tube defects, some skeletal dysplasias, and gastroschisis with herniated liver)

Preoperative issues and preparation:

The following issues must be reviewed for all women going for cesarean section:

- **Consent form**: the procedure including the operation its indication, anesthesia options and postoperative care all should be discussed with the patient as much as it is possible. It should also be documented in the medial records.
- **Reviewing gestational age and Assessment of fetal pulmonary maturity**: by careful history taking of last period and first positive pregnancy test or early scan. In some cases lung maturity should be assessed by amniocentesis and L/S ratio test .
- **Anesthesia:** The choice of the type of anesthesia i.e. regional or general should be discussed. It is influenced by factors such as the urgency of the procedure, maternal status, and physician and patient preference.
- **Antibiotic prophylaxis**: To reduce the risk of postoperative infection, a single intravenous dose of a narrow spectrum antibiotic (e.g., cefazolin 1 or 2 g or ampicillin 2 g) should be administered preoperatively to all women undergoing cesarean delivery
- **Thromboembolism prophylaxis**: All women having cesarean section should have mechanical prophylaxis such as graduated compression stockings, or a pneumatic compression device while in hospital. Pharmacologic prophylaxis should be provided for women with additional risk factors.

Examples of risk factors of include Thromboembolism
- Obesity (BMI ≥30 kg/m2),
- Smoking, recent trauma,
-Inherited or acquired thrombophilia,
- Immobility (>4 days),
- History of thromboembolism.
- Age over 35 years

- **Fetal assessment:** include documentation of the fetal heart with external monitoring and ascertainment of fetal lie and presentation in cases where the indication for delivery is malpresentation (spontaneous cephalic version can sometimes occur).
- **Laboratory testing**: Complete blood count, Rh and ABO blood grouping and saving serum. In some cases (placenta previa) cross-matched blood should be ready in theatre.

Types of Cesarean sections:

According to the uterine incision, cesarean sections are classified into: Lower segment cesarean section and upper segment cesarean section. In the lower segment CS the incisions may be transverse or vertical.

- Transverse lower segment incision:

This the most commonly performed incision.

- The advantages of transverse incision lower segment over vertical incision include: less blood loss, easier reapproximation, and most importantly is a lower risk of rupture in subsequent pregnancies.
- Disadvantage of the transverse incision:
  - If there is a need to enlarge the incision there is high risk of laceration of major blood vessels (uterine blood vessels).
  - In some cases a "J" or inverted "T" extension is required if a larger incision is needed. The "J" extension goes into the lateral fundus and the angles of the inverted "T" incision are poorly vascularized, both of which potentially result in a weaker uterine scar.

➢ Vertical incision: There are two types of vertical incisions, the low vertical and the classical vertical (upper segment).

- The low vertical is performed in the lower uterine segment: Its major disadvantage is the possibility of extension cephalad into the uterine fundus or caudally into the bladder, cervix, or vagina. It is also difficult to determine that the low vertical incision is truly low, as the separation between lower and upper uterine segments is not easily identifiable clinically.
- Upper segment vertical incision "classical": This is rarely performed because in subsequent pregnancies it is associated with a higher frequency of uterine rupture and higher rate of maternal morbidity (infection, adhesions…etc)

The risk of uterine rupture

- Classical CS (4 to 9 %) compared with
- Low vertical (1 to 7 %)

However in very limited circumstances a vertical upper segment CS may have to be undertaken such as:

- Poorly developed lower uterine segment especially if extensive intrauterine manipulation is anticipated (e.g., extremely preterm breech presentation, back down transverse lie)
- Lower uterine segment pathology that prevents a transverse incision (e.g., large leiomyoma)
- Densely adherent bladder

- Anterior placenta previa or accreta
- Postmortem delivery

Postoperative care and complications of CS:

The post operative care following cesarean section is similar to the care provided after any major surgery in addition to the special requirements for postpartum care.

➢ In the immediate postoperative period,

- The woman is monitored for evidence of uterine atony, excessive vaginal or incisional bleeding, and oliguria.
- Blood pressure is monitored to assess for hypo or hypertension, which could be signs of intra-abdominal bleeding or preeclampsia, respectively.
- Analgesia: adequate analgesia should be provided taking in consideration those requirements varies among patients.
- Early ambulation, and oral intake (within four to eight hours of surgery) are encouraged.
- Breast-feeding: is encouraged early with support and help.

➢ Complications:

- The major short-term complications related to cesarean delivery are infection, hemorrhage, injury to pelvic organs, and thromboembolic disorders. In addition anesthetic complications especially with general anesthesia and intubation such aspiration pneumonia.

➢ Long-term risks are:

- The major long-term risks to be considered are the risk of abnormal placentation and issues relating to route of delivery in future pregnancies. Studies have shown that the risk of placenta previe, and placenta prevai with accreta increases as the number of cesarean sections increases (talbe 19-2). Those two complications are particularly important in societies where large families are usually favored.
- Less common complications are complications of scars such as kelloid formation or rarely incisional hernia (more with midline abdominal incision).

- Local numbness or pain around and at the site of the incision: this is due to severance of branches of the ilioinguinal nerve and the

iliohypogastric nerve by transverse abdominal incisions. Pain around the same area or radiating pain could be due to nerve entrapment

Number of cesareans	Previa (percent)	Accreta (percent)	Accreta in patients with previa (percent))
Two	1.33	0.31	11
Three	1.14	0.57	40
Four	2.27	2.13	61
Five	2.33	2.33	67
Six or more	3.37	6.74	67

Table 19-2: Risk of placenta previa and accreta according to number of previous cesarean deliveries
The baseline risk of placenta previa in the general obstetrical population is one in 200 deliveries. Placenta accreta occurs in fewer than one in 500 deliveries.
Adapted from Silver, RM, Landon, MB, Rouse, DJ, et al. Obstet Gynecol 2006; 107:1226.

Reference and Further readings:

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Chapter 20

Early Fetal Wastage

Dr Fatma Al Etebi

For women and their husbands particularly for couples who suffer from recurrent pregnancy loss the experience of miscarriage is a tragic one. Both single and repeated miscarriage can be associated with the same etiologies a fact that creates uncertainness as to when investigations should be initiated. This chapter discusses several aspects related to miscarriage including; etiology, types of miscarriage, treatment and the approach to management of patients with recurrent miscarriage.

By the end of this chapter you should be able to:

- **Define** the single and recurrent miscarriages and the frequency of each.
- **List** the important causes and associated.
  - Genetic: The most common cause of early pregnancy loss.
  - Endocrine: LPD, Thyroid diseases, PCO, Poorly controlled diabetes
  - Uterine anomalies: Ashermans syndrome, Müllerian fusion defects, cervical incompetence and uterine fibroids.
  - Infection: bacteria, mycoplasmas, viruses and parasites
  - Immunological disorders: Auto and Allo immune disorders.
  - Environmental factors: Smoking, environmental toxins, alcohol…etc
  - Thrombophilia: congenital and acquired.
- **Describe** the clinical types of Miscarriage, diagnosis, and option of management for each Threatened, Incomplete, complete, inevitable, and missed miscarriage.
- **Describe** the approach to the management of patient with recurrent miscarriage**.**
- **Describe the** definition, legal and ethical regulations for induced miscarriage.
- **Define** septic abortion and principle of management.

Definitions:

A miscarriage (abortion) is defined as termination of a pregnancy before 20 weeks gestation or of a fetal weight less than 500 g. The term abortion is

better reserved to cases in which termination of pregnancy "TOP" is induced.

Frequency:

Miscarriage is one of the most common, if not the commonest, complications of pregnancy. It is estimated that 70% of all concepts do not reach viability; two thirds of those are lost before the first missed period (pre-embryonic loss), even before the woman realize that she is pregnant. From the remaining clinically recognizable pregnancies about 15 % ends with clinical miscarriage (Figure 20-1).

However the rate of clinical miscarriage is affected by several factors. The most important ones are the women age at conception and history of previous miscarriage. For example the risk of spontaneous miscarriage varied from approximately 8% among women in their twentieth to more than 80% among women in their late forties years of age.

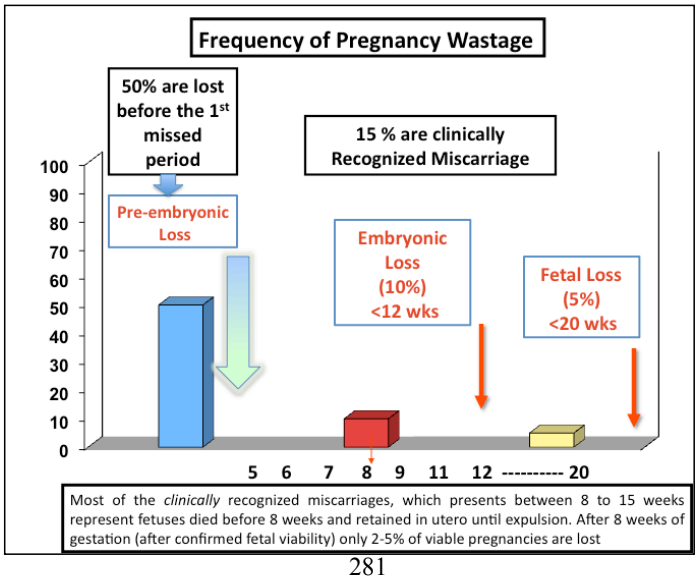

Figure 20-1: Frequency of pregnancy wastage and miscarriage.

Recurrent early pregnancy loss "Recurrent miscarriage":

Patients who experience recurrent miscarriage, defined as the loss of three or more consecutive pregnancies. For any single patient to fall into the 15% risk of miscarriage repeatedly on three consecutive occasions is a rare event. Therefore they are usually looked at differently from one who experiences an isolated miscarriage. It is estimated that recurrent miscarriage affects about 1% of all women.

Causes of fetal wastage and miscarriage:

There is a long list of factors that may be associated with the occurrence of miscarriage. The presence of any one does not necessary mean that it is the cause of miscarriage. Only in few occasions one can define a single cause such as in cases if one of the parents is a carrier of a balanced structural translocation or as in cases of proven antiphospholipid syndrome. Most of the remaining are associated factors -not necessarily causative- that should be considered and searched for especially in cases of recurrent fetal wastage or miscarriage (Figure 20-2). To finally decide that one of those factor is the cause of miscarriage require careful consideration particularly if the treatment entails surgical intervention that may be potentially harmful.

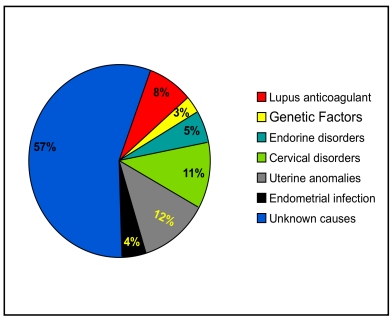

Figure 20-2: Disorders in 671 women with a history of at least three consecutive miscarriages. (Stray-Pederson-Recurrent miscarriage- 1996)

I. Genetic Causes:

Genetic and chromosomal anomlaeis are the most common causes of first trimester miscarriage. Its incidence decreases as pregnancy progresses.

Frequency of chromosomal abnormalities among miscarriages and fetal loss

- In 1st trimester: 70%.
- In 2nd trimester: 30-40% (*mostly of the types observed in live born infants: trisomies 13, 18, and 21; monosomy X; and sex chromosome polysomies*).
- In 3rd trimester losses (stillborn infants) 5%, a frequency that is still higher than the rate of 0.6% in live born

Approximately one fourth of chromosomal abnormalities are due to error in maternal gametogenesis (usually non disjunction). In very small percentage (2%-3%) one of the parents may be carrier for balanced structural chromosomal rearrangement (balanced translocation or balanced chromosomal inversion), which results in abnormal gametes and embryo.

II. Endocrine factors:

Luteal phase deficiency (LPD):

Luteal phase deficiency is a term that describes a state of inadequate progesterone production and/or action.

Progesterone plays a crucial role in inducing the endometrial secretory changes, which is essential for embryonic implantation and subsequent maintenance of the pregnancy. In the early days after ovulation and prior to production of sufficient progesterone by the trophoblast the corpus luteum is the source of progesterone.

Luteal phase deficiency (LPD)

Theoretically LPD may be treated with progesterone, clomiphene citrate, or gonadotrophin (hCG). However because no randomized studies have validated LPD as a genuine entity no treatment is of proven efficacy.

Diagnosis: the diagnostic of LPD is made if the histological secretory change in a luteal phase endometrial biopsy is lagging more than two days behind the normal expected changes following ovulation.

- Polycystic ovarian syndrome "PCO": The high level of luteinizing hormone in patients with PCO have been associated with both infertility and high rate of miscarriage.
- Thyroid Disorder:

Clinically overt hypo and hyper thyroidism has been associated with decreased conception rate and increased pregnancy loss rate. However the role of subclinical hypothyroidism in either isolated or recurrent miscarriage is not determined.

- Diabetes Mellitus:

Patients with poorly controlled diabetes and high hemoglobin A1c level in first trimester is at higher risk of miscarriage and fetal malformation. This however does not apply to women with well-controlled diabetes mellitus who do not seem to run a higher rate of miscarriage-because of their diabetes- than normal non-diabetic women.

III. Uterine Anatomical Factors:

Uterine factors include acquired and congenital factors, in addition to cervical incompetence, which may also be congenital, or acquired.

Acquired uterine factors include:

- **Intrauterine Adhesions "Ashermans Syndrome":**

Miscarriage can occur due to decrease in the area of functioning endometrium that could support implantation. Intrauterine adhesions can be a complication of over-curettage of the endometrium especially if the procedure, performed post abortion or post delivery.

The diagnosis is suspected by hysterosalpingogram showing multiple filling defects, but confirmed by hysteroscopy (figure 20-3). The treatment is by hysteroscopic lysing of adhesions.

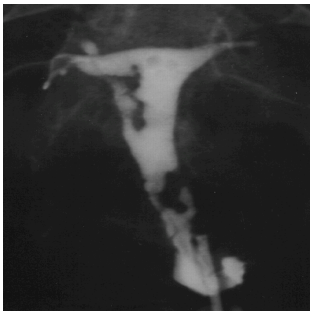

Figure20-3: Hysterosalpingogram shows partial intrauterine adhesions (areas without large volumes of contrast material)

- **Uterine Leiomyomas:**

Uterine leiomyomas "fibroid" can be associated with reproductive failure and other complications. The site of the leiomyoma is of more clinical significance than its size . Submucous leiomyomas can interfere with implantation and result in early miscarriage by causing endometrial thinning and defective decidual vascular supply (Figure 20-6).

Other possible mechanism include red degeneration with or without infection. Also a large myoma may encroach upon the uterine space required for fetal development.

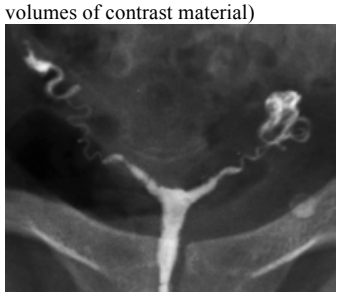

Figure 20-4: T shaped hypoplastic uterus of patient who had been exposed to diethylstilbestrol during her embryonic life.

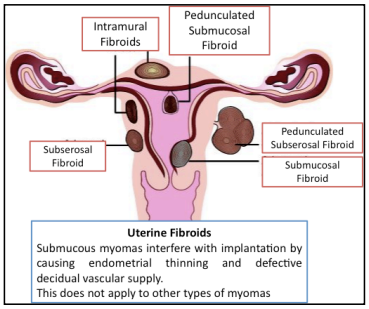

Figure 20-6: Uterine Fibroids sometimes can be associated with pregnancy complication depends on the site more than the size

○ **Congenital Uterine anomalies**:

Congenital uterine anomalies are usually due to incomplete Müllerian tubes fusion; on rare cases it may be induced secondary to in utero exposure to diethylstilbestrol (Figure 20-4 and 5).

Incomplete Müllerian tubes fusion: In general uterine anomalies are more likely to cause secondary trimester loss and/or late pregnancy complications. But the one anomaly that has strong association with spontaneous early and recurrent miscarriage rate of up to 65% is *Septate uteri*. This is explained early miscarriage if implantation of the embryo occurs on the fibrous uterine septum, which , has poor blood supply. Resection of the septum improve pregnancy outcome with an 80% successful delivery rate.

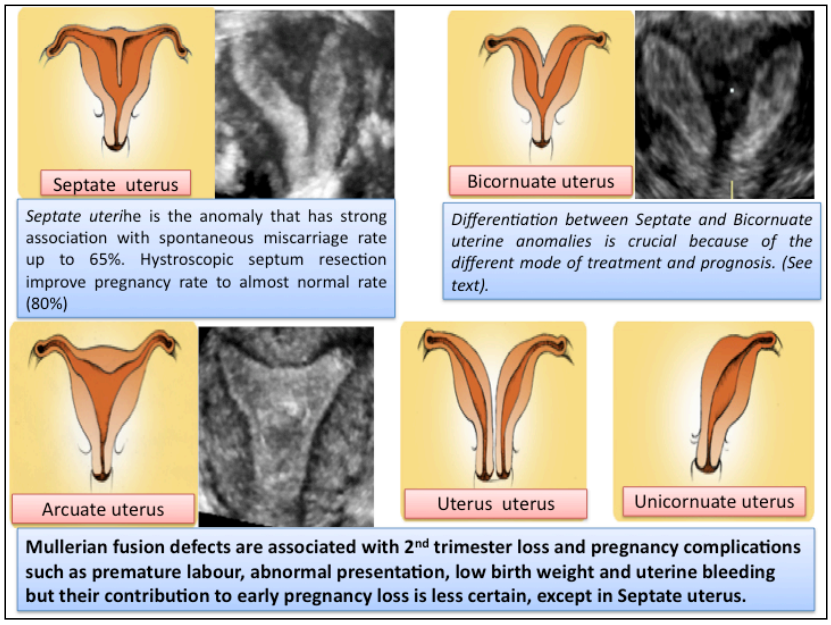

Figure 20-5: The common Müllerian duct fusion anomalies associated with pregnancy loss. The current diagnostic method depends on 3 D ultrasound as shown in the figure.

With *unicornuate uterus* the pregnancy loss rate is up to 50%. Possible etiologies include reduced intramural volume or inadequate vascular supply to the developing fetus and placenta. *Bicornuate uterus* is also associated with 30% - 40% rate of miscarriage.

However Müllerian fusion tubes defects are present in about 1-3% of the general population but can reach up to 40 % among women with recurrent miscarriage and pregnancy loss. This indicates that not all cases with uterine anomalies will end in miscarriage. Furthermore the discovery of uterine anomalies does not necessary means that it is the cause of miscarriage. What is more important is that surgical correction of uterine anomalies should not be undertaken except after careful consideration and evaluation of other causes of fetal loss. This is because surgical procedures for correction of major anomalies *has its own potential compilations and may not necessary improve the outcome.*

o Cervical Incompetence:

Cervical incompetence is defined as the inability of the cervix to support pregnancy until term due to a functional or structural defect

Cervical incompetence is a recognized cause of second trimester miscarriage and premature labour. It complicates approximately from 0.1% to 2% of all pregnancies.

- Causes of cervical incompetence*:*
    a) Congenital disorder (e.g. congenital mullerian duct abnormalities, diethylstilbestrol exposure in utero). This could explain cervical incompetence that develop in primigravidas in the absence of a predisposing factor (see below)
    b) Connective tissue disorder (e.g. Ehlers-Danlos syndrome).
    c) Surgical trauma of the cervix (Leep conization or amputation resulting in substantial loss of connective tissue).
    d) Trauma due to repeated cervical dilatation associated with previous termination of pregnancy.

- The diagnosis of cervical incompetence:

Diagnosis of established cases of cervical incompetence during pregnancy based on symptoms and sings is usually a late diagnosis with poor prognosis. Therefore attempts should be made to identify women at risk of cervical incompetence either before or early in their pregnancy and plan intervention before symptoms or signs of cervical incompetence develops.

Diagnosis during pregnancy: The diagnosis of established cases of mid-trimester miscarriage or preterm labor due to cervical incompetence is based on signs and symptoms. Unfortunately however once a patient has developed the typical clinical picture of cervical incompetence the only treatment options are either conservative management or emergency surgical cervical cerculage. In such late cases both options have poor prognosis.

- **Symptoms**: In typical cases patients are usually in the second trimester (17-20 weeks). The complaint is increased watery dischargee, and some lower pelvic heaviness and pressure like pain. Alternatively patients may presents with symptoms suggestive of rupture of membrane not preceded by pain or contractions.
- **Sings:** on examination uterine contractions or tightness may or may not be present. Vaginal digital examination usually reveals an effaced and dilated cervix with or without herniating membrane.
- **Investigation**: In typical cases (i.e. with signs of cervical effacement and dilatation) no further tests are required. In non-typical cases measurement of cervical length using transvaginal ultrasound is currently the gold standard for diagnosis of cervical incompetence.

Diagnosis of women at risk of cervical incompetence: Identifying women at risk of cervical incompetence are important because there are evidences that prophylactic treatment with cervical cerculage is effective in prolonging the pregnancy. However it is not an easy decision. It is primarily triggered based on obtaining detailed history of the previous pregnancy loss. A typical history is that of second trimester loss or preterm labor, which is often, described as “painless” labor. In this context the word painless refers to the process of cervical dilatation and effacement, which takes place over several days with no or minimal pain.

More recently the use of transvaginal ultrasound for measurement of cervical length plays an increasing role in identifying cases that are more likely to benefit from surgical intervention. (see preterm labor because of cervical incompetence in chapter on preterm labor).

In non-pregnant women: In non-pregnant women there is no effective test for the diagnosis of cervical incompetence. Hysterosalpingography to demonstrate a wide cervical canal (≥ 8 mm at the level of the internal os) and /or painless accommodation of a given size of cervical dilator (Number 8 Hegar) with minimum resistance through the cervical canal have been described as diagnostic tests for cervical incompetence. **None of them are reliable hence they are currently not used in clinical practice.**

- Treatment of cervical incompetence: The treatment of cervical incompetence is "surgical cerclage" that aims to strengthen the cervical competence at the level of the internal os. (see chapter on surgical obstetric procedures)

Infection:

Infections with number of organisms including bacteria, mycoplasmas, viruses and parasites (Table 20-1) can cause miscarriages through several mechanisms:

- Severe affection of fetal organogenesis during early weeks of gestation (e.g. rubella virus, parvovirus B19, cytomegalovirus (CMV).
- Unfavorable implantation from endometrial infection caused by secondary ascending infection (e.g. mycoplasmas and herpesvirus).
- Transplacental fetal blood born infection (as in Treponema pallidum and Toxoplasma gondii)
- Intra-amniotic infection following bacterial invasion of the amniotic cavity, degradation of membranes collagen and early rupture of the membranes.
- Direct effect on the ovum or the fertilization process by infected spermatozoa (Ureaplasma urealyticum).

Bacteria:

- Listeria monocytogenes
- Chlamydia trachomatis
- Ureaplasma urealyticum
- Bacterial vaginosis

Viruses:

- Cytomegalovirus
- Herpes simplex virus
- Human immunodeficiency virus

Parasites:

- Toxoplasma gondii
- Plasmodium falciparum
- Spirochetes
- Treponema pallidum

Table 20-1: Infections that been associated with pregnancy wastage.

Immunological factors:

Immunological disorders are associated with reproductive failure –both inability to conceive (infertility) and inability to keep a pregnancy (pregnancy wastage).

In the context of miscarriage and pregnancy wastage, both alloimmune and autoimmune reactions could be responsible for pregnancy wastage.

- Alloimmune reactions: is an immunological reaction against foreign tissues. The growing conceptus, which in essence is a foreign "allogenic graft", is normally tolerated by the maternal immune system. The mechanisms behind this maternal "immunological tolerance" are not fully understood. But in principle; in normal pregnancy the maternal immune system recognize the fetal tissue as foreign because it carries a different paternal HLA system. In response to that the maternal immune system produce "blocking antibodies" which protects the new conceptus from being rejected by the maternal cell mediated anti-fetal response. If this mechanism fails for example due to significant degree of similarity between the HLA

of the husband and wife then the maternal immune system will not recognize the conceptus as foreign and blocking antibodies will not be produced. The maternal immune system will then mount a cell mediated immune rejection reaction which leads to abortion of the growing embryo.

- Autoimmune reactions: is the body immunological reaction against its own tissues. It includes organ specific autoantibodies such as antithyroid antibodies and non- specific auto-antibodies such as antiphospholipid antibodies "aPL".

Antiphospholipid Antibodies (aPL): In contrary to other immunological causes, antiphospholipid antibodies are a recognized cause of pregnancy wastage. The antiphospholipid antibodies syndrome is a recognized cause of late pregnancy complications and wastage including severe fetal growth restriction, stillbirth and delayed miscarriage. With treatment the risk of these complications can be reduced from 80% to approximately 8-10 %. (See chapter on collagen diseases in pregnancy and antiphospholipid antibodies syndrome).

However the association between APA and early first trimester fetal loss (≤ 10 weeks) is less evident.

Environmental factors:

Several environmental factors have been associated with increased risk of miscarriage and pregnancy wastage. The postulated mechanisms are different and involve direct and indirect effects on the growing conceptus. In addition many of those factors are confounded by each other and by other social and medical characteristics. Nevertheless in patient management those factors should be addressed.

- Cigarette smoking and Caffeine:
- Alcohol:
- Environmental Toxins and chemicals: e.g. anesthetic gases, formaldehyde, lead, and benzene. The contribution of these and other environmental and industrial toxins to spontaneous abortion should if any be very little.

Thrombophilia:

Thrombophilia refers to a group of blood clotting disorders, either inherited "genetic" or acquired, in which there is a predisposition to thrombosis due to a procoagulant state. The most common acquired thrombophilias are lupus anticoagulant and anticardiolipin antibodies (Table 20-2).

Inherited Thrombophilia
Factor V Leiden mutation
Prothrombin gene mutation
Protein S deficiency
Protein C deficiency
Antithrombin (AT)
Factor V Leiden mutation

Table 20-2: Inherited Throbmophilia

Mechanism of pregnancy loss in Thrombophilia:

Thrombosis of spiral arteries and the intervillous space on the maternal side of the placenta can impair adequate placental perfusion. The resulting abnormalities of the uteroplacental circulation may cause late fetal loss, intrauterine growth restriction, placental abruption, or preeclampsia.

As in case of antiphospholipid antibodies syndrome the relationship with early pregnancy loss is less clear and may be restricted to specific thrombophilic defects that have not been completely defined, or the presence of multiple defects.

Treatment of Spontaneous Miscarriage:

A miscarriage is a serious psychological disappointment for almost all women. The recurrence of miscarriage particularly in a consecutive pattern is a very distressing experience and requires a great deal of understanding and support from the clinical attendance.

When a woman presents with symptoms and signs of miscarriage it is the duty of the gynecologist to decide upon the type of miscarriage which may belong to one of four clinical categories; threatened, inevitable, incomplete, and missed.

- Threatened miscarriage:

Threatened abortion is a common event that complicates approximately 25% of pregnancies.

- Symptoms: usually presents with bloody vaginal discharge or bleeding during the first half of pregnancy. The bleeding is often slight in amount but may persist for days or even weeks. It is usually either painless or associated with mild pelvic or low back pain.

- Examination: In the absence of pain there is no indication for pelvic examination. However if it is performed it should begins with vaginal speculum followed by gentle digital examination. The examination reveals a closed the cervix and may be slight vaginal bleeding.
- Ultrasound examination: Is the gold standard. It confirm the location of the pregnancy, gestational age and fetal viability. It can also show abnormalities such as large areas of amnion-chorion separation or subchorionic hemorrhage.

However other causes of pain in early pregnancy should be excluded such as distension or rupture of corpus luteum cyst, extrauterine (ectopic) pregnancy, or torsion of an unsuspected ovarian cyst.

- Treatment of threatened miscarriage is mainly conservative (see below). In about 50% of cases the condition may progress into inevitable miscarriage.

➢ Inevitable miscarriage:
- Symptoms: are usually the same as with threatened except but the bleeding and the pain are usually more pronounced. There may also be history of loss of fluid which suggests rupture of the membranes.
- Examination: Vaginal speculum examination under antiseptic measure rather than manual examination should be performed to demonstrate cervical dilatation which is the hallmark for the diagnosis of inevitable miscarriage.
- Ultrasound examination will again help in confirming fetal viability and may show signs of diminished amniotic fluid within the gestational sac.

In such cases there is very little that can be done to salvage the pregnancy. In the majority of cases bleeding and pain do not subside but rather increases , which will require emptying of the uterus. In rare cases if bleeding and pain subside and the membranes are intact (or no further loss) conservative treatment with bed rest and observation for fever or sings of infection can be offered. If the patient condition remains stable for 24-48 hours, she may be allowed gradually move out of bed but no vaginal examination.

➢ Incomplete miscarriage:

The miscarriage is said to be incomplete if part of the products of conception, the fetus and or the placenta remains within the uterus. This is more likely to occur in miscarriage after the 10th weeks of gestation.

The bleeding in advanced pregnancy can occasionally be massive even fatal unless prompt measures are taken. A patient may present in state of shock which may be out of proportion to the amount of bleeding. In such cases partial cervical distention with placental or fetal tissue protruding through the cervical canal should immediately be suspected. Gentle removal of the protruding products from the cervical canal with ring forceps usually result in immediate stabilization of the patient condition.

Incomplete miscarriage should be treated by uterine evacuation using suction curettage. Cervical dilatation is usually not required.

- Complete miscarriage:

This diagnosis is made if there is firm evidence of complete passage of all fetal and placental tissue, the cervix is closed and the symptoms of bleeding and pain have almost disappeared. Ultrasound examination will confirm that the uterus is empty. No further treatment is needed.

A confusing picture may occur in ectopic pregnancy when the passage of a thick decidua could simulate trophoblastic tissue.

- Early fetal demise (Missed miscarriage):

Early fetal demise (missed miscarriage) is defined as in utero retention of the dead products of conception for few days or weeks. The exact period is not defined.
The diagnosis is suspected in women who gradually indicate regression of the normal sings of pregnancy and may even starts to loose weight. Eventually she will notice that the uterus ceases to increase in size. Alternatively the condition may be discovered during routine ultrasound examination.

- Complications: there are usually no serious complications but occasionally after prolonged retention of a dead fetus, particularly if the gestation had reached second trimester, serious coagulation

defects may develop. Therefore before surgical evacuation of cases of missed miscarriage a screening for coagulation profile should be performed and any defects should be corrected.

The treatment of missed miscarriage is by uterine evacuation. The method of evacuation depends on the weeks of gestation and uterine size. Surgical dilatation and curettage is usually performed for pregnancies less than 12 weeks. The operation however requires experience and skill to ensure complete evacuation. Incomplete evacuation is not uncommon and may latter be complicated with infection and/or bleeding.
Other options of treatment include expectant conservative treatment and medical evacuation using with prostaglandin analogues.

Management of miscarriage:

1. The first line of management includes:
   - Assessment of patient hemodynamic stability.
   - Ascertain of pregnancy status and location by ultrasound examination and by urine and/or blood ß-hCG test.

   The following differential diagnosis should be considered:
   1) Abnormal pregnancy (ectopic, hydatidiform mole)
   2) Normal pregnancy with other causes of bleeding (cervical erosion, polyp, vaginitis, cancer)
   3) Normal pregnancy with other causes of pain (rupture corpus luteum, appendicitis).
   4) Non pregnant conditions; amenorrhea followed by bleeding (metropathia hemorrhagica, ovarian cysts…etc.)

An office ultrasound will sort out most of the list of differential diagnosis. In cases of an empty uterus and a positive pregnancy test the most important differential diagnosis is ectopic gestation.

- Investigations: Blood should be withdrawn for measurement of hemoglobin, blood group and Rh typing. Non-sensitized women who are D negative should receive anti-D immunoglobulin.

Further management depends on the type of miscarriage as described before.

- In threatened miscarriage no intervention is necessary. Bed rest is often described but it has no proven benefit. The patient may continue her normal activities using common sense, but abstain from intercourse for 2 to 3 weeks. Progesterone is sometimes prescribed but there is no evidence that it is effective in preventing the miscarriage.

- Surgical evacuation, by curettage or suction evacuation is necessary if bleeding persists, especially with significant hemodynamic alterations of patient condition or if there is sings of infection. The procedure should be carefully done as there are associated serious morbidities including: uterine perforation; cervical tears, intra-abdominal trauma, intrauterine adhesions (if over curettage is performed) and hemorrhage are reported in about 2% of cases.

- Expectant management: which entails awaiting spontaneous expulsion of the uterine products. This approach is usually successful in more than 90% of cases of incomplete miscarriage but may be less successful in patients with early fetal demise or anembryonic miscarriage.

- Medical evacuation: can be accomplished with the use of prostaglandin analogues (gemeprost or misoprostol) with or without antiprogesterone priming agent (mifepristone). Success with medical evacuation is related to the type of miscarriage, dose and route of administration of misoprostol

Tissue obtained either by surgical or medical evacuation should be sent for histological examination in order to confirm the diagnosis of miscarriage and exclude ectopic pregnancy or gestational trophoblastic disease.

2. *Emotional support*: miscarriage is a traumatic event for women and their husbands. They normally would like to know why it happened. There is often a feeling of disappointment and may be guilt that they are responsible for the miscarriage by doing or not doing something appropriately. The immediate obligations of obstetrician in face of patient

with miscarriage are: 1) inform the woman of the normal frequency of clinically recognized miscarriage rate (10 to 12 %) and its likely etiology (at least 50% are genetic diosorder) 2) Provide recurrent risk rates 3) undertake necessary investigations according to the clinical situation. This is usually required for patient with recurrent pregnancy loss (Figure 20-7).

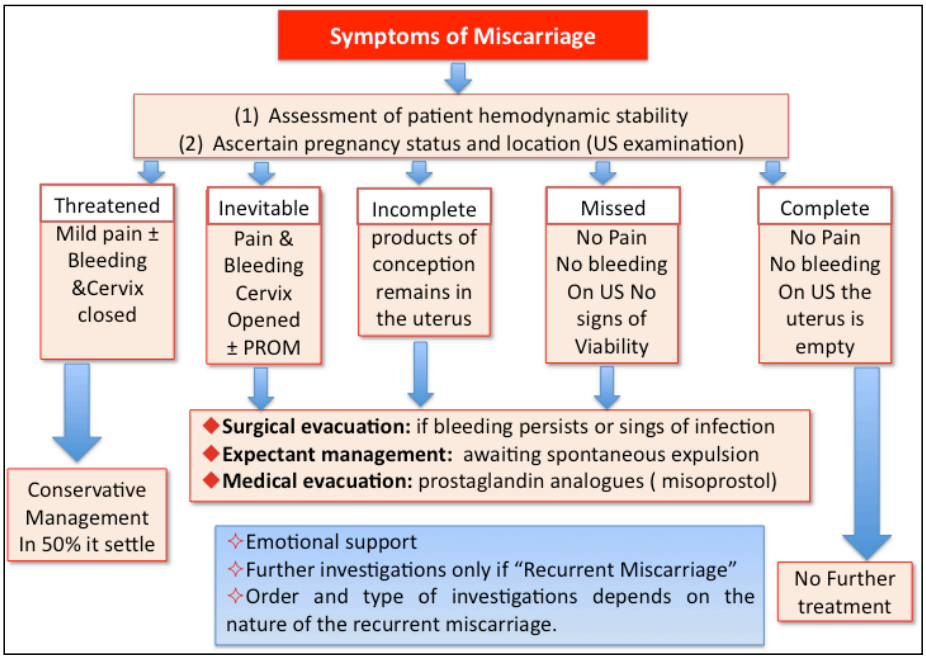

Figure 20-7: Summary of management of miscarriage. In all cases DD should be made of (1) Abnormal pregnancy (ectopic, hydatidiform mole) (2) Normal pregnancy with other causes of bleeding (cervical erosion, polyp, vaginitis, cancer) (3) Normal pregnancy with other causes of pain (rupture corpus luteum, appendicitis). (4) Non pregnant conditions; amenorrhea followed by bleeding (metropathia hemorrhagica, ovarian cysts…etc.)

Approach to management of patients with recurrent miscarriage:

The diagnosis of recurrent miscarriage is usually made after three consecutive miscarriages. The incidence of recurrent miscarriage is around 1%.

The figure three was agreed upon because commencing investigations after two losses gives negative results in the majority of cases. However in special circumstances e.g. older women, a positive genetic pedigree or medical history that is relevant to the risk of miscarriage investigations may be ordered after two or even one miscarriage.

- *History*: A full history should include:
  - The ages of the wife and husband.
  - Past medical and family genetic histories.
  - Direct enquiry should be made about medications or symptoms that might suggest systemic medical disorders or endocrinopathies known to increase risk of miscarriage such as connective tissue diseases, renal disorders, uncontrolled diabetes or thyroid diseases.
  - Social factors including smoking, alcohol or drug abuse and potential adverse occupational exposures should be ascertained.

- Detailed descriptive history of the previous miscarriages: Early miscarriage suggests fetal factors while late ones suggest uterine factors. However the exact gestational age at miscarriage may not be informative since pregnancies are often lost weeks after in utero fetal demise had already occurred.

History suggestive of cervical incompetence should be inquired upon since it will offer a good chance for therapeutic intervention in coming pregnancies.

- Menstrual history should be carefully taken. It might suggest the presence of PCO disease.
- *Physical Examination*: General examination for signs of endocrinopathies such as obesity, hirsutism, galactorrhea, and thyroid diseases.
- Pelvic examination including transvaginal ultrasound should be performed with the objective of looking for uterine anomalies, fibroids and ovarian morphology (PCO).
- *Investigations*: can be very costly therefore it should be limited to those tests with proven value. The order and type of tests performed varies from patient to patient depending on history, examination and potential etiology:
  - Peripheral blood karyotyping of both parents:

The frequency of chromosomal abnormality, most commonly a balanced reciprocal or Robertsonian translocation, among of parents, who present with recurrent pregnancy is about 3% to 5%. Such patient should be referred for counseling with a clinical geneticist. They are advised to have prenatal diagnosis in any future ongoing pregnancies since they have a 5-10% chance of giving birth to a child with unbalanced translocation. Translocation carriers may also be offered preimplantation genetic diagnosis to ensure conception with genetically normal gametes.

- Investigations for congenital and/or acquired uterine anomalies: currently this can be preformed by 3 D transvaginal ultrasound examination. Other more invasive methods include hysterosalpingogram or hysteroscopy.
- Screening tests for antiphospholipid antibodies:
- The diagnosis of APS syndrome require two positive tests at least six weeks apart for either lupus anticoagulant and/or anticardiolipin antibodies of IgG and/or IgM class in medium or high titre.
- Microbiological tests: Tests for infections are not helpful in cases of recurrent miscarriage because of acquired immunity after the first episode of infection. However in high-risk cases screening and treating positive cases of genital infection e.g. C. Trachomatis, bacterial vaginosis…etc. is justifiable. If a cervical culture reveals Ureaplasma urealyticum both partners should be given antibiotics (doxycycline 100 mg per day for ten days or erythromycin 250 mg QID for ten days if allergic to tetracycline).
- Hormonal studies: Tests such as glucose tolerance tests (for diabetes) and thyroid function tests should only be ordered as necessary based on clinical gourds.

Induced Abortion:

Induced abortion is defined as medical or surgical termination of pregnancy before the time of fetal viability.

Legal and Ethical Aspects for Induced abortion: (see chapter on prenatal diagnosis)

Induction of abortion may be undertaken for fetal or maternal reasons:

- If continuation of the pregnancy seriously threaten the life of the woman or impair her health. An example for that are persistent heart diseases after pervious decompensation or advanced hypertensive vascular disease or invasive carcinoma of the cervix.
- When pregnancy has resulted from rape or incest.
- When continuation of pregnancy is likely to result in the birth of a child with severe physical deformities or mental retardation provided that the diagnosis of such abnormalities was undertaken within the legal permissible period for induced abortion.

Methods of induction of Abortion:

- General evaluation:

All cases must have minimum hemoglobin and blood grouping including Rhesus tests. Ultrasound evaluation of gestational age should be performed. Care should be taken when doing ultrasound of the patient special circumstances. The examination should be done in an office rather than in a general antenatal scan department where wanted pregnancies are being examined.

- *Induction of abortion for pregnancies < 7 weeks of gestation*: At this gestational age conventional suction termination is not recommended. Alternatively medical termination using mifepristone plus prostaglandin is more appropriate. A technique called "menstrual aspiration or mini-abortion" has also been described for confirmed pregnancies within 1 to 3 weeks after missed period. In this technique a flexible 5 or 6 mm Karman cannula and syringe is used for aspiration of the endometrial cavity.
- *Induction of abortion for pregnancies between 7-15 weeks of gestation*: the choices within this gestational age range between medical and surgical evacuation. Between 7-9 weeks medical induction of abortion may be undertaken using the same regimens as for gestation < 7 weeks. Suction evacuation may also be used between 7-15 weeks although many would prefer to offer medical abortion at gestation above 12 weeks in order to reduce potential morbidity associated with surgical evacuation. In all cases consideration should be given to cervical preparation. If the cervix is unripe the use of Gemeprost 1 mg vaginally, or misoprostol 400 micrograms (2×200 micrograms tabs) vaginally 3 hours prior to surgery has been recommended.

- *Induction of abortion for pregnancies greater than 15 weeks of gestation*: Beyond 15 weeks surgical induction of abortion is performed by dilatation and evacuation (D&E). This consists of wide cervical dilatation (prior cervical preparation is often required) followed by mechanical destruction and evacuation of fetal parts. It should only be performed by persons with sufficient experience in such procedure in addition it require the presence of special instrumentation and large bore vacuum curette. A dilatation and extraction (D&X) is similar to D&E except that with the term "extraction" means that part of the fetus is first extracted through the dilated cervix to facilitate the procedure.

Complications of elective abortion:

Induction of abortion is generally a safe procedure if performed in a prepared medical set up and especially within the first two months of pregnancy. However potential complications should be considered which sometimes could be very serious or even fatal.

The risk of death from abortion preformed during the first 2 months is about 0.6 per 100,000 procedures. Furthermore the relative risk of dying as the consequence of abortion is approximately doubled for each 2 weeks of delay after 8 weeks' gestation. A proportion of those deaths are related to general anesthesia.

Table 20-3 describes various complications and potential risks of induced abortion and their frequency. The earlier the pregnancy and the more experienced the operator the lesser is the rate of complications. All methods of first trimester abortion carry a risk of failure to terminate the pregnancy, which will necessities a further procedure.

Morbidity	Reported Frequency
Hemorrhage:.	1.5/1000 abortions overall. The rate is lower for early abortions (1.2/1000 at <13 weeks; 8.5/1000 at >20 weeks).
Uterine perforation:	1-4 per 1000. The rate is lower for abortions performed early in pregnancy and performed by experienced clinicians
Cervical trauma:	< 1%. The rate is lower when abortions are performed early in pregnancy and when they are performed by experienced clinicians.
Failed abortion/on-going pregnancy:	all methods of first trimester abortion carry a risk of failure to terminate the pregnancy, thus necessitating a further procedure. The rate for surgical abortion is around 2.3/1000 and for medical abortion around 6.0/1000.
Post-abortion infection: genital tract infection of varying degrees of severity, including pelvic inflammatory disease	10% of cases. The risk is reduced when prophylactic antibiotics are given or when lower genital tract infection has been excluded by bacteriological screening.
Future reproductive outcome:	There are no proven associations between induced abortion and subsequent infertility or preterm delivery.
Psychological sequelae:	Early distress, although common, is usually a continuation of symptoms present before the abortion.

Table 20-3: Morbidities associated with Induction of abortion: Source National evidence based guild lines of the RCOG # 7

Septic Abortion:

Septic abortion is a term that has been associated with criminal (illegal) abortion. It includes serious complications of hemorrhage, sepsis, bacterial shock and acute renal failure.

Septic abortion and its compilations may still be seen, but at a much lower rate, in neglected incomplete spontaneous miscarriage. The most common bacterial organisms are due to anaerobe and gram negative bacterial infection. Treatment of septic abortion includes prompt evacuation along with broad spectrum antimicrobials given intravenously.

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Chapter 21

Preterm Birth

Dr Wafa Sait

Preterm labors "PTL" is the primary cause of neonatal mortality and morbidity. Despite advancement in fetal and maternal care, neither the incidence nor the consequences of preterm birth have declined. In fact in many occasions it has increased. On one hand this is due to the increased rate of multifetal gestation induced by assisted reproduction technology, on the other hand the extremely premature babies who once were considered as "non-viable" births are now, with the advancement in neonatal care are considered survivable.

By the end of this chapter you should be able to:

- **Define**: Term and Preterm labor, low, very low and extremely low birth weight, appropriate, small and large for gestational age and premature fetus.
- **Describe the risks and consequences of Preterm Birth**: Mortality, short and long term morbidity
- **Describe the frequency of Preterm labor:** Indicated and spontaneous Preterm birth.
- **Describe the pathophysiology of preterm Birth**: :
  - Uterine distension.
  - Placental hemorrhage.
  - Fetal and maternal distress.
  - Infection systemic or local.
- **Describe the approach for prevention of preterm labor:** Identifying patient at risk of preterm labor and possible preventive measures: Progesterone, cervical cerculage, rest…etc.
- **Describe approach to management of preterm labor:**
  - **Management of patient presents with threatening symptoms of preterm labor:**
    - Confirm diagnosis, evaluate fetal and maternal condition.
    - **Tocolytics:** Its role, indication, contraindication.
    - **Steroid: and Antibiotics:** Role and indications.
    - **Transfer to Tertiary units:**
  - **Management of established advanced preterm labor**
- **Define the approach to preterm Premature rupture of membrane:** diagnosis, and management

Definitions:

Term birth: A term birth is birth that occurs between 37 completed weeks and less than 42 of menstrual age.

Preterm birth: A birth that occur before the completion of 37 menstrual weeks of gestation, regardless of birth weight.

Low Birth Weight infant: an infant weighting < 2500 gm regardless of gestational age.

Very low birth weight (VLBW) infant: an infant weighting < 1500 gm.

Extremely low birth weight (ELBW) infant: an infant whose birth weight is less than 1000 g.

Appropriate for gestational age: An infant whose birth weight between the 10th and 90th percentiles.

Small for gestational age: An infant whose birth weight less than the 10th percentile for gestational age.

Large for gestational age: birth weight above the 90th percentile.

Premature infant: an infant that has not achieved functional maturity Because maturation of the fetal lungs is the primary concern at birth, it is the most important function to be considered in the management of preterm birth.

⇒**Consequences of preterm birth**:

Preterm labor accounts for 85% of infant mortality and 50% of the surviving infants' neurologic disorders. Figure 21-1, displays the inverse relation between gestational weeks at birth and rate of neonatal mortality morbidity.

It is also obvious that babies born before 32 weeks, are more likely to be develop serious morbidity such as: visual and hearing impairment, chronic lung disease, cerebral palsy, and delayed development in childhood.

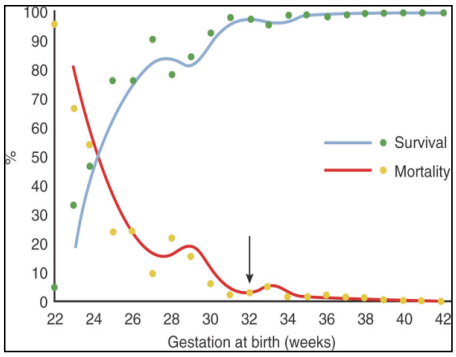


Figure 21-1: Neonatal mortality and morbidity are inversely related to gestational week at birth, particularly before 32 weeks

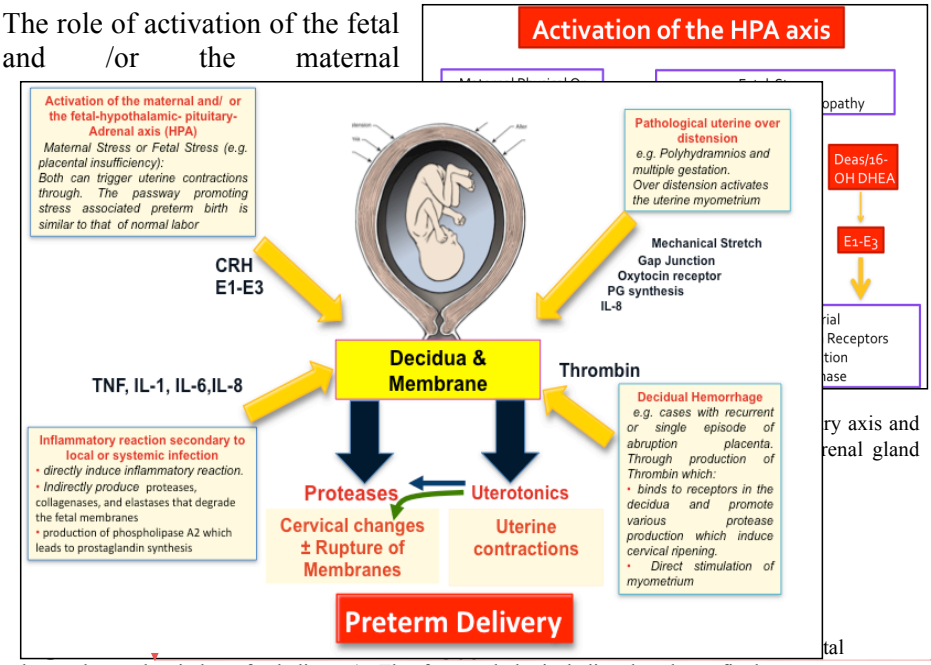
⇒**Frequency of Preterm and Low Birth Weight Delivery:**

Preterm birth occurs in about 10 to 12 percent of live births. The frequency may vary depending on the studied population and prevalence of risk factors (see below). The majority (75%) is due to spontaneous preterm labor, while about 25% are indicated (induced) preterm births (e.g. because of severe medical or obstetric conditions such as severe preeclampsia, maternal cardiac disease or severe uncontrolled diabetes….etc.)

⇒Pathophysiology of Spontaneous Preterm Labor:

The exact path-physiologic mechanism that trigger uterine contractions before term is not known. However there are four major pathological conditions that could lead to preterm birth, these are: **(1)** Activation of the maternal and/or fetal hypothalamic pituitary-Adrenal axis (HPA), **(2)** Pathologic uterine overdistension, **(3)** Decidual hemorrhage, and **(4)** inflammatory reaction secondary to systemic or local genital infection. **Although each has a unique biochemical mediators but all the four share common final biologic pathway that lead to cervical changes and uterine contractions with or without membrane rupture** (Figure 21-2).

The role of activation of the fetal and /or the maternal



ry axis and renal gland

tal hemorrhage also induce fetal distress). The four pathological disorders have final common pathway by acting on the decidua and membranes to induce **uterotonic effect** (prostaglandin, rise in E level, gap junction, rise oxytocin receptors), which induce uterine contractions, and/or **proteases** (collagenases, matrix metalloproteases), which induce cervical changes ± rupture of membranes. CRH(corticotrophic hormone), IL (interleukins), PG (prostaglandins), E1 and E3 (estrone and estriol

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hypothalamic pituitary axis and secondary stimulation of the fetal and or maternal adrenal gland in precipitation of preterm uterine contraction and birth is similar to that which occur in physiological labor.
Figure 21-3 displays the cascade in such conditions.

However in addition to the aforementioned four causes other immunological and genetic factors that are not yet known could explain why not all women exposed to the same pathologic factors (e.g. infection or stress) have the same response.

⇒**Prevention of Preterm Birth:**

Prevention of preterm labor is the first step in the management of preterm birth. Most of the effort is directed towards identifying patients who are at increased risk of going into preterm labor because of one or more of the recognized epidemiological risk factors (figure 21-4).

The more the number of risk factors (risk score) a patient have the higher the risk of preterm labor. The most predictive risk factors are history of

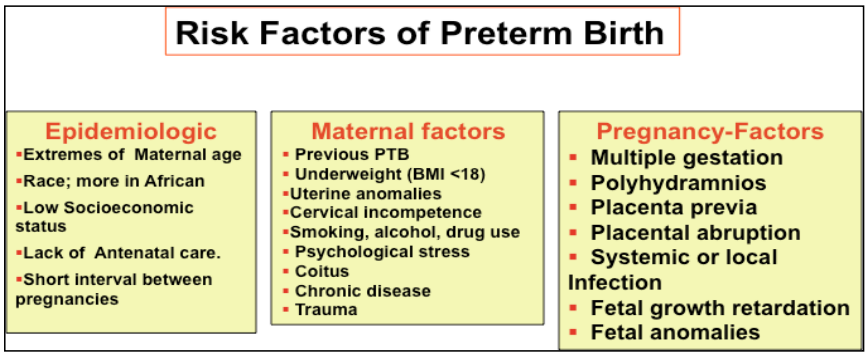

Figure 21-4: Risk factors that epidemiologically were found to be associated with increased risk of preterm labor. But association does not mean causation. The more the risk factors (risk score) a patient have the higher her risk of going into preterm labor

previous preterm labor, multiple gestation and uterine anomalies including cervical incompetence.

A history of preterm birth confers an approximately twofold increase in the risk of early delivery in subsequent pregnancies. The risk rises as the

number of prior preterm births increases. Also in multiple gestations the risk of preterm birth rises with the number of fetuses.

However it should be noted that more than 50% of cases of preterm labor occur in women with no previously identified factors.

⇒Management of patients at high risk of preterm labor:

An important objective of the of antenatal care is to identify patient at high risk of preterm labor based on one or more of the above mentioned risk factors. Those patients should receive general health advice, which include avoidance of strenuous work and stress, cessation of smoking, prevention of anemia and good nutrition. In addition one or more of the following measure may be offered depending on the nature and type of risk:

- Screening and treatment for vaginal and systemic infection: Bacterial vaginal swab for bacterial vaginosis and urine test by microscopy with or without culture is performed. In some cases this may be repeated every few weeks.
- Measurement of cervical length by transvaginal ultrasonography: This may begin at around 18 weeks. If sings of cervical incompetence are discovered early, cervical cerclage can be offered (Figures 21-5, 6).

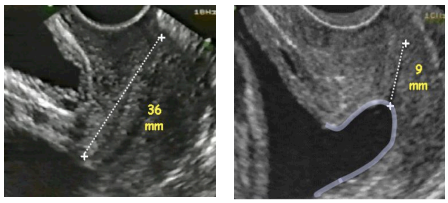

Figure 21-5: A, B normal and short cervix. The relative risk of preterm birth before 35 weeks is increased six- to eightfold in woman whose cervical length is less than the 10th percentile (25 mm) when compared with women with a cervical length above the 75th percentile (40 mm) at 20 to 24 weeks

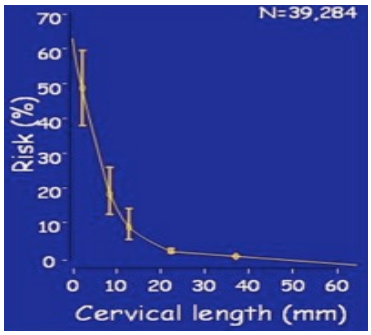

Figure 21-6: the risk of spontaneous premature birth increases as the cervical length decreases (see reference)

- Prophylactic Cervical Cerclage: this surgical procedure aims to strengthen what sought to be "incompetent cervix". It is probably effective in cases with cervical incompetence. However problem is in identifying cases with true cervical incompetence. Therefore in most cases a balance should be made between the possible benefit and the potential risk of the procedure (see chapter on operative obstetrics). It is normally placed between 12-16 weeks and removed at 36 week. Unfortunately large randomized studies did not prove the effectiveness of this procedure in reducing the perinatal mortality and morbidity from preterm labor.

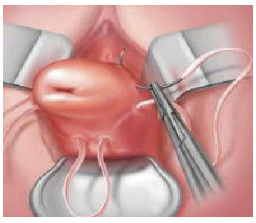

Figure 21-7: Simple cerclage suture being placed "McDonald technique" as prophylactic in cases at high risk of cervical incompetence.

- Progesterone supplementation: The current evidence suggests that progesterone supplementation (*as weekly intramuscular injections of 250 mg of 17α-hydroxyprogesterone caproate or daily 400 mg progesterone vaginal suppositories*) is effective in prevention of preterm labor in women with a prior preterm birth. Although the appropriate dose, timing and route of administration is not yet very clear.
- Biochemical screening tests: the presence of fetal "Fibronectin" in vaginal fluid in patients at high risk of preterm labor. A positive test in asymptomatic women at 24 weeks was shown to indicate high risk of delivery within 2 weeks of sampling.

What is Fibronectin: is a glycoprotein of fetal origin. It is normally present at the decidual-chorionic interface. If there is decidual separation or damage it leaks out which is a sign of threatened labor.

⇒**Management of patient presenting with threatened (early symptoms) of preterm labor:**

The diagnosis of preterm labor should be considered in any patient who present in the second trimester with recurrent lower abdominal pain. In such cases the patient should be evaluated with the following objectives:

1. To confirm the diagnosis of preterm labor: the diagnosis of PTL is confirmed if cervical dilatation is > 2 cm and effacement is > 80% in the presence of regular labor like uterine contractions. However in cases associated with cervical incompetence "painful contractions" may either be absent or not a prominent sign.

In cases if there is doubt about the diagnosis the patient has to be admitted to the hospital for further evaluation. This entails monitoring for uterine contractions by cardiotocogram and investigations such as Fibronectin test or vaginal sonography for measurements of cervical length.

2. Assessment of maternal condition: some acute maternal conditions may require immediate delivery even if the fetus is premature such as with severe preeclampsia, placental abruption, bleeding placenta previa, chorioamnionitis…etc.
3. Assessment of fetal condition: some fetal conditions require immediate delivery or specific management plan such as cases with severe fetal growth restriction especially if there is oligohydramnios and abnormal heart rate tracing. Also the presence of fetal malformations. In those cases the potential benefit for *in utero* versus *ex utero* treatment should be assessed

Subsequent management and intervention depends on the following factors: (1) the gestational age, (2) if labor is already advanced or not, (3) facilities available for neonatal care.

Once preterm labor has been confirmed, the pregnancy less than 34 weeks, and no fetal or maternal indication for immediate delivery administration of one of the tocolytic agents should be considered.

- If labor is not already advanced: it may be administration of tocolytics may succeed tin the arrest of labor.
- If labor is advanced: tolcolytics can not stop labor but in such cases the aim is give time for transfer of patient to tertiary units for neonatal care – if it is necessary- and for glucocorticoids administration for lung maturity to take effect.. Glucocorticoids require 48 hours to achieve optimum results. The regiment are either Betamethasone (two doses of 12 mg given intramuscularly 24 hours apart) or Dexamethasone (6 mg given intramuscularly 12 hours apart).

- Administration of antibiotics: to reduce neonatal morbidity from lung infection.

Figure 21-8 describes the algorithm for management of women presenting with symptoms of threatened preterm labor.

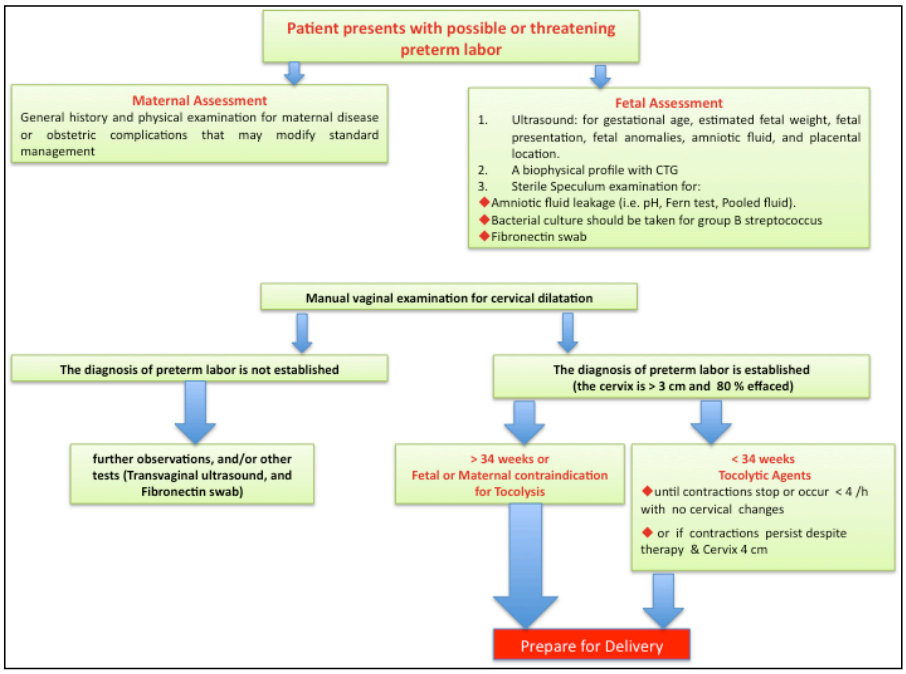

Figure 21-8: Summary for management of patient presenting with threatening preterm labor. Tocolytic therapy should be discontinued if cervical dilatation reach > 4 cm. In the remaining cases with no cervical dilatation will mostly stop contractions after the Tocolytic is discontinued. Cx =cervix, BPP=biophysical profile, EFW= estimated fetal weight, CTG= cardiotochogram, AF amniotic fluid

The use of tocolytic drugs in preterm labor

Tocolytic agents are drugs used to arrest uterine contractions in established preterm labor with or without rupture of membranes. There are many Tocolytic agents. Table 21-1 summaries the mechanisms of action and potential side effects of the currently used agents (Table 21-1).

Although sometimes tocolytic agents may succeed in stopping uterine contractions but **the main objective of administration of Tocolytic agent in cases with established diagnosis of preterm labor is not to prevent labor** but to delay the preterm birth for sufficient period to allow **(1)** maternal transfer to a center with a tertiary neonatal care **(2)** administration of glucocorticoids course to the mother which enhance fetal lung maturation and reduce risk of intraventricular hemorrhage **(3)** administration of prophylactic antibiotics for group B streptococcus GBS.

Calcium Channel Blockers (Nifedipine)	
Mechanism of Action	Inhibition of calcium entry into smooth muscle cells, resulting in a direct decrease in intracellular calcium as well as decreased release of calcium from intracellular storage sites.
Dose	10- 20-mg initial dose, repeated every 3 to 6 hours until contractions are rare, followed by long-acting 30 or 60 mg every 8 to 12 hours for 48 hours.
Maternal Side effects	Related to hypotension such as headache (20 percent), flushing (8 percent), dizziness, and nausea (6 percent)
Fetal side effects	No significant fetal adverse effects
Magnesium Sulfate	
Mechanism of Action	Magnesium competes with calcium either at the motor end plate, reducing excitation, or at the cell membrane, reducing calcium influx into the cell.
Dose	Loading dose of 4 to 6 g is given over 30 minutes, followed by an infusion of 1 to 4 g per hour.
Maternal Side effects	Flushing, nausea, vomiting, headache, generalized muscle weakness. Serious effects: Chest pain and pulmonary edema, Mg Sulfate toxicity (cardiopulmonary arrest). (see chapter on PET for monitoring of Mg Sulfate)
Fetal side effects	No significant fetal adverse effects
Cyclooxygenase Inhibitors (Indomethacin)	
Mechanism of Action	Inhibit Prostaglandin Synthesis
Dose	Loading dose 50 mg followed by 25 -50 mg 6 hourly (for 2-3 days) Should not be used after 32 weeks
Maternal Side effects	- GIT effects: nausea, heartburn, and vomiting. - Serious GIT bleeding, asthma in aspirin-sensitive patients, -Renal injury
Fetal side effects	Constriction of the ductus arteriosus, oligohydramnios, and neonatal pulmonary hypertension. The likelihood of ductal constriction increased from 5 to 10 percent before 32 weeks to 50 percent after 48 hours of treatment at 32 to 35 weeks.
β- sympathomimetic drugs (Terbutaline, Ritodrine, and others)	
Mechanism of Action	Stimulation of the β-receptors
Dose	Terbutaline: SC 0.25 mg (250 µg) every 4 hours / Ritordrine (follow manufacture

	regiment)
Maternal Side effects	Cardiopulmonary Complications: fall in diastolic BP (5- to 10-mm Hg) , and the extensive peripheral vasodilatation, tachycardia, palpitation, tremor chest dicomfort, with risk of pulmonary edema. - Metabolic Complications. β-mimetic agents induce transient hyperglycemia and hypokalemia during treatment
Fetal side effects	Neonatal hypoglycemia, hypocalcemia, and ileus
The oxytocin antagonist (Atosiban)	
Dose	According to manufacture regiment
Maternal Side effects	Few except for injection site inflammation
Fetal side effects	FDA did not approve Atosiban because of an unexpected finding of more perinatal deaths among infants born to women enrolled into Atosiban arm before 26 weeks

Table 21-1: Summary of the Tocolytic agents in use. The main objective of its use is to delay preterm birth for enough time to transfer patient to tertiary care center and for administered steroid to take effect on maturation of fetal lung.

Contraindication to Tocolysis:

- Cases that require immediate delivery for maternal conditions e.g. Hypertension, bleeding, and cardiac disease.
- If the pregnancy is more than 34-35 weeks.
- The presence of other serious fetal conditions such as lethal anomaly or evidence of acute or chronic fetal compromise.

⇒**Management of patient in established advanced preterm labor:**

Patients in advanced preterm labor (cervix more than 4 cm dilated) should not be placed on Tocolytic therapy. The management of labor and delivery in such cases require careful surveillance of the fetal condition. Not only because of the infant is preterm but because in many cases there is underlying complications such as hypertension, amnionitis, abruption, oligohydramnios, or fetal growth restriction that increase the chance of intrapartum fetal compromise.

- Labor and delivery should take place in a tertiary care center with high standard of neonatal care.
- Careful monitoring of the fetal condition and the progress of labor should take place. The active phase and the second stage may be particularly short and quick . Care should be taken to ensure that the fetus does not have a precipitous delivery without control of the fetal head to reduce the risk of trauma or intraventricular hemorrhage from fast delivery.

- The neonatal care team should be alerted to the circumstances of a preterm birth well in advance of the delivery so that appropriate personnel and equipment are available.

- Cesarean section: Routine cesarean delivery of all preterm or VLBW infants is not justified, as it does not benefit the infant while increases maternal morbidity.

- For preterm infants in breech presentation, the potential benefit of cesarean section delivery is to avoid trapping of the after-coming head and other manipulations that could lead to trauma or hypoxia. However the delivery of preterm breech through cesarean section can also be difficult due to inadequate abdominal or uterine incision and poorly developed lower segment. The decision and management of such cases requires senior obstetrician experience and skill.

Preterm Premature rupture of membranes (PPROM)

Definitions:

Premature rupture of membranes (PROM) is defined as membrane rupture in the absence of uterine contractions.

Preterm PROM (PPROM)": this term is the term used when the pregnancy is less than 37 completed weeks of gestation.

In the majority of times PROM will be followed by labor within 24 to 48 hours. If labor does not occur there is increasing risk of development of chorioamnionitis.

Incidence: PPROM occurs in 3 percent of pregnancies and is responsible for, or associated with, approximately one-third of preterm births.

Etiology and Risk Factors for PRROM:

The risk factors for PPROM are similar to those for preterm labor (Figure 21-4). Of particular significance are; PPROM in a previous pregnancy, genital tract infection, antepartum bleeding, and cigarette smoking which were found to have strong association with PPROM.

DD of vaginal/perineal wetness: Urinary incontinence, vaginal discharge, and perspiration

Clinical manifestation and diagnosis:

The diagnosis of PPROM based on combination of a characteristic history (symptoms) and visualization

of amniotic fluid on physical examination (signs) and if necessary investigations.

- History: The classic clinical presentation of PPROM is a sudden "gush" of clear or pale yellow fluid from the vagina. However, many women describe intermittent or constant leaking of small amounts of fluid or just a sensation of wetness within the vagina or on the perineum.
- Physical examination: An almost definite confirmation of the diagnosis of PROM is made by direct observation of amniotic fluid coming out of the cervical canal or "pooling" in the vaginal fornix. If amniotic fluid is not immediately visible, the woman can be asked to push "Valsalva strain", or cough to provoke leakage of amniotic fluid from the cervical os.

  Vaginal digital examination should be avoided because it may increase the risk of intrauterine infection. Instead speculum examination should be performed under complete aseptic precaution. A high vaginal swab should be taken for bacteriology examination.

- Investigations:

- **Nitrazin test**: is a test for the pH of the vaginal fluid. The amniotic fluid usually has a pH range of 7.0 to 7.3 compared to the normally acidic vaginal pH of 3.8 to 4.2 (figure 21-9)

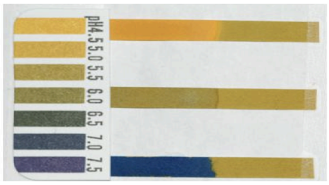

Figure 21-9: (A) normal, (B) bacterial vaginosis, (C) pregnant woman with PROM

False-negative and false-positive nitrazin tests results occur in up to 5 percent of cases. False negative tests results can occur when leaking is intermittent or other vaginal fluids dilute the amniotic fluid. False positive results can be due to the presence of alkaline fluids in the vagina, such as blood, seminal fluid, or soap. In addition, the pH of urine can be elevated to near 8.0 if infected with Proteus species.

- **Fern test**: Fluid from the posterior vaginal fornix is swabbed onto a glass slide and allowed to dry for at least 10 minutes. Amniotic fluid produces a delicate ferning (arborization) (figure 21- 10)

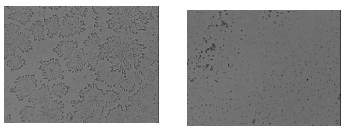

Figure 21-10: (A) negative fern test (B) Positive fern test.

Ultrasonography: Sonography can confirm diagnosis especially if there is oligohydramnios combined with characteristic history suggestive of rupture of membranes.

Placental alpha microglobulin-1 protein assay (AmniSure): AmniSure® is a rapid slide test that uses immunochromatographic methods to detect trace amounts of placental alpha microglobulin-1 protein in vaginal fluid. An advantage of this test is that it is not affected by semen or trace amounts of blood. It has a sensitivity of almost 100%. But still rather expensive, therefore is reserved for cases where it is still in doubt after examination and Nitrazin test.

The patient herself using a commercially available kit can do the test. A sterile swab is inserted into the vagina for one minute, then placed into a vial containing a solvent for one minute, and then an AmniSure test strip is dipped into the vial. The test result is revealed by the presence of one or two lines within the next 5 to 10 minutes (one visible line means a negative result for amniotic fluid, two visible lines is a positive result, no visible lines is an invalid result).

Management of PPROM:

As in preterm labor the management of PPROM begins with assessment of maternal and fetal conditions that require immediate delivery e.g. severe pre-eclampsia, sings of chorioamnionitis, fetal distress, fetal anomalies…Etc. In such cases pregnancy need to be terminated and any attempts to prolong pregnancy is contraindicated.

In cases with PPROM with no indications for immediate delivery the decision is based on the balance between the two main risks of PPROM: the risk of prematurity versus the risk of infection. The risk of prematurity should take in consideration the availability of neonatal intensive care service and the ability to assess fetal lung maturity (Figure 21-11).

- If PROM occurs in pregnancy > 34 weeks the risk of chorioamnionitis out

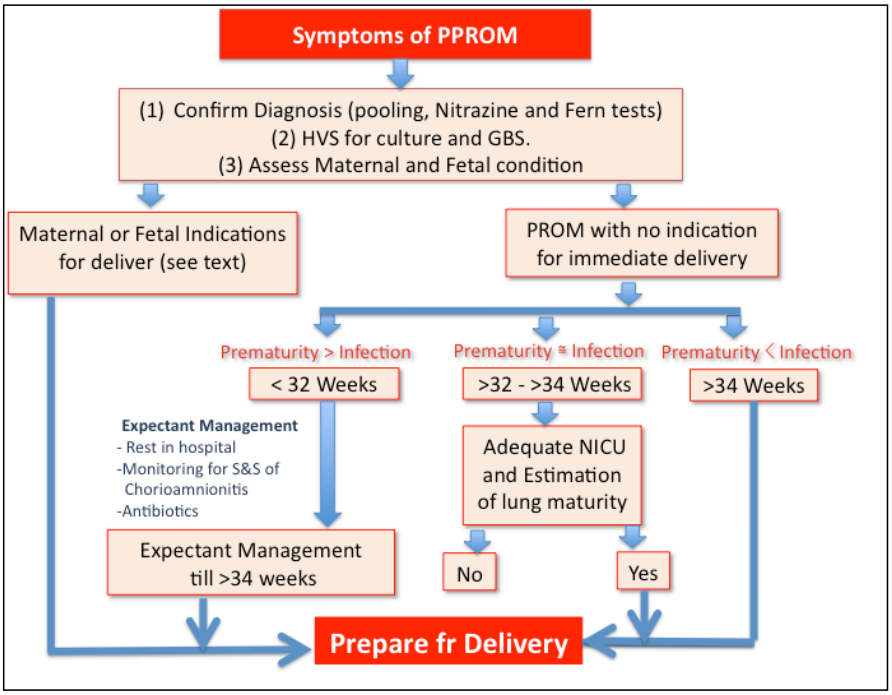

Figure 21-9: Algorithm for management of PPROM (see text). HVS=high vaginal bacteriology swab, GBS: group B streptococcus, NICU: Neonatal intensive care unit

weight the risk of prematurity. Therefore at or beyond this age and expedite delivery is recommended.

- If PROM occurs in pregnancy < 32 weeks the risk of prematurity exceed the risk of infection. In such cases the patient is managed expectantly until at least 32 weeks. At 32 weeks, the fetal lung maturity can be tested

by measuring Lecithin/Sphinogmyelin ratio (L/S ratio) in a sample of amniotic fluid aspirated form the vagina. If testing shows a low risk of neonatal respiratory problems, the patient may be delivered. If this cannot be done or the lung is still immature it is better to continue expectant management until 34 weeks of gestation.

- Pregnancy between 32 to 34 weeks are managed in similar manner, i.e. to initiate delivery if fetal lung maturity can be tested, otherwise continue observation till 34 weeks.

Earlier delivery is indicated if the patient developed clinical evidence of infection or abruption, labor pain started spontaneously, or fetal assessment was not-reassuring.

Expectant management of patient with PPROM:

Expectant management involve:

- Hospitalization: most patients with PROM should be admitted to hospital for rest and surveillance for early signs of chorioamnionitis (maternal temperature, uterine tenderness and contractions, maternal and fetal heart rate, change in color or smell of vaginal discharge)
- Antibiotic prophylaxis: To reduce the frequency of maternal and fetal infection and delay the onset of preterm labor.
- Fetal surveillance: e.g., kick counts, non-stress tests, biophysical profile [BPP]) to provide the clinician and patient some assurance of fetal well-being.

Method of delivery of patient with PPROM: the method of delivery depends on several factors. However if there is no obstetric complication (e.g. breech presentation) other than PROM the aim should be for vaginal delivery. A digital cervical examination is performed to assess whether cervical ripening has occurred. If the cervix is favorable, oxytocin is administered for induction according to standard protocols.

If cervix is not rip one or two doses of prostaglandin can be used to induce cervical ripening followed by oxytocin infusion.

Reference and Further readings:

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Chapter 22

Multiple gestations

Dr Nisma Manosuri

Multiple gestations usually twins and less commonly higher order (e.g. triplets, quadruplets or more) is always a fascinating biological phenomenon. While it is usually received by joy and happiness from the parent's point of view, obstetricians and pediatricians are full aware that multiple gestation and multiple birth carries significantly higher fetal and maternal risks. This chapter discusses the phenomenon of twin gestations, its associated maternal and fetal risks and its management during pregnancy and labor. Higher order pregnancies are associated with even higher rate of potential complications.

By the end of this chapter you should be able to:

- Define Chorionicity and Zygosity.
- List the frequency of each of MZ and DZ twins.
- **List the** complications of twin pregnancy:
    - Increased rate of pregnancy associated complications: hyperemesis gravidarum, pressure symptoms, anemia, PET, polyhydramnios with its associated complications and placental complications.
    - Fetal: miscarriage and the vanishing twin, genetic abnormalities, FGR, and Preterm Birth.
    - Unique complications of Monochorionic twin: TTTS, TRAP syndrome, Fetal Growth discordance, Twin reversal transfusion syndrome and conjoined twin.
- **Describe** the management of twin during pregnancy and the role of US
- **List** the specific complication during labor
- **Describe** the princple of management of twin during labor

Pathophysiology

Twins can be either monozygotic (MZ) or dizygotic (DZ).

Zygosity refers to the genetic make-up of a pregnancy.

- DZ twins: develop when 2 ovum each fertilized by a separate sperm. Such twins are genetically distinct as much as other children born to the same parents .

- MZ twins: develop when a single ovum at some points after fertilized splits into two distinct individuals. Such twins are not only of the same sex but almost always genetically identical. On very rare occasions genetic discordance may occur secondary to genetic mutations in one of the twin , which result in phenotypic and chromosomal dissimilarities between MZ twins.

Chorionicity: Refers to the pregnancy's membranes and placentas composition.

In DZ twin each embryo will have its own placenta and amniotic sac "dichorionic diamniotic placentas". Even if the placentas appears "fused" together, there is no real vascular connection (Figure 22-1)

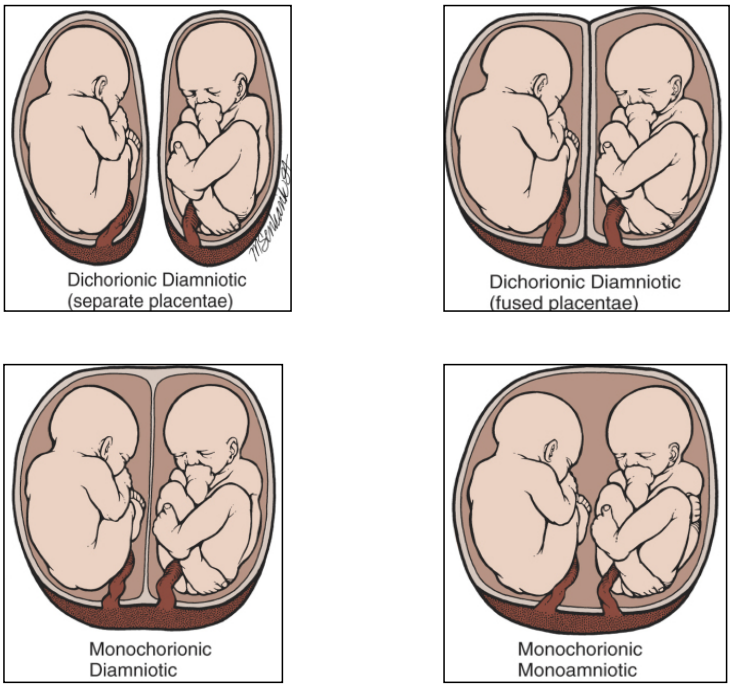


Figure 22-1: A and B Dichorionic Diamniotic Twins. No Vascular connection even if the placentas appears fused. D and E Monochorionic Diamniotic and Monoamniotic vascular communication and risk of TTTS in 15 % of cases.

- **In MZ twin** the type of placenta that develops is determined by the timing of cleavage of the fertilized ovum (Figure 22-2)

- Cleavage in the first 2 to 3 days, before the formation of the chorion, results in dichorionic diamniotic MZ twin" (30% MZ twins).

- Cleavage between the 3-8 days, after formation of chorion results in diamniotic monochorionic placenta (70% of MZ twins).

- Cleavage between 8th - 13th day, after the amnion is already formed, results in monoamniotic and monochorionic (1% of MZ twins).

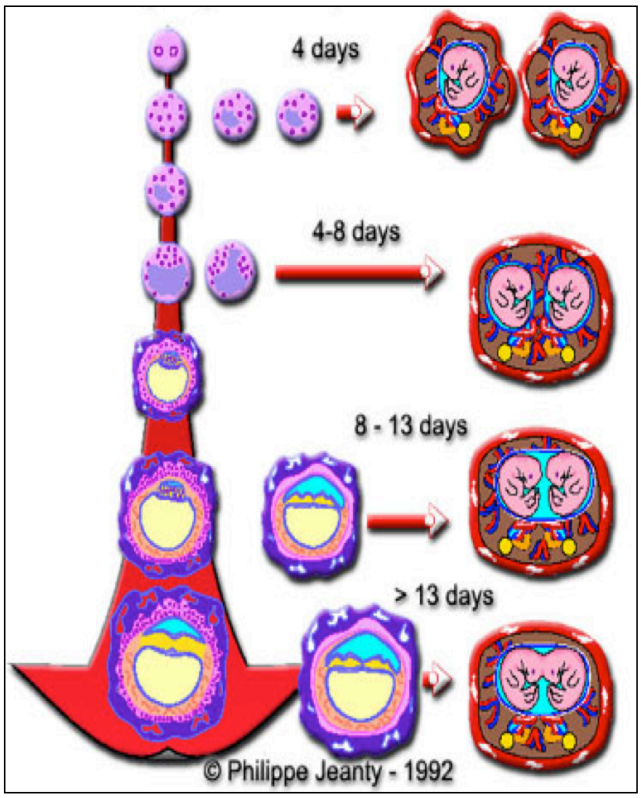


Figure 22-3: Relation of time of cleavage after fertilization to Chorionicity in MZ twins

- Embryonic cleavage between the 13th and 15th days will result in conjoined twins within a single amnion and chorion; beyond that point, the process of twinning cannot occur.

Frequency:

- Dizygotic twins: form approximately two thirds of twins. Its incidence, however, varies between **races** and is affected by several other factors

including **maternal age** and **parity (**it increases with age and parity**)**. In general, the frequency of DZ twins is low in Asians, intermediate in whites, and high in blacks. In some African it can reach as high 45 twins per 1000 live births.

- Monozygotic Twins: In comparison to DZ twins the incidence of monozygotic twins is constant worldwide (approximately 4 per 1000 births).

Frequency of Higher order gestation: Naturally occurring triplet births occur in approximately 1 per 7000-10,000 births; naturally occurring quadruplet births occur in approximately 1 per 600,000 births.

However the prevalence of multiple gestations is increasing worldwide due to the widespread use of assisted reproductive techniques and advancing maternal age at conception.

Mortality/Morbidity

Multifetal pregnancies are associated with increased rate of morbidity and mortality for both the mother and the fetus during pregnancy and in labor.

Complications during pregnancy:

- The general pregnancy "complications": such as hyperemesis gravidarum, anemia and pressure symptoms occur at higher rate and may be more severe with mutifetal pregnancy than in singleton pregnancy.
- Serious complications that occur more often in twins:
  - Pre-eclampsia is more frequent with multiple gestations and specifically it develops earlier in multifetal than with singleton gestation.
  - Polyhydramnios: A recognized complication of multiple gestation. It contributes to the increased risk of preterm labor, premature rupture of membranes, and abnormal fetal lie.
  - Placental abnormalities and complications: such as placenta previa, abroptio placenta. Vasa-previa with the risk of fetal exsanguinations occur more frequently in multifetal gestation

which is attribute to velamentous cord insertion.

- However the two major complications of multiple fetal pregnancies that are responsible for the increased perinatal mortality and morbidity are **preterm delivery**, **and fetal growth restriction**.

Approximately 50 % of multiple pregnancies are premature (< 37 weeks) compared to about 10% of singletons. Similarly about 60% of multiples are low birth weight (<2500 g) compared with about 6% of singletons. The mean gestational age at delivery and mean birth weight correlate with the fetal numbers.

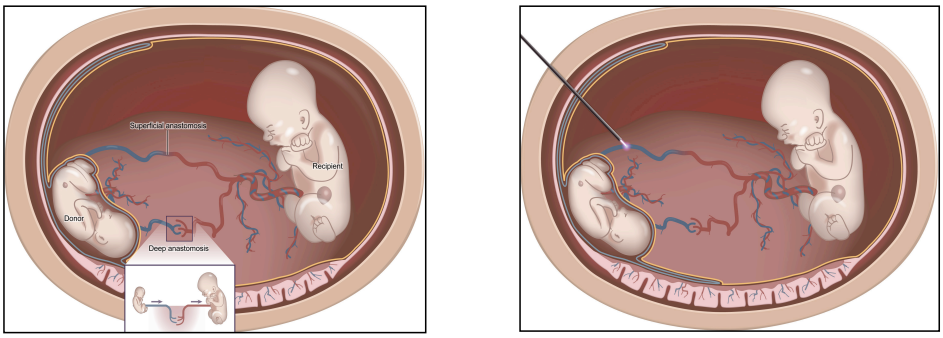
- Complications specific to Twin (multifetal gestations):

A a number of fetal complications are specifically associated with twin gestation (and multiple fetal gestation)

- Congenital anomalies and genetic disorders: occur at higher rate in multiple gestations compared to singleton. In addition the prenatal diagnosis is more complicated as well as counseling and management if one of the fetuses is abnormal while the other is normal.
- Early fetal Wastage (miscarriage): The widespread uses of early ultrasound scanning have shown that a large proportion of twin pregnancies scanned in the first trimester will turn up into single birth. This is often described as the "vanishing twin" phenomenon. The condition usually has no adverse effects on a coexisting fetus.
- Twin-to-Twin Transfusion Syndrome (TTTS): TTTS is a specific complication of monochorionic pregnancies. In almost all of monochorionic pregnancies there is vascular communication between the twins at the placental site. For reasons that are not clear, in only 15 percent to 20 percent of monochorionic diamniotic twins, the blood flow through these blood vessel connections becomes unbalanced, resulting in a condition known as twin-twin transfusion syndrome (TTTS). It causes under-perfusion of the donor twin and over-perfusion of the recipient. Both twins are at risk. The donor twin often develops fetal

growth restriction "FGR" and oligohydramnios, whereas the recipient experiences volume overload and polyhydramnios that may lead to heart failure and hydrops. The syndrome can present at any gestational age. Earlier onset is often associated with poorer prognosis. Without treatment the perinatal mortality in TTTS exceeds 80% (Figure 22-4).

- The treatment options of TTTS: include amnio-reduction, septostomy, selective feticide and laser ablation of placental vasculature, all are procedures that can only be performed in highly specialized fetal medicine unit.



"A" "B"

Figure 22-4: "A" In TTTS, the donor twin does not get enough blood, its growth is restricted, and develop oligohydramnios. The Recipient twin is overloaded and at risk of cardiac failure, and polyhydramnios. "B" Show treatment with laser coagulation of the communicating vessels.

- Twin-reversed arterial perfusion (TRAP) sequence (Twin Acaria): It is an unusual form of TTTS that occurs in about one in 15,000 pregnancies in which one twin develops normally while the other twin fails to develop heart (the acardiac twin) as well as other

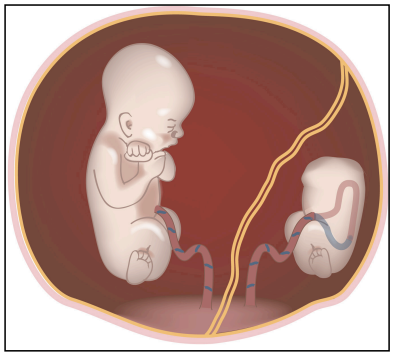


Figure 22-5: TRAP

body structures. The blood flow directly from the normal twin (called pump twin) into the acardiac twin. Because of functional overload the pump twin eventually develop heart failure and polyhydramnios. In some cases the blood flow from the "Pump twin" to the "Acardiac" twin stops on its own and the acardiac twin stops growing. In others the flow continue and acardiac twin increase in size.

Without treatment, more than 50 percent of cases of TRAP will result in the death of the pump twin.

Growth Discordance: This complication is diagnosed if the difference between the estimated weights and/or the abdominal circumferences of the two fetuses is more than 20%. This complication occurs in both MZ and DZ twins. In MZ twins the most common cause is TTTS. In DZ twins it could be due to uteroplacental insufficiency, gestational hypertension, velamentous cord insertion, and antenatal bleeding. It could also indicate genetic abnormality in one of the twins.

- Conjoined Twins: Conjoined twins occur with a frequency of about 1 per 50,000 deliveries and are an extremely rare complication of monochorionic twinning. The precise etiology of conjoined twinning is unknown, but the most widely accepted theory is that incomplete division of a MZ embryo occurs at approximately 13 to 15 days' post ovulation. The prognosis and management depends on the type and the organs shared between the twins.

- Death of One Twin in Utero: This complication occurs in approximately 0.5 to 6.8 percent of twin pregnancies with more frequency in MZ than DZ twins.

In multiple gestation death of one of the fetuses can adversely affect the surviving fetus or fetuses in several ways: (1) in case of monochorionic pregnancies, the surviving twin is at risk for multiorgan damage, including severe neurologic compromise most

probably due to acute hypotension and/or intravascular thrombi affecting the circulation of the surviving twin (2) preterm labor and delivery (3) in rare instances the mother may be at risk, albeit theoretical, of developing coagulopathy.

Complications during labor: The increased complications during labor are due to several factors include:

- Increased rate of operative delivery.
- Higher rate of fetal hypoxia and distress, particularly for the second twin due to increased risk of placental and cord accidents such as abruption placenta or cord prolepses.
- After deliver the mother is at risk of postpartum hemorrhage due to uterine over distension and larger placental bed.

Diagnosis of Multiple pregnancies:

In modern obstetric practice the diagnosis of multiple pregnancies is made during routine ultrasound scan examination, which is currently available in almost all obstetrics units.

In the absence of ultrasound examination multiple pregnancy should be suspected in the following cases:

- Presence of exaggerated symptoms of nausea and vomiting (hyperemesis gravidarum) especially in patient with family history of multiple pregnancy or who have ovulation induction.
- Polyhydramnios or large for gestational age uterus in the second half of pregnancy.
- The palpation of multiple fetal parts during routine examination and auscultation of two heart rates of > 20 bpm difference.

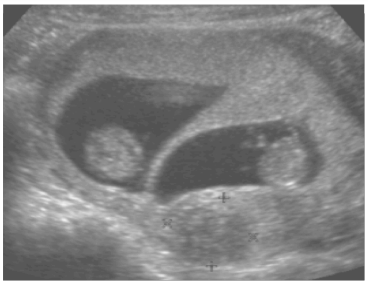
Management of Twin Pregnancy:

The management of twin pregnancy can be considered under the following sections: 1) Management during pregnancy and 2) management during labor.

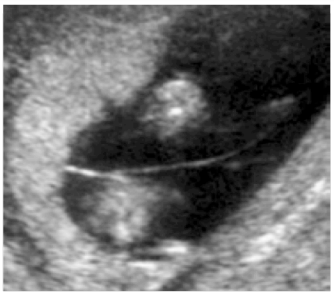
Management during pregnancy:

Once a diagnosis of multiple pregnancies is made patient should be referred for specialized ultrasound examination. The specific objectives of this examination are: (1) to determine the number of fetuses (2) to determine the

amnionicity/chorionicity of the twins (3) To screen for nuchal translucency and fetal anomalies. The differentiation between monochorioinc and dichorionic gestation can by made by ultrasound scan early in gestation (before 14 weeks) by the presence of two sacs and a thick chorionic tissue in between, which gives characteristic sign on ultrasound examination known as the "lambda sing". As pregnancy progress this sign disappear and the determination of chorionocity becomes difficult especially if the twins are of the same sex with adjacent placentas.



"A"



"B"

Figure 22-6: "A" ultrasound picture at 9 weeks gestation shows the thick chorionic tissue between the two sacs "lambda sing" in cases of dichrionic twins. "B" the lambda sing is absent in a pregnancy of the same gestation. The "lambda sing" disappear as pregnancy progresses and diagnosis of chorincity becomes difficult if twin are of the same gender.

Follow up visits: During the follow-up visits the parents should be educated as to the specific issues of a multifetal pregnancy.

- The potential complications that need special care during the routine antenatal follow up include anemia, monitoring of blood pressure for early detection of pre-eclampsia, and general advice for diet and rest.

- The risk of preterm labor is higher in twin pregnancies. Although there is no effective prophylactic measure, but patient should be advised to observe for signs of early labor, in some cases steroids for lung maturation may be administered around 26 weeks and arrangement should be made ready with pediatric units if labor begins.

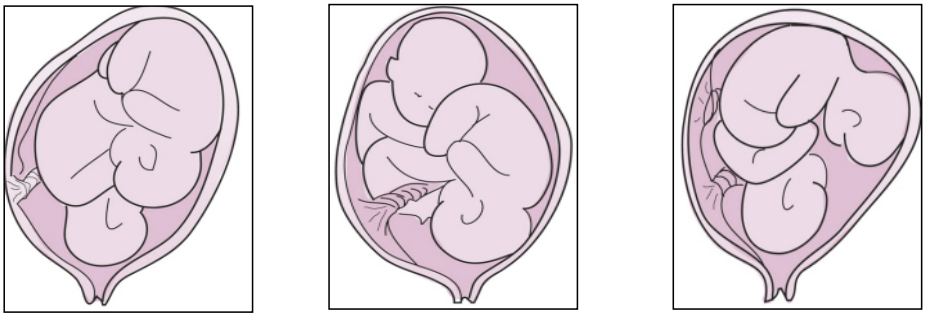
- For monitoring of fetal growth serial ultrasound examination should be initiated from approximately the 26 weeks and every 3-4 weeks.

Generally in low risk twin (dichorionic, diamniotic) with no signs of growth discordance or anomalies the prognosis is usually good and follow up may be scheduled as usual. Other cases however will require specialized care and follow up in high-risk pregnancy clinic.

- As the patient reach 34 or 36 weeks arrangement for delivery should be discussed with the patient including the mode of delivery.

Management during labor:

The mode of delivery: It depends on several factors most importantly are the gestational age and estimated weights of the fetuses, their positions relative to each other (figure 22-6). The most common presentation of twins is vertex- vertex presentation, which can usually be delivered vaginally. When the first presenting twin is in a nonvertex presentation (breech or transverse) delivery is usually by cesarean section. However if the presenting fetus is vertex and the second is in breech or transverse lie the optimum mode of delivery is controversial and should be discussed with the patient.



A B C

Figure 22-7: If both twins are vertex the delivery is usually vaginally (A). If only the first twin is vertex, the mode of delivery is controversial (B) and (C). If the first twin is non vertex the delivery is by.CS.

Management in labor: In addition to the standard preparation and care for normal labor, the management of patients with multifetal gestation requires additional care.

- The first stage: Fetal monitoring should be undertaken for both fetuses. The best approach is to monitor the first twin internally by scalp electrode and the second twin by external monitoring.
  Epidural analgesia: is the preferred method since in addition to its analgesic effect it allows manipulation and intervention if that becomes necessary with the delivery of the second twin.

- The second stage:
  - Pediatric neonatologists (at least two) should be present and ready to take care of the newborns. Also the anesthetist and the theatre team should be available and ready for immediate intervention if needed.
  - Once the first twin is delivered the lie of the second twin should be ascertained by abdominal palpation and or ultrasound examination if necessary. The second twin is at risk of acute fetal hypoxia due to placental compression, abruptio placenta or cord prolapse, therefore the fetal heart of the second twin should be carefully monitored. The interval between the delivery of the first and second twin may be as long 30 minutes but usually less. The optimum treatment if the second baby has not been delivered after half an hour in the absence of signs of fetal distress is not clear. The options include, instrumental delivery with ventous or forceps, breech extraction (under epidural anesthesia) or cesarean section. The choice depends on the presenting part, the dilatation of the cervix, fetal size, and operator skill.
- The third stage: Since multiple gestations is one of the recognized risk factors for postpartum hemorrhage, the third stage should be carefully attended and actively managed. In all cases of multiple gestations it is prudent to maintain blood cross-matched and ready if needed.

Immediately after delivery the neonatologist should take care of the babies as necessary. The mother should be maintained under observation for fear of

uterine atony and postpartum hemorrhage before she is returned back to her room.

Chapter 23

Fetal Growth Restriction

Fetal growth is a complicated process that is primarily determine by the genetic make up of the conceptus but is also be influenced by several intrinsic and extrinsic factors in fetus, mother or the placenta.

During pregnancy the diagnosis of pathologically abnormal fetal growth is challenging not only because it is difficult to accurately estimate the fetal weight but also because not all fetuses within the "normal" range are necessarily normal, similarly not all fetuses outside those ranges are abnormal. Inaccurate diagnosis may results in either overlooking a compromised baby or over treating a healthy constitutionally small baby. Therefore one of the primary objectives of antenatal care is to detect fetuses who are failing to achieve their growth potential, assess their wellbeing and accordingly plan for appropriate management.

By the end of this chapter you should be able to:

- **Define**: Small for gestational age vs. intrauterine fetal growth restriction.
- **List the complications and Risks of SGA**: Short, long term and adulthood morbidity
- **Describe:** the normal pattern of fetal growth and pathogenesis of FGR.
- **List** the main etiology and associated factors of of SGA & FGR: Fetal, placental and maternal factors.
- **Describe** the steps in the diagnosis of FGR. **:** first suspected then confirmed.
- **Describe** the principle of Management of GRF: Depends on Etiology, Severity and Gestational age.

⇒ The Small for Gestational Age Fetus (SGA):

-

A small for gestational age fetus is defined as fetus whose weight is below the tenth percentile for the gestational age. This definition is controversial because it comprise heterogeneous group of healthy and unhealthy fetuses. In other word not all fetuses below the tenth percentile for a given gestational age are unhealthy (i.e. suffer from growth restriction "GR"), similarly not all fetuses within the normal range are healthy (they may sill suffer from GR) (Figure 23-1).

⇒**Fetal Growth Restriction**: Is a pathological condition in which the fetus does not achieve its destined size or weight. A fetus may suffer from "growth restriction" even though its absolute weight might be within the "normal" range for the gestational age.

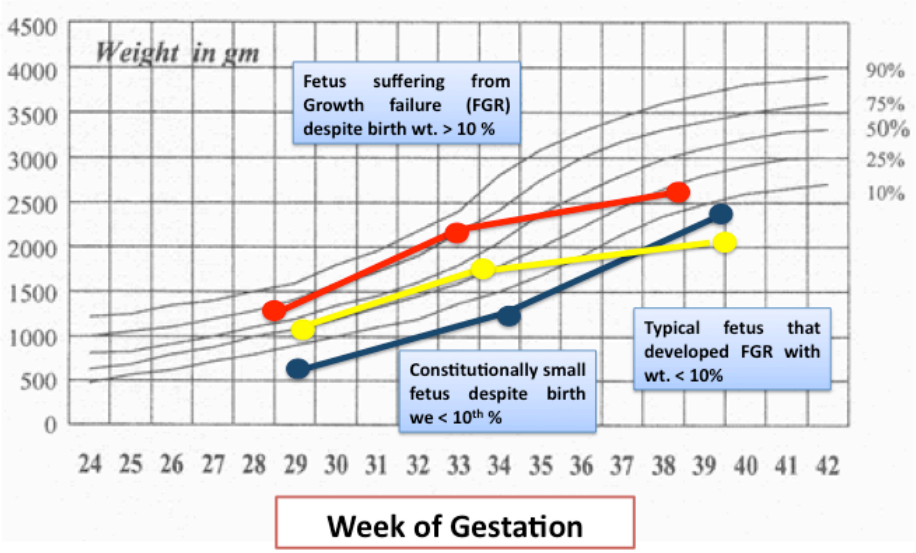


Figure 23-1: Three patterns of fetal growth: the "blue line" is constitutionally small baby. The "yellow line" true fetal growth restriction. The "red line" a growth restricted fetus that is still weight above the 10th percentile.

⇒Prognosis and Risks of SGA:

Fetal growth is important because there is an inverse relationship between the fetal/neonatal weight percentile and adverse perinatal outcome, with the greatest risk at weights below the third percentile for gestational age. This is because most of fetuses below the third percentile are suffering from growth restriction and not simply constitutionally small (Figure 23-2).

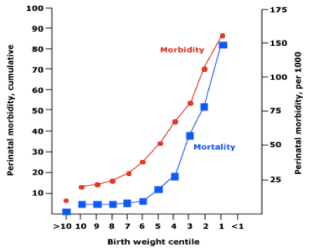


Figure 23-2: Fetal morbidity and mortality increase sharply with birth weigh <5 % .

Epidemiological observational data have shown that there is increase in the short and long term morbidities in association with low birth weight.

Short-term morbidities: include impaired thermoregulation, hypoglycemia, polycythemia/hyperviscosity, and impaired immune function. Increased risks of acidemia, respiratory distress, intraventricular hemorrhage, and necrotizing enterocolitis.

Long term morbidities: the IUGR babies are more prone to various degrees of impaired neurodevelopment that range from slight delayed performance at school to cerebral palsy. The worst outcomes have been observed in growth-restricted infants who in addition to exposure to in-utero hypoxia are also born preterm.

Adulthood morbidities: More recent data have shown that low weight at birth is associated with increased risk of development of some adulthood disorders such as hypertension, hypercholesterolemia, impaired glucose tolerance, and ischemic heart disease. The hypothesis proposes that the endocrine-metabolic reprogramming that enable the growth restricted fetus to compensate for the hostile intrauterine environment predispose to development of such disorders in adulthood.

⇒Pathogenesis of FGR:

Fetal growth is accomplished through a combined process of cellular hyperplasia and hypertrophy. In the embryonic and early weeks of fetal growth, hyperplasia dominates, but as pregnancy progress the role of hypertrophy becomes more important.

This pattern of fetal growth forms the basis of the clinical classification of fetal growth restriction "FGR" into the two major varieties:

- **Symmetric FGR**: It refers to a proportional restriction of fetal growth. It comprises 20 to 30 percent of growth-restricted fetuses. It usually results from insults at the early stages of fetal cellular hyperplasia, which causes decrease in the total fetal cellular mass "number". The typical examples are FGR due to genetic diseases and early fetal infection,. FGR in such cases is characterized by symmetrical decreases in the whole fetal size and organs.
- **Asymmetric FGR:** refers to disproportionate FGR. It comprises 70-80% of cases FGR. It is due to insults that develop in the second half of gestation at the stage of cellular hypertrophy. In response to such insults the fetus tries to adapt to the diminished nourishment (and hypoxia) by redistribution of blood flow to the vital organs (i.e. brain, heart, and adrenals) at the expense of non-vital organs (e.g., abdominal viscera, lungs, skin, kidneys). The typical examples are asymmetrical FGR due to placental insufficiency as in cases of preeclampsia or severe maternal nutritional deficiency in the second half of pregnancy. FGR in such cases reflects the fetal attempts to spare the vital organ therefore there is greater decrease in abdominal size (e.g., liver volume and subcutaneous fat tissue) than head circumference. This sometimes is described as "brain sparing phenomenon" or feature.

However it should be remembered that there is considerable overlap between the two verities of FGR. Therefore while defining the type of FGR help to identify the cause this is not always a straightforward matter.

⇒**Etiology of Fetal Growth restriction**:

Fetal growth restriction may be caused by fetal, placental, or maternal factors, often with contributions from multiple factors.

- **Maternal factors**:
  - Poor Nutrition: Maternal undernutrition is associated with increased risk of FGR. Studies have shown that maternal weight at the

beginning of pregnancy and maternal weight gain during pregnancy are related to fetal growth.

- Hypoxemia: Women residing at high altitude are at higher risk of having FGR than women residing at sea level. Also some chronic diseases that cause maternal hypoxemia such as chronic lung diseases, cyanotic heart diseases, and severe anemia (sickle cell anemia) increase the risk of FGR.
- Pro-thrombotic disorders: Hematological and immunologic disorders that cause thrombosis of the intervillous space and thus decrease uteroplacental perfusion (e.g. antiphospholipid syndrome).
- Hypertension and vascular diseases: could be due to maternal medical disorders (e.g. nephropathy, collagen vascular disease) or obstetrical complications (e.g. preeclampsia) associated with vasculopathy and diminished uteroplacental perfusion.
- Infections: Viruses and parasites (e.g. rubella, toxoplasmosis, cytomegalovirus, varicella-zoster, malaria) especially if it occurs early in pregnancy are associated with symmetrical type of FGR.
- Substances abuse: including cigarette smoking, alcohol consumption, and illicit drug use can cause FGR either by a direct cytotoxic effect or indirectly from related variables, such as inadequate nutrition.
- Toxins: Toxic exposures, including various medications such as Warfarin, anticonvulsants, antineoplastic agents, and folic acid antagonists, can produce FGR with specific dysmorphic features.
- Socio-Demographic factors: such as race, pregnancy at the extremes of reproductive life, and previous delivery of a FGR neonate.

- **Placental Factors:**

  - Placental insufficiency could be idiopathic or secondary to maternal diseases such as thrombophilia and type I diabetes with vasculopathy or obstetric complications such as preeclampsia.
  - Other gross placental conditions that have an association with FGR include: single umbilical artery, velamentous umbilical cord insertion, bilobate placenta, placental hemangioma, abruptio placenta and, placenta previa.

- **Fetal Factors:**

- Genetic: Genetic factors contribute to approximately 40 percent of the variation in birth weight, with the remainder due to environmental factors. Therefore a large proportion of SGA fetuses are constitutionally and not pathologically small (i.e. do not suffer from restriction of growth). It is important to identify this subgroup of SGA in order to avoid unnecessary intervention.
- Chromosomal abnormalities: The presence of a chromosomal abnormality often results in the appearance of FGR early in pregnancy, most likely of the symmetric type.
- Congenital anomalies: Major congenital anomalies are frequently associated with failure to maintain normal fetal growth.
- Multiple gestations: Fetal growth in multiple gestations has a direct relationship to the number of fetuses present. Growth of twins is similar to that of singletons until 28 to 30 weeks and then slows such that the weight of an individual fetus of a multiple gestation is 15 to 20 percent less than that of singletons of the same gestational age.

⇒Diagnosis of FGR fetus:

The diagnosis of "pathological" FGR can be difficult. Approximately 50-70% of the fetuses suspected to have growth restriction are simply healthy (constitutionally) small for gestational age (SGA) fetuses (Figure 23-1). The challenge is to identify the 25% who suffer from growth restriction and intrauterine hypoxia.

In practice the first step is to suspect FGR based on the clinical history and/or examination. The second step is to confirm or refute the diagnosis based on further tests for assessment of fetal wellbeing. The management then will depend on the cause of FGR and gestational age.

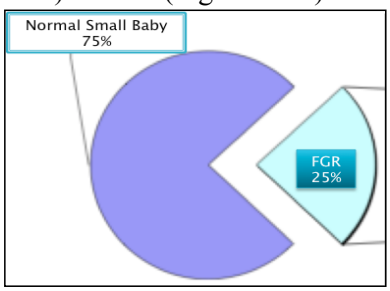


Figure 23-3: Approximately75% of SGA Fetuses/infants are healthy constitutionally small while 25% will turn out to have GR

- Suspecting FGR is usually based on:
  - The maternal history: which might identify one or more of the risk factors associated with fetal growth restriction (Table 23-1).
  - The obstetric examination: the finding of more than three centimeters discrepancy between the "symphysis fundal height" measurements and the gestational age.
- Confirmation of the diagnosis: the suspicion of FGR is then confirmed or refuted by sonographic examination. The primary role of ultrasound is to differentiate between healthy constitutionally small fetus and the fetus that suffer from pathological growth restriction and hypoxia.

Conditions associated with IUGR
Maternal history
Prior history of IUGR pregnancy
Low pre-pregnancy weight
Malnutrition
Residing at high altitude
Smoking, Drug abuse, Alcohol
Use of prescription drugs warfarin (Coumadin, phenytoin)
Medical conditions (of mother)
Chronic hypertension
Preeclampia early in gestation
Diabetes mellitus
Systemic lupus erythematosus
Chronic kidney disease
Inflammatory bowel disease
Severe lung disease
Infectious diseases
Syphilis
Cytomegalovirus
Toxoplasmosis
Rubella
Hepatitis B
Herpes simplex virus 1 or 2
HIV-1
Congenital disorders (of fetus)
Trisomy 21 (Down syndrome)
Trisomy 18 (Edwards syndrome)
Trisomy 13 (Patau syndrome)
Turner's syndrome

Figure 23-1: Risk factors of FGR

The ultrasound diagnosis of IUGR is based on taking various fetal biometric measurements and correlates those measurements with established normal ranges for gestational age. Ideally the normal standard should be derived from the population being examined or even customized to the mother weight and height. The most sensitive measurements for the diagnosis of small for gestational age (SGA) are ultrasound estimated fetal weight and fetal abdominal circumference (AC) that are below the normal range (usually the 10^{th} percentile) for the gestational age.

In addition ultrasound examination can help to define the type of IUGR whether symmetrical or asymmetrical by estimating the fetal head to the

abdominal circumferences ratio. In asymmetrical FGR the ratio of the FH/AC measurements is above the normal standard for the gestational age .

⇒Management of IUGR:

There is no treatment or for fetal growth restriction i.e. there is no intervention that can make the fetus grow.

However once the diagnosis of FGR is confirmed the management of depends on: (1) the etiology of FGR, (2) the severity of the condition and (3) the gestational week at diagnosis (Figure 23-3).

Based on those data the plan of management is to decide on the appropriate time and mode of delivery. Until that time the frequency and extend of monitoring of fetal growth and wellbeing is designed according to the severity of the case.

- The etiology:

- A detailed history should be taken for maternal factors or systemic diseases that may be the cause of fetal GR. Tests for congenital and acquired thrombophilic disorders should be considered, especially when FGR is recurrent or early and severe or when there is a maternal or family history of thrombosis. Some maternal diseases such as severe preeclampsia or uncontrolled diabetes may require early delivery regardless of the fetal condition.
- A detailed sonographic examination should be performed for fetal anomaly. Fetal karyotyping should be considered if FGR occurs early (<32 weeks), severe (<3rd percentile), or accompanied by polyhydramnios (suggestive of trisomy 18) or in the presence of structural anomalies. The presence of fetal anomaly or genetic disease will often change the management plan according the type and degree of abnormality.
- Maternal serum should be examined for evidence of seroconversion if there is clinical suspicion of viral infection (e.g. maternal or fetal signs/symptoms of cytomegalovirus, rubella, and varicella).

In the majority of cases however there is no obvious cause for FGR and the management depends on the severity of the FGR and the gestational age.

- Severity of FGR:

- The severity of FGR, which is, the extent of intrauterine hypoxia is evaluated by the measures for fetal surveillance, which include: Ultrasound examination of biophysical profile, particularly amniotic fluid volume, and fetal Doppler blood flow study (see chapter on antenatal fetal surveillance).
- In FGR, Doppler velocimetry study (e.g. of umbilical and cerebral blood flow) is the primary surveillance tool. The use of Doppler velocimetry can significantly reduce perinatal death. A normal blood flow pattern is rarely associated with significant morbidity. Thus it allows prolongation of pregnancy and avoids unnecessary induction of labor in the preterm growth restricted fetus.

- The gestational week:

- At term or near-term a growth restricted fetus should be delivered.
- When FGR is mild with reassuring antepartum fetal testing results delivery can be delayed until at least 37 weeks when pulmonary maturity is likely.
- Fetuses remote from term, may be allowed to achieve further fetal maturity while under close monitoring provided the fetal Doppler velocimetry studies are within normal range. However, absence or reversal of diastolic umbilical Doppler blood flow is an ominous finding; in these cases prompt delivery is often indicated because of a high risk of fetal demise.

The mode of delivery and Management in labor:

The mode of delivery whether by elective cesarean section or induction of labour depends on (1) the fetal condition and whether or not it can stand the stress of labour and (2) the cervical Bishop score which predict the chances of success of labour.

If it is decided to allow for trial of vaginal delivery the overall management of labor is the same as in normal pregnancy. But it is important to realize

that the GR fetuses already exist in a state of mild-to-moderate chronic oxygen and substrate deprivation. The stress of labor is likely to aggravate such situation. Therefore close continuous intrapartum fetal monitoring should be performed to detect nonreassuring fetal heart rate patterns. Preparation for intervention should be ready with the presence of immediate skilled neonatal care.

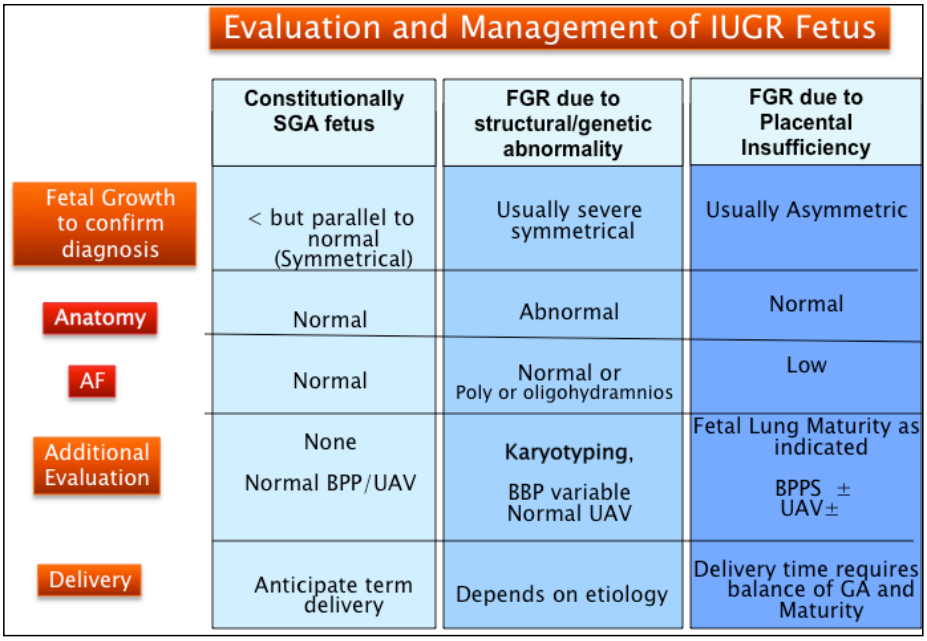


Figure 23-3: Summary of evaluation and management of SGA fetuses. 75% of cases will be constitutionally normal SGA and require standard follow up anticipating normal delivery. Of the remaining 25% some FGR will have genetic abnormality. The majority will be due to placental insufficiency the monitoring, timing and mode of delivery depends on surveillance tests. SGA=Small for gestational age, FGR=Fetal growth restriction, FH=fetal heart, UAV=umbilical artery Velocimetry, GA=gestational age, FM=Fetal movement, FH=Fetal heart.

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Chapter 24

Prolonged Pregnancy

Dr Nisma Manosuri

Fetal growth and maturation are continuous process, while the placenta has limited life span. Signs of placental aging are often observed towards the end of gestation. There is usually no problem as long as labor and delivery takes place at the expected time or shortly after (term + 2 weeks). If pregnancy is pregnancy beyond term the fetal requirements exceeds the capacity of the aging placenta and a state of relative placental insufficiency ensue. Such condition is known as post-term pregnancy. In postterm pregnancy both mother and fetus are at higher risks of serious complications compared to normal term pregnancy.

By the end of this chapter you should be able to:
Define Term, post-term pregnancy and post-maturity
"Prolonged pregnancy" "Postterm pregnancy" and "Post maturity"
List the fetal and maternal risks associated with post-term pregnancy
Counsel patients for appropriate management of posterm pregnancy.
Describe the principle of management of post-term pregnancy and labor.

Definition: "Prolonged pregnancy" "Postterm pregnancy" and "Post maturity" are terms that refers to a pregnancy that has extended to or beyond 42 weeks of gestation or 294 days from the first day of the last menstrual period. Accurate pregnancy dating is critical to the diagnosis.

Prevalence: The exact prevalence is not known because it depends very much on accurate dating. However among pregnancies dated by first trimester ultrasound examination, the prevalence of postterm pregnancy is only about 2 percent.

Risk factors:
The majority of postterm pregnancies have no known cause. It tends to be more common among primigravid and obese women. A history of prior postterm pregnancy is the most common identifiable risk factors. It is possible that there is genetic predisposition to such condition.

In rare instances postterm pregnancy may be associated with "placental sulfatase" deficiency or fetal anencephaly (in the absence of polyhydramnios).

Morbidity and mortality:
Postterm pregnancy is associated with increased in both fetal and maternal risks.

➢ **Fetal risks:**

1. The Perinatal mortality (i.e., stillbirths plus early neonatal deaths) at ≥42 weeks of gestation is twice that at term (4 to 7 versus 2 to 3 per 1000 deliveries) and increases four-fold at 43 weeks and five- to seven-fold at 44 weeks. Part of the increase in perinatal mortality is due to a higher rate of congenital anomalies among the postterm fetuses. The fetal mortality is mostly "intrapartum" and neonatal rather than during pregnancy.

2. Increased rate of macrosomia (4500 g) (2.5-10 versus 0.8-1 percent at term). This could lead to other complications such as prolonged labor, cephalopelvic disproportion, and shoulder dystocia, all of which increase the risk of birth injury.

3. Development of the "fetal dysmaturity (postmaturity) syndrome," This complicate about 20 percent of postterm fetuses. This syndrome is characterized by feature of chronic intrauterine malnutrition due to "relative placental insufficiency".
   - Oligohydramnios, which increases, risk of umbilical cord compression, nonreassuring fetal antepartum or intrapartum assessment tests.
   - The infant shows loss of subcutaneous fat and dry craked skin
   - Meconium staining and risk of meconium aspiration.

- Short-term neonatal complications (e.g. hypoglycemia, seizures, respiratory insufficiency, asphyxia and death).
- Long-term neurologic sequelae.

➢ **Maternal risks**: Maternal risks of postterm pregnancy are related to fetal macrosomia and operative intervention for nonreassuring fetal assessment which include: perineal lacerations, and cesarean delivery.

Management:
Patients who reach term should be counseled as to the options of management available and the evidence in support of each one.
The options of management are:
➢ Delivery at 41 + weeks or
➢ Expectant management with close fetal surveillance. Delivery should be initiated if fetal assessment is not reassuring or spontaneous labor does not occur.

Fetal surveillance should start around 41 weeks with twice weekly testing. The fetus is monitored by nonstress testing and the biophysical profile (BPP) or modified BPP test. The oxytocin challenge test, or a combination of these modalities may be used (see chapter 7 on antenatal fetal surveillance).

However patient should be informed that the weight of evidence from metanalysis of large number of randomized studies support delivery by induction of labor at 41+ weeks rather than expectant management. Studies have shown that induction at 41+ weeks was associated with significantly less perinatal mortality, and lesser rate of cesarean section compared to expectant management.

Management of labor:
In addition to the standard management, cases with postterm fetus are at higher risk of intrapartum fetal heart rate abnormalities and passage of meconium than the term fetus. For this reason, continuous electronic fetal monitoring should be applied.

Long-term prognosis:

The long-term outcome of the general intelligence quotient, physical milestones, and frequency of intercurrent illnesses are the same for term infants and those from postterm pregnancies.

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Chapter 25
RhD Isoimmunization in Pregnancy

Dr Entesar Al Madani

RhD isoimmunization remain a significant clinical reality and contributor to fetal and neonatal morbidity and mortality. Remarkable advances regarding this hemolytic disease process, however, have been made over the past decades. Still, there remains a 1% isoimmunization rate among women who are RhD negative, which warrant spending effort understanding the disease process and the current management regimens. This chapter describes the basics of RhD alloimmunization, including current prenatal testing and management techniques. In addition it addresses the appropriate consensus use of anti –D immunoglobulin.

By the end of this chapter you should understand:

- **Types of antibodies "iso-immunization" during pregnancy:**
- **Biochemistry and Genetic of Rh Antigen:**
- **Genetic Expression (Antigenicity of the Rh surface protein):**
- **Exposure the maternal immune system to fetal Antigen (Rh positive fetal cells):** The occasions of Maternal Immunization to Rh +ve Fetal Red Cells.
- **Determination of the presence of fetal cells in maternal blood:** The Kleihauer test
- **The Mechanism of Development of the Rh Immune Response:** the first and second immune response and the characteristics of each
- **Exposure to maternal antigen in utero "the grandmother theory":**
- **Factors that influence the risk of Development of Maternal Isoimmunization:** why only 16 % of exposed Rh negative mothers develop isoimmunization
- **Prevention of Maternal Isoimmunization:**
- **Pathogenesis of Fetal Alloimmunization:** And factors that influence variation in disease severity
- **Management of the Rh Isoimmunization:**
    - Prevention in Rh negative non-immunized women:
    - Management of Rh negative immunized women:
        - Role of antibodies Titer in screening and management
        - Role of Ultrasound and MCAV Doppler studies
        - Role of Amniocentesis and the Lilly's curve

Hemolytic disease of the fetus and newborn is a condition in which the life span of the fetal or neonatal red blood cells is shortened by the action of maternal antibodies against antigens present on the fetal or neonatal red cells. When fetal blood group factor inherited from the biological father is not possessed by the mother, antepartum or intrapartum fetomaternal hemorrhage (FMH) may induce immune reaction by the mother.

CDE (Rhesus) And Other Blood Group Incompatibilities there are hundreds of erythrocyte antigens that have been described in the literature, but only few are clinically important causes of maternal isoimmunization that lead to fetal cell hemolysis. Alloantibodies known to cause hemolytic disease of the newborn include antigens against the Rh blood-group system (c, C, D, e, E) and those of the Kell, Duffy, and Kidd and M, N, S, and s systems. The most notorious is the anti-D antibody that is directed against the D antigen of Rh blood group system. RhD negative women who are exposed to RhD- positive fetal red blood cells can produce this antibody during their pregnancies.

The CDE genes are inherited independent of other blood group genes and are located in the short arm of chromosome 1. They appears early in embryonic life and has been demonstrated on the red blood cells as early as 38 days after conception. There is no difference in the distribution of the CDE antigens with regard to sex, but there are important racial differences. Native Americans, Inuits, and Chinese and other Asiatic people are almost all D positive (99 percent). Approximately 92 to 93 percent of African Americans are D-positive, but only 87 percent of Caucasians carry the D antigen. Of all racial and ethnic groups studied thus far, the Basques show the highest incidence of D-negativity (34 percent). Individuals with an Rh-positive blood type have the D antigen present in their erythrocytes, whereas individuals with Rh-negative blood type do not.

The physiologic role of the Rh peptides is uncertain, but the few persons who express no Rh peptides may potentially develop hemolytic anemia. Thus, the Rh antigen is thought to play role in maintaining erythrocyte membrane integrity. The expression of the Rh antigen on the red blood cell membrane is genetically controlled, not only in term of the structure of the antigen but also the number of specific Rh antigen sites present.

The description of various Rh phenotypes and gentypes is beyond the scope of this chapter; however, one should realize that gene dosage has an effect on the

number of specific Rh antigen sites that express antigen. Individuals who are homozygous for a particular genotype have up to twice as many antigen sites as individuals who are heterozygous. In short, not all pregnant Rh-negative women will respond in the same way to an RhD-positive invasion and, thus, the effect on the fetus will vary from case to case even when FMH is held constant.

In case of RhD, the primary Immune response results in generation of Immunoglobulin M (IgM) which, due to its high molecular weight, unable to cross the placenta. With a secondary antigenic challenge, the immune response appear more quickly, attains a higher titer, and consist predominantly of IgG which is of lower molecular weight and thus able to cross the placental barrier and destroy red blood cells. The pathogenesis of hemolytic disease of the newborn is similar for all antibodies.

ABO blood group Incompatibility has been shown to afford protection against RhD sensitization. Typically the mother is type O and the fetus type A or B. With intermixing of blood, the naturally occurring antibodies in the maternal circulation (anti-A or anti-B) bind to the corresponding antigen on the surface of the fetal erythrocytes, causing complement fixation with subsequent hemolysis. Theoretically, this occurs prior to recognition by maternal immune system leading to immunization.

Source of Immunization the most common cause of Rh alloimmunization is fetal maternal transplacental hemorrhage. As determined by the Kleihauer acid eluation test, a transplacental hemorrhage occurs with 75 percent of pregnancies. Sixty percent have transplacental hemorrhage of less than 0.1ml, less than one percent has greater than 5 ml, and less than 0.25 percent has greater than 30ml. As little as 0.1ml of RhD-positive blood from transplacental hemorrhage is sufficient to cause alloimmunization in Rh-negative women. The incidence and volume of transplacental hemorrhage increases with advancing gestation. Five to fifteen percent women in the first trimester have transplacental hemorrhage of less than 0.1 ml compared to 45 percent of women in the third trimester with more than 0.1 ml transplacental bleeds. There is also estimated risk of transplacental hemorrhage associated with: spontaneous abortion (5 – 10%), therapeutic abortion (20 -25%), amniocentesis (2.5%), chorionic villus sampling (14%), external cephalic version (2-6 %) and ectopic pregnancy.

Blood transfusion remain the most common cause of alloimmunization with atypical or irregular (non-RhD) antibodies, as blood prepared for transfusion is matched only for ABO and RhD .

- Biochemically: The Rh antigen is a complex lipoprotein which is the products of the Rh gene distributed throughout the erythrocyte membrane in a nonrandom fashion. It cannot be seen by routine microscopy, but can be identified by specific antisera.

Rh antigen lipoprotein complex is formed of three components: the C, D, and E antigens. Two of these antigens (proteins), namely C and E have alleles that can be identified immunologically (again can be detected by specific antisera). However for the third component, D antigen, no antigenic allele has been identified i.e. no antisera specific for a "d" antigen has been found.

Thus there are three pairs of Rh antigens, commonly Dd, Cc, and Ee. The presence of D indicates an Rh (D)-positive person. The absence of D, not the presence of d, which has never been proved to exist, denotes an Rh (D)-negative person.

Inheritance: The antigens are inherited in two sets of three, one set from each parent. Thus the Rh genotype of a person is designated by the appropriate three letters e.g. CDe, c(d)e, phenotypically this person is Rh positive.

About 50 % of people are homozygous for D (*i.e.,* they have inherited a set of antigens containing D from both sets of parents). The remainders are heterozygous for D (*i.e.,* they have inherited a D-containing set from only one parent).

⇒**Epidemiology:** Rh negativity (absence of D antigen) is a trait of white people. In most whites, the incidence is 15% to 16%. It has wide variation among other races: about 1%; American blacks, 7% to 8%; Indo-Eurasians, about 2% to 4%; Asiatic Chinese and Japanese, almost zero. Among local population in Saudi Arabia the rate of Rh negative is around 4%.

⇒ **Genetic Expression (Antigenicity of the Rh surface protein):**

Factors, which affect the degree of expression of the Rh antigen on the erythrocyte membrane, include:

- The degree of genetic expression of the D antigen. Incomplete expression may result in a weakly positive patient e.g. D^u variant (they may even be determined as Rh negative). A mother with D^u Rh blood group may become

sensitized from a D-positive fetus (although she herself is genetically positive) or the other way around may take place.
- The relative position of the alleles, and the presence or absence of regular genes.
- Interaction of other components of the Rh blood group: For example, erythrocytes of individuals of genotype Cde/cde express less D antigen than do the erythrocytes of individuals of genotype cDE/cde. Thus, the presence of the C antigen seems to affect the expression of the D antigen.
- The exposure of the antigen protein on the surface of the red cell membrane.

⇒**Exposure the maternal immune system to fetal Antigen (Rh positive fetal cells):** Studies show that 75% of women have a fetomaternal transplacental hemorrhage "TPH" during pregnancy or at the time of delivery. In about half of these women, the TPH does not exceed 0.1 mL of fetal blood. Less than 1% has more than 5 mL, and less than 0.25% has more than 30 mL of fetal blood in their circulations. The amount of TPH necessary to cause Isoimmunization is not known. But studies on Rh-negative men volunteers showed that as little as 0.1 mL of Rh-positive could induce sensitization.

The following are specific circumstances for occurrence of transplacental hemorrhage (TPH):

- -At the time of delivery (occur in 15-50 % of births) the risk increase with procedures such as cesarean section or manual placental removal.
- -Complications such as miscarriage or ectopic pregnancy are other sources of exposure of the maternal immune system to fetal antigen. After spontaneous abortion fetomaternal hemorrhage and subsequent risk of development of isoimmunization is about 1.5% to 2%. The risk is higher with therapeutic abortion (about 4%).
- -Procedures such as amniocentesis or external cephalic version.
- -Antepartum hemorrhage.
- -Massive fetomaternal hemorrhage can also occur sometimes spontaneously but not uncommon in cases of abruptio placenta or placental manipulation after delivery (manual removal of placenta).

⇒**<u>Exposure to maternal antigen in utero "the grandmother theory":</u>**

- This theory explains the development of fetal isoimmunization in a primigravida, who has no history of exposure to incompatible Rh blood. If a fetus is Rh negative and the mother is Rh positive, the fetus may be exposed to the maternal Rh antigen through materno-fetal transplacental bleed. In such cases the fetus immune system develops a permanent template (memory) for the Rh-positive antigen.
- When the fetus becomes a mother herself and exposed to a new load of D antigen from her fetus (hence the grandmother connection) the immune memory is recalled and a secondary immune response occur.

⇒ **Determination of the presence of fetal cells in maternal blood:**

The Kleihauer-Braun-Betke test: It is based on the fact that an acid solution (pH 3 to 3.5) can preferentially denaturant the maternal but not fetal hemoglobin. The denatured maternal hemoglobin leaks out from the RB Cells leaving only the stroma. Thus under light microscopy the maternal red cells appears as "ghost cells" while the fetal cells retain their normal color. This test can detect as little as 0.01 mL of fetal blood mixed in the total maternal blood volume (as high as 8 L).

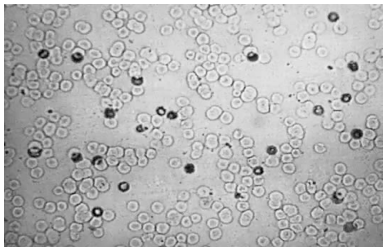


Figure 25-1: Acid elution technique of Kleihauer. Fetal RBCs stain with eosin (appear dark), adult RBCs do not stain (appear as ghosts). This maternal blood smear contained 11.2% fetal RBCs, representing a

⇒**The Mechanism of Development of the Rh Immune Response:**

The maternal immune system responds to the exposure to an Rh antigen (Rh positive fetal RBCs) in two phases:

- The primary immune response (Figure 25-2): The Rh antigen will be cleared by macrophages; processed and transferred to plasma stem cell precursors. The plasma cells that have almost long life permanent immunologic memory produces antibodies specific to the Rh antigen. However the response is a slow one (6 weeks to 6 months), and the antibodies produced mostly of the IgM antibodies, which has a molecular weight of 900,000 that does not cross the placenta.

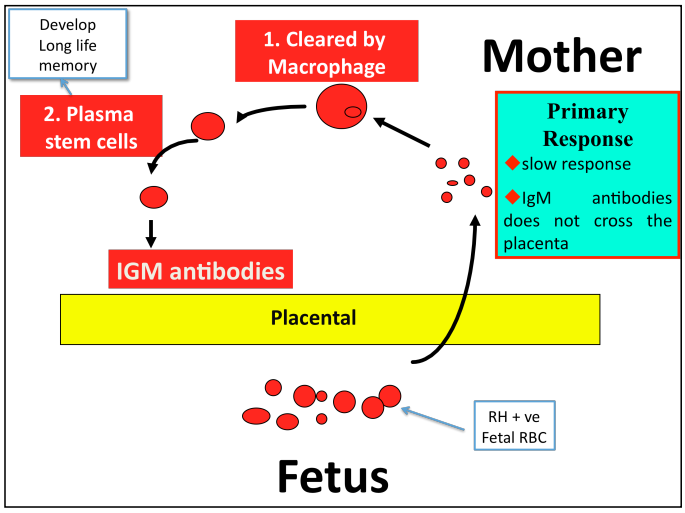


Figure 25-2: Primary immune response (see text)

The primary response may be influenced by several factors such as:
- Non-responders: Not all Rh-negative individuals can be sensitized.
- ABO incompatibility: exerts a protective effect against the development of Rh sensitization (see later)

➢ The secondary immune response (Figure 25-3): With subsequent exposure the plasma cell line proliferate to produce humeral antibodies. The secondary response is fast (within few days) and the antibodies are mostly of the IgG variety which has molecular weight of 160,000 that is capable of crossing the placenta.

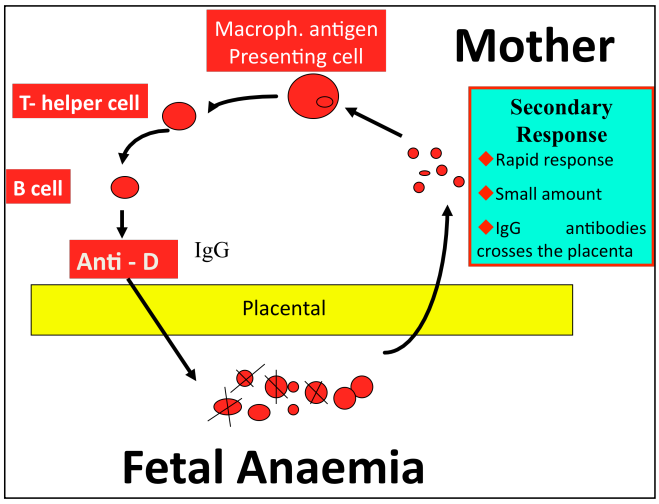


Figure 25-3: Secondary response (see text)

The extent of the secondary response (IgG antibodies production) may vary according to the antigen load, frequency of exposure, and the specific subclass of IgG antibody, which varies in their effects.

⇒**Risk of Development of Maternal Isoimmunization:**

Not all Rh-negative mothers develop Rh immunization. The overall risk of Rh immunization that occurs as a result of the first Rh-positive ABO-compatible pregnancy is about 16%. There are several factors which are responsible for the less than expected number of affected Rh-negative susceptible mothers:

- The husband may be heterozygous: It is estimated that 60% are heterozygous Rh positive, with a 50% chance of having an Rh-positive offspring.
- ABO incompatibility: confers substantial protection against the primary Rh immune response(figure 25-4). The incidence of Rh immunization 6 months after delivery of an ABO-incompatible Rh-positive infant is 1.5% to 2.0%.

- The non-responders: Not all Rh-negative individuals can be sensitized (produce a primary immune response) even when challenged with large volumes of Rh-negative blood. It has been estimated that about 30 % of Rh-negative women are non-responders

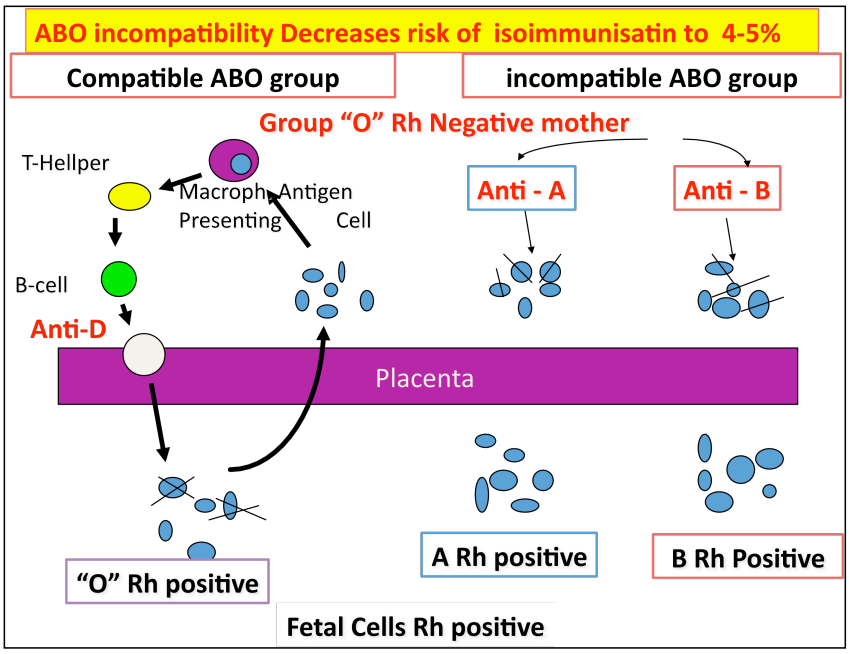


Figure 25-4: Illustration of the protective effect of ABO

⇒**Prevention of Maternal Isoimmunization:**

Prevention of maternal isoimmunization against D antigen (immune prophylaxis) is based on the principle of antibody Mediated Immune Suppression (AMIS) which is prevention of **Active** immunization by **Passive** immunization (i.e. administration of an antibody specific to a given antigen). In this case the Anti-D immunoglobulin the antibody being used. The precise mechanism of AMIS is not clearly understood.

The amount of Anti-D antibodies required to induce AMIS depends on the amount of Rh-positive cells entering the circulation, from studies on volunteers it seems that 20 μg of anti-D immunoglobulin will be sufficient for 1mL of fetal D positive red cells.

In practice the standard dose being given ranges between 150 to 300 μg. Under certain circumstances (e.g. massive feto-maternal hemorrhage) the proper dose of anti-D should be given after quantitative estimation of the amount of fetal cells in the maternal circulation is performed using the Kleihauer test or flow cytometry.

Source of commercial Anti-D: Up till now Anti-D immunoglobulin is being produced from human blood products collected from donors with high levels of anti-D antibody as a result of previous natural exposure or immunized Rh negative volunteers.

Who should be given Anti-D? Administration of Anti D immunoglobulin for prophylaxis should only be given to non-immunized Rh negative women who are pregnant in Rh positive infants. The immunoglobulin should be given within 72 h of delivery after testing the infant Rh blood group. However, even late administration (> 15 days) is of value in prevention of the development of isoimmunization.

Prophylaxis administration of Anti-D: It was found that nearly 2 % of Rh sensitization would occur before delivery. With prophylaxis administration of anti-D around 28 weeks (some times again at 34 weeks) reduced the incidence of sensitization to < 0.1 %.

⇒**Pathogenesis of Fetal Alloimmunization**:

Normal Fetal Erythropoiesis: Erythropoiesis normally starts in the yolk sac of the human embryo by the third week of gestation. Rh antigen has been found in the RBC membrane by the sixth week. By 8 to 10 weeks' gestation, RBC production shifts to the liver and spleen. But gradually moves to the bone marrow. By the sixth month of gestation all erythropoiesis becomes confined to the bone marrow.

Pathogenesis of Fetal Erythropoiesis Fetalis:

- The fundamental cause of erythroblastosis

However since the anti-D antibodies –unlike other antibodies such as anti A or B- does not fix complement the mechanism RB Cells destruction is different. The fetal RB Cells coated with the anti D antibodies adhere to the macrophages, forming rosettes, particularly in the spleen, where the circulation slows and the hematocrit increases, thus the fetal cells are destroyed extravascularly, primarily in the spleen.

fetalis is fetal anemia induced by hemolysis of Rh-positive fetal RB Cells by maternal anti-D IgG antibody.

- Fetal anemia results in increased erythropoietin production, which stimulates and increased erythropoiesis.
- When marrow red blood cells production cannot compensate for the increasing anemia, extramedullary erythropoiesis recurs primarily in the liver but also the spleen, kidneys and adrenal glands.
- Immature nucleated "erythroblast" red cell precursors are released in the circulation in large amounts. Thus the full picture of "Erythroblastosis Fetal" is established.
- Hepatomegaly, distortion of the normal architecture of the liver with reduction of hepatocyte function and hepatic failure occur with its consequences of hypoprotienemia, portal hypertension, ascetis and generalized edema.

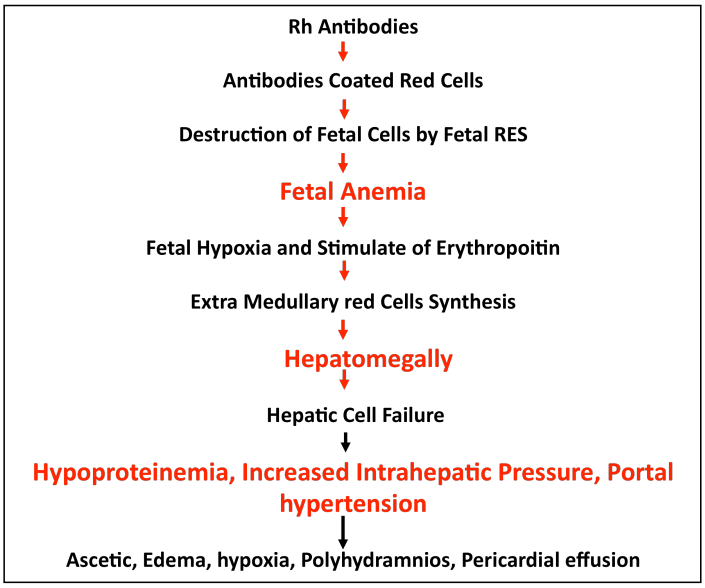


Figure 25-5: Pathogenesis of Fetal Erythroblastosis Fetalis (see

The amount of maternal anti-D IgG present, its avidity for the D antigen, and the ability of the erythroblastotic fetus to replace the hemolyzed red blood cells without developing hepatic damage determine the degree of severity of the disease in the fetus. Therefore the disease may be mild, moderate or severe:

In mild cases:

About 50% of affected infants are mildly or not anemic at birth (cord hemoglobin exceeds 12 g/dl). They are not dangerously hyperbilirubinemic (cord bilirubin levels are less than 3.5 mg/dl). Their RBCs, however, are coated with anti-D, making them direct antiglobulin (Coombs' test) positive. They usually require no treatment.

Moderate Cases:

In about 25% of affected infants, the disease is more severe. Erythropoiesis is adequate to prevent severe anemia but not so great that hepatic hypertrophy and circulatory obstruction occur. The fetus is delivered in good condition at or near term. But while before birth, the products of fetal RBC hemolysis are transported across the placenta and metabolized by the mother, after delivery the fetal liver cannot deal with the products of RBC destruction. The heme component of hemoglobin is converted to indirect bilirubin, which is neurotoxic.

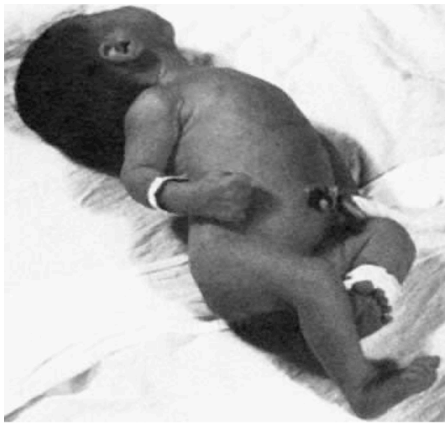


Figure 25-6: Newborn with kernicterus: note spasticity and opisthotonos

Indirect bilirubin is water insoluble and lipid soluble and can circulate only if it is bound to the plasma protein carrier albumin. When the bilirubin-binding sites on albumin are saturated, unbound free indirect bilirubin appears. It cannot remain in a watery medium such as plasma and diffuses into high lipid content tissues. Free indirect bilirubin diffuses across the lipid-containing neuron membrane and interferes with vital metabolic processes, causing ballooning of the neural mitochondria. The neuron dies. Bilirubin accumulates within the dead neurons, producing the characteristic yellow color found at autopsy (kernicterus).

Infants who develop bilirubin encephalopathy (kernicterus) are deeply jaundiced. Signs of brain dysfunction appear on the third to the fifth day. They become lethargic and hypertonic, lying in a position of opisthotonos (Figure 25-6). Apnea develops, and death occurs in 90% of such infants. In the remaining 10% of infants, jaundice lessens, and hypertonicity diminishes. Initially, the neonates appear well. As they grow older, signs of severe neurologic damage inevitably appear.

Severe Cases:

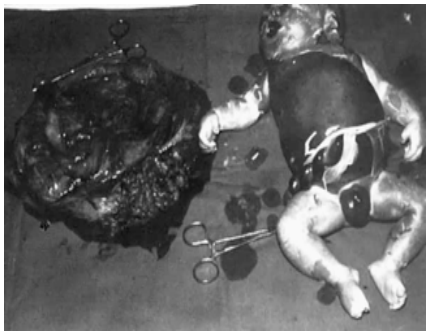


Figure 25-7: Stillborn fetus with hydrops fetalis: note the edema and markedly enlarged placenta

About 20% to 25% of the cases of erythroblastosis fetalis are severely affected. Hepatic erythropoiesis and hepatic enlargement and failure occur. Portal hypertension results into transudation of fluid into the peritoneal space (ascites). Generalized anasarca, pleural and pericardia effusion will further ensure as a result of (hypoalbuminemia. Death in utero usually occurs. If a hydropic fetus is born alive, ventilation usually is impossible because of pulmonary edema and compression hypoplasia of the lungs. Thus portal hypertension, and hepatocellular damage—not anemia—are the basic causes of the condition.

⇒Clinical Management of the Rh Isoimmunization:

All pregnant women on their first antenatal visit should have tests for their blood group, Rh status and antibody screening. Subsequent management depending on the results will be either:

- Prevention of development of isoimmunization in women who are Rh negative with no antibodies detected, or.
- Treatment for those who are immunized (have antibodies) according to the severity of the disease along the lines to be explained.

⇒Prevention of isoimmunization in RH-negative non-immunized women:

An Rh-negative woman who is not immunized (Rh antibodies negative) should have:

- Determination of the husband ABO and RH status. If the father is Rh negative, the infant should be Rh negative and the mother at no risk of immunization.
- If the father is Rh positive then there is 50% risk of the fetus being Rh positive. In this case the mother should have regular screening for antibodies beginning at around 20 weeks and every four weeks thereafter.
- Prophylactic Anti D should be administered during pregnancy whenever there is risk of fetomaternal hemorrhage such as threatened miscarriage, antepartum hemorrhage, or performance of procedures such as external cephalic version and amniocentesis. Normally a standard dose of 150-300 microgram is given. If a higher dose is required a Kleihauer test should performed.
- Prophylactic dose of Anti D is also administered between 28 -34 weeks since it was found that nearly 2 % of Rh sensitization occurs before delivery. This policy reduce the incidence of senitization to < 0.1 %.
- Management after birth: All non-sensitized women who give birth to Rh-positive babies should receive a standard prophylactic dose of Anti D immunoglobulin. The immunoglobulin should be given within 72 h of delivery, however even late administration (> 15 days) is of value in prevention of the development of isoimmunization. A Kleihauer test should be preformed if there is doubt that the amount of TPH above average e.g. following operative procedures such as cesarean section and manual removal of the placenta.

⇒**Management of women who have developed Rh isoimmunization**:

Women who are found to be positive on antibody screening test require further evaluation and diagnostic tests to predicts the severity of the disease (i.e. degree of fetal affection) and accordingly determine the need for intrauterine fetal therapy with blood transfusion or induction of labor depending on the gestational age. The management should be undertaken in specialized fetal units with facilities for therapeutic intervention.

Evaluation of the severity of the disease depends on: (1) history of preceding disease, (2) maternal antibody titers, (3) Determination of fetal Rh blood group, if the technology available (4) Doppler assessment of the fetal blood middle cerebral artery peak systolic velocity for prediction of fetal anemia (5)

amniocentesis for amniotic fluid spectrophotometric measurements, and (6) direct fetal blood sampling (7) Ultrasound evaluation.

1. History:

The classical pattern of erythroblastosis fetalis is that it tends to become progressively worse. A previous history of hydrops gives a 90% chance of recurrence usually at the same time or earlier in gestation. A benign history (no previously affected pregnancies) is reassuring.

However depending on the history of previous diseases have several limitations since subsequent Rh disease may depend greatly on the size and frequency of further Rh-positive fetomaternal RBC TPH in the succeeding pregnancy. Furthermore history is not helpful in the first affected pregnancy, where in 8% to 10% of fetuses become hydropic before term. It is of little value when there is a history of hydrops but the father is heterozygous.

2. Determination of the Fetal Rhesus blood group:

This may be attempted if the father is tested and found to be heterozygous Rh positive, which indicate that the fetus has 50% chance of being negative.

The diagnosis of the Rh status of the fetus is currently possible through one of the following technology:

- DNA analysis of fetal cells from amniotic fluid or chorionic villus samples.
- Prediction of fetal D status by PCR (polymerase chain reaction) and analysis of fetal DNA sequences. Fetal DNA is obtained either from nucleated fetal erythroblast cells or fetal DNA isolated from maternal circulation.

3. Measurement of maternal antibody titer:

The antibody titer is the reciprocal of the highest dilution still giving a positive reaction. Thus, if a 1:32 dilution is positive and a 1:64 dilution is negative, the titer is 32. Measurements of antibody titer, especially serial ones, are of value in predicting the risk of severe hemolytic disease. Each laboratory must determine the antibody titer that puts the fetus at risk. Generally speaking an albumin titer of 16 or an indirect antiglobulin titer of 32 to 64 puts the fetus at about a 10% risk of becoming hydropic.

4. Doppler assessment of the fetal middle cerebral artery peak systolic velocity waveform (PMCA-SWF):

This technology has now become the standard tool for the prediction and determination of fetal anemia. It is based on the fact that the anemic fetus maintains oxygen delivery to the brain by increasing cerebral flow. Since the anemic fetal blood has low viscosity it will have high velocity that increases in

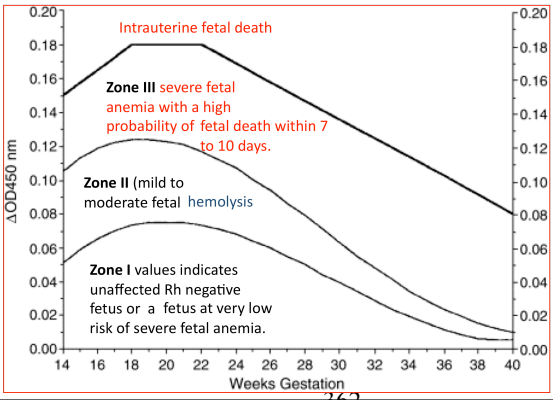
correlation with the degree of anemia. Currently this method has replaced invasive methods such as amniocentesis for measurement of amniotic fluid bilirubin and fetal blood sampling.

5. Amniocentesis for measurement of Amniotic fluid Bilirubin and the Lileys' curve:

The objective of amniocentesis is to measure the bilirubin in the amniotic fluid. Normally fetal bilirubin is present in decreasing amounts as pregnancy progress. It reaches the amniotic fluid from fetal pulmonary and tracheal diffusion. Abnormal rise in amniotic fluid bilirubin correlates with the degree of fetal hemolysis and anemia. The procedure can lead to fetomaternal hemorrhage and a rise in maternal antibody titer and should not be performed unless its benefits is more than its potential risks especially that once amniocentesis is performed it should be repeated to follow the trend in amniotic fluid bilirubin at approximately 10 day to two week intervals depending on the results.

The Liley's curve and its modification: Interpretation of amniotic fluid bilirubin is based on the spectrophotometric technique described by Lilly in 1961. The technique allows accurate comparison of measurements from one laboratory to another. Amniotic fluid must be protected from light, which destroys bilirubin and falsely lower the result. It is based on the fact that bilirubin absorbs visible light at wavelengths between 420 and 460 nm. The amount of light absorption can be most accurately measured by spectrophotometry.

The results of the change in optical density of amniotic fluid at 450 nm are plotted on a normative curve based upon gestational age. The original curve developed by Lilly was divided into three zones and began from 27 weeks). It has been modified to include pregnancies earlier than 27 weeks (Figure 25-8):



Queenan curve (Deviation in amniotic fluid optical density at a wavelength of 450 nm in Rh-immunized pregnancies from 14 to 40 weeks' gestation)

Figure 27-8: modified Lilly's curve

Interpretation of Amniotic Fluid Bilirubin: on serial measurements the decision are based of the results of amniotic fluid bilirubin levels as follow:

- **A Falling Curve (Zone I):** Is reassuring: i.e. An Unaffected Or RhD-negative Fetus Zone one with no rising level.
- **A Plateauing Or Rising Curve** : in zone one or two suggests active hemolysis (Require Close Monitoring And May Require Fetal Blood Sampling And/Or Early Delivery).
- **A Curve That Reaches To Or Beyond The 80th Percentile Of Zone II or Zone III:** suggest a severely affected fetus that need either treatment in utero by intrauterine transfusion of delivery depending on the gestational age.

6. Fetal Blood Sampling:

Fetal blood sampling is by far the most accurate means of determining the degree of severity of fetal hemolytic disease and the need for fetal treatment measures. It is also the most invasive method with the highest risk of fetal mortality and of TPH. Fetal blood sampling may be possible as early as 18 weeks' gestation; it usually is feasible by 20 to 21 weeks' gestation.

At the time of the procedure it is advisable that preparation for intrauterine transfusion be undertaken as well (e.g. patient consented, Packed group O Rh negative blood ready and all necessary equipments)

7. Ultrasound evaluation - parameters of fetal affection:

Ultrasound plays a key role in the management of the alloimmunized pregnancy. A variety of ultrasonographic parameters have been used to determine whether fetal anemia is present. These parameters include: placental thickness; umbilical vein diameter; hepatic size; splenic size; and polyhydramnios and lastly fetal hydrops. It must be realized that sings of fetal hydrops (e.g., ascites, pleural effusions, skin edema) are not observed until the fetal hemoglobin deficit is at least 7 g/dl below the norm for gestational age.

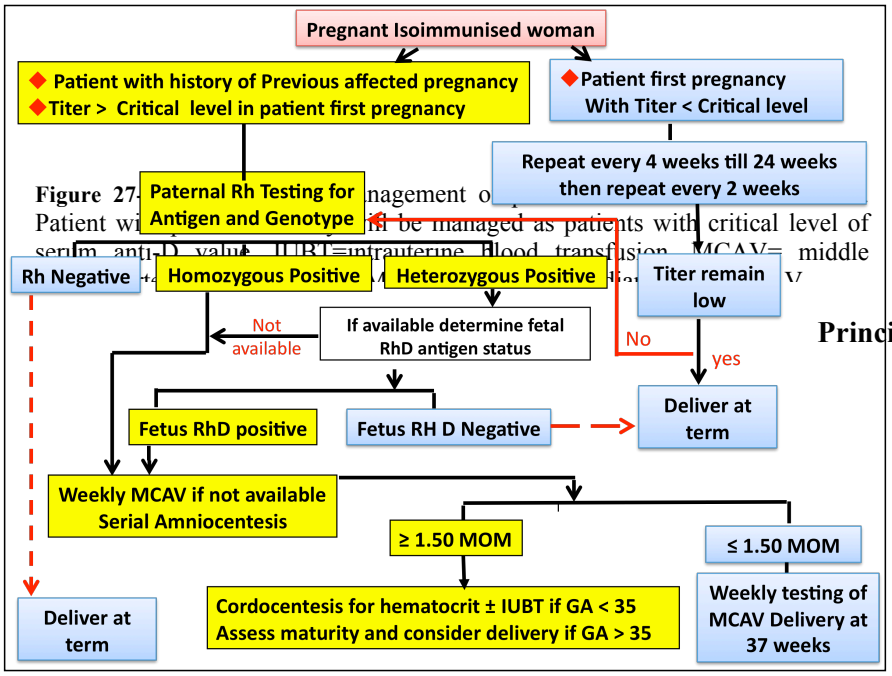


Figure 27- nagement o
Patient wi be managed as patients with critical level of
serum anti-D value. IUBT=intrauterine Blood transfusion. MCAV= middle
[illegible] V

Principle of

management for fetal Rh alloimmunisation (Figure 27-9):

The absence or presence of history of previously affected pregnancy plays an important role in planning the management of Rh alloimmunisation.

➢ <u>In case of no history of previous affected pregnancy (The First pregnancy with maternal isoimmunisation)</u>

1. Maternal anti D titer is measured and followed up monthly until 24 weeks, then every two weeks until delivery. A critical level is determined for each obstetric unit but generally if it is < 1/8 or 1/16 follow up can continue.
2. If the critical titer is reached (1:16 or 1:32 depending on the laboratory), the fetus should be evaluated for the presence of severe anemia. This is currently performed using middle cerebral artery peak systolic velocity (MCA-PSV) at one to two weeks' intervals. MCA-PSV above 1.5 multiples of the median is predictive of severe anemia. If this is not available then, serial measurement of amniotic fluid bilirubin levels using spectral analysis at 450 nm (OD450) can be performed every 10

days to two weeks and the results interpreted using the modified Lilly's curve.

3. If serial MCA-PSV remains <1.5 MoM's, labor may continue and be induced at 37 to 38 weeks of gestation.
4. If MCA-PSV ≥1.5 MoMs then subsequent management depends on the gestational age:
    - For pregnancies <35 weeks of gestation with an MCA-PSV or delta OD450 value suggestive of severe fetal anemia, fetal blood sampling should be performed followed by transfusion if severe anemia is confirmed.
    - For pregnancies at 35 to 37 weeks of gestation, induction of labor may be considered after assessment of lung maturity.

➢ In case of history of previously affected pregnancies it is difficult to rely on maternal antibody titers in following the degree of fetal anemia. In such cases reliance should be on evaluation of MCA-PSV or amniocentesis which ever is available.

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Chapter 26

Mechanism and causes of Genetic Diseases

Currently the care for fetal health is as important as caring for its development. The fetus is not just part of the mother but has become a distinct entity that can be subjected to examination, diagnosis and therapy. As the public awareness grows obstetricians are increasingly encountering parents who have worries about particular genetic problem or disorder. It is therefore essential that obstetricians understand the basic principles of genetic inheritance, be aware of the methods used for prenatal screening and diagnosis and their limitations.

By the end of this chapter you should be able to:
List the estimated rate of congenital abnormalities at different phases of human life
List the causes of congenital anomalies
Describe the difference between: polygenetic, and single gene disorders
List the difference between autsomal and sex linked disorders
List the difference between recessive and dominant disorders.
Describe the types of chromosomal disorders Numerical and Structural aberrations.
Describe the different types of translocation
Describe the role of environmental factors and teratogens as causes of congenital anomalies.

Overview of birth defects scope of the problem:

Congenital abnormalities are frequent occurrence in human reproduction. Table 26-1 shows the estimated rate of congenital abnormalities at different phases of human life:

Among first trimester spontaneous abortions	> 50%
Among Stillborn infants	- 6-12 % have chromosomal anomalies - 25 -23% with intrinsic anomalies at autopsy
Among live birth	- 3% major congenital anomalies or genetic disorder
By the age of 25	7-8% have genetic condition or birth defect

Table 26-1: Frequency of congenital abnormalities

Causes of congenital anomalies

The causes of congenital anomalies can be categorized into three groups:

(1) M**ultifactorial (polygenetic) causes**: Multifactorial inheritance is defined as inheritance by combination of multiple genetic factors (i.e. polygenic, or large number of genes with small, equal, additive effects, from each one) with or without other environmental factors. Polygenic inheritance is responsible for the majority, approximately 65% to 80% of birth defects. Its inheritance does not follow specific pattern but once happened it indicate a higher than average risk of recurrence.

Examples of polygenic disorders include structural anomalies such as cardiac defects, cleft lip, neural tube defects, gastroschisis, and clubfoot.

(2) **Genetic causes**: Is responsible for about 10% to 25% of birth defects. It could results from mutation in a single gene or chromosome.

- **Single-gene mutations:** It is estimated that over 4000 human diseases are caused by single gene defects. There are two major types of single-gene inheritance: **Autosomal**, and **X-linked**. Each type may be either dominant or recessive (Table 26-2). There are important differences in the features and inheritance of each (Table 26-3).

There is a third less common type of genetic mutation, which is mutation of Mitochondrial genes. This type of inheritance is known as maternal inheritance, because only the ovum cells contribute mitochondria to the developing embryo, therefore only mothers can pass on mitochondrial conditions to their children. An example of this type of disorder is Leber's hereditary optic neuropathy

Autosomal		X-Linked	
Dominant	**Recessive**	**Dominant**	**Recessive**
Familial hypercholesterolemia	Sickle cell disease	Duchene Muscular Dystorophy	Hemophilia
Polycystic kidney disease	Cystic fibrosis	Galactosemia	
Marfan Syndrome	Tay-Sachs disease		
Huntington Disease	Phenylketonuria		

Table 26-2: Some examples of single gene disorders

There are however important points that should be taken in consideration when counseling patient in relation to genetic disease:

- Genetic disorders are not always inherited but in many occasions are the result from de novo genetic mutation.
- The phenotype of genetic disorder depends on the degree of **penetrance** and **expression** of the gene.
- The division between recessive and dominant types is not sharp one, still recessive inheritance may express some feature of the disease either clinically or at biochemical level.
- In Y-linked disorders *every* son of an affected father will be affected. While the female off-springs of affected fathers are *never* affected.

Penetrance refers to the proportion of individuals with the mutation who exhibit clinical symptoms (phenotype), it is an all or non-phenomenon. E.g. penetrace 95% autosomal dominant disorder mean that 95% of those with the mutation will develop the disease, while 5% will not.

Expressiveness refers to the degree of expression of a given trait. A typical example is "Multiple Neurofibromatosis", an autosomal dominant trait that widely varies in clinical severity "i.e. expression".

Remember Y chromosome is relatively small and contains very few genes, there are relatively few Y-linked disorders. The most common Y chromosome mutatins are associated with infertility. This is important when counseling infertile couples due to male factors who seek in-vitro fertilization. They can transmit the Y infertility mutation to their sons.

Autosomal-Recessive Inheritance	Autosomal-dominant Inheritance	Sex Linked Inheritance
Two copies of the gene must be mutant for a person to be affected by an autosomal recessive disorder.	Only one mutant copy of the gene for a person to be affected.	- Males are always affected whether the X linked disease is dominant or recessive (because they only one X chromosome) - Female are only affected in X dominant disorders. - Y-linked disorders are rare
-Has a "horizontal transmission" -Recessive genes may remain silent in a family until the chance of pairing of a couple with the same recessive gene.	Has "Vertical transmission" (appear in every generation) *Exception to this rule:* *1. Cases of fresh mutations.* *2. Non-penetrance. or if the expression is very mild*	-The gene is never transmitted directly from a father to his son (but to 50 % of his grandsons through his daughter). -Heterozygous females are usually unaffected, but some may express the condition with variable severity if by chance the normal X chromosome becomes inactive.
If the parents are carriers of mutant genes they have 25% chance in each pregnancy of having a child affected by the disorder.	There is a 50% chance that a child of an affected person will inherit the mutated gene.	- The sons of a man with an X-linked recessive disorder will not be affected, and his daughters will carry one copy of the mutant gene. - A woman who is a carrier of an X-linked recessive disorder has a 50% chance of having sons who are affected and a 50% chance of having daughters who is carriers.
An affected person usually has unaffected parents who each carry a single copy of the mutated gene (and are referred to as carriers).	Phenotypically normal family member do not transmit the phenotype to their children.	

Table 26-3: Features of Autosomal and sex linked inheritance, in recessive and dominant situations

- **<u>Chromosomal disorders</u>**:

Chromosomal disorders or aberrations are clinically important cause of genetic disease. It account for a large proportion of reproductive wastage, congenital malformations, and mental retardation. It also plays an important role in the pathogenesis of malignancy.

<u>Incidence:</u> It is estimated that chromosomal abnormality is present in about 0.7% of live births, 2% of all pregnancies in women over 35 years of age, and in 50% of all spontaneous first trimester abortions.

There are two major categories of chromosomal aberrations: numerical or structural chromosomal aberrations:

Numeric Aberrations: either polyploidy or aneuploidy.

- **Polyploidy** is the presence of one or more extra haploid set of 23 chromosomes e.g. Triploidy (3N = 69) and Tetraploidy (4N = 92). The majority of poliploid blastocysts do not grow. If a polyploidy balstocyst is implanted and grows its development and phenotypic expression depend on the source of the extra set of chromosome. Extra paternal set of chromosome causes partial hydatidiform mole, while extra set of maternal chromosomes usually abort early.
- **Aneuploidy:** is the gain or the loss of single, whole chromosomes. The former condition is referred to, as "Trisomy" while the latter is known as "Monosomy". Either of the two aberrations could affect the autosomes or the sex chromosomes (Table 26-2).

<table>
<tr><th colspan="2">Aneuploidy of the Autosomes</th><th>Aneuploidy of the Sex Chromosome</th></tr>
<tr><th>Autosomal Monosomy</th><th>Autosomal Trisomy</th><td rowspan="3">45X (Turner Syndrome) its hallmarks are short stature and infantilism with or without other Turner stigmata.
Klinfelter Syndrome 47XXY are phynotypically male but azoospermia with small testes, elevated levels of FSH and LH hormones and decreased testosterone.
Polysomy Y in Males (47, XYY and 48, XXYY): is a rather common aberration
Plolysomy X in Females (47, XXX; 48,XXXX; 49, XXXX): Most of those female have normal reproductive system. But there is a risk of delivering child with abnormal chromosomal complement.</td></tr>
<tr><td rowspan="2">is usually lethal</td><td>- Comprise about 15% of all 1st trimester miscarriages.
- Affects about 0.5% of newborns</td></tr>
<tr><td>E.g.
Trisomy 21 (Down Syndrome the most common).
Trisomy 13 (Patau syndrome) & and trisomy 18 (Edwards Syndrome).</td></tr>
</table>

Table 26-3: Aneuploidy of autosomes and sex chromosome and its consequences .

- Common features of all Trisomies: include fetal growth restriction (FGR), presence of U/S markers that may enable prenatal diagnosis. After delivery there is often dysmorphic features, high prevalence of internal organs malformations, and mental retardation.

- Causes of Aneuploidy:

1. **Non-disjunction** i.e. failure of a pair of chromosomes to disjoin in the normal way during meiotic division. This is the most common cause for anueploidy (Figure 26-1). If non-disjunction occurs late in a mitotic division of the zygote, a **Mosaicism** may result, which is the presence of normal cell lines together with trisomic ones.

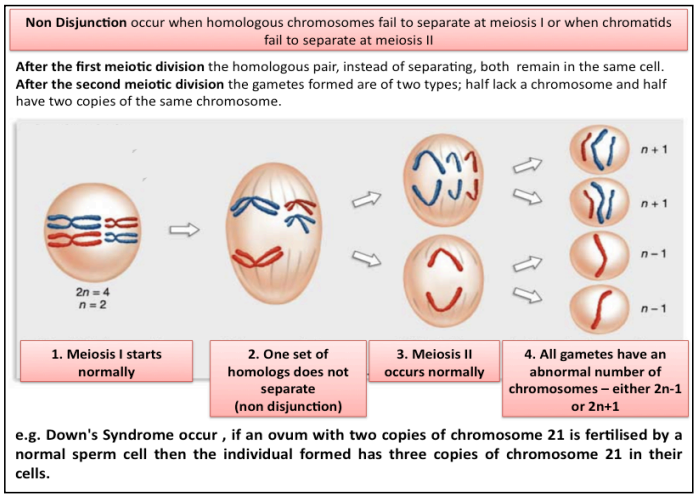


Figure 26-1: Non disjunction may occur at Meiosis I or II

2. **One of the parents carrier of balanced translocation:** The trisomy may not be due to primary disjunction but rather secondary to the presence of balanced translocation (a common translocation is 45, t (14q; 21q) in one of the parents. The parent him or her self

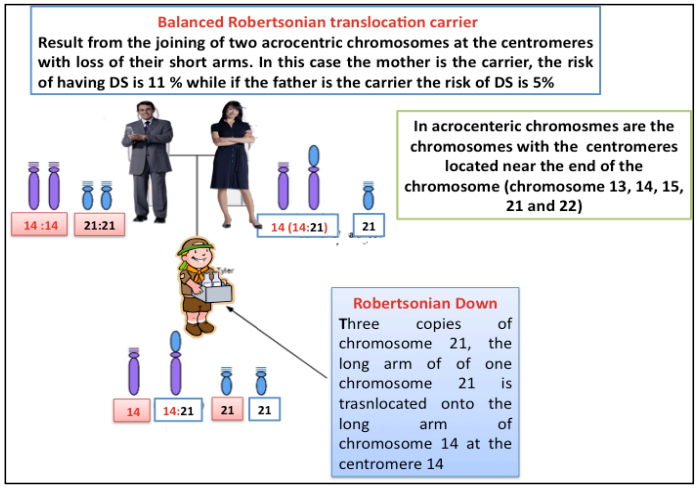


Figure 26-2: Down syndrome inherited from a Robertsonain translocation carrier

appears normal (Figure 26-2)

Structural Aberrations:

Structural Aberrations results from chromosomal breakage, followed by rearrangement in an abnormal combination (Figure 26-4). The result could be **balanced** or **unbalanced** rearrangement.

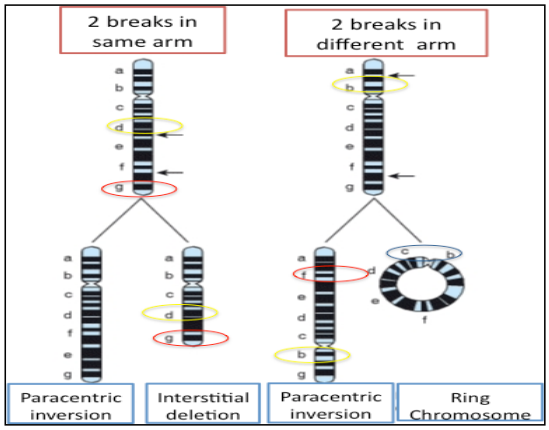


Figure 26-4:Examp;es of structural aberrations in chromosomes. The phenotype depends on the amount and function of the resulting genetic imbalance

- **Unbalanced Rearrangement:** Persons with unbalanced rearrangement display abnormal phynotype because there is either loss (deletion) or duplication of genetic material**.**

- **Balanced Re-arrangement:** Persons carrier of balanced chromosomal rearrangement have normal phynotype because there is NO loss or gain of genetic material .

Individuals with balanced chromosomal rearrangements (e.g. translocation) have no immediate adverse effects but run the risk of producing abnormal gametes. The two common types of translocation are:

- **Reciprocal Translocation:** Results from breaks in two chromosomes, either in the long or short arms, with reciprocal exchange of the broken segments.
- **Centric Fusion "Robertsonian translocation"**: involves two acrocentric chromosomes that fuse near the centromere region with loss of the short arms. The most frequent type of this translocation is between 13 and 14 followed by centric translocation that involve chromosome 21 with chromosomes 13, 14, 15, 21 and 22. In individuals carrier of 21 centric translocation; 20% of pregnancies end in abortions, and about 50% end in live-birth balanced translocation carriers. The risk of having live born Down syndrome is 11% if the maternal parent is the carrier of the translocation and about 5% if the paternal parent is the carrier (Figure 26-2).

(3) **Environmental causes**: refers to external influences that may affect an otherwise normal embryo. This group includes factors such as maternal diabetes; maternal use of alcohol, prescription drugs, and nonprescription drugs; congenital infections; and mechanical constraint problems. Collectively it may be responsible for approximately 10% of birth defects.

Chapter 27

Screening and Prenatal diagnosis of Genetic Diseases

With the technological advances in ultrasound imaging and genetic analysis many congenital and genetic disorders can now be diagnosed at an increasingly earlier stages of pregnancy. Although prenatal diagnosis is usually performed by specialized perinatologists, general Obstetricians and Gynecologists need to be aware of the basic principles of genetic counseling; the different techniques of prenatal diagnosis and their limitations in order to appropriately advise their patients to the best available care.

By the end of this chapter you should be able to:

- **Define** Screening vs. diagnosis
- **List** the indications of prenatal Screening:
  - Screening at individual level, Specific Population screening, and Universal screening.
- **List** the objectives of prenatal diagnosis
- **List** the methods of prenatal diagnosis:
  - the pros and cones of each method:
    - Non-Invasive methods: Ultrasound, analysis of fetal DNA and fetal blood in maternal serum.
    - Invasive Methods: Amniocentesis, Chorion villus sampling and fetal blood sampling.
- **Describe** the principle and place of Preimplantation genetic diagnosis:
- **Counsel** patients on prenatal diagnosis
- **Describe** the Ethical issues in relation to prenatal diagnosis

Screening for Genetic Diseases:

The usual approach to detection of genetic diseases includes screening and diagnosis. A clear distinction should be made between diagnostic tests and screening tests.

- Diagnostic tests are undertaken to confirm whether or not a patient have the genetic disease in question. Most diagnostic tests carry measurable risks. Therefore they are not offered except if there is strong indication that justifies the potential risk of the test.

- Screening tests: In general a screening tests refers to tests that are offered to apparently healthy individuals. screening tests usually carries either no or

negligible risk. The results of a screening test give an estimate of the "probability" or likelihood that a patient may or may not have the genetic disease in question. A screen "positive" test results mean that the person has significantly high risk that justify offering a diagnostic test. At the same time a screen "negative" test result mean that the risk of the patient having the disease is low enough that it does not justify offering a diagnostic test. But does NOT mean that the disorder in question is absent.

A good screening test should be sensitive and specific. Mean it should have high sensitivity in detecting affected individuals (high true positive rate) and high specificity in excluding healthy ones from being falsely labeled as affected (low false positive rate)

Methods of screening of genetic diseases:

The obstetrician has an important role to identify couples at risk of having a baby with an inherited genetic disorder, and advice them regarding the appropriate screening test. This should ideally begin at the time of pre-conception counseling.
Screening for genetic disease may be: 1) specific for patient or couple at known risk, or 2) population screening for certain race, or 3) universal screening for all pregnant women:

- Specific patient or couple related risk:
  Patients may be at increased risk of having genetic disease because of age, family history of inherited disease, previous history of having genetically abnormal baby or exposure to some teratogen. Advancing maternal age has a well-known association with increasing risk of chromosome aneuploidy, in particular autosomal trisomies, most commonly Down syndrome (Table 1)

Maternal age at term (yr)	Trisomy 21	Any Chromosomal Abnormalities
20	1/1480	1/525
25	1/1350	1/475
30	1/940	1/384
35	1/353	1/178
40	1/85	1/62
45	1/30	1/18

Table 27-1: risk of Trisomy 21 or any chromosomal abnormality at delivery

- Population-based carrier screening: certain population at higher risk for genetic disease than others. Of the most common examples of population based carrier screening program are:

- Screening for hereditary disorders of hemoglobin synthesis among Africa, Mediterranean and Asian descended population .
- Screening for Cystic fibrosis among individuals of Northern European background where Cystic fibrosis is the most common severe autosomal-recessive..
- Screening for Tay-Sachs disease: Tay-Sachs disease is a lysosomal storage disease caused by a deficiency of the enzyme hexosaminidase A. It is an autosomal-recessive disorder, most common among Ashkenazi Jewish with a carrier rate of 1 in 30 as

compared with the background rate of 1 in 300.

- Universal screening for birth defects: Universal screening for chromosome aneuploidy and birth defects is now a standard in prenatal care. The two primary screening methods are ultrasound and maternal serum screening using specific biochemical substances. Recently, screening has focused on using an approach that combines those two modalities i.e. ultrasound, looking for specific sings or markers that indicate a high risk of DS, combined with biochemical markers associated with genetic anomalies.

- Ultrasound markers for DS (and other aneuploidy): The most common ultrasound marker found to be associated with increased risk of Down syndrome is increased fetal Nuchal Translucency "NT" between 11 and completed 13 weeks (Figure 27-1). Approximately 70-80 % of fetuses with Down syndrome were found to have NT greater than the 95th percentile.
- Serum markers for Down syndrome screening: Alpha feto-protein, a special protein produced by the fetal liver, was the first biochemical marker to be used for prenatal screening. A high level of alpha-fetoprotein was found to be associated with Neural Tube Defects. Later on a low level was found to be associated increased risk of Down syndrome.

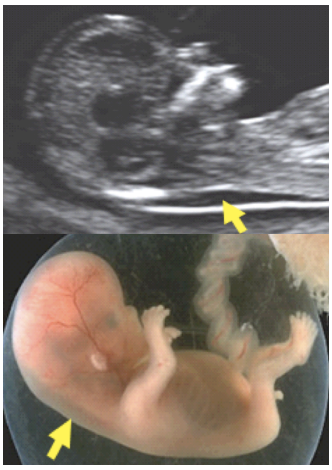


Figure 27-1: On the top is the US picture of fetus at 12 weeks showing a normal NT. The lower picture shows the NT which is the fluid filled skin behind the fetal neck

Currently several biochemical markers either produced by the fetus or the placenta are found to have independent association with Down syndrome risk. Using these markers, in combination increase the detection rate for Down syndrome thus reducing the need for invasive diagnostic tests. Several protocols that combine biochemical markers with ultrasound findings that improve the detection rate of Down syndrome have been developed .

Objectives of Prenatal diagnosis:

It must be emphasized that the primary goal of prenatal diagnosis is not termination of abnormal pregnancies. It has several other important objectives such as:

1. Provide reassurance and reduce anxiety: This is because in the majority of times the results of prenatal diagnosis are normal.
2. In some situation prenatal diagnosis allows couples at risk of having a child with a specific defect, who otherwise might forgo having children, to begin a pregnancy

if they know that the presence or absence of the disorder in the fetus can be confirmed by testing.

3. Provide time for those patients with abnormal test results to adapt and prepare for the birth of an abnormal child (e.g. Down syndrome child).
4. Planning for the time, mode and place of delivery in cases identified to have abnormal fetuses e.g. prenatal diagnosis of cardiac disease require delivery in specialized units.
5. In some cased prenatal diagnosis will help in avoiding unnecessary intervention for the mother or the baby: e.g. the prenatal diagnosis of lethal anomalies such as renal agenesis when operative delivery for fetal indication and/or active neonatal resuscitation should be avoided.
6. Termination of pregnancy: in some cases the patient may wish to consider termination of pregnancy according to the prevailing ethical and legal regulations.

Genetic counseling and prenatal diagnosis:

In all cases adequate genetic counseling should be undertaken prior to prenatal screening or diagnosis procedure. Genetic counseling entails dealing with the following points;

- An estimation of the risk that the fetus in a particular case will be affected.
- The nature and probable consequences of the specific disorder (e.g. haemoglobinopathy or Down syndrome).
- The risk and limitation of the diagnostic procedures to be used including the time required before a result is available, failure rate, need for repeating the test…etc.
- The plan and options available if the test result is positive.

The aim of genetic counseling is to provide expectant parents with as much objective information as possible to help them arrive at a decision that is based on their own desires, values and ethics.

Indications for prenatal diagnosis:

The most two common indications for undertaking prenatal diagnosis are chromosomal disorder and single gene disorder. Other situation where prenatal diagnosis may be requested is exposure to teratogens e.g. medications, infections, radiations or other environmental factors.

I. **Prenatal diagnosis for chromosomal disorders**:

There are number of situations where the risk of chromosomal disorders is considered high enough that prenatal diagnosis should be considered.

- Advanced maternal age: Unlike all other anomalies (e.g. Spina bifida), which have no relation to maternal age, Trisomy particularly, Down syndrome has direct relation to maternal age, which seems to increase significantly and exponentially after the age of 35 (Figure 27-2).

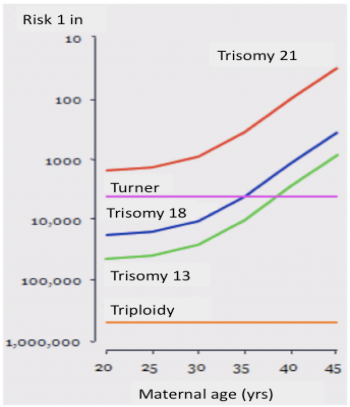


Figure 27-2: Note that all except Turner syndrome are associated with increased maternal age

- If one of the parent is carrier of chromosomal aberrations: (e.g. Robertsonian Translocation) (see Chapter 26).

- Previous birth of a child with chromosomal aberration. Couple who gave birth to a baby with chromosomal abnormalities and who themselves are not carrier of chromosomal aberration run a higher risk of recurrence of the same abnormalities than the general population; 1 in 100 compared to 1 in 800.

- A positive screening test: either a biochemical tests e.g. a positive triple test and/or the presence of a positive ultrasound marker for trisomy such as increased "Nuchal Translucency" or others markers for trisomy.

-The diagnosis of structural anomalies on ultrasound scan: in such cases the prenatal diagnosis of fetal chromosomal make up if performed before viability will help in making the decision regarding continuation of pregnancy. While after viability it directs the managing clinician for the appropriate mode of delivery and subsequent management of the newborn.

II. **Prenatal diagnosis for single gene disorders**:

This is usually undertaken if the parents are discovered to be carrier through population screening studies (e.g. thalassemia) or following the birth of affected child. Single gene disorders have either a dominant or recessive pattern of inheritance (50% and 25% risk of inheritance respectively). The list of single gene disorders that is amenable to prenatal diagnosis is rapidly increasing as the human genome map unfolds together with developments in the technology of DNA analysis.

III. **Other Indications:**

Other indications for genetic counseling and possibly diagnosis include previous stillborn or recurrent abortions, maternal exposure to some teratogens such as cytomegalovirus infection, exposure to irradiation or chemotherapeutic.

Methods of Prenatal Diagnosis:

Methods of prenatal diagnosis may be invasive (the majority) and non-invasive.

- **Non-Invasive Methods**:
  1) **Ultrasound Diagnosis**: High-resolution ultrasound is probably the most powerful method of prenatal diagnosis. In addition it is the back bone of all other methods of prenatal screening and diagnosis since it all depends on accurate ultrasound dating and guidance (see chapter on ultrasound in obstetric).
  2) **Isolation of fetal cells and fetal DNA from maternal serum**: This depends on isolation of fetal DNA and fetal RBC from the maternal circulation and subsequent genetic analyses with PCR and FISH technology. However these methods are still not yet available for clinical application on a wide scale.

- **Invasive Method of Prenatal diagnosis:**

A wide variety of invasive methods are available for prenatal diagnoses. It depends on obtaining fetal cells or tissue biopsy for biochemical and/or genetic analysis. Each invasive method carries some degree of risks primarily to the fetus.

1) **Amniocentesis:** Genetic amniocentesis for prenatal diagnosis is traditionally performed in the second trimester, around 16 weeks of gestation. At that time the amniotic fluid volume is about 200 ml and the ratio of viable to nonviable cells is relatively high. It involves aspiration of small amount of amniotic fluid (one ml for each week) under ultrasound guidance.

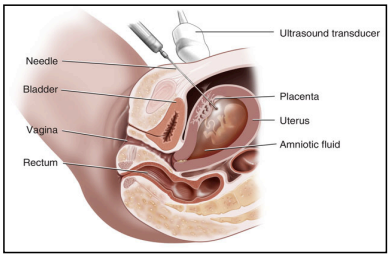


Figure 27-3: amniocentesis with US guidance

Fetal cells (usually fibroblasts) are isolated from the amniotic fluid and cultured for chromosomal genetic studies. The results take on average 2 weeks. Using FISH (Fluorescent In Situe Hybridization) technology can give rapid results (within 24 hours) for the common disorders involving XY, 13, 18 and 21 chromosomes.

Risks of Amniocentesis:

- Maternal complications: are very rare but may include:

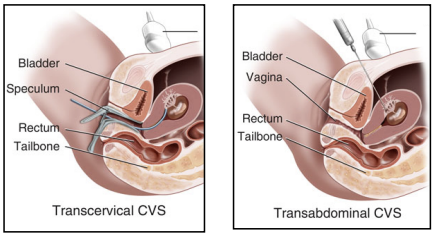
  - Injuries of intrabdominal maternal viscera with subsequent infection, bleeding from laceration of blood vessels have been reported.

- Isoimmunisation of Rh negative patients. Although the risk is small (about 1%) prophylactic (Anti-D IgG) immunoglobulin should be administered (300 µg).

- Fetal complications: include fetal loss and fetal injuries.

  - Fetal loss occurs in < 0.5 % of cases provided the procedure is performed by experienced person and under ultrasound guidance.
  - Leakage of small volume of amniotic fluid, or vaginal spotting after genetic amniocentesis occurs in approximately 1% of all cases but usually transient.
  - On the long term higher rate of skeletal deformities, and respiratory distress were noted to occur among newborns who have been subjected to amniocentesis.

2) **Chorion Villus Sampling:** In this procedure a sample of the chorionic villi is obtained under ultrasound guidance. It has the advantages over amniocentesis of providing earlier diagnosis because it is usually performed after 11 weeks of gestation. Furthermore because the cells of the chorionic villi are in mitotic state it can be fixed and quicker result can be offered. Also culture will take on average one week (Figure 27-4).



- Complication of CVS: maternal complications are the same as in amniocentesis and are very rare. However fetal complications are more common with procedure related fetal loss rate about 1%.

In some cases there is discrepancy between fetal and placental chromosomal make up (the placental karyotype is abnormal while in reality the fetus is normal). This condition is known as confined placental mosaicism "CPM". If CPM is suspected patients are usually offered amniocentesis at 16 weeks to determine the karyotype of the fetus.

3) **Fetal Blood Sampling:** A sample of fetal blood is obtained, usually from the umbilical cord, under ultrasound guidance using a fine needle. The procedure is known as PUBS (percutaneous umbilical cord blood sampling) or cordocentesis.

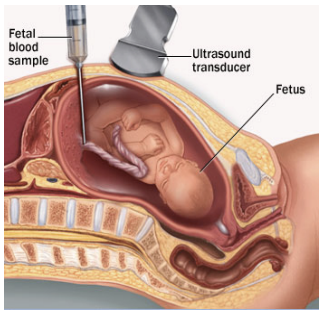


Figure 27-4: PUBS under US guidance

For prenatal genetic diagnosis PUBS has a limited place except for anomalies discovered late in pregnancy when genetic diagnosis would help in determining the mode of delivery. In addition the method require higher skill and associated with significantly higher fetal risks compared to the previous two methods (Figure 27-4).

Pre-implantation genetic diagnosis: Preimplantation genetic diagnosis (PGD) is an alternative method of conception rather than a method of prenatal diagnosis.

The technique: PGD is based on genetic testing of oocytes or embryos obtained, after invitro fertilization. Only normal embryos are transferred back to the patient. PGD is performed either by testing single blastomeres or a few trophectoderm cells removed from preimplantation embryos. Also before fertilization (preconceptional) it is possible to chose the healthy oocyte by removing and testing either the first or the second polar bodies (Figure 7-4). Each method has its advantages and disadvantages.

Advantage: PGD provides an alternative to prenatal diagnostic procedures (i.e. amniocentesis or chorionic villus sampling), which may be followed by the difficult decision of pregnancy termination if results are unfavorable.

Indications: originally the main indications of PGD are when one or both parents have a known genetic abnormality (e.g. blood Hemoglobinopathies).

However the indications for PGD has extended to include other, sometimes ethically unacceptable or controversial indications such as:

- Screening of embryos after IVF to avoid risk of aneupoidy (Down syndrome in older mothers).
- Screening embryos for blood group incompatibility, or for any of the late onset disorders that have genetic predisposition (e.g. cancer, diabetes…et), which may never happens?
- PGD for sex selection, which is ethically not acceptable in many countries including Saudi Arabia.

- Treatment of siblings requiring stem cell transplantation through pre-selection of unaffected and HLA matched embryos.

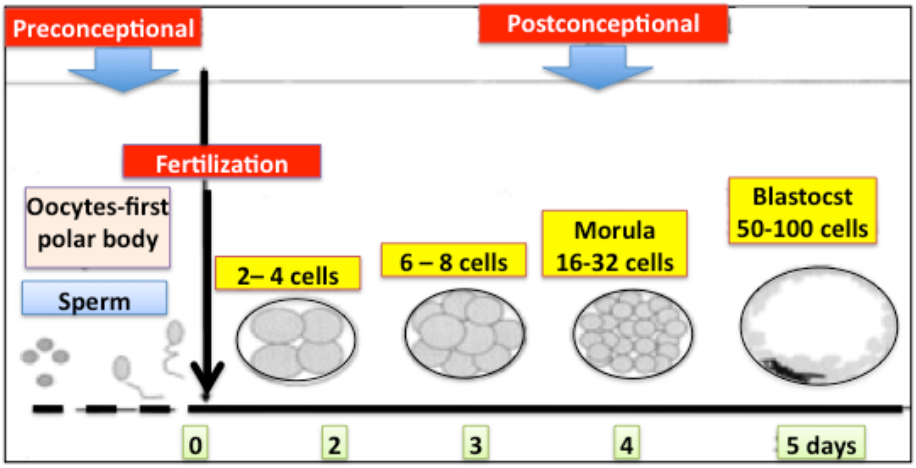


Figure 27-5: PGD may be performed by genetic analysis of the first polar body [preconception], in this case neither the gender of the embryo nor paternally derived genetic abnormality will be known. Postconception testing may be genetic testing of one or two blastomeres at the Morula stage or few trophoectoderm at the Blastocyst stage. Only healthy embryos are replaced back

Ethical and legal issues in prenatal diagnosis and termination of pregnancy – The Islamic views:

Prenatal diagnosis:

Islamic legislation encourages all scientific activities that aim to initiate, maintain and achieve healthy life and livening. Appropriate utilization of the technology of prenatal diagnosis does not violate this Islamic principle; hence the Islamic *Shari'ah (Islamic ruling)* approves it. There is no doubt however those methods, which enable early rather than late diagnosis are preferred in case a decision for abortion has to be made.

In this context pre-implantation diagnosis would be the ideal technique since it eliminate the issue of abortion altogether.

Termination of pregnancy:

However the issue of termination of pregnancy has always been a hot topic that raises different views ranges between those who sees that no indication justify abortion and those who will allow it "on demands" with or without restriction by weeks of gestation.

The Islamic approach to the issue of abortion is very balanced and based on rather clear principles

- **The first principle is the Sanctity of Life**

"***On that account we decreed upon the Children of Israel that whosoever kills a soul for other than manslaughter or corruption in the land, it shall be as if he killed all mankind, and whosoever saves the life of one, it shall be as if he saved the life of all mankind***". (5:32)

Based on this and several other verses and Prophet saying in Islam the human life is sacred, and should not be taken away except upon indications singled out and specified by the law (none of these ever falls within the domain of the medical profession). Human life is a value, and its sanctity covers all its stages including the intrauterine phase.

- The principle of the lesser of the two evils known in Islamic legal terminology as the principle of *al-ahamm wa 'l-muhimm* (the more important and the less important): based on this priciple, *Shari'ah* allows abortion only when doctors declare with reasonable certainty that the continuation of pregnancy will endanger the woman's life. The reason for this is that the mother is the origin of the fetus; moreover, her life is well established with duties and responsibilities, and she is also a pillar of the family. It would not be possible to sacrifice her life for the life of a fetus which has not yet acquired a personality and which has no responsibilities or obligations to fulfill.

- Prenatal diagnosis and the malformed fetus: Modern technology (like ultra sound scan and genetic testing) has made it possible to know whether or not a child has a defect long before he is born. In this respect there has been some diverse views but the one that is mostly accepted by the majority of

Muslim jurists have agreed unanimously that after the fetus is completely formed and has been given a soul, abortion is forbidden "*Haram"*. It is also a crime, the commission of which is prohibited to the Muslim because it constitutes an offense against a complete, living human being.

- The time of insoulment (when the sole enter the body) thus transforming it for living tissue "e.g. plant life" to a "life", has been debated. However currently and based on the statement from the Prophet (s) that refers to a human being starting as a fertilized ovum in the uterus of the mother for forty days, then it grows into a clot for the same period, then into a morsel of flesh for the same period, then an angel is sent to that fetus to blow the *Ruh* "soul" … etc. it is believed that the soul enter the body by 120 days from the day of fertilization (this equal roughly 134 days from the first day of the last menstrual period.
  That however does not mean that the embryo before that date is not to be respected. Indeed once conception occurs it mean a potential life being created.

Based on those principles the Islamic League in Makka Al Mokarama in 1990 has issued regulation in relation to abortion which summaries the majority of Muslim jurists views (see the declaration Figure). It is based on the principle that termination of pregnancy in Islam is forbidden. The only situations when it may be allowed are:

- If it is reliably shown that the continuation of the pregnancy would necessarily result in the death of the mother or serious harm to her health.
- Termination of pregnancy may be undertaken before 120 days from the day of conception provided that trusted specialists have confirmed that the fetus has serious anomaly that is not amenable to treatment and is either incompatible with life or associated with severe ill and unhealthy living.
- Muslim jurists have agreed unanimously that after the fetus is completely formed and has been given a soul (>120 days from

the date of conception), abortion is *Haram* except for saving mother's life.

القـرار الرابــع

بشـأن موضــوع إسقـاط الجـنين المشـوه خـلقياً.

الحـمـد لله وحـده، والصـلاة والسـلام على من لانبي بعـده، سيـدنا ونبـينا محمد وعلى آله وصحبه وسلم.

أما بعد:

فإن مـجلس المجمع الفـقـهي الإسـلامي، برابطة العـالم الإسـلامي، في دورته الثـانيـة عـشـرة، المنعـقـدة بمكة المكرمة، في الفـتـرة من يوم السبت ١٥ رجب ١٤١٠هـ الموافق ١٠ فبراير ١٩٩٠م إلى يوم السبت ٢٢ رجب ١٤١٠هـ الموافق ١٧ فبراير ١٩٩٠م قد نظر في هذا الموضوع، وبعد مناقشته من قبل هيئة المجلس الموقرة، ومن قبل أصحاب السعادة الأطباء المختصين، الذين حضروا لهذا الغرض، قرر بالأكثرية مايلي:

– إذا كـان الحـمل قـد بلغ مـائة وعـشـرين يومـاً، لايجوز إسـقـاطه، ولو كـان التشخيص الطبي يفيد أنه مشوه الخلقة: إلا إذا ثبت بتقرير لجنة طبية، من الأطباء الثقات المختصين، أن بقاء الحمل، فيه خطر مؤكد على حياة الأم، فعندئذ يجوز إسقاطه، سواء كان مشوهاً أم لا، دفعاً لأعظم الضررين.

– قبل مرور مائة وعشرين يوماً على الحمل، إذا ثبت وتأكد بتقرير لجنة طبية من الأطباء المختصين الثقات– وبناء على الفـحـوص الفنية، بالأجـهـزة والوسـائل المختبرية –أن الجنين مشوه تشويهاً خطيراً، غير قابل للعلاج، وأنه إذا بقي وولد في مـوعـده ، ستكون حيـاته سيـئـة ، وآلامـاً عليـه وعلى أهله، فـعندئذ يجـوز إســقــاطه بناء على طلب الوالدين، والمجلس إذ يقــرر ذلك: يوصي الأطبــاء والوالدين، بتقوى الله، والتثبت في هذا الأمر.

والله ولي التوفيق....

Chapter 28

Teratogenesis and Congenital Anomalies

Congenital anomalies are relatively common occurs in about 2-3 % of live born infants, with a higher incidence among stillborns and spontaneous abortions. The term teratogenesis is derived from the Greek word *Tera* meaning *monster*; hence teratogenesis means study of '*monster making*'.

By the end of this chapter you should be able to:
Define what is teratogenic agent or effect
Define each of:
- Malformations
- Deformations
- Disruptions

List the etiology of malformations:
- Genetic causes: (20 to 25 percent).
- Environmental factors "Teratogen": (10 percent).
- Unknown (65 to 75 percent):

List the factors that determine a teratogenetic effect
- The Developmental stage at time of teratogenic insult:
  - The early embryonic period: *all or none period.*
  - From 5 to 10 menstrual weeks: is the period of organogenesis.
  - Fetal period.
- Dose and duration of exposure;
- Species specificity:
- Genetic susceptibility:
- Teratogen characteristics and placental transfer:
- Drug interaction:

List criteria for proof of teratogenesis:
- A specific malformation or group of malformations.
- The teratogen present at the time of organogenesis
- Experimental animals

Types of Congenital anomalies:

Congenital anomalies may be divided into three varieties:

- Malformations are alterations in normal development that occur as a result of an intrinsic abnormality in the formation or developmental process.
- Deformations result from an abnormal mechanical pressure on an otherwise normal fetus (e.g. the development of clubbed foot under the pressure from oligohydramnios).

- Disruptions are due to the disruption of an otherwise normal developmental process, often due to vascular accidents (e.g. gastroschisis, which is thought to result from a vascular disruption in the fetal anterior abdominal wall).

Etiology of Malformations:

- **Genetic causes:** single gene defects and chromosomal abnormalities (20 to 25 percent).
- **Environmental factors "Teratogen":** (10 percent). The term "Teratogen" refers to any factor that alters normal intrauterine development includes drugs and environmental exposures, maternal medical conditions, and infectious agents. The potential teratogenic effects of environmental agents are altered by several factors (see later).
- **Unknown (65 to 75 percent):** Either genetic factors that have not yet been discovered or combination of genetic and environmental factors.

Factors that determine the teratogenetic effects:

1) The Developmental stage at time of teratogenic insult: fetal development occurs in phases (figure 27-1). The early embryonic phase is characterized by cellular hyperplasia and organogenesis. Subsequent phases are mostly cellular hypertrophy, differentiation and functional maturation of different organs. Hence the effect of a teratogen varies depending on the time of fetal exposure.

- The early embryonic period, the first two weeks after conception (until fourth week by menstrual age) is often known as the *all or none period.* At this stage the embryo is formed of few undifferentiated cells. A teratogenic insult during this period either causes loss of the whole embryo or normal development continues. This is because if some cells are damaged the remaining surviving undifferentiated embryonic cells can replace the cells destroyed or damaged by the teratogen.
- From 5 to 10 menstrual weeks is the period of organogenesis, period of differentiation of fetal organs and tissues. This is the most vulnerable period. Exposure to a teratogen during this period can affect the organ systems that are developing at this time.
- The remainder of pregnancy is characterized by cell growth and differentiation. Exposure to teratogenic agents at this time may decrease the cell population by cell death, retard cell growth, or inhibit differentiation. An example is repeated exposure to antenatal corticosteroids in the third trimester may decrease birth weight and while single exposure accelerates morphologic development of the type I and type II pneumocytes.

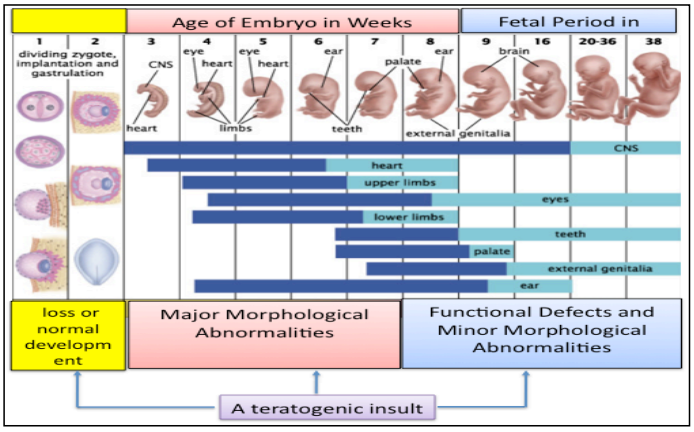


Figure 28-1: Effect of teratogen varies with gestational age (see text). Blue Bars indicate time period when major morphological abnormalities can occur
Light blue bars correspond to periods at risk for minor abnormalities and functional defects.

2) Dose and duration of exposure: most drugs have a threshold dose for teratogenic effects. This of course is species specific (differs from experimental animals and humans)
3) Species specificity: teratogenic agents may have different effects in different species. As an example, thalidomide is not teratogenic in rabbits, but has devastating effects in humans. Glucocorticoids on the other hand, cause facial clefts in animals, but not in humans.
4) Genetic susceptibility; some individuals may be more susceptible to the genetic effect of some drugs or substances than others.
5) Teratogen characteristics and placental transfer: examples of which are molecular weights of the drugs (drugs with a molecular weight > 1000 daltons *do not* cross the placenta), lipid solubility, rate of placental transfer…etc are all factors that determine whether or not the drug reaches the fetus and the drug dose (see chapter 2 on placental physiology).
6) Drug interaction: some drugs interact to enhance and others to reduce the teratogenic effects, e.g. folic acid administration with antiepileptic drugs reduces the rate of teratogenic effects of the antiepileptic drug.

Proof of teratogenesis: to prove that an agent or a drug is a teratogen is not easy and must satisfy strict criteria of which the most important are:

- A specific malformation or group of malformations is consistently associated with exposure to the teratogen.
- The teratogen was present at the time of organogenesis when the anomaly likely to occur, e.g. *Phocomelia*, was almost nonexistent before the introduction of *thalidomide*.
- Experimental animals develop the anomaly if given the presumed teratogen at the appropriate stage of organogenesis.

Chapter 29
Ultrasound in Obstetrics

Dr Nisma Manosuri

Although in Obstetrics the ultimate goal has always been safety for the mother and the fetus, in reality there was no way to know any thing about the fetus until the introduction of ultrasound technology in obstetrics. The fetus has become a real identity that can be examined, and followed up throughout pregnancy. Therapeutic intervention both medical and surgical for fetal disorders became possible. Fetal medicine has emerged as a recognized sub-specialty of obstetrics.

By the end of this chapter you should be able to:
-Describe the Basic principle of ultrasonography
-List the application of US in each of trimester.
-Describe the use of US in determination of GA and fetal weight: The different methods and sensitivity of each in prediction of GA
-Describe the value of US in the diagnosis and evaluation of early pregnancy complication
-Describe the methods of evaluation of amniotic fluid volume by US:
-Describe the current application of US in screening and diagnosis of fetal malformation:
-List the applications of TV - US in obstetrics:
-Describe the use of 3 and 4 D US in obstetrics:
- Describe the value of Doppler Ultrasound in obstetrics**:**
-List some of the application of US in labor:
-Counsel patient regarding the optimum schedule and frequency of US Examination:
- Describe the safety of US:

⇨Basic principles:

The term "ultrasound" (ultra=beyond) refers to sound waves of a frequency greater than that which the human ear can appreciate, namely frequencies greater than 20,000 cycles or Hertz (Hz) per second. To obtain images of the

pregnant or nonpregnant pelvis, frequencies of 2 to 10 million Hertz (2 to 10 megahertz [MHz]) are typically required. Most often sound waves of frequency between 3.5 to 7.0 megahertz (i.e. 3.5 to 7 million cycles per second) are used for this purpose.

The waves are emitted through special crystal transducer. The returning waves are displayed as real time imaging, in which a continuous picture of the moving fetus can be depicted on a monitor screen. Movements such as fetal heart beat and malformations in the fetus can be assessed and measurements can be made accurately on the images displayed on the screen.

⇨Obstetric Scanning:

The application of ultrasound in obstetrics span the whole weeks of pregnancy. The basic indications however vary according to the period of gestation.

Specific obstetrical indications for ultrasound examination in relation to the trimester of pregnancies are listed in the table (table 1).

Components of a first trimester ultrasound examination
➢ Gestational sac *(location, diameter if no embryo identified) An embryo is usually visible when the gestational sac diameter is ^{3}20 mm, and cardiac motion is usually detected when the embryo is ^{3}5 mm (transvaginal examination)*
➢ Presence or absence of a yolk sac (diameter)
➢ Presence or absence of an embryo
➢ Presence or absence of cardiac activity
➢ Crown rump length, if technically possible
➢ Number of embryos
➢ Amnionicity and chorionicity of multiple gestations
➢ Anatomic survey
➢ Evaluation of the uterus and adnexae
Components of second and third trimester ultrasound examinations
➢ Presence or absence of fetal cardiac activity, cardiac rate and rhythm
➢ Fetal number
➢ Fetal presentation
➢ Assessment of amniotic fluid volume
➢ Placental location
➢ Fetal biometry *(biparietal diameter and/or head circumference, femoral length, abdominal diameter and/or circumference) Biometry can be used to estimate gestational age (if not previously determined), fetal weight, and*

fetal growth (by comparing two or more examinations over an appropriate time interval).
➢ Evaluation of the uterus, cervix, adnexa when clinically appropriate
➢ Fetal anatomic survey

Table 29-1: Components of US examination in different trimesters. ACOG Practice Bulletin No. 98. Ultrasonography in pregnancy. Obstet Gynecol 2008; 112:951.

⇨**Determination of gestational age and assessment of fetal size**:

One the most important activities in the first prenatal visit are to determine the gestational age and expected delivery date (EDD). Not uncommonly women either do not know or give an approximate date for their last menstrual period. In such cases early ultrasound scanning plays an essential role in determining the gestational age.

The ultrasound parameters used for estimation of gestational age are the following:

- Measurement of the gestational sac diameter (MSD): The sum of 30 and the sac size in millimeters is equivalent to the gestational age in days. This method can be used prior to visualization of the embryo at five to six weeks menstrual age.
- Crown-rump length (CRL): When embryonic or fetal pole can be visualized at 7 to 10 weeks of gestation, the Crown-rump length (CRL) is the most accurate measurements of pregnancy dating (±3 days). However, after 10 weeks of gestation, the accuracy of the CRL falls with a margin of error of ±5 days at 10 to 14 weeks and ±8.4 days by the 15th week.
- In the early second trimester, the biometric measurements of choice are the biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC).

A sonographically derived estimated date of delivery (EDD) should be relied upon if it differs from that calculated using the last menstrual period (LMP) by more than five to seven days in the first trimester and by more than 10 to 14 days in the second trimester or by 8 percent.

The reliability of the different fetal biometric measurement in prediction of gestational age decreases rapidly as the pregnancy advances. Prior to 20 weeks, they can be used to estimate gestational age with an accuracy of within one week. In the mid to late third trimester, the margin of error for estimation of gestational age is three to four weeks therefore it should not be used alone to estimate the gestational age.

This significant variation is likely due to the increase in normal biological variation in fetal shape as pregnancy advances e.g. near term babies of the same gestational age can have different head size.

The abdominal circumference: Differ from other fetal biometric parameters in that it is not used for prediction of gestational age until late in the second trimester and usually in combination with other measurement. From mid second and third trimester the primary value of the AC is for estimations of fetal weight and for follow up of fetal growth with serial measurements rather than gestational age assessment.

The various ultrasounds biometric measurements used for determination of gestational age are shown in the table 29-2.

Parameter	*Gestational age, weeks*	*Accuracy, days*
Mean sac diameter	4.5 to 6	± 5 to 7
Crown-rump length	7 to 10	± 3
	10 to 14	± 5
	15	± 8.4
Biparietal diameter, head circumference, femur length	14 to 20	± 7
	21 to 30	± 14
	Over 30	± 21 to 28

Table 29-2: Fetal biometric parameters for estimation of gestational age and the range of accuracy for each parameter

Pregnancies with unknown last menstrual date: In pregnancies with unknown or uncertain last menstrual period and late first sonogram ultrasound may be used to check for sings of fetal maturity. Ossification of the distal femoral epiphysis suggests a fetal age of at least 32 weeks and

ossification of the proximal tibial and humeral epiphyses suggests a fetal age of at least 35 weeks.

⇨Diagnosis and confirmation of early pregnancy:

The gestational sac can be visualized as early as four and a half weeks of gestation and the yolk sac at about five weeks. The embryo can be observed and measured by about five and a half weeks.

➢ To confirm the site of the pregnancy "Diagnosis of ectopic pregnancy": It is possible to discriminate between intrauterine and extra uterine pregnancy by correlating ultrasound findings with the serum level of hCG.

In most institution intrauterine pregnancy should be visualized at serum hCG level of 1500 or 2000 IU/L with transvaginal ultrasound "TVS" (the level is higher 6500 IU/L with transabdominal ultrasound). If there is no positive sign of intrauterine pregnancy at this hCG level an ectopic pregnancy should be suspected.

The discrimination Zone
It is defined as the serum hCG level above which a gestational sac should be visualized by ultrasound examination if an intrauterine pregnancy is present.

⇨Vaginal bleeding in early pregnancy:

A visible heartbeat is usually detectable by pulsed Doppler ultrasound at about 6 weeks and is usually clearly detectable by 7 weeks. Ultrasound is the main and perhaps the only test that one need to perform in-patient presents with bleeding in early pregnancy in order to confirm viability, identify the cause of bleeding and decide on plan of management and prognosis.

The prognosis may be guarded in cases of early vaginal bleeding with subchorionic hematoma. It also allow early diagnose of cases of Trophoblastic tumors .

Prognosis in early vaginal bleeding in early pregnancy
The probability of a continued pregnancy is ± 90% if a viable embryo can be detected. Missed abortion and or blighted ovum gives typical picture of deformed sac with or without absent fetal poles.

⇨Vaginal bleeding in late pregnancy "antepartum hemorrhage":

Ultrasound is essential in order to excluding placenta previa before any digital pelvic examination can be performed. It also provides assessment of the degree of placenta previa, hence the options of management. It is however of limited value in cases of placental abruption.

⇨**Estimation of fetal weight:**

Estimation of fetal weight is one of the most important benefits of ultrasound in obstetrics. The weight of the fetus at any gestation can be estimated with great accuracy using polynomial equations containing the BPD, FL, and AC measurements, computer software and readily available charts. In pregnancy estimation of fetal weight is required in many cases such as:

- In confirming a clinical diagnosis of fetal growth restriction: In this respect fetal weight and AC measurements are the gold standard for the diagnosis of FGR.
- In the follow up of fetal growth. (See Chapter 23 on Fetal growth restriction)
- Diagnosis of fetal macrosomia (fetal weight > the 90th percentile)

⇨**Ultrasound estimation of amniotic fluid volume**: Estimation of amniotic fluid volume by ultrasound examination is the only practical clinical method of assessing amniotic fluid volume. Different methods are proposed. The most commonly used ones are:

- **Single deepest pocket technique**: This is the method commonly used when performing the fetal "biophysical profile". In this method the vertical dimension of the largest pocket of amniotic fluid that does not contain umbilical cord or fetal extremities is measured at a right angle to the uterine contour. The results are interpreted as follow:
  - Oligohydramnios: depth of 0 to 2 cm
  - Normal: depth of 2.1 to 8 cm
  - Polyhydramnios: depth greater than 8 cm
- Amniotic fluid index: The amniotic fluid index (AFI) measurement is calculated by first dividing the uterus into four quadrants using the linea nigra for the right and left divisions and the

The ability of AFI to detect abnormal amniotic fluid volume (low or high) is poor because many pregnancies with normal amniotic fluid volume will be falsely characterized as abnormal and a large number with truly abnormal amniotic fluid volumes will be missed.

umbilicus for the upper and lower quadrants. The maximum vertical amniotic fluid pocket diameter in each quadrant not containing cord or fetal extremities is measured in centimeters; the sum of these measurements is the AFI. The result are interpreted as follow:

- Oligohydramnios: 0 to <5 cm
- Normal: 5 to 25 cm
- Polyhydramnios: greater than 25 cm

- Subjective assessment: In this method the ultrasonographer scans the uterine contents and subsequently reports the amniotic fluid volume as oligohydramnios, normal, or polyhydramnios.

⇨Diagnosis of fetal malformation:

Ultrasound is currently the most powerful tool for screening and diagnosis of fetal malformation. The sensitivity and specificity of ultrasound examination in diagnosis of fetal malformation are continuously improving, as experience and equipments are getting better. More and more anomalies can now be diagnosed at earlier stages of gestation. This increasingly creates both clinical and ethical challenges.

It should however be emphasized that prenatal ultrasound cannot diagnose all malformations and problems of an unborn baby (the sensitivity of prenatal diagnosis of abnormalities range from 40 to 98 percent). Factors such as fetal positon, amniotic fluid volume, obesity and nature course of the anomaly can affect the sensitivity of prenatal diagnosis. Therefore a normal scan report does not guarantee that the baby will be completely normal. Therefore it is important that the benefits and limitations of ultrasonography should be discussed with all patients, before its application for that purpose.

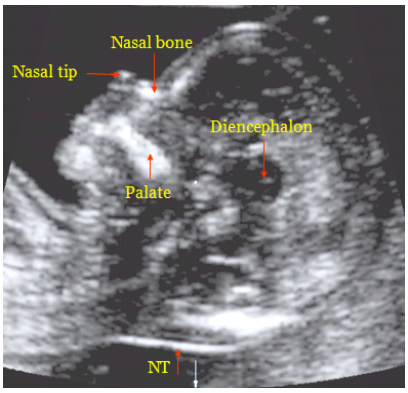


Figure 29-1: Shows the details of some of the important first trimester soft marches for DS. NT = nucal transluecency,

The benefits of prenatal diagnosis of congenital malformations have already been discussed (Chapter 27 screening and prenatal diagnosis).

➢First trimester screening for Down syndrome and fetal anomalies with

scanning between 11 and 13 weeks has become a standard element of prenatal care in many countries. First trimester ultrasound "soft" markers for chromosomal abnormalities such as the absence of fetal nasal bone, an increased fetal nuchal translucency (the area at the back of the neck) are now offered either alone or in combination with biochemical markers (serum BhCG, Papa, AFP) as a universal screening tool for all pregnant women (Chapter 27)

- Second trimester genetic sonsography with or without biochemical tests (triple test: AFP, BhCG, non-conjugated estriol) are also offered for those who do not present early enough in the first trimester.
- Ultrasound is also essential in the application of other diagnostic procedures in prenatal diagnosis such as amniocentesis, chorionic villus sampling, and cordocenteis and fetal therapy such as intrauterine blood transfusion.

⇨**Multiple pregnancies**.

Ultrasonography is invaluable in determining the number of fetuses, the chorioncity, fetal presentations, evidence of growth restriction and fetal anomaly, the presence of placenta previa, and any suggestion of twin-to-twin transfusion (Chapter 22 Multiple Gestation).

⇨**Transvaginal Ultrasound:**

With specially designed probes placed in the vagina of the patient, ultrasound scanning can be performed. The image provided is usually better because the scan head is in closer proximity to the uterus and the sound frequency used is higher.

In pregnancy transvaginal scanning has many applications such as:

- In patients who are obese and/ or in the early stages of pregnancy when fetal pulsation can be seen as early as 6 weeks of gestation.
- When it is necessary to differentiate between intra and extra uterine pregnancy.
- An increasing number of fetal abnormalities can now be diagnosed in the first trimester using the vaginal scan.
- In the second trimester and latter for measurement of cervical length in suspected cases of cervical incompetence and/or diagnosis of preterm labor.

- To confirm a diagnosis of placenta previa particularly posterior placenta previa or border line low-lying placenta (Figure 29-2).

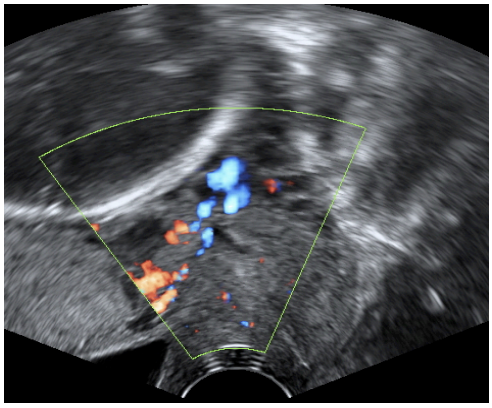


Figure 29-2: TV scan with color mapping shows posterior placenta previa, the edge of the placenta cover the cervical canal

⇨**Three-dimensional sonography**:

This technology depends on capturing volume of data (three dimension) rather than single section. The captured volume can then, using sophisticated software be analyses in two-dimensional displays in different planes. Therefore the use of three-dimensional technology can reduce scanning time by capturing a volume and then analyze it when the patient had already gone.

In addition with three-dimensional it is possible to have surface rendering image of the fetus (figure 29-3). It increases psychological bonding between the parents and the baby. It also demonstrates abnormalities such as facial abnormalities and neural tube defects very clearly. However the ability to obtain

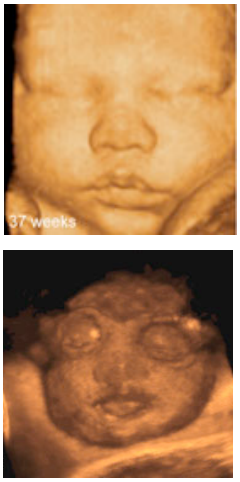


Figure 29-3: Top render picture of normal fetus at 27 weeks. Bottom picture of anencephalic fetus

a good 3-D picture depend not only on the operator skill but also on other factors such as the amount of liquor (amniotic fluid) around the fetus, its position and the degree of maternal obesity.
When movements are added to the 3D scan the image is known as 4D. The 3D and 4D scanning are not yet standard method of scanning but as time goes by the application and benefit of 3 and 4 D scanning in patient management are being defined.

⇨Doppler ultrasound:

The Doppler shift principle has been in use long time in fetal heart rate detectors (The handheld device to detect fetal heartbeat).
In recent years it was further developed into Doppler ultrasound technology, which currently have many application in obstetrics.

- Doppler flow velocity waveforms analysis: in this technique blood flow characteristics in the fetal blood vessels can be assessed. Various ratios of the systolic to diastolic flow are used. Diminished flow, particularly in the diastolic phase of a pulse cycle is associated with compromise in the fetus. The blood vessels commonly examined are the umbilical artery, the aorta, the middle cerebral artery and the maternal uterine arteries (Figure 29-4).
- Color flow mapping: This clearly depict the flow of blood in fetal blood vessels in a real-time scan, the direction of the flow being represented by different colors. Color Doppler is particularly indispensible in the diagnosis of fetal cardiac and blood vessel defects
- Power Doppler (Doppler angiography). It uses amplitude information from Doppler signals rather than flow velocity information to visualize slow flow in smaller blood vessels. A color perfusion-like display of a particular organ such as the placenta overlapping on the 2-D image can be very nicely depicted. It can clearly delineate a low-lying placenta (Figure 29-2).

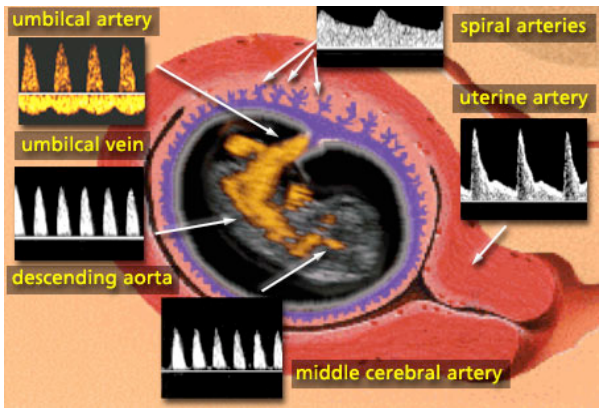


Figure 29-4: common vessels studied by Doppler in pregnancy

- Fetal Venous Doppler Blood Flow:

  More recently venous blood flow in the fetus mainly in the Ductus venosus, inferior vena cave and pulmonary veins using Doppler technology is being utilized in assessment of cases of FGR. It was found that in some cases it yield more sensitive information as to the degree of fetal adaptation and compensation to a hostile hypoxic environment thus helps in deciding optimum timing for delivery.

- Common application of Doppler in obstetrics include:
  - Monitoring fetal wellbeing in cases of intrauterine growth restriction. (Chapter 7, Antepartum Fetal Surveillance and Chapter 23, of Fetal Growth Restriction)
  - Evaluating the fetal cardiovascular system, in fetal echocardiography.
  - Evaluation of fetal anemia and timing for further intrauterine transfusion by assessing peak systolic flow in the middle cerebral artery (Chapter 25 Rh isoimmunization). This method has greatly replaced the invasive method of amniocentesis for measurement of amniotic fluid bilirubin.

⇨ **Intrapartum Ultrasound scanning:**

Intrapartum application of ultrasound has limited place but it can provide very valuable information. For example in determining the presentation of a second twin, or in cases of suspected abnormal cephalic presentation such as face or brow presentation.

⇨**Schedule and Frequency of ultrasound examination in pregnancy:**

There is no hard and fast rule as to the number of scans that should be performed during her pregnancy. In normal cases the following scan schedule can be applied:

- The first scan is generally booked at about 7 weeks to confirm pregnancy, exclude ectopic or molar pregnancies, confirm cardiac pulsation and measure the crown-rump length for dating.
- Between 11to14 weeks to measure the fetal nuchal translucency and to examine for other soft markers of Down syndrome with or without blood test biochemical markers at the same visit. Multiple pregnancies can be firmly diagnosed and dates and growth can also be assessed.
- Between 18 to 20 weeks mainly to look for congenital malformations, particularly for fetal cardiac examination. At this age the fetus is large enough for an accurate survey of the fetal anatomy. Placental position is also determined. Further scans may be necessary if abnormalities are suspected.
- Further scans may be required at around 32 weeks or later to evaluate fetal size (to estimate the fetal weight) and assess fetal growth. Or to follow up on possible abnormalities seen at an earlier scan.

The most common reason for having more scans in the later part of pregnancy is in cases of fetal growth retardation.

⇨**Prediction of pregnancy disorders:** this is a new emerging role of early ultrasound examination. Recent studies yield some strong evidence that prediction of patients at risk of developing disorders such as severe PET, preterm labor or fetal growth restriction is possible by ultrasound examination early in the second trimester. Various parameters have been suggested including maternal uterine artery Doppler blood flow, or cervical length measurements in addition to some biochemical markers. The use of those parameters together with other risk factors as obtained from patient history can define subgroup of women at high risk of developing such complications. The whole concept of “Predictive medicine” and its application in clinical practice is a promising and emerging application of ultrasound in obstetrics.

⇨Safety of Ultrasound:

Unlike X-rays, ionizing irradiation is not present and embryotoxic effects associated with such irradiation should not be relevant. However in laboratory situations the use of high intensity ultrasound is associated with the effects of "cavitations" and "heating" which can be occur with prolonged insonation.
No harmful effects on cells have been observed in embryos and offspring of animals and humans in the large amount of studies.

The greatest risks arising from the use of ultrasound are the possible over- and under- diagnosis that may occur as a result of inadequate training of staff, and or the use of poor equipment. It can create either unnecessary anxiety and perhaps intervention or alternatively missing important diagnosis of abnormality

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Chapter 30

Diabetes and Pregnancy

Diabetes is probably the second most common medical disorder, following anemia, encountered in pregnancy. Before the discovery of Insulin as a therapeutic agent (in 1920) the prognosis for a diabetic mother and her fetus was very poor. The incidence of maternal mortality may reach up to 20 % whereas perinatal mortality was around 60 %. However following the discovery of insulin and with better understanding of the pathophysiology of diabetes mellitus, maternal mortality has almost been eliminated and the perinatal mortality is almost similar to that of non-diabetics.

By the end of this chapter you should be able to:
Describe the changes in carbohydrate metabolism**.**
Describe the pathophysiology of gestational diabetes
Describe the types and classification of diabetes in pregnancy
List the effects of pregnancy on diabetes:
List the effects of diabetes on pregnancy:
- First Trimester Complications:
- Second and Third Trimester Complications:
- Neonatal Complications:

Outline the principle of management of diabetes in Pregnancy
Gestational Diabetes:
Define GD
List the methods of screening for GD
List the Diagnostic criteria for diabetes
Describe the principle of management of diabetes in labor
Postpartum Management: At short and long term

Definitions:

Three types of diabetes may be encountered in pregnancy these are; Type I diabetes (insulin dependent diabetes) or Type II diabetes (non-insulin dependent diabetes). The third variety is known is **"Gestational diabetes" which refers to abnormal glucose tolerance discovered for the first time during pregnancy**. Gestational diabetes is the type of diabetes that creates most of the controversies. There are different views as to its entity and definition, how to screen and how to diagnose and even the management options.

Incidence and Prevalence:

The prevalence of diabetes is influence by genetic as well as environmental variables. Type I diabetes is relatively more common among Western population than Type II diabetes, whereas Type II diabetes is more prevalent in developing countries of Africa and Asia.

The incidence of gestational diabetes (GD) i.e. glucose intolerance discovered for the first time in pregnancy depends on the population and the diagnostic criteria being used. GD is higher among Eastern than Western population. In some parts of Saudi Arabia gestational diabetes had prevalence up to 20% among hospital population. While in Western countries the reported prevalence of gestational diabetes varied between 3-8 %. A proportion of cases of GD are in fact cases of NIDD that is discovered for the first time in pregnancy.

Carbohydrate metabolism in Pregnancy:

The key features of carbohydrate metabolism in pregnancy is that all the changes aim to ensure that all at times whether it is maternal fed or starving stat the fetus gets "glucose" as its primarily metabolic substrate. This explain most of the following facts about carbohydrate metabolism in pregnancy:

- Glucose is freely transported to the fetus across the placenta by a process of facilitated diffusion. Thus there is a positive correlation between maternal and fetal plasma glucose level.

- In a fasting state the maternal body quickly switch to alternative fuels (mainly fat) to spare glucose for the fetus. Thus in pregnancy the fasting maternal blood glucose is normally below non-pregnant values to a level between 55 and 65 mg/dl. In the mean time free fatty acids, and plasma ketone bodies concentrations are several times higher, particularly after an overnight fast. This state is known as 'accelerated starvation'. Its aims are to use alternative fuels for maternal metabolism, while glucose is spared for fetal consumption.

- The placenta produces hormones that have strong anti-insulin action. The most important ones are human plancetal lactogen (HPL) and also the steroid hormones (estrogen and progesterone). Those hormones compete with the maternal insulin at cellular level to prevent the maternal body from utilizing glucose, and ensure its availability to the fetus. The production of those hormones increases as pregnancy progress in parallel with the increasing demands of the growing fetus for glucose.

- In response to the rising level of the "placental anti-insulin" hormones the B cells of the maternal pancreas undergoes a process of hyperplasia and hypertrophy to produce increasing amount of Insulin.

Renal handling of Glucose in Pregnancy:

In the non-pregnant state almost all the glucose that filtrates through the glomeruli is reabsorbed by the tubules, unless the amount of the glucose filtered exceeds the renal threshold or the capacity of the renal tubules to reabsorb it. In normal pregnancy the glomerulare blood flow and the glomerular filtration rate increases by approximately 50% from the non-pregnant state. Thus the filtered glucose load increases. In the mean time the renal threshold i.e. the capacity of the tubules to reabsorb glucose is diminished. The net effect of those two changes is that glycosuria is not common among pregnant women who are not diabetic, especially in the second and third trimester. Thus in pregnancy the presence of glycosuria does not necessary means an increase in the plasma glucose level and there is no correlation between the level of glycosuria and the blood glucose level.

The Pathophysiology of Gestational Diabetes:

The increased production of diabetogenic hormone put increasing demands on the maternal pancreas to produce more insulin, particularly during the second half of gestation as the level of the placental diabetogenic hormones increases. In addition the rate of insulin degradation during pregnancy rises due to the action of the placental enzyme 'insulinase'.

To compensate for the increasing demands of insulin, the B cells of the pancreases undergoes hyperplasia and hypertrophy to produce more insulin. But if it fails to meet those requirements then, hyperglycemia or gestational diabetes develops.

The maternal hyperglycemia results in fetal hyperglycemia. In response to the fetal hyperglycemia, the B-cells of the fetal pancreas undergo hyperplasia to produce increasing amount of insulin (fetal hyperinsulinemia). Thus a state of fetal hyperglycemia and hyperinsulinemia develop.

The resultant fetal hyperglycemia and hyperinsulinemia are the two factors responsible for most of the fetal complications in GD. The extent of those complications depends on the severity and time of onset of the hyperglycemia (GD).

In fact in addition to the hyperglycaemia the fetus of the uncontrolled diabetic mother have a surplus of other metabolic substrates namely amino acids. These excessive nutrients in the presence of fetal hyperinsulinaemia results in fetal macrosomia

Effect of Pregnancy on Diabetes:

Pregnancy in itself does not worsen the course of diabetes or accelerate the development of diabetic complications. However patients of type I diabetes of long duration and already established vascular or neurogenic complications should have special care. Despite the clear benefits to the fetus of strict glycemic control, there are two potential hazards to the mother: hypoglycemia and worsening of diabetic retinopathy. The degree to which this occurs during pregnancy is related to the baseline level of retinal disease and to the magnitude of

the reduction of chronic hyperglycemia. The worsening of diabetic retinopathy is thought to be mediated by closure of small retinal blood vessels that were narrowed but patent. Frequent retinal evaluation during pregnancy is important in women with baseline retinopathy and hyperglycemia who then become euglycemic.

A diabetic woman with already compromised renal function is at increased risk of renal complications even renal failure during pregnancy from urinary tract infection.

Minor other complications such as recurrent infection of the genital tract e.g. yeast and bacterial infection of the urinary tract seems to occur more frequently among diabetic pregnant women.

Diabetic patients on oral hypoglycemic have to change to insulin therapy. Unlike insulin oral hypoglycemic agents have a small molecular weight and cross the placenta. Early in pregnancy during the embryonic phase there is a potential risk of teratogenic effect, whereas in late pregnancy because of immaturity of the fetal liver enzymes the concentration of hypoglycemic agents in the fetal circulation may expose the fetus to prolonged period of hypoglycemia. Recently there have been some evidences that some oral hypoglycemic may be used during pregnancy in selected cases.

Effect of Diabetes on Pregnancy:

Diabetes creates an abnormal metabolic environment that places the fetus at increased risk of variable complications. The perinatal outcome is related to the onset and duration of glucose intolerance and the severity of the disease. Complications are minimal in infants of mothers with gestational diabetes. The most difficult pregnancies for the mother and fetus occur in diabetic women with renal, cardiac, or retinal disease.

Diabetes in pregnancy has been classified into categories depending on the age of onset, the duration of maternal diabetes and the presence or absence of vasculopathy, The classification know as White classification (devised by Priscilla White in 1949) which is used to estimate the prognosis and risk factors for fetal compromise (Table 30-1).

Class	Age at Onset	Duration in (years)	Vascular Diseases	Insulin Needed
Gestational diabetes				
A_1	Any	0	0	0
A_2	Any	0	0	+
Pre-gestational Diabetes				
B	>20	<10	0	+
C	10-	Or 10-	0	+
D	<10	Or	+	+
F	Any	Any	+	+
R	Any	Any	+	+
T	Any	Any	+	+
H	Any	Any	+	+

Table 30-1 -- Modified White Classification of Pregnant Diabetic Women *Modified from White P: Pregnancy complicating diabetes. Am J Med 7:609, 1949.*

- **First Trimester Complications**:

1. Congenital Malformations: The incidence of fetal anomalies among diabetics' women is about 3 times that of non-diabetic women. The risk is related to the severity of hyperglycemia and other metabolic abnormalities during the time of organogenesis. Hence hyperglycemia-induced teratogenicity occurs almost exclusively in pregestational "frank" diabetes. While in typical cases of GD, since there is no metabolic disturbance at the time of embryogenesis there is probably no increased risk of fetal anomalies over non-diabetics.

Any type of anomalies can occur. The most common are skeletal, central nervous system and cardiovascular anomalies. One of the pathognomonic anomalies that have been observed with diabetes, though in itself is a very rare anomaly is caudal regression syndrome (sacral agenesis).

2. High Rate of Miscarriage: The risk of spontaneous abortion is higher among diabetic women. This again may be due to increased risk of fetal anomalies as well as to abnormal metabolic milieu. Hence it is more common among poorly controlled Type I and Type II diabetic women.

- **Second and Third Trimester Complications**:

1. Fetal Macrosomia and its adverse effects:

Insulin is an anabolic hormone, hence fetal hyperinsulinemia in the presence of excessive substrate of glucose as well as amino and fatty acids leads to increase deposition of fat and glycogen particularly in the insulin sensitive tissue. The fetus becomes large (macrosomic) with characteristic facial appearance due to excessive fat deposition around the face, neck and shoulders areas (Figure 30-1). The consequences of diabetic macrosomia are increased rate of operative delivery and shoulder dystocia with its complications to the mother and fetus.

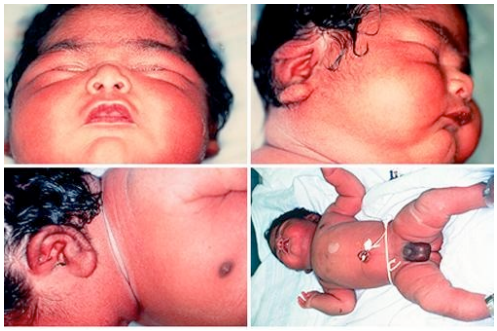

Figure 30-1: the macrosomic infants of diabetic mothers appear large and plethoric have larger shoulder and extremity circumferences, a decreased head-to-shoulder ratio, higher body fat, and thicker upper extremity skin folds compared to nondiabetic control infants of similar weight and length

2. Fetal Growth Restriction (FGR): Although macrosomia is the typical complication of diabetes in pregnancy, intrauterine growth restriction — IUGR can occur in IDDMs, especially when diabetes is complicated by vasculopathy (White's class F and above), which causes placental insufficiency. Other possible causes of FGR in diabetics are; development of preeclampsia, a frequent complication of diabetic pregnancies and congenital anomalies.

3. Preterm birth: the rates of both indicated and spontaneous preterm birth are higher in

women with pre-gestational diabetes mellitus compared to healthy controls. Indicated preterm delivery is related factors such as preeclampsia, worsening nephropathy, macrosomia, and poor glycemic control, which is associated with a higher risk of late fetal death. Preterm infants are at increased risk of hyaline membrane disease, especially in the setting of poor maternal glycemic control.

4. Polyhydramnios: and its adverse effects include maternal discomfort, preterm labor, unstable lie, operative delivery, and postpartum hemorrhage. Polyhydramnios occur because of fetal polyuria secondary to fetal hyperglycemia. It is therefore a sign of uncontrolled diabetes.

5. Fetal hypoxia: Although fetuses of poorly controlled diabetic mothers with IDD are typically large for date (macrosomic). They suffer from hypoxia due to several factors:
- Elevated metabolic rate leads to increased oxygen consumption
- Increased proportion of glycosylated hemoglobin (hemoglobin combined with glucose), which has a poor O2 carrying capacity.
- Associated vasculopathy in long standing cases of Type I diabetes.

Fetal hypoxemia has a variety of adverse effects: it stimulates the synthesis of erythropoietin, which can result in polycythemia, it promotes catecholamine production, which can lead to hypertension and cardiac hypertrophy; and it may contribute to the 20 to 30 percent rate of stillbirth seen in poorly controlled diabetic pregnancies. It also increases rate of intrapartum fetal complications such as fetal heart rate abnormalities, low Apgar scores, and intrauterine death.

5. Intrauterine fetal death: Intrauterine fetal death at term is not uncommon occurrence with poorly controlled IDD diabetes considering the adverse metabolic environment those fetuses' lives in. Chronic hyperglycemia, together with hyperinsulinaemia and state of relative hypoxia makes the fetus very vulnerable to irregular fluctuation in blood glucose, particularly if complicated with attacks of diabetic ketoacidosis.

Neonatal Complications:

1. Respiratory Distress syndrome: Respiratory distress syndrome (RDS) occurs more frequently at all gestational ages in infants of diabetics than those of normal pregnancies. Most probably due to delayed maturation of surfactant synthesis caused by hyperinsulinemia.

To ensure lung maturity in diabetic pregnancies when elective delivery is planned, phosphatidylglycerol should be present in amniotic fluid and the ratio of lecithin to sphingomyelin (L/S ratio) should be more than 2.0 or even 3.5

2. Neonatal hypoglycemia: Hypoglycemia is defined as blood glucose levels below 40 mg/dL (2.2 mmol/L). Hypoglycemia is most common in macrosomic infants. It

occurs because of persistent hyperinsulinemia in the newborn after interruption of the intrauterine glucose supply from the mother.

3. Hyperbilirubinemia: Poor maternal glycemic control increases the risk of neonatal hyperbilirubinemia. Jaundice occurs due to both plycythemia that increases the hemolysis load and liver enzyme prematurity.

4. Neonatal Hypocalcemia and Hypomagnesemia: more common in IDD mother who has low birth weight and or premature ones. Its extend is related to the severity and duration of IDD.

5. Perinatal asphyxia: IDMs are at increased risk for intrauterine or perinatal asphyxia.

6. Hyperviscosity syndrome: Fetal hypoxia stimulates fetal erythropoietin production, which results in increased fetal red cells mass (Polycythemia), which causes hyperviscosity. The hyperviscosity syndrome include vascular sludging, ischemia, and infarction of vital organs and renal vain thrombosis seen in IDD.

Management of Diabetes in Pregnancy:

⇒ Pr-pregnancy counseling:

The aims of pre-pregnancy counseling are:

- Patient education: informing women about the risks of diabetes on pregnancy and the pregnancy on diabetes and the importance of attaining strict glycemic control before and during pregnancy.
- Evaluation of the disease severity: This evaluation should include information on the duration and type of diabetes, history of acute complications (infections, ketoacidosis, severe hypoglycemia) and chronic complications (retinopathy, nephropathy, neuropathy, hypertension, cardiovascular disease).
- Pre-conception glycemic control: Pre-conception glycemic control plays an important role in reducing the risk of fetal and neonatal complications. Therefore Pregnancy should not be attempted before achieving optimum glycemic control, which is best, evaluated by measurement of maternal glycosylated hemoglobin (A_1C). A_1C reflects the average blood glucose concentration over the previous 8 to 12 weeks (NR for non pregnant < 6%).

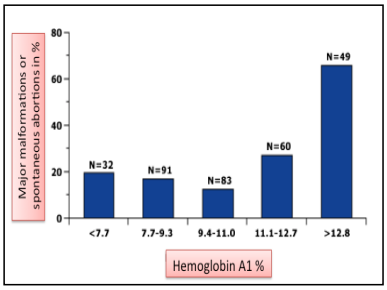

Figure 30-2: the bars shows positive association between HBA1c at the time of conception and rate of fetal anomalies or miscarriage

⇒ Management of pregnant women with pre-gestational diabetes (Type I and II):

Successful management of diabetes is multidisciplinary

team dependant. It requires cooperation between obstetrician, diabetologist, education nurse and dietitian. The aims of management of a pregnant diabetic are:

1) Management of the diabetes: which include:
    a. Glycemic control.
    b. Screening, monitoring, and intervention for maternal medical complications (e.g., retinopathy, nephropathy, hypertension, cardiovascular disease, ketoacidosis, thyroid disease).
2) Monitoring and management of fetal and obstetrical complications (e.g. congenital anomalies, preeclampsia, macrosomia)

The first prenatal visit: the objectives in this visit are; to assess the baseline severity of the disease and educate the patient regarding the potential risks of the uncontrolled diabetes as well as the routine aspect of pregnancy care.
The severity of the disease can be categorized according to the White classification. However because complications are known to occur more in women with vasculopathy, a simpler categorization of "vascular disease present" or "vascular disease absent" has been proposed instead of the White classification.

Tests and investigations: the following are the main tests that should be considered for assessment of the severity of the diabetes, in addition to the standard prenatal tests.

- Maternal glycosylated hemoglobin concentration.
- Baseline renal functions.
- Thyrotropin (TSH) and free thyroxin (T4), as the incidence of thyroid dysfunction in women with type 1 diabetes is as high as 40 percent.
- Electrocardiogram, as a screen for ischemic heart disease, especially in women with evidence of diabetic vasculopathy.
- Ophthalmic examination to detect retinopathy.

Strategy for Control of Blood Glucose:

The main objective of management of diabetes in pregnancy is to induce a state of near euglycemia. The target of desirable blood glucose is as shown in Table 30-2 for fasting, one and two hours postprandial.

Test	Glucose levels (mg/dL (mmol/L)
Fasting	<96 (5.35)
One hour Post Prandial	<140 (7.75)
Two hours Post Prandial	<120 to 127 (6.65 to 7.05)

Table 30-2: Treatment Targets for Women with Gestational Diabetes

The strategy for control of blood glucose includes (1) Diet modification, (2) exercises, (3) pharmacotherapy. While the first two methods are the first option in cases

of gestational diabetes, in pre-gestational diabetes pharmacotherapy is almost always required. In standard practice this pharmacotherapy means insulin therapy. Most patients will require multiple doses per day of combined short and human regular (NPH) insulin. The type of insulin used should be human insulin with the least immunogenic activity in order to minimize the transplacental transport of insulin antibodies.

The dosage of insulin regimen varies according to the gestational age, patient's body mass index, glucose levels, and lifestyle. However Insulin is typically started at a dosage of 0.7 units per kg per day (based on prepregnancy weight), given in divided doses. Two thirds of the total insulin dose is given in the morning, with the remainder given before dinner. The morning dose should be two thirds NPH and one third short acting insulin, and the pre-dinner dose should be equal parts NPH and short-acting insulin. As pregnancy progress the requirement of insulin expected to increase.

Follow up:
Admission to the hospital may be required for initial evaluation and for education. However in the majority of times diabetes educators can advice patients on diet, insulin administration, and use of self-glucometer for blood glucose monitoring. The frequency of follow up depends on several factors such as the severity of diabetes and the patient compliance.

Obstetric management:
The obstetrical management of diabetic mothers should include in addition to the standard antenatal care special strategy for:

- Screening for fetal congenital malformations: by first and/or second trimester screening.
- Monitoring for fetal wellbeing: usually begins around 32 weeks.
- Ultrasound assessment for estimated fetal weight and macrosomia: in the third trimester.

The extend and frequency of fetal monitoring depends on several factors including the degree of diabetes control, fetal condition and presence of other obstetrical complications such as pre-eclampsia.

Deliver and labor:
The timing and mode of delivery depends on several factors including: the degree of glycemic control, estimated fetal weight and wellbeing, the presence of other maternal diseases (e.g. PET, cardiac disease) and other factors (e.g. previous obstetrics history, maternal age).

However patients on insulin therapy even with well-controlled blood glucose are advised to be delivered at the expected delivery date (40 weeks). Also studies have shown that diabetic fetuses with estimated weight more than 4500 gm are better delivered electively by cesarean section, which probably reduce their risk of having shoulder dystocia.

Special care is needed to maintain blood glucose during labor and prevent hypoglycemia. Capillary blood glucose should be measured every one or two hours. If insulin therapy is needed it should be given either as subcutaneous doses or intravenous infusion.

Gestational Diabetes:

Screening and Diagnosis:

The diagnosis of gestational diabetes is made following a positive glucose tolerance test (GTT) i.e. if two or more of the plasma glucose measurement exceed a threshold levels. Table 30-3 shows the most two commonly used GTT tests and the diagnostic thresholds for each.

	Plasma or serum glucose level			
	Mg/dl	mmol/l	Mg/dl	mmol/l
Fasting	95	5.3	≥125	6.9
One hour	180	10.0		
Two hours	155	8.6	≥140	7.8
Three hours	140	7.8		

However GTT is a cumbersome, time and money consuming test, and should only be performed if there is significant risk for having GD. The presence of one or more of the following clinical markers is considered as risk factors for development of GDM (i.e. indication for GTT):

- Family history of first degree relative with diabetes mellitus e.g. parents or sibling.
- Obesity.
- Previous bad obstetric history: repeated miscarriage (>3), delivery of macrocosmic babies, stillbirth, neonatal death, or previous congenital malformations.
- Present obstetric risk factors: Macrosomic babies, Polyhydramnios, fetal

The 3 hours 100 gram OGTT: Glucose concentration greater than these values at two or more time points is a positive test.	The 2 hours 75 gram OGTT: Glucose concentration greater than any one value is a positive test

Table 30-3: The two diagnostic criteria for gestational diabetes mellitus. The modified National Diabetes Data group 100 gm test and the World Health Organization 75 gm Glucose Tolerance test.

anomaly.
- Glycosuria: before 18 weeks gestation, or repeated and heavy glycosuria, or second fasting sample of urine glycosuria.

However if we depend on those risk factors alone, only 50% of cases of GD will be diagnosed, while the remaining 50% of GD develop in women who have no obvious risk factor. Therefore it is proposed that all pregnant women, particularly older than 25 years of age should have some form of screening test for GD.
However so far there is no ideal screening test i.e. cheap, reliable, and sensitive test. The following are some of the most commonly used screening tests for GD.

Screening tests for GDM:

- The 50 g glucose challenge test:

In order to have a standard challenge for the pancreas; all women are given one dose of 50 g of glucose. There is no need for fasting or especial preparation before administration of glucose. After one hour a venous blood sample is obtained for measurement of plasma glucose level. The test is considered positive if the blood glucose level is above a predetermined cut off level, usually above 140 mmol/l (7.8 mmol/l).

- Two-hour 75-g GTT:

A simplified 75 g glucose tolerance test may be more cost-effective than the three-hour test. Sometimes this test may be used as one step approach for both screening and diagnosis

- Urine test for Glycosuria:

Is probably the most widely used screening test, being cheap and easy to perform. However the specificity of this test is poor because a large proportion of normal non-diabetic pregnant women may have glycosuria due to the normal renal physiological changes in pregnancy rather than hyperglycemia, except perhaps first trimester glycosuria.

- Random and Fasting blood glucose (RBG and FBG) measurement:

FBG may also be used as screening test. If the result is above a predetermined cut-off value then the patient is likely to have GDM and is referred for a GTT. Again, the test may be easy to perform but it is difficult to have all patient in a fasting state. In addition patients who develop postprandial hyperglycemia are missed.
Also in case of random blood glucose measurement, the results are very variables depending on the time and nature of the last food or drink the women might have had.

Optimal timing of screening:
Screening is best performed at time when the stress of the placental daibetogenic hormones of pregnancy is at its maximum. Therefore it is usually undertaken between 24 and 28 weeks of gestation. However, in special cases (e.g., marked obesity, personal history of GDM, glycosuria, or strong family history of diabetes) screening may be performed at the

first prenatal visit as in such cases it is possible that the patient has undiagnosed type 2 diabetes

Management of Gestational Diabetes:
The principle and objective of management of GD are the same as in patients with pre-gestational diabetes i.e. *maintain euglycemia* and *obstetrical surveillance for fetal wellbeing*.

However, the risks for the fetus and the mother for patients with GD is far less than among patients with frank diabetes. Most of the fetal complications are related to third trimester hyperglycemia namely polyhydramnios and fetal macrosomia.

Blood glucose control in patient with GD: The primary option in patient with GD is "dietary medication" and exercises. If both failed to achieve the target blood glucose control; patients have to start insulin therapy following the same regimen described before.

Oral hypoglycemic are generally not used in pregnancy. However recent studies have shown that some types of oral hypoglycemic namely the sulfonylurea Glyburide and Metaformin (Glucophage) can be used in pregnancy. Despite the available data, the absolute safety of these agents is yet to be established.
Labor and Delivery:

In patients with diet-controlled GD labor will be allowed to start spontaneously at term i.e. usually there is no need for induction of labor unless for obstetrical reason or if there is other risk factors.

During labor patients on diet control usually do not require active glucose monitoring; however, it is advisable to measure blood glucose levels on admission to the labor room. In contrast, women who are taking medication for gestational diabetes require more frequent glucose monitoring, typically with hourly evaluations.

Postpartum Management:
Most women with gestational diabetes do not require insulin therapy following delivery, although it is prudent to check glucose levels before discharge.

Approximately 50 percent of women with gestational diabetes will develop type 2 diabetes within five to 10 years. Those women are also at risk of gestational diabetes in subsequent pregnancies. Thus, regular screening for type 2 diabetes should be strongly encouraged (every 2 to 3 years). Patients should be advised to adopt a lifestyle that promote postpartum weight loss include breastfeeding, exercising at a moderate intensity for at least 150 minutes per week, and modifying the diet for specific weight-loss goals.

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Chapter 31

Hypertensive Disorders in Pregnancy

Professor Hisham Ramadani

Four types of hypertensive disorders may be encountered in pregnancy:

- **Preeclampsia - eclampsia:**
- **Pre-existing hypertension:**
- **Preeclampsia superimposed upon preexisting hypertension:**
- **Gestational hypertension:**

Preeclampsia, the pregnancy specific hypertensive disorder is still one of the important causes of maternal and fetal morbidity and mortality particularly in developing countries.

By the end of this chapter you should be abl:
Deince and describe the diagnostic criteria for each of: PET, eclampsia, gestational hypertension, superimposed PET, and HELLP syndrome.
Describe the pathophysiology of PET
List the materal and fetal morbidity and mortality of PET
List the risk factors of PET
List the criteria of severe PET
Describe the prinicpel of management of different types of severity of PET
Describe the principel of managnet of eclampsia
Describe the principle of manangement of HELLP syndrome

Incidence:

Hypertensive disorders complicate 5 to 10 percent of pregnancies, depending on the study population.

- Preeclampsia occurs in approximately 3 to 14 percent of all pregnancies worldwide.
- Preexisting hypertension complicates about 3 percent of pregnancies.
- Gestational hypertension occurs in about 6 percent of pregnancies.

Preeclampsia and Eclampsia

Definition: Preeclampsia refers to the syndrome of new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman.

Diagnosis:
The criteria for diagnosis of preeclampsia are:
(1) Systolic blood pressure of 140 mmHg or Diastolic blood pressure 90 mmHg and
(2) Proteinuria of 0.3 grams or greater in a 24-hour urine specimen.
The rise of blood pressure should be present on two occasions at least 6 hours apart.
Preeclampsia is classified into severe and mild, depending on the elevation of blood pressure. Patients with severe disease have one or more of the findings in Table 31-1.

Criteria for severe preeclampsia
Symptoms of central nervous system dysfunction:
Blurred vision, scotomata, altered mental status, severe headache
Symptoms of liver capsule distention:
Right upper quadrant or epigastric pain Nausea, vomiting
Hepatocellular injury:
Serum transaminase concentration at least twice normal
Severe blood pressure elevation:
Systolic blood pressure 160 mm Hg or diastolic 110 mm Hg on two occasions at least six hours apart
Thrombocytopenia:
Less than 100,000 platelets per cubic millimeter
Proteinuria:
5 or more grams in 24 hours
Oliguria
Severe fetal growth restriction

Table 31-1: From Diagnosis and Management of Preeclampsia and Eclampsia. ACOG Practice Bulletin #33, January 2002 and Working Group Report on High Blood Pressure in Pregnancy.

Eclampsia refers to the development of grand mal seizures in a woman with gestational hypertension or preeclampsia.

The pathophysiology of preeclampsia:
The general consensus is that the pathological changes responsible for the development of preeclampsia begins early in pregnancy at the stage of placentation. Accordingly 3 distinct, sequential phases are necessary for its evolution.

- The first phase: failure of normal placentation, demonstrated by failure of invasion of the trophoblast into the intima and muscle layers of the spiral uterine artery within the endmetrium. This result in "placental underperfusion" In

Thromboxane: has a vaso-occlusive effect and increases platelets aggregation.
Prostacylin: has a vaso-relaxing effect and diminishes platelets aggregation.
In normal pregnancy there is a positive balance in favor of Prostacyclin.

normal pregnancy this process converts spiral arteries into a low resistance vessels in order to ensure adequate placental perfusion.

- The second phase: The resultant placental underperfusion/hypoxia/ischemia, cause local placenta damage, increased level of Thromboxane in relation to Prostacyclin, and to release of "stress factors" into the maternal circulation that alter maternal endothelial function and initiate the third phase.

- The third phase: In severe cases the local placental pathology and release of vaso-occlusive substances induce systemic complications and the maternal preeclamptic syndrome is detected clinically, as it starts to affects other body systems (Figure 31-1)

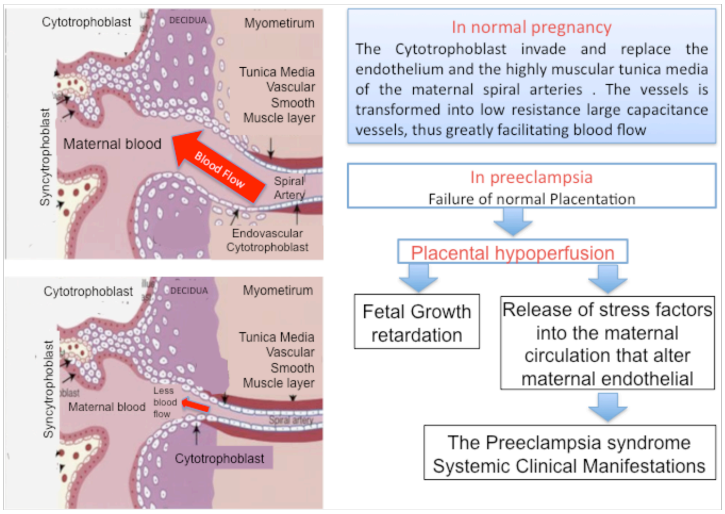

Figure 31-1: Diagrammatic presentation of the pathogenesis of pre-eclampsia. It begins with failure of remodeling of the spiral arteries with trophoblastic invasion. Remodeling of the spiral arteries probably begins in the late first trimester and is completed by 18 to 20 weeks of gestation

Risk Factors for Preeclampsia:

An important objective of ante partum care is to recognize risk factors for preeclampsia. In general PET is a diseases of primigravidas particularly at the extreme of the reproductive ages. Table 31-2 shows some of the risk factors for preeclampsia. A previous history of PET particularly severe with early onset places the women at a very high risk of recurrence. Some maternal diseases such as severe hypertension and antiphospholipid antibody syndrome, renal diseases, diabetes increases the risk of development of PET.

Risk factors for PET
Nulliparity
Preeclampsia in a previous pregnancy
Age >40 years or <18 years
Family history of preeclampsia
Diabetes mellitus
Chronic hypertension
Chronic renal disease
Antiphospholipid antibody syndrome or inherited thrombophilia
Vascular or connective tissue disease
Diabetes mellitus (pregestational and gestational)
Multifetal gestation
High body mass index
Male partner whose previous partner had preeclampsia
Hydrops fetalis

Table 31-2: risk factors for PET

Clinical Manifestation of Preeclampsia:

Preeclampsia is a systemic disease characterized by generalized endothelial dysfunction, small vessels vasospasm and disturbed endothelial control of vascular tone. The results are **hypertension**, increased vascular permeability results in **edema** and **proteinuria**, and abnormal endothelial expression of procoagulants leads to **coagulopathy**.

These changes cause ischemia of target organs, such as the liver, kidney, and placenta, the cerebrovascular circulation, sometimes with life-threatening results.

- Hypertension — Pregnancy related hypertension is defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg in a woman who was normotensive prior to 20 weeks of gestation.
- Proteinuria — significant proteinuria is defined as ≥ 0.3 g protein in a 24-hour urine specimen or persistent 1+ on dipstick. Proteinuria is due, in part, to impaired integrity of the glomerular barrier and altered tubular handling of filtered proteins (hypofiltration) leading to increased protein excretion
- Edema and intravascular volume — Most pregnant women have edema, whether or not they have preeclampsia. Therefore, the presence of edema is no longer part of the diagnostic criteria. However, sudden and rapid weight gain (e.g. >3 kg/week) and facial edema warrant evaluation for other clinical manifestations of preeclampsia.

  It must be remembered that the intravascular volume is lower than in normotensive pregnancy, despite sometimes severe edema.

- Hematologic changes: The most common coagulation abnormality in preeclampsia is thrombocytopenia due to formation of microthrombi. The prothrombin time, partial thromboplastin time, and fibrinogen concentration are not affected unless there are additional complications, such as abruption placentae or severe liver involvement.
- Microangiopathic hemolysis: may also occur and is detected by examination of a blood smear for schistocytes and helmet cells or elevation in the serum lactate dehydrogenase concentration (LDH).
- Liver: The clinical manifestations of liver involvement include right upper quadrant or epigastric pain, elevated transaminases and, in the most severe cases, subcapsular hemorrhage or hepatic rupture.
- Central nervous system and eye : CNS manifestations of preeclampsia include headache, blurred vision, scotomata, and, rarely, cortical blindness. Seizures in a preeclamptic woman signify a change in diagnosis to eclampsia. One in 400 mildly preeclamptic and 2 percent of severely preeclamptic women will develop eclamptic seizures. Stroke leading to death or disability is the most serious complication of severe preeclampsia/eclampsia, but is also rare.
- Cortical blindness is typically transient, but may be permanent if related to retinal pathology, such as retinal artery or venous thrombosis, retinal detachment, optic nerve damage, retinal artery spasm, and retinal ischemia, may be permanent .

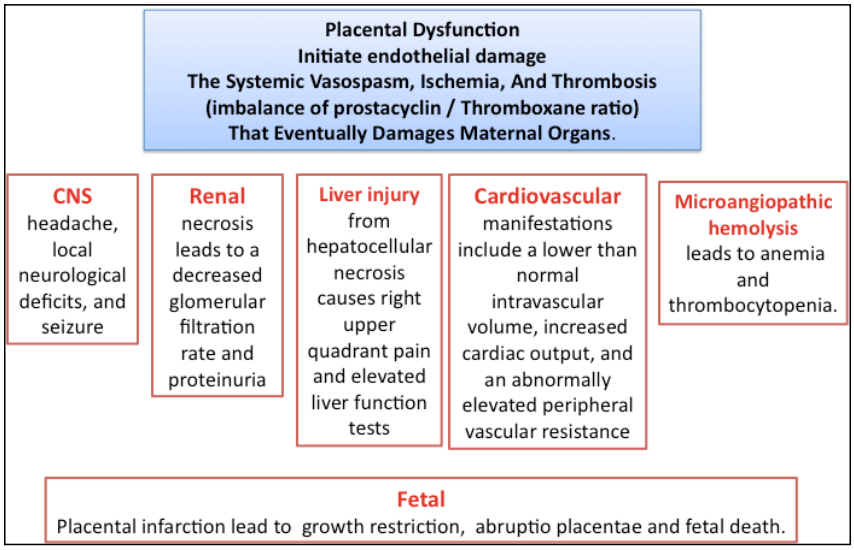

Figure 31-2: summary of the systemic features of pre-eclampsia

- Heart — Preeclampsia does not directly affect the myocardium. However, decrements in left ventricular performance can occur and reflect a physiologically appropriate response to increase after load.
- Pulmonary edema: can develop due to multiple factors, which include excessive elevations in pulmonary vascular hydrostatic pressure (PCWP) compared to plasma oncotic pressure, capillary leak, left heart failure, and iatrogenic volume overload.
- HELLP Syndrome: (Hemolysis, Elevated Liver function tests, Low Platelets) (see later).
- Fetus and placenta — The fetal consequences of chronic placental hypoperfusion are fetal growth restriction and oligohydramnios.
- Abruptio placenta although infrequent (less than 1 percent) in women with mild preeclampsia, but has been reported in 3 percent of those with severe disease.

Long-term maternal risks

Compared with women with no history of the disease, women with preeclampsia are, on the long term, at increased risk of developing hypertension, ischemic heart disease, stroke, and venous thromboembolism. The absolute risk that a woman with or without a history of preeclampsia would develop one of these cardiovascular events at age 50 to 59 years was estimated to be 17.8 and 8.3 percent, respectively.

Management of PET:

The management of preeclampsia should start with the following:

1. To confirm the diagnosis by excluding other disorders characterized by hypertension and proteinuria.
2. Assess the severity of disease; whether mild or severe.
3. Evaluate fetal age and wellbeing.

These goals are achieved as follow:

- History and examination: to gather risk factors for PET and or systemic diseases. On examination special attention should be paid to the symptoms and signs of severe pre-eclampsia namely: persistent occipital headache, blurring vision, epigastric pain or tenderness. Eye fundal examination for sings of vascular changes, and neurological examination (Knee jerk reflex is exaggerated in cases of severe PET)
- Investigations: include a full 24 hours urine collection for volume and protein loss. In addition to the blood tests shown in table 31-2.
- Fetal evaluation: by a nonstress test or biophysical profile including amniotic fluid volume. In addition, fetal growth should be evaluated in relation to gestational age.

Test	Interpretation
Blood hematocrit	Hemoconcentration supports the diagnosis of preeclampsia but hemolysis, if present, can decrease the hematocrit
Platelet count	Thrombocytopenia is a criterion of severe disease
Quantification of protein excretion	300 mg or more in 24 hours is necessary for diagnosis or at least 1+ protein on dipstick of two urine specimens collected at least four hours apart; 3+ or greater or 5 g or more per day is a criterion of severe disease.
Serum creatinine concentration	An elevated or rising level suggests severe disease.
Serum alanine and aspartate amino transferase concentrations (ALT and AST)	Elevated or rising levels suggest hepatic dysfunction indicative of severe disease
Tests for Microangiopathic hemolysis	Elevated Serum lactate dehydrogenase (LDH) and red cell fragmentation (schistocytes or helmet cells) on peripheral blood smear

Table 31-2: Tests for confirmation of the diagnosis and evaluation of severity of PET.

Treatment of Preeclampsia:

Pre-eclampsia is a progressive diseases, its underlying pathology, as explained before, begins at the early stages of placentation. It is not exactly known why in some cases the diseases takes an aggressive course and why in others it continue as mild cases of preeclampsia.

The only definitive treatment of preeclampsia is delivery to prevent development of maternal or fetal complications from progression of the diseases. Whether or not to deliver the fetus is based upon:

- **Gestational age**
- **Maternal and fetal condition**
- **The severity of preeclampsia**

In general patients at term are best delivered. Preterm delivery is not always in the best interests of the fetus. Therefore more conservative approach is often considered in selected women remote from term. Maternal end-organ dysfunction and nonreassuring tests of fetal wellbeing may be indications for delivery at any gestational age.

- **Management of Mild preeclampsia (Figure 31-3)**:

o Women with mild PET at term: are treated by induction of labor provided there are no contraindications to vaginal birth. This minimizes the risk of progression to severe disease and its complications. Cervical ripening agents may be needed with unfavorable cervices.

- Women with mild disease remote from term: can be managed expectantly, to enable further fetal growth and maturation. Expectant management include:
  - Follow up Laboratory tests: The minimum laboratory evaluation should include platelet count, serum creatinine, serum ALT and AST. These tests should be repeated once or twice weekly in women with mild preeclampsia to assess for disease progression. Other tests such as coagulation profile, collection of urine over 24 hours for measurement of protein may be indicated in some cases.
  - Treatment of hypertension: The use of antihypertensive drugs to control mildly elevated blood pressure does not alter the course of the disease or diminish perinatal morbidity or mortality.
    The only indication for antihypertensive therapy in preeclampsia is to protect against cardiovascular or cerebrovascular events namely stroke. If it is administered the target therapeutic level of blood pressures is 130 to 150 mm Hg systolic and 80 to 100 mm Hg diastolic.
  - Assessment of fetal well-being and fetal growth: A minimum of daily fetal movement counts and twice weekly fetal nonstress testing with assessment of amniotic fluid volume, or biophysical profile should be undertaken. Doppler velocimetry is useful for assessing fetal status if fetal growth restriction is present

Indications of antihypertensive in pre-eclampsia

- SBP: 150 and 160 mm Hg and DBP between 100 and 105 mm Hg.
- If there are symptoms (e.g., headache, visual disturbances, chest discomfort)
- If the baseline blood pressure was low (< 90/75 mmHg).

Delivery should be undertaken at any time if progression to severe PET is noted (Table 31-1 for sings of severe PET).

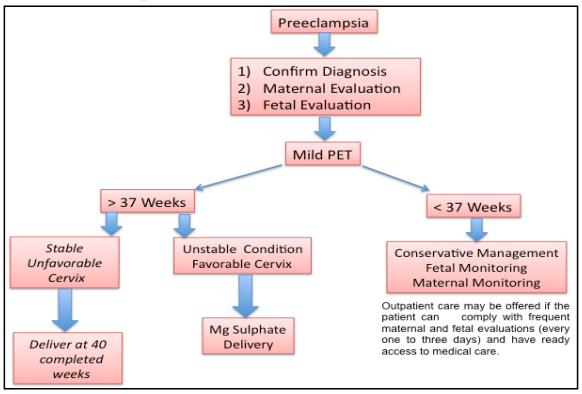

Figure 31-3: Algorithm for management of mild PET

➢ **Management of Severe preeclampsia (Figure 31-4):**

Severe preeclampsia is generally regarded as an **indication for delivery, regardless of gestational age**, to minimize the risk of development of maternal and fetal complications. The management should be undertaken in hospitals, which have appropriate personnel and facilities for care of the preterm neonate especially if the pregnancy is < 34 weeks.

While in high proportion of cases delivery will be accomplished by cesarean section but in all cases consideration for cervical ripening and induction of labor should be given.

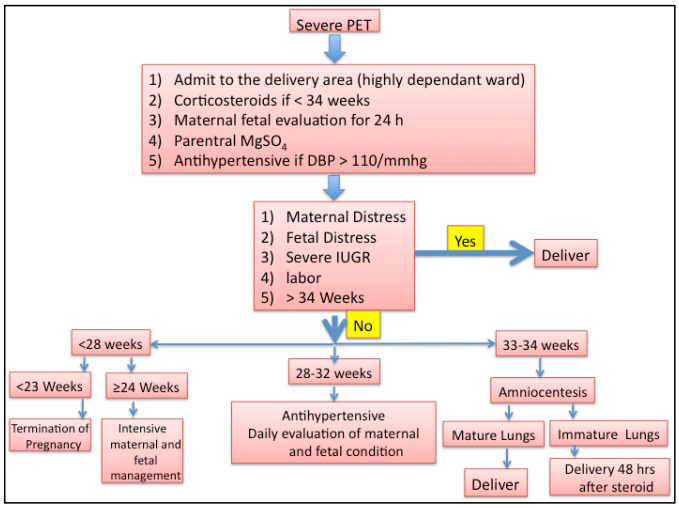

Figure 31-4: Algorithm for management of severe PET

➢ **Management of Severe PET during labor:** The following three principles should be applied:

1. Intrapartum maternal and fetal monitoring:

- Close, continuous maternal monitoring is necessary to identify worsening hypertension, deteriorating maternal hepatic, renal, cardiopulmonary, or hematologic function.
- Fetal monitoring: For uteroplacental insufficiency or abruption placentae (often manifested by nonreassuring fetal heart rate tracings and/or vaginal bleeding).

2. Anticonvulsant Therapy: Anticonvulsant therapy is generally initiated during labor, or prior to cesarean section. It should be continued for 24 hours postpartum (range 12 to 48 hours), after which the risk of developing seizures is low.

Magnesium sulfate: is the drug of choice for the prevention of eclampsia and prevention of recurrent eclamptic seizures (Other drugs such as phenytoin may be used but less effective).

Since the kidneys excrete magnesium sulfate, dosing should be adjusted in women with renal insufficiency (defined as a serum creatinine greater than 1.0 mg/dL). Such women should receive a standard loading dose, but a reduced maintenance dose (1 g per hour or no maintenance dose if the serum creatinine is greater than 2.5 mg/dL) and close monitoring of their serum magnesium level every six hours.

Magnesium Sulfate

Dose: loading dose of 6 g intravenously over 15 to 20 minutes followed by 2 g per hour as a continuous infusion.

The toxic dose: Over dose of Mg Sulfate could lead to cardiorespiratoy arrest.

Monitoring: for early sings of toxicity

- Patellar reflex: loss of reflexes being the first manifestation of symptomatic hypermagnesemia.
- Respiratory rate: Should be > 12 per minute.
- Urine output: Should be > 100 mL /h.

The antidote for MgSO4 toxicity: is Calcium gluconate (1 g intravenously over 5 to 10 minutes).

Magnesium sulfate is contraindicated in women with myasthenia gravis since it can precipitate a severe myasthenic crisis.

The "therapeutic range" of serum magnesium levels is 4.8 to 8.4 mg/dl. However measurement of serum level MgSO4 is not required if the woman's clinical status is closely monitored for evidence of potential magnesium toxicity.

3. Antihypertensive therapy:

The blood pressure should be closely monitored and maintained within the safe range of approximately 130 to 150 mm Hg systolic and 80 to 100 mm Hg diastolic. In some cases parental antihypertensive medication may need to be administered. The drug of choice are labetalol or hydralazine (Table 31-4).

Postpartum Care:

Hypertension and proteinuria due to preeclampsia resolve postpartum, often within few days, occasionally it may take few weeks. Severe hypertension should be treated; some patients will have to be discharged on antihypertensive medications that can be discontinued when blood pressure returns to normal levels. Elevated blood pressures that remain 12 weeks postpartum are unlikely to be related to preeclampsia and may require long-term treatment.

Eclampsia

- **Definition**: Eclampsia refers to the occurrence of one or more generalized convulsions and/or coma in patient with preeclampsia and in the absence of other neurologic conditions.

- **Incidence:** An eclamptic seizure occurs in 0.5 percent of mildly preeclamptic women and 2 percent of severely preeclamptic women.

However in about 20% of cases eclampsia may occur in women with apparently normal blood pressure who are in fact has "relative hypertension" (i.e., blood pressure elevated compared with patient's baseline, but less than 140/90 mmHg) and no proteinuria

The over all incidence of eclampsia is 4 to 5 cases per 10,000 live births in developed countries. But it is much higher in developing countries, among low socioeconomic classes, and young primigravidas.

- **Diagnosis and Clinical feature**:

Eclampsia may develop anytime from the second trimester to the puerperium. In general the timing of eclampsia in relation to pregnancy is as follow: antepartum (38 to 55 percent), intrapartum (13 to 36 percent), less than or equal to 48 hours postpartum (5 to 39 percent), and greater than 48 hours postpartum (5 to 17 percent).

Eclamptic seizures take the feature of generalized tonic-clonic convulsions and/or coma. It is almost always self-limiting (and seldom last longer than three to four minutes (usual duration 60 to 75 seconds).

Imminent signs of eclampsia (before the seizure): these are the sings which precedes the occurrence of eclampsia, it include: persistent frontal or occipital headache, blurred vision, photophobia, right upper quadrant or epigastric pain, and altered mental status in preeclamptic women.

- **Differential diagnosis of Eclampsia**:

Eclamptic seizures are clinically and electroencephalographically indistinguishable from other generalized tonic-clonic seizures. In typical cases the diagnosis is directly made and no need for further tests such as MRI for the brain.

Stroke (hemorrhage, arterial or venous thrombosis)
Hypertensive disease (hypertensive encephalopathy, pheochromocytoma)
Space-occupying lesions of the central nervous system (brain tumor, abscess)
Metabolic disorders (hypoglycemia, uremia, water intoxication e.g. high dose of oxytocin)
Infection (meningitis, encephalitis)
Thrombotic thrombocytopenic purpura or thrombophilia
Idiopathic epilepsy
Use of illicit drugs (eg, methamphetamine, cocaine)

However in non typical cases other causes of convulsions and/or coma should be excluded (Table 31-3:)

➢ **Maternal and Fetal complications of Eclampsia:** Eclampsia especially in developing countries and in absence of prenatal and intrapartum care is associated with high rate of maternal and fetal mortality and morbidity.

Table 31-3: DD of Seizure in pregnancy. History, clinical examination and investigations should clarify the diagnose

The primary cause of maternal mortality is intracranial hemorrhage, which is also responsible for permanent brain damage and disabilities. Table 31-4 shows the maternal and fetal risks in cases of eclampsia. The perinatal mortality is directly related to the week of gestation.

Outcome	%
Abruption	7 to 10
Disseminated intravascular coagulation	7 to 11
Pulmonary edema	3 to 5
Acute renal failure	5 to 9
Aspiration pneumonia	2 to 3
Cardiopulmonary arrest	2 to 5
Liver hematoma	1
HELLP syndrome	10 to 15
Perinatal death	5.6 to 11.8
Preterm birth	50

Table 31-4: Maternal and fetal outcome adopted of eclampsia from Sibai, BM. Obstet Gynecol 2005; 105:402.

➢ **Management:**

Development of eclampsia is an absolute indication for delivery regardless of the gestational age.

The principles of management are:

1. **Prevention of maternal hypoxia and trauma**: maintenance of airway patency and prevention of aspiration in addition to protection of the patient from injuring her tongue or mouth. The patient should be rolled onto her left side and protected from trauma (A bed with raised, padded side rails provides protection from trauma).
2. **Management of severe hypertension**: as in severe preeclampsia.
3. **Prevention of recurrent seizures**: as in severe preeclampsia
4. **Evaluation for prompt delivery**: the mode of delivery depends on several factors including gestational age, the cervical ripeness, and whether or not the patient in labor.
5. **Close monitoring for maternal and fetal conditions**:

Preexisting Hypertension

Preexisting hypertension is defined as systolic pressure ≥ 140 mmHg and/or diastolic pressure ≥ 90 mmHg that antedates pregnancy, or is present before the 20th week of pregnancy, or persists longer than 12 weeks postpartum.

It can be primary (essential hypertension) or secondary to a variety of medical disorders.

There is often difficulty in differentiation between pre-existing hypertension and pre-ecalmpsia in women presenting for the first time in pregnancy after 20 weeks of gestation.

- **The risks of preexisting hypertension to pregnancy include**:

- Development of "Superimposed preeclampsia", is the most significant risk, its incidence is two to four folds higher than in the general obstetric population.
- Abruptio placenta (0.7 -1.5 percent)
- Preterm birth <37 weeks (12 to 34 percent)
- Fetal growth restriction (8-16 %).

Superimposed PET
This diagnosis is made if there is worsening hypertension with new onset proteinuria in a woman with preexisting hypertension.

Those risks are higher among women with severe preexisting hypertension in the first trimester

- **The management of women with preexisting hypertension**:

1. Exclude causes of secondary hypertension (Table 31-5).
2. Maternal evaluation for evidence of "target organ" damage due to chronic hypertension: fundoscopic examination of the retinal vessels, and assessing the carotid, femoral, and peripheral pulses. Baseline laboratory tests include urinalysis, urine culture, and serum creatinine, blood urea nitrogen, glucose, and electrolytes. An electrocardiogram should be obtained in women with long-standing hypertension. All patients should also have a complete evaluation for other cardiac risk factor (e.g., hypercholesterolemia, smoking, diabetes, family history, sedentary lifestyle)

Causes for hypertension	Associated Symptoms, Sings and Tests
Endocrine	
Pheochromosytoma	Attacks of headache, palpitation and sweating
Thyroid diseases	TSH measurement
Hperaldosteronism	Serum postassium measurement
Cushing disease	Evidence of moon facies and centripetal obesity
Hypercalcemia	Serum calcium measurement
Renal	
Renal Disease	Serum creatinine measurement and urine analysis
Renal artery stenosis	Examine patients for renal bruit
Cardiac	
Coarctation of the aorta	Delayed or absent femoral pulse

Table 31-5: cause of secondary hypertension

3. Antepartum assessment and follow up for early diagnosis of preeclampsia and fetal growth delay: This is best accomplished by frequent prenatal visits for monitoring maternal blood pressure, proteinuria, and assessment of fetal growth. The frequency and intensity of fetal surveillance depends on presence of complications such preeclampsia or signs of intrauterine growth restriction.

4. Indications for treatment of hypertension: The goal of treatment of hypertension is to minimize the risk of maternal cardiovascular or cerebrovascular events.

Indications for antihypertensive therapy
- Persistent DBP of 95 to 99 mmHg, SBP ≥ 150 mmHg.

- Signs of hypertensive end-organ damage (e.g., ventricular dysfunction, retinopathy).

The goal of BP control is SDP between 140 and 150 mmHg and DBP 90 and 100 mmHg.

Neither the patient nor the fetus appears to be at risk from mild hypertension during pregnancy and more than 85 percent of hypertensive women will have uncomplicated pregnancies.

Drug of choice: if antihypertensive is continued or initiated, it should be realized that all antihypertensive drugs cross the placenta thus the drugs with the most safety record are usually preferred (Table 31-6).

- **Delivery:** Women with mild, uncomplicated preexisting hypertension can be allowed to go into spontaneous labor and deliver at term. Earlier delivery can be considered for women with severe hypertension, superimposed preeclampsia, or pregnancy complications

Drug	Dose and mechanism of action
Labetalol	Has both alpha- and beta-adrenergic blocking activity. **For regular use**: Starting dose by 100 mg twice /day. **For Acute therapy**: 20 mg intravenously followed at 10 minute intervals by doses of 20 to 80 mg up to a maximum total cumulative dose of 300 mg. The fall in blood pressure begins within 5 to 10 minutes and lasts from three to six hours. A constant infusion of 1 to 2 mg/min can be used instead of intermittent therapy
Methyldopa	Mild antihypertensive agent, however it has some side effects such as mental depression, anxiety, nightmares, drowsiness, headache and dry mouth
Calcium channel blockers	Long-acting nifedipine (30 to 90 mg once daily as sustained release tablet, increase at 7 to 14 day intervals, maximum dose 120 mg/day)
Hydralazine: Usually for acute therapy	Is a direct-acting smooth muscle relaxant. **Dose:** 5 mg IV over one to two minutes; if the BP goal is not achieved within 20 min., give 5 to 10 mg bolus depending upon the initial response. The maximum bolus dose is 20 mg. The fall in blood pressure begins

	within 10 to 30 minutes and lasts from two to four hours.
Diazoxide	Rarely necessary if adequate blood pressure control cannot be achieved with labetalol or hydralazine.
Antihypertensive drugs contraindicated in pregnancy: -Nitroprusside: is contraindicated in the later stages of pregnancy due to possible fetal cyanide poisoning. -Angiotensin converting enzyme (ACE) inhibitors -Angiotensin II receptor blockers (ARBs), both have teratogenic effect.	

Table 31-6: Common antihypertensive drugs used in pregnancy

Gestational Hypertension

Gestational hypertension refers to elevated blood pressure first detected after 20 weeks of gestation in the absence of proteinuria.

The risks of gestational hypertension are mostly due to:

- The risk of development of preeclampsia: About 50 percent of women who develop gestational hypertension go on to develop preeclampsia. The risk is high among women who develop gestational hypertension before 30 weeks.
- Cases with severe symptoms and signs such as severe hypertension, persistent headache, visual changes, growth restriction, oligohydramnios, epigastric or right upper abdominal pain, thrombocytopenia, or liver function abnormalities.

In these two situations, women with gestational hypertension should be treated as though they have preeclampsia (or HELLP syndrome), even in the absence of proteinuria since they are at high risk of maternal and/or fetal morbidity.

The indications for and choice of antihypertensive therapy in women with gestational hypertension are the same as for women with preeclampsia.

HELLP Syndrome

Definition: HELLP syndrome refers to a syndrome characterized by the triad of hemolysis with a microangiopathic blood smear, elevated liver enzymes, and a low platelet count.

HELLP syndrome and severe preeclampsia are probably part of a disease spectrum as the syndrome represents a severe form of preeclampsia. However approximately 15 to 20 percent of HELLP syndrome cases occur in the absence antecedent hypertension or proteinuria.

Incidence:
Its overall incidence in pregnancies is about 1-2 per 1000, while it is about 10-20% among women with severe preeclampsia/eclampsia. The syndrome typically develops in the third trimester between 28 and 38 weeks (70%). But it also has been reported in the second trimester around 17-20 weeks in 2-3% of cases, and in the postpartum period in approximately 20% of the cases.

Clinical manifestation and diagnosis: The condition usually develops in the third trimester. It is more common if there are symptoms and sings of severe PET. However the final diagnosis is based on the result of the investigations.

- Symptoms and signs:. The most common clinical presentation is abdominal pain and tenderness in the midepigastrium, right upper quadrant, or below the sternum.

- Investigation:
  - Microangiopathic hemolytic anemia: with characteristic schistocytes (also called helmet cells) on blood smear (Figure 31- 5). Other signs suggestive of hemolysis include an elevated LDH (≥600 IU/L) or indirect bilirubin (≥1.2 mg/dL) and a low serum haptoglobin concentration (≤25 mg/dL).
  - Platelet count ≤100,000 cells/microL
  - Serum AST ≥70 IU/L

Hypertension (blood pressure ≥140/90) and proteinuria are present in approximately 85 percent of cases, *but it is important to remember that either or both may be absent in women with otherwise severe HELLP syndrome*.

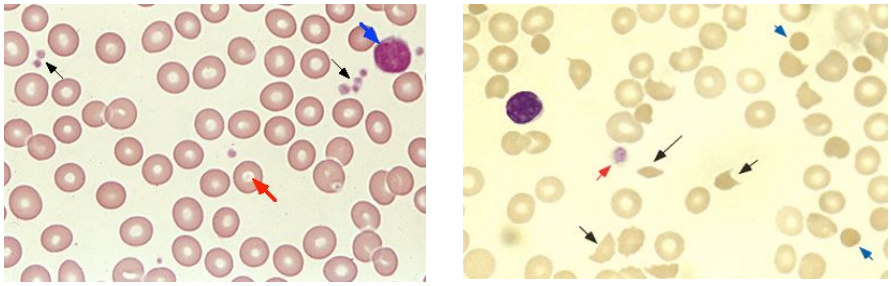

Figure 31-5: Peripheral blood smear of normal case (Left) and patient with microangiopathic hemolytic anemia (right) note marked red cell fragmentation. The smear shows multiple helmet cells (small black arrows), other fragmented red cells (large black arrow); microspherocytes are also seen (blue arrows). The platelet number is reduced; the large platelet in the center (red arrow) suggests that the thrombocytopenia is due to enhanced destruction. In the normal (left) smear note the red cells are of relatively uniform size and shape, several platelets (black arrows) and a normal lymphocyte (blue arrow) can also be seen.

Morbidity of HELLP Syndrome:
Serious maternal morbidity has been reported either before or after the development of HELLP syndrome. This includes disseminated intravascular coagulation (DIC), abruptio placentae, acute renal failure, pulmonary edema, subcapsular liver hematoma, and retinal detachment. Jaundice and ascites may also be present. *Some patients may remain asymptomatic for the initial period of the disease.*

Differential diagnosis: The DD diagnosis of HELLP syndrome include other diseases complicating pregnancy such as: acute fatty liver of pregnancy, gastroenteritis, hepatitis, appendicitis, gallbladder disease, idiopathic thrombocytopenic purpura, lupus flare, antiphospholipid syndrome, hemolytic-uremic syndrome, or thrombotic thrombocytopenic purpura. Careful history, examination and investigations are necessary in order to reach the correct diagnosis.

Management:
Maternal stabilization and monitoring in highly dependant unit with multidisciplinary team is required in order to reduce the high rate of morbidity and mortality in such cases. However HELLP syndrome is managed along the guidelines of management of severe PET with **the cornerstone of therapy being delivery**.

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Chapter 32

Cardiac Diseases in Pregnancy

Dr Nawal Al Sinani - Dr Ahmed Merstani

Cardiac diseases encompasses a wide spectrum of pathology, including congenital, acquired, functional or structural defects. Each has its own hemodynamic, genetic, obstetric, and social implications.

Cardiac diseases in pregnancy are considered the most common non-obstetric cause of maternal mortality. The specific causes of mortality include pulmonary edema (main cause), pulmonary hypertension, infective endocarditis, thromboembolism, and fulminating peripartum cardiomyopathy. Hence it is important for obstetrician to appreciate the maternal and fetal risks associated with cardiac diseases, and be able to set a clear management plan for pregnancy, labor and the postpartum period including prescribing appropriate contraception.

By the end of this chapter you should be able to:

- **Describe** the cardiovascular and hemodynamic changes in pregnancy:
- **Describe** the diagnosis of cardiac diseases in pregnancy:
- **List** the principle of preconception management:

- Element of counseling
- Functional assessment: (NYHA grading system)
- Pathological assessment:

- **Describe** the effect of the pregnancy on the cardiac disease:

The three risk levels: low, intermediate, and high

- **Describe** the Effect of heart dieses on pregnancy:
- **Describe** the principle of management in pregnancy:

- Assessment of the cardiac state and Patient education:
- Ultrasound examination: with fetal echocardiography scan. ,
- Anticoagulant drugs and other specific medication:
- Follow up visits: S&S suggestive of cardiac decompensation.
- Fetal monitoring:

- **Describe** the principle of management in labor: (Decision on mode of delivery)

<u>In the first stage of labor</u>:

- Posture.
- Appropriate analgesia
- Maintaining fluid balance
- Frequent assessment of air ventilation

<u>In the second stage:</u>

- Avoid straining and holding breath for long time.
- Shortening of the second stage

<u>Third stage:</u>

- Risk of hemorrhage vs. of autotransfusion

- **Describe** the postpartum management and contraception: the prose and cons of each method.

Cardiovascular and hemodynamic changes in pregnancy:

Major hemodynamic alterations occur during pregnancy, labor and delivery and the postpartum period. Those changes begin early in the first trimester reach its peak in the second trimester and remain at an almost plateau until delivery (see Chapter 4 on Physiological adaptation of pregnancy) it include:

- Increase in intravascular blood volume (by 40-50%).
- Increase in the cardiac output: (30-50% above baseline).
- Decrease in the peripheral vascular resistance
- Increase in blood coagulability.

These changes impose significant burden on the maternal cardiac function, throughout pregnancy particularly during labor and the immediate postpartum period (Figure 32-1). While it is well tolerated by healthy individuals, in patients with underlying cardiac diseases it imposes major physiological challenge that may be complicated with heart failure, pulmonary edema and mortality.

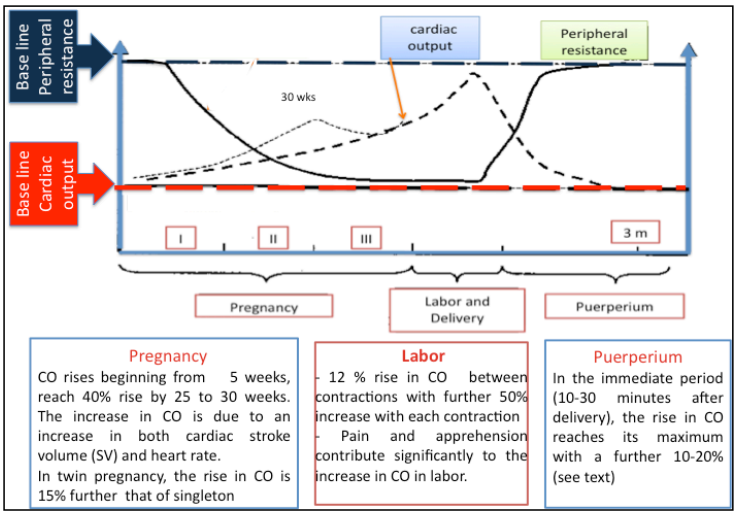

Figure 32-1: illustration of hemodynamic changes in pregnancy and labor

Cardiac Diseases and Pregnancy:

Incidence:

The reported incidence of cardiac diseases in pregnancy is approximately 1% to 3%. However the true incidence is probably higher since it is possible that cases, especially mild forms of cardiac diseases, that are not known prior to pregnancy, are overlooked also cases that end in miscarriage are not included.

Causes of cardiac diseases: The profile of cardiac pathology varies between developed and developing countries. In developing countries rheumatic heart diseases is the most commonly type, whereas in developed countries congenital heart diseases are more common and most of it have already been operated upon before pregnancy.

Most Frequent causes of heart diseases:
- Rheumatic heart disease
- Congenital heart disease
- Arrhythmias
- Ischemic heart disease

Diagnosis of cardiac diseases in pregnancy:

Patients may present with already known cardiac disease. However about 50 % of cases of heart diseases are diagnosed for the first time during pregnancy. The diagnosis of heart diseases in pregnancy require high index of suspicion, since the normal cardiovascular hemodynamic changes in pregnancy gives both symptoms and even signs that mimic cardiac diseases.

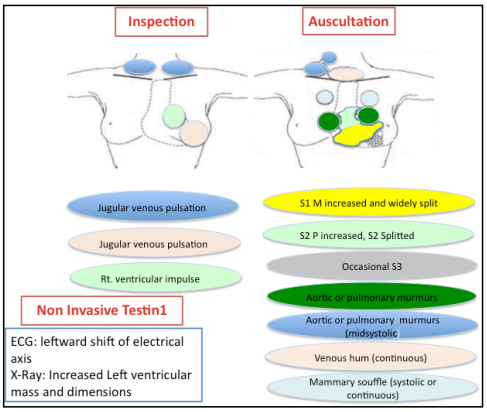

Figure: 32-2: Normal signs and testing in pregnancy that mimic cardiac disease conditions

Symptoms such as shortness of breath, palpitations, dizziness, edema, and murmurs (mostly systolic) are not uncommon in pregnancy. Nevertheless it should not be dismissed as

normal without careful history, examination and if necessary referral to a cardiology specialist for further evaluation.

Management of patient with heart disease:

The management should be undertaken in a specialized center for high-risk pregnancy. In many cases a multidisciplinary team that include cardiologist, cardiac surgeon, genetic counselor, obstetric anesthetist and pediatrician may have to be involved.

Preconception management:

Ideally women with heart disease should seek appropriate counseling about short and long-term impact of the pregnancy on the cardiac disease and the cardiac disease on the pregnancy and the fetus. Maternal fetal specialist and cardiologist and geneticist may be involved in the patient counseling after assessing patient pathological and functional status of the disease with appropriate history, examination and investigations.

In counseling, six areas should be considered:

1. The underlying cardiac lesion
2. Maternal functional status.
3. The possibility of further palliative or corrective surgery
4. Additional associated risk factors
5. Maternal life expectancy and ability to care for a child
6. The risk of CHD in offspring

Functional assessment: The most commonly used tool for assessment of functional cardiac status is the New York Heart Association (NYHA) classification (Figure32-3). The functional classification was found to correlate well with maternal and fetal morbidity and mortality e.g. premature delivery, growth restriction, and neonatal death

Pathological assessment: to identify the specific cause

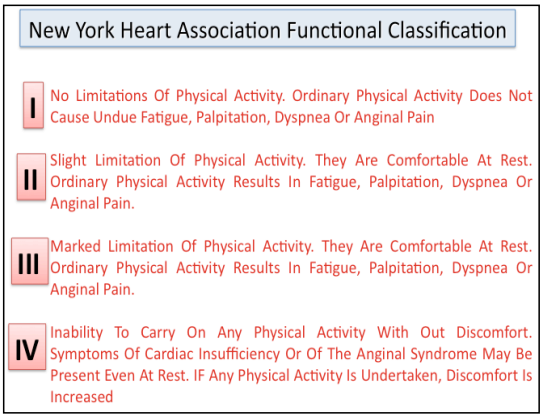

Figure 32-3: Dobbenga-Rhodes YA, Privé AM. Assessment and evaluation of the woman with cardiac disease during pregnancy. J Perinat Neonat Nurs 2006; 20: 295-302 (from the *American Heart Association)*

(congenital or acquired. .etc) and the anatomical lesion (e.g. mitral, tricuspid valves…) of the heart diseaes.

- **Effect of the pregnancy on the cardiac disease:** According to the functional and structural assessment the majority of patient can be stratified into three risk groups: low, intermediate and high (table 31-2). The high-risk group is associated with increased maternal and fetal mortality and patients in this group should be advised against pregnancy.

Sometimes pregnancy may be postponed until a period of remission (e.g. in cases of viral myocarditis or lupus). Also in some cases surgical repair of structural abnormalities may be advised before conception (e.g. valvular disease or shunts).

Maternal Cardiac Lesions and Risk of Cardiac Complications during pregnancy	
Low Risk	Mortality
▪ Small left-right shunt (atrial septal defect, Ventricular septal defect, Patent ductus arteriosus) ▪ Aortic regurgitation with normal LV function ▪ Mitral valve prolaps ▪ Mitral regurgitation with normal LV function ▪ Mild or moderate Mitral stenosis ▪ Mild or moderate Pulmonary stenosis ▪ Repaired acyanotic congenital heart disease without residual cardiac dysfunction	< 1%
Intermediate Risk	
▪ Large left to right shunt ▪ Coarctation of the aorta ▪ Marfan syndrome with a normal aortic root ▪ Moderate or severe MS ▪ Mild or moderate AS ▪ Severe PS	5-15%
High Risk	
▪ Eisenmenger's syndrome ▪ Severe pulmonary hypertension ▪ Complex cyanotic heart disease ▪ Marfan syndrome with aortic root or valve involvement ▪ Severe aortic stenosis with or without symptoms ▪ NYHA Class III or IV symptoms History of prior peripartum cardiomyopathy	25-50%

Table 32-1: Maternal cardiac lesions and the risk of mortality during pregnancy according to the severity group

- **Effect of heart dieses on pregnancy:**

There is an overall increase in the rate of fetal and neonatal complications among women with cardiac disease. It include increased rate of spontaneous abortion as well as fetal mortality and morbidity due to prematurity and fetal growth restriction.
However the extend of adverse outcome depends on the risk factors present, which include:

- The NYHA functional class (table 1) is a major determinant of fetal mortality, with incremental risk ranging from virtually zero for gravidas who are asymptomatic at all levels of activity to about 30 percent for gravidas in NYHA class III or IV (e.g. pregnant women with Eisenmenger syndrome, for example, only 15 to 25 percent of pregnancies progress to term)
- Cyanosis at the baseline prenatal visit, left heart obstruction (aortic and/or mitral stenosis).
- The presence of other risk factors: e.g. smoking, multiple gestations, and the use of anticoagulants throughout pregnancy.

➢ **Management of pregnancy (Prenatal Care):**

• The First Antenatal Visit:

In addition to the routine, history, examination and investigations the antenatal care for women with cardiac disease involves the following additional elements:

1. Assessment of the cardiac state: If it has not been done before. It involves determining the exact pathology and anatomical cardiac lesion and assessment of the functional status of the heart using the NYHA classification. It should also be realized that the functional status of the heart is not static throughout pregnancy, thus a patient assigned to low Grade cardiac lesion may under certain circumstances may develop cardiac failure and pulmonary edema.

In cases belong to the high-risk group, the continuation of pregnancy caries significantly high risks of maternal as well as fetal mortality, and termination of pregnancy should be strongly considered.

2. Ultrasound examination: Early ultrasound examination is important to confirm gestational age; numbers of embryos and a detailed anomaly scan. In addition fetal echocardiography scan, should be scheduled around 20-22 weeks to screen for cardiac anomalies.

3. Patient education:

- The patient should be made aware of the potential complications and the warning symptoms of cardiac decomposition e.g. increasing dyspnea, cough, early sings of infection...etc.
- Iron supplementation should be emphasized to prevent anemia, which is an independent risk factor.
- Advice should be given regarding modification of physical activities and the need for rest. Women compliance with the treatment team's recommendations should be emphasized.
- Admission to hospital should be undertaken whenever it is necessary, in some cases it has be to arranged for prolonged period of time.

4. Anticoagulant drugs and other specific medication:

The need for anticoagulant and/or specific medications such as inotropic cardiac drugs or antiarrhythmia agents should be revised. Anticoagulants are indicated in cases at high risk of thromboembolic complications such as: recurrent deep vein thrombosis, pulmonary embolism, rheumatic heart disease with atrial fibrillation, prosthetic valves, or cyanotic congenital heart disease (figure 32-4).

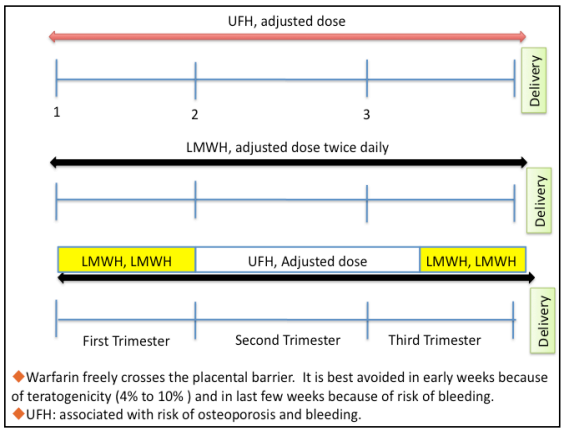

Figure 32-4: Three commonly used regiment for anticoagulants. (UFH) unfractionated heparin, (LMWH) low molecular weight heparin and Warfarin. The prose and cones of each strategy should be explained and discussed with the patient..

- Subsequent antenatal visits:

Visits for the obstetric and specialized cardiologist care is best arranged in a combined clinic in order to improve patient compliance. In each visit enquiry and examination for, symptoms and signs suggestive of cardiac de-compensation should be recorded.
Admission to the hospital is recommended whenever signs of decompensation, infection, or anemia are present. Patients in functional class IV often need hospitalization throughout pregnancy

Symptoms of and signs suggestive of heart failure:
Unexplained cough, hemoptysis, and increase severity of dyspnea or orthopnea.
-Weight gain, tachypnea, and distension of neck veins, rales, wheezes, and newly palpable liver edge.

- Fetal monitoring:

The fetal risk correlate positively with the cardiac functional grade.
For women in classes I and II there is probably no increase in fetal risk and normally there is no special additional need for fetal monitoring.
But for women in functional classes III and IV, left-sided heart obstruction or regurgitation and cyanosis; fetal monitoring should begin at around 28 weeks of gestation because of the increased risk of fetal growth restriction and fetal wastage in cyanotic gravida.

Plan of labor and delivery:

The plan of labor and delivery should be discussed with the patient, including the mode of delivery and analgesia to be used in labor or cesarean section.

- **Management in Labor**:

- The decision of the timing of delivery depends on:

1. The functional status of the heart as determined by the current NYHA.
2. The fetal condition (e.g. intrauterine growth restriction, oligohydramnios, or nonreassuring fetal testing)

Women in functional classes I and II and without fetal indications for delivery are allowed to go into labor spontaneously.

Women in functional classes III and IV should be electively delivered, in a tertiary care center. Elective delivery has the advantage of arranging the optimum care that such patient often need e.g. cardiologist, anesthesiologist, pediatrician, and intensivist should be around and alerted.

- The mode of delivery the objective is to achieve vaginal delivery, unless there is an obstetric indication, since cesarean section in itself is an independent risk factors for several complications *(increases the risk of hemorrhage, postpartum infection, pulmonary morbidity etc)*. However, in some cases cesarean section will be the preferred method either for obstetric reason e.g. unripe cervix, or severe fetal growth restriction or for the cardiac condition such as: in women with Eisenmenger's reaction, severe aortic stenosis, aortic dilatation, or dissection; and women with a history of recent myocardial infarction.
- Intrapartum management:

Labor whether spontaneous or induced, presents an additional burden on the cardiac function at each of the stages of labor. Therefore throughout labor:

- The progress of labour should be carefully monitored on a partogram.
- The maternal condition should be closely monitored including blood pressure, pulse and respiratory rate. Oxygen saturation should be monitored with pulse oximetry.
- In certain situations invasive monitoring measure such as insertion of pulmonary artery catheter may be required as in women in functional class IV, recent myocardial infarction, peripartum cardiomyopathy, and obstructive cardiomyopathy.

The following measures are adopted to prevent / reduce the risk of pulmonary edema and or heart failure from the exaggerated stress of labor:

In the first stage of labour:

(1) The patient should be managed in the left lateral or semi-sitting position.

(2) Appropriate analgesia to alleviate patient anxiety and relieving pain. Epidural analgesia is the first choice unless contraindicated e.g. patient on anticoagulants, low or fixed cardiac outputs such as aortic regurgitation, and in potential or actual right-to-left shunts.

(3) Maintaining fluid balance with an input and output chart.

(3) Frequent assessment of air ventilation and intermittent humidified oxygen administration should be undertaken.

In the second stage:

- The patient should be refrained from holding her breath for long time.
- Shortening of the second stage by using outlet forceps or ventouse, as appropriate, is recommended especially in patients with cyanotic congenital heart disease

Third stage:

In this stage there are two opposing risks, each one can precipitate cardiac failure. One from acute decrease in the cardiac preload if there is excessive postpartum hemorrhage the other is acute overload from "autotransfusion" that results from strong uterine contraction. Therefore "Ergot preparations" that induce sustained tonic uterine contractions should not be used. Uterine massage with intramuscular Syntocinon administration (not intravenous as it induce hypotension) is normally the preferred method.

In the fourth stage: During the few hours after delivery the patient should be carefully observed because it is still associated with hemodynamic instability.

Endocarditis prophylaxis: The current evidence suggest that delivery by cesarean section and vaginal delivery (in the absence of infection) do NOT require endocarditis prophylaxis except in high-risk patients (Table 32- 1)
If prophylaxis is required it should be started 30 to 60 minutes before procedure or labor. Amoxicillin 2g orally or Ampicillin 2gm (IM or IV), alternatively if patient is sensitive to penicillin Clidnamycin 600 mg may be administered.

- **Postpartum management**:

- During the postpartum period the patient should be encouraged to mobilize.
- Anticoagulant may be administered or resumed if the patient was already on anticoagulant.
- Lactation should be encouraged.

Contraception:

Most patients with cardiac disease can use all kinds of contraception. However each of the available methods has its advantages and disadvantages, which should be balanced against the risk of unplanned pregnancy.

- The use of intrauterine devices (IUCD) is contraindicated in patients with a history of endocarditis or valvular prostheses, or receiving chronic anticoagulation. But may be used in other patients considering a low risk of endocarditis.
- Oral contraception may be associated with slightly higher risk of inducing high blood pressure and thrombosis especially in cyanotic patines. In these patients, the combined use of low-dose aspirin with the oral contraceptives has been suggested. Patients on anticoagulants (warfarin) can have inadequate control of contraception and anticoagulation for the first few months due to the interaction between the two drugs.
- Parenteral contraception (medroxyprogesterone acetate) has low profile of complications in women with cardiac disease, but associated with the problem of weight gain and amenorrhea.
- Barrier methods are safe and effective if used correctly.
- For some patients, in whom pregnancy is associated with high mortality rate, or those who completed family, surgical sterilization should be considered.

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Chapter 33

The Renal System in Pregnancy

Dear Dr Sara Ghazali - Dr Bandr Kutbi

Pregnancy involves significant anatomical and physiological changes in the urinary system. Those changes must be taken into account when interpreting the normal parameters of renal function in pregnant women. Some of those changes e.g. ureteric dilatation and urinary stasis render pregnant women more vulnerable to complications such as urinary tract infection.

Acute renal failure is one of the serious complications that may occur in pregnancy. Also it is not uncommon to see pregnant women suffering from chronic renal disease or following renal transplant. It is therefore important that obstetricians understand the effect of renal diseases on pregnancy and the effect of pregnancy on renal function and renal diseases.

By the end of this chapter you should be able to:
List the causes and DD of proteinuria in pregnancy.
Describe the methods of testing for proteinuria: Qualitative testing vs. Quantitative tests.
Describe the factors that increases women susceptibility for UTI in pregnancy:
Define asymptomatic Bacteriuria (ASB):
Acute Pyelonephritis:
List the causes, maternal and fetal complications
Describe the treatment of pyelonephritis in pregnancy
The Nephrotic Syndrome:
Describe the Causes of Nephrotic Syndrome in Pregnancy:
Acute Renal Failure (ARF) in pregnancy:
List the Causes of ARF in pregnancy
Describe the diagnostoic criteria of ARF in pregnancy
Chronic Renal Disease (Failure) with Pregnancy
- How to Counseling patient with chronic renal diseases:
- Describe Principles of Management of pregnancy with chronic renal disease:

Describe the potential complications and management principles of each of the following situations:
- **Pregnancy and Renal dialysis (End Stage Renal Diseases):**
- **Pregnancy after Renal Transplant:** Criteria must be fulfilled prior to pregnancy:
- **Urinary Calculi (Urolithiasis):** The diagnostic dilemma.

Proteinuria in pregnancy, Causes and DD

Screening urine for excessive amounts of protein (or albumin) is an integral part of the antepartum care strategy for detecting preeclampsia. There are two methods for evaluation of proteinuria; qualitative and quantitative tests.

- Qualitative testing "Dip stick test": This test is the commonly performed test in routine antenatal visits. The test is performed on a fresh clean voided midstream urine specimen obtained before pelvic examination to minimize the chance of contamination from vaginal secretions. A paper strip impregnated with dye that changes color according to the concentration of protein (principally albumin) is dipped into the urine and interpreted as follows:

- Negative:
- Trace: - between 15 and 30 mg/dl
- 1+: - between 30 and 100 mg/dl
- 2+: - between 100 and 300 mg/dl
- 3+: - between 300 and 1000 mg/dl
- 4+: - more than 1000 mg/dl

Being a qualitative method, it is prone to false negative and false positive results. False positive reactions, due to differences in the osmolality (concentration) of urine (high urine concentration can give false positive results), also if urine is contaminated with blood or semen. False negatives can occur with low specific gravity (<1.010), high salt concentration, highly acidic urine, or with non-albumin proteinuria.
However if the results show +3 or persistent +2 especially in the presence of other signs (edema or hypertension) it is important to proceed to one of the following quantitative tests.

- 24-hour collection: This method requires a 24-hour urine collection to directly determine the daily total protein or albumin excretion. An extra benefit of this approach, if creatinine is also measured, is that it provides the information necessary to estimate the glomerular filtration rate (GFR) from the values of creatinine clearance rate.

- Urine protein to creatinine ratio: This method relies on a random untimed urine sample from which the protein-to-creatinine ratio or albumin to creatinine ratio is calculated, this accounts for the differences in the urine osmolality (concentration). This method has a good correlation with the 24-hour urine collection technique. It has the advantages that it minimizes collection and laboratory errors, saves time in obtaining results and is far more convenient for the patient. However it is less sensitive than the direct measurement of protein output in a 24 hour urine sample.

DD of Proteinuria in pregnancy:

The DD of significant proteinuria in pregnancy includes: Renal diseases, pre-eclampsia and Nephrotic syndrome. Careful history as to the onset of proteinuria, its severity and associated symptoms could help in making the diagnosis.

Urinary Tract Infection in pregnancy

Urinary tract infection (UTI) is one of the most common types of infections in pregnant and non pregnant women. In pregnancy the anatomical and physiologic changes in the urinary tract increases women susceptibility to UTI. The progesterone effects and the mechanical compression by the gravid uterus impair complete emptying of the bladder and increase urinary residual volume and vesicoureteric reflux. Furthermore the increase in GFR causes increase urine glucose concentration and urine alkalinity, both facilitate bacterial growth.

Factors that increase women susceptibility to UTI in pregnancy:

1. Impaired complete emptying of the bladder (Increased residual volume)
2. Increase vesicoureteric reflux
3. The physiological glucosuria
4. Urine alkalinity

Bacterial pathogens of UTI: The most common bacterial pathogens in all types of UTI are Enterobacteria, including *Escherichia coli*, this is the primary pathogen in 80% to 90% of initial UTIs and 70% to 80% of recurrent infections. Other gram-negative pathogens include *Klebsiella pneumoniae* and *Proteus mirabilis*. Further pathogens include *Pseudomonas*

aeruginosa and gram-positive organisms, *Streptococcus agalactiae*, and *Staphylococcus saprophyticus*.

UTI in pregnancy includes:

1. Asymptomatic Bacteriuria.
2. Cystitis
3. Pyelonephritis.

1. Asymptomatic Bacteriuria (ASB):

Definition and Diagnosis: Is defined as significant bacterial colonization of the urinary tract without symptoms.

Bacterial colonization is considered significant if there is more than 100,000 colonies/ml of a single bacterial organism in culture from a clean catch voided sample of urine.

The incidence of ASB is around 4-7% among pregnant and non-pregnant women.

Complications of ASB: The difference is that among pregnant women ASB is associated with the following complications:

- Can progress to symptomatic cystitis and pyelonephritis in about 30 % of cases.
- Two-fold increase in the risk of preterm labor, premature rupture of membrane.
- Low birth weight infants.

Screening for ASB: All pregnant women should be screened for ASB in their first antenatal visit by culture of a midstream sample of urine (MSU).

Treatment: Appropriate antibiotics according to the culture and sensitivities results should be administered for 7-10 days course. In addition the patient should be encouraged to increase the fluid intake. A reculture of a urine sample should be ordered one or two weeks after treatment.

Recurrence of infection requires repeated courses of treatment. In some cases long term “suppressive” therapy with low dose antibiotics throughout the pregnancy should be considered.

Patients with resistant and recurrent infection should have evaluation of the renal tract for possible underlying abnormalities. This is important because in 18-50% of patients with ASB there is radiologic evidence of abnormalities of the urinary tract.

2. Cystitis:

Acute bacterial cystitis presents with clinical signs and symptoms of urgency, frequency, dysuria, pyuria, and hematuria without evidence of systemic illness. Cystitis complicates 1% to 4% of all pregnancies. Diagnosis, although mostly clinical, includes a positive urine culture with at least 10^5 CFU/mL of a single uropathogen.

The treatment regiment is the same as in ASB. Follow-up surveillance, including monthly urine cultures for the duration of the pregnancy, is recommended.

Women may present with symptoms that are consistent with cystitis but with a negative urine culture. After confirming the lack of recent antibiotic use, the diagnosis of **urethral syndrome** should be considered. Urethral cultures for *Chlamydia* should be performed, followed by appropriate treatment.

3. Acute Pyelonephritis:

Acute Pyelonephritis is the most common renal complication of pregnancy. Its incidence is around 1-2 %. It affects the right kindney more than the left because of the dextrorotation of the uterus.

The risk factors include those of ASB in addition to a previous history of pyelonephritis, urinary tracts malformations and calculi.

Complications:

-Maternal: bacterial endotoxemia, if not adequately treated can lead to endotoxic shock, adult Respiratory Distress Syndrome (ARDS), hemolytic anemia. Furthermore it can leads to renal insufficiency due to permanent damage to of renal tissues.

-Fetal: pyelonephritis is associated with increased rate of fetal complications such as preterm labor, premature rupture of membranes (PROM) and fetal growth restriction (IUGR).

The diagnosis

- Systemic signs and symptoms. These include fever; flank pain; dysuria, costovertebral angle tenderness (CVAT); shaking chills; nausea and vomiting.
- The diagnosis is confirmed with the identification of significant pathogenic organisms in the midstream urine (MSU) culture.. Additional diagnostic signs include the presence of pyuria or leukocyte casts.

The treatment includes:
- Hospitalization and parenteral antimicrobial therapy. The choice of antibiotics is based on knowledge of the common pathogens in cases of UTI. If there is no clinical improvement by 48 to 72 hrs of IV antibiotic, then sonography is recommended to look for urinary tract obstruction or malformation.
- Adequate intravenous hydration and close monitoring of urine output.
- Antipyretics and analgesics.
- At the same time blood and urine samples are sent for culture and sensitivity. However change of the antimicrobial agents is usually guided by the clinical response rather than the results of culture.
- Other laboratory tests: complete blood count and serum chemistry evaluation should be requested.

The antibiotics should be changed from Parenteral to oral once the patient is afebrile. The patient may be discharged from the hospital when she is afebrile for 24hrs with continuation of oral antimicrobial therapy for further period of 7-10 days.

The Nephrotic Syndrome

Clinically the hallmark for the diagnosis of Nephrotic syndrome is heavy proteinuria > 3.0 g/day, hypoalbuminemia, hyperlipidemia, and edema.
Patients have reduced ability to excrete sodium and are prone to develop generalized edema and ascites. Hypertension may be present.

Causes of Nephrotic Syndrome in Pregnancy:
Nehrotic syndrome may be due to:

- Preexisting renal disease.
- Renal disease, which first develops during pregnancy.

- Preeclampsia.

Criteria for differentiation between the different causes depend on the time of clinical presentation of proteinuria and hypertension, and the severity of symptoms.

Treatment of Nephrotic Syndrome: It should be directed towards the major clinical problems, which are:

- Treatment of oedema.
- Treatment of hypertension.
- Treatment of anaemia.
- Fetal surveillance.

Acute Renal Failure (ARF) in pregnancy

Acute Renal Failure (ARF) is a sudden decrease in renal function characterized by:

- Rapid increase in serum creatinine levels (of at least 0.5 mg/dL/day (44 µmol/L/day) and oliguria with urine output of less than 400 mL in 24 hours. While oliguria is a common clinical finding, approximately 20% of the patients diagnosed with ARF will maintain normal urine volumes.

Incidence: The incidence of ARF that require dialysis is less than 1 in 10,000 - 15,000 pregnancies.

Causes of ARF: traditionally the causes of ARF are described as **prerenal**, **renal** or **postrenal**.

Prerenal conditions are the most common causes of ARF and usually result from inadequate perfusion of the kidneys (e.g. hemorrhage)

In obstetrics the important causes that may be encountered are:

- ARF following septic abortion.
- Renal obstruction.
- Pyelonephritis: occur in 1-2% of cases
- Preeclampsia and Eclampsia: Although the occurrence of ARF in preeclampsia is a rare event, it contributes significantly to obstetric causes of ARF. The picture is similar to acute tubular necrosis and recovery of renal function is the rule.

- Severe Hemorrhage, abruptio placenta, amniotic fluid embolism, and retained dead fetus.
- Hemolytic-Uremic Syndrome (HUS): This unusual cause of ARF can develop following several precipitating events including infections, pregnancy, and certain drugs. It occurs 7-10 days after a seemingly normal pregnancy. There is microangiopathic hemolytic anaemia, thrombocytopenia, with variable degree of neurologic symptoms. The prognosis of this disease is generally poor (61% mortality rate for cases reported prior to 1979). Recently it has markedly been improved with plasma exchange using plasmapheresis.
- Acute Fatty liver of Pregnancy:
- Lupus Nephritis:

Once ARF is suspected a multidisciplinary approach should be adopted including critical care specialists, maternal-fetal-medicine specialists, nephrologists, and neonatology specialists.

Complications of ARF:

- ARF is associated with high mortality rate that ranges from 20% to 60%, mostly from the underlying cause e.g. sepsis and hemorrhage.
- Development of chronic renal failure: bilateral renal cortical necrosis (BRCN). This complication is particularly common with abruptio placenta. Some patients might have slow recovery of the renal function for up to 3 years after the onset and can achieve a satisfactory lifestyle without dialysis.

Pregnancy with chronic Renal Disease (Failure)

The two important concerns in the management of a woman with chronic renal diseases who is pregnant or planning to conceive are:

- The effect of the pregnancy on the kidneys function:
- The effect of the kidney disease on the pregnancy:

The answer to those questions depends on several factors, which include: the cause of renal disease (e.g. diabetes, SLE ...etc.) and the renal function at the time of conception (mild, moderate or severe).

- Women who have chronic renal disease with well-preserved renal function (serum creatinine level > 1.4 mg/dL, or 125 umole/L) and normal blood pressure can be reassured that the pregnancy is likely to be associated with a good fetal outcome and no permanent adverse effect on maternal renal function

- However with moderate and severe forms of renal disease (serum creatinine level of 1.5 to 2.5 mg/dL, or 125 to 250 umole/L), and those with severe disease (creatinine level ≥ 2.5 mg/dL, or 250 umole/L) the risk of preterm labor and intrauterine growth restriction increases with worsening degree of renal insufficiency. Also there is increased risk of further decline in renal function as a consequence to pregnancy.

However it is important when counseling an individual patient to realize that:

- There is no way of preventing or predicting a decline in renal function during pregnancy.
- Furthermore, once renal failure occurs, termination of pregnancy does not generally reverse the course of the disease. The fact is that most women with severe chronic renal impairment will ultimately progress to renal failure.

Principles of Management of pregnancy with chronic renal disease:

The management requires multidisciplinary team of an obstetrician specialized in high-risk pregnancy, to ensure careful fetal monitoring and a specialized nephrologist for follow up of renal function. The principles of management includes the following:

- Treatment of Hypertension:
- Treatment of anemia:
- Assessment of renal function monthly up to 28 weeks and then every 2 weeks until term by creatinine clearance, BUN, serum creatinine level and electrolytes.
- Assessment of fetal wellbeing and growth: Non-stress testing is indicated from 26 weeks until delivery. The interval of testing depends partly on the severity of renal disease and hypertension. Ultrasonographic

measurements of fetal growth should be performed at 26, 32, and 36 weeks.

- Prevention of UTI and other types of infection: Since patients with renal disease are susceptible to infection. Antibiotics that are nephrotoxic (particularly the aminoglycosides, cephaloridine, and methicillin) should be avoided.

With proper care the chances of fetal survival is good (as high as 80%). If renal failure occurs dialysis should be instituted before the development of uremic symptoms.

Pregnancy and Renal dialysis (End Stage Renal Diseases):

With end stage renal disease pregnancy is rare because of infrequent and irregular menstruation, anovulation and hormonal imbalance. However with renal dialysis the chances of pregnancy could increase. Hence patients on renal dialysis still need to use contraception. Regarding the risk of pregnancy and its implication on their management. Both peritoneal and hemodialysis have been used in pregnant patients with renal failure.

Fetal Risks: include high incidence of pregnancy wastage including miscarriage, intrauterine death, and fetal growth restriction. The risk increases as the duration of years of dialysis preceding pregnancy increases.

Patient Risk: Patients on dialysis should also be aware that in pregnancy the frequency and duration of dialysis is likely to increase to almost daily sessions (intensive dialysis regiment) to maintain the BUN below 70 mg/dl and serum creatinine below 5 mg/dl. Maternal death still occurs at a high rate in developing countries.

Pregnancy after Renal Transplant

An increasing number of women are now getting pregnant after kidney transplant. The main concerns in such cases are:

1. Whether subsequent pregnancy will jeopardize the graft.

2. Medical criteria that must be fulfilled before a transplanted patient is allowed to get pregnant.

3. The effect of medication i.e. immunosuppressive therapy on the fetus.

The general advice is that pregnancy should be deferred for 1 - 2 years after transplantation. At the end of this period the following criteria must be fulfilled before the patient can safely allowed getting pregnant:

1. General good health for at least 2 years post transplantation.
2. No proteinuria.
3. No significant hypertension.
4. No evidence of graft rejection.
5. Serum creatinine < 2 mg/dl.
6. Drug therapy <= 10 mg prednisone and <= 3 mg /kg azathioprine.

- Studies have shown that pregnancy does not seem to increase the rate of graft rejection in patients who fulfill the required criteria for pregnancy after transplant.
- However the management of such patients requires a highly specialized multidisciplinary team.
- In pregnancy there is an increased risk of developing pre-eclampsia and contracting infections (being on immunosuppressant drugs).
- The delivery should be normal; the transplanted kidney rarely obstructs normal labor and delivery. Cesarean section should only be undertaken for obstetric reasons.

Urinary Calculi (Urolithiasis)

In pregnancy the incidence “urinary calculi” varies between 0.03 and 0.35 %. The condition is considered a serious pathology that can lead to permanent parenchymatous damage if not properly treated, in addition to the risk of serious systemic infection.

The diagnosis can be difficult and a high index of suspicion is needed. Ultrasound scan is not very helpful in the late pregnancy. In the mean time there is usually hesitancy in using radiological examination. However if used judiciously it is not contraindicated.

The management depends on several factors such as the degree of obstruction, the presence or absence of infection, the general condition of the patient and the stage of pregnancy.

Although medical intervention is often tried first, surgical intervention is not contraindicated.

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Chapter 34

Thyroid disease and pregnancy

Dr Bandr Kutbi

The importance of thyroid disease and pregnancy is due to several factors:

- It is the second most common endocrine disorder that affects women during their childbearing age.
- Its diagnosis requires high index of suspicion because the physiologic changes of pregnancy can mimic thyroid disease.

The thyroid hormones have an important role in fetal brain development

By the end of this chapter you should be able to:
List the key points in the maternal physiological changes in thyroid function.
List the key points in fetal thyroid development: The Fetal Thyroid gland functional developmentover two phases
Describe the importance of and challenge in the diagnosis of thyroid diseases in pregnancy:
Why important: relatively common, difficult to diagnose, thyroid hormone affect fetal brain development.
List the effects of pregnancy on thyroid gland and thyroid function: rise in total thyroxin and triiodothyronine but not the free fraction.
Hyperthyroidism and pregnancy:
- **List the Causes:** Graves' disease, gestational trophoblastic disease, nodular goiter or solitary toxic adenoma, viral thyroiditis, and tumors of the pituitary gland or ovary (struma ovarii).
- **Describe the effect of hyperthyroidism on pregnancy**: increase pregnancy wastage.
- **Describe the diagnosis and treatment:** antithyroid drugs (e.g. carbimzole) cross the placenta and induce fetal hypothyroidism.

Hypothyroidism and pregnancy:
- **List the causes:** iodine deficiency and WHO recommondation.Hashimoto's thyroiditis an autoimmune disorder.
- **Describe the effect of hypothyroidism on pregnancy:** can impair fetal cognitive functions and neurologic development.

Define postpartum thyroiditis: an autoimmune disorder affects 6% to 9% of women who do not have a history of the thyroid disease.

Effects of pregnancy on thyroid gland and thyroid function:

The changes in physiology of maternal thyroid gland begins early in the first trimester it include:

- Increase hepatic production of thyroid-binding globulin “TBG” secondary to an estrogenic stimulation and reduced hepatic clearance of TBG. This result in increase in the levels of total thyroxin, and total

triiodothyronine but the free resin triiodothyronine uptake (RT_3U) is decreased.

- A transient decrease in TSH between weeks 8 and 14 of gestation secondary to the peak rise in human chorionic gonadotropin, which has a weak thyroid stimulator action. In most pregnant women, this change has minimal clinical consequences.
- Reduction in plasma iodide level secondary to fetal use of iodide and increased maternal renal clearance of iodide (which explain the increase demands of iodine intake in pregnancy). This may explain the increase in the size of thyroid gland "Physiological goiter" which occurs in approximately 20% of patients.

The Fetal Thyroid gland functional development:

The fetal thyroid functional development takes place over two phases.

The first phase begins during the first trimester as the fetal thyroid starts to traps iodine by 12 weeks and evidence of T_4 products appear by the 14th week of gestation. However during this phase the supply of thyroid hormones to the fetus depends almost exclusively on the maternal thyroid.

The second phase begins around mid-gestation as the fetal thyroid function mature and become under the fetal pituitary TSH control. During this phase maximum fetal brain growth begins and extends to 2 to 3 years of age. During this time, the supply of thyroid hormones is first fetal and then neonatal in origin.

Maternal T_4 and T_3 cross the placenta, whereas maternal TSH does not.

Hyperthyroidism and pregnancy:

Hyperthyroidism occurs in 0.2% of pregnancies. Some of the symptoms of hyperthyroidism (e.g. tachycardia, nervousness, tremors, heat intolerance, weight loss, goiter, frequent stools, excessive sweating, palpitations, and hypertension) may be difficult to differentiate from normal physiologic changes of pregnancy.

- Causes:

Graves' disease (organ-specific autoimmune disease mediated by thyroid stimulatory immunoglobins) is the most common cause of hyperthyroidism during pregnancy and accounts for 95% of the causes. Other causes of hyperthyroidism during pregnancy include gestational trophoblastic disease, nodular goiter or solitary toxic adenoma, viral thyroiditis, and tumors of the pituitary gland or ovary (struma ovarii).
Transient hyperthyroidism may also occur as in cases of hyperemesis gravidarum and gestational transient thyrotoxicity (GET).

- Effect of hyperthyroidism on pregnancy:

Severe maternal hyperthyroidism is associated with increased risk of miscarriage, preterm delivery, intrauterine growth restriction, preeclampsia, stillbirth and heart failure.
In Grave's disease the anti-thyroid antibodies can cross the placenta and cause neonatal Graves' disease (hyperthyroidism) or neonatal hypothyroidism.

- Diagnosis:

In hyperthyroidism, TSH is depressed and fT_4 and fTI are increased. The RT_3U that is normally decreased in pregnancy is increased in hyperthyroidism.

- Treatment:

The goal of treatment of hyperthyroidism during pregnancy is to keep the patient euthyroid with the free T_4 in the upper limit of normal range so as not to cause fetal or neonatal hypothyroidism. Most of the antithyroid drugs (e.g. carbimzole) cross the placenta and induce fetal hypothyroidism.

In Grave's disease if there is concern for fetal thyroid dysfunction ultrasound can be used to assess for signs of fetal hypothyroidism, including fetal bradycardia, goiter, and growth restriction. In addition amniocentesis or cordocentesis can be performed to assess fetal thyroid function. Amniotic fluid measurements of TSH, T_4, and T_3 levels reflect fetal serum levels.

Hypothyroidism and pregnancy:

- Effect of hypothyroidism on pregnancy:

Untreated maternal hypothyroidism is associated with increased rates of miscarriage, preeclampsia, placental abruption, growth restriction, prematurity and stillbirths. Of particular significance is the association of maternal hypothyroidism with impaired fetal cognitive functions and neurologic development.

- Diagnosis:

Symptoms of hypothyroidism can be masked by the hypermetabolic state of pregnancy. Mild symptoms include modest weight gain, lethargy, decrease in exercise capacity, and intolerance to cold. The diagnosis is confirmed by thyroid function tests showing elevated level of TSH with or without suppressed levels free T_4. Diabetic patients have high risk of associated hypothyroidism.

- Causes:

The most common cause of hypothyroidism, worldwide, is iodine deficiency. If not treated it result in endemic cretinism, which is the most common cause of mental retardation worldwide. The World Health Organization recommend an increase of the daily intake of iodine from 150 micrograms per day for the non pregnant to 200-300 micrograms/day of iodine for pregnant women. Other causes include primary hypothyroidism, Hashimoto's thyroiditis an autoimmune disorder, which accounts for most cases of hypothyroidism during pregnancy.

- Postpartum Thyroiditis

Is an autoimmune disorder affects 6% to 9% of women who do not have a history of the thyroid disease. The diagnosis is made by documenting abnormal TSH (elevated or suppressed) levels during the first year postpartum. The classical presentation is a transient hyperthyroid phase that occurs 6 weeks to 6 months postpartum followed by a hypothyroid phase that lasts for up to 1 year postpartum. Some cases develop permanent hypothyroidism.

Screening for thyroid diseases:

Because of the importance of maternal euthyroidism for normal fetal cognitive development, universal screening for hypothyroidism has been recommended by some authorities. However the current evidence do not support such approach. Instead testing of pregnant women for thyroid dysfunction should be undertaken if a woman is symptomatic or have a family history of thyroid disease.

Chapter 35

Hemoglobinopathies
And inherited blood coagulation disorders in pregnancy

Dr Sama Nazer

Hemoglobinopathies can be divided into two major types: the thalassemias, which are hemoglobin disorders due to decreased globins chain production (quantitative defect), and the sickle cell anemia (and its variants as hemoglobin C disease) which are hemoglobin disorders due to production of a variants type of globins (qualitative defect). Hemoglobinopathies are chronic, debilitating, and often fatal. Worldwide sickle cell disease and thalassemia are among the most common genetic diseases. The diagnosis and management of most blood disorder require close cooperation between the obstetric and the hematology teams.

By the end of this chapter you should be able to:

Describe the Diagnosis and screening of Hemoglobinopathy in pregnancy.

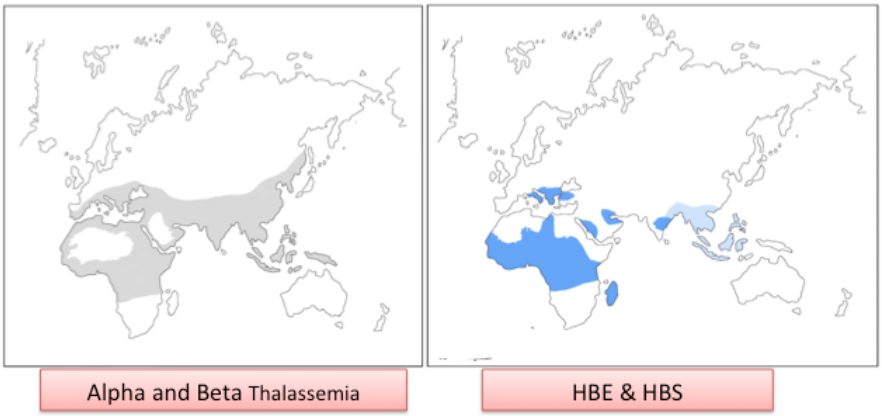
- **Sickle cell Disease**:
  - **List** the maternal and fetal risks
  - **List** the principle of management in pregnancy and labor.
- **Thalassemia:** alpha and Bet thalassemia and pregnancy
- **Counsel:** patients at risk of giving birth to newborn affected with Hemoglobinopathie**s.**
- **Describe** the pathology of Von Willebrand's disease its course and potential complications in pregnancy and management principle.

Structure of normal adult and fetal hemoglobin:

Hemoglobin is a tetrameric protein composed of two pairs of polypeptide chains with a heme group attached to each chain. The normal adult hemoglobin A_1 comprises 95 percent of hemoglobin. It consists of two α-chains and two β-chains. The remaining 5 percent of hemoglobin usually consists of hemoglobin A_2 (containing two α-chains and two δ-chains) and

hemoglobin F (with two α-chains and two γ-chains). In the fetus, hemoglobin F (fetal hemoglobin) declines during the third trimester of pregnancy, reaching its permanent nadir several months after birth.

The prevalence of hemoglobinopathies: has distinct geographical and racial variation (Figure 35-1).



- **Figure 35-1:** Persons of African, Southeast Asian, and Mediterranean descent are at increased risk of carrying hemoglobinopathies (WWW.DCP2.org)

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Diagnosis of hemoglobinopathies:

- Red blood cell indices: Microcytic red blood cells (MCV <80 fL) in the absence of iron deficiency suggests thalassemia. It is recommended that all pregnant women should be screened for thalassemia by having complete blood count with red blood cell indices. Women who have: An MCV <80 fL in the absence of iron deficiency should have additional studies for confirmation of diagnosis (Figure 35-2)

Indication for Hemoglobin electrophoresis
Identifying at-risk patients

- Medical history: of chronic anemia or obstetric history of stillbirth.
- Family history: of hemoglobinopathy.
- Women living in endemic areas or from known ethnic groups at high risk of hemoglobinopathy.

- Hemoglobin electrophoresis: can detect the presence of abnormal and excess or deficient quantities of globin chains. Hemoglobin electrophoresis should also be performed in all at risk patients (see box)

- DNA-based testing: When abnormalities are noted, secondary tests such as DNA-based testing for alpha globin gene deletions may be required in order to establish a diagnosis.

In cases determined to be carriers the father should be evaluated with hemoglobin electrophoresis to determine the risk for the offspring.

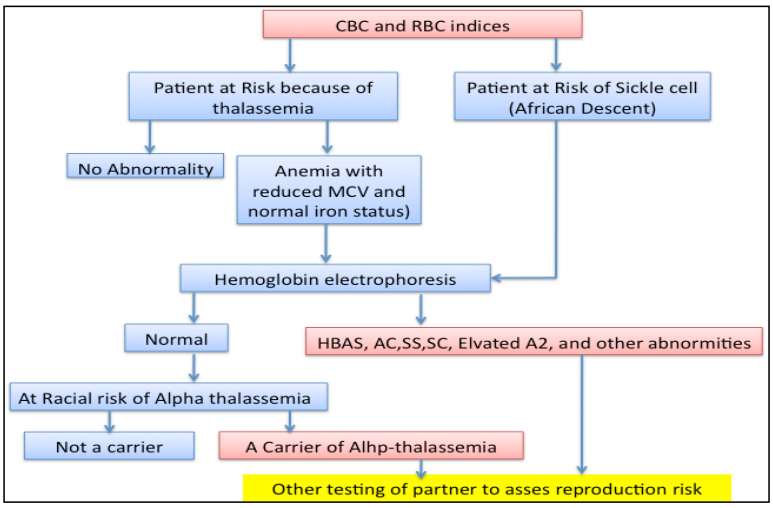

Figure 35-2: Algorithm for specialized antepartum evaluation for hematologic assessment of patients at risk (CBC = complete blood count; Hb = hemoglobin; MCV = mean corpuscular volume; RBC = red blood cell.) *Adapted from ACOG Practice bulletin no. 64.2005*

Hemoglobin S "Sickle Cell Hemoglobin"

Pathology and pathogenesis:

Hemoglobin S, aberrant (abnormal) hemoglobin results from a single substitution of valine for glutamic acid at the sixth position in the β-polypeptide chain. This alteration causes two significant pathological changes

(1) At low oxygen tensions (e.g. dehydration, hypoxia, or acidosis) the

RBCs containing hemoglobin S assume a sickle shape, and sludge in small vessels, resulting in microinfarction of the affected organs

(2) Shorten the life span of sickle cells to approximately 5 - 10 days, compared with 120 days for a normal RBC.

A person may be a heterozygous carrier to sickle cell trait (hemoglobin AS) or have the sickle cell disease or homozygous (hemoglobin SS).

Infants affected by sickle cell disease, have no antenatal, perinatal, or immediate postpartum manifestations of the disease until the production of fetal hemoglobin is replaced by the production of hemoglobin S. This usually takes 6 to 12 months of age after birth.

Diagnosis:

Patients are usually known cases of disease because of family or medical history. Carriers are either discovered during screening program for at risk patients or because of history of affected family memebers.

Pregnancy and sickle cell:

The complications depend on whether the patient is having sickle cell disease (SS) or a trait (SA).

Pregnancy with Sickle cell homozygous "Sickle cell anemia" (hemoglobin SS): Patients with Hemoglobin SS run multiple maternal and fetal risks:

Maternal Risks:

- Increased risk of painful vaso-occlusive crisis: this is because in pregnancy there is increase in metabolic demands, hypercoagulable state, and vascular. The most common sites for vaso-occlusive episoeds are the extremities, joints, abdomen, and the lungs which result in pulmonary infarction.

- Recurrent infection:particularly the urinary tract with increased risk of pyelonephritis. Sickling may also occur in the renal medulla, in which oxygen tension is reduced, resulting in papillary necrosis.
- Jaundice: due to hemolysis and decreased RBC survival. Biliary stasis commonly occurs during crisis, and cholelithiasis is seen in about 30 percent of cases.
- High-output cardiac failure may occur because of chronic anemia. left ventricular hypertrophy, and cardiomegaly are common.

Fetal Risk:

Fetal complications are related to decreased placental blood flow as a result of sickling in the uterine vessels. This result in high rate of spontaneous abortion (up to 25%), increased perinatal mortality rate (approximately 15 percent) due to multiple factors including preterm birth, fetal growth restriction and low birth weight.

Pregnancy with Sickle cell heterozygous "trait" (hemoglobin AS): Patients who are carriers run much lower risk than homozygous (Hemoglobin SS) patients. However they still need careful follow up. Studies have shown that sickle cell trait patients are at increased risk of preeclampsia, giving birth to low birth weight babies and postpartum infection namely endometritis.

Management: Management should be in a tertiary care center. It includes two elements: (I) the management of the disease with the objectives of prevention and early intervention, and (II) specific management of the pregnancy with fetal monitoring and early detection of obstetric complications.

(I) The management of the disease:

- Prevention and treatment of anemia: Folate supplementation at 4 mg/day (higher than the standard recommended dose), routine iron supplementation should not be given unless there is evidence of iron deficiency (low serum Ferritin).
- Prevention and Management of vaso-occlusinve crises In first trimester prevention of dehydration from nausea and vomiting. If crisis develop the management is along the same lines as in non-pregnant women by analgesia, oxygen, and hydration. *However hydroxyurea should not be used in pregnancy because of teratogenicity.*

Prophylactic transfusions to replaces the patient's sickle cells with normal RBCs, has been proposed but its effectiveness is still controversial, and the evidence of significant improvement in outcome are lacking.

- Prevention and management of infection: Frequent test for urinary tract infection is advisable and any infection requires aggressive management.

(II) Specific management:

- Fetal and pregnancy monitoring: The signs and symptoms of common pregnancy complications (e.g., decreased fetal movement, vaginal bleeding, preterm contractions, abdominal pain, headache) should be reviewed with the patient at each visit. Antepartum fetal surveillance with non-stress tests and ultrasound monitoring of fetal growth and well-being are indicated during the last trimester, or earlier if maternal or fetal complications arise

  Labor: the principle is to await spontaneous onset of labor. Induction and cesarean section should be performed only for the usual obstetrical indications. During labor and delivery the woman should be well oxygenated and hydrated to prevent sickling and the fetus should be monitored continuously. Analgesia or regional anesthesia is useful to reduce maternal cardiac demands secondary to pain and anxiety.

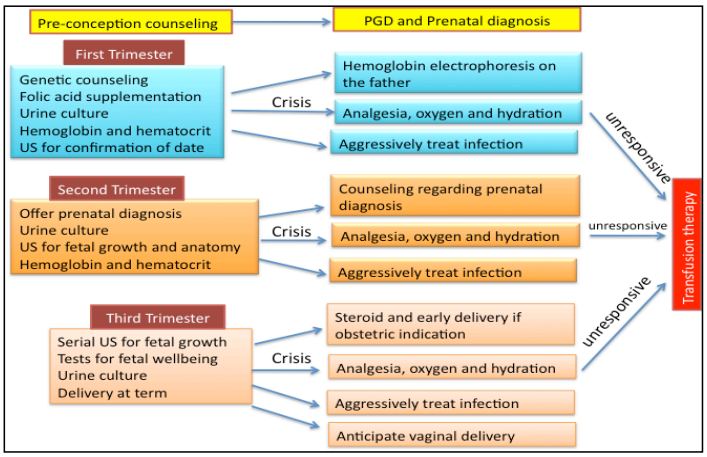

Figure 35: Algorithm for management of patients with Sickle cell diseases in pregnancy

Hemoglobin SC Disease

Hemoglobin C is another β-chain variant. It results from a G to A point mutation in the first nucleotide of codon 6. The gene is present in 2 percent of blacks. Women with both S and C hemoglobin suffer less morbidity in pregnancy than do patients with only hemoglobin S. As in sickle cell disease, however, there is an increased incidence of early spontaneous abortion and pregnancy-induced hypertension.

Because patients with SC disease can have only mild symptoms, this hemoglobinopathy may remain undiagnosed until a crisis occurs during pregnancy.

During gestation, patients with hemoglobin SC should receive the same program of prenatal care outlined for women with hemoglobin SS.

Thalassemia

Pathology and pathogenesis:

Thalassemia is due to a defect in the rate of globin chain synthesis. Any of the polypeptide chains can be affected. As a result, there is production and accumulation of abnormal globin subunits, leading to ineffective erythropoiesis and a decreased life span of RBCs. The disease may range from minimal suppression of synthesis of the affected chain to its complete absence. Either α- or β-thalassemia can occur. Heterozygous patients are often asymptomatic.

- **Homozygous α-thalassemia**

Homozygous α-thalassemia results in the formation of tetramers of β-chains known as hemoglobin Bart. Since there is no compensation for the alpha globin chain in utero, this **hemoglobinopathy** often result in severe fetal anemia and hydrops fetalis.

- **β-Thalassemia:**

β-Thalassemia is the most common form of thalassemia. It is either homozygous or heterozygous.

- **Heterozygous β-Thalassemia**: It has different forms of expression. Patients with thalassemia minima have microcytosis but are asymptomatic. Those with thalassemia intermedia exhibit

splenomegaly and significant anemia and may become transfusion dependent during pregnancy. These patients should be managed with a treatment program similar to that followed for patients with sickle cell. Folic acid should be routinely administered but iron supplementation should be given only if there is evidence of iron deficiency since there is real risk of iron overload.

- **Homozygous β-thalassemia**: is known as thalassemia major, or Cooley's anemia. Patients with this disorder are transfusion dependent. Affected individuals have high rate of infertility, short life span, often die of infections or cardiovascular complications before they reach childbearing age.

Counseling and prenatal diagnosis for patients with hemoglobinopathies:

Patients with hemoglobinopathies should be counseled regarding the risk of fetal inheritance of the disorder and the available modalities for prenatal diagnosis.

The firs step is to test the husband (or the proposed husband if it is pre-marital counseling), for hemoglobinopathies. If both are hemoglobinopathy carriers their offspring may be either normal (25%), carrier (50%), or affected (25%) the probability follow the basic Mendelian inheritance pattern.

Parents who are hemoglobinopathies carriers should be advised to either go for pre-implantation genetic diagnosis or prenatal diagnosis that can be accomplished by DNA analysis from chorionic villi or amniocytes (see chapter 27 on prenatal diagnosis)

VON WILLEBRAND'S DISEASE

Von Willebrand's disease (vWD) is the most common congenital bleeding disorder in humans. It is estimated that up to 1 percent of the population may have some form of the disorder. Type 1 is an autosomal dominant disorder, whereas type 3 and occasionally type 2 are autosomal recessive.

Pathology and pathogenesis:

vWD is related to quantitative or qualitative abnormalities of von Willebrand's factor (vWF), a glycoprotein serves as carrier protein of factor VIII, prolonging its life span in plasma. It also promotes platelet adhesion to the damaged vessel and platelet aggregation. In type 2B, the only clinical symptom in **pregnancy** may be thrombocytopenia. Therefore, this diagnosis should be considered in the gravida presenting with isolated thrombocytopenia during **pregnancy**.

Clinical features:

The clinical severity of vWD is variable but the concentration of factor VIII appears to determine the risk of hemorrhage.

Menorrhagia, easy bruising, gingival bleeding, and epistaxis are common.

Heavy bleeding may be encountered in patients with vWD undergoing elective or spontaneous first-trimester abortion because the levels of factor VIII have not yet risen.

During pregnancy bleeding is not common because the levels of factor VIII and vWF increase. However, shortly after delivery, it drop which increases the risk of severe and even fatal postpartum hemorrhage.

Treatment:

If the factor VIII level is less than 50 percent, treatment during labor and delivery should be initiated. Hemorrhage can also occur several days postpartum. Therefore, factor VIII levels should be checked before the patient goes home after delivery.

The treatment of choice is Desmopressin. It elicits the release of vWF from endothelial cells. Intranasal preparations of 300 mg are usually employed. In emergent or preoperative situations, 0.3 mg/kg of desmopressin can be given intravenously over 30 minutes

Reference and further readings:

- ACOG Practice bulletin no. 64. Hemoglobinopathies in pregnancy. Obstet Gynecol 2005;106:206.

- WWW.DCP2.org

Chapter 36

Autoimmune Connective Tissue Diseases in Pregnancy

Dr Estabraq Al Hachim

Pregnancy is a unique immunological experience in which the fetus that is for the maternal body is basically immunologically foreign tissue is not only accepted but also nourished and protected. Normally this occur secondary to major alterations in the cellular and humoral components of the maternal immune system.

Therefore disorders of the maternal immune system are likely to affect the normal immune adaptive mechanism of pregnancy. Conversely pregnancy-induced immunological alteration can modulate the clinical course of maternal immune tissue disorders.

By the end of this chapter you should be able to:

- **Describe** the definition of connective tissue disorders and its general features:
- **Describe an over view of the common autoimmune connective tissues disorders:**

SLE, Anti-phospholipid syndrome, Rheumatoid arthritis, Scleroderma

For each syndrome:

- Diagnostic criteria:
- Epidemiology:
- Effect of Pregnancy on the disease:
- Effect of the disease on pregnancy:
- **Management:**
    - Preconception counseling
    - Management during pregnancy
    - Maternal surveillance:
    - Fetal surveillance:
    - The Delivery
- **Puerperium and contraception**:

General features of autoimmune connective tissue disorders:

Connective tissue disorders are a term that describes non-organ specific diseases of the connective tissues. It comprise two major categories; autoimmune connective tissues disorders also known as collagen vascular diseases and inherited disorders of connective tissue synthesis or

metabolism such as Ehlers-Danlos syndrome, Marfan syndrome, osteogenesis imperfecta. The discussion in this chapter focuses on the autoimmune connective tissue disorders.

Autoimmune connective tissue disorders have general features in common these are:

- Its diagnosis is usually based on a set of clinical and laboratory features. These features are laid down by international bodies and revised from time to time to improve and sharpen its diagnostic sensitivity and specificity.
- For unknown reasons connective tissue disorders are two to three times more common in females than in males.
- When considering the effect of the disease on the pregnancy it is important to consider the adverse effect of drugs and medications (Table 36-2).
- Autoimmune connective tissue disorders, normally have spontaneously waxing and waning courses. Furthermore pregnancy is often associated with changes and diseases that mimic autoimmune connective tissues flare such as various erythemas, thrombocytopenia, dilutional anemia, hypertension and proteinuria.

Systemic Lupus Erythematosus

SLE is a chronic autoimmune disorders characterized by wide diversity of clinical and laboratory manifestation. It can affect any organ or tissue in the body.

Clinical course: SLE clinical course is characterized by remissions and exacerbations with some patients manifesting relatively benign diseases and others experiencing rapidly progressive and even fatal course. Infection, lupus flares, end-organ failure including nephritis, and cardiovascular disease account for most of the deaths.

Antiphospholipid antibodies and SLE: at least one third of cases of SLE are also positive for antiphospholipid antibodies, either anticardiolipin (in approximately 30%) or lupus anticoagulant (in approximately 10%) or both. The documentation of either of these antibodies in patient with SLE confers significantly higher

Most cases of fetal loss and pregnancy complications associated with SLE seem to be related to the presence of antiphospholipid antibodies.

risk of thrombosis, neurological disorders and thrombocytopenia.

Epidemiology: It mostly affects women between the ages of 15 to 64 years with a prevalence of 1 in 500 among women in the reproductive age group.

Effect of Pregnancy on SLE: generally unpredictable but at least in some cases pregnancy may increase the risk of flare up of SLE. This risk can be reduced if conception occurs during a period in which the disease is controlled.

Patients should be advised not to conceive during time of increased lupus activity as this increases the chance of flare up during pregnancy. A period of quiescence of 5 to 6 months is preferable.

Effect of SLE on pregnancy: There is increased risk of fetal loss, pre-eclampsia, and hypertension. However most if not all fetal deaths in women with SLE seems to associated with the presence of antiphospholipid antibodies

Neonatal lupus: Is a rare and unusual syndrome occurs in about 5 to 10% of cases. It consists of any or all of the following findings: a (transient) photosensitization rash, congenital complete heart block, thrombocytopenia, liver abnormalities and hemolytic anemia

Management: Pregnancy with SLE is a high-risk pregnancy. Optimum management requires collaboration between immunologist and perinatologist.

Preconception counseling: Evaluation of patient disease with careful serology testing for antibodies in addition to renal function tests. Before conception patient should be on minimum drug therapy and in a quiescent period for 6 months.

Management during pregnancy:

- Maternal surveillance: The aim of maternal surveillance is to monitor changes in diseases activity (renal and hepatic function in addition to hematological evaluation) and detection of superimposed preeclampsia.

The differentiation between preeclampsia and flare up of SLE is difficult yet it is important to make since the treatment of PET is delivery while the treatment of lupus flare is increasing dose of steroids and possibly azathioprine therapy. Hypertension, as well as edema, proteinuria and thrombocytopenia are present in both conditions

Unfortunately it is sometimes impossible to distinguish between the two conditions lupus flare and severe preeclampsia. The patient should continue her SLE medication as necessary (see table 36-2 for drug therapy)

- Fetal surveillance; starts with early ultrasound examination to accurately determine gestational age. From 20 weeks of gestation serial ultrasound for fetal growth should be performed at approximately 2-3 weeks gestation. From 28 weeks onwards, assessment of fetal wellbeing should include amniotic fluid volume and fetal cardiotocography once then twice weekly. Fetal echocardiography should be performed from 20-24 weeks especially if anti SSB (la) antibodies are present.

The Delivery and Puerperium:

Decision regarding timing and route of delivery are primarily dictated by the status of the fetus but also may be influenced by the maternal SLE and its complications such as severe maternal illness, thrombocytopenia and total hip replacement.

Long term Management for women with SLE: Because of increased risk and morbidity in association with each pregnancy, women should be advised to limit their family size. Tubal sterilization should be offered. Estrogen containing hormonal contraceptives should probably be avoided. Progestin only implants and injection may be used. Contraceptive devises should not be used for patients on immunosuppressive therapy.

Antiphospholipid Antibodies syndrome (APS)

Definition: Antiphospholipid antibodies represent a broad category of autoantibodies that bind to negatively charged phospholipids, proteins or a protein-phospholipid complex. The most clinically relevant ones are lupus anticoagulant (LAC) antibodies and anticardiolipin antibodies.

The diagnosis: The Diagnosis of APS syndrome is based on laboratory and clinical features. At least one or more of the laboratory features and one or more of the clinical features cited in

Clinical Features	Laboratory Features
Pregnancy Morbidity - Fetal death > 10 weeks - Premature birth <34 weeks with feature of placental insufficiency or severe PET - ≥ unexplained spontaneous abortions at less than 10 weeks.	1. Lupus Anticoagulant 2. Anticardiolipin antibodies IgG, medium or high positive
Thrombosis Venous Arterial, including stroke	3. Anticardiolipin Antibodies IgM, modium or high positive and lupus anticoagulants
Autoimmune thrombocytopenia	
Other Coombs positive hemolytic anemia Livedo reticularis	

Table 3-1: Clinical and laboratory criteria for the diagnosis of APS. The laboratory feature should be positive on two occasions 8 or more weeks apart

table 36-1 should be present for labeling a patient as having antiphospholipid antibodies syndrome

Patient either has primary APS if there is no underlying disease or secondary APS if superimposed on underlying diseases, such as SLE or malignancy.

Other antiphospholipid antibodies such as phosphatidylserine, phosphatidylinositol, phosphatidylglycerol have been identified. However its clinical implications are questionable and its essays have not been subjected to any standardization

More recently attention have directed to the protein Beta$_2$-glycoprotien "ß$_2$-GP-I" which could actually be the cofactor through which antiphospholipid antibodies interact to mediate its pathogenic function. ß$_2$-Glycoprotein-I is an abundant circulating glycoprotein with several anticoagulant properties in vitro.

Other phospholipid binding proteins which may be involved in the pathophysiology of APS include protein C and protein S, both are endogenous anticoagulants, and annexin V, a placental antithrombotic product that coats the syncytiotrophoblast in high concentration. Thus antibodies that bind protein C or S would result in venous, arterial or decidual thrombosis, while binding of annexin V would result in coagulation and thrombosis in the intervillous space.

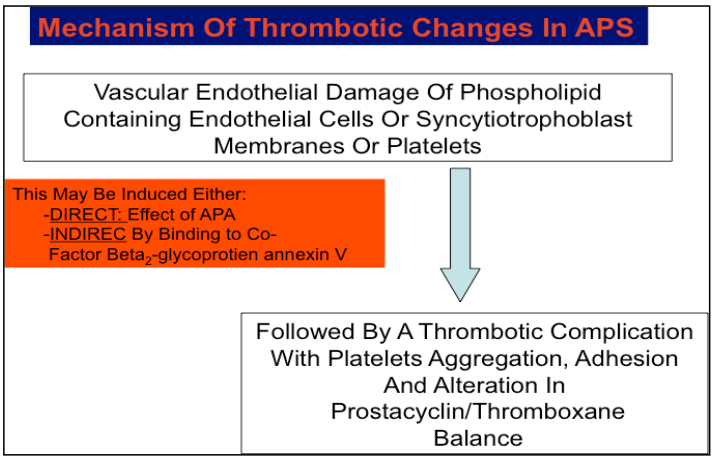

Figure 36-1: Antiphospholipid antibodies induce its thrombotic effects by direct and indirect action through binding to a cofactor such as B2-Glycorproein-1, Annexin which has an anticoagulant properties
Annexin (placental anticoagulant protein I): coats the syncytiotrophoblast. Binding of Annexin V results in coagulation and thrombosis in the inter villus space

Clinical features of APS:
Any of the medical complications shown in Table 36-2 should be indication to screen for APS.

Indications for testing for APS
• Recurrent pregnancy loss • Unexplained second or third trimester loss • Early onset severe preeclampsia. • Venous or arterial thrombosis. • Unexplained fetal growth restriction. • Autoimmune or connective tissue disease. • False positive serological test for syphilis. • Prolonged coagulation studies. • Positive autoantibody tests

Table 36-2: Indications for testing of APA

Obstetric Complications of APS:
Several studies have demonstrated a positive link between the presence of aPL antibodies and some obstetrics morbidities;

- Fetal wastage particularly late (i.e. second and third trimester) but not early (first trimester) pregnancy loss.

- *FGR and Preeclampsia*: Intrauterine fetal growth restriction is reported in approximately one third of pregnancies in women with APS. Similarly a high rate, approximately 10% of cases of severe and early pre-eclampsia are positive to antiphospholipid antibodies

Pathogenic Mechanism of APS and Pregnancy:
In most cases of APS pregnancy loss has traditionally been ascribed to thrombosis of the uteroplacental vasculature and subsequent placental infarction.

Obstetric Management of Antiphospholipid Syndrome:

Management of APS in pregnancy includes; patient counseling regarding the potential risks and management plane during pregnancy, drug management of the diseases, fetal surveillance, postnatal care and contraceptive advice.
The management strategy of APS is to combat the vascular thrombotic effect of the disease. Currently the recommended regiment for women with APS syndrome is a combination of low dose aspirin and heparin. Therapy is usually initiated after confirmation of a viable embryo with cardiac activity.

Postpartum management: Thromboprophylaxis should be continued during the postpartum period because of a real risk of thromboembolism.
As in case of SLE, patients with APS should be advised to limit their family size. The appropriate method for doing that should be discussed along more or less the same guidelines as in women with SLE.

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease characterized by synovitis and serositis (inflammation of the lining surfaces of the joints, pericardium, and pleura) in addition to a variety of other systemic manifestation. Articular involvement is the hallmark of the disease. It varies in severity and course from progressive to intermittent one. As a chronic disease it results in progressive development of various degrees of symmetric joint destruction, deformity, and a significant decline in functional status.

It has a prevalence of about 2%. The onset of the diseases is usually between 20 and 60 years of age. Women are three times affected more than men. All races are equally affected.

Effect of pregnancy on the disease: Rheumatoid arthritis is one of the few immune disorders for which almost all studies have demonstrated that pregnancy has a favorable effect on the course and severity of the disease while in the postpartum period the symptoms exacerbate.

Effect of the disease on pregnancy: there is no adverse effect of rheumatoid arthritis on pregnancy or perinatal outcome. However concern may arise in relation to; the drug treatment of rheumatoid arthritis (Non steroidal anti-inflammatory agents NSAIDs) Prednisone and Immunosuppressive therapy (see table 36-2).

Delivery: The aim is to achieve vaginal delivery however in some cases hip or knee involvement may preclude vaginal delivery or position of the patient on the delivery table. Also induction of anesthesia and intubation might be difficult in patients with spinal involvement.

Scleroderma and Progressive systemic sclerosis (PSS)

Both are forms of systemic collagen diseases of unknown etiology, its prevalence average 1 in 10,000 with a 3 to 1 female to male ratio and an onset between the ages of 30 to 50 years. In its systemic form (PSS) the disease is characterized by fibrosis of skin, blood vessels and visceral organs. The term scleroderma is used if the disorder is localized to the skin.
The mortality is high with renal and pulmonary involvement and the 10 years survival is less than 50%. There is no effective treatment. Therapy is symptomatic with corticosteroids.

Effect of the disease on pregnancy: there are no specific effects of scleroderma or SPP on pregnancy. With careful timing of pregnancy in women without renal, pulmonary or cardiac disease and with careful monitoring successful pregnancy are achievable for both mother and fetus.

Delivery is expected to be vaginal unless soft tissue changes due to scleroderma cause soft tissue dystocia. Tracheal intubation may be difficult because those women have limited ability to open their mouths.

Effect of the pregnancy on the disease:
Pregnancy does not seem to specifically worsen the course of the disease. Several studies have shown that the rate of progression is the same whether or not the woman was pregnant.

Women with advanced systemic disease involving renal, vascular, cardiac or pulmonary involvement do poorly. Termination of pregnancy should be considered in the presence of rapidly worsening cardiac or renal disease.

Drug	Dose, Mechanism of action, and side effects	
Aspirin	• Low dose aspirin are used for antiphospholipid syndrome (see text). • Block the conversion of arachidonic acid to thromboxane A_2 in favor of sparing prostacyclin (thromboxane A_2 has vasoconstrictive action and increase platelets aggregation while prostacyclin has a vasodilator action).	
Nonsteroidal ani-inflammatory drugs ***NSAIDs***	• Cause premature closure of the ductus arteriosus and subsequent persistent of the fetal circulation (pulmonary hypertension). • Impair fetal renal function and precipitate oligohydramnios These effects appear to be reversible and gestation-age dependent. It should not be used beyond 32 weeks of gestation.	
Steroids ***Prednisone is the drug of choice. It is metabolized in the mother to the active form prednisolone***	• Prednisolone: 10 to 15 mg daily. The placenta converts Prednisolone to an inactive active metabolite. The fetal/maternal concentration of the drug is approximately 1:10 • Animal studies have showed increase in the background incidence of cleft palate after exposure to chronic corticosteroid administration but not in human	**Untoward Effects** - Fluid retention. - Worsening of striae and acne. - GIT discomfort and ulceration. Steroid induced GDM
Dexamethasone and Betamethasone	• Unlike Prednisone cross the placenta more freely resulting in maternal fetal concentration of almost 1:1 with little conversion to inactive form For this reason are used for enhancing fetal lung maturity	
Immunosuppressive and Cytotoxic agent ***Azathioprine*** ***Cyclophosphamide***	• Cyclophosphamide regularly causes amenorrhea and infertility. Should not be used in early weeks of pregnancy because of its teratogenicity and abortifacient property. • Azathioprine is less toxic (recommended oral dose are 2 to 3 mg/kg/day).	
Heparin ***Unfractionated heparin (UFH)*** ***Low Molecular Weight Heparin (LMWH)***	• **Heparin**: Does not cross the placenta • **Mechanism of action**: - Prevent venous and arterial thrombotic episodes. -Prevent thrombosis in the microcirculation of the decidual-trophoblastic interface **UFH dose**: 5000 to 10,000 units SC every 12h. Prolonged administration of heparin is associated with a number of complication including bleeding, thrombocytopenia, osteopenia and osteoporosis **LMWH**: has the advantages of once daily injection without the side effect of UFH	

Table 36-2: the commonly used drugs in connective autoimmune disorders, their doses, maternal and fetal effects.

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Chapter 37

Liver Diseases in Pregnancy

Liver diseases in pregnancy encompass a diverse range of problems. Some of these disorders are unique to the gestational state, whereas others may affect pregnant as well as non-pregnant women.
Surgical diseases Cholelithiasis occurs in 6 percent of pregnancies; complications can, safely be treated with surgery in the first or second trimester. Women with chronic liver disease or cirrhosis are often anovulatory but if pregnancy occurs it is associated with a higher risk of fetal loss during pregnancy.

By the end of this section you should be able to:

- **Describe** the physiologic changes of liver function tests in pregnancy
- **List the** most common disorders of liver in pregnancy:
  - Liver diseases specific to pregnancy: intrahepatic cholestasis, Acute fatty liver.
  - Liver diseases develop as complications of pregnancy specific diseases: e.g. hyperemesis gravidarum and preeclampsia, (HELLP).
  - Liver disease not specifically related to pregnancy: e.g. Acute viral hepatitis
- **Develop** a problem-oriented approach to the diagnosis and treatment of liver disorders in pregnancy.
- **Describe** the fetal and neonatal risks of the different types of hepatitis in pregnancy
- **Describe** the screening and Prophylaxis against viral hepatitis in pregnancy

Liver disorders in pregnancy can be considered as follow:

- **Liver diseases specific to pregnancy:** e.g.
  - Intrahepatic cholestasis of pregnancy
  - Acute fatty liver of pregnancy

- **Liver diseases develop as a complication of pregnancy specific diseases:**

- Hyperemesis gravidarum
- Preeclampsia, which may be complicated by the syndrome of hemolysis, elevated liver enzymes and low platelets (HELLP).

- **Liver disease not specifically related to pregnancy**: e.g.
  - Acute viral hepatitis.
  - Cholelithiasis, thrombotic diseases (such as Budd-Chiari syndrome).

Physical and physiological changes of the liver in pregnancy:

Normal pregnancy is associated with important changes that have important bearing on the diagnosis of hepatobiliary diseases. These changes affect both physical examination and liver function tests.

- Physical changes: some of the features of chronic liver diseases such as spidar angiomas and palmer erythema are also present in pregnancy, in both conditions it is due to hyperestrogenemia. In late pregnancy the enlarging uterus and stretched abdominal muscles makes physical examination for hepatomegally difficult.

- Liver function tests in pregnancy: In normal pregnancy most liver biochemical tests are either normal or slightly increased or decreased but still within the normal range. The following table summaries the pattern of liver function tests in pregnancy:

Liver tests affected by pregnancy (these tests are increased or decreased in relation to values in non-pregnant women)	
Albuminemia	Decreased from the first trimester due to hemodilution
Alkaline phophatase levels	Increased from second half of pregnancy - mainly from placental origin
Gamma glutamyl transferase	Slightly decreased in late pregnancy (within normal)
Serum fibrinogen	Increases in late pregnancy
Liver tests not affected by pregnancy	
The bilirubin level "Total, free and conjugated bilirubin"	
Serum aminotransferase levels (ALT, AST)	
Prothrombin time	

Table 37-1: Physiological changes liver test in pregnancy

- Functionally: The sex hormones (estrogen and progesterone) induce mild relaxation of the smooth muscle of the biliary tree, leading to increased gallbladder volume and decreased contractility. In addition there is increase in the relative concentration of cholesterol, phospholipids, and bile acids. This could explain the association between high parity and increases rate of gallstones development.

Approach to a pregnant woman who has signs or symptoms of hepatobiliary disease:

The approach to the diagnosis of hepatobiliary disorders in pregnancy depends on:

- Past medical history: history of similar problems in previous pregnancies, history of drug use or blood transfusions.
- The pregnancy trimester: e.g. Hyperemesis gravidarum should be considered in the differential diagnosis of abnormal liver function tests in the first trimester, "Cholestasis" of pregnancy might also begin to develop in the second trimester, "Acute Fatty Liver" usually develop in the third but may occur in the second trimester of pregnancy.
- The primary or cardinal clinical feature: The clinical presentation of liver diseases encompass wide spectrum of specific and non-specific symptoms and signs. None-specific clinical features include: fever, nausea, vomiting, general malaise and fever. While specific features include: right upper quadrant abdominal pain, jaundice, and pruritis. HELLP syndrome is more often a complication of severe PET.
- Pattern of liver biochemical tests: these include:
  - LFTs which reflects liver cell injury: Aspartate aminotransferase (AST), and Alanine aminotransferase (ALT) (both are markedly elevated in viral hepatitis).
  - LFTs which reflect liver synthetic function: Albumin level and prothrombin level
  - LFTs which reflect Cholestasis and biliary obstruction: Alkaline phosphatase, bilirubin and gamma glutamyl transpeptidase

Table 37-2 shows the common pregnancy related liver disorders, including the cardinal clinical picture, liver function tests and other tests. Both HELLP syndrome and acute fatty liver of pregnancy are emergency conditions that require prompt delivery, intensive care setting and involvement of multidisciplinary team.

However in all cases of liver diseases that present in pregnancy other causes of liver heptobiliary diseases should be considered these include viral hepatitis (the most common cause of jaundice in pregnancy) or drug-induced hepatitis, gallstone disease, or malignancy. These causes have no specific relation to any trimesters of pregnancy (see Figure 37-1).

Liver Disease	Cardinal Clinical Features	Liver Function tests	Treatment
Intrahepatic Cholestasis of pregnancy ICP: - *Usually in the 3rd trimester of* - *Pathophysiology unknown.* - *Associated with a Prematurity (40%) Fetal Distress Perinatal mortality (2-3%)*	• Pruritus 80% • Jaundice 20% • Anorexia, nausea, vomiting. • Upper Quadrant Abdominal pain (mild)	• Elevate Fasting serum level of bile acids (Cholic acid). • Mild elevation of serum bilirubin (mostly conjugated). • Mild elevation in (AST, ALT) • Elevated alkaline phosphates	• Ursodeoxycholic acid (Actigall), 15 mg per kg per day • Cholestyramine (Questran) • Parenteral vitamin K supplementation
HELLP Syndrome	• Severe PET (Not all cases) • Right upper quadrant pain and malaise. • Significant weight gain or edema; • Nausea/ emesis. • Jaundice is rare	• Hemolysis (with elevated bilirubin levels and LDH > 600 IU per L) • Moderately elevated transaminase levels (AST and ALT levels of 200 to 700 IU per L) • Thrombocytopenia < 100,000 per mL (100 × 109 per L).	Expeditious delivery and intensive care
Acute Fatty Liver Disease of pregnancy - *Usually in 3rd trimester.* - *commonly associated with PET.* - *Associated with mortality rate for mother and fetus (18-23% respectively))*	• Upper right quadrant abdominal pain, anorexia and headache. • Nausea, vomiting, generalizes malaise and tiredness • Jaundice is mild and late in onset. • 50% of patients shows clinical sings of preeclampsia	• Varies from mild biochemical abnormalities to fulminate hepatic failure. • Moderate elevations of transaminases. • prolongation of prothrombin time and PTPT, decreased fibrinogen • renal failure. • profound hypoglycemia • Modest and delayed rise in bilirubin levels	Expeditious delivery and intensive care

Table 37-2: Shows the Clinical picture, LFT, and outline of treatment for the hepatic live diseases specific to pregnancy

Viral Hepatitis:

Acute Viral Hepatitis is the most common cause of jaundice in pregnancy. The course of most viral hepatitis infections (e.g., hepatitis A, B, C and D) is unaffected by pregnancy, except in Hepatitis E (waterborne virus spread through fecal-oral transmission) which in pregnancy is associated with markedly increased fatality rates (10 to 20 percent).

Effect of Viral hepatitis on the fetus:

In cases of acute hepatitis B virus infection complicating pregnancy, the prevalence of neonatal infection depends on the time during gestation that maternal infection occurs.

- Neonatal hepatitis B virus infection is rare if maternal infection takes place in the first trimester.
- The infection occurs in 6 percent of neonates of women infected in the second trimester.
- It rises to about 67 percent of those infected in the third trimester and in virtually all of those infected in the immediate postpartum period.

Neonates of mothers experiencing acute hepatitis B virus infection should receive immunoprophylaxis and vaccination.

Screening of pregnant women for HBsAg: chronic hepatitis B infections may be transmitted to neonates. Transmission is effectively prevented with perinatal hepatitis B vaccination and prophylaxis with hepatitis B immune globulin. The risk of chronic hepatitis B virus infection in a neonate who does not receive immunoprophylaxis and vaccination for hepatitis B virus is 40 percent.

The risk of vertical transmission hepatitis B virus to the fetus is proportional to maternal B antigen (HBeAg) and antibody (HBeAb) status. It is estimated as:

- 10 % in mothers with negative HBeAg (**hepatitis B antigen)** and positive HBeAb (**hepatitis B antibody)**

- 90 % if HBeAg is positive.

Table 37-2: Shows the Clinical picture, LFT, and outline of treatment

Hepatitis C Virus The incidence of hepatitis C virus infection is rising most rapidly among persons 20 to 45 years of age.

Fetal Transmission: The risk of vertical transmission of hepatitis C virus infection range from zero to 36 percent. In hepatitis C virus-positive, HIV-negative mothers without a history of active intravenous drug use or transfusion exposure, the risk of hepatitis C virus vertical transmission is zero to 18 percent. The highest reported rate of vertical transmission in this group occurs in infants born to hepatitis C virus-positive, HIV-positive mothers, with transmission rates of 6 to 36 percent.

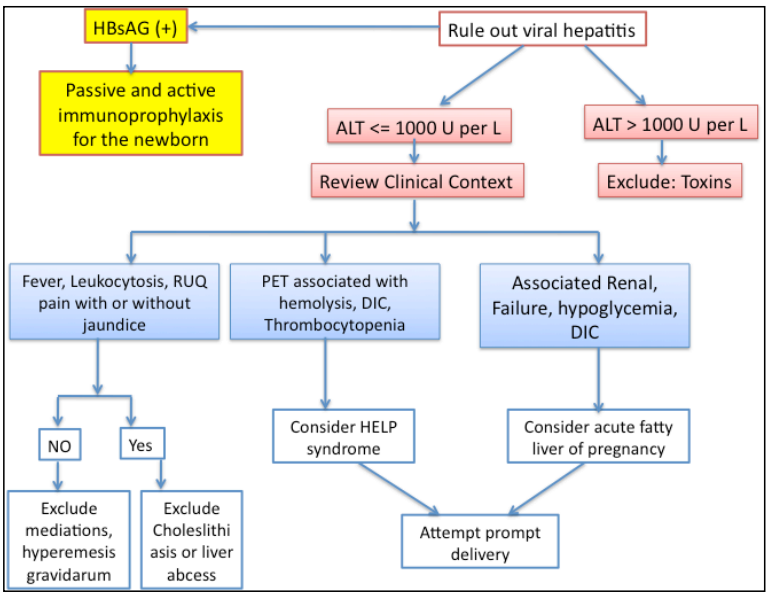

Figure 37-1: Algorithm for the evaluation of alanine aminotransferase elevation during pregnancy. (HBsAg=hepatitis B surface antigen; ALT=alanine aminotransferase; RUQ=right upper quadrant; DIC=disseminated intravascular coagulopathy; HELLP=hemolysis, elevated liver enzymes, low platelets)
Recommended serological tests: Hepatitis A IgM, hepatitis B surface antigen and hepatitis B core antibodies, hepatitis C antibodies, CMV IgM, herpes simplex virus IgM and Epstic Barr virus IgM

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Chapter 38

Acute Surgical Emergency in Pregnancy

In pregnancy as outside pregnancy acute surgical emergency may develop. However in pregnancy not only the diagnosis is a challenging but also delay in treatment can have grave consequences on both the mother and the fetus. There may be hesitation on part of the physician to undertake necessary invasive diagnostic or therapeutic procedures.

An understanding of the anatomical and physiological changes in pregnancy, a detailed history and clinical examination and the use of appropriate laboratory and imaging techniques, including abdominal imaging as necessary, will assist in the early diagnosis and institution of treatment. A multidisciplinary approach is often required in such cases.

By the end of this chapter you should be able to:
Describe why the diagnosis of acute surgical abdomen in pregnancy is challenging?
- Problem with symptoms
- Problem with signs
- Problem with investigations

List Pregnancy-related causes**:**
- Labor pain: -Placental abruption:
- Uterine rupture -Extrauterine pregnancy:
- Severe preeclampsia and HELLP syndrome:
- Intraamniotic infection: -Acute fatty liver:

List Non-pregnancy-related causes
- Acute appendicitis: -Acute cholecystitis and cholelithiasis
- Bowel obstruction: -Inflammatory bowel disease:
- Pancreatitis: -Perforated ulcer:
- Acute pyelonephritis: -Acute cystitis:
- Trauma: -Sickle cell crisis:
- Gastroenteritis: -Pneumonia:

List Gynecologic causes
- Ovarian torsion or cyst rupture:
- Fibroid degeneration:
- -Pelvic inflammatory disease:

Describe the Approach to pregnant patient with acute abdominal pain

⇨Why the diagnosis of acute abdomen in pregnancy is challenging?

There are several reasons that make the diagnosis of acute abdomen in a pregnant woman a rather challenging task that require both clinical skill and knowledge.

- Abdominal discomfort is a common complaint in pregnancy. It may due to a number of normal physiological entities, such as the enlarging uterus, fetal position or movement, Braxton-Hicks uterine contractions (i.e., contractions not associated with labor/cervical changes), and possibly stretching or congestion of the round ligaments. Some patients' particularly young nullipara can experience the discomfort felt by one or more of those changes in a rather severe form.

Remember that
- Sometimes the underlying pathological processes lead to uterine contractions, which may result in cervical changes.
- Pain that is severe, sudden, constant, associated with other symptoms (e.g., nausea, vomiting, vaginal bleeding) or in the upper abdomen suggests the abdominal pain is due to disease.
- The presence of peritoneal signs (rebound tenderness, abdominal guarding) is never normal in pregnancy.

- Nausea and vomiting, which often associated with gastrointestinal pathology, are common features of early pregnancy. Normally however it decrease or disappear by early to middle second trimester.

Remember that
Nausea and vomiting are not normal manifestations of pregnancy when they occur with abdominal pain, fever, diarrhea, headache, or localized abdominal findings.

- The enlargement of the uterus and stretching of the abdominal muscles may affect the presentation and evaluation of abdominal pain. Furthermore together with laxity of the abdominal wall they could mask or delay signs of peritoneal irritation.

- Physiological changes in hematologic parameters may make infection and occult hemorrhage more difficult to diagnosis. White blood cell counts increase to a normal range of 10,000 to 14,000 cells/mm3 during pregnancy, and even as high as 20,000 to 30,000 cells/mm3, during labor to return to normal prepregnancy levels about one week postpartum.

Furthermore low hemoglobin may be simple form of physiological anemia. Thus the modest decrease in hemoglobin concentration (normal hemoglobin ≥10.5 to 11.0 g/dL) coupled with the normal modest increase in heart rate (by 10 to 15 beats per minute) can be mistaken for signs of mild hemorrhage.

Pregnancy-related causes

Labor pain: labor should be excluded in all patients' presents with abdominal pain in pregnancy. However while labor pain may be the primary cause of pain it also may develop secondary to the original pathology.

Placental abruption: An acute, clinical abruption classically presents with vaginal bleeding, abdominal and/or back pain, and tonic uterine contractions. The fetal heart rate pattern may be nonreassuring or in severe cases fetal death may ensue. However sometimes such typical picture may be absent, and there may be no or very slight revealed bleeding (see chapter on Bleeding in pregnancy)

Uterine rupture: Signs and symptoms of uterine rupture include non-reassuring fetal heart tracing or fetal death, uterine tenderness, peritoneal irritation (abdominal guarding), vaginal bleeding, and immanent signs of shock. This complication should be suspected particularly in high-risk cases (patient with previous uterine scar particularly upper segment scar and during labor).
Uterine rupture prior to the onset of labor is rare and usually due to sharp or blunt abdominal trauma.
A scarred uterus may rupture spontaneously in the absence of labor or obvious trauma. This is more likely in patients with previous classical or T shaped cesarean section scar.
Rupture of the unscarred uterus during labor is rare; risk factors include grand multiparity, dystocia (malpresentation, macrosomia), obstetrical procedures (breech extraction, uterine instrumentation, cephalic version), and injudicious use of uterotonic drugs in the presence CPD.

Extrauterine pregnancy: Extrauterine pregnancies usually occur in the fallopian tube, but can occur elsewhere (e.g. attached to abdominal viscera

or within the cervix or a hysterotomy [e.g. cesarean delivery] scar. Non-tubal ectopic pregnancies tend to rupture later in pregnancy than tubal pregnancies, and the ectopic location may not be identified until the second, or even third, trimester (e.g. in congenital rudimentary uterine horn).
An extrauterine pregnancy can occur concurrently with an intrauterine pregnancy; these heterotopic pregnancies can be difficult to diagnose. A risk factor for such condition is a pregnancy conceived via assisted reproductive technology (e.g. IVF).
Clinical manifestations vary depending upon the location; however, abdominal pain is a common symptom of all types of extrauterine pregnancy; vaginal bleeding, nausea, and vomiting may also occur. A high index of suspicion is important for diagnosing these pregnancies.

Severe preeclampsia and HELLP syndrome: Upper abdominal pain due to stretching of the liver capsule, or in severe cases subcapsular hemorrhage or hepatic rupture are signs of severe pre-eclampsia with or without HELLP syndrome. In rare occasion it may be the presenting sign.

Clinically there is abdominal pain and tenderness in the midepigastrium, right upper quadrant, or below the sternum. The condition should be differentiated from nonspecific viral illness or viral hepatitis, particularly if the serum aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) are markedly elevated. Hypertension (blood pressure ≥140/90 mm Hg) and proteinuria are present in approximately 85 percent of cases, but it is important to remember that either or both may be absent in women with otherwise severe HELLP syndrome (see Chapter 37 Hepatic Diseases in Pregnancy).

Intraamniotic infection: The full symptoms and sings of intraamniotic infection are more common in the setting of premature rupture of the membranes. It includes fever, abdominal pain, uterine tenderness, leukocytosis, maternal and fetal tachycardia, and uterine contractions.

Acute fatty liver: This condition should be considered particularly in the third trimester in patients complaining of nausea or vomiting (approximately 75 percent of patients), abdominal pain (particularly epigastric, 50 percent), anorexia, and jaundice.

About one-half of patients have signs of preeclampsia at presentation or sometime during the course of illness.

Non-pregnancy-related causes

Acute appendicitis: Appendicitis is the most common cause of the acute surgical abdomen during pregnancy. Its incidence in pregnancy is approximately 1 in 1500 (similar to the non pregnant female population). The fetal morbidity and mortality with perforated appendicitis ranges between 33% and 43%, and is closely linked to delay in surgical intervention. In the absence of perforation, the fetal loss is 1.5% or less.
The problem of appendicitis in pregnancy is that the diagnosis can be difficult because:

- The symptoms of acute appendicitis, such as nausea, vomiting, epigastric and lower abdominal pain, may be less apparent in pregnancy.
- The signs are not reliable: because right iliac fossa rebound tenderness and guarding may not be very prominent due to the stretched abdominal muscle in advanced gestation. It is also possible that the appendix is rather displaced upward or hidden behind the enlarging uterus. However still in the majority of cases the most common sign is right lower quadrant pain, occurs within a few centimeters of McBurney's point, regardless of the stage of pregnancy.
- The investigations can be misleading because of the physiological leukocytosis of pregnancy.

Acute cholecystitis and cholelithiasis: Pregnancy is associated with an increased risk of gallstone formation. The increased serum cholesterol and lipid levels in pregnancy, as well as decreased gallbladder motility and delayed emptying, are partly responsible. It can lead to acute cholecystits.

- Symptoms and signs: similar to non-pregnant cases except that Murphy's sign is less commonly elicited in pregnancy. The evaluation of tenderness and guarding can be difficult in the third trimester because of the large uterus. Ultrasonography will accurately diagnose more than 90% of gallstones

In the late second and third trimesters, acute cholecystitis is generally managed conservatively by intravenous hydration, gastric suction, the judicious use of narcotics and antibiotics for signs of sepsis. Surgery is reserved for those with failed medical treatment, those experiencing recurrent attacks of biliary colic, suspected perforation, sepsis or peritonitis.
In the first and early second trimester surgical approach should be strongly considered including laparoscopic cholecystectomy.

Bowel obstruction: The risk of bowel obstruction during pregnancy increases as the uterus enlarges into the upper abdominal cavity with advancing gestation. Adhesions and volvulus are the most common causes of the obstruction; intussusception, hernias, and cancer are rare.

Diagnosis is often delayed, as symptoms of cramp-like pain, vomiting and constipation can be mistaken for the pain of labor, abortion or just pregnancy symptoms.
A common misdiagnosis in the second and third trimester is hyperemesis gravidarum,
Diagnosis and treatment are similar to that in nonpregnant individuals. Aggressive intervention is warranted because delay in treatment increases maternal and fetal morbidity and mortality.

Inflammatory bowel disease: The pain of inflammatory bowel disease is likely to be associated with changes in bowel movements (loose, bloody, mucousy); fever and weight loss may occur.

Pancreatitis: Acute pancreatitis is a rare complication of pregnancy; almost all patients have acute and persistent upper abdominal pain. The pain may radiate to the back, may be relieved with leaning forward, and may be accompanied by fever and postprandial nausea and vomiting.

Perforated ulcer: Ulcer perforation should be suspected in patients with a history of peptic ulcer symptoms who develop the sudden onset of severe, diffuse abdominal pain. The characteristics of the pain and associated symptoms and physical findings (e.g. tachycardia, low temperature, peritoneal signs) evolve over the first 12 hours after perforation.

Acute pyelonephritis:
This occurs in 1±2% of pregnancies, most frequently in the second and third trimesters, and is one of the most common reasons for hospitalization in pregnancy. It is usually a sequel to untreated asymptomatic bacteriuria (Chapter 33 Renal diseases in pregnancy).
It is important to remember that the diagnosis is clinical and a negative urine examination does not exclude the possibility of pyelonephritis. Treatment must be aggressive include: hospitalization, adequate hydration and parenteral antibiotic therapy; a penicillin (ampicillin) together with an aminoglycoside (gentamycin) for 5 days is followed by oral therapy for a further 10 days. Symptoms usually resolve within 24±48 hours.

Acute cystitis: This occurs in about 1% of pregnant women. It is more common in the second trimester and is characterized by suprapubic pain, dysuria, frequency, urgency and haematuria.

Trauma: Abdominal pain is a common consequence of blunt or penetrating abdominal trauma. Motor vehicle crashes are responsible for approximately two-thirds of maternal trauma cases in developed countries, while domestic violence, other assaults, falls, and burns account for the majority of the remainder.

Sickle cell crisis: Pain due to vasoocclusive crisis should be considered in patients with sickle cell disease. Such pain may be difficult to distinguish from an acute surgical abdomen (e.g. appendicitis, cholecystitis).

Gastroenteritis: maternal enterovirus infection can cause severe abdominal pain. Other types of gastroenteritis and mesenteric adenitis also may cause an acute abdomen.

Pneumonia: Pneumonia involving the lower lobes of the lung is a common cause of abdominal pain syndromes, presumably related to diaphragmatic irritation, and may be confused with acute cholecystitis or, rarely, an acute abdomen. Abdominal pain is occasionally the sole presenting complaint in a patient with lower lobe pneumonia.

Other causes: *there is a long list of other causes such as rupture splenic aneurysm, Diverticulitis and other less common causes which should be considered in difficult cases.*

Gynecologic causes

Ovarian torsion or cyst rupture: Ovarian torsion in pregnant women typically presents with lower abdominal pain, frequently accompanied by nausea, vomiting, low-grade fever, and/or leukocytosis. It occurs in all three trimesters, but is most common in the first trimester.

Rupture of an ovarian cyst (e.g. corpus luteum cyst) may be associated with the sudden onset of unilateral lower abdominal pain. The pain often begins during strenuous physical activity, such as exercise or sexual intercourse. Rupture may be accompanied by severe bleeding into the pelvis and hemodynamic instability.
Induction of ovulation, which can cause enlarged multicystic ovaries, is a significant risk factor for torsion.

Less commonly the ovarian cyst is ovarian neoplasm. The management of an ovarian neoplasm detected during pregnancy depends on its ultrasonographic characteristics and whether there are associated symptoms.

Fibroid degeneration: Pain is one of the most common complications of fibroids in pregnancy “red degeneration”; the frequency of pain is especially high in fibroids greater than 5 cm in diameter. The majority of patients with a degenerating fibroid have only localized pain, although mild leukocytosis, pyrexia, and nausea and vomiting can occur. The treatment is conservative.

Pelvic inflammatory disease: PID is rare during pregnancy, but the infection can still occur in the first 12 weeks of gestation before the mucous plug and decidua seal off the uterus from ascending bacteria.

Approach to pregnant patient with acute abdominal pain

Pregnant patient who presents with acute abdomen require prompt attention usually with multidisciplinary team. In some cases the diagnosis may be difficult to make on first presentation. Conservative management with close observation of general condition and vital signs of the mother and the fetus may be applied for a short period of approximately 24 hours.
At the end of this period if the symptoms are not resolved and or at any time the condition worsen, active intervention including laparoscopy or laparotomy should be considered. The golden role is that no patient should be left in acute abdominal pain without diagnosis for more than 24 hours. During this period she remains under close observation.

- A thorough history and physical examination is performed with the previous list of differential diagnosis in mind.
- Laboratory tests: are requested as necessary including complete blood count with differential, urinalysis, and tests of liver and pancreatic function (aminotransferases, alkaline phosphatase, bilirubin, amylase, lipase). In the presence of fever or unstable vital signs, blood and urine cultures should be performed.
- The gestational age should be verified and the fetal heart rate should be documented.
- Imaging studies: there is always concern about the possible fetal effects of ionizing radiation in pregnancy. This concern should not prevent medically indicated diagnostic procedures during pregnancy using the best available modality for the clinical situation. It should be realized that almost all diagnostic radiological procedures provide exposures that are below the threshold for congenital malformations, growth restriction, or developmental delay (Table 38-1).

- Surgical intervention and anesthesia: if operative procedures are indicated it should be undertaken without delay e.g. in the case of appendicitis. However as a general role non-urgent or elective non-obstetric surgery are best performed in the second trimester, except in case of the acute abdomen, since delay in intervention will lead to increased maternal and fetal morbidity.

Procedure	Fetal Exposure
Chest radiograph (2 views)	0.02 -0.07 mrd
Abdominal film (single view)	100 mrad
Intravenous pyelography	≥ 1 rad
Hip film (single view)	200 mrad
Mammography	7-2- mrad
Barium enema or small bowel series	2-4 rad
CT scan head or chest	< 1 rad
CT abdomen and lumber spine	3-5 rad
CT pelvimetry	250 mrad

Table 38-1: Estimated Fetal Exposure From Some Common Radiologic Procedures

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Chapter 39

Maternal and Perinatal Infection in pregnancy

Infections acquired in utero or during the birth process are significant causes of fetal and neonatal mortality and an important contributor to early and later childhood morbidity.

Infection in pregnancy may be due to viruses, bacteria, mycoplasmas, fungi, and protozoa. This diversity of causative agents is reflected in a diversity of mechanisms of transmission and pathogenesis.

By the end of this chapter you should be able to:
List the che common TORCH, Cytomegalovirus, Varicella virus, HIV and group B streptococcal infections.
For each type of infections you should be able to list:

- The causative agent, epidemiology and prevalence.
- Maternal infection
- Fetal / Neonatal infection.
- The extend of fetal and neonatal risks
- Diagnosis of maternal primary infection and the limitation of the tests available.
- Methods for prenatal diagnosis of fetal infection
- The importance of neonatal diagnosis
- The prevention and treatment strategy

Overview of infection in pregnancy:

It is possible to group the diseases of interest according to its most significant effect (maternal or fetal) and according to when during pregnancy the disease is likely to cause its greatest damage (Figure 39-1).

Some infections can be teratogenic, particularly if acquired in the first trimester. Other infections although not teratogenic, can be transmitted to the fetus and might have serious or even lethal consequences during infancy or childhood e.g. HIV. In addition there is also important group of

infections which are associated with serious complications to the pregnancy such as premature rupture of the membrane and premature labor e.g. group B streptococcal infection of the genital tract.

In their first antenatal visits women are often requested to have screening tests for the most known teratogenic group of infections, collectively have been described with the acronym TORCH. These include toxoplasmosis, *o*ther (such as syphilis), *r*ubella, *c*ytomegalovirus, and *h*erpes (TORCH).

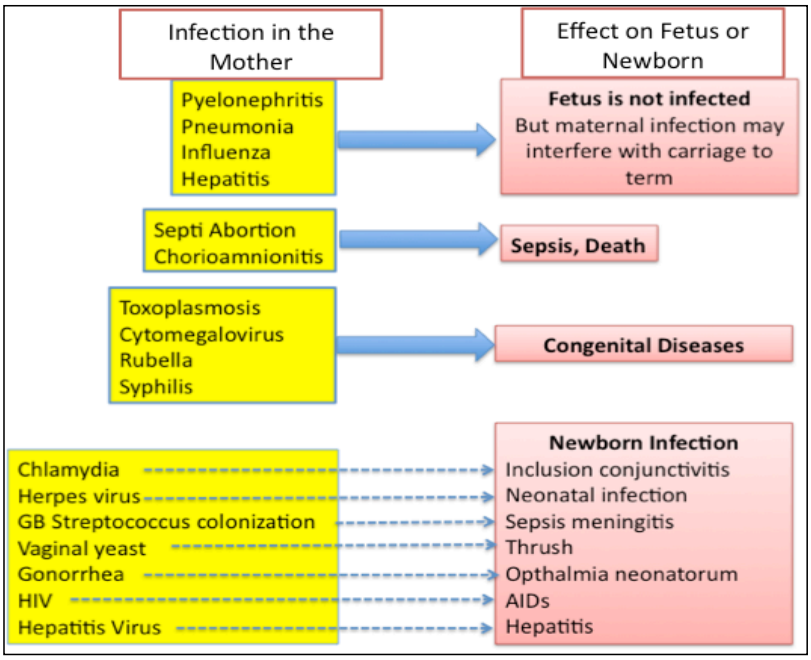

Figure 39-1: Diagram showing the examples of the effect infections on pregnancy, the fetus or the newborn.

Important questions that need to be answered in relations to infections in pregnancy are:

1) What is the prevalence of the infections among pregnant patients?

2) In those women who get the disease, how frequently does the

microorganism reach the fetus?

3) With what frequency does the microorganism seriously and permanently affect the fetus? And finally what preventive measures and/or treatment are available?

Women often go to their obstetricians for advice whenever there is history of exposure or a screening test for infection is positive.

Toxoplasmosis

➢ Prevalence and Epidemiology: Is a parasitic infection, the causative agent is *Toxoplasma gondii.* Based on serologic studies, approximately one third of women in the reproductive-age are seropositive (i.e. already immune), but there is wide geographical variation.
The incidence of maternal infection during pregnancy ranges from 1 to 8 per 1000 susceptible pregnancies, with the highest reported rates in France

➢ Maternal-Fetal Transmission of infection: fetal infection "Congenital toxoplasmosis" via transplacental transmission can occur in approximately one third of cases following primary infection (i.e. infection in a seronegative women). Chronic or latent maternal infection is unlikely to cause fetal injury.

The risk of vertical transmission increases with increasing gestational age at maternal infection.
Estimated to be about:
- 15 percent at 13 weeks
- 44 percent at 26 weeks
- 71 percent at 36 weeks

Although the rate of fetal infection is higher when maternal infection occurs in the third compared to the first trimester, the risks of intracranial lesions and serious neurodevelopmental sequelae decrease with increasing gestational age at maternal infection.

➢ The clinical manifestations of congenital toxoplasmosis: The sequelae of fetal infection include intracranial lesions (calcification or ventricular dilatation), serious neurological impairment (e.g. seizures in early infancy, cerebral palsy), and retinochoroiditis. Stillbirth and growth restriction are rare events. Intracranial lesions and neurological impairment are more likely to occur following early rather than late seroconversion.

Approximately less than half of affected infants who have congenital toxoplasmosis are asymptomatic at birth. They are at high risk of development of late sequlae such as chorioretinitis, intellectual disability (mental retardation), deafness, and seizures if they do not receive treatment.

- Diagnosis of Toxoplasmosis:

Clinically most infections are asymptomatic and the diagnosis depends on combination of tests since no one test alone has adequate sensitivity or specificity.

- Maternal diagnosis:

Serology: Assay for specific IgM and IgG antibodies are the most commonly used primarily screening tests. However the confirmation of primary infection is difficult as IgM antibodies alone does not indicate recent infection since in some women IgM remain positive for years. Therefore the following should be looked for to confirm the diagnosis:

- Diagnosis is made if a minimum of two blood samples at least two weeks apart show seroconversion from negative to positive toxoplasma-specific IgM or IgG.
- A combination of a positive IgM and negative IgG result, with both tests becoming positive two weeks later.

In all cases a reference laboratory should confirm serological diagnosis of acute infection.

- Prenatal / Fetal diagnosis: The objective of fetal diagnosis are: (1) to help decide on initiation of prenatal treatment (2) Some patients may consider termination of the pregnancy if legally appropriate (3) Exclusion of fetal infection by prenatal diagnosis can also prevent unnecessary postnatal treatment in children without clinical signs of toxoplasmosis and at low risk of congenital infection. The methods to be considered for prenatal diagnosis are:

  - Polymerase chain reaction (PCR) for T. gondii DNA in amniotic fluid is currently the method of choice for diagnosing fetal infection.
  - Ultrasound for signs of fetal affection but usually reflect late findings (e.g. ventriculomegaly, intracranial calcifications, microcephaly after 21 weeks).
  - Fetal blood sampling usually after 20 weeks for IgM specific

antibodies or PCR testing. This method is not used any more because of potential fetal risks.

- Neonatal diagnosis:

In high-risk cases the pediatrician should be informed in order to undertake the necessary work up for the diagnosis of congenital infection in newborns. This is necessary to decide on postnatal treatment.

➢ Prevention and treatment in pregnancy:

Pregnant women should be advised to avoid contact with cat litter if at all possible, not to eat rare cooked meat and most importantly to maintain clean habit of hand washing.

In cases of primary infection during pregnancy the mother should be counseled based on the known fact that on one hand there is uncertainty about treatment effectiveness, on the other hand the treatment itself has its own potential risk. In addition most infected babies have a good prognosis and, on average, do not differ in their development at three to four years from uninfected children. If she still opts for treatment the drugs of choice are Spiramycin (1 g orally every eight hours without food) or double agent therapy with Pyrimethamine and sulfadiazine.

Syphilis

Syphilis is a treatable **infection** caused by *Treponema pallidum,* a motile spirochete. **Infection** occurs in four stages: primary, secondary, latent, and tertiary (or late). It is rare to see pregnant women with tertiary or late syphilis.

➢ Maternal infection**:** is acquired by direct sexual contact with ulcerative lesions of the skin or mucous membranes of infected persons.

➢ Maternal-Fetal transmission: occurs through transplacental transmission of T. pallidum from infected mothers with primary or secondary syphilis. Fetal infection can occur at any time during gestation but typically occurs during the second half of pregnancy.

➢ Effect on the fetus**:** *Treponema pallidum* infection can manifest in the fetus, the newborn, or later in childhood. **Immediate effects include**

stillbirth (24%), neonatal death, and overt infection at birth with features such as hydrops fetalis.

However Two-thirds of live-born neonates with congenital syphilis are asymptomatic at birth. Clinical manifestations may appear early (≤2 years of age) or late (>2 years of age)

- Diagnosis:
  - Direct visualization of the spirochetes using dark field microscopy or direct fluorescent antibody tests: can be performed in patients with overt manifestations. It provides definitive diagnosis but is rarely available.
  - Serological tests: A nontreponemal test, e.g. **VDRL** (Venereal Disease Research Laboratory) or **RPR** (rapid plasma reagin), is used for screening. The tests provide quantitative results, which are helpful indicators of disease activity and are used to monitor response to treatment, but are non-specific. If the nontreponemal test is positive, confirmatory testing is performed with a specific treponemal test, such as the **microhemagglutination test** for T. pallidum (MHA-TP) and the **fluorescent treponemal antibody absorption** (FTA-ABS). These latter tests are not quantitative and, once positive, will remain so for life, even after successful treatment.
  - Neonatal diagnosis: Confirmation of neonatal diagnosis is important in order to initiate treatment at early stage. Therefore the obstetrician has duty to inform the neonatologist regarding all high-risk cases e.g. if the mother has a history of contact with an individual with primary or secondary syphilis within 90 days of delivery and/or did not receive treatment.

- Management: Penicillin is the only antibiotic currently recommended for syphilis treatment in pregnancy because of its safety, efficacy, and transplacental passage to treat the fetus. Penicillin-allergic women should undergo desensitization first or receive alternative therapy such as ceftrixone.

All women with syphilis should be carefully evaluated for other sexually transmitted diseases, in particular HIV.

Rubella

Diagnosis: Maternal Rubella infection can be subclinical, but it usually manifests 14 to 21 days after exposure with a maculopapular rash that begins on the face and spreads to the neck, trunk, arms, and legs; other signs and symptoms are lymphadenopathy, malaise, arthalgias, and petechiae.

Suspected **infection** should be documented by specific rubella IgG and IgM measurement or by viral culture of the mother.

➢ Maternal-Fetal Transmission: In the first trimester, fetal infection rates as high as 81 percent have been observed, dropping to 25 percent in the late second trimester and increasing again in the third trimester from 35 percent at 27 to 30 weeks to nearly 100 percent for fetuses exposed beyond 36 weeks. However, the risk of congenital defects after maternal infection is essentially limited to maternal infection in the first 16 weeks of pregnancy.

➢ The most common congenital anomalies include:

- Audiologic defects, predominantly sensorineural deafness (60 to 75 %)
- Ophthalmologic abnormalities (10 to 25 %) particularly cataracts and pigmentary and congenital glaucoma .
- Cardiac malformations (10 to 20 %)
- Neurologic sequelae (10 to 25 %) ranging from meningoencephalitis, to behavior disorders and mental retardation

Congenital Rubella Syndrome

The diagnosis of CRS is made in the presence of any of the recognized defects or laboratory data, i.e. isolation of rubella virus, demonstration of IgM antibody, or a persistently elevated rubella IgG titer that fails to drop twofold dilution per month

- Other features include: intrauterine growth restriction or microcephaly, radiolucent bone disease, hepatosplenomegaly, thrombocytopenia, and characteristic purpura, resulting in the "blueberry muffin" appearance.
- Late manifestation can also occur such as persistent neuromotor deficits.

pneumonitis, diabetes mellitus, thyroid abnormalities, and progressive panencephalitis.

➢ Diagnosis:

- A fourfold rise in IgG titer between acute (with the onset of rash) and convalescent serum specimens (two to three weeks later)
- The presence of rubella specific IgM
- A positive rubella culture e.g. the virus is generally isolated from the pharynx one week before to two weeks after the rash.

Prenatal Diagnosis: currently Rubella specific Polymerase chain reaction (PCR) on CVS samples (rather than amniotic fluid or fetal blood) is the preferred option.
Prevention and Treatment: Prevention program is provided by Vaccination for all children at one year of age using a monovalent rubella vaccine or at 15 months in conjunction with measles and mumps (MMR).
Also (MMR)vaccination should be offered as part of premarital counseling, and in the postpartum period for susceptible women. Since the vaccine is a live attenuated virus pregnancy should be avoided for 28 days following vaccination.
There is no in-utero treatment for CRS. Before 16 weeks patient should be offered the option of termination of pregnancy. Those who decline may receive treatment with immunoglobulin but no evidence that it alter the fetal course of the disease.

Herpes

Genital herpes is usually caused by "Herpes simplex type 2" and usually contracted by sexual contact. However currently 30% to 50% of genital herpes are caused by herpes simplex type 1, which most often causes oropharyngeal herpes.

➢ Maternal infection: There are three types of maternal infections:

- Primary infection: refers to infection in a patient without preexisting antibodies to either HSV-1 or HSV-2.
- Recurrent infection: refers to reactivation of genital lesions in a seropositive person.
- Non-primary genital infection: refers to genital HSV-2 lesions in a

patient with preexisting antibodies to HSV-1; or genital HSV-1 lesion in a patient with preexisting antibodies to HSV-2.

- Clinical Feature and diagnosis:
  - In primary infection the signs and symptoms are highly variable: include painful genital ulcers, dysuria, fever, tender local inguinal lymphadenopathy, and headache. In some cases the infection can be mild, subclinical, or entirely asymptomatic.
  - In non-primary and recurrent infection: the symptoms and signs (lesions) are milder, and often no symptoms at all.
- Diagnosis: Should be confirmed by one the following tests: (1) antibodies specific serology testing of IgG and IgM antibodies for HSV type I and II (2) viral culture: as obtained from active lesions. (3) PCR amplification of viral particle. The choice to testing depends on the clinical presentation.
- Maternal-Fetal transmission: Congenital fetal and neonatal infection can occur through one of two mechanisms:
  - The primarily mechanism is via direct contact with infected vaginal secretions during delivery.
  - Rarely fetal infection occurs via intrauterine transmission from transplacental or ascending infection. This mechanism explain the occurrence of early neonatal infection despite delivery by cesarean section before both labor and rupture of fetal membranes

Risk factors for fetal infection include: Acquisition of HSV infection near the time of labor, premature rupture of the membrane, use of scalp electrode for fetal monitoring.

- Congenital herpes lesions: The risk of congenital infection is 30% to 50% during a primary episode, but less than 1% during a recurrent infection. The spectrum of infection is variable from asymptomatic to fatal one.

- Treatment: Depends on the type of infection (Primary or recurrent) and the timing in relation to labor.

Congenital Herpes

Can be localized to skin, eyes, and the oral cavity, can involve the nervous system, can be disseminated and fatal, or can be entirely asymptomatic

- In primary infection antiviral treatment “acyclovir” (400 mg three times a day) should be offered regardless of the timing of occurrence during pregnancy.
- Patient with recurrent lesions should be offered suppressive antiviral treatment from 36 weeks until labor.
- Cesarean delivery should be offered as soon as possible to women who have active lesions or, in those with a history of genital herpes or prodromal symptoms at the time of delivery. The benefit of CS if the membranes have been ruptured for more than six hours, is less certain.

Cytomegalovirus (CMV)

➢ Epidemiology and prevalence: CMV infection is the most common congenital viral infection. It is estimated that about 1% of live births are infected with CMV. It is a leading cause of deafness and an important contributor to learning disabilities. Its prevalence among the general population ranges between 40% and 100 percent depending upon geography and socioeconomic status and age as most people acquire the virus infection as they grow in age. Approximately 30-50 % of women of the reproductive age group are seropositive.

➢ Maternal Infection: occurs through close contact with infected secretions including sexual contact, and through blood transfusion and organ transplantation.

In pregnancy infection with CMV may be primary (initial acquisition of virus during pregnancy) or recurrent (in women who are already seropositive), and both can result in congenital CMV. However Preexisting maternal CMV seropositivity is associated with less severe fetal disease, suggesting a protective role of maternal immunity.

The risk of seroconversion during pregnancy averages 2.0 to 2.5 percent. Risk factors for seroconversion during pregnancy include young maternal age, having young children at home or at work, poor hygiene, and lower socioeconomic.

➢ Maternal-Fetal Transmission:

Congenital infection is transmitted transplacentally, in addition perinatal transmission can also occur through ingestion or aspiration of cervicovaginal secretions at the time of delivery or ingestion of breast milk after delivery

Primary maternal infection results in 30% to 40% fetal transmission "congenital infection". Ten percent of infants with congenital infection will have clinical disease at birth. Of these, as many as 30% die, while 90% of survivors have sequelae such as deafness, mental retardation, chorioretinitis, and motor deficits. The other 90% of infants with congenital infection are asymptomatic at birth, but 5% to 17% develop long-term sequelae, most commonly deafness and learning disabilities.

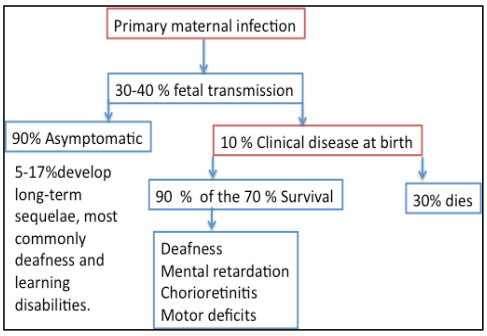

Figure 39-2: Counseling pregnant patient with following primary CMV infection

Secondary maternal infection (infection in immune women) can also result in congenital disease in about 0.2% to 1%. Also the congenital infection due to recurrent disease is far less severe, and less than 10% of affected infants have long-term sequelae.

➢ Diagnosis: Most patients are asymptomatic or have mild generalized symptoms such as fatigue, malaise, fever, lymphadenopathy, and pharyngitis. Suspected CMV infection should be documented by serology or cultures of the cervix, amniotic fluid, or maternal urine.

- Serology: is used to diagnose maternal infection and determining past exposure to CMV infection but has limitation in diagnosis of recent infection, because:
  - The detection of CMV-specific IgM antibodies, suggesting recent seroconversion is not certain because IgM from previous infection can be detected for up to one year.
  - Even rise in CMV-specific IgG titers (up to four folds) in paired specimens obtained at least two to four weeks apart also suggest recurrent or recent infection.

Prenatal diagnosis: Depends on multiple approaches which include:

- Ultrasonographic markers suggestive, but not diagnostic, of fetal CMV infection includes: Cerebral ventriculomegaly, Microcephaly, hyperechogenic fetal bowel, hepatosplenomegaly, ascites, intracranial calcifications, fetal growth restriction, and placental enlargement.

However, a normal ultrasound examination does not exclude the possibility of neonatal abnormality.

- Amniocentesis, and/or cordocentesis (fetal blood sampling): to confirm fetal infection using PCR technology for amplification of viral DNA and viral culture. Viral culture of neonatal urine can confirm the diagnosis after birth.

➢ Prevention and treatment: Routine screening of the pregnant population is not currently recommended because present laboratory methods are limited in the differentiation between primary and recurrent infection.
Preventive efforts are based on good hygiene, limiting intimate contact with infected children, and responsible sexual practices. *CMV vaccine is still under development*.

Human Immunodeficiency Virus

Human immunodeficiency virus (HIV) is a retrovirus transmitted through infected secretions, most often sexually, also blood and blood products transfusion.

➢ Fetal infection: The most serious consequence of HIV infection in pregnancy is fetal infection, resulting in the birth of a congenitally infected newborn. Maternal HIV is not teratogenic or associated with increased fetal loss (except for end-stage disease).
With out treatment the risk of fetal transmission is around 30%. The quantity of viral load (HIV-1 RNA) in the mother appears to be a significant risk factor for fetal infection.

➢ Management: The goals of management in pregnancy are:

(1) Identifying the disease
(2) Preventing perinatal transmission.

- Diagnosis of HIV: In some communities screening with an enzyme-linked immunosorbent assay (ELISA) for HIV is recommended and should be offered to all pregnant women. Women at risk (e.g. those with hemophilia, intravenous drug users, and female partners of infected men) should be screened more than once during the pregnancy. Suspected cases i.e. positive screen tests should be confirmed with more specific tests such as Western blot.

- Counseling of women with positive HIV test: such cases should best be counseled in a center familiar with HIV treatment and management. Counseling include education about the diseases and its potential consequences, the need for treatment during pregnancy, screening for other family members…etc.

- Prevention of perinatal transmission: All women who are HIV positive should be advised to take antiretroviral therapy "Zidovudine" during pregnancy and delivery to decrease perinatal transmission of the virus. Evidences have shown that Zidovudine administration in HIV-infected pregnant women from 14 to 34 weeks' gestation decreased perinatal transmission from 25.5% to 8.3%.

- Mode of delivery is controversial: many experts recommend cesarean section at 38 weeks for women with a viral load greater than 1000 copies per mL. If vaginal delivery is contemplated in women with lesser viral load, artificial rupture of membranes and placement of a scalp electrode onto the fetal head to monitor the fetal heart rate are contraindicated.

- Care of the newborn: breast-feeding is contraindicated in HIV-infected women. The newborn should be followed up and testes with specific tests for up to 6 months or one year.

Varicella (or chickenpox)

The causative agent is Varicella-zoster virus (VZV), is also the causative agent of herpes zoster (shingles). VZV is a member of the herpesvirus family along with herpes simplex types 1 and 2, cytomegalovirus. VZV is highly contagious virus transmitted by respiratory droplets or close contact. Primary varicella generally confers lifelong immunity, although there are reported cases of re-infection. VZV remains latent in the dorsal root ganglia and may be reactivated, often associated with impaired cell-mediated immunity.

It mainly occur in children, with only about 2 percent occurring in adults 20 years of age or older. In pregnancy the incidence of varicella is estimated to be 1 to 5 cases per 10,000 pregnancies.

- Diagnosis: Depends on the typical clinical lesions (erythematous macules, papules, and vesicles rashes). Serologic tests can help to document acute infection; Specific IgM and IgG antibodies can be detected as early as three and seven days respectively after varicella symptoms. PCR can identify VZV-specific DNA from vesicular fluid or throat swabs.

- Management: In adults the VZV infection carries high risk of development of varicella pneumonia, which is a significant risk among pregnant women.

Maternal infection:

- Prevention strategy includes ascertaining VZV status prior to pregnancy in women without a clinical history of infection and offering the live attenuated VZV vaccine (Varivax, Merck) to susceptible women. Pregnancy should be deferred for one month following vaccination.

- Management of pregnant woman with a negative history of VZV (non-immune) exposed to varicella: Within the first 72 hours (and up

to 96 h) from exposure VZIG (varicella virus immunoglobulin) should be administered (also if serology testing can not be obtained in time). In addition prophylactic acyclovir should also be administered (800 mg PO five times daily for 5 to 7 days starting within 9 days of exposure).

Varicella pneumonia in pregnancy is a medical emergency. The main risk for women is the development of pneumonia. The clinical course is unpredictable and may rapidly progress to hypoxia and respiratory failure. The mortality rate in untreated pregnant women is in excess of 40 percent.

- Maternal-Fetal transmission and the "congenital varicella syndrome:

The precise mechanism of in utero VZV infection is unknown. It is postulated that the fetus develops chickenpox in utero followed by resolution and subsequent infection of the dorsal root ganglia. This results in cell destruction of nerve tissue, which may account for the limb denervation changes seen in the congenital varicella syndrome. Thus the herpes zoster and zoster encephalitis can explain most of the fetal anomalies of the congenital varicella syndrome and the specific segmental nature of these anomalies.

- Risk of fetal infection: the overall risk of congenital varicella syndrome appears to be small (0.4 to 2 percent). The highest risk to the fetus occurs with maternal infection between 13 and 20 weeks' gestation. No congenital malformations have been observed when maternal infection occurs after 20 weeks.

Neonatal VZV: is serious complication with mortality rate of 20-30%. The newborn is most susceptible for infection if the mother develops varicella between 5 days before and 2 days after delivery. In this short period the women would not have produced enough IgG antibodies to protect her neonate. After birth varicella zoster immune globulin (VZIG) should be given to the newborn. The infant should also be isolated from the mother until all vesicles have crusted over to prevent transmission of VZV. If possible, delivery should be delayed until 5 to 7 days after the onset of maternal illness to potentially prevent neonatal VZV through allowing time for maternal IgG antibodies to reach the fetus, which can reduce the risk of neonatal VZV.

Group B Streptococcal Infection

Group B *Streptococcus* asymptomatically colonizes the vaginal or rectal areas of 10% to 30% of pregnant women. Group B streptococcal (GBS) infection has been associated with preterm labor, premature membrane rupture, urinary tract infections, chorioamnionitis, postpartum endometritis, postpartum wound infection, septic pelvic thrombophlebitis, endocarditis, and sepsis.

An intrapartum infection is strongly associated with 5-minute Apgar scores less than 6, neonatal seizures, and unexplained spastic cerebral palsy in infants of normal birth weight.

Up to 2% of maternal carriers deliver infants with invasive GBS disease, most of which is caused by in-utero infection. In population with high prevalence of GBS population screening for all pregnant women is recommended by vaginal-rectal culture at 35 to 37 weeks' gestation.

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Chapter 40

Vital Statistics in Obstetrics

Dr Sameera Al Basri

An alarming report of the World Health Organization has revealed that more than half a million maternal deaths worldwide, which is almost about 1500 women/day die from pregnancy or childbirth-related complications (WHO report 2005). Most of these deaths occurred in developing countries, and most are avoidable deaths. The report also reveals that every year 3 million babies are stillborn. Almost one quarter of those die during birth because of causes similar to the causes of maternal deaths.

Unfortunately international efforts to combat those calamities have achieved rather limited success. In many of the developing countries the high maternal mortality rate is due to limited resources. However another important factor is lack of vital statistics of births, true causes of infant and maternal mortality hinders proper planning of health care and distribution of resources.

By the end of this chapter you should be able to:

- **Describe** the importance of "Vital Statistics" at hospital and national level.
- **Define and explain each of the following terms:**
- **Maternal Statistics**
  - Maternal death Rate
  - Late maternal death
  - Non-Maternal death

Describe and differentiate between "Direct" and "Indirect" obstetrics causes of maternal death.

Define and differentiate between: **Maternal mortality ratio vs. rate**

Define Reproductive mortality rate

List causes of death among women of reproductive age (15-44 years of age):

Define the following "Infant statistics":

- Live birth
- Stillbirth and common causes.
- Fetal death rate (stillbirth rate)
- Neonatal mortality rate
- Perinatal mortality rate
- Infant mortality rate (IMR)

⇨Why Vital Statistics are vital:

Advances in public health depend on effective interventions at a populations level, and proper utilization of available resources. This requires the development of appropriate tools for measuring birth rate, maternal and infant death rate and causes "i.e. vital statistics". The benefits of maintaining accurate statistics that is vital for planning health care intervention can be summarized in the following:

1. To identify priority areas of deficiency that requires intervention.
2. To enable monitoring and evaluation of the intervention results.
3. Allow comparison between different institutes at national and international level.

⇨Important definitions used in vital statistics:

Birth rate

The birth rate is the number of livebirths per 1000 population per year.

The birth rate is a gross measure of a population's growth rate. Less-developed areas tend to have very high birth rates. However, the "birth rate" should be interpreted together with the infant and childhood mortality rate.

Fertility rate

The fertility rate is the number of live births per 1000 women aged 15-44 years. It is a gross measure of the rate at which women of reproductive age are successfully reproducing. Of note, in this definition live births are specified, it does not include miscarriages although a woman who conceives and miscarries is considered as fertile.

Maternal Statistics

Maternal death: is the death of a woman while pregnant or within 42 days of termination of pregnancy from any cause related to or aggravated by the pregnancy or its management, irrespective of the duration of the pregnancy or its site, but excluding accidental or incidental causes of death.

Maternal Mortality Rate:
The maternal mortality rate is defined as the number of maternal deaths in a given period per 100,000 women of reproductive age (15 to 49 years of age) during the same time period. Since the frequency of pregnancy in women of childbearing age is a factor in calculating this rate, it is altered by differences in the frequency of pregnancy or birth in the population even though the risk of maternal death per pregnancy/birth remains unchanged.

Maternal mortality ratio: The maternal mortality ratio refers to the number of maternal deaths during a given time period per 100,000 live births.
The denominator is live births rather than all pregnancies because of the difficulty in ascertaining the number of miscarriages and abortions in the population.
This is the most commonly used measure of maternal mortality since unlike the mortality rate the ratio serves as an indicator of the risk of death once a woman has become pregnant.

$$\frac{\text{Number of maternal Deaths} \times 100,0000}{\text{Number of life Births}}$$

Late

maternal death: The death of a woman from direct or indirect obstetrical causes more than 42 days, but less than one year, after termination of pregnancy.

Categories of maternal death:
For purpose of optimum planning of population's health needs three categories of maternal death rates have been distinguished. In all of them the denominator is 100,000 live births.

Direct and indirect obstetric death
- **A direct obstetric or maternal death: refers to** maternal death from complications of pregnancy, delivery, or the puerperium; e.g. death from complications such as preeclampsia, hemorrhage, and chorioamnionitis

➢ **Indirect obstetric or maternal death:** refers to death from underlying medical conditions aggravated by but not caused by the pregnancy. E.g. complications from connective-tissue disease or cardiac conditions.

While the majority of direct maternal deaths can be preventable, indirect maternal deaths are more difficult to prevent. This is because they may simply reflect the natural course of the underlying disorder. In some cases, a woman may voluntarily choose to conceive despite the known risks.

➢ **Non-maternal death rate:** refers to deaths of pregnant or postpartum women that were neither caused by nor aggravated by the pregnancy (e.g. motor vehicle accidents, homicides).

Lifetime risk of maternal death: The lifetime risk of maternal death takes into account the cumulative probability of dying as a result of pregnancy across a woman's reproductive years. It is calculated by multiplying the maternal mortality rate by the length of the reproductive period (approximately 35 years).

Reproductive mortality rate: Refers to deaths resulting from contraceptive use (trying not to get pregnant) plus direct maternal deaths (deaths from getting pregnant) per 100,000 women.

Function: It measure of a population's ability to provide safety for its most vulnerable and valuable segment.

⇨ **Causes of maternal mortality:**

The overall causes of maternal mortality have been attributed to "Delay" which can take place at several points in both direct and some of the indirect causes of mortality:

- Delay in the decision to seek care (eg, unrecognized life-threatening illness, women needing to seek permission from family members before obtaining care)
- Delay in arrival to an appropriate medical facility (e.g. poor or no transportation, long distance from care facility)

- Delay in receiving adequate care once a woman arrives to medical facility (e.g. unrecognized or under-treated life-threatening condition, inadequate facilities for severity of disease)

⇨Causes of death among women of reproductive age (15-44 years of age):

At worldwide level the leading cause of death for women age 15 to 44 is "pregnancy-related disorders," which account for approximately 15 percent of deaths in this age group.

The frequencies of some other major causes of death in this age group are tuberculosis (10 percent), suicide (7 percent), war (4 percent), traffic accidents (3.7 percent), HIV (3.4 percent), and stroke (2.7 percent). Globally, breast cancer is the leading cause of female cancer deaths, followed by stomach, lung, and cervical cancer. Cervical cancer is the leading cause of gynecologic-related cancer deaths in developing countries.

⇨Maternal Mortality at Global level "Why do mother die?"

Women die from a wide range of complications that is directly related to pregnancy, childbirth or the postpartum period. In some cases the death is due to preexisting illnesses that is aggravated by the pregnancy e.g. preexisting cardiac or chronic renal diseases.

The distribution of causes maternal mortality and its frequency varies between different countries and even within the same country depending on existing health care facilities and contribution of the three "Delays" model. Figure 40-1 shows the distribution of causes of maternal mortality at global level which account to about 80% maternal deaths.

The four major killers are:

1. Severe bleeding (mostly bleeding postpartum)
2. Infections (also mostly postpartum infection)
3. Hypertensive disorders in pregnancy (eclampsia)
4. Obstructed labor.

Complications after unsafe abortion contribute to 13% of maternal deaths. Among the indirect causes (20%) of maternal death are diseases that complicate pregnancy or are aggravated by pregnancy, such as malaria,

anemia and HIV.

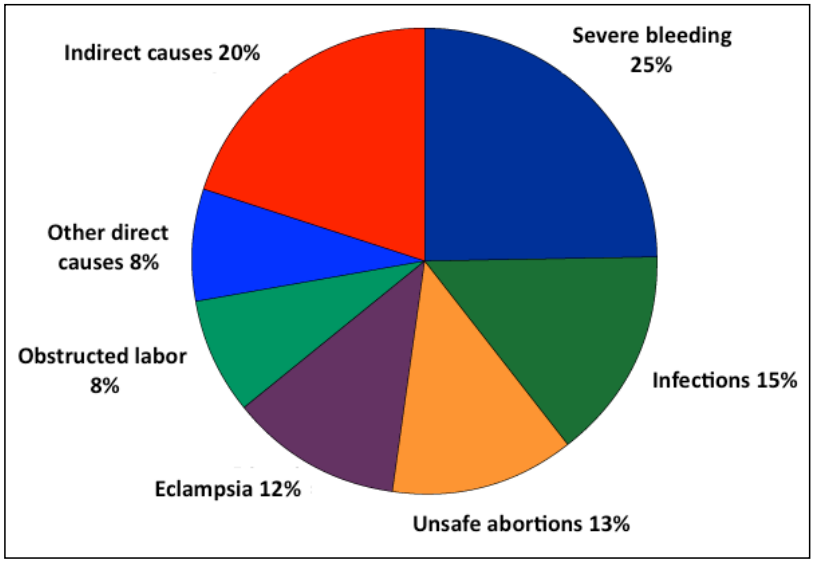

Figure 40-1:The World Health Report 2005: Global Distribution of the main causes of maternal mortality

Infant Statistics

Study of the mortality rates in the perinatal period is one of the very important parameter that is used to evaluate the outcome of pregnancy and monitor the quality of perinatal (prenatal and neonatal) care.

The perinatal mortality rate encompasses late fetal and early neonatal mortality. When comparing figures between different institutes or countries it is important to confirm consistency in definitions and the criteria used for

inclusion.

Live birth

Delivery after 20 weeks' estimated gestational age "EGA" in which any activity is noted is classified as a live birth. This is a difficult definition, as the lower limit of reasonable viability currently remains around 23 weeks' EGA. However a spontaneous delivery at 21 weeks' EGA with reflex motion but no ability to survive with or without intervention would still be considered a live birth.

Stillbirth

Delivery after 20 weeks' "EGA" (or > 500 g birth weight) in which the infant displays no sign of life (gasping, muscular activity, cardiac activity) is considered a stillbirth.

⇨**Causes of fetal death (stillbirth):** Approximately one-third of fetal deaths are unexplained. In the remaining two-thirds fetal death could be attributed to one of the following main categories of causes:

- Fetal causes (e.g. structural defects, syndromes, and aberrant growth)
- Placental causes (e.g. abruption, large chorioangiomas, hypertensive disorders of pregnancy)
- Maternal causes (e.g. acute chorioamnionitis, diabetes mellitus, rheumatologic disorders)

Fetal death rate (stillbirth rate)

The fetal death rate is the number of fetal deaths ≥20 weeks gestation that occur during a year divided by the sum of live births plus fetal deaths during the same year (total number of birth), and expressed per 1000 live births plus fetal deaths.

Neonatal mortality rate

The neonatal mortality rate reflects losses between the moment of birth and 28 days of life (inclusive). The denominator is 1000 live births, a slightly different number than the fetal death rate (which is per 1000 births). This

rate is often divided into early (first 7 d) and late (8-28 d) rates, as etiologies within these 2 categories vary somewhat. Early neonatal death is more likely to have obstetrically related cause.

The causes of neonatal death vary widely among different population. However of the leading causes are: prematurity, infection and congenital malformation.

Perinatal mortality rate

Perinatal mortality rate (PMR) is the sum of late fetal deaths (stillbirth) plus early neonatal deaths (i.e. deaths within the first seven days of birth) during a year divided by the sum of live births plus late fetal deaths (stillbirths) during the same year, expressed per 1000 live births plus late fetal deaths.

Infant mortality rate (IMR): The infant mortality rate (IMR) is the number of infant deaths under one year of age (O to 365 days of life) during a year, divided by the number of live births reported during the same year, expressed per 1000 live births.

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Chapter 41

Ethical and Legal Issues in Obstetrics and Gynecology

Dr Sameera Al Basri

Ethical and legal issues are increasingly influencing medical practice at worldwide level. In this respect of all medical branches, obstetrics ranks at the top of the list in being associated with ethical dilemmas and potential conflicts of interest. This is perhaps inherent in the nature of obstetrics practice where the majority of patients are healthy young adults, almost always anticipating healthy outcome. In addition the "fetal rights" became a recognized issue since technological development have made enabled the fetus to be an independent entity that can be identified, examined and accessed from early stages in pregnancy. In turn the public expectation for the "perfect baby" has put more demands and responsibility on medical care providers.

By the end of this chapter you should understand:

Genetic Counseling, Screening and Prenatal Diagnosis.

Ethical and legal issues in prenatal diagnosis and termination of pregnancy – The Islamic views:

Maternal Fetal conflict:

– Responsibility of the Obstetrician

Fetuses Near The Edge "Threshold" Of Viability:

– Ethical issues related to viability

– Definition of viability

Ethical Issue in Assisted Reproductive Technology – The Islamic principles:

Miscellaneous Ethical and Legal Issues:

In the practice of obstetrics it is not uncommon for the physician to find him/her self in conflict with the basic ethical principles of autonomy, beneficence or non-maleficence. Furthermore the limits and definition of those principles are inevitably influenced by local social, ethical and religious concepts. In conservative Islamic communities the religious beliefs have the upper hand in defining the limits of ethical practice in medicine. Hence the subtle but significant difference that should be observed by health

cares providers practicing in Islamic community.

Genetic Counseling, Screening and Prenatal Diagnosis

Prenatal diagnosis has become an established element in prenatal care. This fact has put legal and ethical responsibilities on obstetrician. Currently in most developed countries women have the right to be informed about their potential risks of having a disabled child and the available measures for screening and or diagnosis. Failure to inform the patient of her due rights mounts to incompetence and / or negligence on part of the physician that bring legal action against the doctor.

In developing countries including Saudi Arabia the matter falls within the realm of ethical problem and not yet a legal issue. This however may well change in the near future.

There are however important and sometimes difficult ethical issues that in relation to genetic counseling and prenatal diagnosis. In term of ethical matters and responsibilities these include:

- The physician does not guarantee a healthy child, but he or she has the duty to offer the patient reasonable expectation of possibilities and degree of disability that the child might have.
- The physician should give physicians should give accurate information to parents and forbids withholding material information from them.
- Furthermore the patient should be informed of alternative ways to proceed for prenatal diagnosis and or action if the results of a screening or diagnostic test isresults of a screening or diagnostic test are positive.
- Some physicians may have personal reservation or conflict with issue related to genetic counseling or prenatal diagnosis. However they should not impose their views on the patient. Furthermore they are obligated to alert prospective parents that a potential genetic problem does exist, that the physician does not offer genetic services, and that the patient should seek medical genetic counseling from another qualified specialist.
- To ensure the patient's interest in both autonomy and privacy: This mean

that no information obtained in genetic counseling or screening should be disclosed to any third party (e.g. including insurers and employers) without the patient's informed consent (unless there is specific legal indication that would justify breaching confidentiality).

However in certain situation for example if there is a risk on other patient's family or relatives (e.g. the discovery of recessive inherited infantile polycystic kidney disease) the physician should attempt to persuade patients to make disclosures of important information to potentially affected relatives.

- The limitations of screening tests, especially the fact that negative results cannot guarantee a healthy infant; the possible need for additional, invasive tests such as chorionic villus sampling or amniocentesis, to establish a definitive diagnosis; the reproductive options that might have to be considered, such as prenatal diagnosis, abortion, or acceptance of risks all should be discussed with the patient at length.
- If carrier status is detected in the woman, it must be emphasized that the husband should also be screened.

Ethical and legal issues in prenatal diagnosis and termination of pregnancy – The Islamic views:

Prenatal diagnosis:

Islamic legislation encourages all scientific activities that aim to initiate, maintain and achieve healthy life and livening. Appropriate utilization of the technology of prenatal diagnosis does not violate this Islamic principle; hence the Islamic *Shari'ah (Islamic ruling)* approves it. There is no doubt however that those methods which enable early rather than late diagnosis are preferred in case a decision for abortion has to be made.

In this context pre-implantation diagnosis would be the ideal technique since it eliminates the issue of abortion altogether.

Termination of pregnancy:

However the issue of termination of pregnancy has always been a hot topic that raises different views ranges between those who sees that no indication

justify abortion and those who will allow it “on demands” with or without restriction by weeks of gestation.

The Islamic approach to the issue of abortion is very balanced and based on rather clear principles

- **The first principle is the Sanctity of Life**

"***On that account we decreed upon the Children of Israel that whosoever kills a soul for other than manslaughter or corruption in the land, it shall be as if he killed all mankind, and whosoever saves the life of one, it shall be as if he saved the life of all mankind***". (5:32)

Based on this and several other verses and Prophet saying in Islam the human life is sacred, and should not be taken away except upon indications singled out and specified by the law (none of these ever falls within the domain of the medical profession). Human life is a value, and its sanctity covers all its stages including the intrauterine phase.

- The principle of the lesser of the two evils known in Islamic legal terminology as the principle of *Agl Al Darareen* (Bearing the least of two harms): based on this principle, *Shari'ah* allows abortion only when doctors declare with reasonable certainty that the continuation of pregnancy will endanger the woman's life. The reason for this is that the mother is the origin of the fetus; moreover, her life is well established with duties and responsibilities, and she is also a pillar of the family. It would not be possible to sacrifice her life for the life of a fetus which has not yet acquired personality and which has no responsibilities or obligations to fulfill.

- Prenatal diagnosis and the malformed fetus: Modern technology (like ultra sound scan and genetic testing) has made it possible to know whether or not a child has a defect long before he/she is born. In this respect there has been some diverse views but the one that is mostly accepted by the majority of Muslim jurists have agreed unanimously that after the fetus is completely formed and has been given a soul, abortion is forbidden “*Haram”*. It is also a crime, the commission of which is prohibited to the Muslim because it constitutes an offense against a complete, living human being.

- The time of insoulment (when the sole enter the body) thus transforming it from a living tissue “e.g. plant life” to a “human life”, has been debated. However currently and based on the statement from the Prophet (s) that

refers to a human being starting as a fertilized ovum in the uterus of the mother for forty days, then it grows into a clot for the same period, then into a morsel of flesh for the same period, then an angel is sent to that fetus to blow the *Ruh* "soul" … etc. it is believed that the soul enter the body by 120 days from the day of fertilization (this equal roughly 134 days from the first day of the last menstrual period.
This however does not mean that before that date the embryo is not to be respected. Indeed once conception occurs it means a potential life being created.

Based on those principles the Islamic League in Makka Al Mokarama and Islamic jurisprudence council in 1990 has issued regulation in relation to abortion which summaries the majority of Muslim jurists views (see attached declaration). It is based on the principle that termination of pregnancy in Islam is forbidden. The only situations when it may be allowed are:

- If it is reliably shown that the continuation of the pregnancy would necessarily result in the death of the mother or serious harm to her health.
- Termination of pregnancy may be undertaken before 120 days from the day of conception provided that trusted specialists have confirmed that the fetus has serious anomaly that is not amenable to treatment and is either incompatible with life or associated with severe ill and unhealthy living.
- Muslim jurists have agreed unanimously that after the fetus is completely formed and has been given a soul (>120 days from the date of conception), abortion is *Haram* except for saving mother's life.

القـرار الرابــع

بشـأن موضــوع إسقـاط الجـنين المشـوه خـلقياً.

الحـمـد لله وحـده، والصـلاة والسـلام على من لانبي بعـده، سيـدنا ونبـينا محمد وعلى آله وصحبه وسلم.

أما بعد:

فإن مـجلس المجمع الفـقـهي الإسـلامي، برابطة العـالم الإسـلامي، في دورته الثـانيـة عـشـرة، المنعـقـدة بمكة المكرمة، في الفـتـرة من يوم السبت ١٥ رجب ١٤١٠هـ الموافق ١٠ فبراير ١٩٩٠م إلى يوم السبت ٢٢ رجب ١٤١٠هـ الموافق ١٧ فبراير ١٩٩٠م قد نظر في هذا الموضوع، وبعد مناقشته من قبل هيئة المجلس الموقرة، ومن قبل أصحاب السعادة الأطباء المختصين، الذين حضروا لهذا الغرض، قرر بالأكثرية مايلي:

– إذا كـان الحـمل قـد بلغ مـائة وعـشـرين يومـاً، لايجوز إسـقـاطه، ولو كـان التشخيص الطبي يفيد أنه مشوه الخلقة: إلا إذا ثبت بتقرير لجنة طبية، من الأطباء الثقات المختصين، أن بقاء الحمل، فيه خطر مؤكد على حياة الأم، فعندئذ يجوز إسقاطه، سواء كان مشوهاً أم لا، دفعاً لأعظم الضررين.

– قبل مرور مائة وعشرين يوماً على الحمل، إذا ثبت وتأكد بتقرير لجنة طبية من الأطباء المختصين الثقات– وبناء على الفـحـوص الفنية، بالأجـهـزة والوسـائل المختبرية –أن الجنين مشوه تشويهاً خطيراً، غير قابل للعلاج، وأنه إذا بقي وولد في مـوعـده ، ستكون حيـاته سيـئـة ، وآلامـاً عليـه وعلى أهله، فـعندئذ يجـوز إســقــاطه بناء على طلب الوالدين، والمجلس إذ يقــرر ذلك: يوصي الأطبــاء والوالدين، بتقوى الله، والتثبت في هذا الأمر.

والله ولي التوفيق....

Maternal Fetal conflict

Maternal fetal conflict occurs when the pregnant woman's interests, as she defines them, conflict with the interests of the fetus, as defined by the woman's physician.

This is uncommon situation because normally a mother will do whatever it takes to save the life and wellbeing of her unborn child.
In rare situation the mother may refuse a therapeutic advice which is believed to be for the interest of the fetus wellbeing the typical example for such behavior is refusal for cesarean section for fetal and/or maternal life saving indications e.g. refusal of delivery by CS for non-reassuring CTG, or a major placenta previa or scarred uterus at significant risk of rupture. In some cases with some refusal of blood transfusion that is deemed to be life saving may be an issue.

This can create a difficult situation, since forcing operative and or medical intervention in such cases will not only break the trust relationship between the physician and his/her patient but also undermines the fundamental principle of autonomy and informed consent that every adult sane person should enjoy. On the other hand the obstetrician has responsibility towards the fetus and his duty the society.

According to Islamic regulation the fetus has a full respected identity once it is conceived (see section on abortion). In normal cases the mother is the first one to guard the right of her unborn child. No one, even his/her parents have the right to hurt the fetus either intentionally (by abortion) or non-intentionally by perhaps preventing or refusing therapeutic intervention. Hence if a CS is deemed to be necessary for life saving matter neither the patient nor her husband has the right to refuse intervention (Patient autonomy is not absolute). In such cases the duties of the obstetrician include several issues:

- He or she has important duty as educator and counselor, weighing the risks and benefits to the patient and making sure she understand the issues involved and addresses all her questions.
- Consultation with others includes colleagues realizing that tests, judgments, and decisions are fallible should be strongly considered.
- Consultation with an institutional ethics committee
- The use of authorities or legal power to resolve such a conflicts should almost never become necessary except after exhausting all other measures.

However by doing so the physician will balance the principle of fetal beneficence over that of the mother autonomy.

Fetuses Nearnear The Edge "Threshold" Of Viability

Fetal viability is defined as "the point in time in fetal development at which the fetus becomes potentially able to live outside the mother's uterus even though that it require artificial aid"

Defining an exact age for fetal viability has both legal and ethical implications. In the past newborn infants of less than 28 completed weeks' gestation (birth weight approx. <1000g.) rarely survived and were termed 'previable'. With the development of neonatal intensive care, the age of survival continued to decrease. Now survival has become possible after a gestation as short as 22 weeks. This led the World Health Organization "WHO" in 1993 to define the perinatal period as commencing at 22 completed weeks of gestation (154 days; birth weight approx. 500g.) Infants born 22 - < 28 weeks gestation (approx. equivalent to 500-1000g.) have been termed as having "threshold viability".

However there is strong negative association between gestational age and the chance of survival and/or disability (Table 41-1).

Summary Of Outcomes Among Extremely Preterm Children				
Outcome	22 weeks	23 weeks	24 weeks	25 weeks
	Number (Percent)			
Died in delivery room	116 (84)	110(46)	84(22)	67(16)
Admitted for intensive care	22 (16)	131(54)	298(78)	457(84)
Died in Neonatal intensive care	20 (14)	105(44)	198(52)	171(40)
Survived to discharge	2 (1)	26(11)	100 (26)	186(44)
Death post discharge	0	1(0.4)	2(0.5)	3(0.7)
Lost to follow up	0	3(1)	25(7)	39(9)
At 6 years of age				
Survived with severe disability	1 (0.7)	5(2)	21(5)	26(6)
Survived with moderate disability	0	9(4)	16(4)	32
Survived with mild disability	1(0.7)	5(2)		
Survived with no impairment	0	3(1)		

Table 41-1: Data from the EPICure study: www.epicurestudy.com

Therefore dealing with patients presenting with threatened delivery at the "threshold age of fetal viability" can creates serious ethical dilemmas in respect to appropriate management both before and after delivery which include:

- Whether elective delivery for fetal indication is appropriate. Taking in consideration the potential risks of exposing the mother to cesarean section. The risks in such cases are not only the operation itself but also the long-term risks on the mother reproductive function because a cesarean section at this early age in gestation involves hysterotomy incision of the upper uterine segment (the lower uterine segment is not well developed yet). At the same time the chance of intact neonatal survival may be very limited depending on the gestational age.
- Whether intensive care should be provided following delivery, as opposed to comfort care (i.e. warmth, offer of oral nourishment and

human contact). Again neonatal morbidity, mortality, and cost…etc should all be considered.

The responsibility of obstetrician in management of pregnancies at the threshold of viability:

The perinatal management of the threshold-viability fetus and infant is a multi-disciplinary matter requiring close collaboration between obstetricians, pediatricians, midwives, nursing staff and other supporting professionals. There is no single one answer to the correct management of all cases. The management will varies depending on the gestational age, parentsparent's expectation, facilities available, chances of in-utero transfer to tertiary centers with better facilities are important factors that influence management in individual cases. The following guidelines are important in the course of management:

- The obstetrician and neonatologist should be aware of the up-to-date statistics on infant mortality and morbidity outcome according to gestational age at both the national level and the local level within their own hospital. This should include the incidence and severity of disability amongst survivors at the age of 2 years or more.
- The parents should be counseled honestly and accurately as regards the realistic chances of neonatal survival, short and long term outcome. The discussion should include the place of delivery and whether or not in utero transfer should be considered.
- The parents and or the care givers may want to do every thing possible but their should be realistic appreciation of the difference between "doing every thing that can be done" and doing "what is reasonably possible in term of survival on the short and long term". There is a need to balance maternal well being against the likely neonatal outcome. Caesarean section in the baby's interest can rarely be justified prior to 25 weeks' gestation because of the poor prognosis for the baby and the risks for the mother. If parents insist then a second senior obstetric opinion is advisable.
- Fetal heart monitoring in labor may be important in the perinatal management, but on such occasions when the fetus is at the threshold of viability and may not survive, monitoring should be only undertaken after sensitive explanation to the mother. It should be silent and unobtrusive. Intermittent auscultation provides an alternative method.

- The doctor counseling parents on such condition should be senior and experienced. He or she may wish to consult colleagues or, in exceptional circumstances, an ethics committee.
- The doctor counseling parents should be careful not to impose his or her own cultural and religious convictions. When a doctor's beliefs prevents the disclosure of all possible management options open to the parents, the doctor has a duty to refer them to a colleague who is able to do so.
- Islamic principle dictate that every effort should be made to save a life, but at the same time balancing priorities and the least of two harms are important principle in decision making.

Ethical Issue in Assisted Reproductive Technology

Assisted reproduction refers to procedures that aim to enhance fertilization by artificial or partially artificial means. The two most common procedures included under this heading are intrauterine insemination and in-vitro fertilization.

There are whole ranges of legal and ethical issues related to such procedures that specialist in infertility has to be aware of it. The examples include: sperm or egg donation, the use of surrogate mothers, embryo cryopreservation and the disposing of unused embryos.

As technological development is taking place further ethical matters continuously come up, for example genetic screening, pre-implantation diagnosis, embryo selection, cloning and embryonic stem cell research and therapy. Such developments have important clinical applications but also carry potentially important ethical and legal issues.

The legal regulations and ethical stands toward many of those procedures vary among different countries from complete permission to total prohibition.

In Islamic countries that derive its ethical principles from *Shari'ah (Islamic low)*, infertility is considered a disease and the desire for a cure by an infertile couple is natural and acceptable. However the following ethical and legal regulations have to be followed:

- In Islam, all forms of assisted reproductive technology (ART) are permissible between husband and wife during the span of marriage using the husband's sperm and the wife's ovaries and uterus.
- No third party involvement is allowed e.g. donation of sperm, ova and embryo.
- The death of one of the spouse terminates the marriage contract on earth, thus frozen sperm from husband cannot be used.
- Any form of surrogacy that involving a third person is not permissible e.g. surrogate uterus.
- Additional embryos produced by IVF between husband and wife can be discarded or given for genetic research byafter his their own permission.
- Currently in Saudi Arabia pre-implantation genetic diagnosis is allowed for genetic disease but not for sex selection.

There are other legal and ethical issues related to the subject of assisted reproduction such as; clinic record keeping, informed consent, reporting, and statistical methods that should be observed by specialists in this field.

Miscellaneous Ethical and Legal Issues

The following section is a brief review of important issues, which are among the common ones that can create ethical and / or legal claims in any medical specialty. In obstetrics and gynecology, however, it has special importance because of the unique relationship between the physician and his/her patient that often involve sensitive and personal matters.

- **Abandonment:** Abandonment refers to unilateral dismissal of the patient by the physician without informing her and/or setting up proper arrangement plan. There are many examples for abandonment such as;
  - Failure to keep a promise (e.g. of being present for a delivery, or treating with a particular modality)
  - Failure to give proper discharge instructions.
  - Delegating your authority to another individual without prior arrangement.

- **Coverage Arrangements:** Improper coverage arrangements may lead to charges of abandonment. Not uncommon a physician is being faced with cases that he/she had not previously been informed about her. Serious

ethical and legal problems may arise not only from charge of abandonment as mentioned earlier but also from poor communication among coverage groups which frequently leads to offended patients and can be the first step on the path to a malpractice suite.

- **Informed Consent:** Informed consent has little to do with a "form". Informed consent has to do with the physician's professional duty to his or her patient. The fact is that after adequate explanation the patient chose the treatment method that she thinks the best for her and the physician is the one to consent to undertake her chosen approach. Which indicate that in reality it is an "informed choice" rather than "consent".

It is the physician's duty to give the patient all the information needed for the patient to make an intelligent decision about the therapies suggested. The information given must be:

- Accurate for published studies and compared with the physician's own figures.
- Presented in language the patient in question can understand in view of her education, intelligence, experience, and social standing.
- The information should include the diagnosis; a description of the suggested treatment; an explanation of what the treatment is thought to accomplish; the hoped for prognosis with the treatment; the possible side effects and possible adverse happenings with treatment.
- The therapeutic alternatives, their benefits, and possible adverse and side effects; and the patient's prognosis with the alternative and including no therapy.

- **Laboratory Tests:** One of the most common reasons for malpractice suits is the unreported abnormal laboratory or X-ray finding. E.g. failure to communicate the results of an abnormal pap smear, glucose tolerance test, or mammogram to a patient can have disastrous legal consequences.

- **Medical High-Risk Patients:** High-risk cases e.g. elderly, frail women with or without serious concomitant conditions should be recognized at early stage and given the necessary care. In this respect it is the treating consulting duty to make sure that all participating members of the treating team are aware of the risk factors and the extra care that the patient need.

- **Medical Records:** As it is appropriately stated more by Wag in 1930 "Medical records are the malpractice witness that never dies!", . Ttoday this statement still true. All records should be written or dictated contemporaneously with the event described. All writing should be objective as possible, clear without confusion or ambivalence, dated, timed, signed legibly, and kept in chronological order. Abbreviations should not be used.

- **Prescriptions:** Adverse drug events are among the most common medical errors. It is estimated that more than two thirds of all adverse drug events are caused by physician error. Physicians are not expected to memories all forms of medications. They should always refers to reliable resources for dosage, interaction…etc. and ensure that patients have clearly understood the instructions for the prescribed drugs.

- **When Things Are Not Going as Expected:** it is inevitable that errors occur or patient's illness may not follow the anticipated medical course. In such cases it is the duty of the treating consultant to recognize such issues as early as possible, confront patient, consult with colleagues or with hospital ethical committee as necessary.

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