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A MONOGRAPH

PLACENTA

Examination and Pathology

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PREFACE

Please do read these lines:
Placenta is generally considered to be a **"Throw away after birth"** which actually is a complete organ. It is infact a unique amazing organ that grows with the foetus from the very first cell division. Placenta has a great historic reputation: it holds the position of being a second child who has its own spirit that resides in the umbilical cord (The Baganda of Uganda believe it); during the Cleopatra and the previous civilisations; it was practiced by Egyptians that when placenta is of royal blood, it is ritually preserved and even carried in a procession by a high ranking officer. Perhaps we should honor the place of honor throughout the history that placenta held. We should also recognise the wisdom of the ancients and see that placenta is more than just some messy after birth to be discarded and ignored in the excitement and joy over the birth of a beautiful new baby. Here we are one step ahead, we do not only ignore the placenta, but it goes into the bucket in the labour room then perhaps to an incinerator or disposed off in garbage bin.

It may be reminded that placenta is a complete organ which is very firmly connected to the mother and rather loosely connected to the developing foetus through the umbilical cord. The life of the foetus depends upon the welfare of the placenta and the life of placenta depends upon the welfare of the mother to whom it is so intimately attached. Hence this triad of **mother → placenta → foetus** becomes very important in the whole process of development of the foetus (baby) and the birth. The three points of this triad tell us the story of each other; so that one can take care of any problems that arise before and during the stages of pregnancy.

Hence the examination of a freshly delivered placenta can give us immense information about the mother as well as foetus. This preliminary examination takes only 3 – 5 minutes for the attending doctor. If any unusual finding is observed one can always get the help of a pathologist who can examine the placenta in a great detail using a very scientific approach. Presently there are now numerous pathological techniques available even to the extent of immunohistochemistry, genetical parameters and even electron microscopy.

Placenta also needs your attention to inform you about various developmental anomalies, for changes in eclampsia, pre-eclampsia, in liver disorders, hypertension, diabetes mellitus, kidney abnormalities and many genetical disorders. Before I close this preface to the monograph I would like to leave a piece of advise, please do not just throw away placenta, spend 2 – 3 minutes on its gross examination and if required fix it and send it to a pathologist for further look after. You may get much more useful information about the newborn and the mother required for future pregnancies.
God bless you!

AHN

EXAMINATION OF PLACENTA

INTRODUCTION

This monograph on the "Pathology of Placenta" will give you a brief description of various abnormalities of placenta due to placental diseases, abnormalities in maternal systems and fetal abnormalities. Like any organs of human body placental pathology here has been categorised for the sake of convenience into different groups, e.g. developmental abnormalities, vascular and coagulation problems, inflammation and placental associations with various clinical syndromes / diseases of mother and various neoplastic lesions.

The importance of placenta is historic since the ancient civilizations. Placenta gained a great respect in many countries of Africa, Egypt, and Indonesia etc. It is known that placenta and the baby grow together, entwined and connected in the womb. In other words this amazingly unique organ grows with the baby from the very first cell division. Malaysians consider the placenta to be the older sibling to the new born. When the baby smiles unexpectedly, it is said that he is playing with his brother. Many African tribes believe that placenta has its own spirit that resides in the umbilical cord. In Egypt when the child was of royal blood, the placenta was ritually preserved and carried in procession by a high ranking officer. Placenta therefore has held a place of honour through our history. Perhaps we should recognise the wisdom of the ancients, and realise that the placenta is more than just some messy after birth to be discarded and ignored in the excitement and joy over the birth of a beautiful new born – baby. Now when the world has become more realistic and scientific the value of placenta has become health or disease oriented of the fetus / new born as well as the mother. In other words it becomes a triad of mother, fetus and placenta. The placenta being health indicator of the mother and fetus, it must be carrying out some very important functions which if disturbed; they can disturb the anatomy and physiology of the other two members of the triad.

Placenta has two major functions, nutrient exchange and protection of the fetus. In the former it must continuously adapt, maximise maternal supply and fetal extraction of nutrients without compromising the integrity of the two circulatory systems i.e. maternal and fetal. On the other hand in the latter it responds to danger signals by mounting an inflammatory response. The maternal and fetal placental vasculatures are dynamic structures which can undergo significant alterations by their abnormal development, luminal abstraction and physical loss of integrity.

The functional and anatomical disturbances are associated with various pathological abnormalities. They can be seen in the placental haemodynamics such as thrombotic lesions; infarcts, inflammations, malformations, villous abnormalities, placental chromosomal abnormalities, abnormalities of umbilical cord and of membranes. The following pages will describe a systematic approach to examine placenta in disease and otherwise.

EXAMINATION OF PLACENTA

Placenta needs to be examined at the time of birth (by the delivering physician) as well as a part of pathological examination (by a patho-logist).

Examination of Placenta at Birth

A quick examination of freshly delivered placenta is the duty of the delivering obstetrician who can observe if there are any obvious abnormalities or it is normal. Placental changes can be associated with various congenital / genetic abnormalities or even certain haemodynamic effects. At times it is of paramount importance to examine placentas at birth so that it may be beneficial both to the fetus and mother. If the attending doctor notices any abnormalities of placenta, umbilical cord and membranes, he / she must refer that placenta for pathological examination. This must accompany the relevant history of the mother, fetus and the stages of delivery. The findings of the initial examination of placenta be recorded in the record file of patient. This information may be essential for protecting the attending doctor in case there is an adverse maternal or fetal outcome.

The examination of placenta at the time of delivery can yield information that may be important in the management of mother and infant. Although some experts argue that all placentas should be examined by a pathologist, most hospitals do not practice this idea. Ideally this should be the responsibility of the attending obstetricians to refer the placentas to the pathologist which require a detailed pathological examination. In some situations decisions need to be made soon after the initial examination of fresh placenta. Hence he has to examine it thoroughly and accurately. In the examination of a fresh placenta one needs to know and observe the following features.

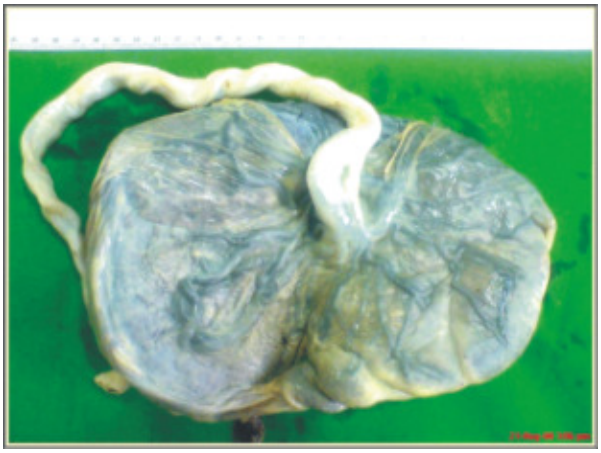

Fig 1.1: *Fetal surface of a normal placenta and the cord.*

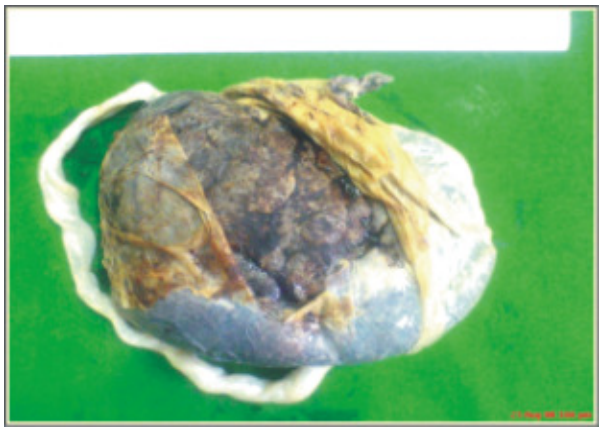

Fig 1.1a: *Maternal surface of a normal placenta showing cotyledons.*

Fig 1.2: *Slices of a placenta showing normal thickness.*

Characteristics of Normal Placenta

- The normal placenta at term measures about 22 cm in diameter and 2.0 to 2.5 cm thick. It generally weighs about 470 gr. However these measurements are variable (Fig 1 and 1.1a).
- Maternal surface of placenta is dark maroon in colour and shows lobules or cotyledons which are complete.

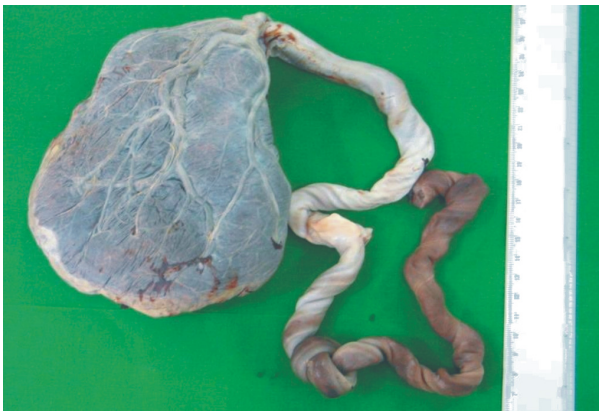

Fig. 1.3: *A placenta with an infracted cord and marginal insertion. The cord also shows a kit.*

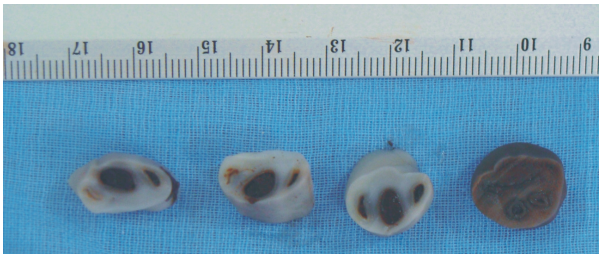

Fig. 1.3a: *Cross section of a cord showing vascular thrombosis.*

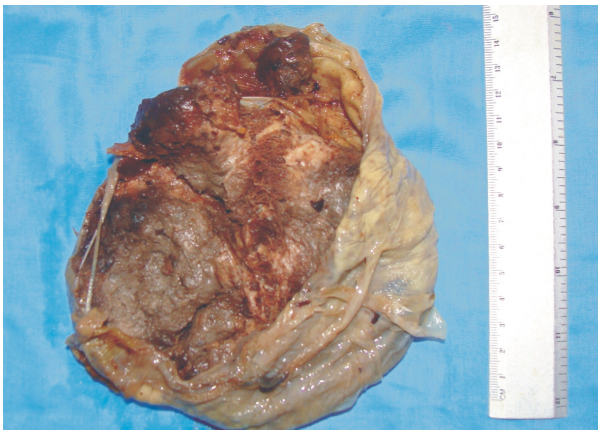

Fig. 1.4: *A placenta showing a small chorangioma.*

- Fetal surface of the placenta is usually shiny, gray and translucent.
- At term the typical umbilical cord is 55 – 60 cm in length, with a diameter of 2.0 to 2.5 cm. It should contain enough Wharton's jelly, and no true knots, or thromboses be present. This needs to be measured in the delivery room. The cut section of normal umbilical cord shows two arteries and one vein. These vessels should be

examined either in the middle third of the umbilical cord or near the fetal third of the cord. These vessels at times, are fused close to the placenta hence may be difficult to differentiate.
- Fetal membranes are usually gray, variably wrinckled, translucent and shiny.
- The placental membranes have a peculiar metallic odour. Placenta and the fetal membranes are not malodorous.

LIKELY ABNORMALITIES OF THE PLACENTA

Placental Completeness
- Ensuring placental completeness is of critical importance in the delivery room. Retained placental tissue is frequently associated with infection and haemorrhage.
- The cotyledons on the maternal surface be examined, see if all are complete and none is missing.
- The fetal membranes need to be examined at the edges of the placenta. Prominence of vessels (large vessels) beyond the edges indicate that a placental lobe may have been retained (accessory lobe). All or part of the placenta is likely to be retained (in placenta accreta, placenta increta and placenta percreta).

Placental Thickness
- A reduction in placental thickness i.e. less than 2.5 cm is usually associated with intrauterine growth retardation of the fetus. When a placenta becomes thicker than normal i.e. more than 4 cm in thickness, it is usually associated with fetal hydrops, maternal diabetes mellitus and intrauterine fetal infection (Fig 1.2).
- A very thin placenta may represent placenta membranacea that lines the uterine cavity. Such a placenta is associated with a poor fetal outcome.

Placental Shape
- Look for extra placental lobe. They are important because they may result into retained placental tissue.
- A large blood clot may disfigure placental shape when it is attached to area close to the margin or at the margin. This type of clot may represent an abruption. The dimensions of the placenta are to be measured.

Placental Surface and Consistency
- Placenta needs to be palpated with both hands. Both maternal and fetal surfaces need to be palpated.
- Maternal surface: As already mentioned the placenta of a normal term is dark maroon coloured. In a premature delivery placenta is light coloured. In fetal anaemia that could be associated with haemorrhage.
- Clots which are centrally located on the maternal surface may represent placental abruption.
- Fetal surface: The circumvallated placenta (a thick ring membrane on the fetal surface). This is associated with prenatal bleeding, abruption, prematurity, multiparity and early fluid loss.
- A circum marginate placenta (a thinner ring of membrane tissue), this does not carry any significance.
- Amnion nodosum (squamous metaplasia) are seen as many small, firm, white, gray or pale nodules on the fetal surface. It is associated with renal agenesis, oligohydramnios and a poor fetal outcome.
- A nodular or thickened fetal surface may be due to vanished twins. The vanishing (decreased) twin may co-exist with the normal fetus.
- Amnionic tissue bands may strangle and even amputate fetal parts such as an entire limb, digit, head, neck or even trunk. In such cases a detailed examination of placenta is needed.

Placental Parenchyma
- In fresh samples placental parenchyma is soft to feel.
- Firm areas in placenta may represent fibrinous changes and infarcts. Fresh infarcts are red, and the old infarcts are gray to pale. Fibrin deposits are grayish pale. Multiple infarcts are associated with growth retardation of fetus. When fibrin deposits and infarcts occupy less than 5% of the placental substance they do not carry a significant importance.
- When placenta is diffusely soft and is thickened, it may represent infection.
- Focal dark red fleshy areas represent chorioangiomas. These benign vascular lesions (haemangiomas) occur in only 1% placentas. Large chorioangiomas can result in fetal anaemia, thrombocytopaenia, hydramnios, hydrops, fetal growth retardation, prematurity and still birth.
- The gestational trophoblastic neoplasia, include benign hydatidiform moles, invasive moles and choriocarcinoma. They rarely coexist with viable gestations. Moles appear as grape like clusters, whereas choriocarcinoma appears similar to a fresh infarct.
- Subfetal membrane haemorrhage or a dark coloured cyst may represent a Breus'mole associated with Turner's syndrome (45, X) and with fetal death.

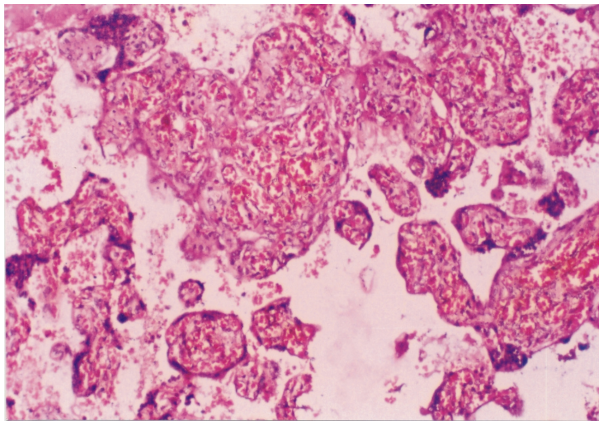

Fig. 1.5: *Morphological appearance of a villous chorangiosis.*

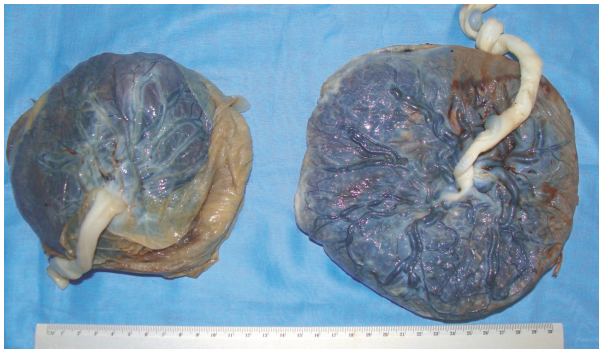

Fig. 1.6: *A normal placenta (right) and a placenta of pre-eclampsia (left). None small size of the latter.*

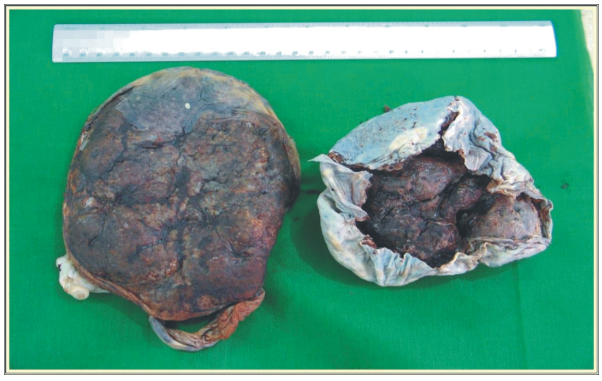

Fig. 1.7: *Two placentas showing pre-eclampsia changes (left) and a very small size placenta of eclampsia (right).*

Umbilical Cord

- The length of umbilical cord is variable between 40 and 70 cm; more between 55 and 60cm. The length of the umbilical cord is increased by the tension the fetus produces on the cord. It means a short cord is associated with less active fetus; fetal malformation, Down's syndrome, myopathies, neuropathies and oligohydramnios. Short cord may result in rupture, haemorrhage and stricture. In addition long cord may result into many fetal problems, which will be discussed later.

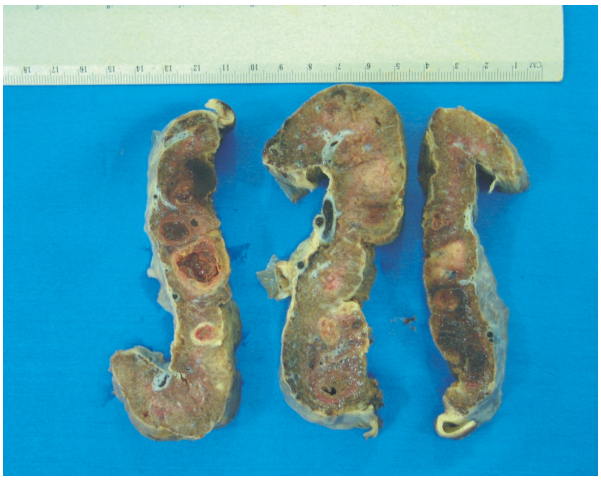

Fig. 1.8: *Multiple fresh infarcts of placenta on cross section.*

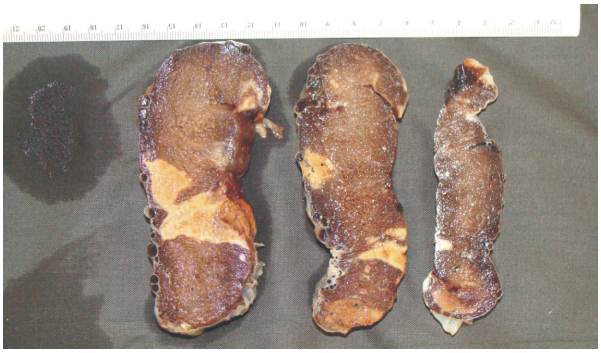

Fig. 1.8a: *Cross sections of a placenta showing infarcts undergoing organization.*

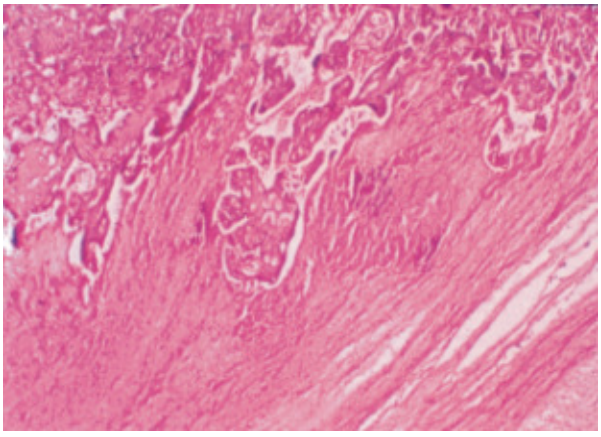

Fig. 1.9: *Microscopic appearance of a placental infarct showing extensive necrosis.*

- The cord diameter: The cord is 2.0 to 2.5 cm thick. Any narrow areas (due to deficient Wharton's jelly) can lead to torsion and fetal death. A thick oedematous cord is associated with haemolytic anaemia, prematurity, pre eclampsia, eclampsia and diabetes mellitus. Cord oedema can be associated with respiratory distress syndrome. Focal oedema of cord can be seen in trisomy 18; and omphalo cord etc. Inflammatory and necrotising inflammations, calcifications and thrombosis can also be seen.
- Cord is normally inserted near its center (about 90%). It may be inserted at the placental margin (it does not cause any harm). Vilamentous cord insertion is associated with fetal haemorrhage, vascular compression and thrombsis, advance maternal age, diabetes mellitus, smoking and fetal malformation.
- A cord knot may be true or false. The true cord can be harmful by leading to fetal asphyxia due to the cutting off of the blood supply.
- Cord contains two arteries and one vein.
- Thrombosis of cord blood vessels must not be overlooked as they can result into fetal injury (Fig 1.3 and 1.3a).

Fetal Membranes

- Normal fetal membranes are thin, grayish, and glistening.
- Thick and smelling membranes indicate infection.
- Green coloured fetal membranes are due to meconium staining or some times the infection.

Pathological Examination of the Placenta

At the time of childbirth any abnormality of clinical significance needs the attention of the pathologist for a complete pathological examination. Hence there are many indications for pathological examination of placenta (table 1).

a. *Poor Pregnancy Outcome:*
   - ♦ Prematurity.
   - ♦ Intrauterine growth retardation.
   - ♦ Perinatal death.
   - ♦ Fetal asphyxia.
   - ♦ Congenital anomalies.
   - ♦ Suspected fetal infection.
   - ♦ Fetal haematological abnormalities.

b. Obstetrical indications:
   - ♦ Intra uterine fetal death.
   - ♦ Maternal disease.
   - ♦ Maternal infections.
   - ♦ Gestational hypertension.
   - ♦ Antipartum haemorrhage.
   - ♦ Postpartum haemorrhage.
   - ♦ Abnormal placenta at birth.

PREREQUISITES FOR SUBMISSION

- ♦ Indications for placental examination should be known to the sending clinician who must write his impression on the requisition.
- ♦ The clinicians and pathologists should reach an understanding so that codal formalities are completed in sending the placenta e.g. fixation in sufficient quantity of 10% formaline. Some people keep the placenta in a refrigerator that does not interfere with the morphological examination. The specimen container need to be properly labelled (i.e. the name, age, hospital registration No:, name of the physician, brief indication(s) that need placental examination). When placenta is to be transported from an out station, and if the fixative is not handy, it may be kept in a refrigerator for up to five days (table 2). If an infection is suspected one may not fix it in formaline and sent it fresh.
- ♦ The pathologist has to understand the clinical scenario before undertaking placental examination. If needed he may discuss the obstetrical and clinical background with the clinician.

STEPWISE HANDLING OF PLACENTA

Practical handling of placenta is variable; however the essential / universal precautions are the same. The procedures used in the author's laboratory, University of Health Sciences is described below.

1. When clinical information of the mother indicates an infection or there is a known case of HIV infection one may take the necessary material for microbiological examination before it is fixed in a large volume of 10% formaline, for 10 – 15 days.
2. Remove the placenta from the container, let it drain, mop it with cotton cloth; and remove gently the loose clots.
3. Prepare two membrane rolls and put them in a formaline container (rolls should measure about 3 cm wide). Remove the remaining membranes.
4. The umbilical cord is to be measured and removed. Take two sections, one about 5 cm from the free end, and another about 15 cm from the point of insertion; or even the mid length of cord.
5. Measure the placental disc and the distance of cord insertion from the closest margin.
6. Weighing of placenta: This is done after removal of the membranes and the umbilical cord.
7. After inspection of the fetal and maternal surfaces, slice the placenta into 1.5 cm to 2 cm thick

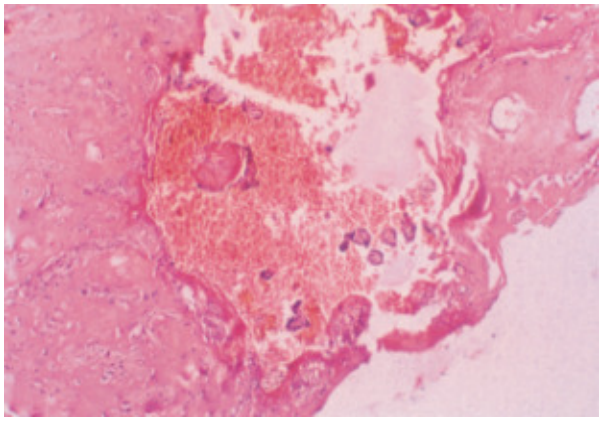

Fig. 1.10: *Microscopic appearance of an intra-placental haemorrhage.*

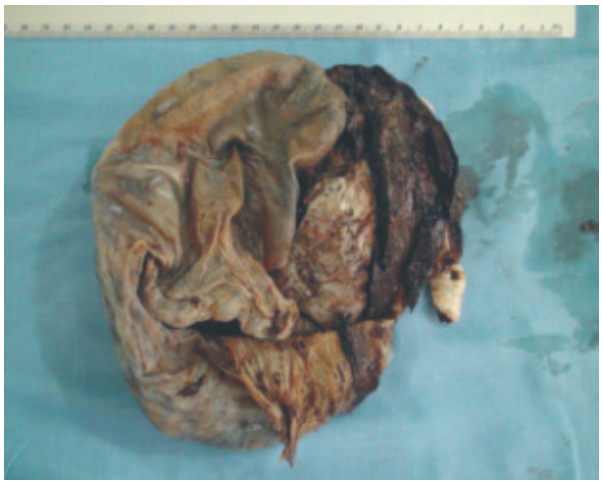

Fig. 1.11: *A placenta of pre-eclampsia showing marginal haematoma (arrow).*

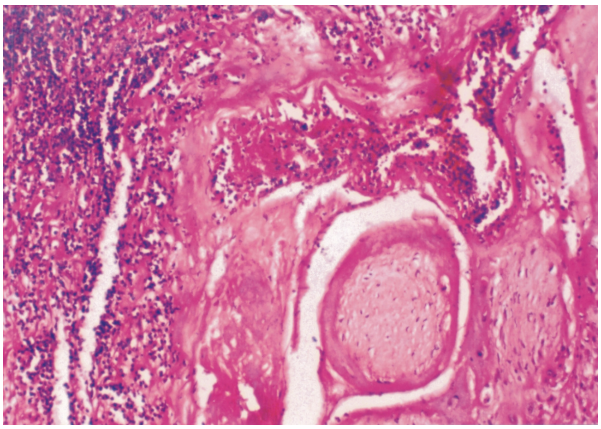

Fig. 1.12: *Microscopical appearance of a placenta showing an evidence of severe acute inflammation and perivillous fibrin (arrow).*

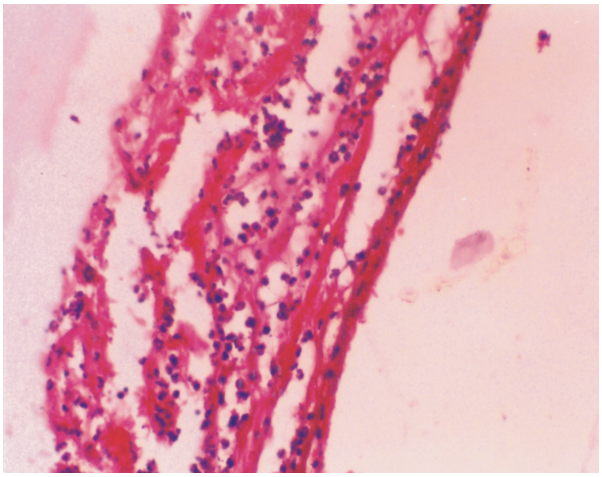

Fig. 1.13: *Microscopical appearance of a placental membrane showing acute inflammatory reaction (membranitis).*

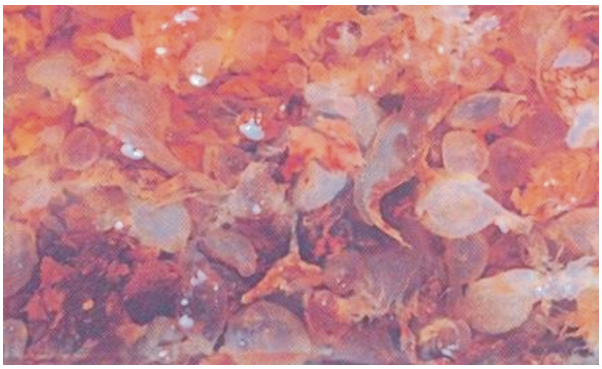

Fig. 1.14: *Gross appearance of a hydatidiform mole in a uterus. Numerous moles are visible.*

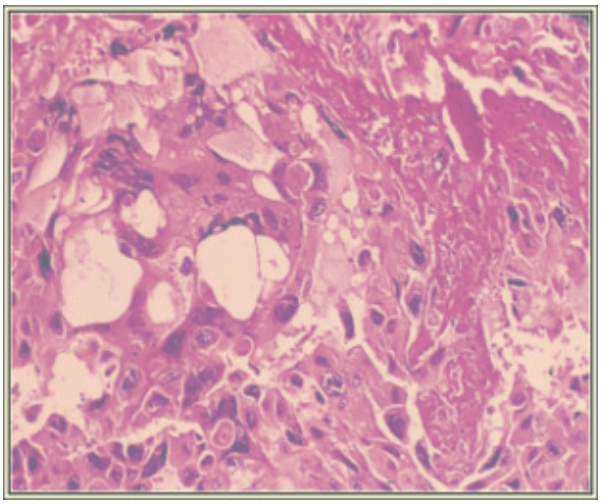

Fig. 1.15: *Microscopic appearance of a choriocarcinoma.*

slices. The fetal surface may remain intact. Remove these tissue blocks from the placenta (2.5 to 3 cm wide) and put them in formaline before they are processed. The remaining placental sli-

ces be stored in the original container. In case of any further examination the remaining placenta can be used.

8. The rest of the placenta should be kept for no less than six weeks before it is discarded.

Table 1

Points to note in placenta, cord and membranes when the placenta is to be sent for pathological examination, consider using the term "approximately" when referring to dimensions; let the pathologist document accurate measurements. Please tick the boxes:

Placenta

Complete: - ❒ Yes
❒ No
If incomplete, amount apparently missing: _____%

Intact: ❒ Yes
❒ No

Diameter: _____ cm

Thickness: _____ cm

Shape: ❒ Discoid
❒ Oval
❒ Bilobed
❒ Succenturiate lobe present
Other anomaly present _____

Consistency: ❒ Normal
❒ Soft
❒ Firm

Haemorrhage: ❒ Yes
❒ No
Size of haemorrhage: _____ cm
Consistency of haemorrhage:
_____
Adherence of clot:
❒ Yes
❒ No

Other abnormalities: ❒ Amnionic nodules
❒ Staining of amniotic surface
❒ Mal-odour

Umbilical cord

Insertion: ❒ Central
❒ Eccentric
❒ Marginal
❒ Velamentous

Length: _____ cm

Diameter: _____ cm

Knots: ❒ No
Yes (describe)_____
_____
_____

Number of vessels: _____

Single artery: ❒ No
❒ Yes

Thrombosis: ❒ No
Yes (describe)_____
_____
_____

Wharton's jelly: ❒ Present
❒ Absent

Fetal membranes

Velamentous vessels present:
❒ No
❒ Yes

Studies performed

❒ Placenta sent for pathological examination
❒ Cord blood-gas
❒ Maternal cultures/serologies
❒ Fetal cultures/serology –

Other maternal, fetal and / or placental reasons for sending placenta to pathology:

Maternal conditions:
❒ Diabetes
❒ Abruption placenta
❒ Oligohydramnios
❒ Hypertension
❒ Infection
❒ Fever
❒ Repetitive bleeding episodes
❒ Substance abuse
❒ Maternal history of reproductive failure

Fetal and neonatal conditions

❒ Stillbirth
❒ Depressed one – minute Apgar score
❒ Multiple births
❒ Neurological problems, including seizures
❒ Prematurity
❒ Hydrops
❒ Suspected infection
❒ Fetal growth retardation
❒ Perinatal death
❒ Admission to neonatal intensive care unit
❒ Congenital anomalies
❒ Postmaturity
❒ Apgar score of 3 or less at five minutes
❒ Thick meconium

Placental conditions (any gross abnormality of the placenta, the placental membranes or the umbilical cord):

GROSS DESCRIPTION

While writing the gross description of placenta; it should be concise and complete, how variations

from case to case can be seen. However, the key points that need to be noticed are the following.

1. Presence or absence of fixative.
2. Weight of placental disc (trimmed).
3. Length of umbilical cord; its colour, number of twists per inch, its point of insertion and the appearance of membranes.
4. Completeness of membranes or if ruptured, its distance from placental margin.
5. Appearances of fetal surface; number of lobes, colour etc.
6. Appearances of maternal surface.
7. Any abnormalities on cut surfaces.

How to do the Tissue sampling?

How to get the samples from the placenta, may vary from one institution to another, but the goal is the same. Hence the minimum number of blocks, their labelling and processing are the same every where. The approach to take blocks is as follows and is also shown in the figure. We prefer that placenta is fixed before tissue blocks are removed.

1. Membranes: Two rolls, one section from each roll. The examinations of membranes give us the information about inflammation, maternal decidual vasculopathy, exogenous substances, meconium, haemosiderine, and various other pathological changes.
2. Umbilical cord: Two pieces – one 5 cm away from the fetal end and one from the proximal part of the placental 3rd i.e. just beyond the mid length. This is used to assess the number of arteries and veins; vasculitis, thrombi and Wharton's jelly.
3. Parenchyma: 2 –3 full – thickness tissues i.e. from maternal to the fetal surface. The examination of the parenchyma gives us idea about the villous pattern, vasculopathy, thrombosis, infarction, syncytial knots, chorangiosis and the tumours of placenta. In addition pigment deposition, necrosis, abscesses etc.

Notes

- One may take a block if an interesting finding is seen in another area.
- In twins or multiple pregnancies, each placenta should be treated individually or under gross and microscopic examination.
- All the blocks are processed in the tissue processor, sections stained in haematoxyline and eosin for the microscopic examination. We can select certain blocks containing areas that need to be further explained. One can do further morphological stains to explain the morphological changes.

SPECIAL STAINS: (HISTOCHEMICAL STAINS)

1. Gomori methamine silver (GMS).
2. Periodic Acid – Schiff (PAS).
3. Gram stain.
4. Silver impregnation stains (Warthin's Steiner; Dieterl).
5. Prussian blue (Perl's; Gomori's iron).
6. Phosphotungstic acid haematoxyline (PTAH).
7. Alcian blue.

IMMUNOHISTOCHEMISTRY

Many markers can be demonstrated using immunohistochemical staining techniques. Some of the markers which can be used on placental tissue include:

- CD_{68} — To demonstrate the nature of intervillous infiltrate.
- CD_{34} — Capillary endothelial – lineage marker.
- CDC — For T – lymphocytes
- CD_{56} — Natural killer cells (Nk cells)
- CEA, HMB – 45, Cytokeratin — For metastatic tumours
- Keratin, HCG — For trophoblastic subtyping
- HPL — Human placental lactogen
- PAP — Placental alkaline phosphatase

OTHER SPECIAL STUDIES

a) *Polymerase Chain Reaction*

- Viruses such as parvovirus B_{19} infection can be detected.
- DNA extraction from umbilical cord tissue.
- PCR based microanalysis (microsatellite analysis) of decidual placental tissue.

b) *Cytogenetics*

- Placental Karotyping: When fetus is not available or macerated, routine karotyping is not so useful in cases of suspected confined placental mosaicism; because abnormalities are often focal.
- Direct karotype of trophoblast cells and competitive genomic hybridization are more sensitive technique for detecting confined placental mosaicism. This may not be available in most of the pathology department.
- Flowcytometry or image analysis is useful for the confirmation of polyploidy is some partial / complete molar pregnancies.
- FISH: Multicoloured fluorescence is insitu hybridization.

c) *Electron Microscopy (EM)*
- The EM can be useful only rarely to diagnose cases of inborn errors of metabolism.
- In addition viral capsid detection can be used.

d) *Bacterial Cultures*
In over 90% placentas one or another organism is grown on culture. Chorioamnionitis is a typical response to any organism. Hence detection of an organism is not very useful. However, variables such as duration of infection, maternal antibody level and intensity of the fetal inflammatory response are more important.
- Mycoplasma and vaginal anaerobes are more predictable pathogenic organisms.
- Other virulent organisms include: Escherichia coli, group B – streptococci and haemophilus influenza. They rarely alter the clinical scenario.

ABNORMALITIES OF PLACENTAL DEVELOPMENT

The development of placental disc and its adnexa (umbilical cord and membranes) is the result of a developmental programme. Their general features are identical but there are usually some minor variations which are species specific. Placental implantation in human occurs into the uterine body where it extends through the endometrial decidua into the myometrial blood vessels and myometrium. The membranes develop from the chorionic sac by a process of secondary atrophy. The blood supply of fetus is gathered in the umbilical cord that inserts into the placenta at its original site of implantation (central or slightly eccentric).

Abnormalities of development occur by various mechanisms; such as errors in gene expression. Apart from fetal anamolies, developmental abnormalities can arise as the result of abnormal maternal environment. Many genetic and chromosomal abnormalities also occur as the result of the mechanisms such as defects at the initial site of implantation, local oxygen supply and metabolic status of mother.

DISORDERS OF MEMBRANE DEVELOPMENT

1. *Placenta membranacea*

It is a failure in the formation of normal placental membrane. As a result a gestational sac is surrounded by vascularised chorionic villi.

It is between 10 and 14 weeks that the villi in the membranous portion of placenta regress at the time when degenerative changes due to oxidative damage occur in the periphery of the placenta. Hence this supports the view that placenta membranacea may be the result of poor blood supply to decidua basalis and increased vasculature of the decidua capsularis. The failure regression could be genetic in origin. "It has also been proposed that diffuse hypoplasia of endometrium may be a causative factor.

Clinically premature separation, placenta previa, maternal haemorrhage or gravid hysterectomy due to retained placenta are the known complications. Morphologically there is usually a small patch of clear membrane on one side of placental sac. Placenta is very thin with disruption of maternal surface due to placenta accreta. As very often there is a poor pregnancy outcome the fetal areas of haemorrhage need to be examined properly both grossly and microscopically.

2. *Circumvallation / Circummargination*

It is the complete or partial insertion of the fetal membranes in the placental disc away from the peripheral margin. This is a rather common condition occurs in 1 to 7% placentas and is considered to be due to marginal venous haemorrhage or marginal disruption. Clinically circumvallate placentas are associated with recurring vaginal bleeding throughout the pregnancy. This can be seen in marginal haematoma, retroplacental haematoma and placental abruption. Grossly, placenta usually looks small for its age and has many degenerating blood clots. Sometimes greenish discolouration of fetal surface can be due to meconium staining may be seen. Sections are taken from its margins which microscopically show foci of old decidual haemorrhage recognised by the presence of haemosiderin and haemosiderin macrophages.

DISORDERS OF UTERINE IMPLANTATION

They include:
- *Placenta Previa:* When placental implantation occurs in the lower segment of uterus reaching the cervical or when incompletely covered by one edge it is called placenta previa. It is seen in usually < 0.5 percent of deliveries. Placenta previa often results in premature separation of the placenta that leads to profuse vaginal bleeding, premature labour or sometimes both. Such a case is to be treated promptly, on gross examination there is a marginal retroplacental haematoma. Disruption of maternal surface due to placenta accreta is seen commonly. Histology of placenta previa is not very significant.

- *Placenta Accreta, Increta and Percreta:* Placenta accreta is implanted on uterine smooth muscle where it is limited to the superficial myometrium. Placenta increta extends into the myometrium and percreta extends through the myometrium and goes through the uterine serosa. The complications (antepartum) of placenta

accreta include vaginal spotting, concealed haemorrhage, and even rupture of uterus which is confined mainly to placenta percreta. The post partum complications include, post partum haemorrhage, myometritis. Pathologically the maternal surface is usually disrupted and very often incomplete. Focal absence of decidua is a very important diagnostic feature.

- *Superficial Implantation:* This is an underlying abnormality in pre eclampsia that affects < 3% of all pregnancies. It is more common in nulliparous than the multiparous women. Other related problems are fetal growth restriction, maternal thrombophilia and abruption placenta.

Grossly superficially implanted placentas appear normal but are small for their age. Microscopically the most important finding in the presence of muscularised basal plate arteries that underlie the inner two third of the placental disc. The walls of arteries in this area normally contain trophoblastic and fibrinoid matrix. Acute atherosis is seen in the small arteries of placental membranes. As atherosis is seen in muscular arteries, its presence in the basal plate is diagnostic of superficial implantation. In addition one can see numerous placental site giant cells within the basal plate; surrounded by loose decidual tissue.

DISORDERS OF PLACENTAL MIGRATION

a) ***Shape abnormalities***

- An accessory lobe: Separated from the main body by membranes.
- Multilobation: Shows membranous indentations of placental disc involving 50% of its diameter.
- Atrophy: Placental thickness is reduced by 50 percent; involving more than 10% of placental disc.

b) ***Peripheral Cord Insertion***

- Velamentous (membranous) insertion: occurs in 1.3 – 1.6 percent.
- Marginal insertion : occurs in 6 – 9 percent gestations.
- Peripheral insertion : Accentric umbilical cord insertion.

c) ***Disorders of Villous Development***

Distal villous hypoplasia

It is a decreased number of distal villi in the center of placental lobules. The villi are thin, are non branching, poorly vascularised and shows many syncitial knots. The stem villi show prominent hypertrophy of their arterioles and degree of intervillous fibrin.

Grossly: The placenta in distal villous hypoplasia is very small for gestational age. It also shows infarction abruption and changes of severe oligohydramnios.

Microscopically: Distal villi in the center of lobules are deficient. They are thin and unbranched. Tertiary stem villi are fibrotic. Syncitial knots may be prominent.

Distal villous immaturity with placental over growth: This is also called delayed villous maturation. "This is seen in the form of an increased number of large distal villi, with prominent capillaries, stromal macrophages and interstitial fluid. It forms about 7 percent of pregnancies.

d) ***Disorders of Fetal Vascular Development***

- *Chorangioma:* Chorangioma is a tumourous nodular lesion formed by capillaries, stromal cells and surrounding tissue of chorionic villi. Most chorangiomas are an incidental finding with no clinical significance. Infants with placentas containing chorangiomas have a higher than expected incidence of haemangiomas elsewhere.

Trophoblast: It is similar to haemangioma elsewhere. Localised chorangiomatasis tissues have features similar to chorangioma. Chorangioma is seen in about 1 percent of placentas; whereas chorangiomatosis is seen in 0.3 percent placentas.

Grossly: Chorangioma may be a single mass or multiple masses best seen on the cut surface of placenta. They are firm pale to maroon coloured but rarely contain blood. They are well circumscribed. They are seen as subchorionic or marginal as firm masses than surrounding parenchyma. Fibrous septae can form lobules within the chorangioma.

Microscopically: Chorangiomas are composed of small capillary like vessels with a few intermixed large vessels. Occasional cases may show high cellularity, containing area of degeneration and focal calcification or even cellular atypia. They do not undergo malignant transformation (Fig. 1.4).

Clinically significance: Large chorangiomas (> 9 cm) can be associated with arteriovenous shunting amnios and even fetal death. Sequestration of platelets in capillaries of large chorangiomas and multifocal chorangiomatosis can cause disseminated intravascular coagulation (DIC), thrombocytopaenia or a haemorrhagic diathesis in the faetus. In addition polyhydramnios, preterm delivery, antepartum bleeding, hydrops fetalis and fetal anaemia; are also associated with it.

Villous Chorangiosis
This is also called villous hyper capillarisation. Villous chorangiosis is defined as the presence of ≥ 10 capillaries per terminal villous is 10 terminal villi in at least three different regions of placenta. The lesion is called vallous chorangiosis when more capillaries are involved in several areas of the placenta. Chorangiosis is found in 6 –7 percent of placenta. The lesion is usually found in term placentas. Chorangiosis is commonly seen in association with distal villous immaturity (in diabetic pregnancies). In addition it may be prominent in chronic villitis, mild maternal vascular under perfusion and thrombotic vasculopathy. The maternal hyperfusion can increase when placenta is delivered at high altitude.

Grossly: The placentas of chorangiosis are large for gestational age.

Microscopically: It is limited to the distal villi. Capallaries in chorangiosis have clearly visible basement membrane and lack the layer of pericytes that is regularly seen in chorangiomatosis and chorangioma (a point of differentiation). The immunoperoxidase staining for the endothelial antigen using CD_{31} and CD_{34} demonstrates many more capillaries than are seen using HandE stain. Chorangiosis should be differentiated from congestion in which the vessels are usually prominent (Fig. 1.5).

Diffuse Mutifocal Chorangiomatosis
This is a diffuse multifocal lesion recognised by the foci of exclusive capillary growth, with surrounding pericytes and collagen fibers affecting stem cell villi in the entire placenta. It is very rare (0.2 percent of all placentas). It is a change associated with pre eclampsia, congenital anamolies, twin gestation and vascular villi that could perhaps the result of hypoxia.

GENETIC AND CHROMOSOMAL CONDITIONS

Metabolic Storage Disorders

- Hydrops fetalis.
- Isolated organ failure.

Grossly placenta appears normal. Microscopically the placentas show rather pale staining parenchyma. This lighter staining is due to vacuolation of syncytio trophoblasts, villous stromal cells, intermediate trophoblasts and amniocytes.

Villous macrophages show an increase in number and size with foamy cytoplasm. Amniotic epithelium and intermediate trophoblasts are more clear, showing clear cytoplasm. Periodic acid – Schiffs stain and Alcian blue are useful to examine the mucopolysaccharide. These changes are seen in mucolipidosis, galactosialidosis, sialidosis, cholesterol ester storage disease and type IV mucopolysaccharidosis.

Mesenchymal Dysplasia
Mesenchymal dysplasia is placental enlargement associated with cystically dilated abnormal stem villi, fibroblastic stromal over growth and vascular abnormalities. Mesenchymal dysplasia is a term and is used very rarely. The cause(s) of this condition is not known except its association with certain conditions such as omphalocoele, macroglossia and visceromegally. Pre eclampsia is commonly associated.

Grossly, placental weight at term is more than 1000g. Large stem villi are near the chorionic plate and are grossly thickened and may show mural haemorrhage, aneurysmal dilation and thrombosis.

Microscopically fibroblastic stroma is prominent with increased vascularisation and or cystic changes. Associated chorangiomas or localised chorangiomatosis are fairly common. The terminal villi are usually normal.

Genetics and Chromosomal Abnormalities
Majority of chromosomal abnormalities are associated with an in-creasing tendency in advance maternal age. For karyotyping one has to have 1 – 3 percent of all first trimester samples of chorionic villi. Some examples of genetic and chromosomal abnormalities are given below:
Metabolic storage disease:
Fetal metabolic storage diseases.
Galactosialidosis (Vacuolation of syncytiotrophoblasts).
Mucolipidosis II.
Gangliosidosis (GM_1 and GM_2).
Infantile sialic storage disease.
Sialidosis.
Cholesterol ester storage disease.
Type II mucopolysaccharodosis.
Glycogen storage disease.

PLACENTAL PATHOLOGY IN DIABETES MELLITUS

Pathological changes in placenta in gestational diabetes are the main reasons for impaired placental functions; hence they can result in increased frequency of fetal complications. Diabetes in pregnancy is seen in two groups: those with pre existing diabetes as in type I and women having undergone glucose intolerance during pregnancy. The latter group is likely to develop overt type II diabetes in their later life. Gestational diabetes increases the risk for fetal macrosomia and stillbirths along with increased frequency of maternal hypertension and caesarean delivery. These complications are attributed to the abnormalities of placenta. Hence placenta of diabetic women have become an important area and sev-

eral pathological changes in placenta have been described. The major placental changes are hereby described below.

- *Lymphohistiocytic Villitis* was diagnosed by the presence of numerous lymphocytes and macrophages in the villous stroma.
- *Presence* of NFRBC (Nucleated fetal red blood cells) as a mark of fetal hypoxia when present in the umbilical cord or the villi.
- *Ischaemia* was defined when increased maturation and branching of villi (Tenney – Parker changes) were present.
- *Infarction,* assessed at gross examination, was present when at least 10% of the placental volume was infarcted.
- *Villous fibrinoid necrosis,* a condition where villous stroma is replaced by fibrinoid.
- *Villous immaturity* was defined when there was decreased formation of terminal villi and increased presence of immature intermediate villi in relation to gestational age.
- *Chorangiosis*, i.e. vascular hyperplasia of the chorionic villi, was defined as the occurrence of 10 or more villi with 10 or more capillaries in 10 or lower power microscopic fields.
- *Hydropic villi* were diagnosed when large terminal villi were present with oedematous fluid, with an increase of villous macrophages, and with an artifactual separation of the trophoblast lining from the underlying stroma.
- *Fetal vascular thrombosis* was diagnosed when a large fetal stem villous vessel was partially or completely occluded by a thrombus.
- *Avascular villi* were diagnosed when a group of at least 5 fibrotic avascular villi without inflammation or mineralisation was observed.

These above mentioned changes in placenta can lead to impaired placental functions, that further leads to abnormalities of fetus.

PLACENTAL CHANGES IN PRE ECLAMPSIA AND ECLAMPSIA

Pre eclampsia clinically has two components .i.e. Pregnancy induced hypertension and protienuria (1+ or 24 hours collection containing 300 mg or more protein). Generalised oedema though is present, it is rather non specific. Severe preeclampsia is recognised by the blood pressure of more than 160 / 110 mmHg; proteinuria more than 5 mg / 24 hr or more than 3+ about 4 hours apart. In addition clinically headache, visual disturbances, oliguria, right upper quadrant and epigastric abdominal pain, thromhocytopaenia, fetal growth restric-tion, disturbed liver functions, and pulmonary oedema. Eclampsia means preeclampsia and maternal seizures. Clinically it is more severe (Fig. 1.6).

Pathological changes in placentas

Placenta in preeclampria and eclampsia can show two different types of changes. The most common is a small placenta which is frequently delivered prematurely. Multiple infarcts and decidual vasculopathy are seen in the form of acute atherosis. In more severe disease the chorionic villi are small and thin, that is the result of distal villous hypoplasia or villous hypermaturation. The other type is large sized placenta with immature villous cytotrophoblasts. This change may be seen in multifetal gestation. Hydropic placenta (as in moles) and diabetes mellitus. The aetiology of preeclampsia is not known. However placental anoxia and ischaemia followed by endothelial injury, perhaps is due to oxidative stress and some inflammatory effects. In addition one may consider genetic bases as well (Fig. 1.7).

VASCULAR LESIONS OF PLACENTA

a) Acute atherosis.
b) Mural or occlusive thrombosis.

In acute atherosis the decidual spiral arteries show necrotic vessel wall having dense eosinophilia. The lumens in some loops of blood vessels are thrombosed. These arteries in the membranes show accumulations of large foamy macrophages and fibrin. In more severe eclampsia the lumen can be nearly occluded by fibrin mesh. The intermediate trophoblasts become prominent. The basis of acute atherosis, in addition to pre-eclampsia, is also seen in placentae of women with Systemic Lupus Erythematosis, Scleroderma, antiphospholipids antibody syndrome and small for gestational age infants.

In addition in maternal thrombophilic state products of anti fibrinolytic changes are seen. Hence the effects of thrombosis usually seen are the formation of infarcts. The villous changes i.e. hypoplasia is recognized by reduced branches and slender villi. The terminal villi are very small – limited or atrophic (accelerated maturation). These changes are seen in eclampsia of 30 weeks gestation. Another frequent change associated with the damaging placental substance (as in infarcts and villious hypoplasia) is the clustering of syncytiotrophoblast nuclei (also called syncytial knots) which are usually numerous.

Placental Infarcts

Placental infarcts are very frequently seen in preeclampsia. They form about 65% of all placentas of pre eclampsia. This is usually due to the partial or complete abstruction to the blood flow through spiral arteries. In this process multiple spiral arteries are involved hence the number of infarcts may be more than one. Solitary small (< 3 cm) infarcts are of no significance i.e. do not cause placental insufficiency. Many small infarcts are associated with

maternal hypertension. These infarcts occur when spiral arteries are narrowed. Hence multiple spiral arterial insufficiencies result into the formation of multiple infarcts, however small infarcts of less than 3 cm are frequent. They are seen as an incidental finding. Such infarcts are located at the periphery. When damage is caused by infarcts involving more than 50 percent of the placental substance, it can significantly reduce the placental function hence may cause fetal hypoxia.

Grossly: The infarcts are firm and well demarcated. They are maroon coloured when fresh and become pale and even indurated with time. Their cut surface is maroon and later become pale and granular.

Microscopically: The infarcted tissue becomes necrotic. The ghost villi and surviving villi are crowded due to the presence of fibrin. As the infarcted area is ischaemic, the trophoblastic knots also become prominent. What we see is an almost homogenous and pink necrosed structureless tissue or rarely ghost villi are seen.

The closest differential diagnosis of a fresh infarct is intraplacental haematoma, which like fresh infarcts can be multiple. They however are not indurated. Placental damage caused by infarcts depends upon the extent and severity of injury: Placental insufficiency may be the end result of extensive damage to the placental substance (Fig. 1.8 and 1.8a) (Fig. 1.9).

INTRA PLACENTAL HAEMATOMA

Intraplacental haematomas are clots in the maternal inter villious space. They are circumscribed and localized. They can be more than one and usually are 1 – 2 cm in size. Intra placental haematomas are seen in up to 48 percent placentas.

Clinically intervillous haematomas are harmless when they are small and fewer in number. Although most of the bulk of these haematomas are formed by maternal blood, mostly they form due to leakage in fetal circulation. This can result in:

- Fetal anaemia.
- Placenta fetal hydrops.
- Still birth.
- Severe reduction in placental functions.
- Abortion of early gestation.
- Sudden intrauterine fetal death in 3rd trimester.
- Association with inherited thrombophilias.

Grossly: Fresh intraplacental haematomas are dark red and may show laminated appearance. The older lesions are lighter or gray and even pale in appearance.

Microscopically: As it is an intravillous thrombosis the villi are pushed apart and the cavity is filled with blood. The adjoining villi are thus pressed by the expanding clots. When clot becomes older it gradually becomes depigmented. These surrounding villi are infarcted. Among the differential diagnosis (keeping in mind both gross and microscopic appearances) it includes fresh infarcts being common, chorangiomas and perivillous fibrin deposits (Fig. 1.10).

Other placental haemodynamic changes include:

- Retroplacental haematoma and
- Placental abruptions (showing villious oedema).

MATERNAL CIRCULATION

Non vascular lesions:

- Maternal perivillous fibrin deposition and
- Maternal floor infarcts.

Massive perivillous fibrin deposits and maternal floor infarcts will be discussed together. Their morphological features are similar except for the distribution of fibrin in the perivillous spaces; where these variable sized deposits are seen as grayish pale or whitish streaks or masses.

As regard their prevalence clumps of perivillous fibrin are commonly formed in full term placentas. They can involve upto 1/4th of the placental mass hence can significantly affect placental functions. The prevalence of massive perivillous fibrin deposition is highly variable from one center to the other.

The maternal floor infarcts is a misnomer, it actually is seen as perivillous fibrin deposition (PDF) that involves an extensive area (about 3rd of villi adjacent to the basal plate with extension into the underlying decidua) of the parenchyma. It can result in a sudden inutero death of fetus during the 3rd trimester. The fetuses who survive are at risk for growth retardation, preterm delivery, or some serious neurological disturbances. Some women may also show frequency of phlebitis and maternal thrombophilia. Maternal floor infarcts are seen in less than 1% of placentas. It can recover in subsequent pregnancies adjacent to the basal plate with extension into the underlying decidua.

FETAL CIRCULATION DEFECTS

a) Fetal Thrombotic Vasculopathy:

Occlusion of vessels in the circulatory system can involve tributaries of umbilical veins, the vessels of chorionic plate, and the smaller fetal vessel within the chorionic villi. It is because during gestation there is a one continuous circulation between the faetus and the placenta; the extensive thrombotic lesions in the placenta can indicate thrombotic or embolic lesions in the fetal circulation. How common is the fetal thrombotic vasculopathy is not known.

Grossly: Collections of vascular terminal villi appear as pale areas of variable sizes. Microscopically those areas show villi surrounded by dense, eosinophilic but almost acellular stroma with absence of vessels. The villi are normally spaced and intervillous spaces are not collapsed. Another pattern is villous stromal vascular karyorrhexis. It is recognised by karyorrhexis of fetal cells e.g stromal cells, endothelial cells and blood cells. In this, villi are more cellular than in vascular terminal villi, with degeneration of fetal capillaries and fragmentation of red blood cells. Fetal vascular obstruction (due to thrombotic disease) is associated with stasis, hypercoagulability or vascular damage. It may be remembered that 50 – 60% placental mass damage can cause intrauterine or intrapartum fetal death.

b) Subamniotic Haematomas:
They are collections of liquid blood between amnion and chorion of fetal plates. It is the result of trauma to the chorionic plate vessels, during the delivery of the placenta; hence it may form during or after the delivery. They are dark red and soft to feel and beneath the thin amniotic membrane. As majority is noticed after the delivery they are hardly of clinical significance.

CIRCULATORY DISORDERS:
1. Infarcts.
2. Massive perivillous fibrin deposition.
3. Maternal floor infarcts.
4. Subchorionic fibrin deposition.
5. Retroplacental thrombohaematoma.
6. Intervillous thrombohaematoma.
7. Subamniotic haematoma.
8. Marginal haematoma.
9. Massive subchorial thrombosis.
10. Fetal thrombotic vasculopathy.
11. Chorangiomas.
12. Chorangiosis.

Subchorionic Fibrin Deposition
It is a common condition. The deposit is firm, oval, tan white, raised plaques of the fetal surface of placenta beneath the amnion and chorion. The cut surface shows laminated appearance beneath the membranes but above the villious tissue. Microscopically it shows a layer of blood and fibrin beneath the chorion. It may be mentioned that subchorionic fibrin plaques are clinically insignificant.

Retroplacental Thrombohaematomas (RTH)
This is seen in about 4.5% of placentas. They are organized blood clots beneath the maternal surface of placenta that indents the surface. Recent RTH are soft red and can be easily dislodged and can be seen on gross examination in the specimen tray. Older RTH is firm brown and adherent and shows an induration. Morphologically it shows an organizing blood clot and fibrin. Sometimes underlying placental parenchyma may be infarcted. This is due to the duration of RTH that is an important cause of still birth.

Intervillous Thrombohaematomas (IVTHs)
IVTHs are very common, seen in 50% of normal placentas and much more than placentas of complicated pregnancies. Grossly they are rounded, circumscribed and very firm. The cut surface shows a laminated appearance. Recent IVTHs are red and as the age advances they becomes whitish. Their location is between the fetal and maternal surface. Microscopical examination shows layer of red blood cells and fibrin. A rim of infarcted villous tissue may be seen at the periphery.

MARGINAL HAEMATOMA (MH)
MH occurs in about 2% of placentas. They appear wedge shaped clots at the margin of placenta at the junction of the fetal membrane to the placental disc (Fig 1.11). MH clinically is not significant.

Massive Subchorial Thrombosis
This is also called Breu's mole. It is a rare abnormality seen even in less than 1 in 1000 placentas. It is red and is about 1 cm in size. It is located immediately beneath the chorionic plate. Under the microscope it appears like an organizing blood clot. How it occurs is not clear.

Chorangiomas have been discussed else where (see the index).

PLACENTAL INFECTIONS
Infections of placentas can be discussed under two patterns depending upon the routes through which the infections occur i.e. ascending and transplacental routes. In any infection placenta shows acute and more frequently chronic inflammation within the villi termed as villitis that may be of unknown aetiology.

1. *Ascending placental infections:*
Ascending infections are most common and are typically caused by bacteria. They result in inflammation of membranes, chorioamnionitis and that of umbilical cord called funisitis. The causative organisms i.e bacteria include both aerobic and anaerobic bacteria. Some of the bacteria that cause infection of placenta are:
a) Group B streptococci.
b) Coliform bacteria.
c) Mycobacterium tuberculosis.
d) Compylobacter fetus.
e) Mycoblasma.

These infections are initiated from curvix, utrine soft tissue and complicate about 4% of term deliveries but a much higher number of preterm deliveries. Both the mother and the fetus respond to infective agents. The neutrophils from maternal blood emigrate from vessel in decidua through chorion and then amnion. They also emigrate from the umbilical cord vessels (fumigitis). In term gestation there is likelihood of developing chorioamnionitis (after the rupture of membrane).

In the preterm gestation chorioamnionitis preceedes and contributes to the membrane rupture. This acute inflammation can be associated with adverse fetal outcome e.g. neonatal sepsis, chronic lung disease, and necrosing enterocolitis.

2. *Transplacental infections:*
Transplacental infections result from haematogenous routes, the mother being the source. They are usually caused by viruses or protozoa (The Torch organisms) such as:

a) cytomegalo virus.
b) Herpes simplex virus (EBV; varicella zoster).
c) Parvovirus.
d) HIV.
e) Treponema pallidum.
f) Toxoplasma gondii.
g) Histeria monocytogenes.
h) Rubella.
i) Mycobacterium tuberculosis.

Here it may be pointed out; that there are many defenses against infections. Some of such defenses include:

- Anatomical barrier that limits access:
  - Cervical canal and its contents.
  - Decidualised endometrium.
  - Uterine myometrium.
  - A continuous layer of trophoblasts separating maternal immunity in the form of protective antibodies.
- Pre existing maternal immunity in the form of protective antibodies.

Morphological Changes in Placentas
In tissue the infection spreads transplacentally, it is called villitis. Grossly, placenta shows no specific changes except occasionally small yellow nodules on the fetal surface. Microscopically the villi usually are infiltrated with lymphocytes, sometime plasma cells and neutrophills. Occasionally multinucleated giant cells are seen. The villitis may be associated with necrosis (necrotizing villitis) and destruction of trophoblastic membrane with fibrin deposition. The fibrinous deposition causes the villi to agglutinate and is recognized on the scanner of the microscope. Usually villitis is randomly distributed in the placenta; however at times they involve basal villi. The most common transplacental infections are caused by cytomegatovirus; Herpes simplex virus; Parvovirus B_{19}; Human immunodeficiency virus (HIV); Syphilis, Toxoplasma gondii; Listeria monocytogenes (Fig. 1.12 and 1.13).

PATHOLOGICAL FEATURES OF FETAL SURFACE IN INFLAMMATION
Grossly the inflammatory exudate imparts a diffuse dull opaque colour. A prominent green yellow discolouration of membranes is also seen. Microscopical features include maternal inflammatory response in various forms and intensity. For the purpose of descriptions they are grouped into:

Stage I (Early response)

- Acute subchorionitis
- Acute chorionitis

} Characterised by maternal neutrophils in subchorionic membrane

Stage II (Intermediate response)
- Acute chorioamnionitis (maternal neutrophils are in the connective tissues of chorionic plate).

Stage III (Late response)
Necrotising chorioamnionitis:
- Hyper eosinophilia of amnion basement membrane.
- Karyorrhexis of neutrophils.
- Necrosis.
- Sloughing of amnionic epithelial cells.

Inflammatory Lesions of Placenta
- Acute chorioamnionitis.
- Subacute chorioamnionitis.
- Chronic placentitis (TORCH type).
- Acute Villitis (Herpes virus, syphilis, Toxoplasmosis).
- Chronic intervillositis (viral, parasitic, fungal).

Idiopathic inflammatory lesions
- Chronic villitis.
- Chronic idiopathic villitis (maternal T-lymphocytes).
- Intravillositis (maternal macrophages – histiocytosis).
- Chronic deciduitis.
- Maternal plasma cells (lymphoplasmacytic cells).

Acute Fatty Liver of Pregnancy
Acute fatty liver of pregnancy can lead to maternal hepatic failure (1:10,000 pregnancies).

Presentation (in 3rd trimester):
- Jaundice.
- Nausea.
- Coagulopathy.
- Vomiting.
- Profound hyperglycaemia.
- Encephalopathy.
- Epigastric pain.
- Bleeding – death.

Microscopically shows centrilobular steatosis and necrosis.

Placenta and Clinical syndromes
- Essential hypertension (pregnancy induced hypertension).
- Pre-eclampsia (PIH and 1 + or more proteinuria).
- Eclampsia (pre eclampsia + seizure).
- HELLP syndrome: It consists of:
  - Pre eclampsia
  - Maternal RBCs haemolysis
  - Liver enzymes elevation
  - Platelets count – low.

Maternal Thrombophilia
Maternal thrombophilia includes:
- Deep vein thrombosis (DVT).
- Pulmonary infarcts.
- Cerebral vascular accidents (CVA).

Venous thromboembolism is the major maternal risk, however arterial thrombosis can also occurs. This has a strong association with severe pre-eclampsia and diabetes mellitus. Some adverse pregnancy results can be seen in women with thrombophilia. The faetus of a mother with thrombophilia can result in fetal growth restriction or even still birth. Some children can have perinatal or even prenatal coagulation abnormalities. In addition placentas show lesions of maternal thrombophilia i.e. thrombotic vasculopathy, infarction, haematomas and abruption. The major maternal risk is venous thromboembolism, however arterial thrombosis also occurs.

Maternal Anaemias
In anaemias the placental site trophoblasts invades more deeply than in normal placentas. This is contrary to the changes in pre eclampsia. Premature birth is more common. When anaemia is of sickle cell type, it results in placental infarcts. Placenta and faetus are usually smaller than the gestational age. Sometimes placenta may be larger than its gestational age. The villous volume is also reduced. In maternal sickle cell anaemias infarcts can be very common. In addition abruption can occur. Sometimes mother may be thallassaemic. This is due to defective fetal Hb formation. A very anaemic mother can result into hydrops fetalis and even death. The pathological changes in placenta and fetus in maternal homozygous α-thalassaemia and β-thalassaemia differ. Both the placenta and fetus are hydropic. Fetal death occurs in utero / soon after birth. In β thalassaemia placenta and fetus are normal at birth but infant becomes severely anaemic soon. Pregnancy in β-thalassaemia is seen rarely.

GESTATIONAL TROPHOBLASTIC NEOPLASIA

Trophoblastic tissue, like other organs is capable of forming neoplastic lesions. These lesions are divided into those with villi and those without villi. In addition they have also been classified by World Health Organisation. This is as follows.
- Hydatidiform mole.
  - Complete hydatidiform mole.
  - Partial hydatidiform mole.
- Invasive hydatidiform mole.
- Choriocarcinoma.
- Placental site trophoblastic tumour.
- Trophoblastic lesions (Miscellaneous).
  - Exaggerated placental site.
  - Placental site nodule or site.
- Unclassified trophoblastic lesion.

HYDATIDIFORM MOLES

As shown in the classification they may be complete or partial and almost always occur in the reproductive age groups but rarely in post menopausal age. Their risk factors include a personal or family history of gestational trophoblastic disease, two or more previous spontaneous abortions, infertility, smoking and increased maternal age.

Morphological Features
- Grossly evident hydropic villi (vesicles) are characteristic, but on curettage may not be visible (Fig 1.14).

- Cardinal histological features include:
  - Diffuse villous hydrops of variable degree.
  - Diffuse trophoblastic hyperplasia.
  - Hydropic villi are irregular in shape and are of variable sizes (particularly in the first trimester).
  - Villi also show club like extension.
  - Some villi show small cavities.
  - Cytotrophoblasts may show a marked nuclear variations – pleomorphism.

- The syncytiotrophoblasts (contain cytoplasmic vacuoles) for protrusions from the villous surface.

PARTIAL HYDATIDIFORM MOLE (PM)
Partial mole's incidence varies from as common as complete mole to thrice its incidence. Women with PM present with late first trimester bleeding. The uterus may be small or even normal for dates.

Morphological Features
Grossly the examination shows normal appearing immature placental tissue mixed with vesicles which are small and less numerous.

Microscopically
- Two distinct populations of villi, enlarge hydropic villi and fibrosing villi.
- Markedly irregular villi.
- Villi are irregular and show stromal invasion. Villi with central cavities are less common.
- Hyperplastic villous trophoblasts.
- Stromal blood vessels include undated red blood cells. They occur during second trimester.

Behaviour: Tumour persists in < 1% of cases. Rarely partial mole become invasive and even undergoes metastases. Very rarely it develops into choriocarcinoma, placental site trophoblastic tumour or epithelioid to true trophoblastic tumour.

CHORIOCARCINOMA
Choriocarcinoma is twice as common in blacks than the whites. The incidence is 20 – 40 times higher in Asia and Africa and Latin America. It is seen as 1 in > 20,000 pregnancies. Choriocarcinoma is preceded by complete mole in about 50% cases; abortion in 25%, normal pregnancy is about 22% and rarely ectopic pregnancy. In exceptional cases choriocarcinoma was found in term placenta (usually as an incidental finding).

Clinically the most common presentation is vaginal bleeding and raised serum hCG levels. When confined to the myometrium it may be asymptomatic. Many patients come with metastases in lung, liver, brain, kidney, gastrointestinal tract and even skin (Fig. 1.15).

Pathological Features
Grossly: The tumour is red to brown and fleshy in appearance with areas of necrosis and haemorrhages. Myometrium may be replaced by a destructive invasive process. Rarely it can occur in cervix. The tumour may be very small in size.

Microscopically: The choriocarcinoma may be detected only as a small tumour i.e. < 3 cm. It is a combination of cytotrophoblasts and syncytiotrophoblasts, the latter are usually vacuolated. The syncytiotrophoblasts have densely eosinophilic cytoplasm. Villi are absent. Myometrium is invaded by these cells. Post chemotherapy survival is in the region of 90%. These tumours in term placenta may have metastatic tumours in mother or infant.

In the end it will be appropriate to say that **placenta is not an organ to throw away**. The attending obstetrician needs to give **three** minutes to examine placenta physically and better if it is done so after considering the obstetrical history and clinical findings of the previous obstetrical history and if there are any events such as hypertension, proteinuria, infection or diabetese mellitus in it. If 2 – 3 minutes are spent on placenta one can extract may be a very useful information for the wellfare of the mother and the patients.

I should close here praying that you may get into the habit of examining placentae and usefully spend these 2 – 3 minutes.

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