Best Practice No 178

Examination of the human placenta

B Hargitai, T Marton, P M Cox

The human placenta is an underexamined organ. The clinical indications for placental examination have no gold standards. There is also inconsistency in the histological reports and the quality is variable. There is great interobserver variability concerning the different entities. Although there are still grey areas in clinicopathological associations, a few mainstream observations have now been clarified. The histopathological examination and diagnosis of the placenta may provide crucial information. It is possible to highlight treatable maternal conditions and identify placental or fetal conditions that can be recurrent or inherited. To achieve optimal benefit from placental reports, it is essential to standardise the method of placenta examination. This article summarises the clinical indications for placenta referral and the most common acknowledged clinicopathological correlations.

According to the guidelines of the Royal College of Pathology, samples of diagnostic value removed from the human body should be histologically examined, with only a few exceptions. One of the exceptions is the healthy human placenta, but even with valid indications the human placenta is one of the most underexamined specimens. There is also evidence that the quality of reports on the investigation of the placenta is very variable. According to a recent study, there is a considerable discrepancy rate in the diagnosis of placental disease, and it is common for general surgical pathologists not to recognise placental lesions that may have clinical relevance. In this best practice article, we summarise those circumstances in which it is recommended that the placenta should be examined, the minimum criteria of sampling, and the acknowledged clinicopathological correlations.

“It is common for general surgical pathologists not to recognise placental lesions that may have clinical relevance”

Lesions of the placenta often reflect or explain the condition in which the baby was born and some have clinicopathological implications. However, in most cases, there is no clinicopathological relevance to a placental examination, such as in the case of normal pregnancy and delivery.

CLINICAL APPROACH

What do we expect from the pathological examination?

The placenta forms a functional unit between the mother and the fetus. Therefore, any pathological event that concerns the mother or the fetus will influence the normal function of the placenta, occasionally resulting in morphological change. Severe abnormalities of the placenta may lead to adverse fetal outcome. However, placental lesions are not necessarily the cause of unfavourable outcome, and some structural changes may be the consequences of poor fetal condition. The placenta is an easily available specimen and the costs of a routine pathological examination are moderate.

The benefits that can be expected from the examination include revealing the aetiology of stillbirth, preterm delivery, intrauterine growth restriction (IUGR), and neurodevelopmental impairment. It may be possible to decide whether the pathological condition that endangered the well being of the fetus was an acute or a chronic process.

In the case of twin pregnancies, the type of twinning can be identified and pathological aspects of twin pregnancy (for example, twin-to-twin transfusion syndrome) can be studied. Conditions with the risk of recurrence can be recognised, resulting in adequate treatment and preventive measures during subsequent pregnancies.

Placental examination may have medicolegal aspects—for example, concerning the aetiology of longterm neurodevelopmental sequelae or the approximate timing of an intrauterine death.

Which placentas should be examined?

There are different approaches to the examination of the placenta. It would produce a pointless increase in workload if all placentas, including those from normal pregnancies and normal deliveries resulting in a healthy infant, were examined in a routine pathology laboratory setting.

Because it is the decision of the midwife and/or obstetrician which placentas to send to the pathology laboratory, there should be standardised sampling criteria and guidelines for referral to the laboratory.

Abbreviations: AAA, arterio–arterial anastomosis; AVA, arterio–venous anastomosis; IUGR, intrauterine growth restriction; VVA, veno–venous anastomosis
pathology department, a clinically oriented approach (fig 1) may be used to define the indications for histopathological examination.

Referral is not indicated for:

- cholestasis of pregnancy
- hepatitis B, human immunodeficiency virus, etc
- other maternal disease with normal pregnancy outcome
- normal pregnancy
- placenta praevia
- postpartum haemorrhage.

A RATIONAL SORTING OF THE REFERRED PLACENTAS

Figure 2 is an algorithm for selecting which of the referred placentas should be subjected to further study. Figure 3 contains a recommendation for sampling the placentas based on the clinical context.

NORMAL VARIANTS

As mentioned above, many features can be judged only in the clinicopathological context. This is partly because of the loose correlation between some histological changes and clinical symptoms, and partly because of the large reserve capacity of the placenta.

To record the macroscopic appearance of the placenta we recommend the use of a worksheet as shown in fig 4. This proforma can be useful to describe normal placentas; however, each abnormality should be documented individually.

Umbilical cord

The normal length of the umbilical cord at term varies between 40 and 70 cm and cords of less than 32 cm are considered to be short and those more than 100 cm are considered long. The importance of length and coiling should be treated cautiously, because the proportion of the umbilical cord received in pathology laboratories varies and is thus not reliable. Umbilical cords normally show a degree of coiling. The normal coil index is said to be one coil/5 cm.\textsuperscript{91} 0 The normal cord contains three vessels, and this has to be assessed at least 5 cm from the placental insertion.\textsuperscript{11} False knots may be the site of thrombosis, or rarely bleeding, but most often they have no clinical relevance.

Embryonic remnants of the vitelline duct and urachus are normal findings. Cysts may arise from these vestigial remnants. It may be necessary to differentiate the embryonic remnants of the cord from teratomas and haemangiomas.\textsuperscript{12}
Extraplacental membranes and the fetal surface

The importance of circummarginate and circumvallate placentas is uncertain, although an association with IUGR and acute and chronic maternal haemorrhage has been proposed in circumvallate placentas. Amnion nodosum (granular grey/white nodules, consisting of keratin and vernix) are a sign of oligo/anhydramnios, but squamous metaplasia of the amnion is a normal feature.

A small amount of subchorionic fibrin deposition (Langhans fibrinoid) is not pathological, because it accumulates from eddying of the intervillous flow.

Placenta

A low placental weight is found in “small for gestational age” placentas. Normal values of fetal to placenta weight ratio change during the course of gestation, and vary between 1 at 14 weeks and 7.23 at term. Hydrops or congestion can result in a high placental weight, but the placenta weight can vary to some degree (a table of normal values can be found in Benirschke and Kaufmann13). Deviation from the round or oval shape such as an irregularly shaped, bilobed, or multilobed placenta can be attributed to disturbed implantation, but it can be assessed only in the clinicopathological context. Increased calcification has been mentioned in association with maternal smoking and high socio-economic status, but the feature itself has no clinical relevance.

Minor perivillous fibrin deposition is almost always present in term placentas. This is of no clinical relevance if marginal, or if it does not exceed 10% of the villous tissue. A range of values is found in the literature with regard to the amount of the villous tissue loss required to define whether infarction or

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### Table: Indications to examine the placenta

<table>
<thead>
<tr>
<th>Group 1: full examination</th>
<th>Recommended minimum samples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1A</strong></td>
<td><strong>Group 1A</strong></td>
</tr>
<tr>
<td>Rhesus isoimmunisation with admission to the NNU</td>
<td>Umbilical cord x 2</td>
</tr>
<tr>
<td>Any IU anaemia requiring IU transfusion</td>
<td>Membrane roll x 1</td>
</tr>
<tr>
<td>Morbidity adherent placenta</td>
<td>Representative lesions (if any)</td>
</tr>
</tbody>
</table>

| **Group 1B** | **Group 1B** |
| Maternal pyrexia | Umbilical cord x 3 (x 2 if < 10 cm) |
| Prematurity (< 34 weeks and not PET/IUGR) | Membrane roll x 1 |
| Severe fetal distress, admission to the NNU | Representative lesions (if any) |
| Neonatal infection | Paracentral (i.e. not marginal), grossly normal placenta including fetal and maternal surface x 3 |

| **Group 1C** | **Group 1C** |
| IUGR | Umbilical cord x 2 |
| Prematurity (< 34 weeks) due to PET/IUGR | Membrane roll x 1 |
| Severe PET | Representative lesions (if any) |
| Abruptio | Paracentral (i.e. not marginal), grossly normal placenta including fetal and maternal surface x 3 |
| Spiral artery blocks | Spiral artery blocks |

| **Group 1D** | **Group 1D** |
| Hydrops | As 1A, with special investigations if necessary |
| Fetal anomaly | |
| Stillbirth | |

**Group 2: macroscopic examination only and afterwards storage (unfixed, 2 weeks, 4°C, urgent examination on clinical request)**

Abnormal shape

Single umbilical artery

Uncomplicated twin pregnancy

**Group 3: storage (unfixed, 2 weeks, 4°C, urgent examination on clinical request)**

PROM

Prematurity, 34–36 weeks

Gestational diabetes

Rhesus negative mother

Maternal group B streptococcus

Uncomplicated pre-eclampsia
perivillous fibrin deposition is “extensive” or relevant—that is, large enough to account for adverse fetal outcome. The reported percentage of minimal villous tissue loss ranges from 10% to 30% in the case of significant placental infarcts and 20% to 30% in perivillous fibrin deposition. In general, there is no clinical relevance if the lesion is single, marginal, and/or involves less than approximately 5% of the villous tissue. Obviously, the functional reserve capacity of the placenta depends not only on the quantity, but also on the quality of the uninvolved tissue and the original size of the placenta. In the case of a small placenta, a smaller amount of parenchymal loss can lead to fetal demise or morbidity.

X cell islands (extravillous cytotrophoblast islands, X-cell proliferation) are considered to be a normal feature.

The origin of septal cysts is unknown. They are reported to occur more frequently in oedematous placentas, but are of no clinical relevance.13

Examination of twin placentas
Twin placentas should be labelled after the delivery to identify which cord belongs to which fetus. The examination of placentas from multiple gestations should establish the choriocicity of the sample and whether there are signs of twin-to-twin transfusion syndrome. Separated twin placentas have to be examined in the same way as those of singletons. Fused placentas can be monochorionic or dichorionic. The dividing membrane should be studied to identify the choriocicity. The dividing membrane in monochorionic pregnancy is thin and translucent (with no

Figure 4  Worksheet for macroscopic examination. DiDi, dichorionic diamniotic; DiMo, diamniotic monochorionic; MoMo, monochorionic monoamniotic.
### Table 1  The clinical relevance of placental abnormalities

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Clinicopathological correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Umbilical cord</strong></td>
<td></td>
</tr>
<tr>
<td>Short cord (less than 40 cm)</td>
<td>High fetal and neonatal mortality rates and increased frequency of neurological abnormality.</td>
</tr>
<tr>
<td>Long cord (larger than 70 cm)</td>
<td>Maternal factors: systemic diseases, delivery complications, increased maternal age. Fetal factors: non-reassuring fetal status, respiratory distress, vertex presentation, cord entanglement, male sex, increased birth weight. Gross placental features: increased placental weight, overcoiled cord, true knots, congestion, cord prolapse causing fetal distress.</td>
</tr>
<tr>
<td><strong>Marginal cord insertion</strong></td>
<td>IU Gronst, still birth, neonatal death, premature birth, low birth weight.</td>
</tr>
<tr>
<td><strong>Vesiculation of the cord</strong></td>
<td>Fetal demise intolance to labour, IU Gronst, chronic amnionitis.</td>
</tr>
<tr>
<td><strong>Syncytiotrophoblast villous</strong></td>
<td>If tight, associated with perinatal mortality of 10% and umbilical vessel thrombosis.</td>
</tr>
<tr>
<td><strong>Villous stromal fibrosis and sclerosis</strong></td>
<td>Single umbilical artery is associated with fetal malformation chromosome aberration in 25–50%, with IU Gronst and increased perinatal mortality in normally formed infants.</td>
</tr>
<tr>
<td><strong>Thrombosis of umbilical cord vessels</strong></td>
<td>Thromboembolic spread to placental or fetal vessels. The consequences of cord vessel thrombosis for the fetus may be wide. Severe sequelae such as fetal death, cerebral palsy and IU Gronst have been described, but delivery of a healthy, live neonate may also occur.</td>
</tr>
<tr>
<td><strong>Placental abnormalities</strong></td>
<td>Umbilical cord vasculitis and funisitis are associated with cord vessel thrombosis, preterm delivery, amniotic infection, vassopasm of cord vessels.</td>
</tr>
<tr>
<td><strong>Membranes</strong></td>
<td>It is often associated with premature rupture of the membranes, perterm labour, IU Gronst, intrauterine death. Usually seen with acute chorioamnionitis.</td>
</tr>
<tr>
<td><strong>Acute chorioamnionitis (including &quot;subchorial intervillitis&quot;)</strong></td>
<td>Strong association with premature rupture of membranes and perterm delivery. Fetal intrauterine infection may occur. Maternal fever and tachycardia are described, but may be asymptomatic. Recently, chorioamnionitis has been implicated as a risk factor for periventricular leukomalacia and cerebral palsy.</td>
</tr>
<tr>
<td><strong>Chronic chorioamnionitis</strong></td>
<td>Association with premature rupture of membranes, preterm delivery, and prolonged rupture of membranes has been observed. It has been described in herpes virus infection.</td>
</tr>
<tr>
<td><strong>Amnion epithelial vacuolisation</strong></td>
<td>Cell degeneration and necrosis of amniotic epithelial cells can be observed in normal and abnormal pregnancies and the evaluation of these alterations might be fairly uncertain because of artefact effects. Small, lipid containing vacuoles in the cytoplasm are the feature, strongly associated with gastritis.</td>
</tr>
<tr>
<td><strong>Pigmented macrophages, meconium staining</strong></td>
<td>The presence of meconium staining is not necessarily associated with adverse fetal outcome. Meconium staining indicates the danger of meconium aspiration and with other pathological signs of fetal distress may underlie the diagnosis. Vassopasm of cord vessels and fetal choriatic vessels is reported as a consequence of meconium exposure.</td>
</tr>
<tr>
<td><strong>Deciduitis, acute deciduitis, chronic decidual necrosis</strong></td>
<td>Acute deciduitis in the decidua capsularis is often associated with ascending infections of the placental membranes, and may be unimportant in isolation. Severe, necrotising, acute deciduities can be found in placentas with retroplacental haematomata. Chronic deciduitis with scattered infiltration may represent a physiological condition of maternal lymphocyte response.</td>
</tr>
<tr>
<td><strong>Placenta</strong></td>
<td>IU Gronst, pre-eclampsia, increased intervillous fibrin deposition, villitis of unknown origin, and trisomy.</td>
</tr>
<tr>
<td>Low placental weight, below 10th centile for gestational age</td>
<td>Maternal diabetes mellitus, maternal or fetal anaemia, fetal hydrops; may also be seen in congenital syphilis, Beckwith-Wiedemann syndrome, congenital nephrotic syndrome.</td>
</tr>
<tr>
<td>High placental weight</td>
<td>Average thickness less than 2 cm, placenta with large membranous area, high incidence of maternal bleeding, placenta praevia, placenta accreta. Often premature delivery occurs. Possibly more frequent in IU Gronst and maternal smokers.</td>
</tr>
<tr>
<td>Thin placenta (placenta annulare or placenta membranacea)</td>
<td>IU Gronst and maternal smokers.</td>
</tr>
<tr>
<td>Placental haemorrhage</td>
<td>Large retroplacental haematomata can cause extensive infarction involving a significant proportion of the villous tissue to cause fetal hypoxia or lead to placental hypoxia.</td>
</tr>
<tr>
<td>Retrolental haemorrhage</td>
<td>This is a normal finding when patchy, focal, or diffuse. However, subchorionic thromboses of large size have been reported in association with abortion, premature delivery, and live-born infants also potentially life threatening clinical conditions, causing uterine rupture and massive postpartum haemorrhage, or leading to caesarean section if prenatally diagnosed. It is often an indication of postpartum hysterectomy because of excessive bleeding. To make the pathological diagnosis of a placenta accreta, examination of the entire uterus is necessary.</td>
</tr>
<tr>
<td>Subchorionic haemorrhage (massive subchorial thrombosis, Breus's mole)</td>
<td>IU Gronst, stillbirth, pregnancy induced hypertension, IU Gronst, pre-eclampsia, hypertension, diabetes mellitus, maternal diabetes, maternal or fetal anaemia, fetal hydrops.</td>
</tr>
<tr>
<td>Placenta praevia</td>
<td>Placentas with retroplacental haematomata. Chronic deciduitis with scattered infiltration may represent a physiological condition of maternal lymphocyte response.</td>
</tr>
<tr>
<td>Placenta accreta</td>
<td>IU Gronst, pre-eclampsia, increased intervillous fibrin deposition, villitis of unknown origin, and trisomy.</td>
</tr>
<tr>
<td>Placenta increta, placenta percreta</td>
<td>Maternal diabetes mellitus, maternal or fetal anaemia, fetal hydrops; may also be seen in congenital syphilis, Beckwith-Wiedemann syndrome, congenital nephrotic syndrome.</td>
</tr>
<tr>
<td>Placenta accreta, increta, and percreta</td>
<td>IU Gronst and maternal smokers.</td>
</tr>
<tr>
<td>Placenta accreta, increta, and percreta</td>
<td>IU Gronst, pre-eclampsia, increased intervillous fibrin deposition, villitis of unknown origin, and trisomy.</td>
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<tr>
<td>Placental abnormalities</td>
<td>Maternal diabetes mellitus, maternal or fetal anaemia, fetal hydrops; may also be seen in congenital syphilis, Beckwith-Wiedemann syndrome, congenital nephrotic syndrome.</td>
</tr>
<tr>
<td>Placenta praevia</td>
<td>IU Gronst, stillbirth, pregnancy induced hypertension, IU Gronst, pre-eclampsia, hypertension, diabetes mellitus, maternal diabetes, maternal or fetal anaemia, fetal hydrops.</td>
</tr>
<tr>
<td>Placenta accreta, increta, and percreta</td>
<td>IU Gronst and maternal smokers.</td>
</tr>
<tr>
<td>Placental choriatic villi and intervillous space abnormalities</td>
<td>Increased numbers of syncytiotrophoblast knots occur in: pre-eclampsia, hypertension, diabetes mellitus, maternal anaemia, pregnancy at high altitude, thick section (artefact). A correlation between increased syncytiotrophoblast knots and fetal hypoxia has not been reported. An excessive increase of syncytiotrophoblast knots may result from reduced fetal perfusion and placental hypoxia or can be the sign of accelerated maturation if the duration of pregnancy was less than 40 weeks.</td>
</tr>
<tr>
<td>Syncytiotrophoblast knots</td>
<td>No clinical relevance if it is single, marginal, and/or involves less than about 5% of the villous tissue. Involving more than 10% of villous tissue: fetal hypoxia, IU Gronst, stillbirth, pregnancy induced hypertension, IU Gronst, prenatal diagnosis of IU Gronst, IU Gronst.</td>
</tr>
<tr>
<td>Infarct (acute or old)</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>Extensive placental infarction</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>Nucleated RBC</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>Villous basal membrane thickening</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>VSM deficiency</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>Villous stromal fibrosis and sclerosis</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>Villous oedema</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
<tr>
<td>Dysmaturity/immaturity</td>
<td>IU Gronst, stillbirth, acute fetal blood loss, maternal diabetes, and erythroblastosis fetalis.</td>
</tr>
</tbody>
</table>

**Notes:**
- IU = Infarct, U = Umbilical, VSM = Vascular Smooth Muscle
- IU Gronst is a condition where the placenta is partially or completely included in the uterus.
- Pre-eclampsia is a pregnancy complication characterized by high blood pressure and proteinuria.
- Diabetes mellitus is a chronic condition involving the body's inability to properly use or produce insulin.
- Hypothyroidism is a condition where the thyroid gland does not produce enough thyroid hormones.
- Maternal anaemia is a condition where a woman has a low number of red blood cells or haemoglobin.
- Fetal hydrops refers to the presence of excess fluid in the fetal tissues.
- Congenital anomalies are structural abnormalities present at birth.
- Placenta praevia refers to the placenta being located at the lower end of the uterus near the cervix, which can cause complications during delivery.
- Placenta accreta is a condition where the placenta adheres too strongly to the uterine wall.
- Placenta increta is a condition where the placenta invades the muscle layer of the uterine wall.
- Placenta percreta is a condition where the placenta invades through the uterine wall and into other pelvic organs.
- Preterm labour is the onset of labour before the expected date of delivery.
- Fetal death is the death of a fetus before or during birth.
- Low birth weight is defined as a birth weight of less than 2500 grams.
- Chorioamnionitis is an inflammation of the chorion and amnion, which are two layers of the membranes that surround the fetus in the uterus.
- Umbilical cord is a collection of blood vessels that connect the fetus to the placenta.
- Fetal hydrops is a condition where the fetus has excessive fluid accumulation.
- Essential hypertension is a chronic high blood pressure condition not caused by any other medical condition.
- Maternal diabetes mellitus is a condition where blood sugar levels are higher than normal due to problems with insulin production or action.
- Maternal smoking is the practice of smoking cigarettes or other tobacco products during pregnancy.
- Advanced maternal age refers to women who are 35 years or older at the time of delivery.
- Maternal heart failure is a condition where the heart is unable to pump enough blood to meet the body's needs.
- Thromboembolic disease is a condition where blood clots form in blood vessels and can cause damage to the body.
- Preterm delivery is the delivery of a baby before the gestational age of 37 weeks.
Acute transfusion occurs either during labour or after the delivery of the recipient twin. This flow may lead to acute or chronic twin-to-twin transfusion. Chronic twin-to-twin transfusion occurs more frequently in monochorionic placentas. Imbalance in the blood flow between the co-twins may be identified by the presence of an impaired vessel from one twin feeding an area drained by the co-twin. In monochorionic placenta, arteries may be identified in fresh specimens to clarify the type of the anastomosis. Arterio–venous anastomoses (AVA) are associated with poor outcome. The anatomical background of chronic twin-to-twin transfusion syndrome seems to be a unidirectional arteriovenous shunt between the donor and the recipient twin. Injection studies can be performed in fresh specimens to clarify the type of the anastomosis. In fixed placentas, arteries may be identified by the fact that they are always superficial to the veins.

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A properly oriented T section is the best sample to prove chorionicity.
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### Table 1

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Clinopathological correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced maturation/maturitas praecox</td>
<td>Accelerated maturation can be seen in prematurely delivered placentas in pre-eclampsia. It is considered to be an ischaemic feature.</td>
</tr>
<tr>
<td>Mesenchymal dysplasia</td>
<td>Associated with Beckwith-Wiedemann syndrome.</td>
</tr>
<tr>
<td>Perivillous fibrin deposition</td>
<td>When more than 20–30% of the villous tissue and functional placenta is involved it is associated with IUGR and fetal death. In these cases often 70–80% of the villous population is enveloped by fibrin. The maternal serum AFP values is raised, sometimes extremely so.</td>
</tr>
<tr>
<td>Maternal floor infarct, Gitter infarct</td>
<td>Massive basal plate perivillous fibrin deposition is termed “maternal floor infarct” and is associated with high mortality and IUGR. Massive perivillous fibrin deposition in a netlike pattern is the “Gitter infarct”. Neither of these is an infarct. Massive perivillous fibrin can recur (18%) and is associated with IUGR and fetal death.</td>
</tr>
<tr>
<td>Villitis</td>
<td>Clinical consequences depend on the type of the pathogenic agent. Acute villitis is usually associated with severe maternal infection, preterm delivery and might lead to intrauterine infection and IUD.</td>
</tr>
<tr>
<td>Acute villitis</td>
<td>Chronic villitis: more often of unknown aetiology (VUE) than known. Fetal infections causing chronic villitis: CMV, toxoplasma, connatal syphilis. Chronic villitis is associated with: IUGR and/or stillbirth.</td>
</tr>
<tr>
<td>Chronic villitis: basal, parenchymal, granulomatous, and VUE</td>
<td>VUE: IUGR, preterm birth, is often recurrent.</td>
</tr>
<tr>
<td>Chronic histiocytic villitis, perivillous fibrin deposition</td>
<td>Associated with raised maternal serum AFP, recurrent abortion, IUGR, preterm delivery. Malaria infection should be excluded.</td>
</tr>
<tr>
<td>Abnormalities of the fetal vessels</td>
<td>Extensive avascular villi as a result of fetal vessel thrombosis was reported in association with stillbirth, IUGR, maternal and fetal coagulopathy, and fetal thromboembolic disease leading to cerebral palsy.</td>
</tr>
<tr>
<td>Fetal chorionic vessel thrombosis and avascular villi</td>
<td>Neonatal asphyxia, association with disseminated capillary thrombi of fetal vessels. The severity of the fetal consequences depends more on the accompanying lesion, than on the cause of the thrombosis.</td>
</tr>
<tr>
<td>Intervillous haemorrhage and thrombus</td>
<td>Most often intervillous haemorrhage is related to a maternal vessel lesion and is of maternal origin. Its consequence can be fetal compromise or death depending on the functional placenta parenchyma loss and the rest of the unaffected placenta.</td>
</tr>
<tr>
<td>Intimal fibrin cushion</td>
<td>Haemorrhages of the placenta: intervillous haemorrhage and intervillous thrombus.</td>
</tr>
<tr>
<td>HEV and haemorrhagic villitis</td>
<td>Perinatal death, congenital malformation, and cerebral palsy were found to be associated with chorangioma as a response to low grade tissue hypoxia. Although others have supported this observation, it is still unclear how chronic hypoxia results in increased vascularity. The importance of this alteration needs further investigation.</td>
</tr>
<tr>
<td>Abnormalities of the maternal vessels</td>
<td>Uteroplacental or decidual arteriopathy is closely related to pregnancy induced hypertension, maternal essential hypertension, and pre-eclampsia, and results in fetal complications such as IUGR, SGA, and stillbirth. It is associated with APA, SLE, and thrombophilia.</td>
</tr>
<tr>
<td>Failure of physiological adaptation of maternal vessels, uteroplacental fibrinoid necrosis</td>
<td>Most often intervillous haemorrhage is related to a maternal vessel lesion and is of maternal origin. Its consequence can be fetal compromise or death depending on the functional placenta parenchyma loss and the rest of the unaffected placenta.</td>
</tr>
<tr>
<td>Acute atherosis, uteroplacental vessel thrombosis</td>
<td>In some cases, intervillous haemorrhage and thrombus is a sign of fetal bleeding into the maternal circulation, as described by Kline. Only a few of these alterations lead to a large amount of fetal blood loss and stillbirth or severe anemia followed by ischaemic lesions of parenchymal organs.</td>
</tr>
<tr>
<td>Haemorrhages of the placenta</td>
<td>It is important to know the type of twinning because the twin-to-twin transfusion syndrome is associated with diachoronic monochorionic placentas.</td>
</tr>
<tr>
<td>Intervillous haemorrhage and intervillous thrombus</td>
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</tr>
<tr>
<td>Kline’s haemorrhage</td>
<td>Acute villitis is usually associated with severe maternal infection, preterm delivery and might lead to intrauterine infection.</td>
</tr>
<tr>
<td>Twin placenta, chorionicity</td>
<td>Chronic villitis: more often of unknown aetiology (VUE) than known. Fetal infections causing chronic villitis: CMV, toxoplasma, connatal syphilis. Chronic villitis is associated with: IUGR and/or stillbirth.</td>
</tr>
<tr>
<td>Angiomas</td>
<td>Clinical consequences depend on the type of the pathogenic agent. Acute villitis is usually associated with severe maternal infection, preterm delivery and might lead to intrauterine infection and IUD.</td>
</tr>
<tr>
<td>Angioma of the placenta (chorangioma)</td>
<td>Chronic villitis: more often of unknown aetiology (VUE) than known. Fetal infections causing chronic villitis: CMV, toxoplasma, connatal syphilis. Chronic villitis is associated with: IUGR and/or stillbirth.</td>
</tr>
<tr>
<td>Angioma in the cord</td>
<td>Neonatal asphyxia, association with disseminated capillary thrombi of fetal vessels.</td>
</tr>
<tr>
<td>Angioma in the cord</td>
<td>Large lesions often lead to cardiac failure, hydrops, and death of the fetus. Transplacental bleeding and fetomaternal transfusion have been also described, leading to anemia. Chronic villi were reported to be associated with pre-eclampsia, multiple gestation, premature delivery, fetal thrombocytopenia, and fetal anemia (Kasabach-Merritt syndrome).</td>
</tr>
<tr>
<td>The lesion can be associated with raised AFP, fetal DIC, and fetal hydrops; fetal death has been described</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:** AFP, α fetoprotein; APA, anti-phospholipid syndrome; CMV, cytomegalovirus; DIC, disseminated intravascular coagulopathy; HEV, haemorrhagic endovasculitis; IUD, intrauterine death; IUGR, intrauterine growth restriction; NOS, not otherwise specified; RBC, red blood cell; SGA, small for gestational age; SLE, systemic lupus erythematosus; VSM, vasculo–syncytial membrane; VUE, villitis of unknown aetiology.
It is recommended that fused dichorionic placentas should be
separated. Evidence of a vanished twin might be found in
singleton or twin placentas. This varies in appearance from
an amorphous, fibrotic plaque to a well formed fetus
pappaceous. Histological and x-ray examinations are helpful
to identify calcification.46

RECOGNISED CLINICOPATHOLOGICAL
CORRELATIONS

Table 1 summarises the clinical relevance of placental
abnormalities.

CONCLUSION

We recommend that relevant placentas are discussed
regularly at perinatal mortality or morbidity meetings. This
could reveal new clinicopathological correlations, would
increase appreciation of the profession, and would serve
team building and communication between the different
medical teams. We have presented an algorithm of indica-
tions for placental examination and discussed the methods
of histopathological examination. Common placental lesions
with their clinicopathological correlation are reviewed.
Our intent is to outline the acknowledged entities with their
clinical consequences. Often, the clinicopathological cor-
relation appears to be strong, significant, and well documented.
In other instances, lesions may have a tendency to occur
with clinical conditions and in the rest of the cases there
is only an anecdotal association. A major problem with the
literature related to the placenta is that most of it has been
produced based solely on abnormal placentas, so that for
many features it is not clear what is pathologically abnormal
and what is a normal variant. Basic studies are necessary to
analyse normal placentas statistically and to identify the
and what is a normal variant. Basic studies are necessary to
analyse normal placentas statistically and to identify the
normal variants of histological lesions during the course of
pregnancy.

It is also apparent that because function depends on the
reserve capacity of the placenta, several findings can be
decided only in the clinical context: the importance of a
particular lesion depends on its localisation and on the extent
of the lesion (the proportion of the placenta involved and the
size and the condition of the uninvolved placenta). Some
features can be within normal limits in term placentas,
wheras earlier in pregnancy they may be pathological. In
addition, the assessment of the lesions is even more complex
because several pathological conditions can coexist in
the same placenta.

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