Cynthia G. Kaplan

Color Atlas of Gross Placental Pathology

Second Edition

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ЗНАНИЕ

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To my husband Marty
without whose continuing and increasing support this revision
would not have been possible

To Kurt Benirschke
who started me on this path
and remains a friend and continuing resource, and

To the memory of Lauren Ackerman,
who was a great supporter of my work.

Preface to the Second Edition

Interest in the placenta has not waned in the 12 years since the publication of the first edition, and an increasing number of excellent articles and texts are available. While many gross placental abnormalities are included in these references, the need still exists for an illustrated manual of examination.

The material in this book comes completely from my experience in grossly examining virtually all placentas from deliveries at University Hospital in Stony Brook. Since the hospital's opening 25 years ago, there has been marked increase in both high risk and more routine deliveries with an annual total near 4,500.

An appreciation of the spectrum of normal is necessary for the evaluation of abnormal placentas. In this edition, the discrimination of normal variation in the gross placental morphology from the possibly or definitely abnormal will be covered more fully than in the first edition. While many of the original illustrations are still included, there are many new and additional gross photographs.

The move to digital imagery over film has also occurred in the years between editions. Pictures from the first edition and other 2×2 slides have been converted to this format. New images were photgraphed digitally at 4 or 5 megapixels.

Cynthia G. Kaplan, MD

Preface to the First Edition

Careful evaluation of the placenta can often give much insight into disorders of pregnancy in the mother and fetus. It can confirm the clinical suspicion of processes such as hemorrhage or infection, explain problems during labor and lead to specific diagnoses in cases of hydrops, growth retardation, or fetal demise. The placenta also holds clues to the origins of disease unsuspected at birth, manifesting later with significant sequelae. Frequently the placenta has been examined only cursorily and then discarded. This is unfortunate. Many clinically significant macroscopic lesions can be readily identified with a minimum of effort. Additionally, the gross examination often suggests the presence of microscopic abnormalities. Fortunately change is occurring in the handling of placentas. Thorough gross evaluation of placentas from all deliveries is now promoted, with triage for histology of those from pregnancies with significant clinical history or with abnormal initial examination.

The techniques of gross placental examination are not difficult, but a systematic approach is necessary to be complete. While it is possible for others to review microscopic slides, the gross findings will exist only as originally observed and recorded. This book is designed to aid in careful and thorough gross examination by providing the images and vocabulary required. It depicts normal variations and common abnormal findings, with some examples of more unusual pathology as well. Fresh specimens are used predominantly, as placentas are always examined in this state in the delivery room, and frequently in pathology as well. Lesions are presented by site rather than by diseases process, since this is how one actually encounters them in the course of doing the placental evaluation. Important clinicopathologic correlations and related histopathology for major processes are included. Normal tables, selected references, and sample forms are found in the appendices. This material is drawn from the examination of over 20,000 placentas delivered since the opening of University Hospital, Stony Brook in 1980. Gross photography was done in the surgical pathology suite using a copy stand and a 35 mm camera with a Nikon 55 mm 1 : 1 macro lens. Ektachrome 64 and 100 daylight film were used, with processing done on the premises.

Cynthia G. Kaplan, MD

Acknowledgments

I would like to acknowledge the assistance of those individuals in the pathology laboratory who have helped me over the years with my examinations of placentas and encouraged me to write this book and its revision. Many of the alterations in this second edition stem from experiences in teaching residents and pathologists about the placenta and review of placental examinations in medico-legal cases. Much of the original illustrative material is still the work of Media Services at the State University of Stony Brook. Matt Nappo of Pathology did most of the digital photography and conversion to digital format.

Cynthia G. Kaplan, MD

Contents

1

Examination Procedures

Every placenta should be examined, as it reflects disease in the mother and the fetus. Frequently these processes are unsuspected previously. The information the placenta contains is often unavailable from any other source. The necessary examination will vary with the clinical situation and ranges from simple visual inspection to detailed molecular studies.

Site

The two most likely locations for the initial gross examination of the placenta are the delivery room and the pathology suite. This exam need not be done by a pathologist or obstetrician. It can be performed by other trained personnel, such as nurses, or physician's assistants. Further triage is based on the history and the initial evaluation (Figure 1.1). The responsible individual sends all abnormal or potentially abnormal placentas for full gross and microscopic examination. Although the initial triage exam may not be as complete as the gross examination outlined below, it should be reasonably thorough and include assessment of cord length and placental size, as well as careful observation and palpation. In the vast majority of cases, this will take an experienced observer no longer than a couple minutes.

There are maternal, fetal, and placental indications for histology (Table 1.1). The number of placentas examined microscopically will vary with the nature of the obstetrical population, but is unlikely to be less than 15%. The storage of unexamined placentas for several days after delivery allows placenta microscopy in neonates, who develop problems in the first days of life. Using these criteria, most neonates who develop neurologic or other problems later in life will have had their placenta examined. While some of the remaining unexamined placentas will belong to infants who later develop disabilities not predicted from the obstetrical and neonatal history, the vast majority do not. It is unusual for a pathology service to have sufficient manpower to microscopically examine all placentas, or even to archive tissue or blocks for potential microscopy those placentas not initially selected for microscopic examination.

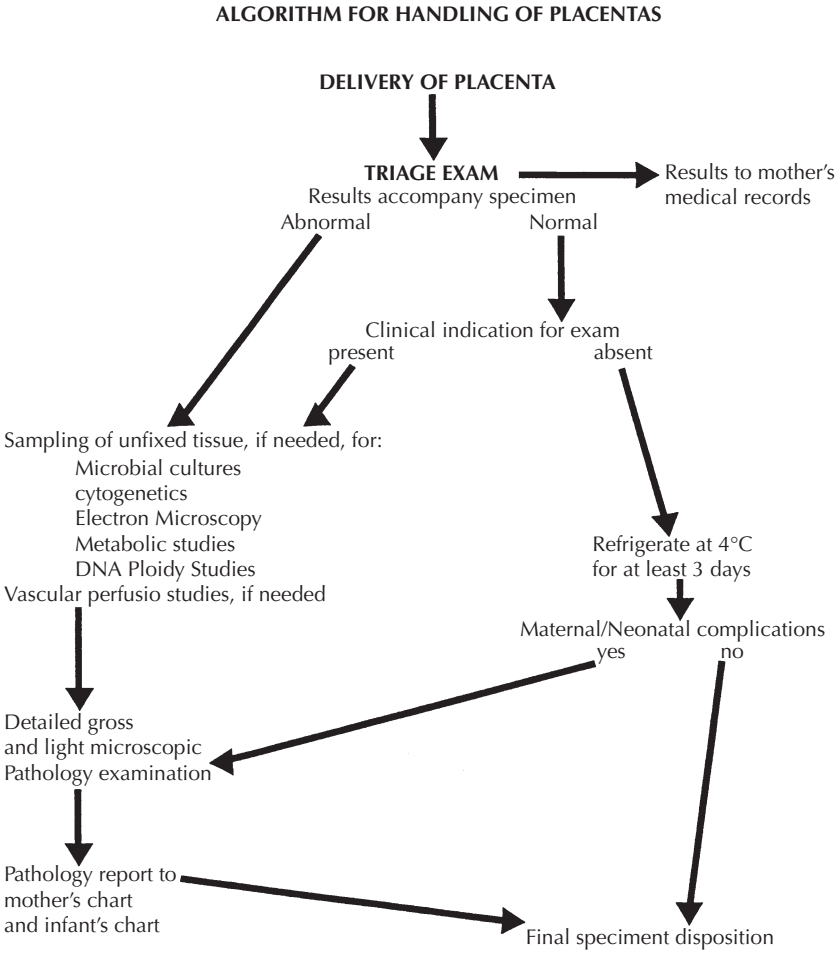


Figure 1.1. Scheme for placental triage. (Adapted from Langston C, Kaplan C, Macpherson T, et al. Practice guidelines for examination of the placenta, Arch Pathol Lab Med 1997;121:449–476.)

Fixation

Bouin's solution has often been used for placental fixation, and has the great advantage of hardening the membrane roll instantly. It does, however, lyse red cells and requires care in histologic processing. Most labs have moved to using buffered formalin as their basic fixative. The question of whether to examine placentas fresh or fixed has long been debated without a definite answer as both methods are useful in various situations. The fresh placenta permits microbiological cultures, freezing of tissue for DNA samples, and the establishment of cell culture for karyotype or other testing. Frozen sections are easiest with fresh tissue. Injection studies in twins can only be done on fresh placentas. Surface changes are much better appreciated and membrane rolls are easily made. The fresh placenta is also more readily palpated for solid lesions. Unfixed pla-

Table 1.1. Indications fory placental examination

Fetal/neonatal
Stillbirth/perinatal death
Hydrops
Multiple gestation
Prematurity (<35 weeks)
Postmaturity (>42 weeks)
Intrauterine growth retardation
Congenital anomalies (major)
Possible infection
Seizures
Admission to Neonatal Intensive Care Unit (NICU)
Compromised condition at birth (e.g., low pH or Apgar scores)
Placental
Abnormal fetal/placental weight ratio
Extensive infarction
Single umbilical artery
Meconium staining
Suggestive of infection
Retroplacental hemorrhage
Excessive fibrin deposition
Villous atrophy
Chorangioma
Amnion nodosum
Maternal
Maternal disorders (e.g., hypertension, collagen disease, diabetes, drug abuse)
Possible infection/fever
Poor reproductive history
Abruptio placenta
Repetitive bleeding
Oligohydramnios
Polyhydramnios

Adapted from Langston C, Kaplan C, Macpherson T, et al. Practice guidelines for examination of the placenta, Arch Pathol Lab Med 1997;121:449–476.

centas may be held for several days refrigerated prior to gross examination. Gross and microscopic changes are minimal, if any, over this time (Figure 1.2). The fixed placenta is more simply transported and stored, is less infectious, and may show infarcted regions better. Good fixation of an intact placenta will require several days' immersion in several times its volume of formalin. Except in cases of stillbirth, hemolytic coloration of the placenta usually indicates improper handling or storage (Figure 1.3).

Some facilities have largely eliminated formalin and use one of several recently developed nonformalin fixatives. These may be adequate for small biopsies but they do not penetrate very well. The placentas remain poorly fixed, even in adequate volumes. These fixatives also markedly change the gross appearance (Figure 1.4). On histology red cells are lysed and inflammatory cells poorly preserved. Postfixation in formalin will result in extensive pigment deposition.

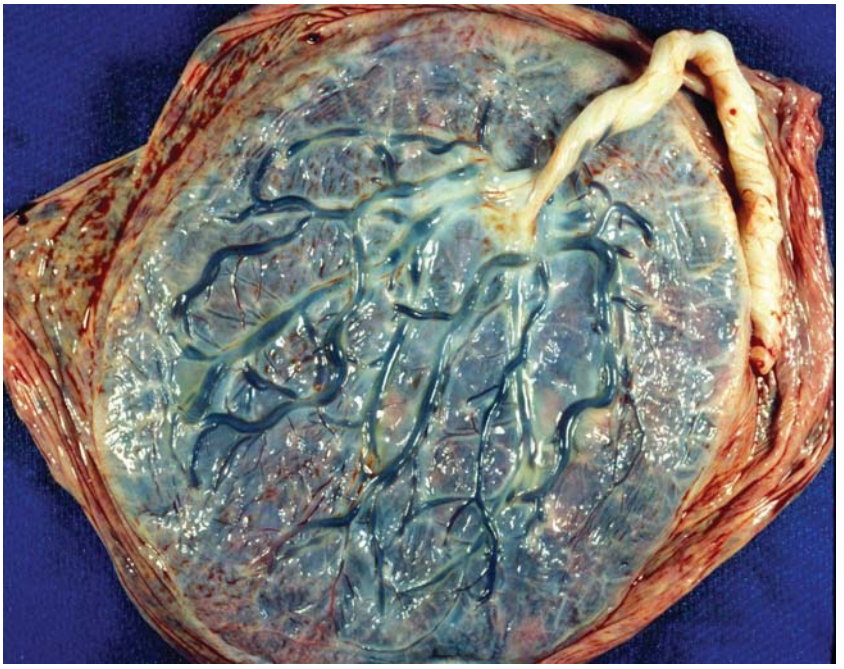


Figure 1.2. This intact fresh normal term placenta shows the fetal surface after refrigerated storage for two days. The surface is bluish with no opacity or unusual coloration. Subchorionic fibrin, usual in mature placentas, leads to the whiter areas. With longer storage or with large amounts of blood in the container, there is often more opacification grossly, without histologic findings. The cord is present inserting just off center. Free peripheral membranes can be seen at the margin.

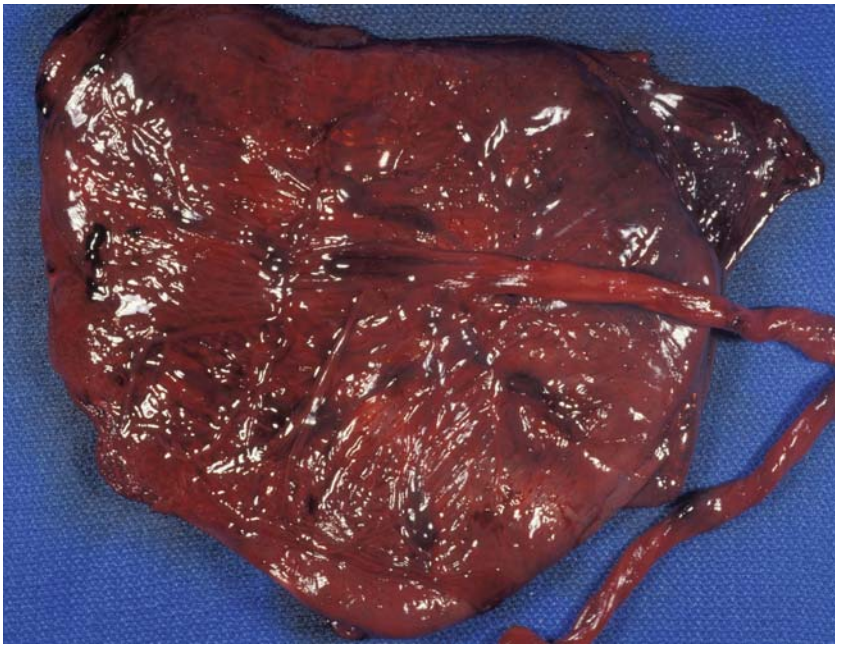


Figure 1.3. This placenta shows severe hemolytic coloration of the cord, membranes and surface. It was inadvertently placed in betadine scrub at delivery. A few bubbles are visible. Similar hemolysis will be seen if the placenta is frozen or left unrefrigerated.

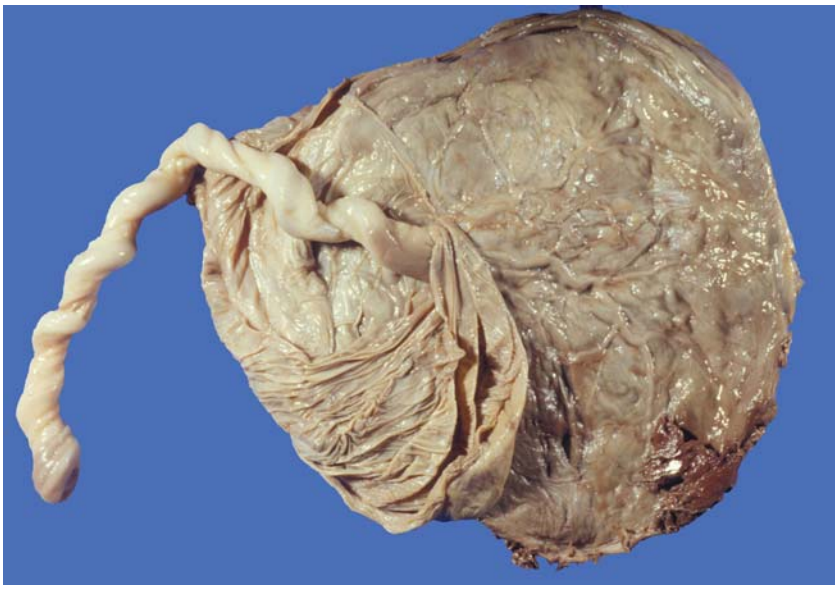


Figure 1.4. This term placenta was fixed in a nonformalin fixative for two days. There is no firming of the tissue as with formalin. Markedly meconium stained placentas will retain a green color, but other membrane changes are not discernable. These fixatives do not penetrate well and only 2 mm of the villous tissue on the maternal surface was fixed.

Technique of Gross Examination

Complete gross examinations and sampling of placentas can be done quite rapidly with some experience. Placentas, whether fresh or fixed, are large, messy specimens and more comfortably handled in an easily cleaned area, such as a table with running water. If the placenta is initially examined fresh, representative portions are saved and fixed. The remainder of the placenta may be discarded, except for those placentas with very unusual findings.

Gross examination of placentas should be done in a fixed routine, so all features are assessed. Individual placentas may require deviations from the routine for optimal assessment. Certain easily obtainable instruments simplify the process (Figure 1.5). It is also useful to have an assistant who notes data on a specialized form (Appendix A.1). The following briefly summarizes the steps. Specific findings are detailed in subsequent chapters.

1. The placental exam begins even before opening the container. In fresh placentas a bulging lid or an unusual odor may indicate bacterial infection. Large amounts of fresh clot are seen in some cases of premature separation (abruption).
2. The general shape of the placenta is assessed and extra lobes noted. The fetal surface is examined for color, fibrin deposition, subchorionic and subamniotic hemorrhages, cysts, vascular pattern, and blood vessel

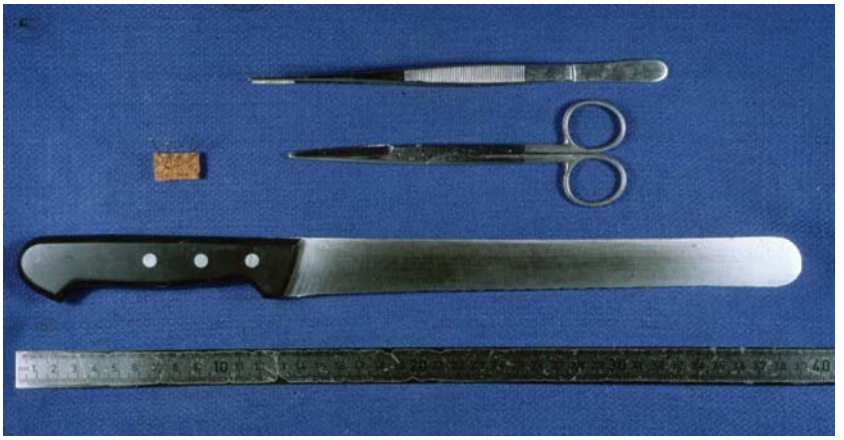


Figure 1.5. Implements useful for gross placental examination include a large thin round-ended knife for the major cutting, a metal meter stick for measurements, a long thin forceps with delicate teeth for membrane rolls, pins to hold the rolls intact in formalin, and scissors for trimming.

changes such as thrombi (Figure 1.2). The maternal surface is inspected for color, completeness, and adherent blood clot. The villous tissue is palpated for lesions (Figure 1.6).

3. The cord length is measured and its site of insertion in the placental disk noted. Measuring the distance of insertion to the margin of the placenta is more precise than the term "eccentric" or "paracentral" insertion. Particular attention should be given to the presence, length and intactness of any velamentous vessels. Extra pieces of cord in the container should be noted and measured.

4. The cord is inspected for true knots, twisting, and discolorations. It is then cut several centimeters from its placental insertion and the cut end examined for the number of vessels and other abnormalities. Maximal and minimal diameters are measured. Portions of the cord from the proximal and distal regions are fixed, without clamp marks, if possible.

5. The peripheral membranes are inspected for the type of insertion into the disk and completeness. If essentially complete, the distance from the point of rupture to the edge of the placenta is measured. This measure should be based on the membranous chorionic tissue as the amnion is freely movable and readily becomes separated. The opening in complete membranes is relatively small. An extensive opening or fragmentation indicates the membranes are incomplete. The color, opacity, and other lesions such as hemorrhages and compressed twins are noted.

6. A strip of membranes is cut from the edge of the site of rupture to the margin of the disk preferably from a thicker portion of the membranes with more attached decidua. A "jellyroll" is made by grasping the end with long thin forceps and rolling toward the placenta. This puts the

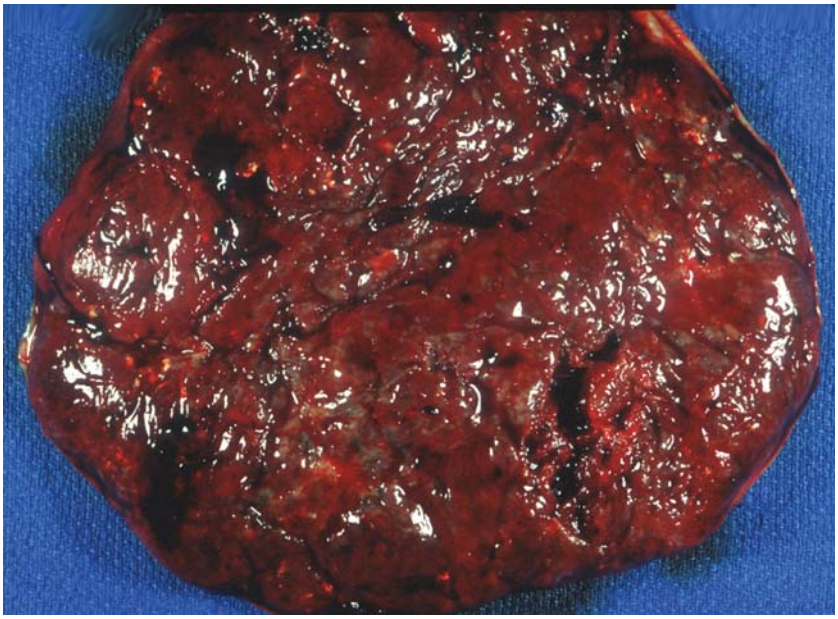


Figure 1.6. This view of the maternal surface in a term placenta shows the villous tissue to be complete, except for a small area of disruption at 5 o'clock. The placental cotyledons are vaguely outlined. A small amount of loose, soft, postpartum clot is present which should be removed prior to weighing and further examination. There are large and small yellow flecks of calcium.

point of rupture at the center of the roll, which is held in place with a pin and cut from the placenta. The weight of the still attached placenta facilitates this process. Rolls can also be made around a small piece of marginal placental tissue. The pin is unnecessary with hardening fixatives such as Bouin's. Rolls are difficult to make once the placenta has been fixed or if the membranes are severely disrupted or "slimy" from meconium (Figure 1.7, Figure 1.8).

7. The remaining membranes are trimmed away (with scissors or knife) and any loose soft clot is removed from the maternal surface. The placenta is now weighed, without cord or membranes, in a hanging pan or other balance. Measurements are taken of greatest diameters and thickness of the disk, and any extra lobes.

8. Transverse cuts are made through the maternal surface at 1-cm to 2-cm intervals. Lesions are measured and described. The degree of calcification and any unusual features such as villous color or texture are noted (Figure 1.9).

9. Representative pieces of the placenta are cut to include the margin, central villi from several cotyledons, and any significant gross lesions (Figure 1.10). Keeping the cord insertion area attached helps retain the amnion as the amnion is continuous with the surface of the cord. The samples are placed in formalin.

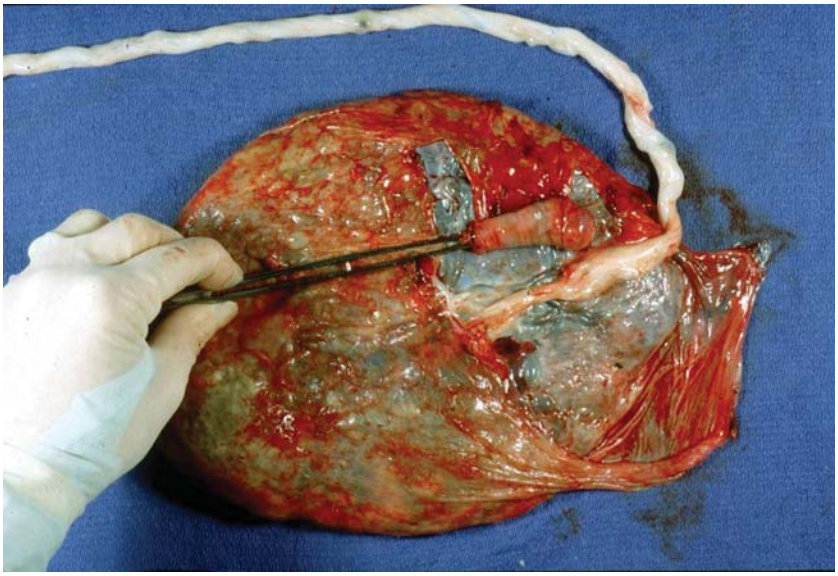


Figure 1.7. The membranes of this normal, term placenta have been placed in their in situ uterine position. With a vaginal delivery, the minimal distance from the hole of rupture to the edge of the placental disk indicates the site of the placenta in the uterus. Shorter lengths indicate low-lying placentas. This shows a membrane roll being made from the rupture point to the margin of the placenta. It is then pinned, cut, and fixed. A larger length of membranes can be rolled and two sections cut from different areas.

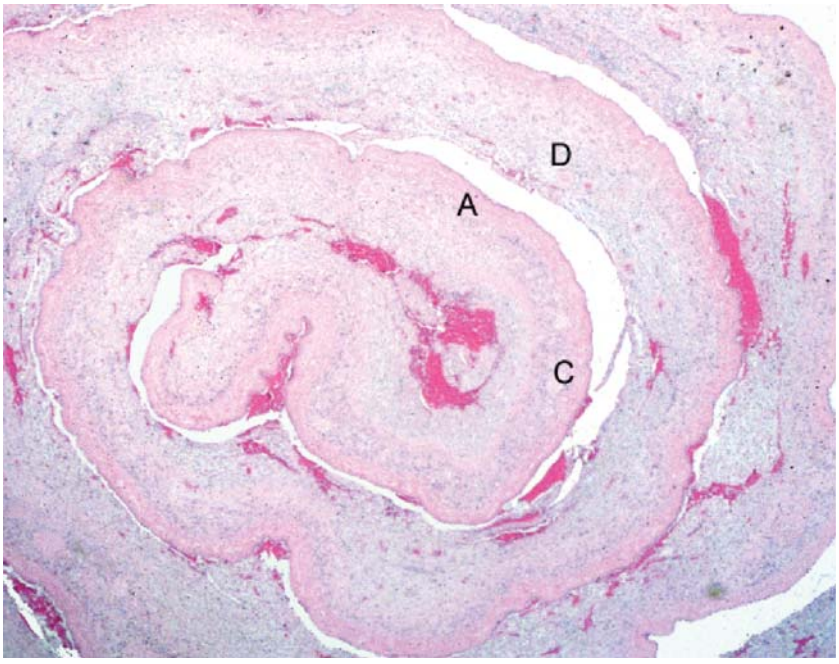


Figure 1.8. Histologic section of a cross section of a membrane roll shows the numerous layers visible by this technique. Amnion (A), chorion (C), and attached decidua (D) with small blood vessels are present.

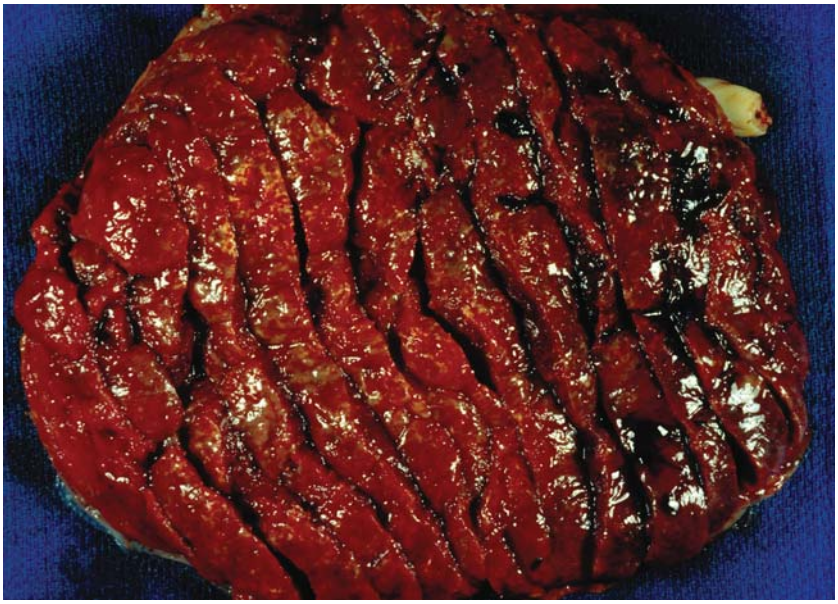


Figure 1.9. Mature placenta after transverse cuts (1.5 cm to 2 cm) have been made on the maternal surface in order to examine the villous tissue. The knife has a tendency to skip over firmer areas and simultaneous palpation of the villous tissue is necessary. The fetal surface is not usually cut and keeps the placenta somewhat intact.

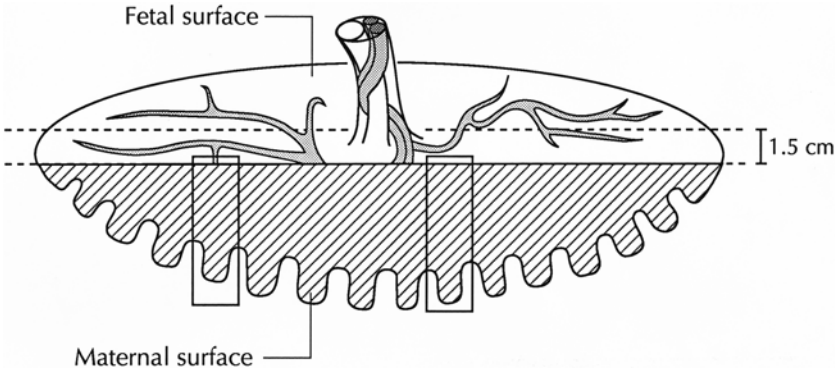


Figure 1.10. A transverse strip of placental tissue from the central region including the cord is routinely saved. This piece should be thin enough to adequate fix. Histologic blocks of villi including small surface vessels are taken from at least two separate areas in the placental midzone (*boxes*). These should not be from areas with thick subchorionic fibrin or hemorrhage as this masks inflammation. The placental margin has substantial artifact and is not ideal for assessing villous configuration. It may show more inflammation or decidual vascular change and can be submitted in addition. Placentas with significant pathologic processes require extra blocks to sample these.

Placental Weight

Placental weight is not a precise measurement and will vary with the methodology of examination. It is affected by fixation, the presence of cord, membranes, and loose clot, the amount of blood retained, and the intactness of the maternal surface. Fresh refrigerated placentas lose a small amount of weight with storage, whereas formalin fixation leads to an increase, no more than 10% in either case. The value of placental weight is largely at the extremes, taking into account the gestational age and weight of the baby. A relatively heavy or light placenta often indicates an abnormal pregnancy. At term, the infant usually weighs about 7 to 8 times the placental weight. The ratio decreases earlier in gestation. Most term placentas weighing more than 750 grams or less than 350 grams will warrant histology. There are standard tables for placental weight by gestational age and by fetal weight as well as those with fetal-placental ratios by gestational age (Appendices B-1, B-2, and B-3).

Histologic Sectioning

Although it is possible to cut blocks from fresh placental tissue, this is far easier after some fixation has occurred. Sharp blades are important to keep the amnion on the placental surface intact. On most placentas cord (2 pieces from different sites), membrane roll, and two to three full thickness pieces of villous tissue including fetal and maternal surfaces are an adequate sample. The pieces of placental villous tissue should be from separate areas (different cotyledons), and *not* from the margin of the placenta, which frequently shows changes of diminished blood flow (Figure 1.10). The fetal surface of the section should include small blood vessels, and be free of substantial subchorionic clot or fibrin. Early changes of ascending infection are often masked in areas with thick subchorionic deposits. If the placental sections are too large to fit in the cassette, they will need to be divided. Additional representative sections of significant lesions or differences in villous character are also taken. En face blocks of the basal plate may be useful for evaluating maternal vasculature. It is not necessary to section every infarct, hemorrhagic lesion, and so forth, as long as they are clearly identifiable grossly and adequately described. Blocking can be done by a trained technician. The specific type of fixation, processing, cutting, and staining may greatly alter the histology of the placental villous tissue. This is particularly important in the assessment of villous structure and maturation. Anyone looking at even a few placentas needs to become familiar with the appearance of villous tissue at different points in gestation as prepared in their histology lab.

Reports

For reports, the form on which the original gross information is recorded can often serve as the actual report or a master for rapid typing of reports. These forms can readily incorporate the microscopic exam and

diagnoses. Some hospitals use placental check lists while in others reports are narrative. The special requirements of twin placentas should be either a separate form or incorporated into the singleton worksheet. (Appendix A1,2)

2

Basic Placental Anatomy and Development

Some appreciation of placental development and structure is necessary to understand its examination and certain pathology. While the placenta shows extensive growth and histologic change in the second and third trimesters, the basic gross morphology is established early in pregnancy, before the end of the first trimester.

Development

Trophoblastic tissue is the major component of the placenta. By 4 to 5 days after fertilization, trophoblasts differentiate from the external cells of the morula as it becomes a blastocyst. The trophoblastic cells proliferate rapidly and surround the inner cell mass, covering the entire surface of the blastocyst. Attachment to the endometrial surface and implantation occur at 5 to 6 days, usually in the upper part of the uterus. Implantation is interstitial and the blastocyst becomes totally embedded in the endometrium. As the developing conception grows, it protrudes into the endometrial cavity. The endometrial stroma undergoes decidual change. At first the entire gestational sac is covered by chorionic villi (Figure 2.1, Figure 2.2). As the sac enlarges, its surface thins, forming the peripheral membranes which are composed of decidua capsularis, atrophied chorion, and amnion. The definitive placenta is left at the base. With continued growth of the conception there is apposition of the membranes with the decidua vera of the opposite side of the uterus, but no true fusion.

The fetal-placental circulation begins at about 9 days when lacunae form in the syncytial trophoblast. By days 10 to 12 these lacunae link with maternal blood vessels which have been eroded by trophoblastic invasion. The intermediate trophoblastic cells are responsible for invasion into the uterine wall and maternal vasculature. The primary fetal chorionic villi have formed by 14 days and consist of cords of cytotrophoblast covered by syncytial trophoblast. Shortly after there is invasion of avascular extraembryonic mesenchyme from the embryonic body stalk into these columns forming secondary villi. Capillaries develop within the villous stroma and form networks by 20 days (tertiary villi).

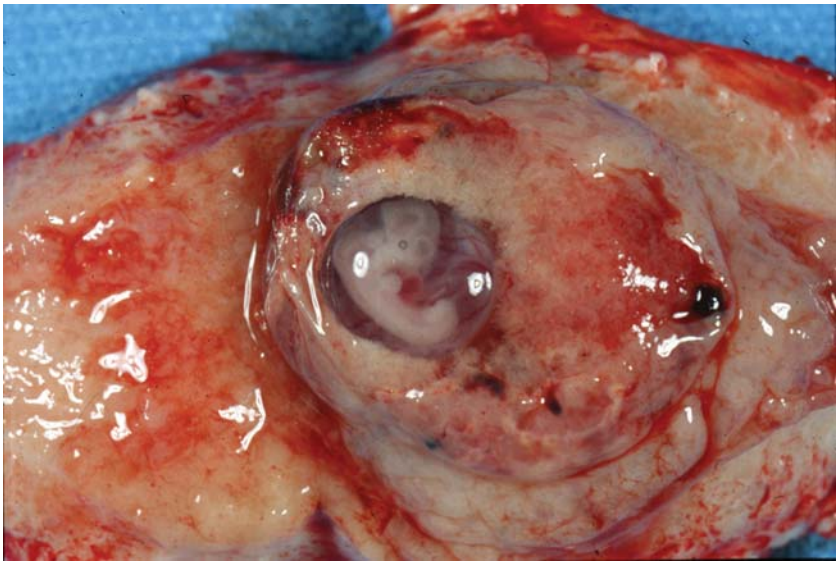


Figure 2.1. This embryo of 6 developmental weeks was removed in situ during a hysterectomy for cervical carcinoma. The decidua has been partially removed to reveal the chorionic villi which cover the entire early gestational sac. Part of the chorion has also been dissected showing the amniotic sac containing the embryo.

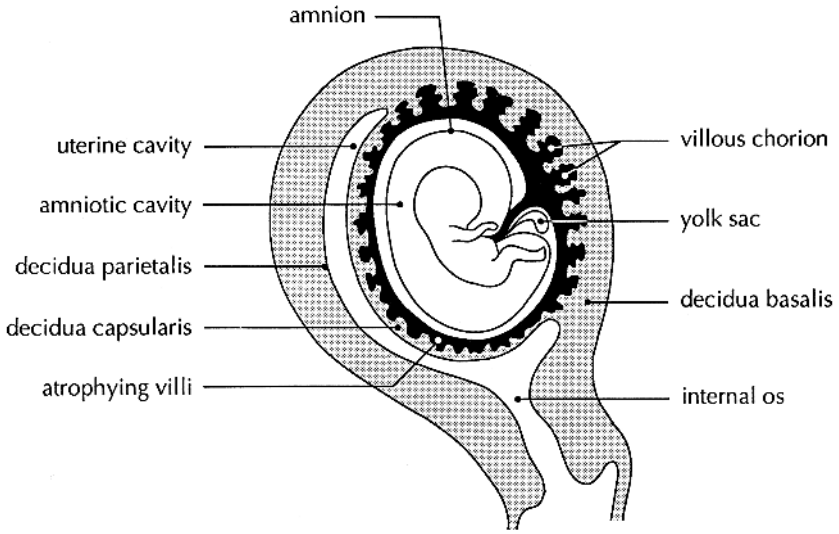


Figure 2.2. The embryo lies within the chorionic and amniotic sacs. Note the yolk sac between them. The capsular chorionic villi associated with the evolving peripheral membranes are undergoing atrophy creating the discoid placenta at the base into which the cord inserts.

These vessels communicate with the fetus through vessels differentiating from the chorion and the connecting stalk, the large surface vessels and umbilical cord. The circulation is functional by the end of the third developmental week. The placenta grows through branching of the villous tree. Primary stem villi break up below the chorionic plate to form

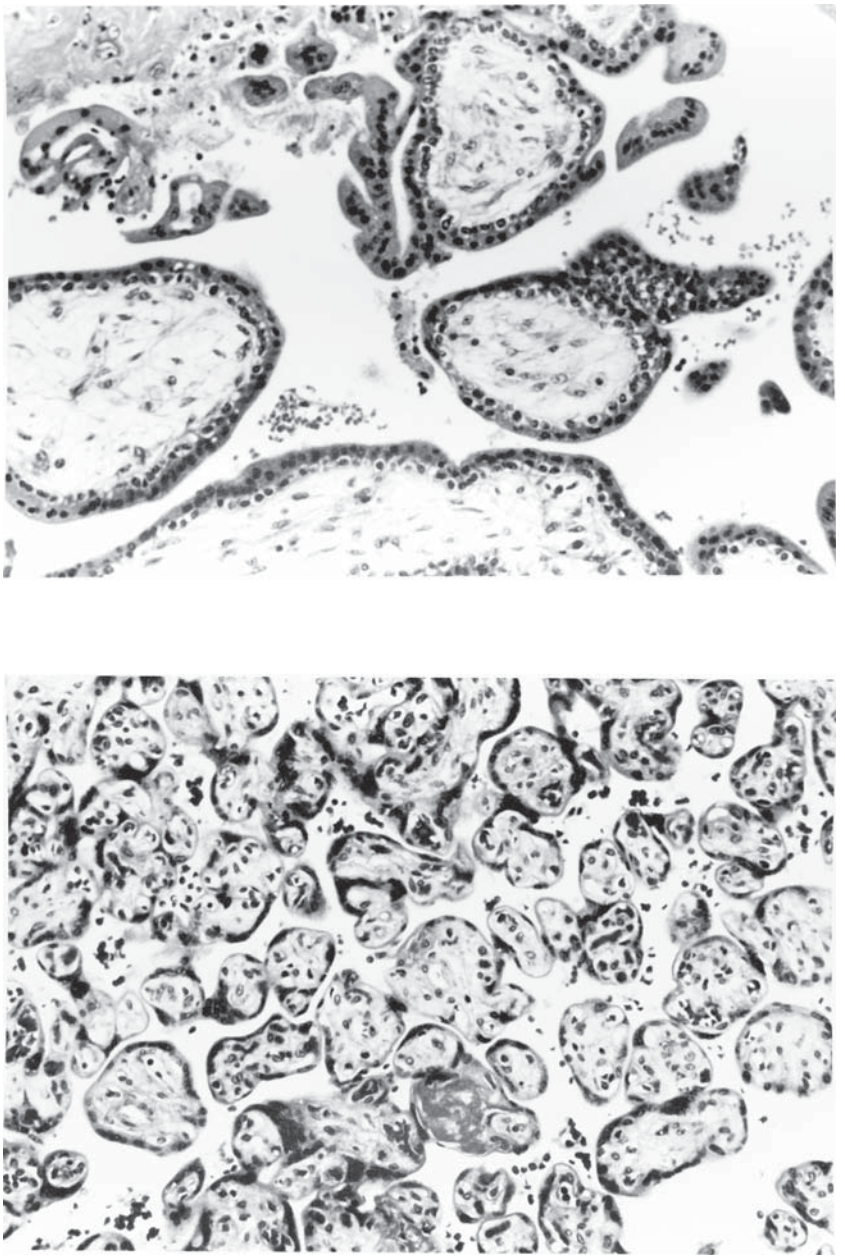


Figure 2.3. Histologic maturation of villi (**A**) Very early first trimester villi show abundant stroma without vessels. Two layers of trophoblast (cyto and syncytiotrophoblast) are present, without syncytial knots. (**B**) At the same magnification, term chorionic villi are much smaller and show little stroma. There are numerous blood vessels and only syncytial trophoblast is visible on the surface with numerous knots.

secondary and tertiary stem villi and finally distal terminal villi. "Anchoring" villi are present at the base of the placenta. Normal maturation of villi entails several features. There is progressive diminution in villous size and stromal content with an increasing portion of the villus composed of blood vessels. The syncytiotrophoblast nuclei become aggregated into "knots," and the cytoplasm thins over vessels forming vasculosyncytial membranes. The originally prominent cytotrophoblastic layer disappears and by term few cytotrophoblasts are recognized on light microscopy (Figures 2.3A,B).

Placental Shape

The shape of the placenta is quite variable. Generally it is round to ovoid and about 18-cm to 20-cm diameter by 1.5-cm to 2.5-cm thick at term. Failure of atrophy of capsular villi leads to succenturiate lobes (Figure 2.4, Figure 2.5). Bilobate placentas result from uterine sulcal implantation (Figure 2.6), while unusually shaped often multilobate placentas may be due to uterine cavity abnormalities (Figure 2.7). A diffuse thin placenta without free membranes is extremely rare and known as placenta membranacea. (Figure 2.8). This may represent a shallow implantation with persistence of virtually all the capsular villi. While these alterations should be described, they are of little significance except for potential problems related to the velamentous vessels that often accompany them and placenta previa.

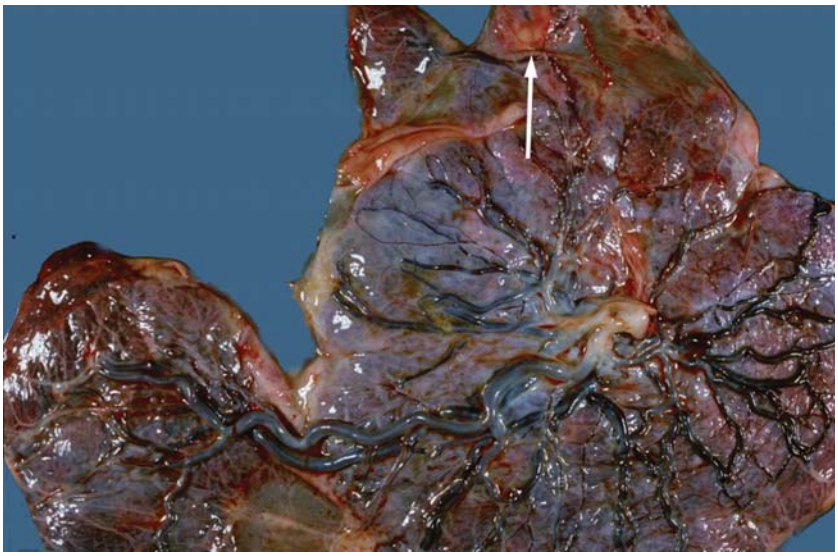


Figure 2.4. Succenturiate lobes are formed if some of the capsular villous tissue fails to atrophy during development. Such tissue can potentially be left behind at delivery leading to bleeding from retained placenta. True succenturiate lobes are connected to the main placental mass by velamentous vessels which can be damaged. This slightly immature placenta shows at least four such lobes, one large and three small. Succenturiate lobes often become infarcted or fibrinous. One of the small lobes is yellow and atrophic (*arrow*).

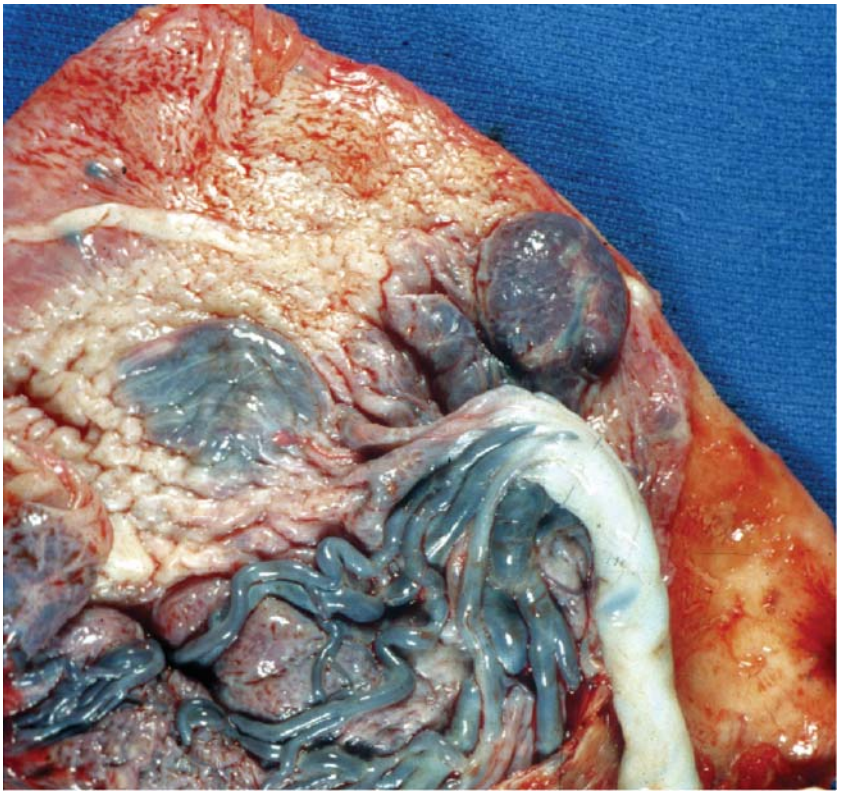


Figure 2.5. The term "partial" lobes can be used to help describe some of the irregularities of outline. These are lobe-like marginal placental areas which are connected by bridges of villous tissue and do not show velamentous vessels.

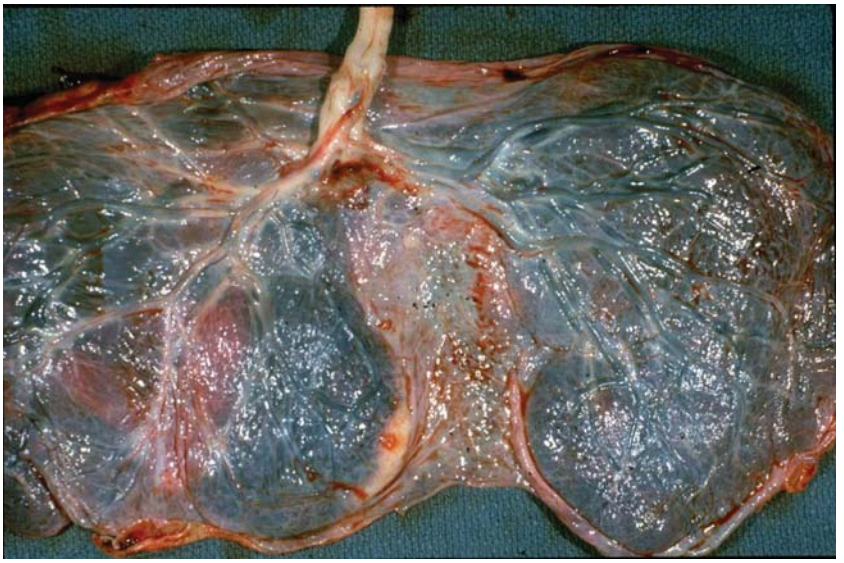


Figure 2.6. This mature bilobate placenta has two distinct lobes of roughly equal proportions. The umbilical cord inserts between them, velamentously into the membranes. Although this resembles a placenta with a large succenturiate lobe, this configuration more likely arises through a different mechanism. Implantation in a lateral uterine sulcus will lead to relatively equal growth along the anterior and posterior walls.

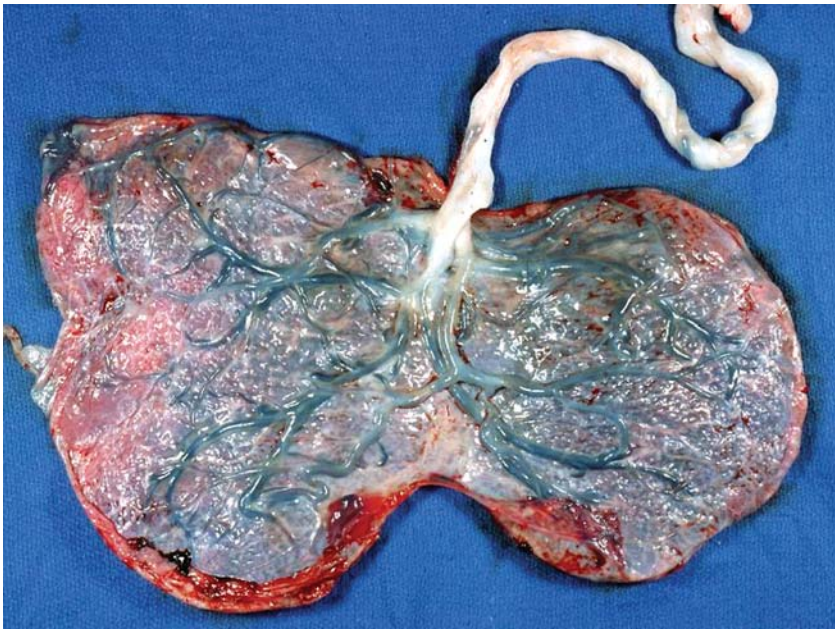


Figure 2.7. An unusual uterine shape, scarring, or intracavitary lesions may be reflected in the placental outline. Such abnormalities impede placental growth in certain areas and the remaining tissue extends into other regions. This large irregular placenta suggests an abnormal uterine cavity.

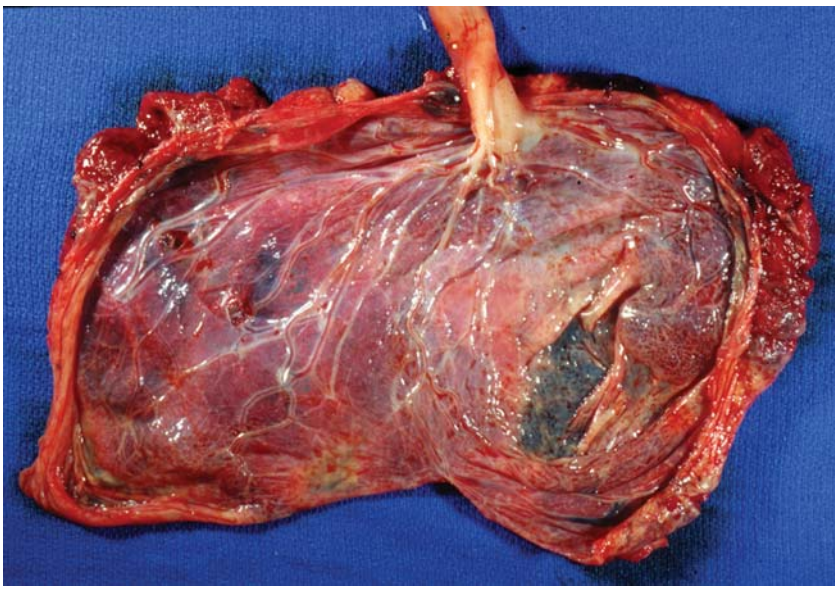


Figure 2.8. This is a very large thin immature placenta with villi covering the entire sac except for small areas of membranes including an enclosed window. It likely covered the cervical os. The placenta was cut through at Cesarean section and was extensively disrupted.

Placenta Previa

When implantation is low in the uterus the point of membrane rupture will be near the placental edge in a vaginal delivery. True placenta previa develops with a low implantation when placental villous tissue covers the cervical opening (Figure 2.9). Complete previas are usually delivered by cesarean. This process is often difficult to confirm on placental examination, particularly if there has not been significant clinical bleeding. The maternal surface may show old or fresh hemorrhage (Figure 2.10) or merely a 1-cm to 2-cm circular deposition of fibrin in the region of the cervix.

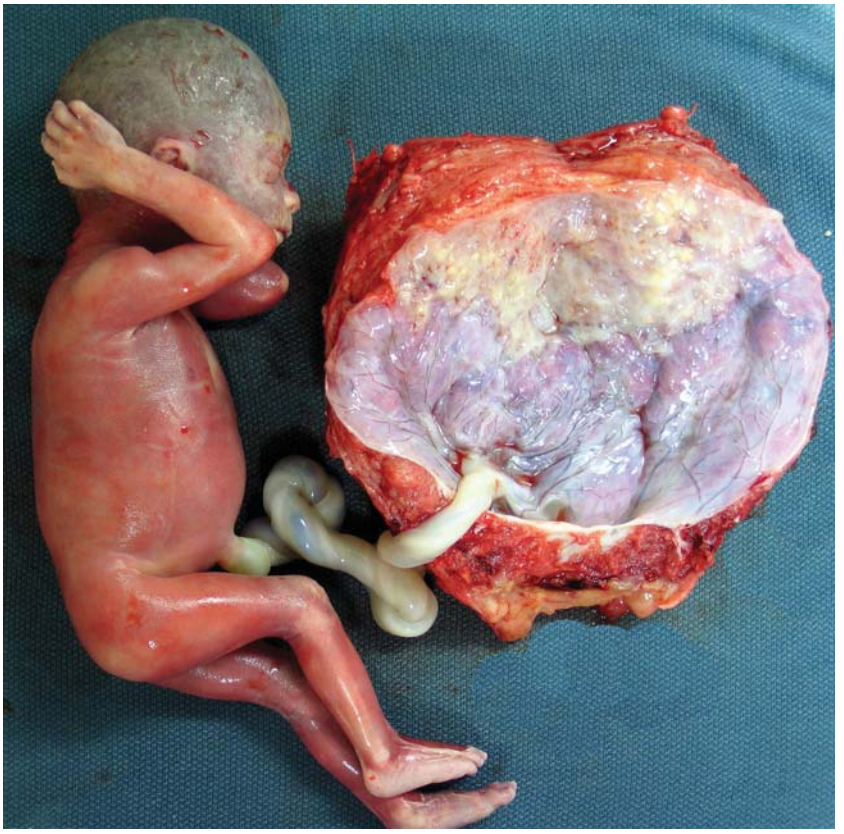


Figure 2.9. This gravid supracervical hysterectomy was done for placenta previa with excessive maternal bleeding at a nonviable gestational age. Note the pale villous tissue completely covering the region of the cervical os at 6 o'clock cervical os and extending around the entire lower uterine segment. The placenta could not be manually removed from the uterus and there was extensive placenta accreta.

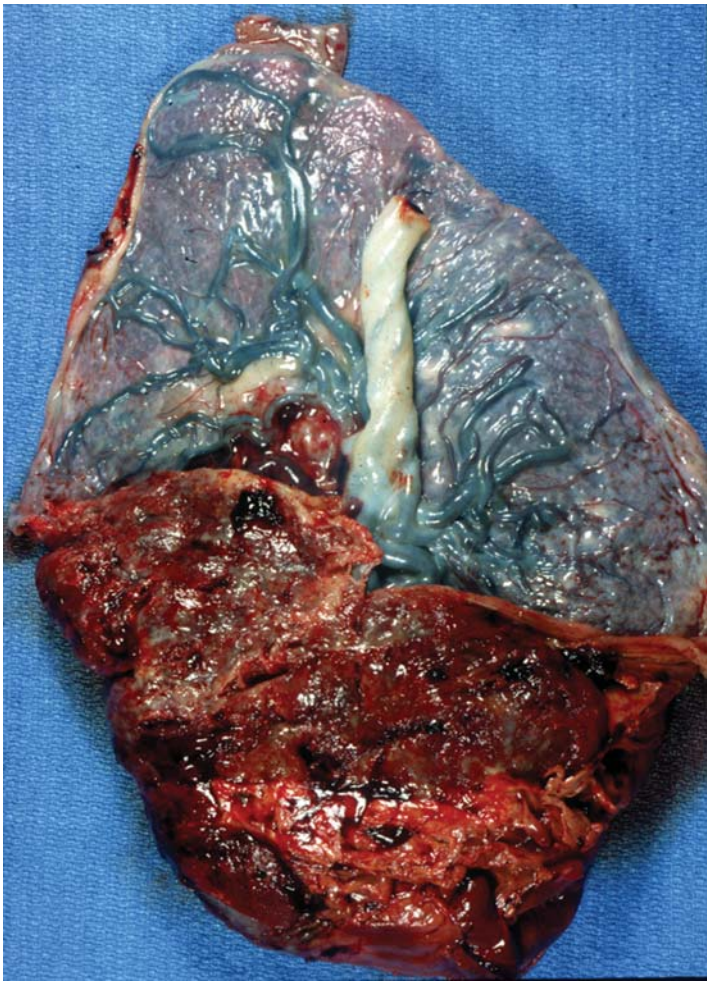


Figure 2.10. This near term placenta with complete placenta previa recapitulates the shape of the lower portion of the uterus, being folded back on itself at the cervix. There is brown, old hemorrhage in the area of the os due to placental separation. No accreta was present.

Placenta Accreta

Invasion of the placenta into the uterine wall should stop before the myometrium is reached, leaving a layer of decidua separating the anchoring villi from the muscle. Decidual tissue apparently limits placental growth. If such limitation does not occur the placenta will adhere abnormally to the uterus and may extend into the myometrium. Placenta acreta, increta or percreta results if there is invasion to, into, or through the myometrium respectively (Figure 2.11 to Figure 2.13). These processes often occur in the setting of damage to the endometrium by previous cesarean sections or other uterine scarring and low

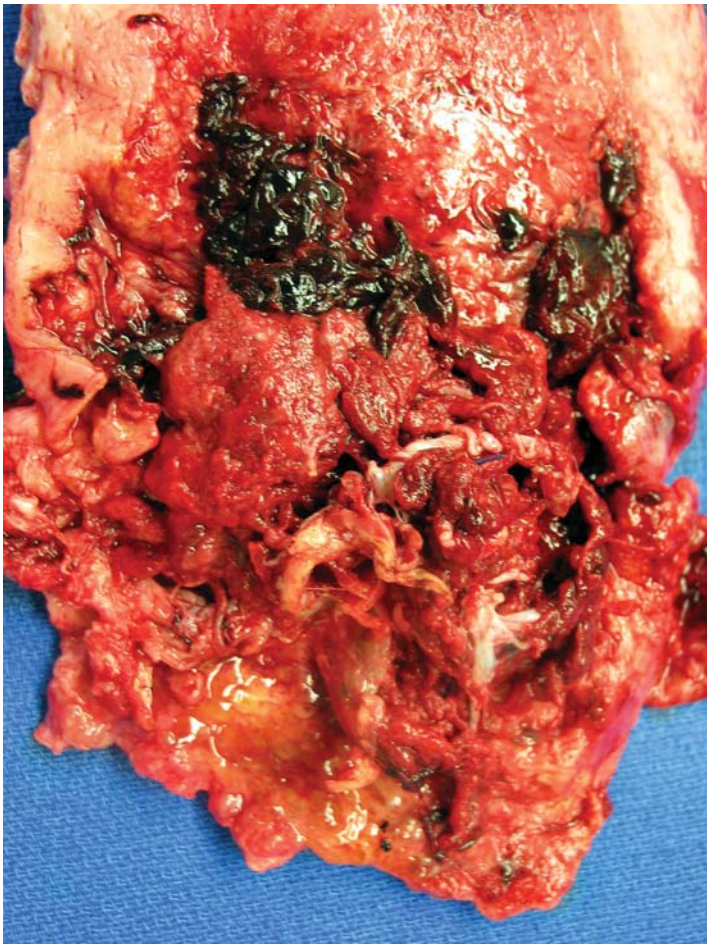


Figure 2.11. This opened post-partum uterus shows extensively invasive adherent placental tissue in the lower segment. Thus this was a placenta previa that had partially separated as well as invaded into the muscle, an increta. Accreta, previa, and placental separation are frequently seen together.

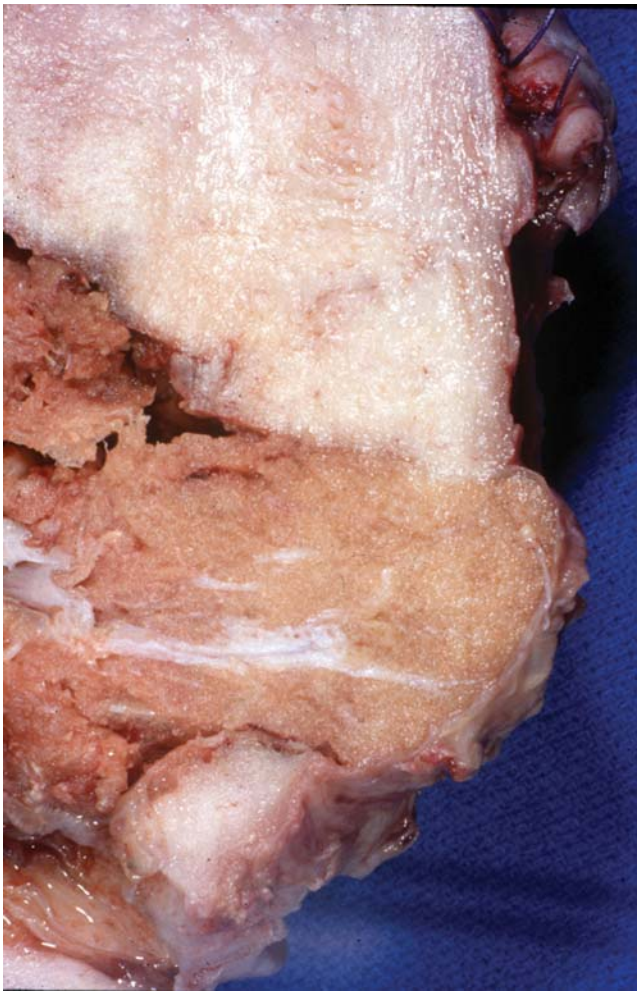


Figure 2.12. This fixed postpartum hysterectomy specimen reveals retained pale placental tissue invading focally nearly through the wall of the uterus, with thinning to less than 1 mm of serosal tissue (placenta increta).

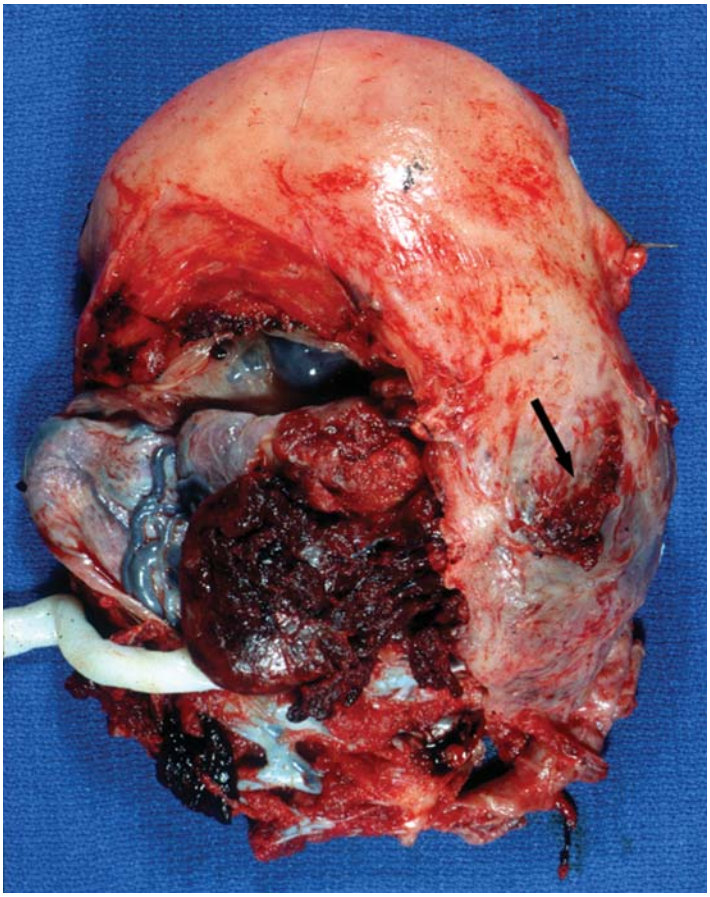


Figure 2.13. This uterus still contains the placenta as it could not be removed readily at delivery and focally the placental tissue has perforated the myometrium (*arrow*). Fibrin and organization of the clot were present on histology. The adjacent thinned lower uterine area appears somewhat blue from the closely underlying placental. An unsutured vertical cesarean section incision is present.

implantation. Accreta is most easily identified in hysterectomy specimens. It is usually not possible to make the gross diagnosis of symptomatic accreta and its more invasive forms in a delivered placenta, and only rarely on placental microscopy. Accreta may be found both grossly and microscopically in post-partum currettings for bleeding (Figure 2.14). Partial myomectomies of regions with increta are occasionally performed (Figure 2.15).

Abnormal adherence of the placenta is not the only cause of life threatening postpartum hemorrhage. Uterine atony is another frequent cause of postpartum hysterectomies (Figure 2.16).

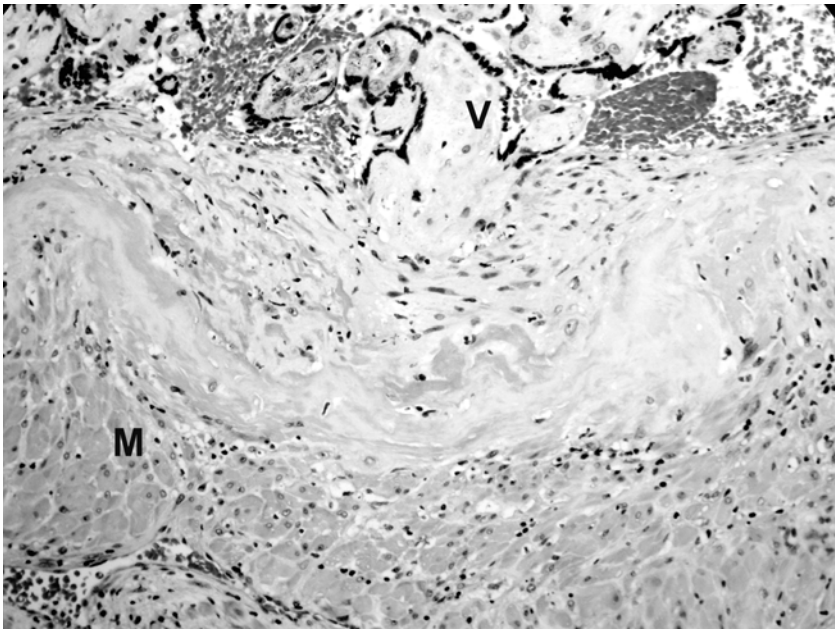


Figure 2.14. This is from the post-partum currettings in a woman with bleeding 3 weeks after delivery. Fibrotic avascular villi (V) can be seen directly adjacent to myometrium (M) without intervening decidua.

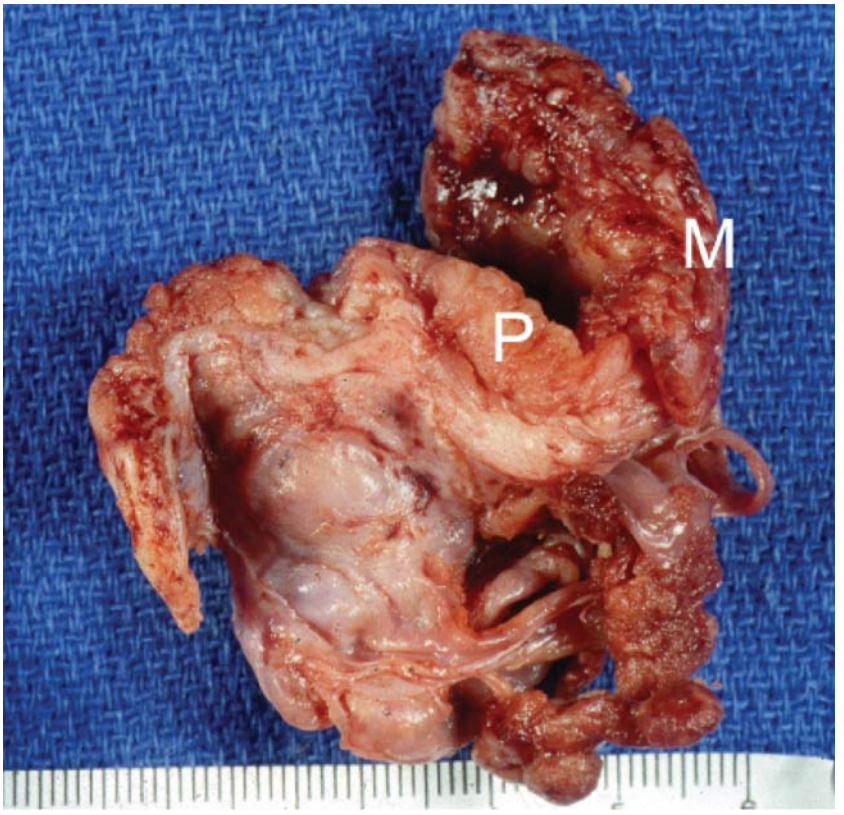


Figure 2.15. This piece of myometrium was resected in a woman with a localized area of accreta. The placental tissue invades well into the muscle.

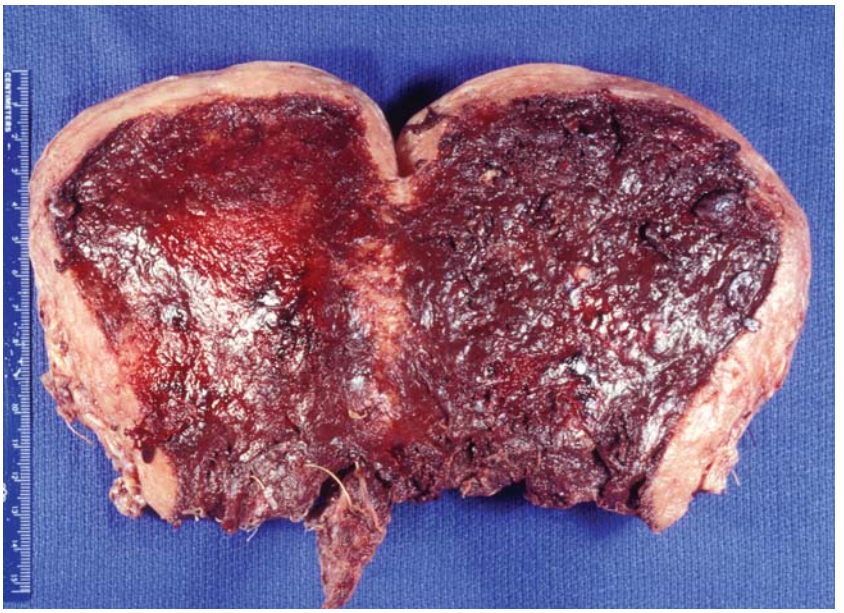


Figure 2.16. This postpartum supracervical hysterectomy was done for uncontrollable bleeding after delivery. The myometrial wall is thin and the fresh uterus was floppy. No adherent placenta was identified on thorough sectioning.

3

Umbilical Cord

The umbilical cord is the lifeline of the fetus. Complete cord occlusion often leads to fetal demise while intermittent obstruction has been associated with intrauterine brain damage. Cord compression and vasospasm are important factors in fetal distress. Careful umbilical cord examination often reveals significant lesions which may be associated with these processes.

Development

The umbilical cord forms in the region of the body stalk where the embryo is attached to the chorion. This area contains the allantois, omphalomesenteric duct, vitelline vessels and evolving umbilical arteries and vein. The expanding amnion surrounds these structures and covers the umbilical cord. Eventually most of the embryonic elements as well as the right umbilical vein disappear, leaving two arteries and one vein (Figure 3.1). Embryologic remnants are frequent on microscopy, but are rarely visible grossly. Allantoic remnants show a transitional-type epithelium and occur most often near the fetal end, between the arteries. Omphalomesenteric remnants may be ductal and lined by gastrointestinal epithelium or vascular (Figure 3.2).

Single Umbilical Artery

The absence of one umbilical artery is a common anomaly, occurring in about 1% of deliveries (Figure 3.3). It is more frequently seen with twins and velamentous cord insertions. About 20% of infants missing one artery will have other major congenital anomalies which may involve any organ system. Many are of chromosomal etiology. The abnormalities are generally apparent in the neonatal period, except for the increased incidence of inguinal hernias. The "nonmalformed" infants missing one umbilical artery are slightly growth-retarded overall and have increased perinatal mortality. Cord accidents have been unusually frequent in this group.

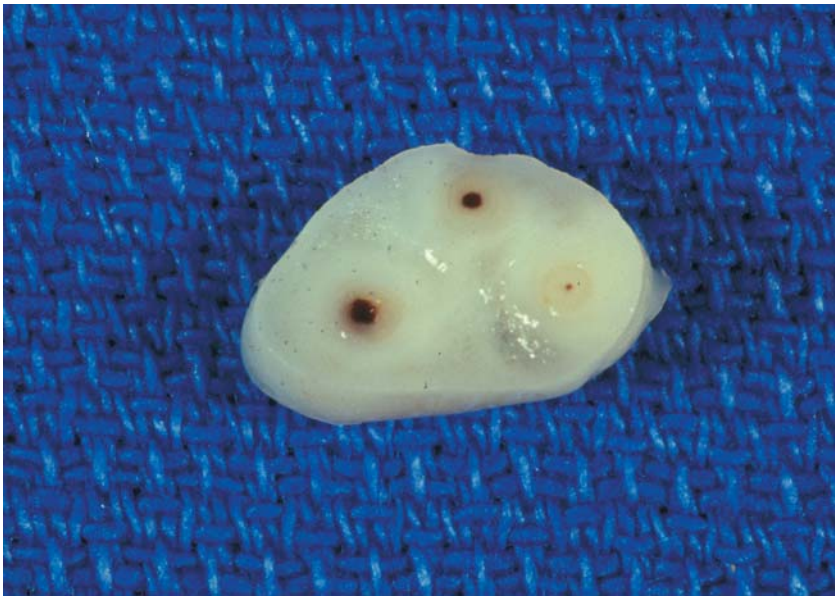


Figure 3.1. A normal three-vessel cord contains two arteries and one vein. The arteries are often more contracted than the vein, but it is not always possible to identify the type of vessel grossly. Most embryologic remnants are too small to be seen by eye.

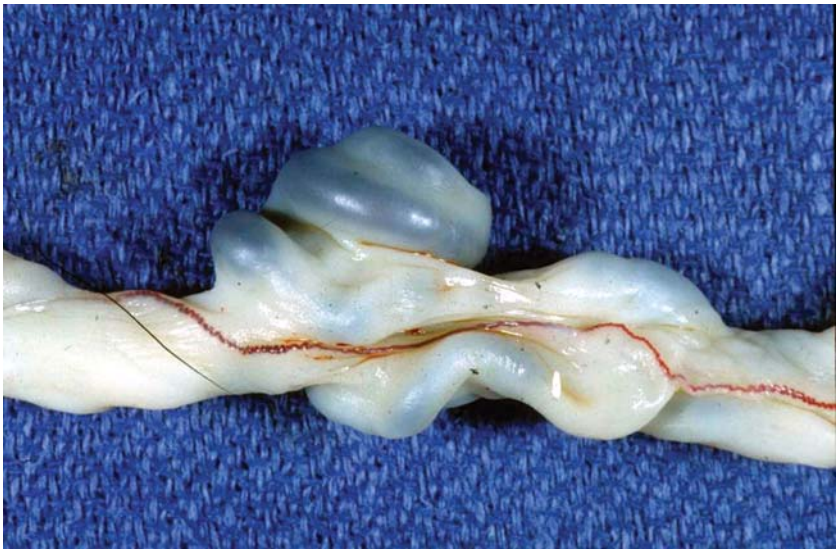


Figure 3.2. The small zigzag vessel on the cord surface is a vitelline vascular remnant. Under the microscope these have no muscular wall and are sometimes multiple suggesting a hemangioma. The dilated blue area is a small "false knot," an area of redundant length of the umbilical vein.

Figure 3.3. An umbilical cord with a single umbilical artery shows only two vascular lumens. Frequently the two arteries fuse in the last few centimeters of cord above the fetal surface, thus multiple cuts along the cord should be made to confirm the number of vessels.

Twist

The spiral twisting of the cord is established early in development (Figure 3.4). Most commonly it is counterclockwise, a so-called left twist (Figure 3.5, Figure 3.6). The etiology of twisting is unknown. It does allow the arteries to surround and help protect the vein from compression. The number of twists in the cord can be counted, as excessive twisting is

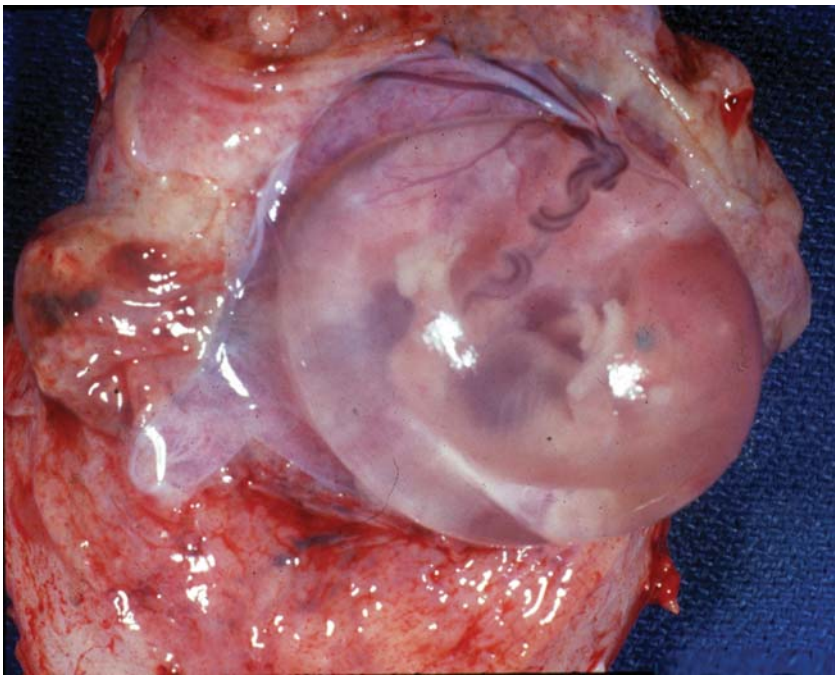


Figure 3.4. Umbilical cord twist is established early in development, as shown in this 10-week gestation. It usually twists in a left or counterclockwise direction (7:1).

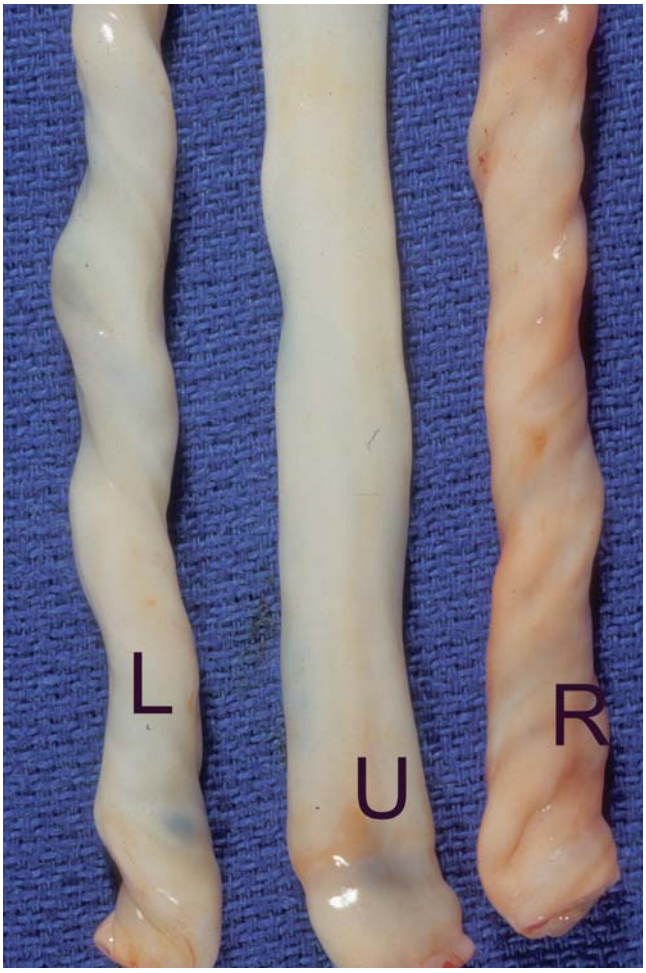


Figure 3.5. Umbilical cords showing left (L), absent (A), and right (R) twists. Infants whose cords lack a twist exhibit more perinatal morbidity. Cords missing one umbilical artery are also more frequently untwisted. No other correlations with fetal outcome have been identified.

Figure 3.6. It is not unusual for a cord to have regions with differing directions and density of twisting. Here a right twisted cord becomes an untwisted one.

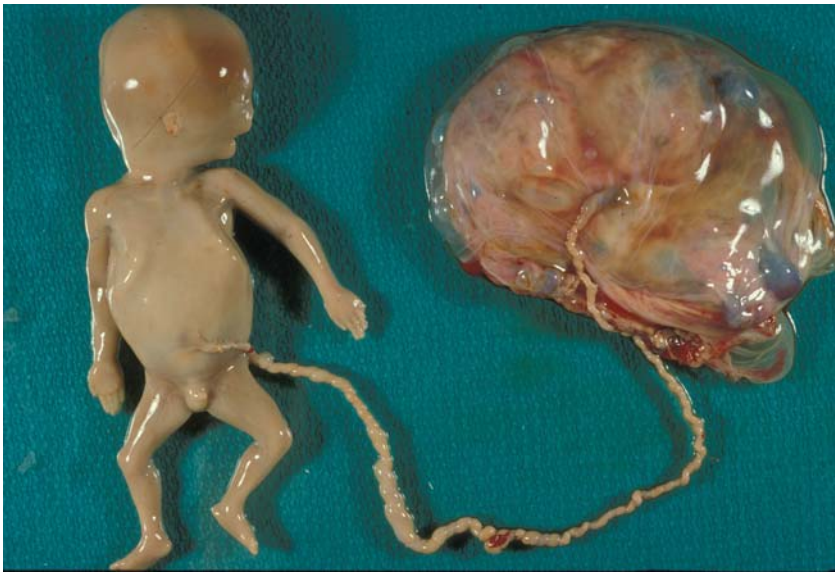


Figure 3.7. This mid-trimester fetal demise shows an excessively long and twisted cord. Markedly twisted cords may be associated with fetal compromise or death. Such twisting is not a postmortem artifact and is seen throughout gestation. No other cause of fetal death was found on complete autopsy with karyotype.

associated with fetal morbidity and mortality (Figure 3.7). In general, one should be cautious in attributing fetal death to this or other cord problems particularly if congestion and/or thrombosis are absent. It may one of several factors, or truly incidental.

Length

One of the most obvious features of the umbilical cord is the length. This increases throughout gestation, although the growth rate slows in the third trimester. Fetal activity and stretch on the cord are major factors determining length. There is a genetic component. Normal tables have been developed (Appendices B-4 and B-5), based on the entire length. Both abnormally long and short cords have significant clinical correlates. Long cords (>75 cm) are well associated with knots and fetal entanglements. They may correlate with later hyperactivity. Congestion and thrombosis in cord vessels are important signs of true obstruction (Figure 3.8 to Figure 3.14).

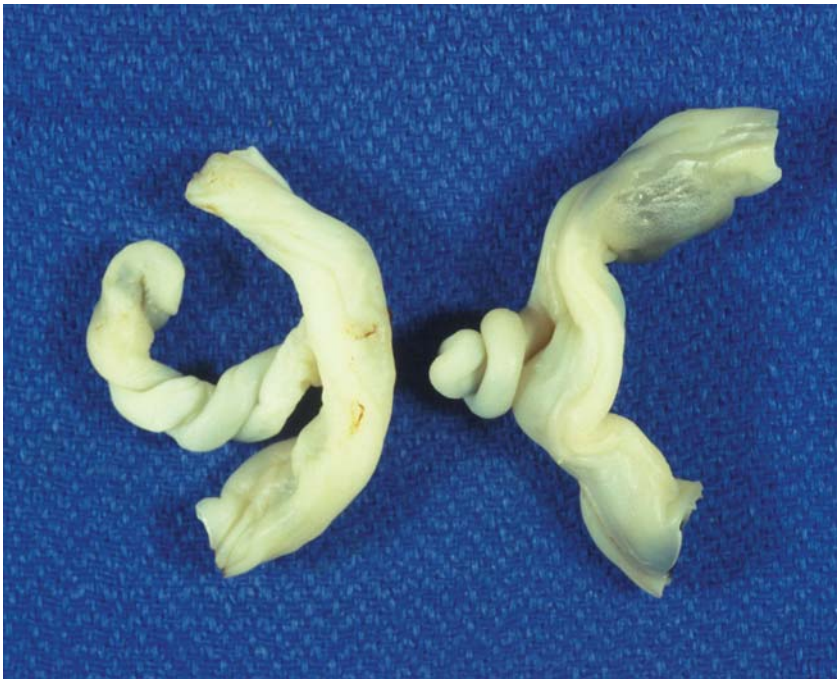


Figure 3.8. The vein redundancy in false knots can be quite impressive. These are of no clinical significance and are not prone to thrombosis or hemorrhage.

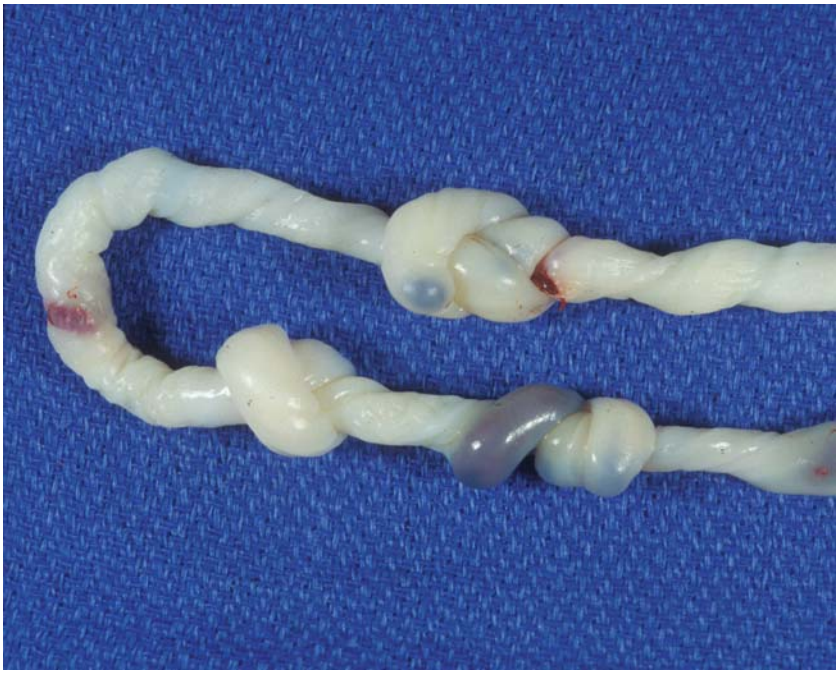


Figure 3.9. These complicated knots occurred in a 31-week infant. There is slight congestion, but no thrombosis was noted. There were no clinical signs of cord compromise. True knots and entanglements are common. Most are not associated with problems. They do occasionally cause fetal distress and death. Knots should be carefully examined for changes which suggest functionally significant obstruction.

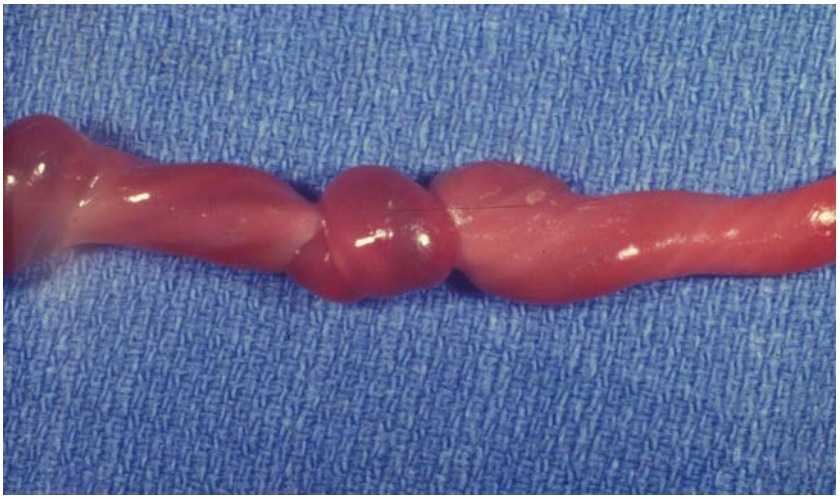


Figure 3.10. In fatal cord compressions, flow in the vein has usually been compromised, leading to congestion on the placental side. Such was the case in this intrauterine demise.

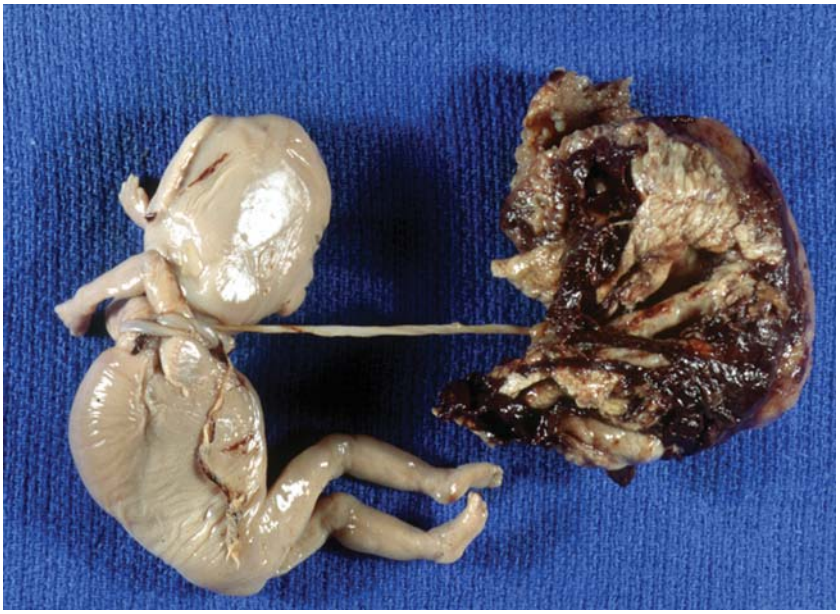


Figure 3.11. This midtrimester loss was thought to be due to true cord entanglement and occlusion. A complete autopsy including cytogenetics failed to reveal other significant pathology.

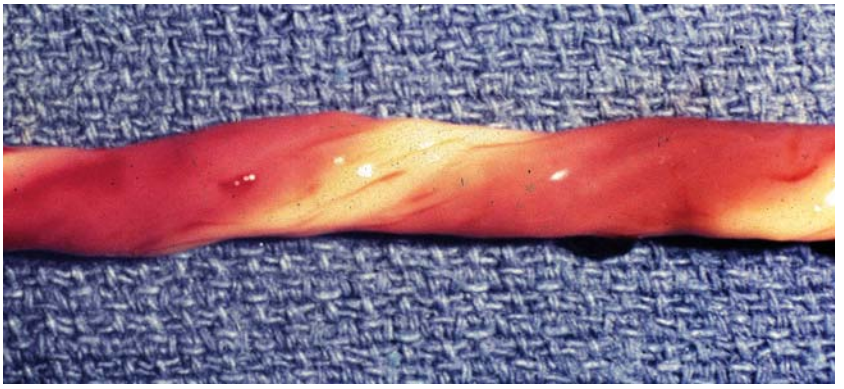


Figure 3.12. The only source of nutrients to the umbilical arteries is the blood flow. If an artery is totally thrombosed the muscle will become necrotic allowing leakage of blood pigments which discolor the cord stroma along its course.

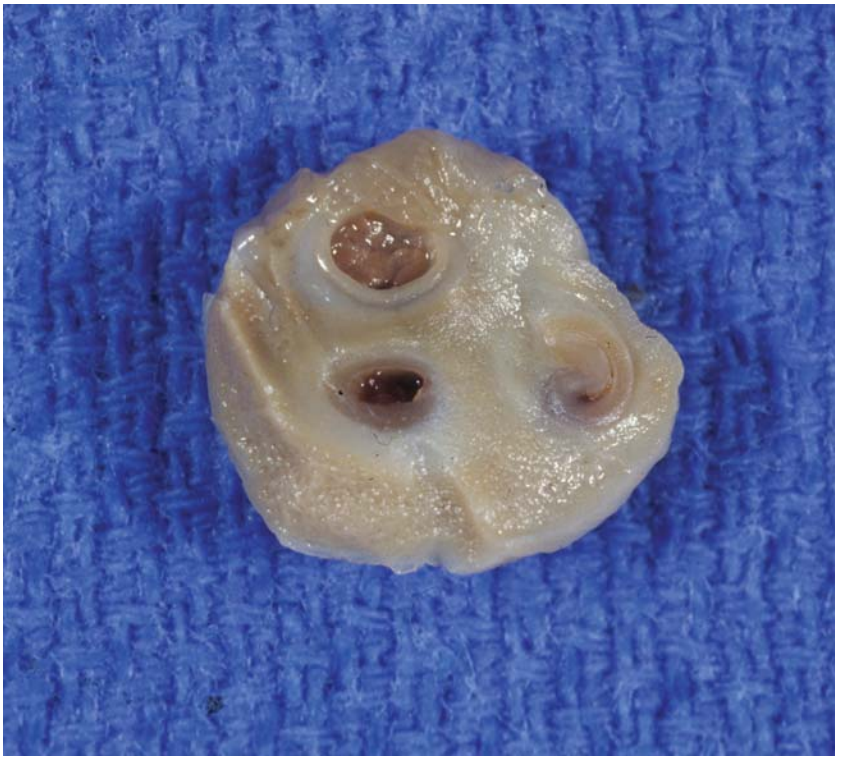


Figure 3.13. This three-vessel cord shows thrombosis of one artery. An occlusive thrombus in one of two umbilical arteries can occur without fetal problems because there are usually vascular anastomoses between the two arteries. This enables perfusion of the entire placenta.

Figure 3.14. This cord cross-section shows a very small artery with pigment in the surrounding tissue. Thrombosis and eventual disappearance of that vessel is a common etiology of single umbilical artery.

A minimum cord length of 32 cm is felt to be necessary for normal vaginal delivery. Undue traction on the cord can cause fetal distress, cord tearing with hemorrhage, and possibly placental separation. The majority of hemorrhages in the cord will be associated with clamp marks and are artifact (Figure 3.15 to Figure 3.17). Entanglement can lead to a functionally short cord. Short cords are known to occur in disorders with

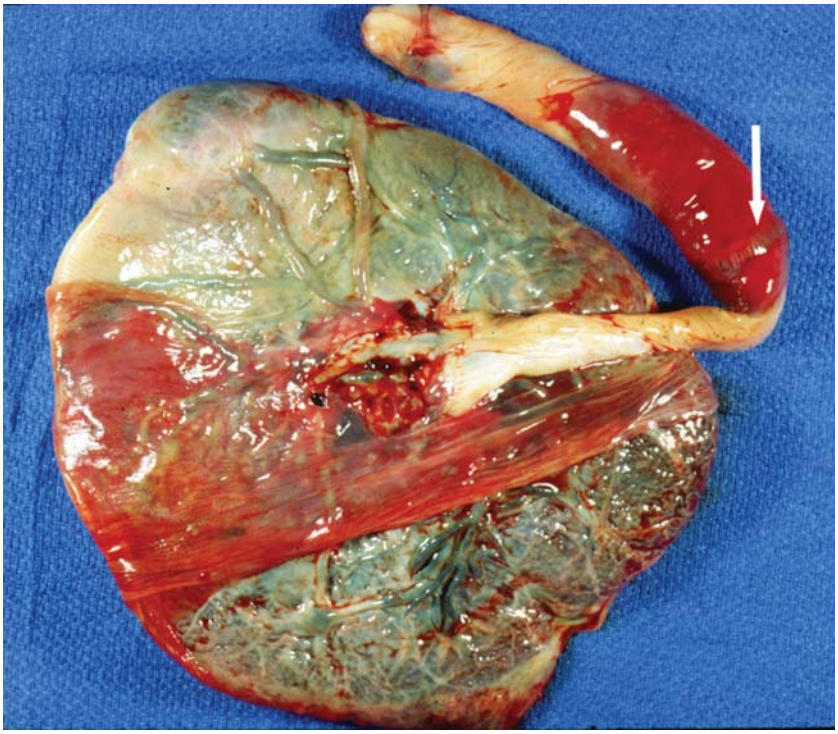


Figure 3.15. The area of hemorrhage shows a clamp mark (*arrow*). It is unlikely this is a true rupture of the cord and is probably not the cause of fetal distress. The majority of cord hemorrhages are an artifact, associated with cord clamping. Ideally, microscopic sections are not taken from such areas. These marks are often quite numerous from cord traction with a clamp during placental delivery.

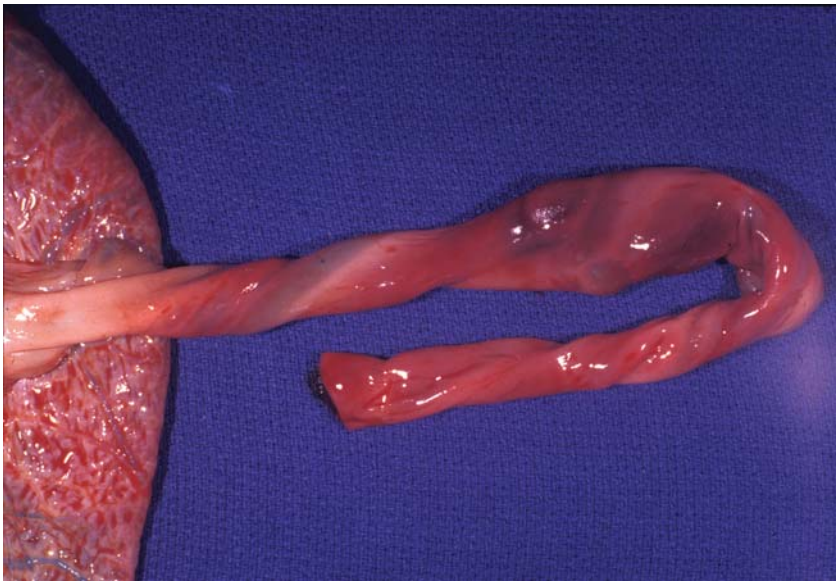


Figure 3.16. This hemorrhage occurred in a stillborn infant with a short cord, complete length of 32 cm. The occlusive hematoma appeared to be arterial in origin and compressed the umbilical vein. Early thrombosis was present.

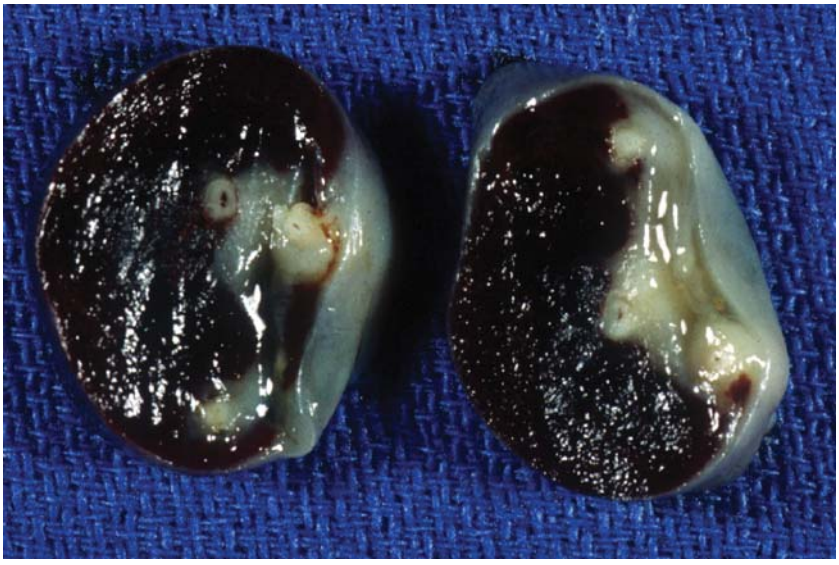


Figure 3.17. Both true cord hemorrhages and artifactual ones have a similar appearance on cross-section. The blood often tracks for considerable distances along the vessels. In problematic cases, multiple microscopic sections from the area may show vital changes.

decreased fetal movement (oligohydramnios, arthrogryposis). They are also associated with more problems in neurological development, suggesting the associated infants may have had longstanding *in utero* problems compromising mobility. Because of these associations, it is extremely important to measure the entire cord length, including that left on the baby or taken for cord gases. Ideally this is done in the delivery room.

Diameter

Premature infants tend to have thicker umbilical cords than more mature babies, while cord substance is often lacking and cords are thin in uteroplacental insufficiency. Edema of the cord can be impressive. It is inconsistently seen in a variety of pathologic states (Figure 3.16). Isolated areas of true cord stricture also occur, particularly near the fetal body wall and at the placenta cord insertion (Figure 3.17).

Insertion

The insertion of the cord into the placental disk occurs in a variety of sites. It may be into the placental substance or into membranes. The position of insertion is due to the plane of implantation of the conception and/or differential placental growth from uterine conditions. Placentas with velamentous vessels are particularly important to evaluate and document, since such vessels can be associated with compression or rupture (Figure 3.18 to Figure 3.25). While these are usually seen with velamentous insertions, small membranous vessels can be present along the edge with normal insertions.

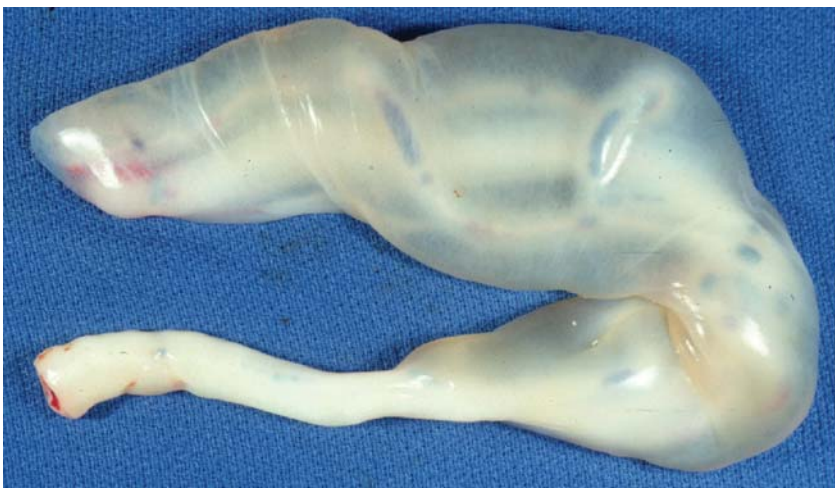


Figure 3.18. Marked edema is present in this umbilical cord. The vessels become cordlike strands within the very loose Wharton's jelly. While such edema may be seen with a variety of perinatal diseases, it is most often an impressive incidental finding.

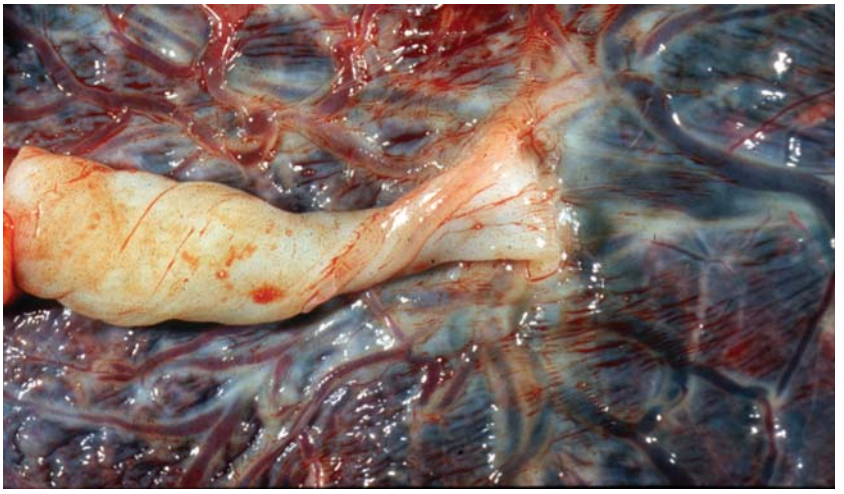


Figure 3.19. This cord becomes narrowed near its insertion into the placenta with reduced Wharton's jelly. Differences in diameter are common along the length. It is usually wider close to the infant. Strictures which are physiologically significant often show microscopic thrombosis.

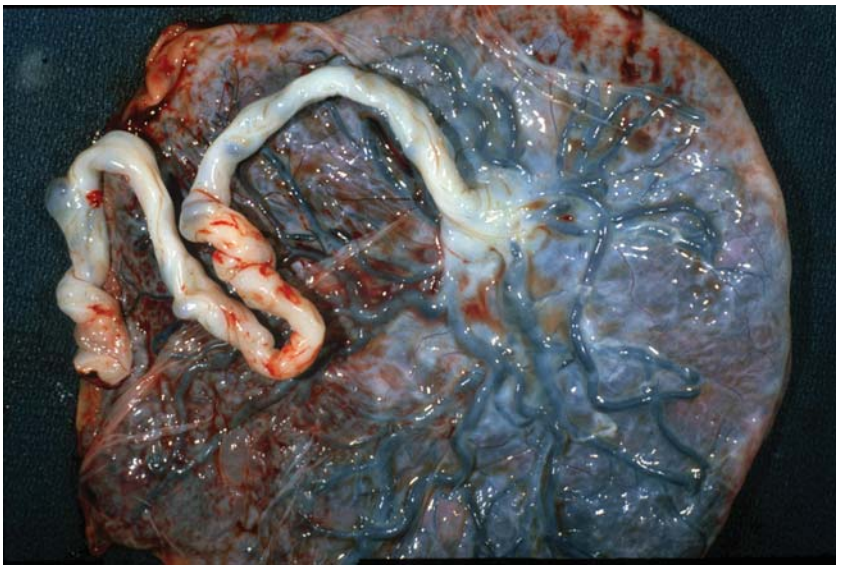


Figure 3.20. Most placentas will have a cord insertion in the center or slightly eccentric in the disk, the latter shown here. The surface vessels disperse from the cord in a relatively even circumferential manner. Even when the cord has been torn from the placenta, examination of the distribution of surface blood vessels usually reveals the site of insertion.

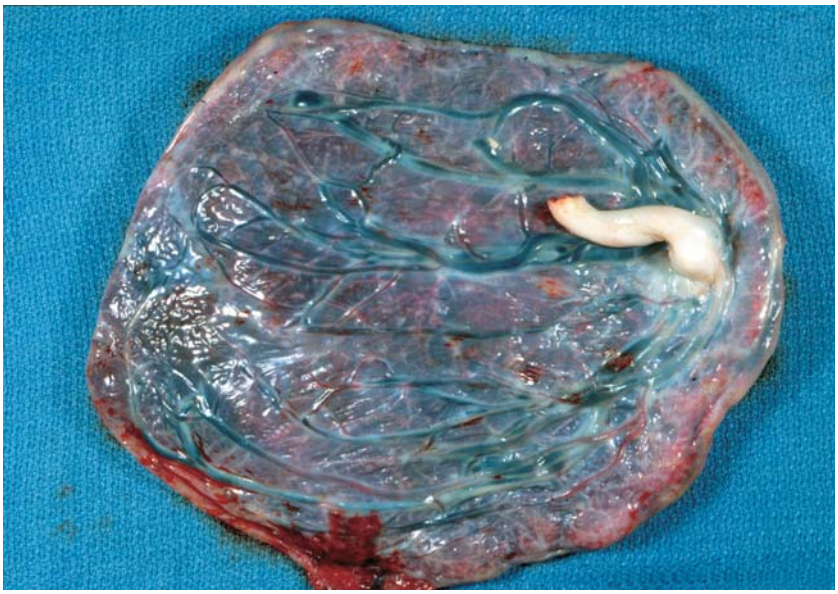


Figure 3.21. This cord inserts close, but not quite at the margin of the placenta. The vessels course in one direction away from the cord. Such a vascular distribution is found in 38% of placentas and is likely somewhat less effective in perfusing the fetus.

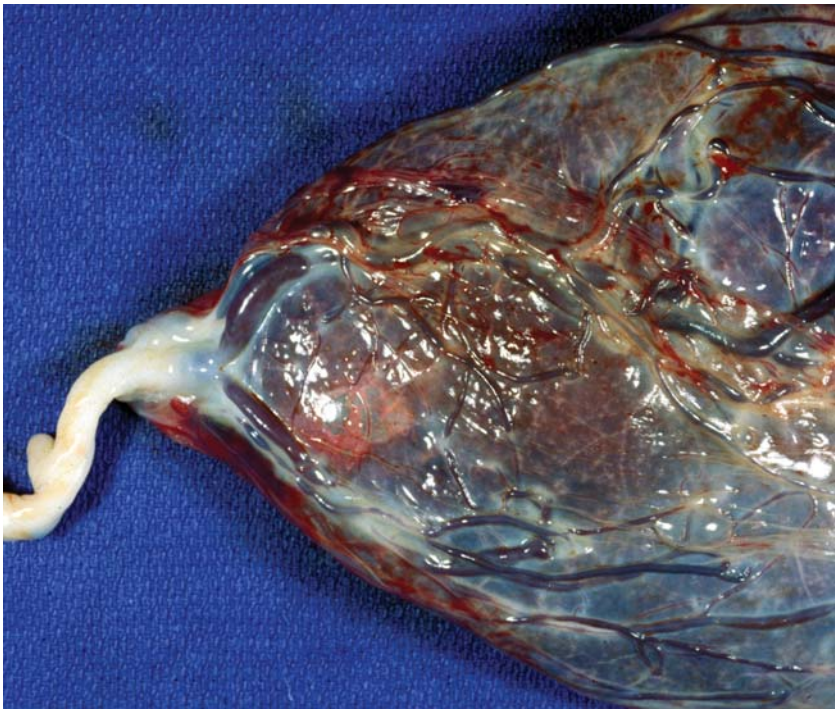


Figure 3.22. A true marginal insertion is present (Battledore placenta). Membranous vessels adjacent to marginal cord insertions are common. Marginal and velamentous cords may be less mobile and more prone to compromise. The infants are slightly smaller on average. In many of the very peripheral insertions, there are a reduced number of fetal surface vessel branches.

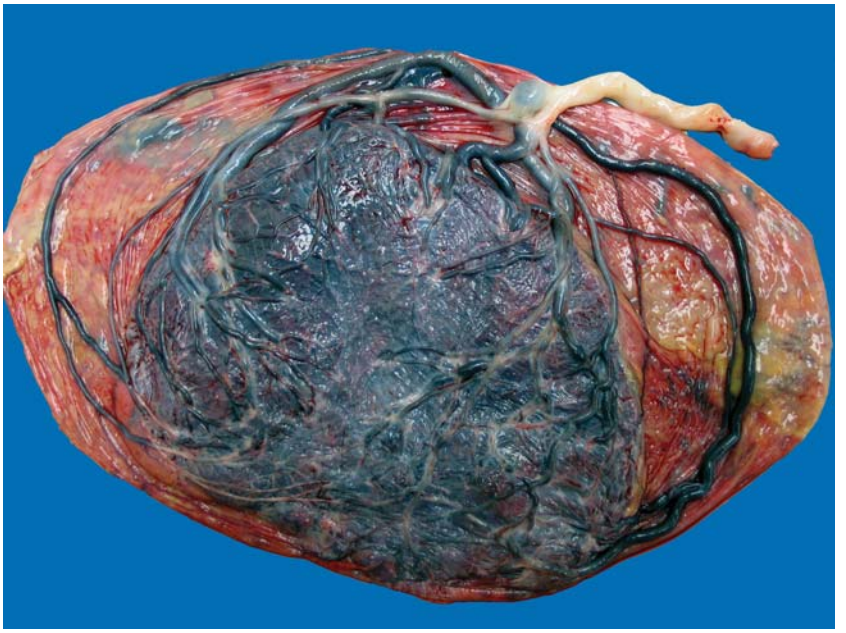


Figure 3.23. Cord insertion into the free membranes (velamentous insertion) occurs in about 1% of deliveries. The vessels must be carefully examined for integrity and extent of membranous passage. Old hemorrhage behind the membranes is sometimes found where the cord attaches.

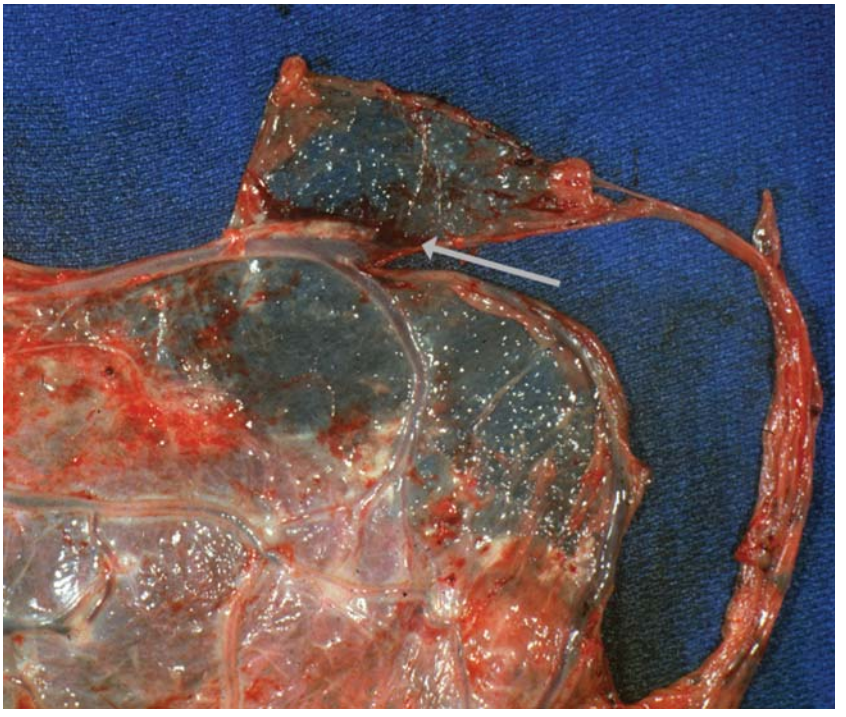


Figure 3.24. Intrapartum rupture of a velamentous vessel occurred in this case (*arrow*) supported by maternal history and neonatal anemia. This infant survived. Hemorrhage from a ruptured vessel is usually found in the sub-amniotic region. Vessels may also be torn after the infant has been born, during placental delivery. While this has no clinical significance, it should be noted since complete historical information may not be available at the time of placental examination.

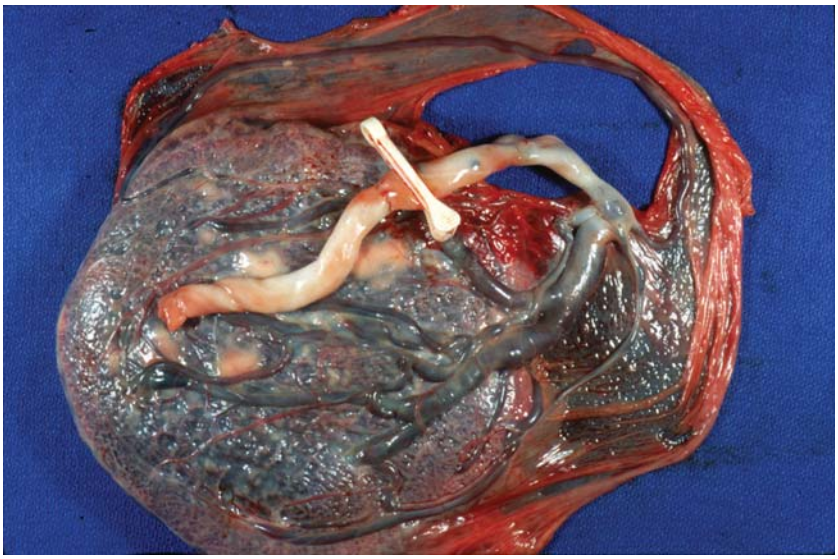


Figure 3.25. Despite the close proximity of the cord insertion and velamentous vessels to the site of membrane rupture in this vaginal delivery, no vascular disruption occurred. Vessels overlying the cervical os (vasa previa) are at the greatest risk of tearing and causing catastrophic fetal blood loss. Velamentous vessels may also be compressed during labor. There is a fleck of calcium in one velamentous vessel which is likely old thrombosis (*arrow*).

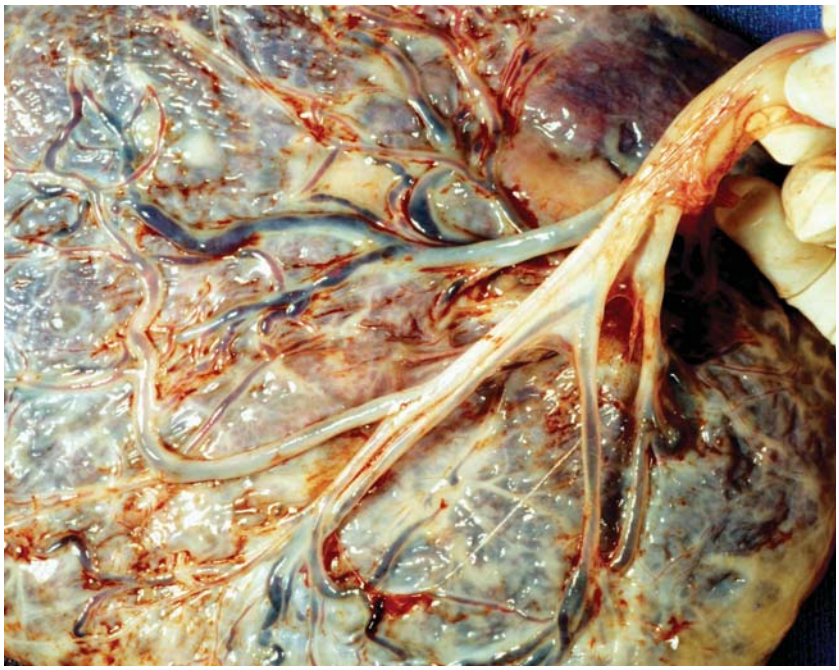


Figure 3.26. This cord divides into vessels which lose their protective covering of Wharton's jelly above the surface of the placenta. Such furcate insertions will have the risks attendant to velamentous vessels.

The vessels in the cord may separate before it reaches the surface (furcate). The unattached surface amnion may also attach to the cord several centimeters before the cord reaches the placental surface (Figure 3.26 to Figure 3.29).

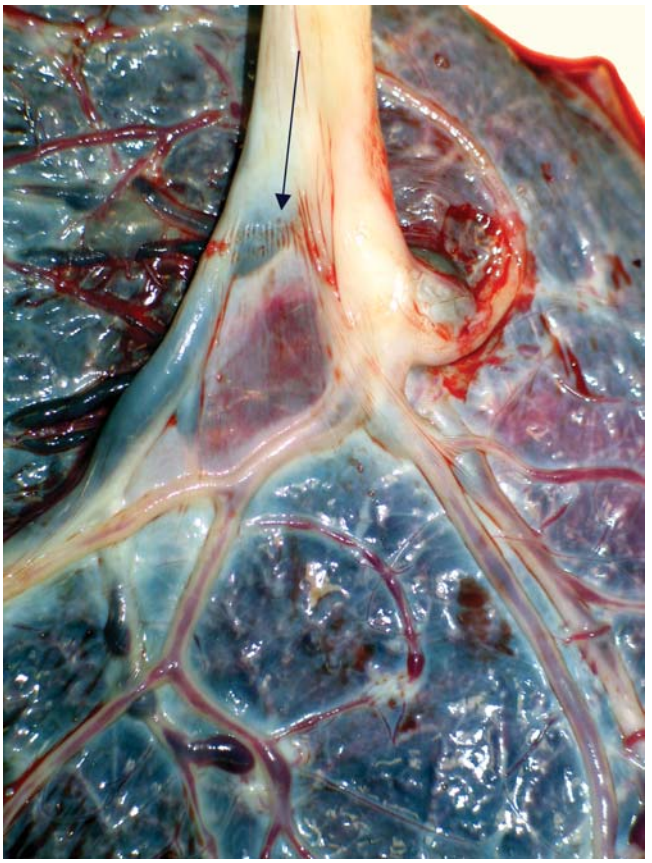


Figure 3.27. At times the cord is partially encased by a fold of amnion at its placental end, a "chorda" or amniotic web. This cord is minimally furcate with a web of amnion enclosing the vessels. A clamp mark is present (*arrow*).

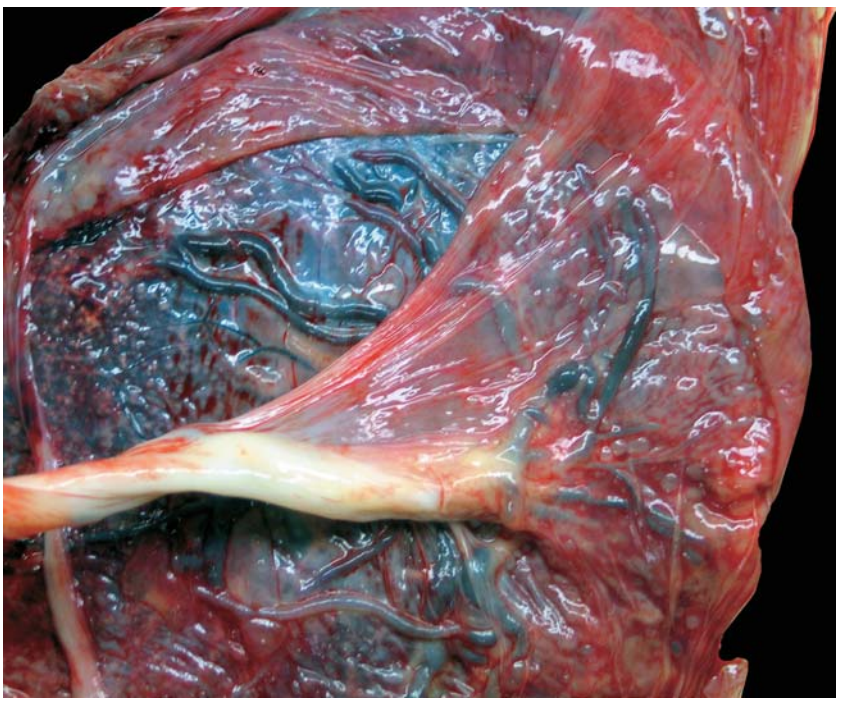


Figure 3.28. Amniotic webs are very common and can extend for several centimeters up the cord. They may be loose or relatively tight and bind the cord to the fetal surface of the placenta. If the amnion is largely detached from the chorion, a web is likely.

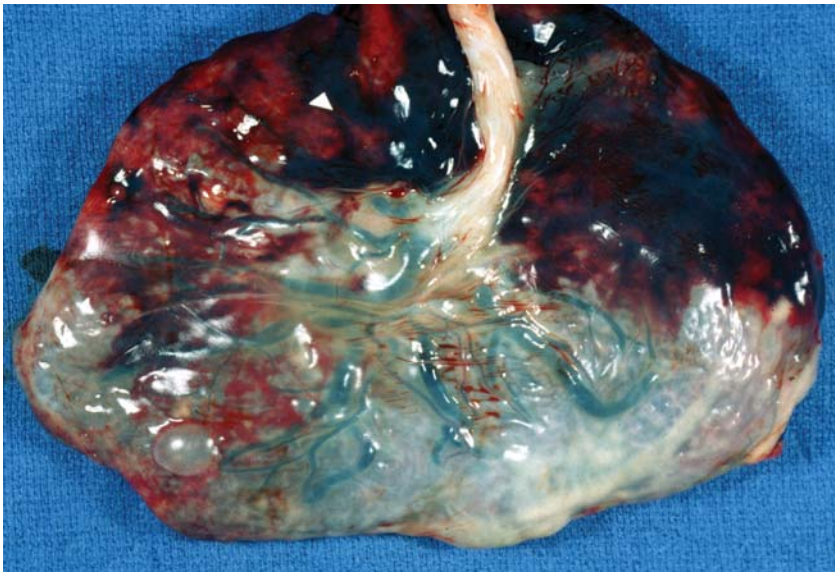


Figure 3.29. A long tight amniotic web is present. Webs may limit the mobility of the cord, potentially compromising blood flow. There is also subamniotic hemorrhage. Although bleeding from vessels between the amnion and chorion is usually an artifact arising during placental delivery, it is common when webs are present, suggesting abnormal stress in this area.

Infections

The cord inflammation seen with most ascending membranous infections (see page 56) is usually not recognizable grossly. Candida is an exception and shows characteristic micro abscesses on the cord surface (Figure 3.30, Figure 3.31). This infection may cause a rash on the infant at birth.

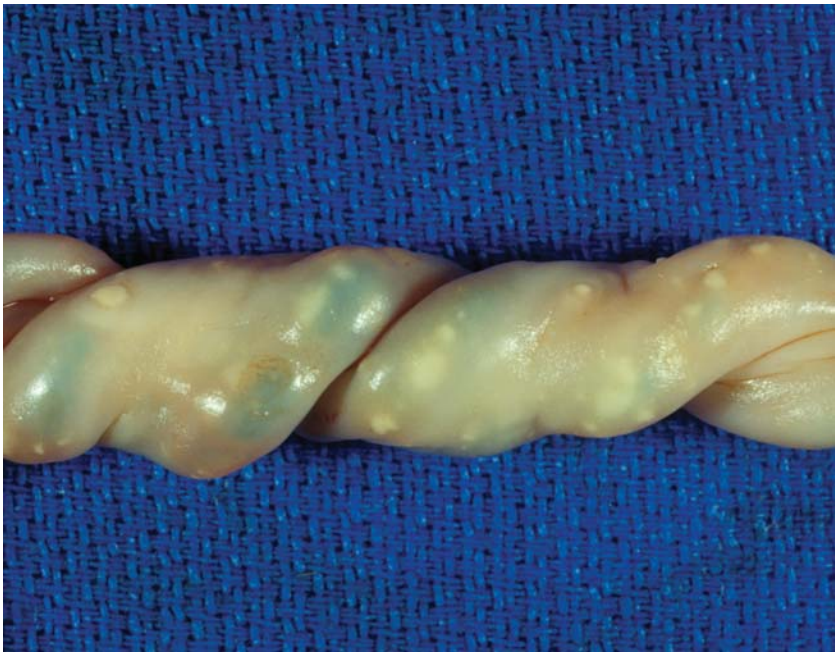


Figure 3.30. Scattered yellow to white 2-mm to 3-mm plaques on the cord are virtually pathognomonic of *Candida* funisitis. They are not seen elsewhere on the placental membranes. There is usually an associated chorioamnionitis.

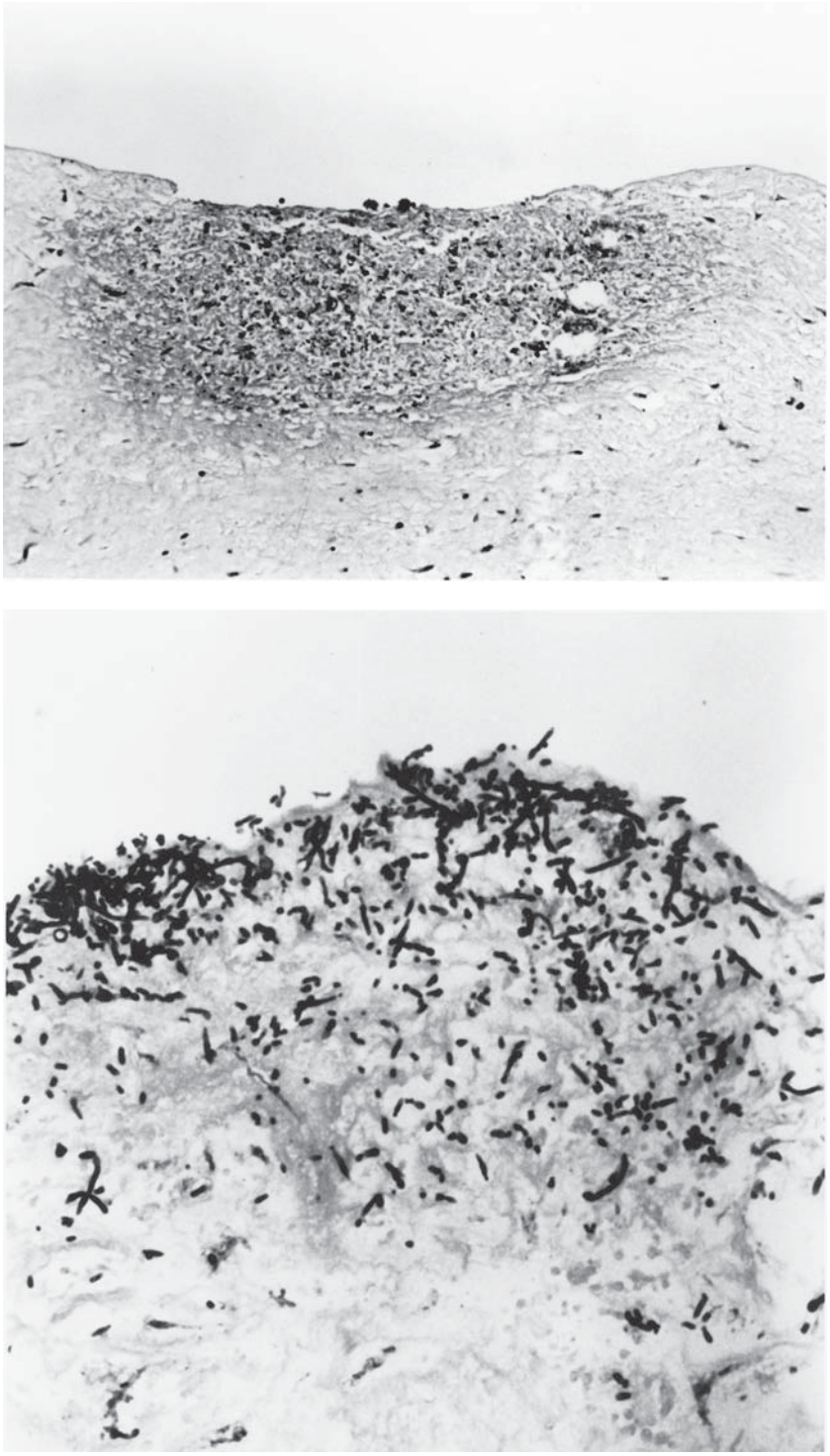


Figure 3.31. (**A**) Histologically *Candida* funisitis shows micro abscesses just under the cord surface. These are filled with necrotic debris, in which it is difficult to identify organisms, (**B**) numerous fungal pseudohyphae and yeasts are present on methenamine silver stain.

It is more likely to cause sepsis in premature infants. The "barber-pole" configuration of chronic necrotizing funisitis is felt to represent a chronic and sometimes healed intra-uterine infection with organisms of low virulence (Figure 3.32, Figure 3.33).

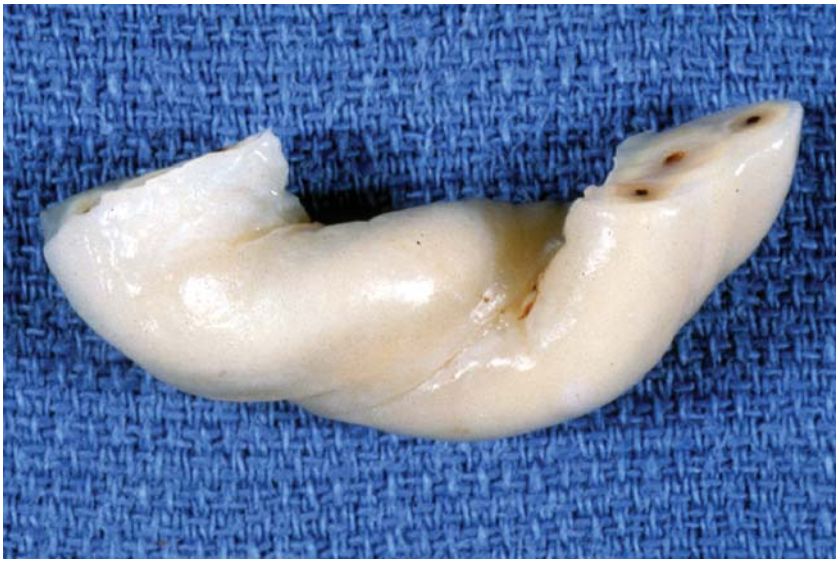


Figure 3.32. Necrotizing funisitis represents a chronic inflammatory process in the umbilical cord, apparently infectious in origin. There is calcification surrounding the vessels leading to an extremely rigid cord. This is at times visible along the length as a white stripe.

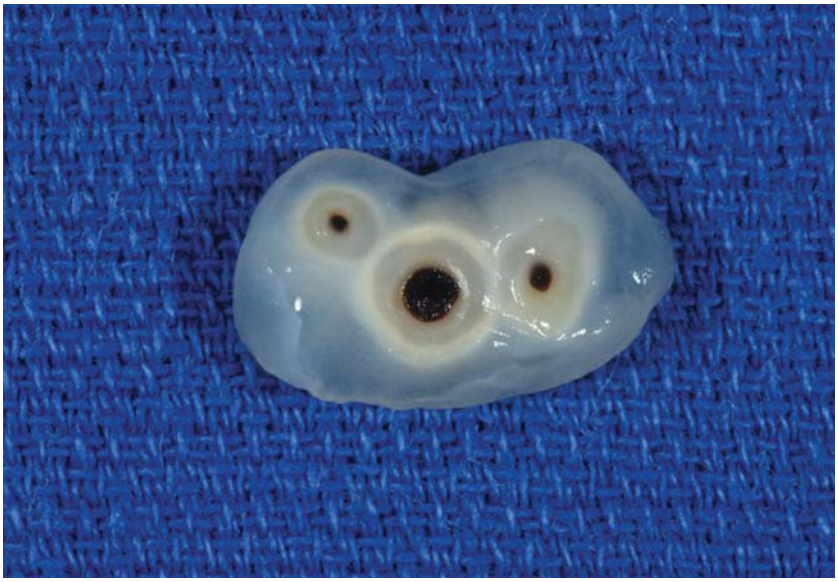


Figure 3.33. Cross-section of a cord with necrotizing funisitis shows white bands suggesting diffusion rings surrounding each of the three vessels. These are composed of necrotic inflammatory cells and calcification.

Ulceration

Loss of Wharton's jelly with ulceration of the cord surface is uncommon, but the associated infants may have significant problems. It is usually related to bile or meconium exposure (Figure 3.34).

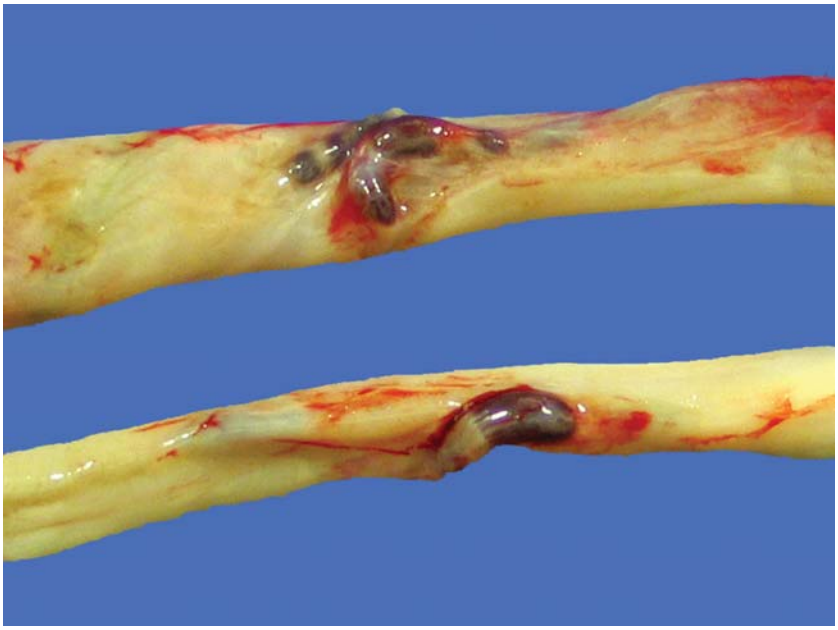


Figure 3.34. Ulceration of the cord occurs in some cases of upper gastrointestinal tract atresia. This infant had proximal jejunal atresia. The exposed vessels may hemorrhage leading to fetal compromise or death. The intestinal obstructions are located below the Ampulla of Vater as the bile, appears to be etiologic. Ulceration also may occur with longstanding meconium exposure.

4

Fetal Membrances and Surface

Layers

The peripheral membranes and fetal placental surface are continuous, and most processes are seen in both. The layer of membrane closest to the fetus is amnion. External is the chorion, which is minimal on the peripheral membranes and more extensive on the disk. The remnant of the yolk sac lies between the amnion and chorion (Figure 4.1). The chorion is continuous with all the villous tissue. There is close proximity of the surface membranes to the maternal blood of the intervillous space, while the peripheral membranes abut the decidua and its blood vessels. This relationship permits maternal cells access to the membranes.

Subchorionic Fibrin and Hemorrhage

Deposits of fibrin from the maternal circulation and thrombosis are common beneath the fetal surface. As pregnancy progresses, the amounts of these materials generally increase (Figure 4.2, Figure 4.3). Subchorionic thrombi eventually become compacted fibrin. The quantity of subchorionic fibrin has been associated with fetal activity. Large nodular subchorionic hematomas, sometimes called "Breus moles," are seen in both liveborns and spontaneous abortions (Figure 4.4). Unusually thick layers of subchorionic hemorrhage can be associated with chronic bleeding and prematurity (Figures 4.5).

Extrachorial Placentation

The membranes normally insert at the peripheral margin of the villous tissue which is usually the outer limit of the vascular plate. Extrachorial placentation exists when villous tissue extends outward beyond the vascular plate. This takes two forms, circummargination and circumvallation (Figure 4.7). In circumvallation there is a redundant, doubled-back membrane fold with enclosed debris and old hemorrhage at the point of membrane insertion (Figure 4.8, Figure 4.9). In circummargination there is a

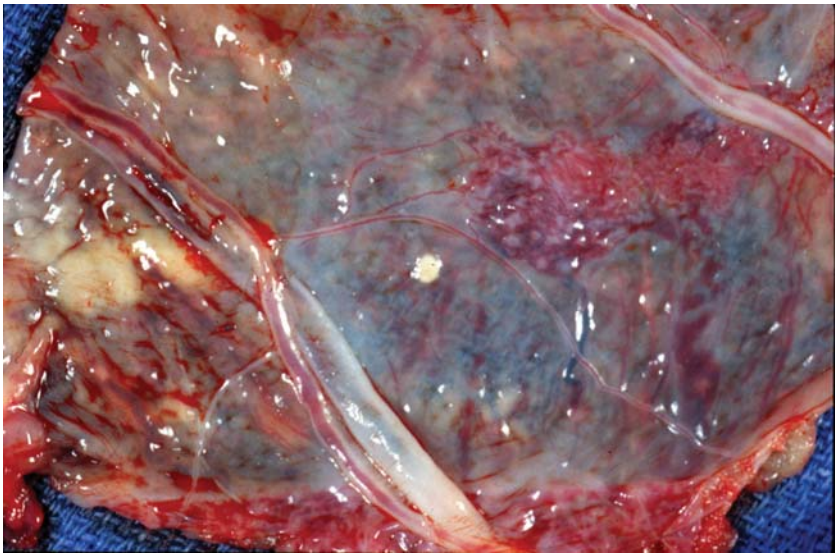


Figure 4.1. The yellow 4-mm nodule is the calcified remnant of the yolk sac. It lies free between the amnion and chorion. These are quite commonly found in normal term placentas and are usually located near the edge of the placenta or in the membranes.

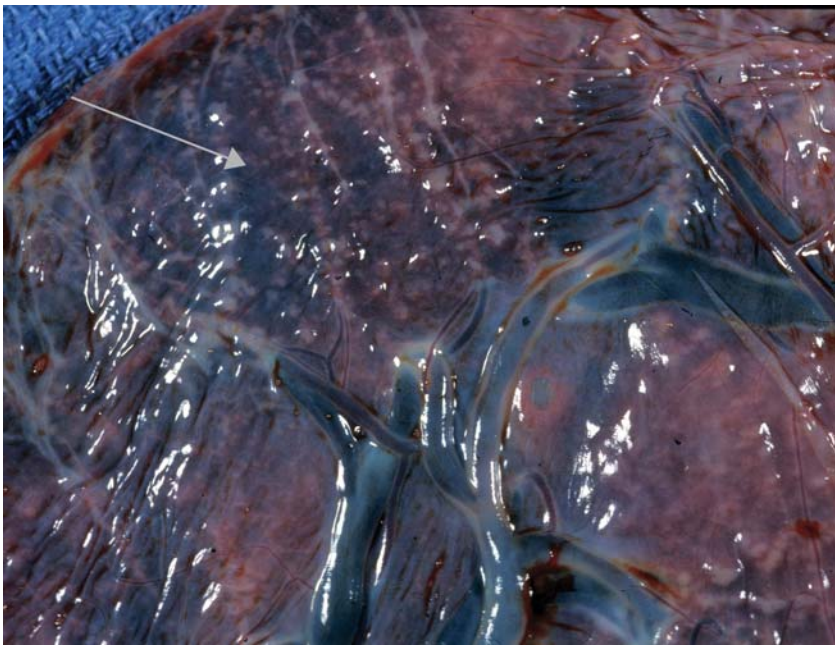


Figure 4.2. Subchorionic fibrin tends to increase with gestational age, although it is quite variable. An immature placenta shows minimal subchorionic fibrin, leading to the deep blue surface coloration commonly seen. The minimal fibrin present appears as tiny nodules under the fetal surface (*arrow*).

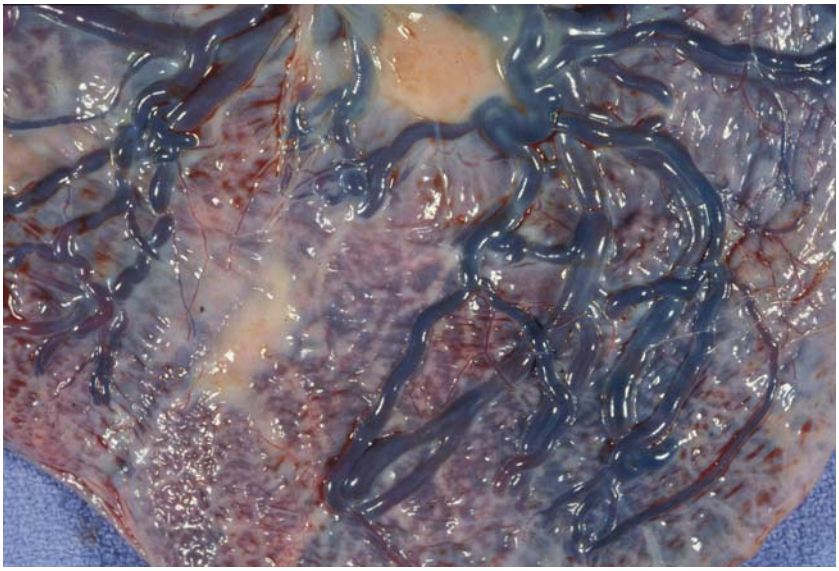


Figure 4.3. Abundant fibrin deposition is often a striking feature of the fetal surface in term placentas. It is composed of larger nodular aggregates of fibrin and old subchorionic hemorrhages which have lost their pigmentation. It may become quite dense, as seen in this term placenta. When possible, histologic sections should not be taken from areas with thick fibrin. Inflammatory processes are often masked in such areas. An increased number of early amniotic sac infections will be diagnosed if thin, more transparent surface areas are sampled.

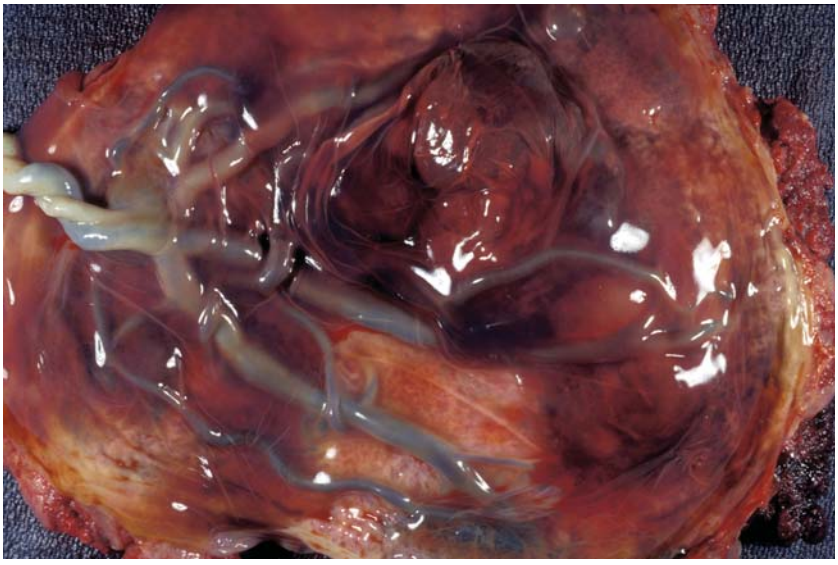


Figure 4.4. Extensive thick clot and hemorrhage undermine the fetal surface in this case, a change which may be seen as early as midtrimester. The membranes are discolored from hemosiderin pigment, and the amniotic fluid may be thick and brown. Placentas such as this are sometimes called "Breus moles."

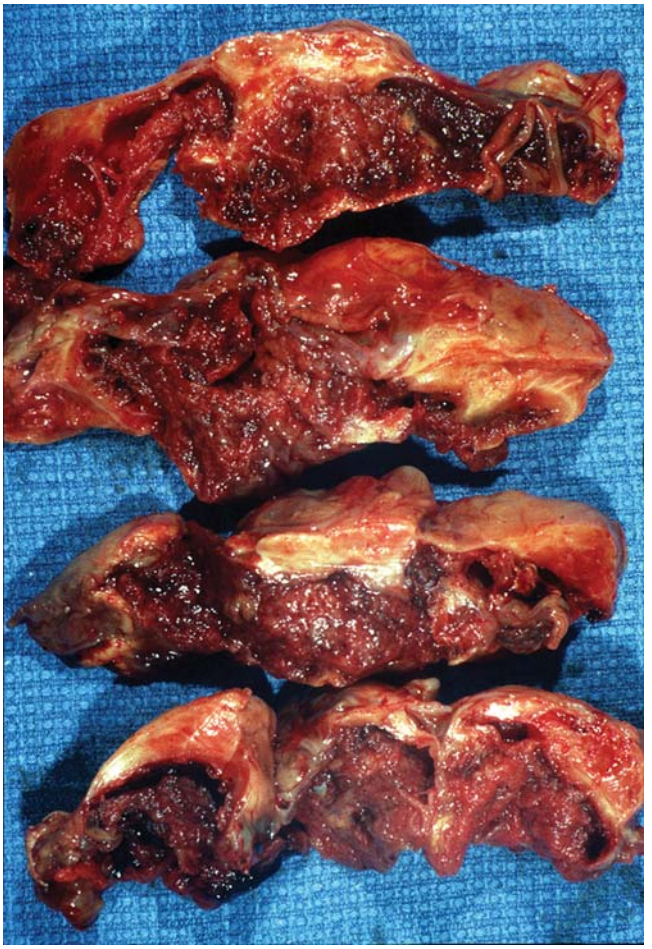


Figure 4.5. Cross-sections of a placenta with excessive subchorionic hemorrhage show the marked extent of the clot in the subchorionic region with separation of the underlying villous tissue from the fetal surface. Such placentas can be associated with early oligohydramnios, bleeding, elevated a-fetoprotein, and preterm delivery of small, nonmalformed infants, who sometimes have pulmonary hypoplasia. The etiology of this process is unknown, but there may be a risk of recurrence.

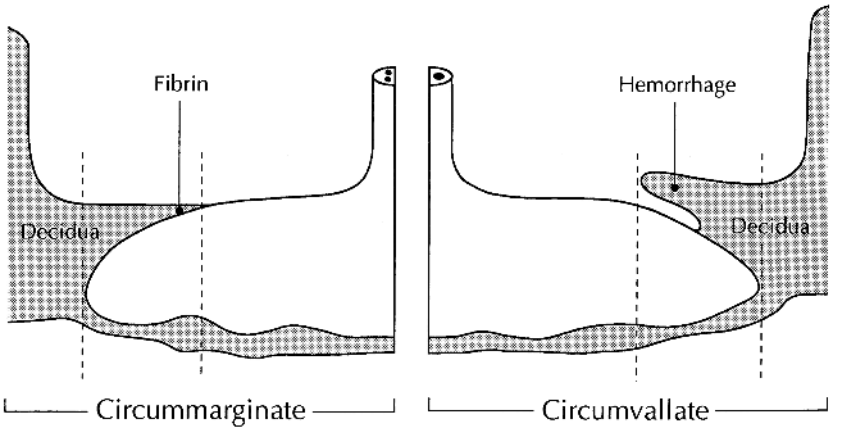


Figure 4.6. Extrachorial placentation is displayed schematically with the extrachorial portion enclosed by dotted lines. The right cross-section shows the redundant membrane fold characteristic of circumvallation. This frequently contains old hemorrhage continuous with the decidua. Such changes are absent in circummargination (left) in which the membranes are flat with a small deposit of fibrin.

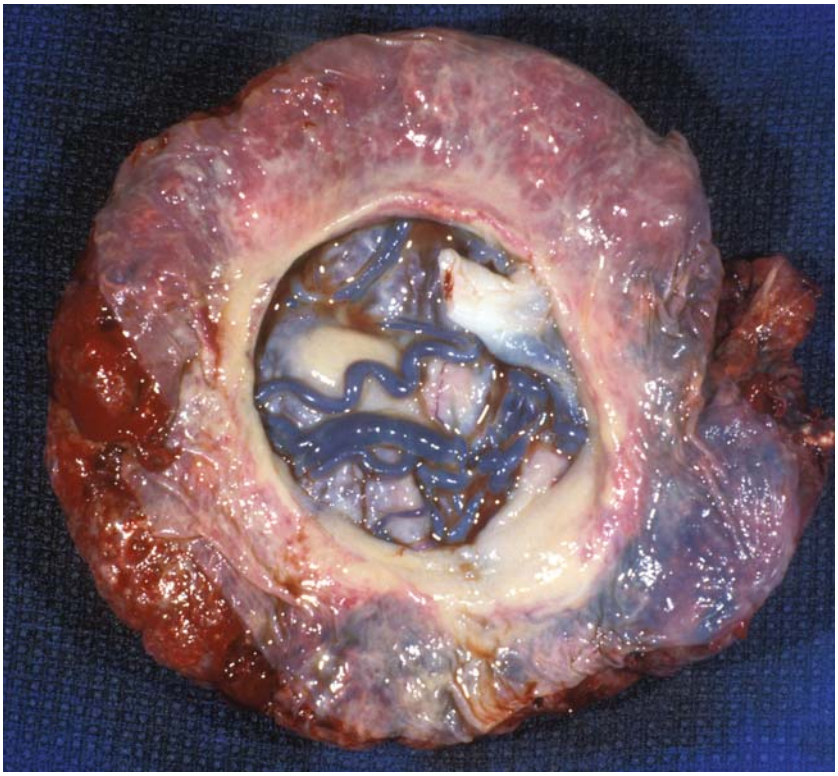


Figure 4.7. This circumvallate placenta shows a complete circumferential fold of membranes where the vascular plate ends. The region of vascular distribution is small. There is decidua, fibrin and sometimes hemorrhage in the overhanging ridge. These placentas are frequently thicker than usual. Here the process is complete, however it may not involve the entire circumference. Circumvallation is at times associated with preterm bleeding and early delivery.

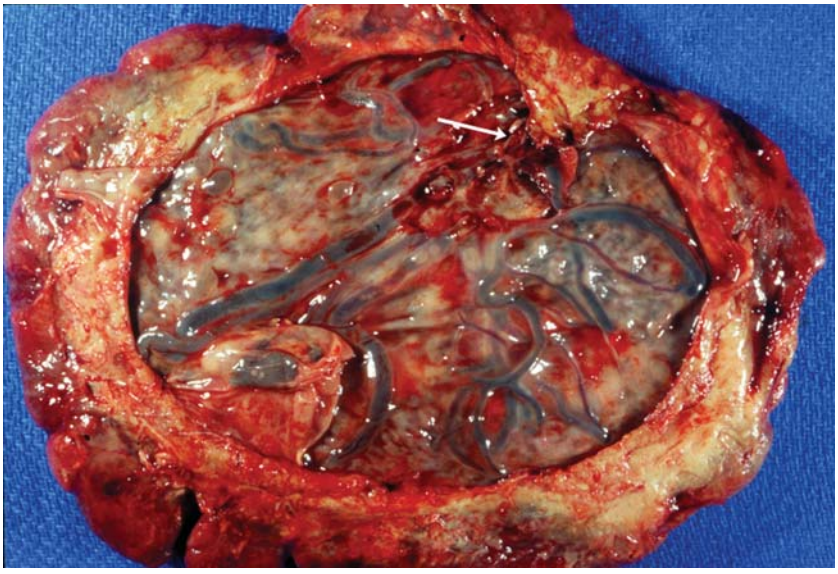


Figure 4.8. Most of the membranes and cord were torn from this circumvallate placenta at delivery. The site of cord insertion is identifiable (*arrow*) at the "margin" of the vascular distribution, the circumvallate ring. The yellow color of the material composing the ring is due to old blood pigment and necrotic decidua.

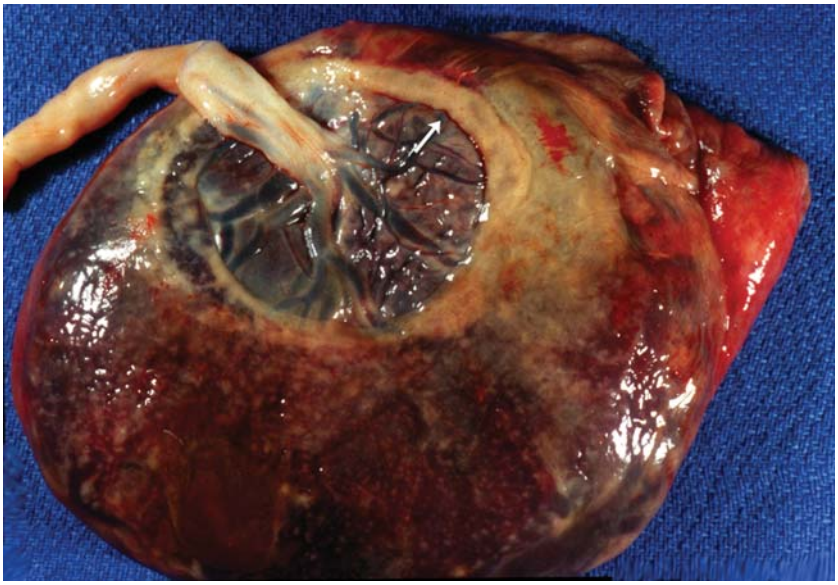


Figure 4.9. This extremely thick placenta is circummarginate with a very wide extrachorial extension of villous tissue. The membranes over the surface are flat with only a thin rim of fibrin where they meet the extension of placental tissue. Circummargination often involves only part of the placental circumference. The remaining tissue is either normal (marginal membrane insertion) or circumvallate. The area at 2 o'clock (*arrow*) suggests circumvallation with a ridge. Circummargination has no pathologic sequelae in the vast majority of cases. However, on observing cases such as this with extensive reduction in the fetal surface vasculature and increased thickness, one must consider possible effects on fetal perfusion.

small ridge of fibrin where the membranes contact the extended placental surface (Figure 4.7). Circummargination is not believed to lead to clinical problems, but prematurity and chronic bleeding are associated with circumvallation. The origin of extrachorial placentation is unclear. Suggestions include abnormal implantation, secondary growth lines, marginal separation, and loss of amniotic fluid pressure.

Amnion Nodosum/Squamous Metaplasia

Small nodules on the amniotic surface are either amnion nodosum or squamous metaplasia. These are important to distinguish. Squamous metaplasia is a normal variant (Figure 4.10), while amnion nodosum is strongly associated with longstanding oligohydramnios, a setting in which pulmonary hypoplasia commonly develops (Figure 4.11 to Figure 4.13).

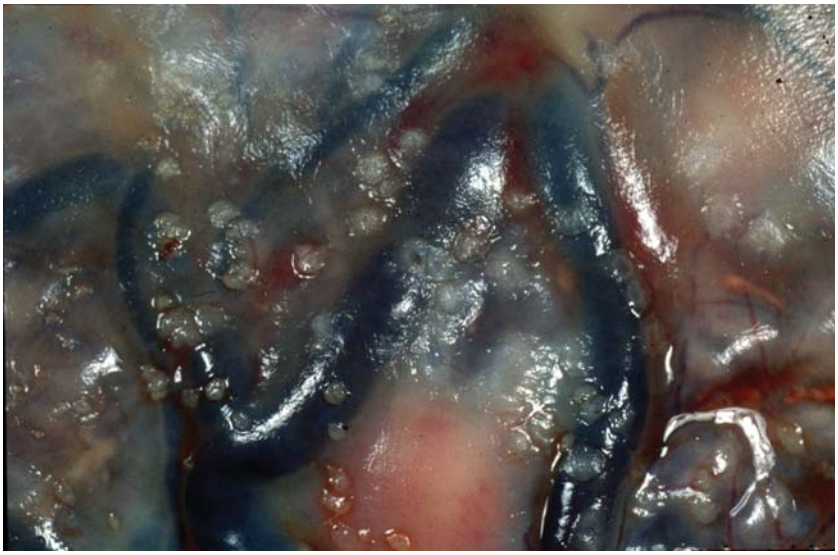


Figure 4.10. Squamous metaplasia is an incidental change in the amnion. The normally cuboidal epithelium becomes nonkeratinizing squamous type. This change is most commonly seen near the cord insertion where it appears as small, dull, white plaques which are not readily removed with scraping.

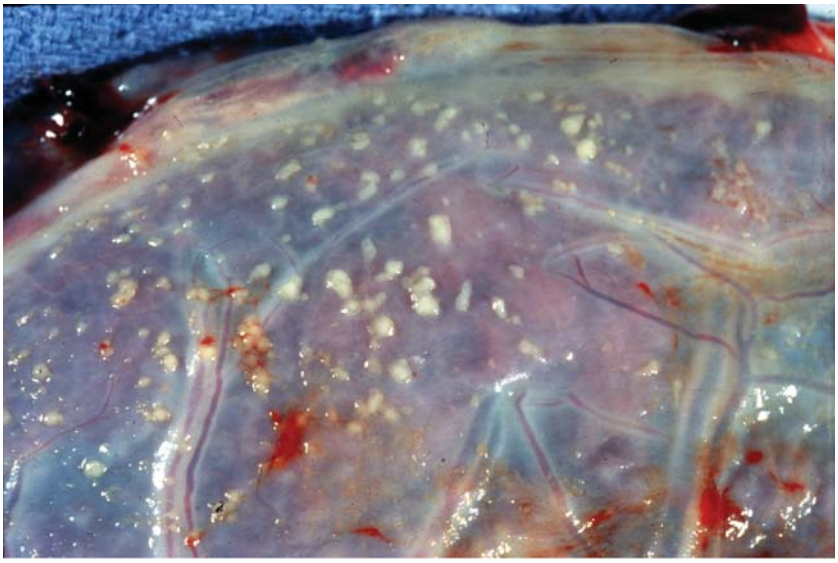


Figure 4.11. Amnion nodosum is a pathologic finding, consisting of yellow-white nodules of hair and squames pressed onto the fetal surface. These nodules are not attached and can be easily removed. They may be found over the placental surface and membranes. Amnion nodosum occurs in the setting of severe oligohydramnios, and is a marker for its prior existence.

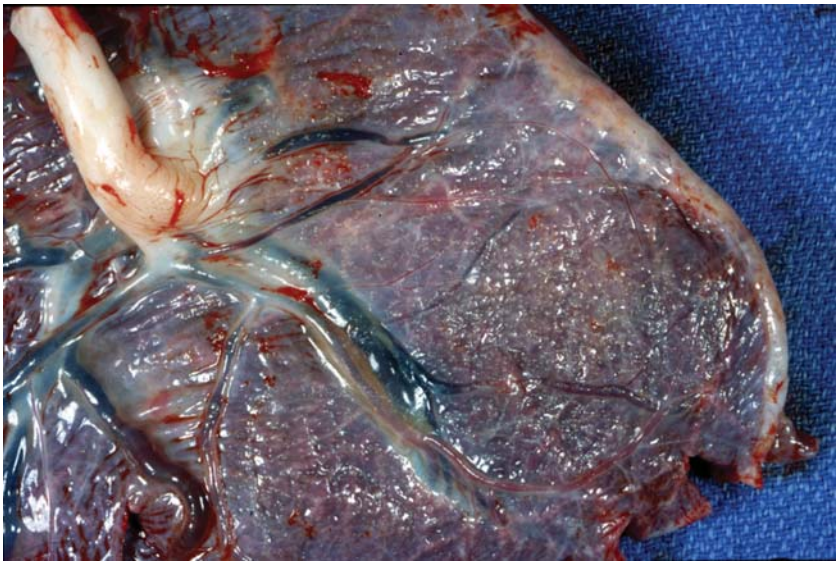
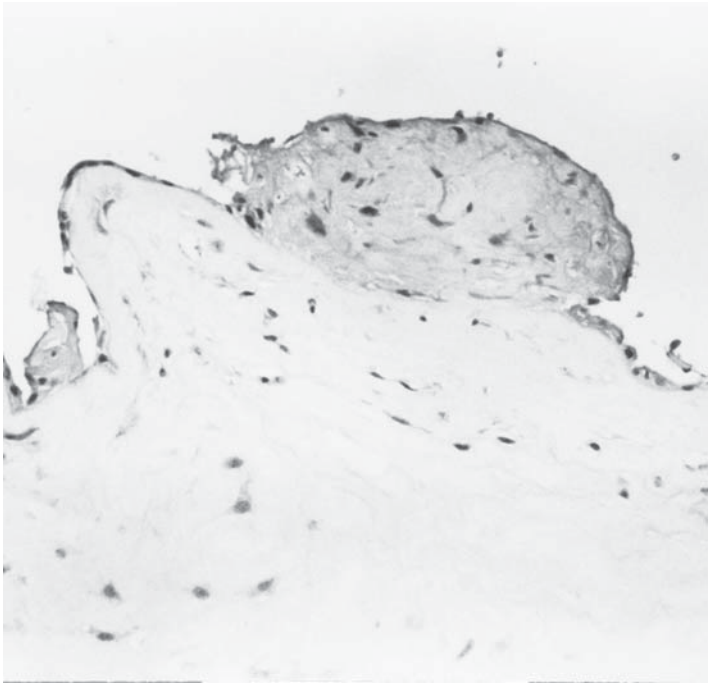


Figure 4.12. Another appearance of amnion nodosum is shown in this placenta which has a finely granular appearance over much of its surface. This is often much harder to recognize. The severity of amnion nodosum tends to be greater later in gestation, but is quite variable.



A

Figure 4.13. Histology of amnion nodosum compared to squamous metaplasia. (**A**) In amnion nodosum nodules of hair, squames, and amorphous material are compressed on the surface, leading to destruction of the underlying amniotic epithelium.

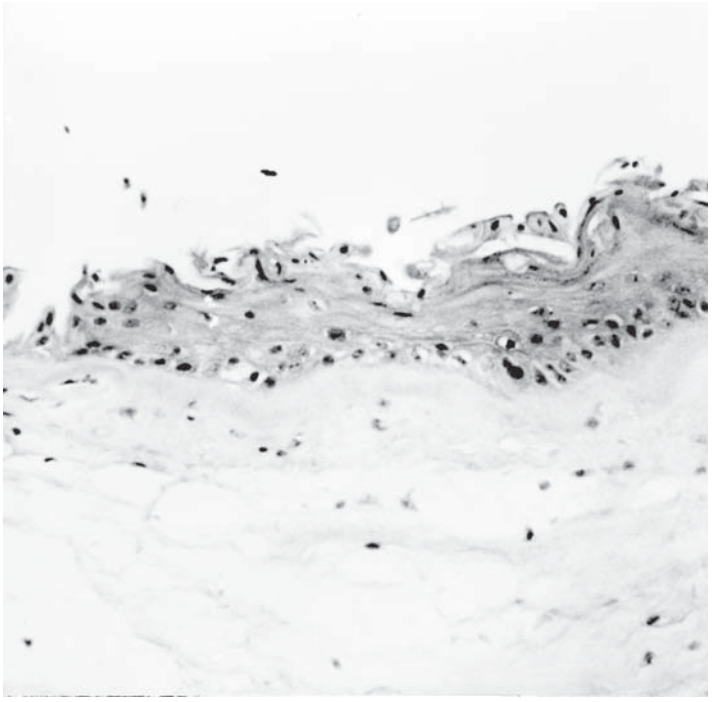


Figure 4.13. (**B**) Squamous metaplasia shows a change in the cuboidal amniotic epithelium to a keratinizing squamous type.

B

Amniotic Rupture

Occasionally the amnion ruptures before delivery. The resulting bands of amnion can entrap and disrupt fetal tissues leading to defects including amputations, clefts, and constrictions (Figure 4.14). They may encircle the umbilical cord and cause fetal death. The denuded chorionic plate may be adherent to the fetus (Figure 4.15). This process has a negligible risk of recurrence and placental examination can often be diagnostic.

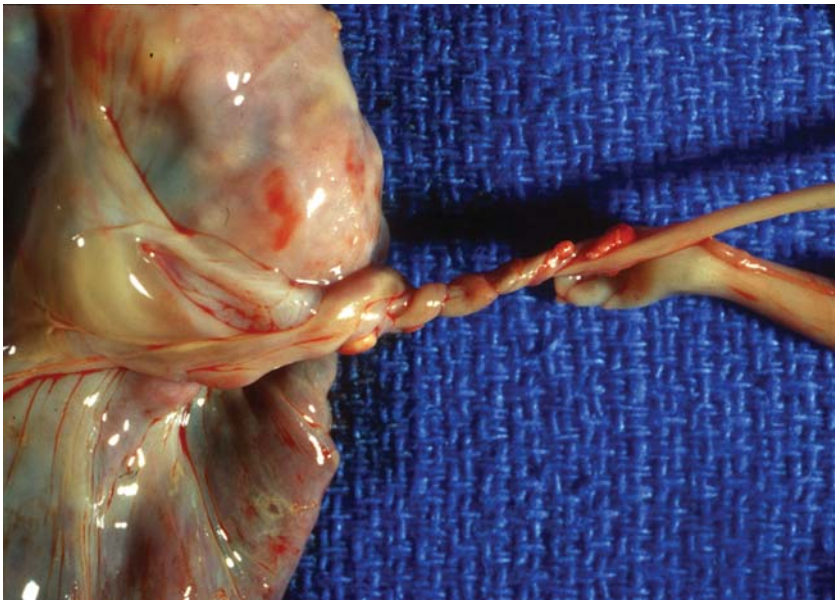


Figure 4.14. A strand of tissue encircles the cord and some digits in this stillborn midtrimester fetus. This is attached to the placental surface and is an amniotic band. Bands can be quite delicate and require careful examination to distinguish them from artifact, particularly in fragmented specimens.

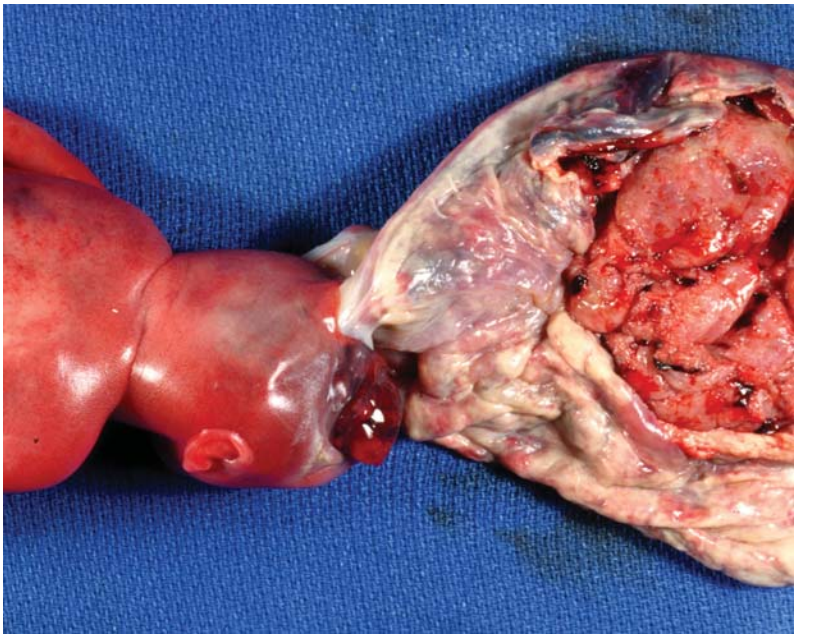


Figure 4.15. After amnion rupture, chorion comprises the placental surface covering and may adhere to the fetus leading to defects. Anencephaly in this fetus was of this etiology and has a different recurrence risk than more typical anencephaly. Squames may become adherent to the surface chorion, similar to amnion nodosum.

Pregnancies in which the fetus develops outside the membranes, extramembranous gestations, also show characteristic placental changes (Figure 4.16). Oligohydramnios occurs with these lesions as the exposed chorion leads to altered amniotic fluid dynamics.

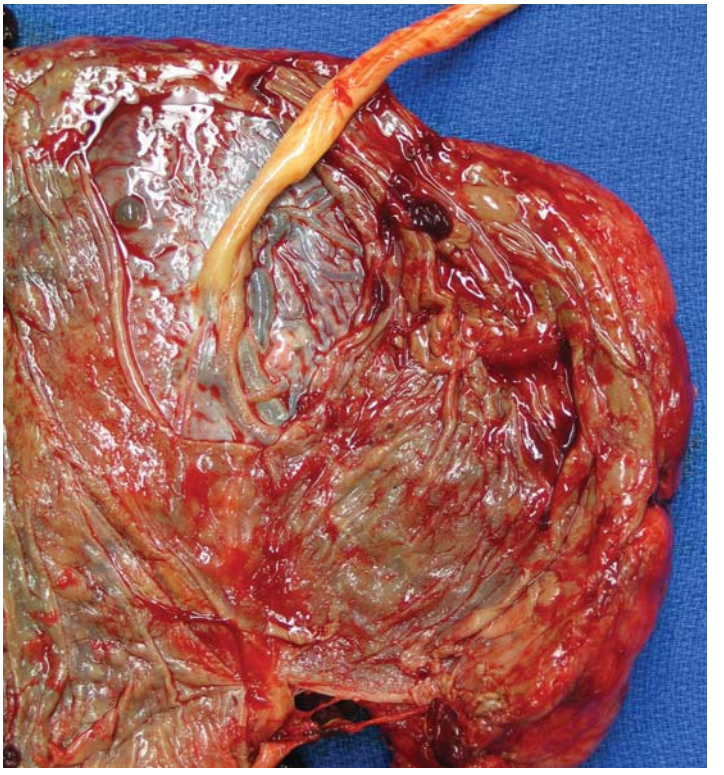


Figure 4.16. This placenta is from an extramembranous pregnancy. The membranes ruptured before delivery and the amniotic sac contracted, extruding the fetus into the chorionic. Note the circular area of shiny amnion which is the opening of the collapsed and contracted amniotic cavity. There is yellow-brown discoloration from old hemorrhage. Squames were embedded in the surface of the chorionic sac containing the fetus.

Cysts

Cysts are frequently found on the surface of the term placenta (Figure 4.17). While most are only a few centimeters in diameter, they are occasionally much larger and may show hemorrhage (Figure 4.18). Cysts are generally seen in placentas with abundant fibrin deposition. Intermediate-type trophoblast ("X" cells) proliferates in fibrinous areas and

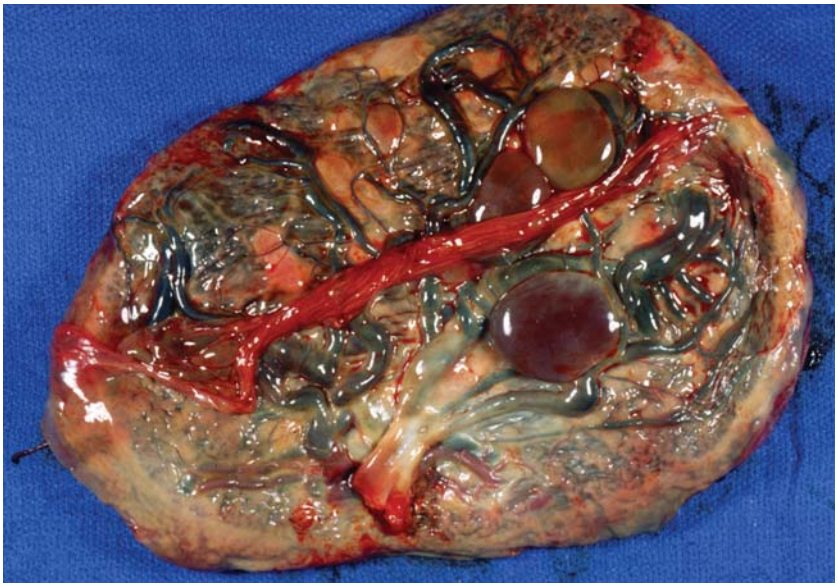


Figure 4.17. This placenta shows abundant subchorionic fibrin, a setting in which surface or subchorionic cysts commonly develop. They lie within the chorion, below the amnion. The cysts are left intact where the amnion has been reflected. Hemorrhage may occur within these, as shown in the red-brown color of the cyst by the cord insertion.

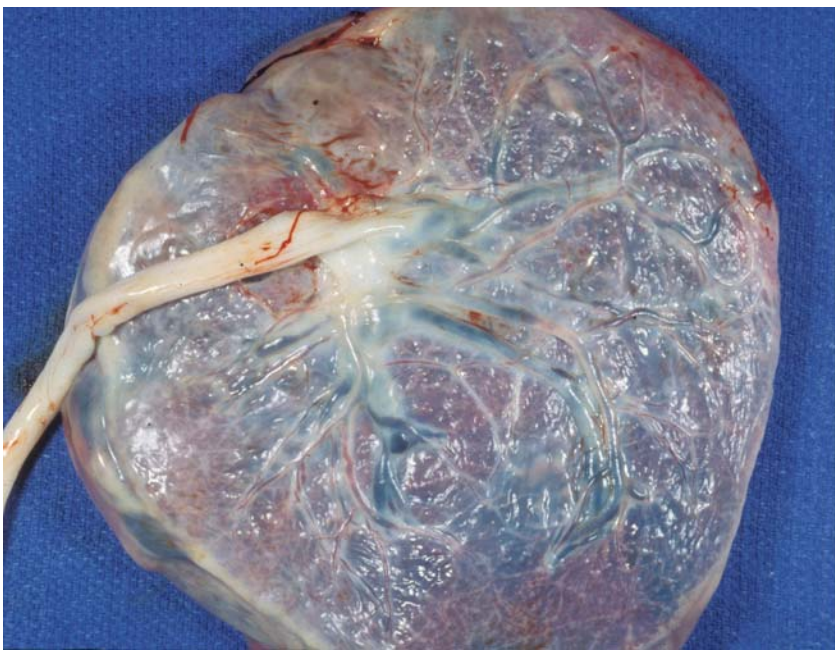


Figure 4.18. This placenta shows a mild degree of surface membrane opacity. While this often indicates ascending infection, membrane edema extended storage, or remote meconium pigmentation may give a similar appearance. It is often difficult to be sure of the etiology on gross.

becomes cystic. Cysts do not appear to have any intrinsic significance to the pregnancy. Similar lesions are seen within placental septae (Figure 5.35).

Infection

Color and translucency of the membranes are quite variable, depending on pigmentation, edema, cellular content, and amount of attached decidua (Figure 4.19). One of the most frequent causes of surface opacity is ascending infection. This is the most common type of placental infection and is due to contamination of the amniotic fluid by organisms from the vaginal tract. The reactive process involves the surface and peripheral membranes. Infiltrates of inflammatory cells, predominantly neutrophils, lead to the opacified appearance (Figure 4.20, Figure 4.21). Frequently this process is clinically unsuspected. The usual agents are clamydia, mycoplasma, and bacteria of low virulence, although *Candida* (Figure 4.22) and herpes simplex also infect in this manner. The vast majority (>95%) of infants with chorioamnionitis do not become septic. However, neonatal sepsis occurring in the first few days of life will be associated with placental changes of an ascending infection. Group B streptococcus is an exception, and may show no inflammation. There are strong indications chorioamnionitis initiates a substantial portion of premature labor and premature rupture of the membranes.

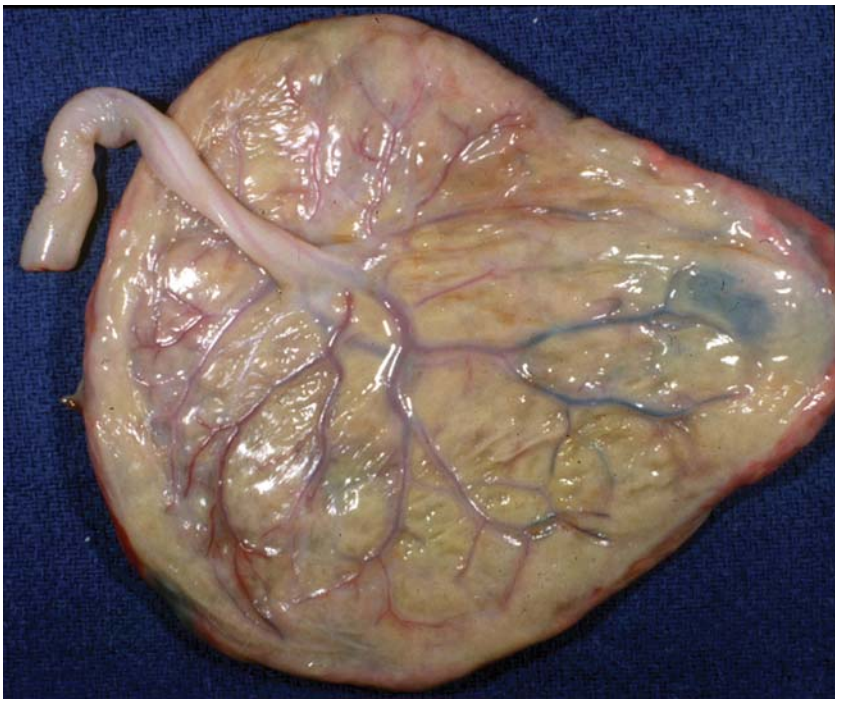


Figure 4.19. There is marked opacity of the fetal surface in this severely infected immature placenta. The slight yellow-green coloration is due to myeloperoxidase from the numerous neutrophils. Such placentas can be foul smelling, particularly in anaerobic infections.

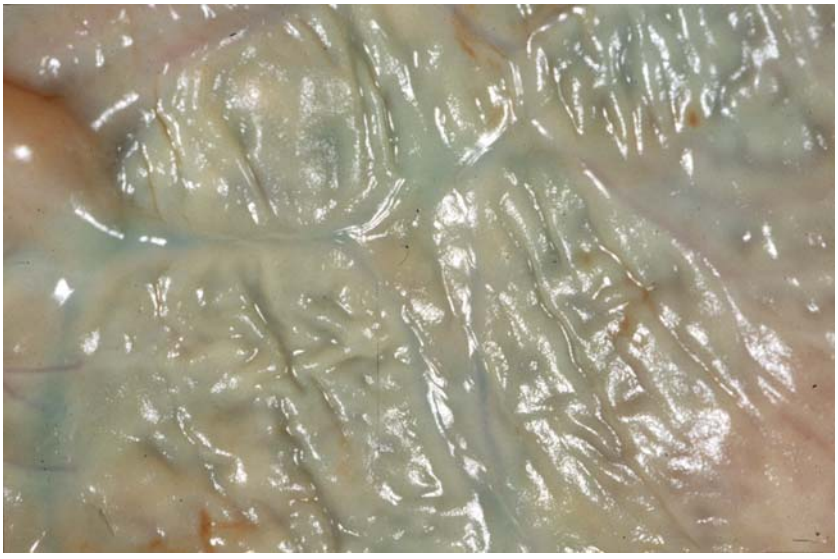


Figure 4.20. The surface of another severely infected immature placenta is extremely opaque and green. The surface vascular pattern is difficult to identify, due to the large number of neutrophils from maternal response and fetal vasculitis associated with the ascending infection. The lack of vascular markings can be helpful in distinguishing inflamed placentas from ones with abundant fibrin.

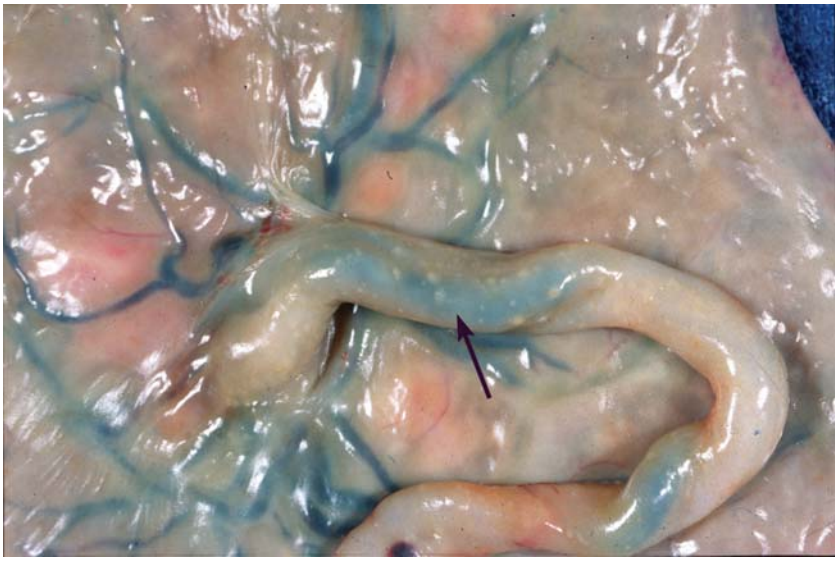


Figure 4.21. This chorioamnionitis was due to candida infection. Note the microabscesses on the surface of the cord (*arrow*), which should be specifically looked for in cases with grossly identifiable chorioamnionitis.

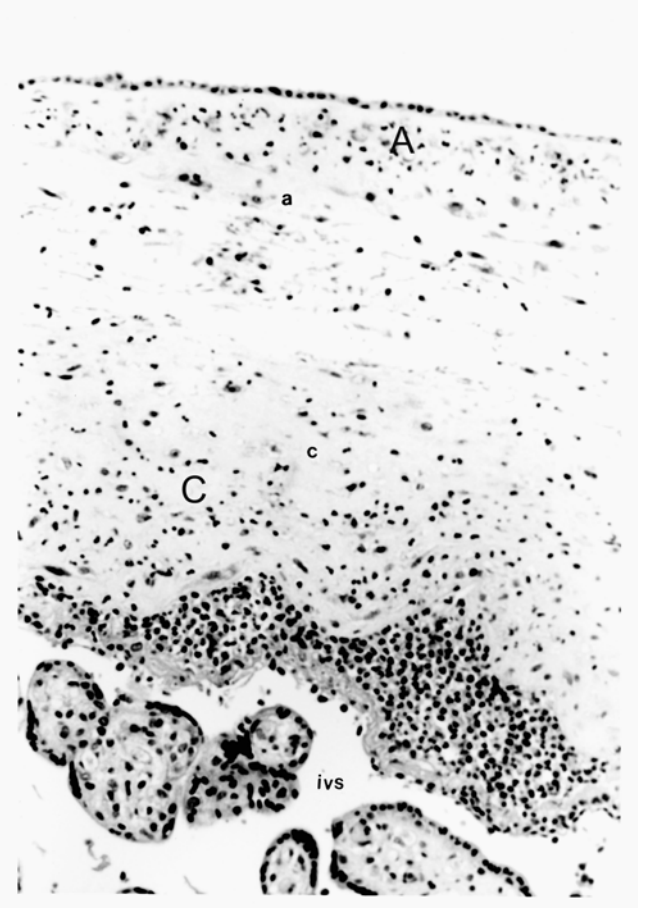


Figure 4.22. Histology of chorioamnionitis reveals neutrophils from the maternal intervillous space (ivs) extending into the chorion (C) and amnion (A).

Meconium

Meconium in the amniotic fluid commonly causes green discolored membranes particularly in late gestation. An exposed placenta can have several gross appearances (Figure 4.23 to Figure 4.25). The entire time course of histologic meconium change is not clearly established. *In vitro* studies suggest meconium rapidly reaches macrophages in the amnion (one hour) (Figure 4.26) and is in the chorion within three hours. Whether this corresponds to the time course *in vivo* is unknown, but alterations occur within hours, not days. The passage of meconium has long been taken as a sign of fetal stress. Current thinking regarding the significance of meconium in the amniotic fluid is less defined. Some, but not all, infants in distress pass meconium, and many infants with meconium have not had hypoxic events. Many term placentas may show a

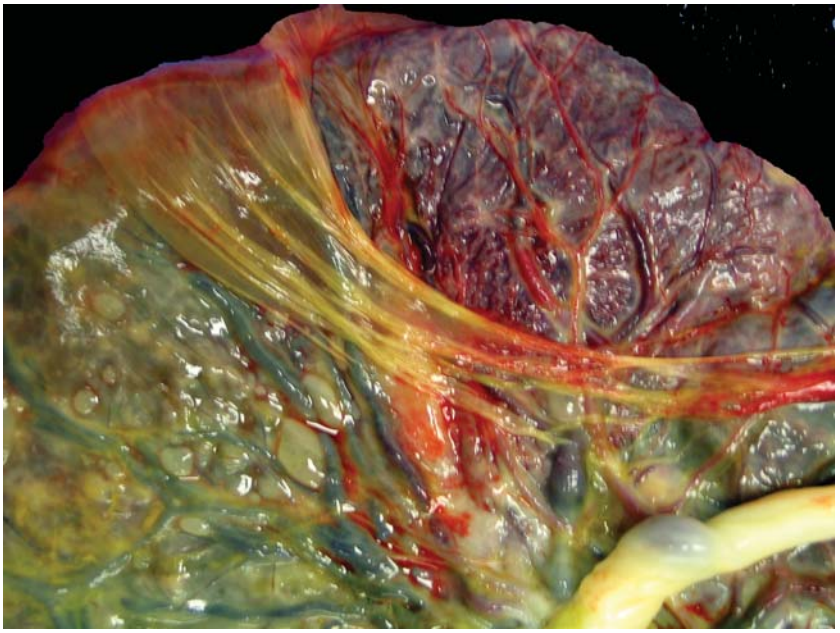


Figure 4.23. Fetal passage of meconium leads to green coloration of the placenta. This is recent meconium, which is in the amnion but does not stain the chorion as revealed by reflection of the amnion. Experimental studies suggest amniotic staining occurs within one hour and chorionic staining in approximately three hours. Meconium has a variety of appearances. It may be thick or thin and color ranges from yellow to dark green.

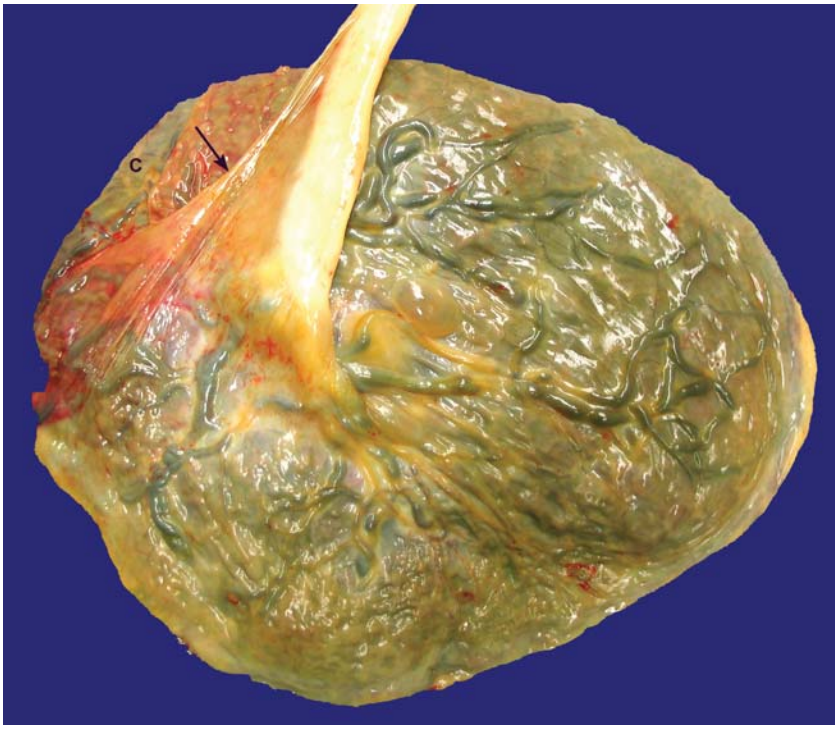


Figure 4.24. This meconium-stained placenta shows yellow-green coloration of the amnion and chorion, suggesting a longer duration of passage. There is an amniotic web (*arrow*) and the adjacent amnion is retracted, revealing the stained chorion (c).

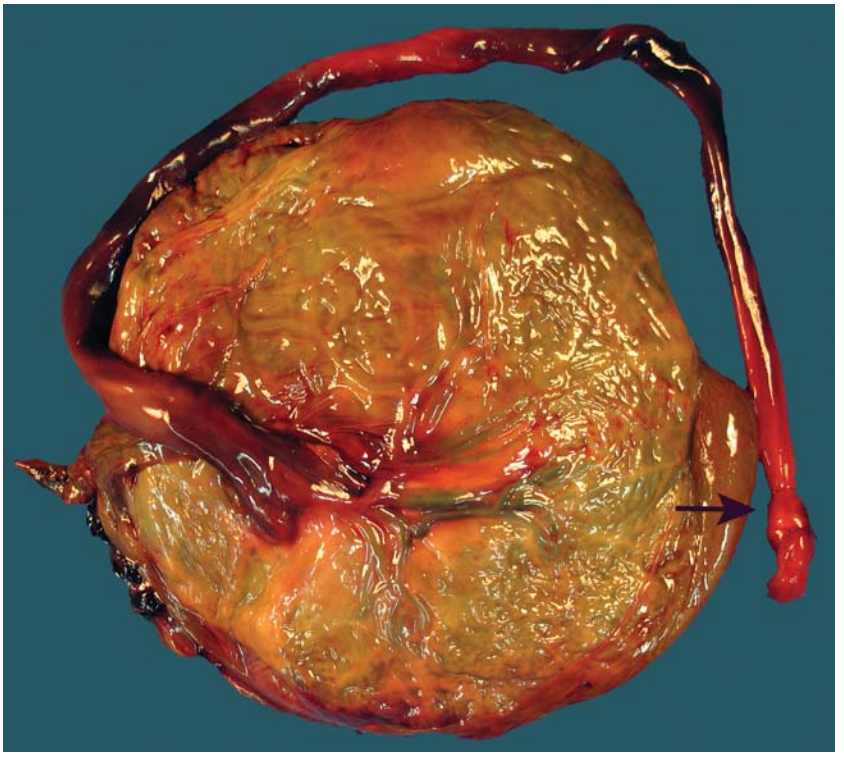


Figure 4.25. This is a near term placenta is from an intrauterine fetal demise and shows severe, longstanding meconium exposure. The cause of death here was the tight cord knot (*arrow*). There is cord congestion on the placental side. On microscopy, inflammation will often accompany meconium.

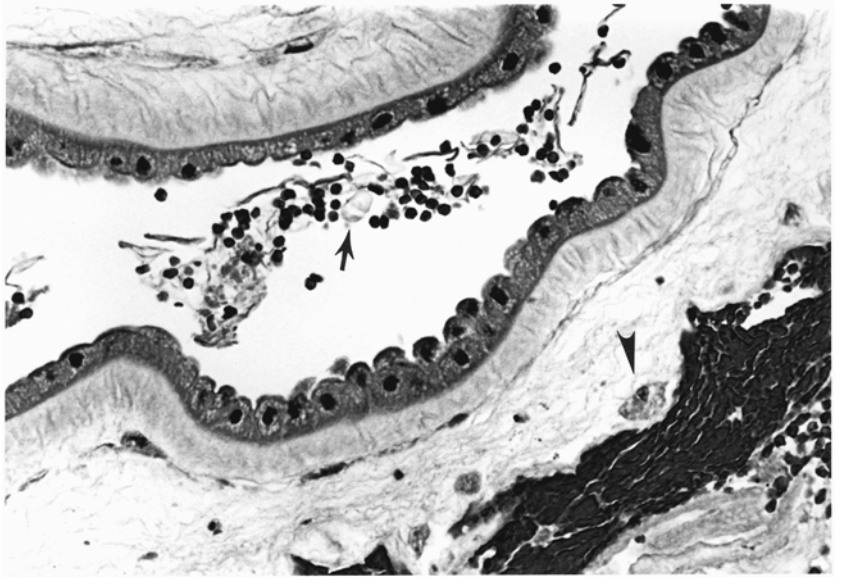


Figure 4.26. Histology of membranes stained with meconium reveals fresh, free meconium containing squames and hair (*arrow*) as well as vacuolated pigmented macrophages in the amniotic connective tissue (*arrowhead*). The pigment does not stain for iron.

vaguely green color with a few pigmented macrophages in the membranes. Subsequent to affecting the membranes, meconium discolors the umbilical cord. All green appearing placentas do not have meconium pigment. Extensive old hemorrhage or severe ascending infection can lead to similar coloration (Figure 4.19 to Figure 4.21). These are important considerations in preterm pregnancies when passage of meconium is less likely.

Retromembranous Hemorrhage

Red-brown thickenings and yellow areas mark old hemorrhages behind the membranes (Figure 4.27, Figure 4.28). These are quite common, particularly in multiple gestations, and result from confined regions of hemorrhage in areas of decidual necrosis. Problems related to these are rare. Other thickenings in the membranes may represent compressed fetuses (Figure 4.29, Figure 4.30) and rarely retained IUD's (Figure 4.31).

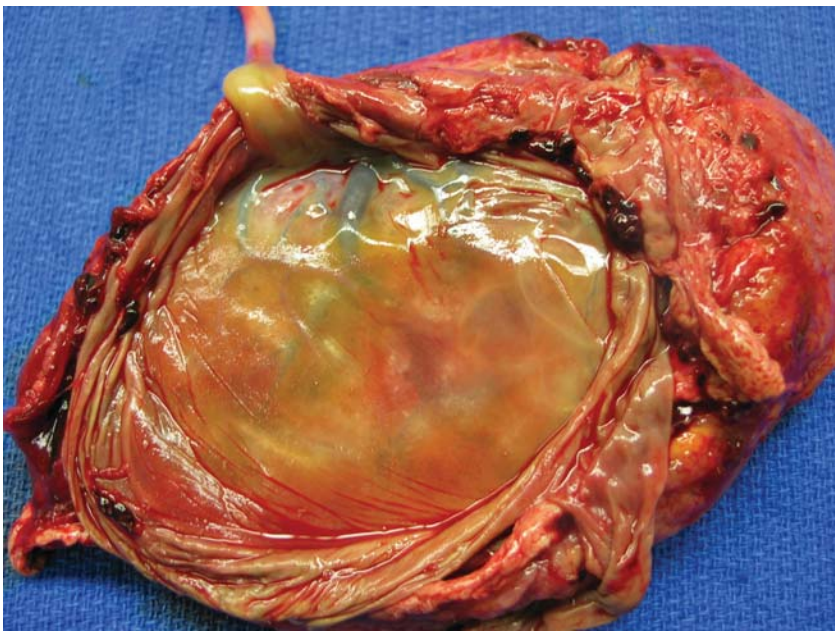
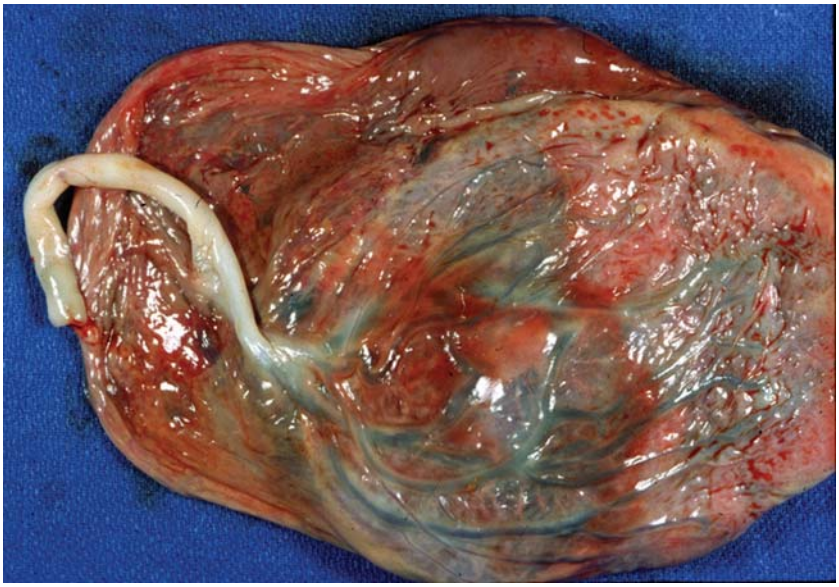


Figure 4.27. This very immature placenta shows marked discoloration and opacity of the fetal surface. This is most likely to be from old bleeding and ascending infection which are common together in extremely premature deliveries.

A



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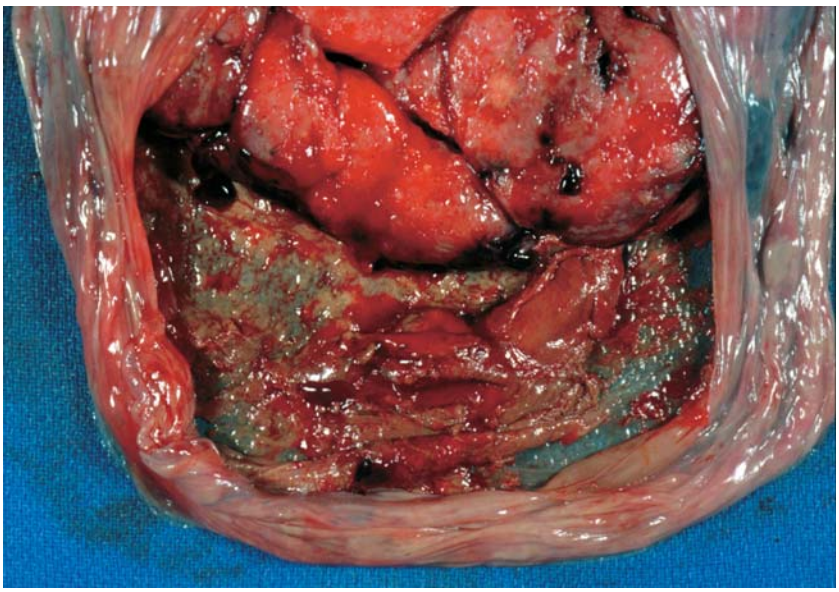


Figure 4.28. (**A**) Brown or yellow discolorations on the membranes usually reflect old, retromembranous hemorrhages. These may be associated with other hemorrhage in the placenta, but are frequently isolated. Such lesions are quite common. A clinical history of mild bleeding can sometimes be elicited. (**B**) The maternal surface better shows the old brown-red clotted blood on the membranes.

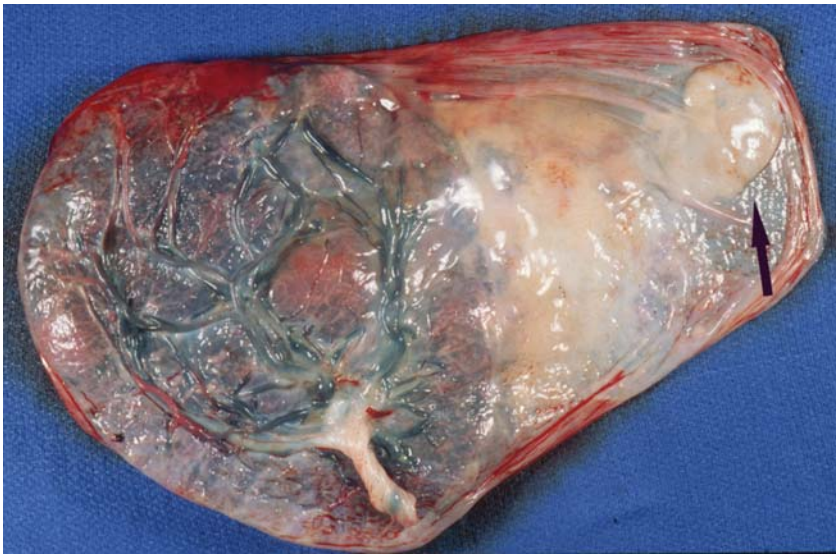


Figure 4.29. Careful examination of the membranes may reveal the presence of an atrophied twin (*arrow*). These are usually firm ovoid nodules with a smooth outline, as distinct from old hemorrhage or decidual necrosis. Eye pigment can often be identified. Examination of the dividing membranes revealed this placenta to be monochorionic and its size suggested 12 weeks gestation.

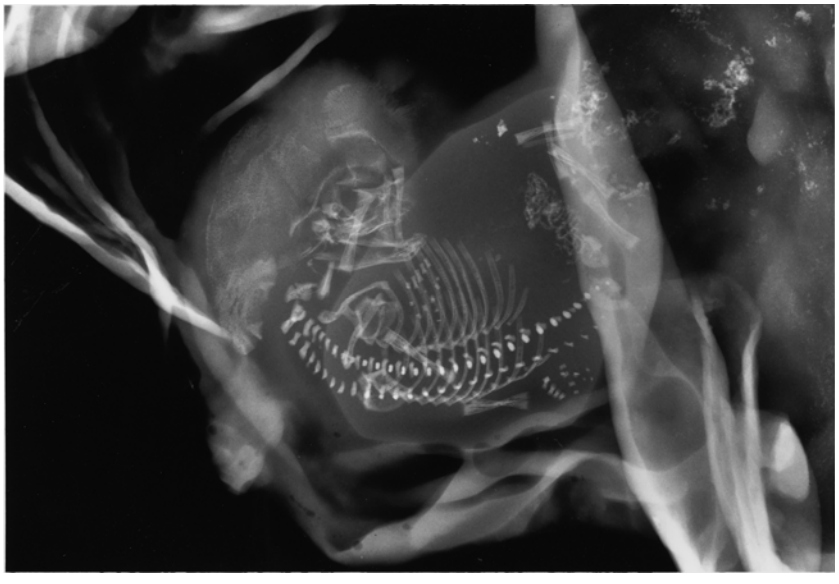


Figure 4.30. Specimen radiograph of the patient in Figure 4-29 confirms the fetal presence. Skeletal examination will reveal gestational age and some anomalies.

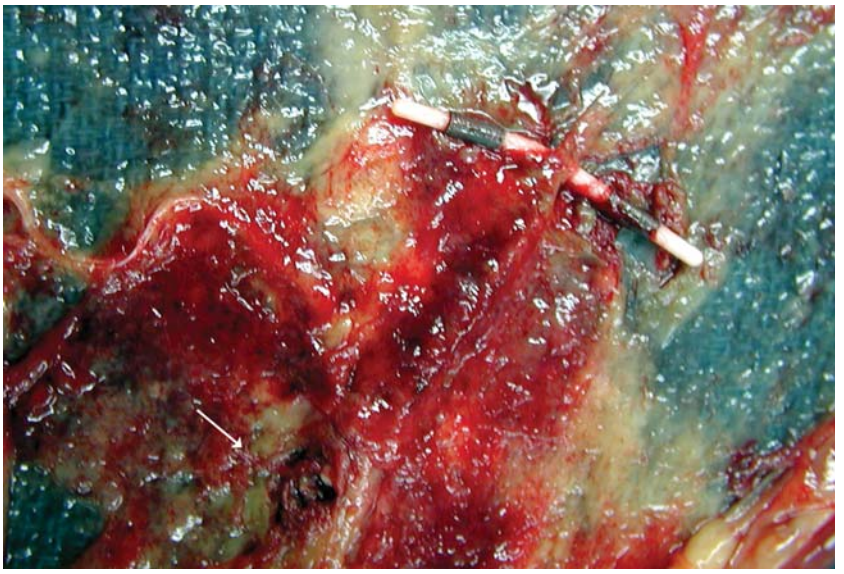


Figure 4.31. Intrauterine contraceptive devices are not always effective in preventing pregnancies. A "copper T" was embedded on the maternal side of the membranes, the characteristic location. There was both old (*arrow*) and recent hemorrhage, with discoloration visible from the fetal side. The pregnancy in this case proceeded normally with a healthy full-term infant. Velamentous cord insertions are common in pregnancies with IUDs in place, perhaps due to the effects on implantation.

Thrombosis

Thrombosis of the fetal surface vessels is an important observation. These occur most commonly in fetal veins (Figure 4.32 to Figure 4.34). Thrombosis is sometimes is associated with inflammation, meconium, or

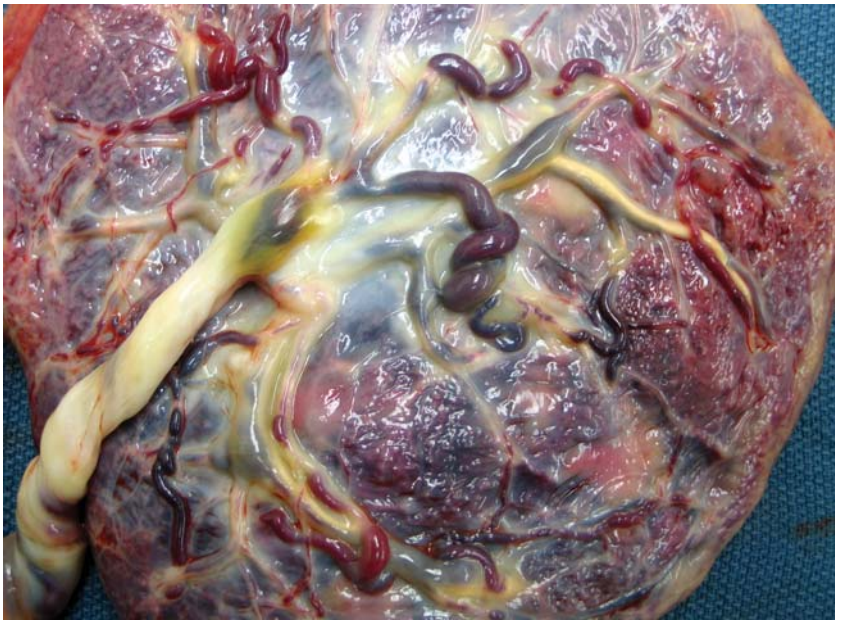


Figure 4.32. Old thrombosis is present in several of the veins on the fetal surface. Veins are the most common vessels to find thrombi. The vessels on the placental surface can be distinguished grossly since fetal arteries cross over veins. Identification of the vessel type is not possible histologically. This placenta was associated with an unusually long and highly twisted cord. The infant did not have problems in the newborn period.

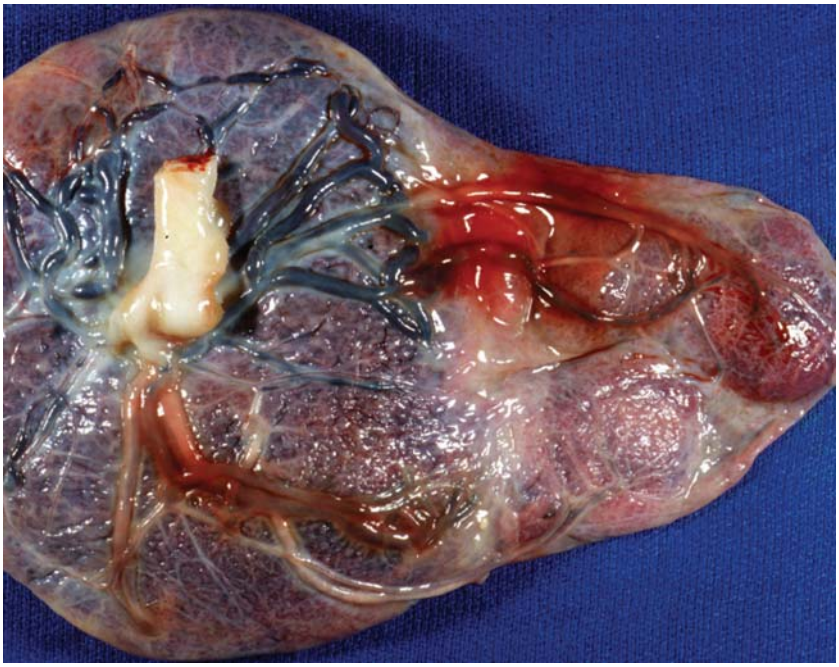


Figure 4.33. Two regions of thrombosed arteries and veins are present on the surface of this slightly immature placenta. Hemolytic coloration of the surrounding membranes is seen in these areas and the variations in color suggest they are of different ages. In one area, several of the thrombosed vessels connect to succenturiate lobes. Since vessels run through thinned placental tissue, it is possible mechanical obstruction was a factor. There was extensive associated villous change.

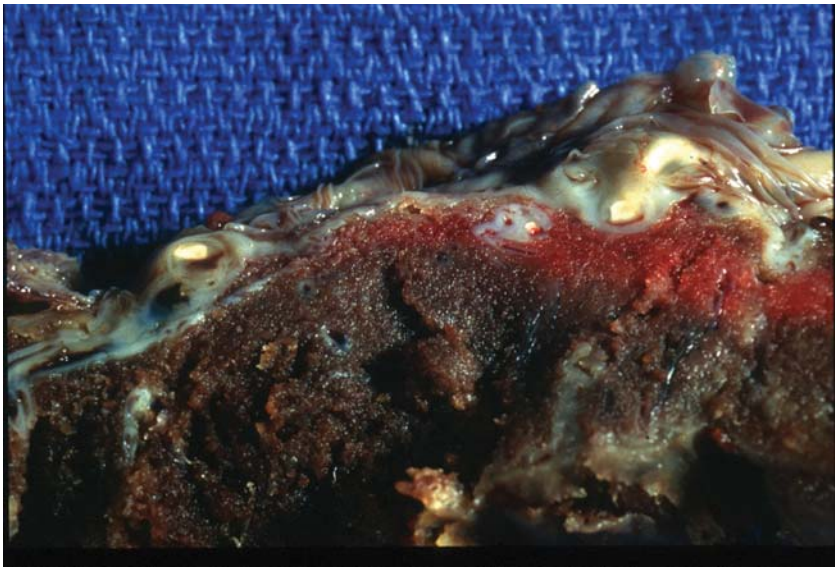


Figure 4.34. Cross-sectional view of surface vessels similar to those in Figure 4.30 shows the nonocclusive nature of many of these lesions which are largely calcified.

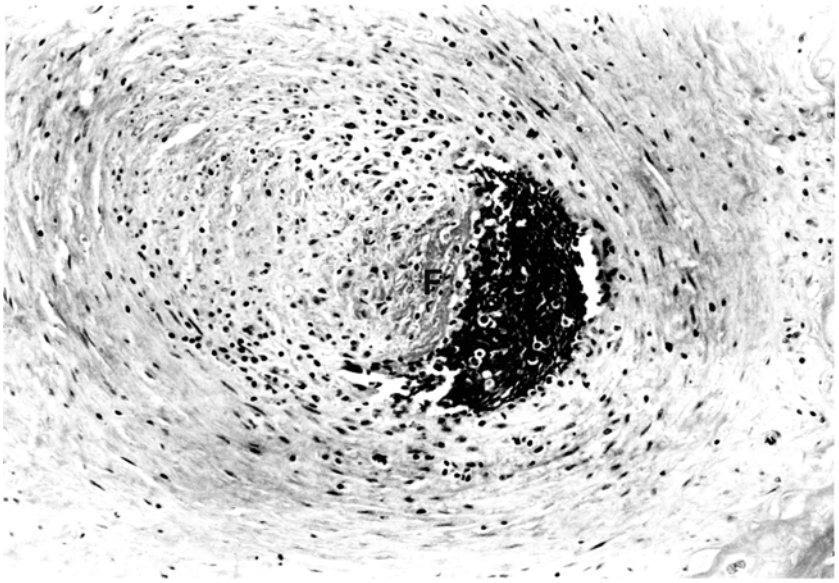


Figure 4.35. Histologic view of a partially occluded large fetal vessel shows fibrinous material on one side.

vascular obstruction, but frequently there is no apparent causation. Calcification of vessel walls represents old thrombosis, and most thrombi are nonocclusive. Many more thrombi will be identified on microscopy (Figure 4.35).

5

Lesions of the Villous Tissue

The general gross morphology of the placenta is established before the end of the first trimester, and further change is largely limited to growth and histologic maturation of villi. During placental examination the villous tissue is examined from the maternal side before and after transverse cuts have been made. While visual inspection is important, palpation of the placenta may be even more revealing of pathologic processes. Most villous lesions show diagnostic gross morphology. The common abnormalities are predominantly related to placental circulation (Figure 5.1). Alterations in the fetal and maternal components can be recognized and distinguished.

Calcification

Calcification may be a striking feature of the maternal surface and villous tissue (Figure 5.2). The degree is quite variable and the etiology is unknown. Even very large amounts have no recognized pathologic sequelae. Generally, calcification increases with gestational age, but is quite variable.

Color

The color of the villous tissue tends to become darken with advancing gestational age. Color is largely determined by fetal hemoglobin content including the level of hematocrit and total blood volume. The placentas of immature infants, who characteristically have lower hematocrits, are paler than those of term infants (Figure 5.3, Figure 5.4). Unusual fetal vascular congestion or fetal blood loss will lead to dark or light villous color (Figure 5.5). In hydrops fetalis the placenta is very pale and coarse (Figure 5.6 to Figure 5.8). There are many etiologies for hydrops including isoimmunization, infection, cytogenetic abnormalities, malformations, and metabolic diseases. Some of these are readily diagnosed through placental histology.

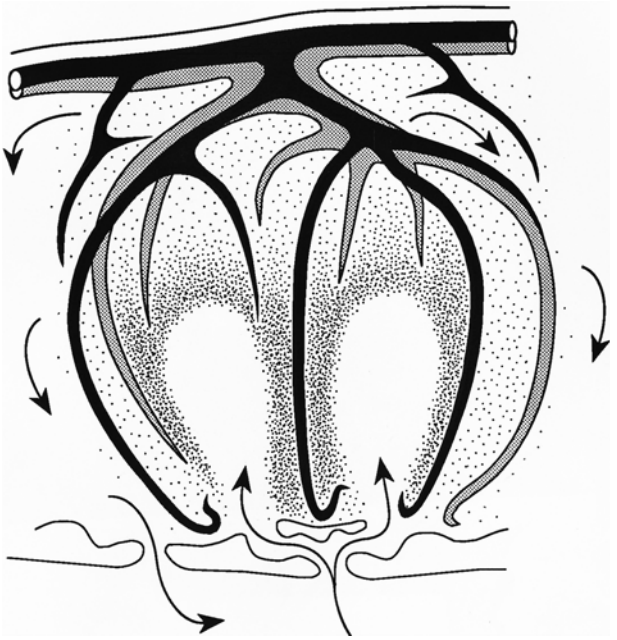


Figure 5.1. In this schematic of a placental district, maternal blood is shown being injected from an altered decidual spiral arteriole (bottom) into the central intervillous space where it often leaves a "hole" (see Figure 5.4). The blood flows toward the fetal surface, and drains back passively to decidual veins. The midzone of the placenta is best perfused, with poorer flow at the base, under the fetal surface, and at the margins. The fetal arteries (*solid*) run over fetal veins (*hatched*) and both branch to capillaries at the villous level.

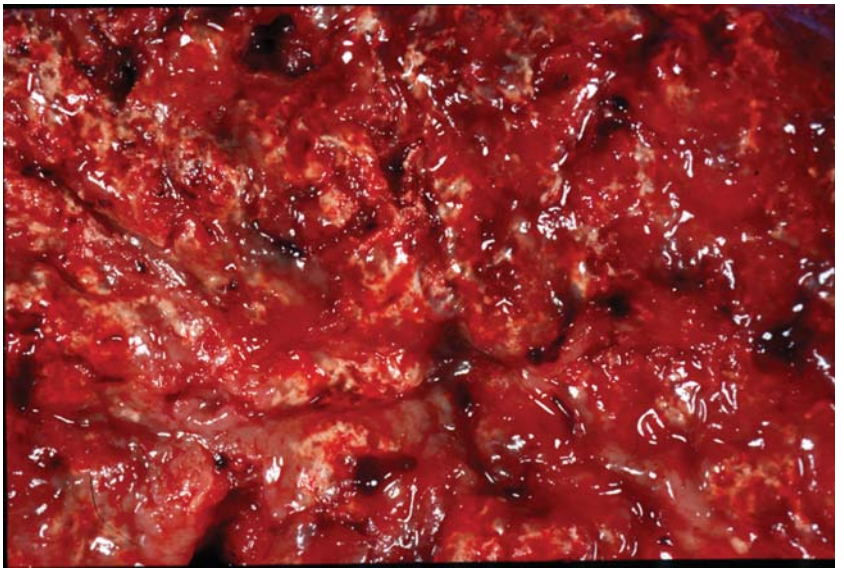


Figure 5.2. Yellow-white areas of abundant calcification can be seen on the red maternal surface of this normal term placenta. It will also be present within the parenchyma, giving a gritty sensation and sound on cutting. Grossly visible calcification is quite variable, but tends to increase with advancing gestation. It is not associated with disease, even if large amounts are present.

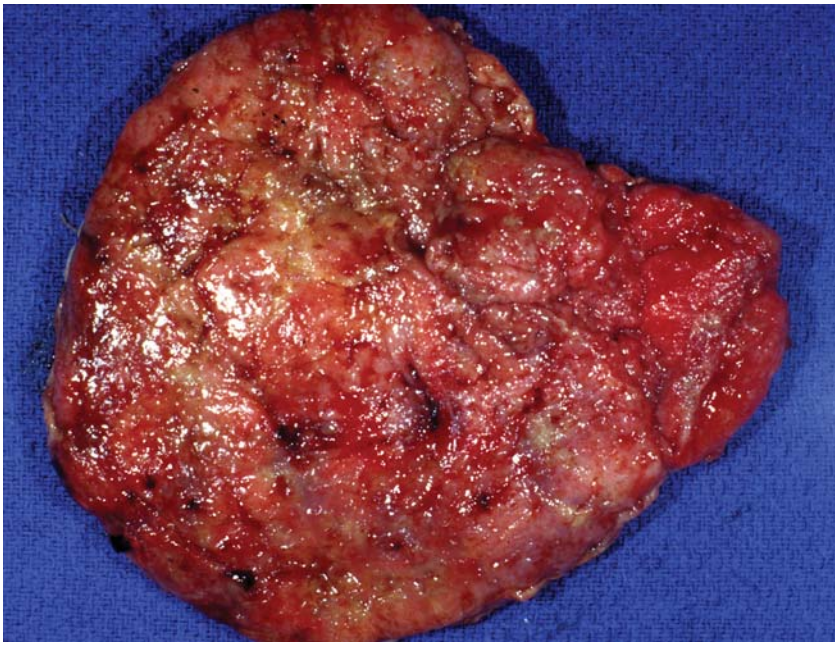


Figure 5.3. The parenchyma of this immature (24-week) placenta shows no calcification and is relatively pale red. Color of the villous tissue is largely related to hemoglobin content. Thus mature placentas have a darker coloration than immature ones (compare also with Figure 1.6).

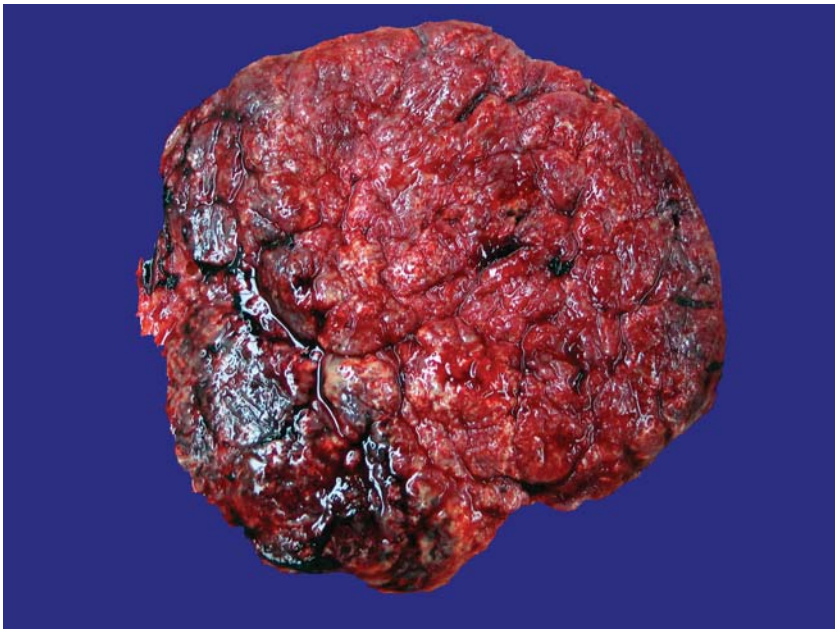


Figure 5.4. The maternal surface of this term placenta shows a rough line from 11 o'clock to 5 o'clock demarcating two zones of differing color. This is an artifact, created by the positioning of the fresh placenta in the container. The darker portion was folded under the slightly paler area. Some of the color difference may be related to dependant congestion. Additionally, the paler red portion was also more exposed to the air and has more oxygenated hemoglobin, an effect common in packaged ground meat.

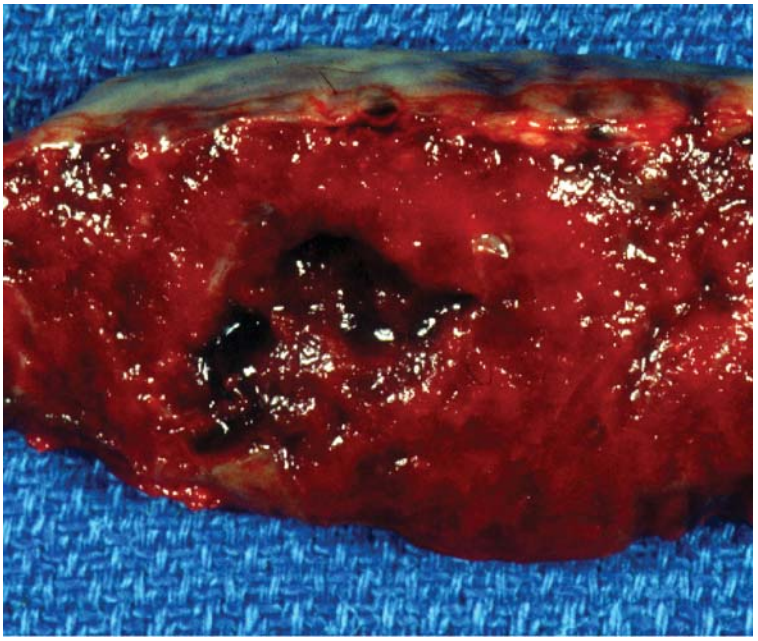


Figure 5.5. In the central portion of the villous tissue there is a rounded depression. This is a site of maternal blood injection into the intervillous space, a normal finding. The placenta is also a very deep red color, which is usually due to congestion of fetal villous vessels with blood. This is commonly caused by early cord clamping, and the infant may be hypovolemic. Dark placentas also occur in some cases of maternal diabetes and with certain microscopic villous vascular abnormalities (e.g., chorangiosis). Such villous tissue may feel unusually soft, particularly in the abnormal deep red placentas.

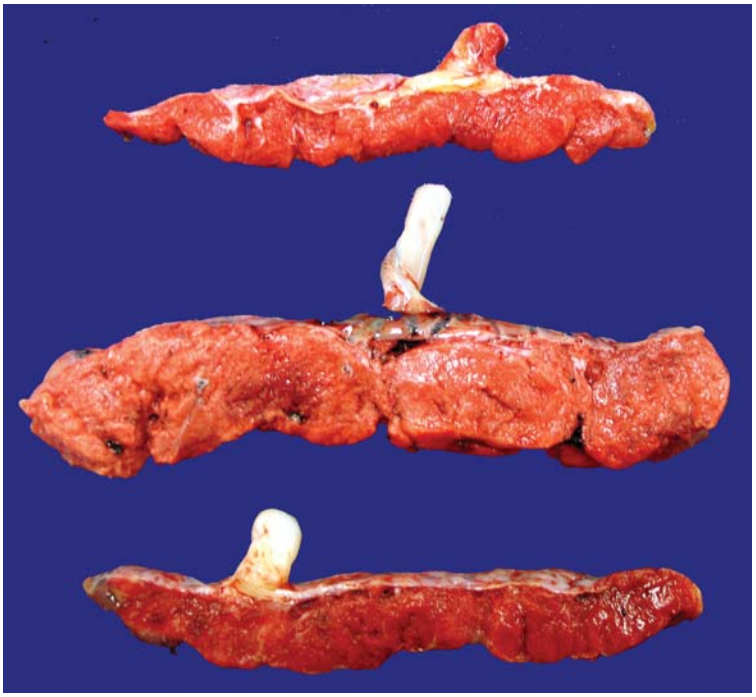


Figure 5.6. A transverse slice of a hydropic placenta (*middle*) is compared with an age matched preterm (*top*) and normal term placenta (*bottom*). Extreme pallor is usually present in hydropic placentas, due to factors including fetal anemia, villous edema, and inappropriately immature villous histology. Such placentas are large and thick with coarse villous structure.

Figure 5.7. A close view of a fixed piece of a hydropic placenta better shows the coarse villous structure. Such placentas may be extremely friable. The pallor here is marked. Placentas also appear pale if they have lost most of their fetal blood either before, during or after delivery (draining the cord, villous disruption). In contrast to hydrops, the gross villous size is normal in such cases.

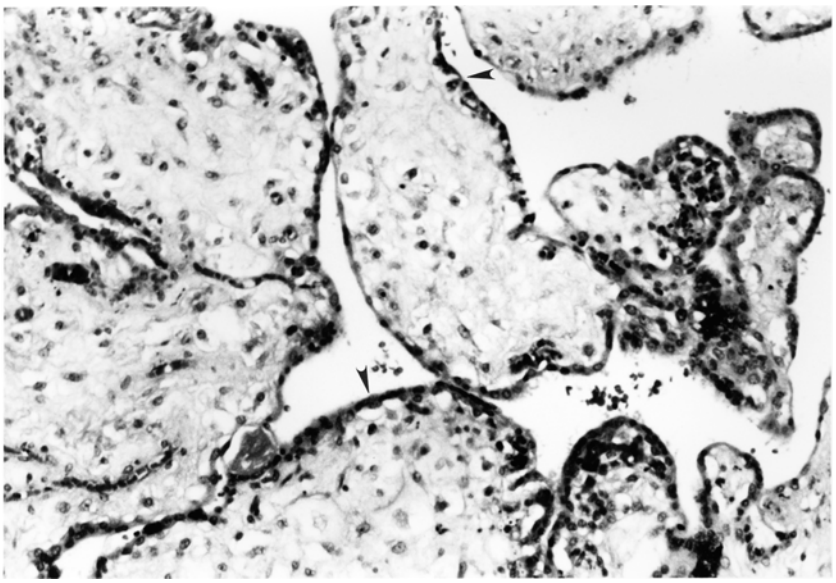


Figure 5.8. Microscopically, these hydropic villi show unusually large size for this near full-term gestation (compare with Figure 2.11, same magnification). The stroma is abundant and edematous. The covering trophoblastic layer shows few syncytial knots, and cytotrophoblasts are easily identified (*arrowheads*), features of abnormal immaturity. There are no specific diagnostic features. The infant showed premature closure of the ductus arteriosus.

Infarcts

True villous infarcts are quite common and usually distinctive on gross exam. These are villous regions that have lost their maternal blood supply. They are based on the maternal surface and have rather linear defined margins (Figure 5.9, Figure 5.10). Infarcts are more solid and feel firmer than the adjacent tissue. They appear granular due to the remaining collapsed villi in varying stages of degeneration. Over time the color changes from red to white. Cystic change and hemorrhagic regions may be seen in infarcts. Infarction is seen most commonly at the placental margin where there is less blood flow. A small (1-cm) lesion of this nature is usually insignificant (Figure 5.11, Figure 5.12). Central and large marginal infarcts suggest maternal vascular disease, particularly if they are extensive or in placentas from preterm births. Examination of the entire sliced placenta is often a good means to assess the extent of villous damage in such cases (Figure 5.13). Fetal problems such as growth restriction are often present with 15% or more infarction. Since infarcts collapse and shrink over time, they actually represent a greater portion of villous tissue than their dimensions would imply. The fetus can survive the loss of more than 50% of its placenta if the increase is gradual.

Histologically infarcts are relatively uninteresting. The early ones show villous congestion and collapse with loss of the intervillous space, accounting for the gross firmness and red color. There is subsequent loss

Figure 5.9. The maternal surface of this 30-week placenta from a mother with severe preeclampsia reveals many infarcts, yellow polygonal areas which feel quite firm. The villous tissue is dark and mature appearing (see Figure 5.2), and the placenta was quite small. Areas of fresh retroplacental blood clot are also identifiable at 2 (*arrow*), 4, and 11 o'clock. Placentas with substantial infarction frequently show premature separation, both processes reflecting maternal vascular disease.

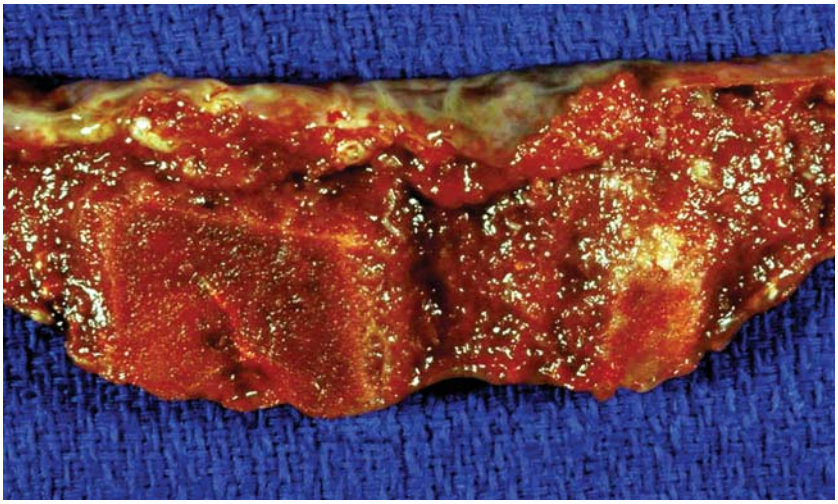


Figure 5.10. Cross-section of a multiply infarcted placenta highlights two central lesions. Infarcts are usually well demarcated, square and based on the maternal surface. There is a spared region under the fetal surface due to cross-circulation between districts. Villous collapse leads to the granular appearance, while color reflects the age of the lesion and degeneration of blood. The dark red lesion is relatively recent. The smaller, paler one has been present longer. The exact time course of these changes is unknown.

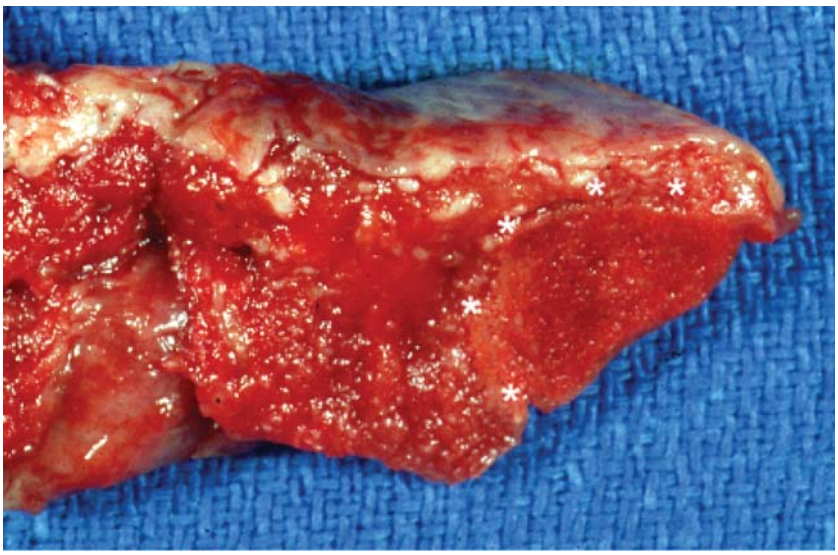


Figure 5.11. A fresh marginal infarct is present at the edge of this placenta (*s). It is minimally different in color, but is more solid and compact. Infarcts at the margin are triangular and often extend to the fetal surface. Such very recent infarcts are often better palpated than seen.

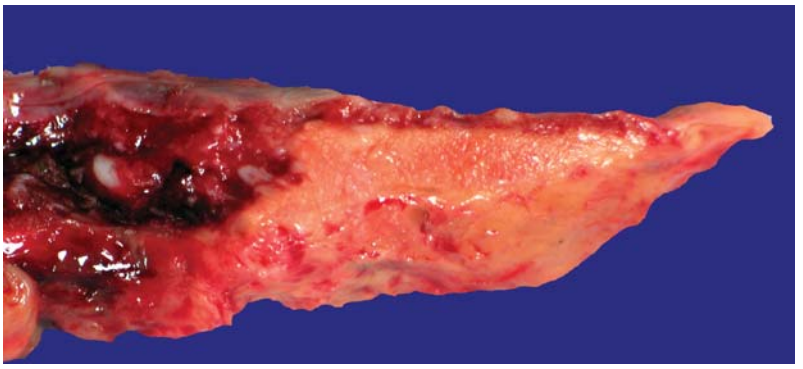


Figure 5.12. Old marginal infarcts are very common, reflecting the poor perfusion near the edge of the placenta. A small lesion is of little significance. This older lesion has lost much of its color. It can be seen to extend on the maternal surface. The placenta shown is thin and the infracted region occurred in a partial lobe. Infarction is particularly common in the periphery of irregularly shaped placentas and relatively large lesions may be seen in otherwise normal placentas.

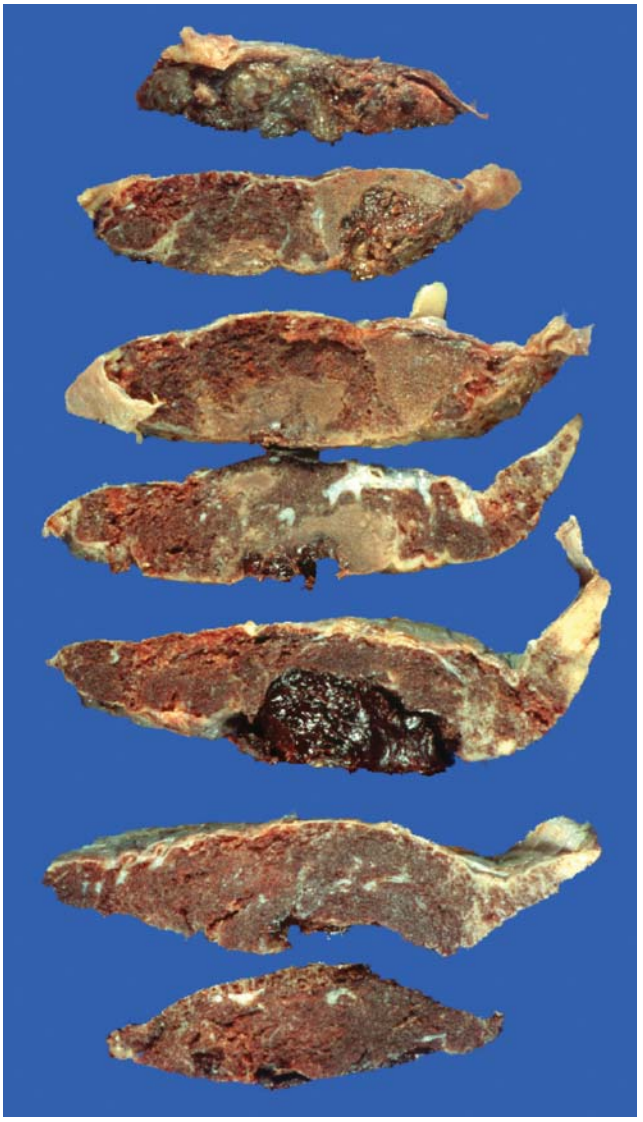


Figure 5.13. The extent of infarction in a placenta can often be better defined if serial slabs are observed simultaneously. As present here, there is often an admixture of areas with infarction of varying ages, some of which is related to premature separation and retroplacental hemorrhage. In this partially fixed placenta, at least 30% to 40% is involved by the lesions.

of staining and fibrin is deposited (Figure 5.14). Associated ischemic villous pathology is seen adjacent to infarcts and often diffusely in the placenta (Figure 5.15). Maternal vascular lesions are sometimes found in attached decidua (Figure 5.16). Vascular disease in the placenta associated with growth restriction and preterm delivery.

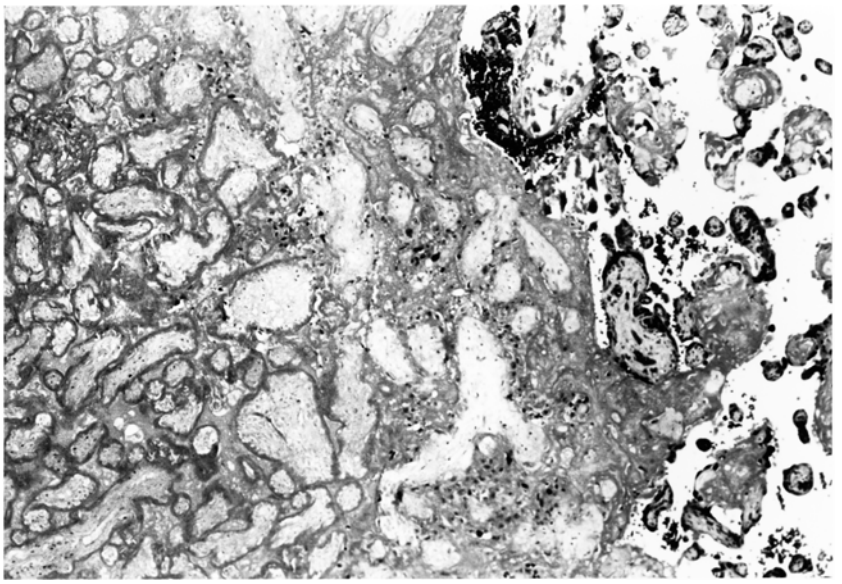


Figure 5.14. Histology of an old infarct reveals ghost outlines of villi enmeshed in fibrin. Nuclear staining has been lost in all the trophoblast and most of the remainder of the villi. Viable small villi are present adjacent to the infarct on the right.

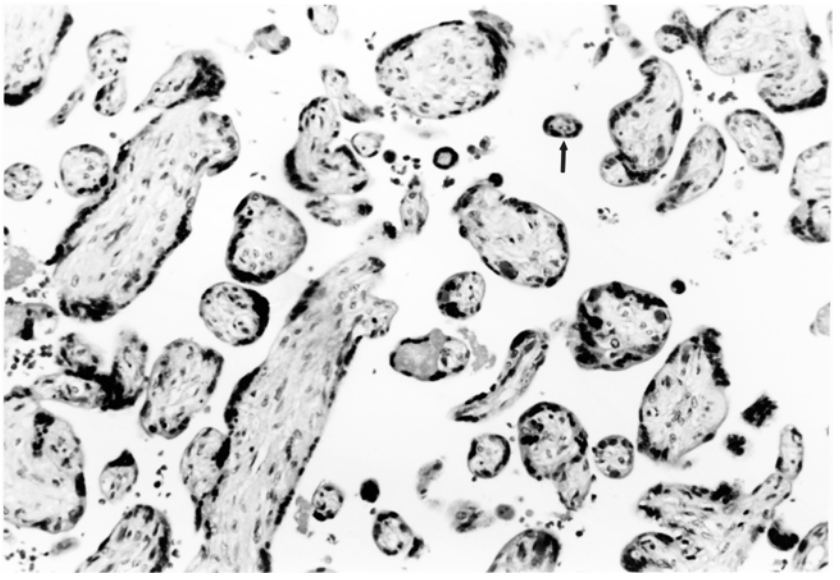


Figure 5.15. Villous structure is often altered in noninfarcted areas of placentas associated with maternal vascular disease. The villi are smaller than expected for gestation with dark smudgy syncytial knots, a change sometimes called "accelerated maturation." Extremely small villi may be present (*arrow*).

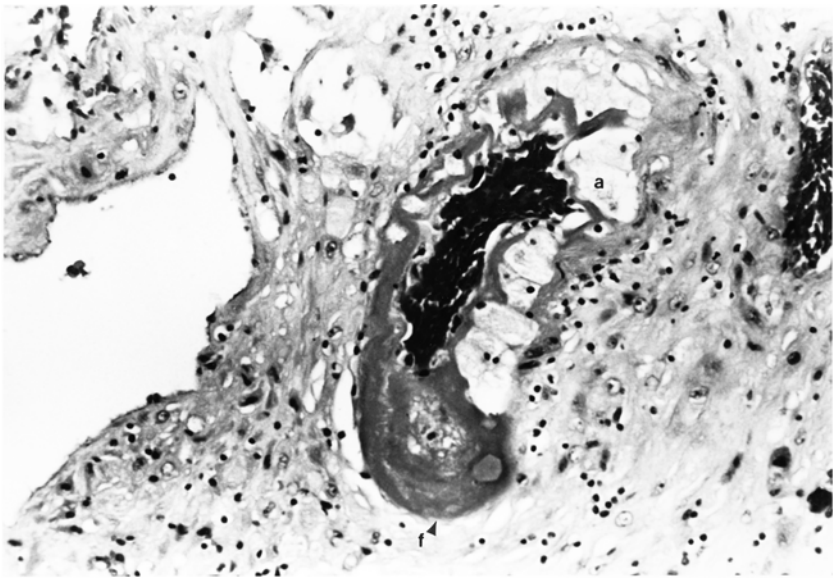


Figure 5.16. Decidual vessels at the base or in the attached decidua may show vascular lesions characteristic of maternal hypertensive disease. This vessel from a severe preeclamptic shows atherosis, a vasculopathy characterized by dense fibrin deposition and lipid-filled atherotic cells (a).

Marginal infarction is overdiagnosed by many observers. Fibrin deposition and necrotic decidua at the edge may be confusing (Figure 5.17). Even occasional small (<0.5 cm) gross infarcts are physiologically insignificant in most cases and the extremely small ones (1 mm–2 mm) do not warrant individual description.

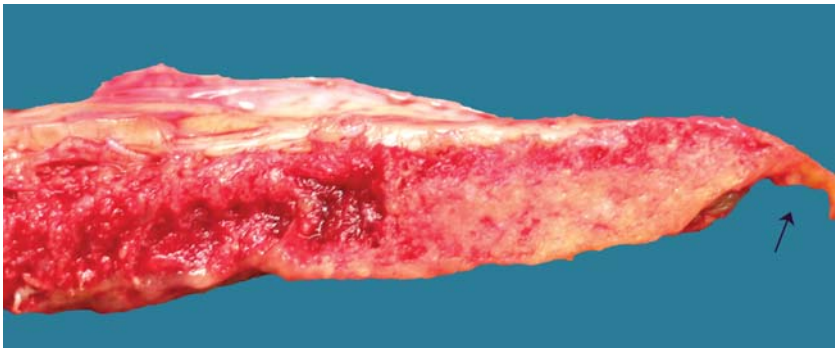


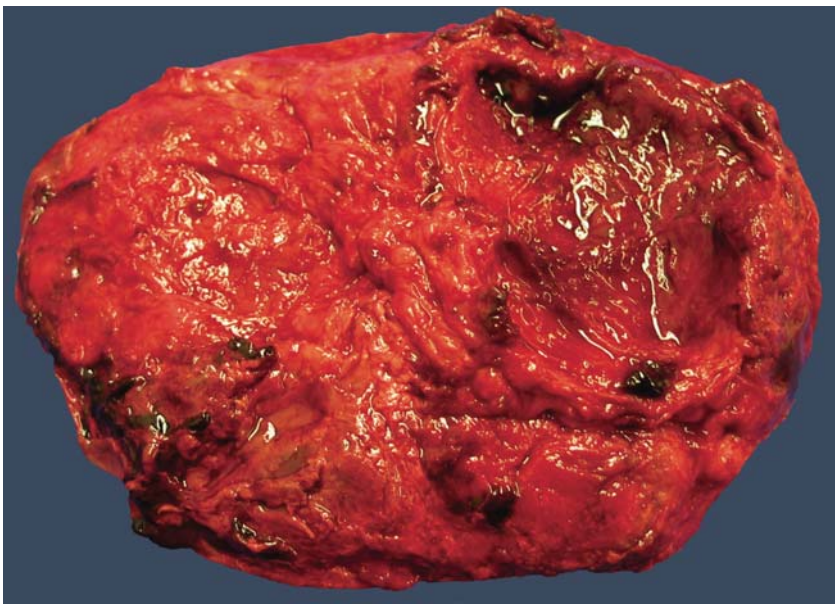
Figure 5.17. There is a yellow-white, somewhat triangular lesion at the margin of this placenta. This is not a marginal infarct. It is shiny and does not have the characteristic solid granular appearance. This is fibrin deposition and there is decidual necrosis on the adjacent membranes (*arrow*). These processes are far more common than true infarction at the placental margin.

Retroplacental Hemorrhage

Blood clots on the maternal surface of the placenta are caused by bleeding from decidual vessels in areas of premature placental separation and may relate to significant maternal or fetal disease. Trauma, hypertensive disorders, chorioamnionitis, smoking, and possibly cocaine use have been associated with retroplacental hemorrhage. It is preferable to use descriptive terms for this process rather than "abruptio placenta," a clinical expression implying pain and bleeding. Although some retroplacental hemorrhages correspond to clinical abruptio placenta, many grossly identified hematomas are unsuspected.

Very recent and at times massive placental separation often has little, if any, gross or histologic change. The placenta may appear to be normally separated. Excessive blood clot received with a specimen, particularly if somewhat granular and formed, may be the first and sometimes only clue to retroplacental hemorrhage. Most genuine fresh retroplacental hemorrhages are at least slightly adherent to the maternal surface, as compared with gelatinous postpartum clot.

The gross morphology of retroplacental hemorrhage depends on the duration and degree of blood trapping. When bleeding is contained behind the placenta, the villous tissue becomes compressed by clot (Figure 5.18). If the pregnancy continues, the separated area will infarct because its blood supply has been lost. Lesions may be subtle on the



A

Figure 5.18. Inspection of the uncut maternal surface is important in recognizing retroplacental hemorrhages. In large lesions the formed clot may become separated from the placenta. A depressed cavity remains on the maternal surface into which the clot will often conform. (**A**) This placenta shows one obvious area of separation on the right with some yellow coloration at the base indicating infarction.

(*Continued*)

B

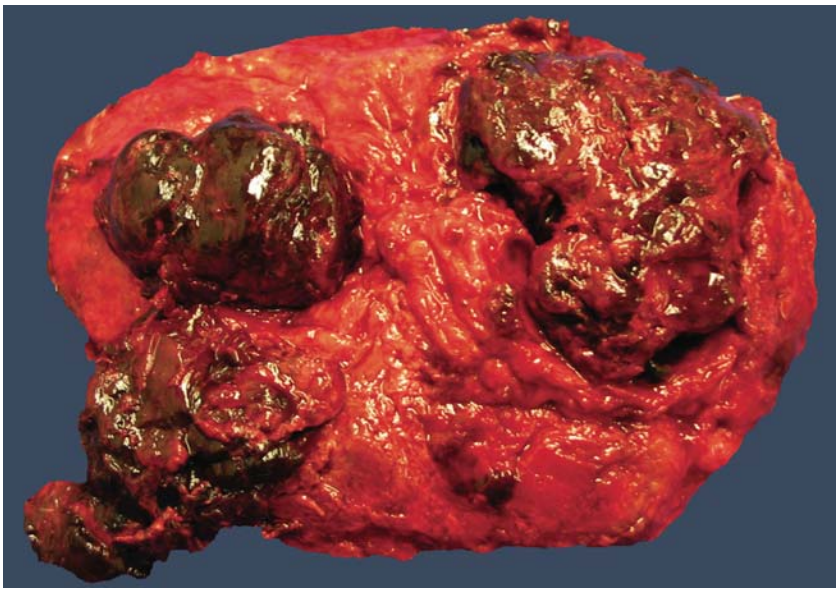


Figure 5.18 (Continued). (**B**) The three large clots received with the placenta fit the large and 2 other more subtle depressions. The involved areas of placental separation will extend well beyond the actual clot.

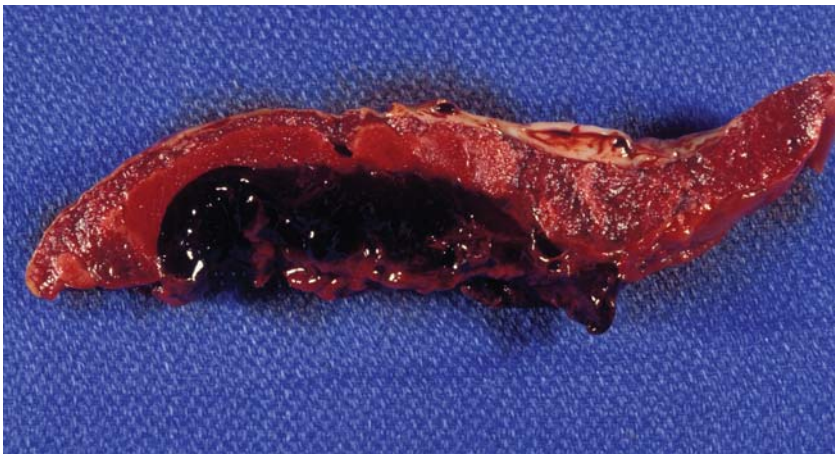


Figure 5.19. Some retroplacental hemorrhages are not raised above the maternal surface and may not be appreciated until cross-sections are done. Trapping of maternal blood led to the large retroplacental clot which compressed the villous tissue. The villi above the blood are solid and pale, having infarcted from the lack of maternal blood supply. The clot does not show significant degeneration.

maternal surface and better seen on cross section (Figure 5.19). Over time the blood breaks down and the infarcts become paler with age (Figures 5.20). The exact time course for these placental changes to occur is unknown. When the blood has a means of egress, villous tissue may not be compressed (Figure 5.21). The blood comprising the clots is

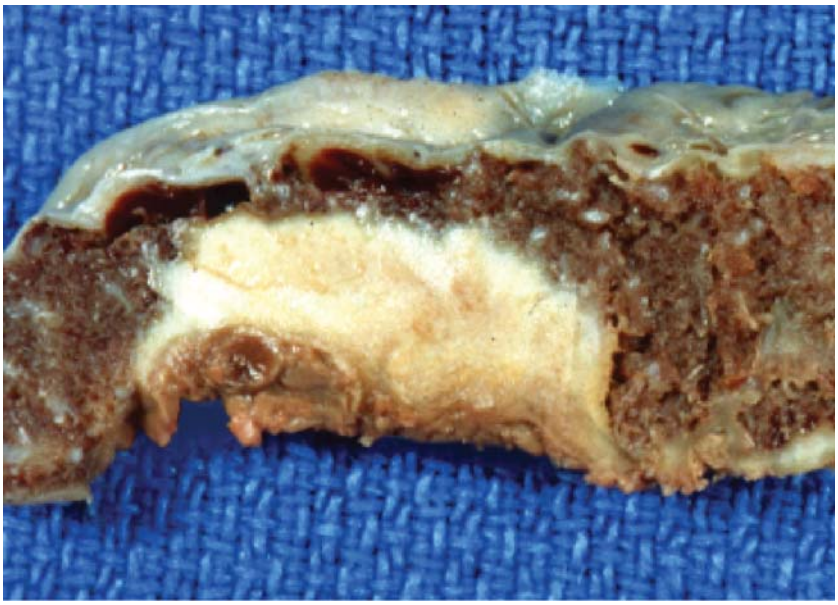


Figure 5.20. If delivery does not occur, the villous tissue will continue through the usual stages of infarction and the blood clot will degenerate, as can be seen in this remote retroplacental hemorrhage. Both processes are of roughly similar ages. If one finds fresh blood overlying old infarction, it suggests a previously infracted area separated prematurely.

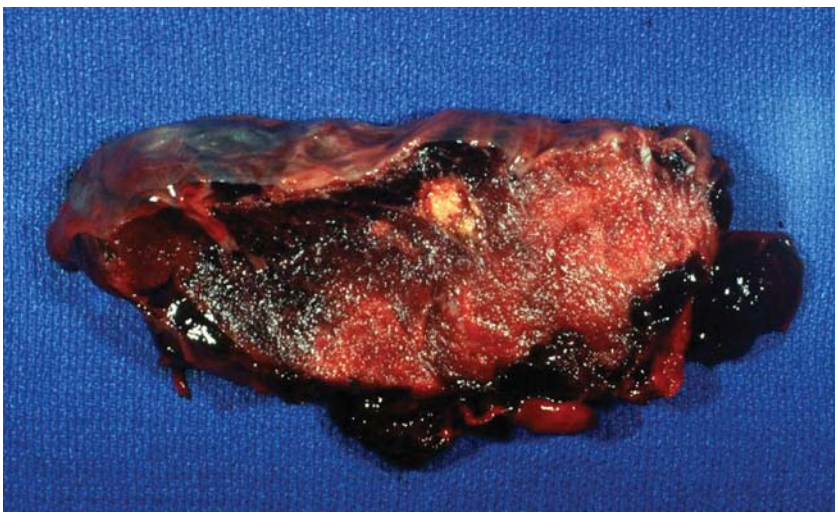


Figure 5.21. In this cross-section of another retroplacental hemorrhage, there is clot on the surface without villous compression. This occurs if blood has a means of egress. Again there is pallor and infarction of the villous tissue adjacent to the clot. This separation involved nearly the entire placenta and led to fetal demise. A small old yellow infarct near the fetal surface suggests preexisting vascular disease.

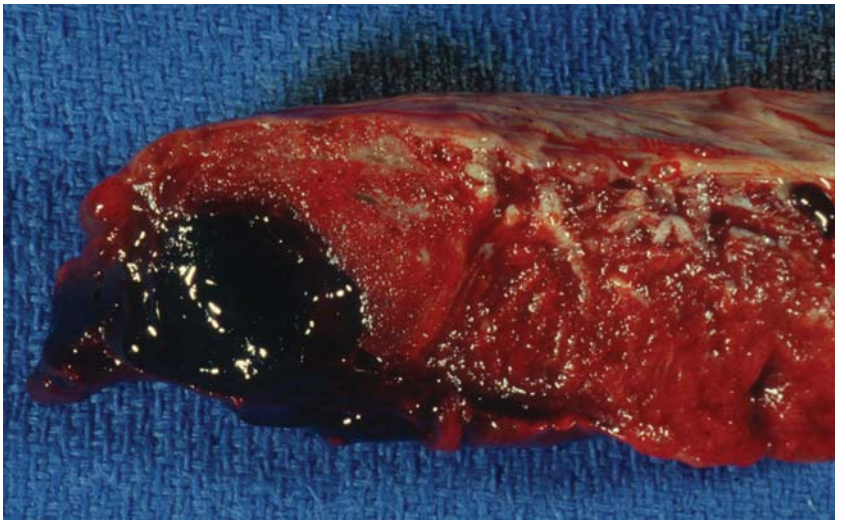


Figure 5.22. Hemorrhage is most commonly seen at the placental margin and many separations start in that region. This fresh hemorrhage undermines the villous tissue and the overlying area is in an early stage of infarction.

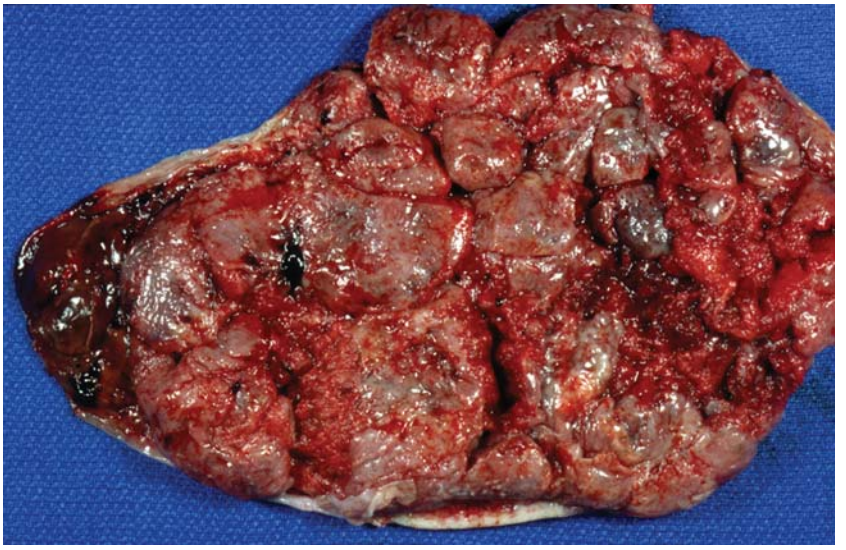


Figure 5.23. Marginal hemorrhage is present in this preterm placenta. It extends onto the membranes and not the villous tissue. The brown color of the blood indicates it is breaking down. These hemorrhages come from marginal sinus bleeding and not placental separation. Note the pale attached decidua on the maternal surface.

largely maternal, occasionally with some fetal bleeding. Retroplacental hematomas occur both centrally and at the margin of the placenta and overlap villous tissue (Figure 5.22).

If placental delivery is delayed or incomplete, one may see fresh retroplacental hemorrhage with slightly adherent blood clot and villous collapse. This, of course, has no implications for the infant. True marginal hemorrhage will also have no fetal effects. It is peripheral, with the aggregate of blood extending onto the membranes, not separating the placenta (Figure 5.23, Figure 5.24). It is a fundamentally different process, related to marginal sinus hemorrhage.

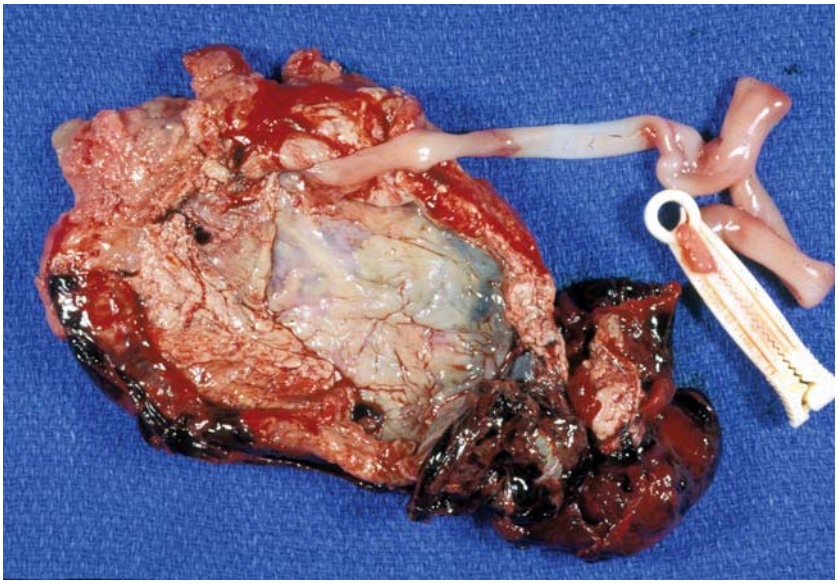


Figure 5.24. This large marginal hemorrhage occurred in an immature placenta. The fetal surface is yellow-green from severe chorioamnionitis. Many severely infected pregnancies deliver prematurely. Such placentas often show substantial hemorrhage at the margin, possibly from necrosis of the infected decidua. This is likely a peripartum event and not the cause of early delivery. The described association of "abruption" with chorioamnionitis is partially due to cases such as this.

Intervillous Thrombi

Intervillous thrombi occur in the intervillous space in central areas of the placenta. The earliest thrombi are fresh red clots, which progress through laminated thrombi to old white lesions (Figure 5.25, Figure 5.26). No true organization occurs. Intervillous thrombi contain both fetal and

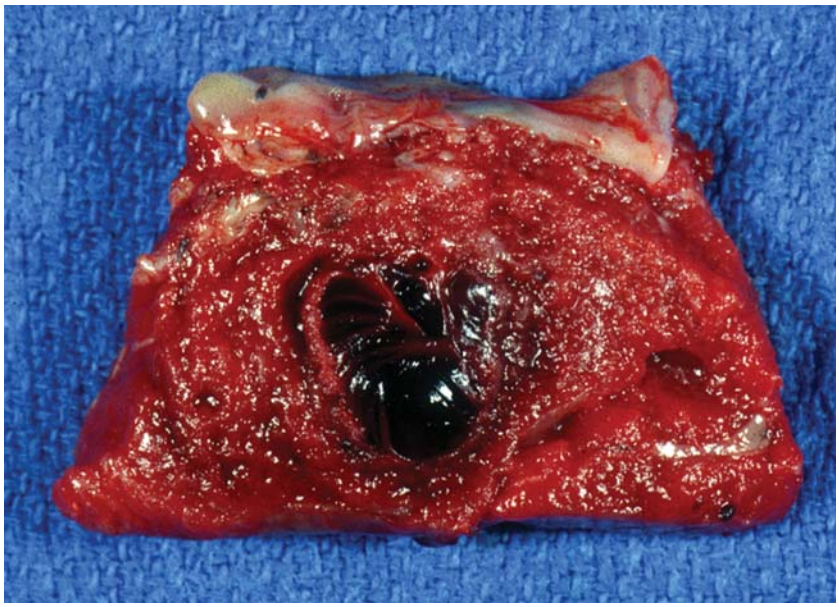


Figure 5.25. Intervillous thrombi will be palpable as firm lesions in the placental tissue. They are shinier and more homogenous in texture than infarcts. Thrombi are usually located in the midportion of the placenta, as shown here by this fresh lesion with minimal stranding of fibrin.

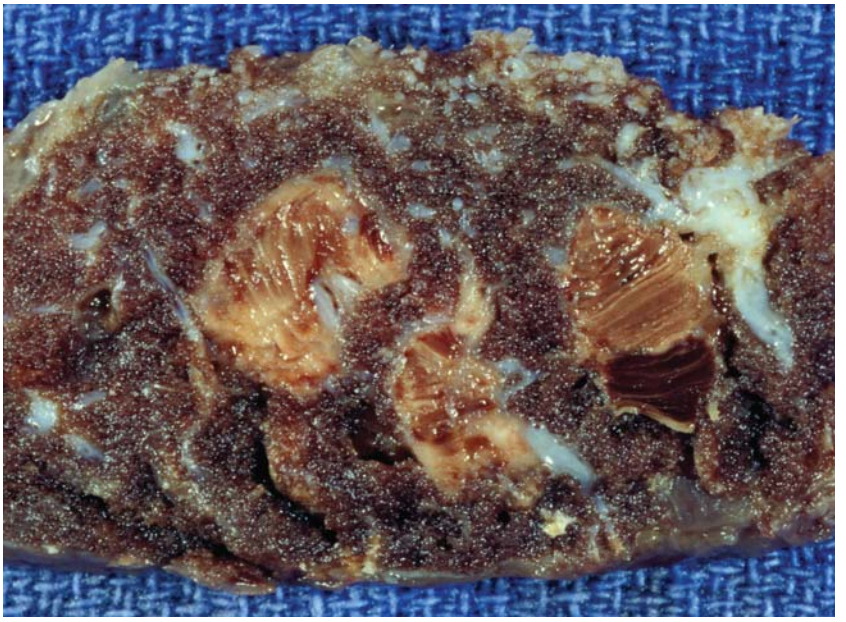


Figure 5.26. These are older thrombi in a fixed placenta. Lines of Zahn can readily be seen. These do not have a marginal rim of infarction.

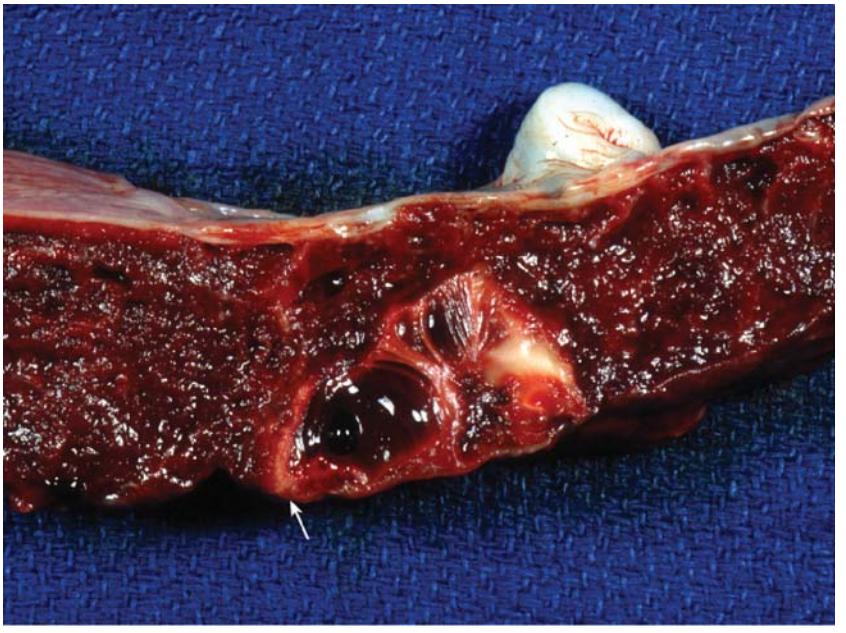


Figure 5.27. This basal intervillous thrombus has several components of different ages. The deep red portion is fresh while the layered material is older. There is a small marginal rim of infarction (*arrow*). Thrombi occur at the base of the placenta and should not be confused with retroplacental hemorrhage.

maternal red blood cells. They are seen more frequently in hydrops and other conditions with large friable placentas. The etiology of these lesions is not clear, but may relate to coagulation at sites of villous damage and fetal bleeding. Infarction may be present as a rim adjacent to intervillous thrombi, which apparently interfere with local villous blood supply. Such associated infarction does not imply maternal vascular disease. Thrombi may also be present at the base of the placenta, where they do not indicate premature placental separation (Figure 5.27).

Fibrin Deposition

Localized areas of perivillous fibrin deposition are seen in virtually all mature placentas and show an irregular lacelike pattern (Figure 5.28, Figure 5.29). Although the entrapped villi eventually die, small amounts of fibrin deposition are not generally thought to be related to fetal or maternal disease, apparently originating from turbulence in the maternal circulation.

Occasionally fibrin deposition is excessive, diffusely involving half or more of the villous tissue (Figure 5.30, Figure 5.31). This degree is abnormal, and associated with preterm delivery, growth retardation, and death.

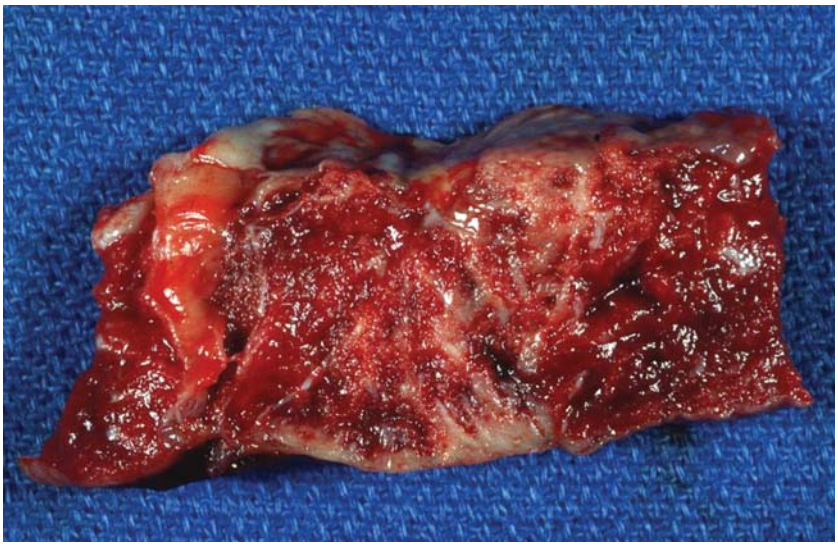


Figure 5.28. This cross section shows a thrombotic lesion (left) and perivillous fibrin deposition (right). The shiny old thrombus is actually an extension of a small, old, subchorionic hemorrhage and not a true intervillous thrombus. Note the irregular outlines of the fibrin deposition and its admixture with normal villous tissue. There is substantial calcification in this area.

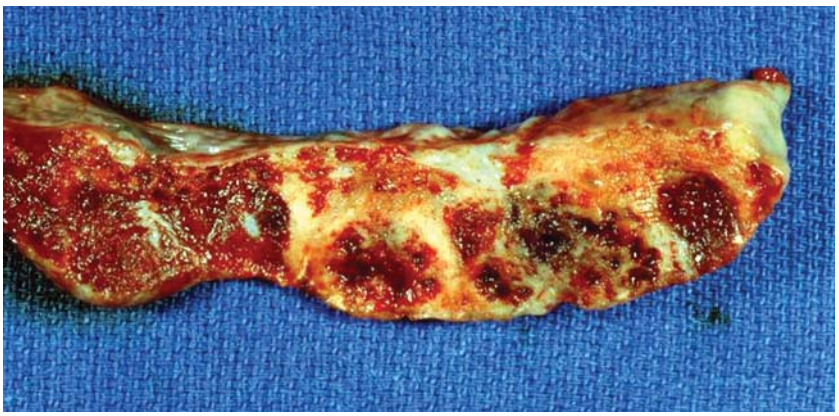


Figure 5.29. The white material deposited in this term placenta is fibrin. Such localized fibrin is common in later gestations. It is deposited in the intervillous space around villi in a lacelike fashion, and usually is quite hard and shiny. Although the entrapped villi eventually die, such fibrin deposition is not usually associated with fetal or maternal disease. At times, relatively large regions are involved, as shown here. The process, however, is still localized and not of concern.

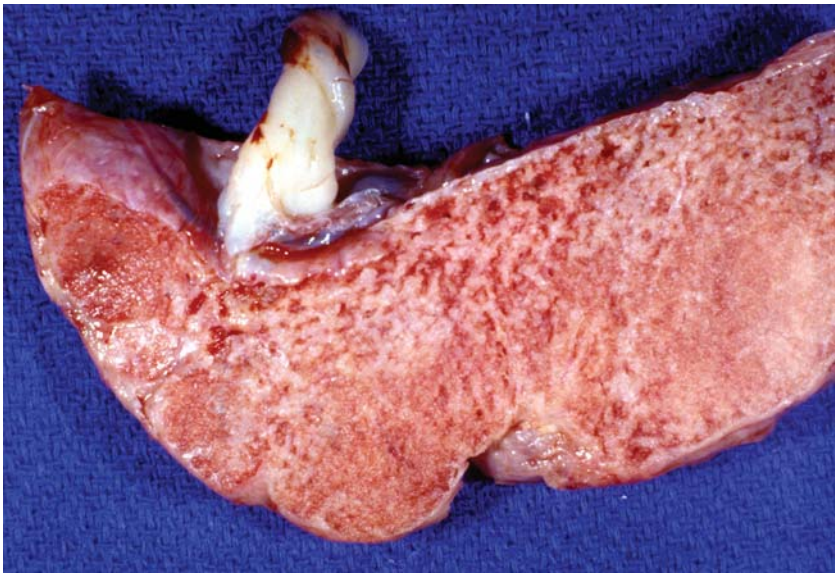


Figure 5.30. Diffuse fibrin deposition involving more than 50% of the placenta is considered abnormal, and is associated with prematurity, fetal growth retardation, and death. The etiology of such massive perivillous fibrin deposition is unknown. This thick, immature, very pale placenta showing a diffuse network of fibrin was associated with intrauterine demise at 25 weeks of a poorly grown infant. Such placentas are usually quite firm and may actually be relatively heavy.

Figure 5.31. Viewing sections of the entire placenta will help determine the extent of the process, as show in another example of massive perivillous fibrin deposition. The material shows a much coarser pattern, the more typical appearance.

"Maternal floor infarction" is a related lesion (Figure 5.32 to Figure 5.34). This is not true infarction, consisting of a layer of bland fibrin deposition around basal villi. It has similar associations to diffuse perivillous fibrin deposition and can be recurrent. The etiology of maternal floor infarction is also unknown. Placentas with excess fibrin, both normal and pathologic, often show surface and septal cysts due to the trophoblastic proliferation which occurs in areas of fibrin. The cysts form within the trophoblastic areas (Figure 4.17, 5.35).

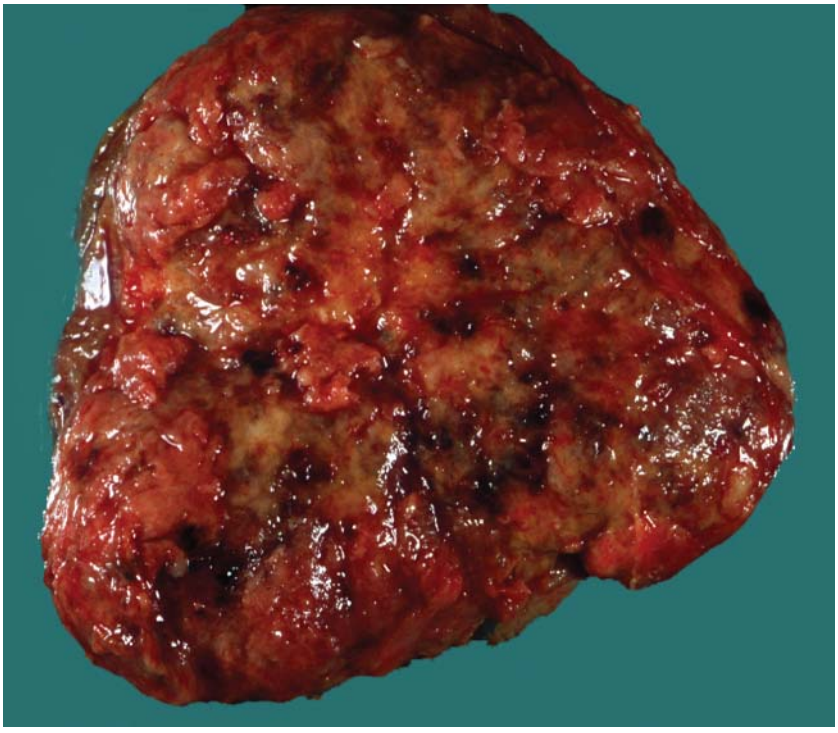


Figure 5.32. Maternal floor of an immature placenta with excess fibrin deposition is shiny and appears stiff showing firm yellow plaques. Such an appearance is suggestive of maternal floor infarction, which is better visualized on cut sections.

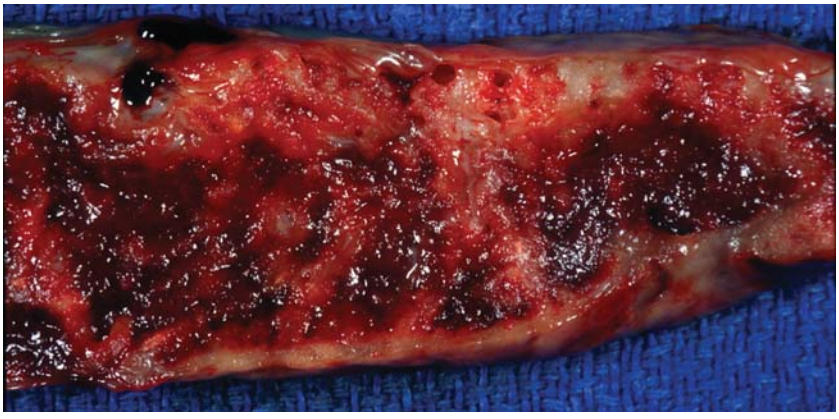


Figure 5.33. "Maternal floor infarction" is a recurring lesion is associated with growth retardation and death. In this process there is a layer of fibrin deposited at the base for 3 mm to 4 mm. Basal villi are entrapped and die, but it is not true infarction. This occurs in combination with some degree of diffuse perivillous fibrin deposition, as shown here. This placenta is from a live-born infant.

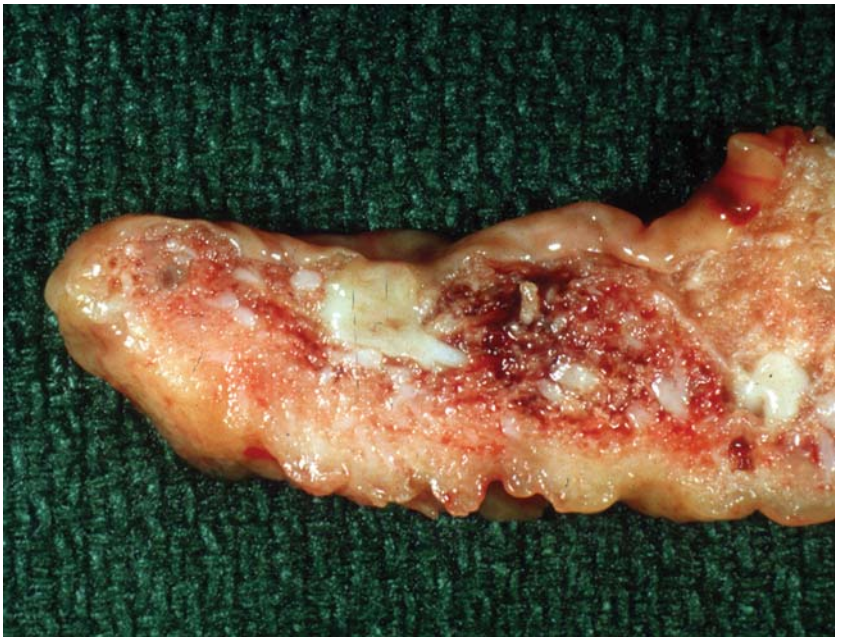


Figure 5.34. This more dramatic example of maternal floor infarction is from a 25 week stillborn.

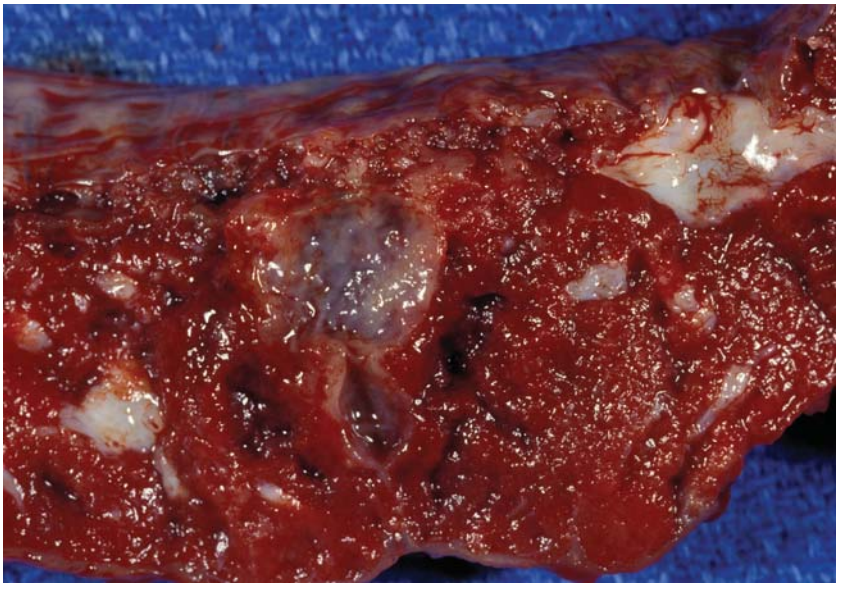


Figure 5.35. This thin-walled cyst is located within a septum of a term placenta. Such cysts also occur on the surface (Figure 4.17). They develop within solid trophoblastic regions and are often adjacent to fibrin deposition. Cysts do not appear to be associated intrinsically with any pathology.

Avascular Villi

The presence of avascular vill (villous atrophy) implies interruption of the fetal blood supply. After fetal demise, the entire placenta undergoes this change if delivery does not occur. It does not infarct since maternal perfusion continues. Occlusion of part of the fetal circulation, as with thrombosis, will lead to zones of atrophic avascular villi, often recognizable grossly (Figure 5.36). Such change may reflect more diffuse fetal thrombotic processes in utero, with the potential for vascular disruptive lesions. Early microscopic change in villi includes vascular breakdown progressing to complete stromal fibrosis (avascular villi) (Figure 5.37). These histologic changes take days to weeks to develop.

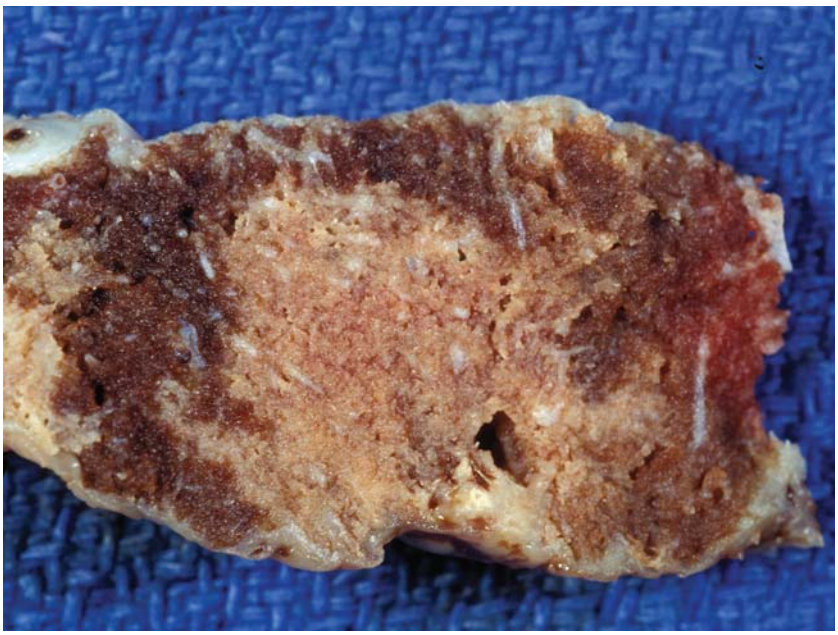


Figure 5.36. Fixed placenta with irregular pale area of atrophy. The light color comes from the lack of fetal blood and fibrosis within the affected villi. No gross thrombosis was noted, which is not unusual; however, fetal vascular thrombi are often found on histology. The tissue is not collapsed or hard and feels similar to adjacent villi.

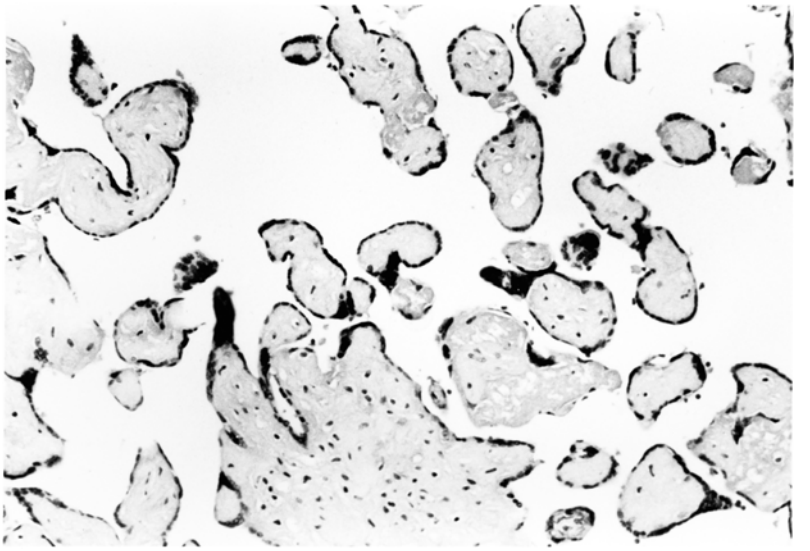
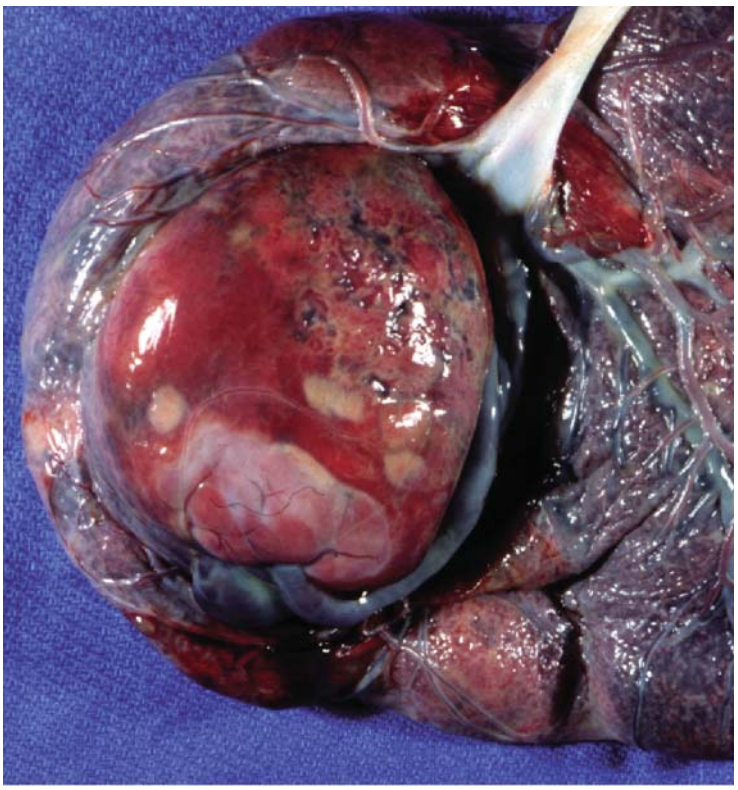


Figure 5.37. Histology of avascular villi reveals a fibrotic stroma without blood vessels. The trophoblast on the surface is viable since it is still perfused by maternal blood. Change of this degree likely takes more than a week to evolve.

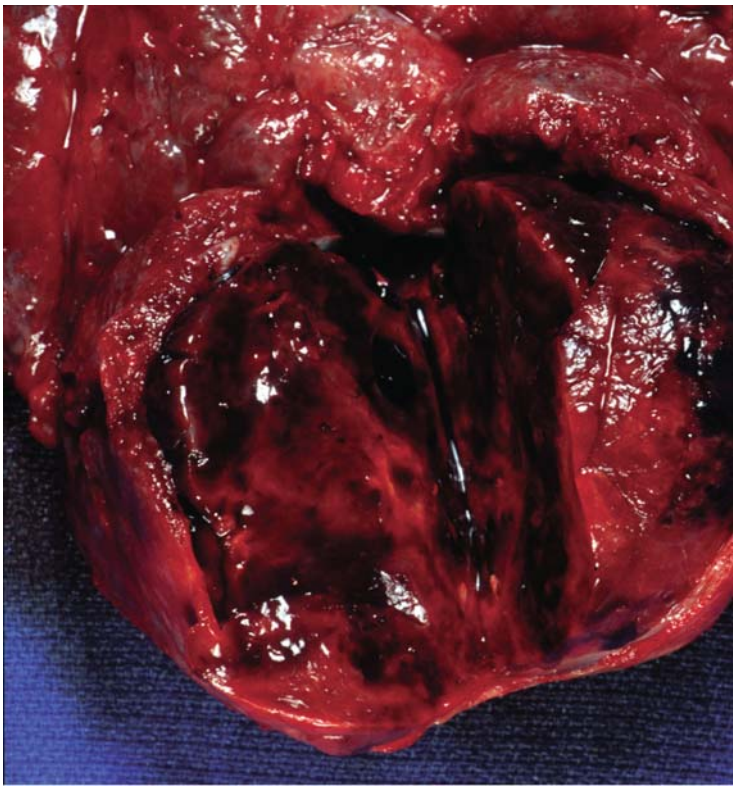
Chorangiomas

Chorangiomas are hemangiomas of the placenta and occur in about 1% of pregnancies. They are best designated as hamartomas. These lesions commonly occur under the chorionic plate (Figure 5.38) and have a variety of appearances, depending on vessel size, perfusion, and viability



A

Figure 5.38. (**A**) The raised red, round solid lesion seen through the fetal surface is a chorangioma or hemangioma of the placenta. These are usually nodular, fleshy lesions connected to the chorionic plate.



B

Figure 5.38. (**B**) The lesion extends nearly to the maternal surface. The cut surface suggests there are large areas of infarction.

(Figure 5.39 to Figure 5.42). Chorangiomas are often confused with other gross lesions (Figure 5.42). Histology is that of a typical hemangioma, usually with small or medium sized vessels (Figure 5.43). Large chorangiomas may lead to fetal hydrops and platelet trapping. Rarely the infants have other hemangiomas.

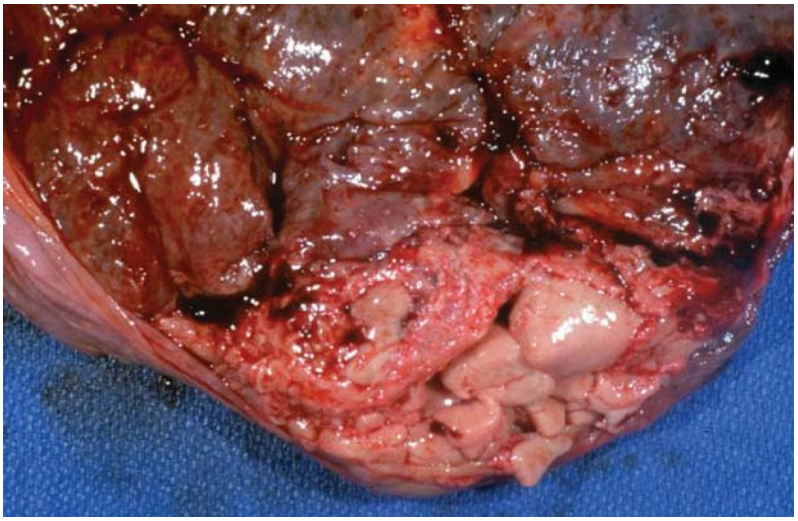


Figure 5.39. Another chorangioma in a preterm placenta is much paler and irregularly lobulated. The size of the vessels, their congestion, and the presence of infarction will determine the characteristics of the mass. Large chorangiomas may be associated with nonimmune hydrops, possibly caused by fetal circulatory overload and shunting. Trapping of platelets and fetal thrombocytopenia may also occur.

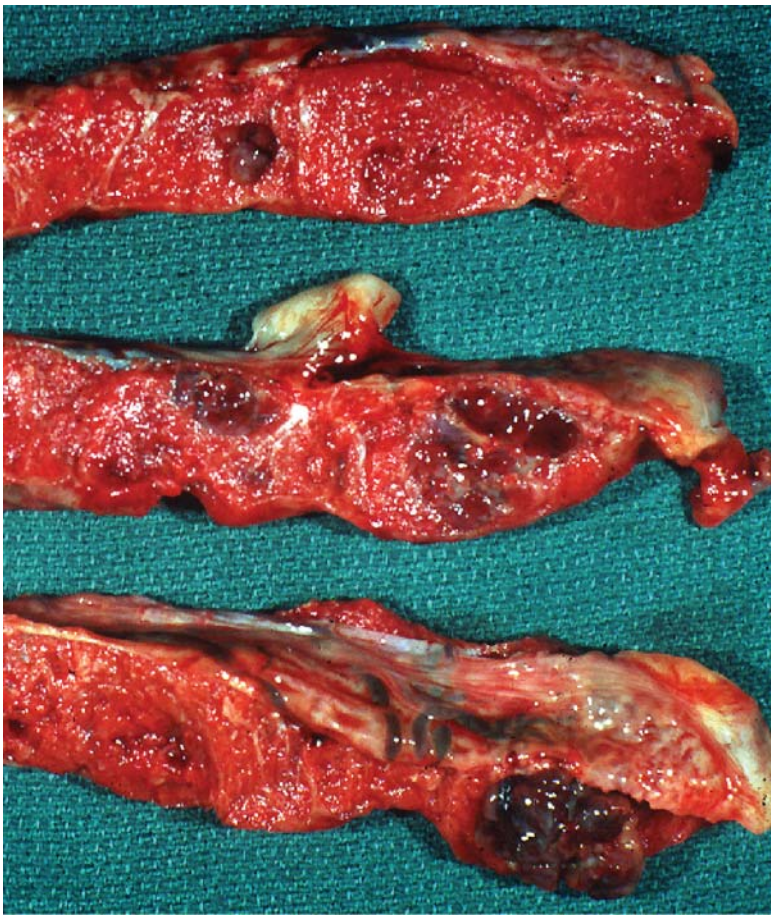


Figure 5.40. Chorangiomas are frequently multiple and may be pedunculated, as shown by the multiple berry-like lesions here.

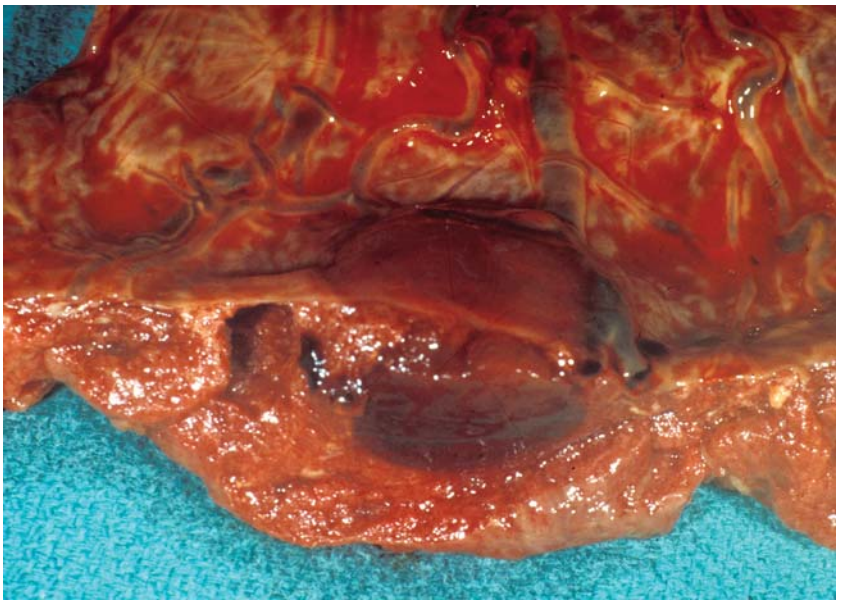


Figure 5.41. The gelatinous ill-defined subchorionic region in this placenta was histologically a chorangioma.

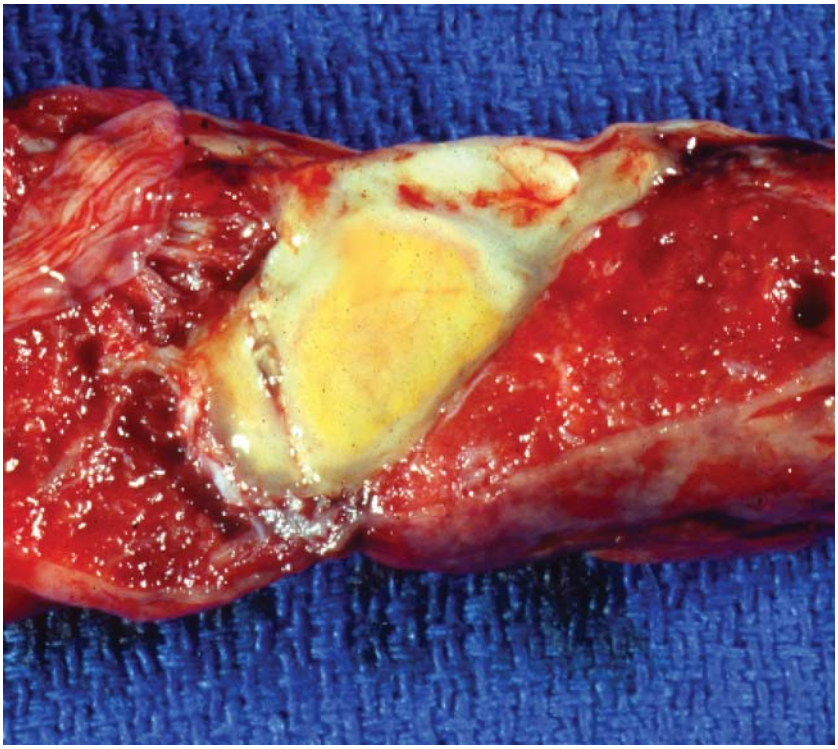


Figure 5.42. Chorangiomas are often confused with other pathologic lesions, particularly if infracted. This thrombus-like mass was actually a chorangioma.

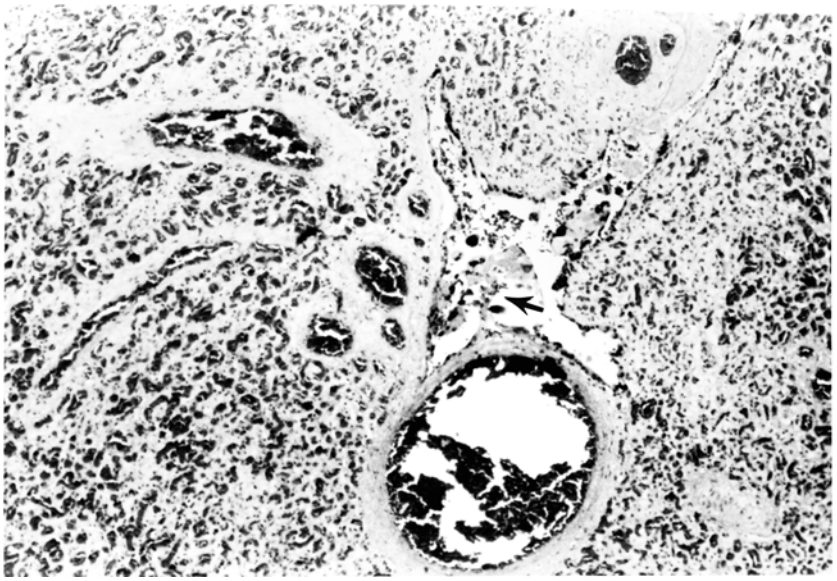


Figure 5.43. Microscopic view of a chorangioma reveals numerous small and a few larger blood vessels in lobulated areas resembling large villi. The vessels are congested. The surface of the chorangiomatous nodules is covered by trophoblast which, as usual, is somewhat hyperplastic (*arrow*).

Mesenchymal Dysplasia

This is a rare disorder of unknown etiology characterized by serpiginous surface blood vessels and large cystic villi, often resembling molar tissue. The most common association is with Beckwith-Weidemann syndrome (Figure 5.44).

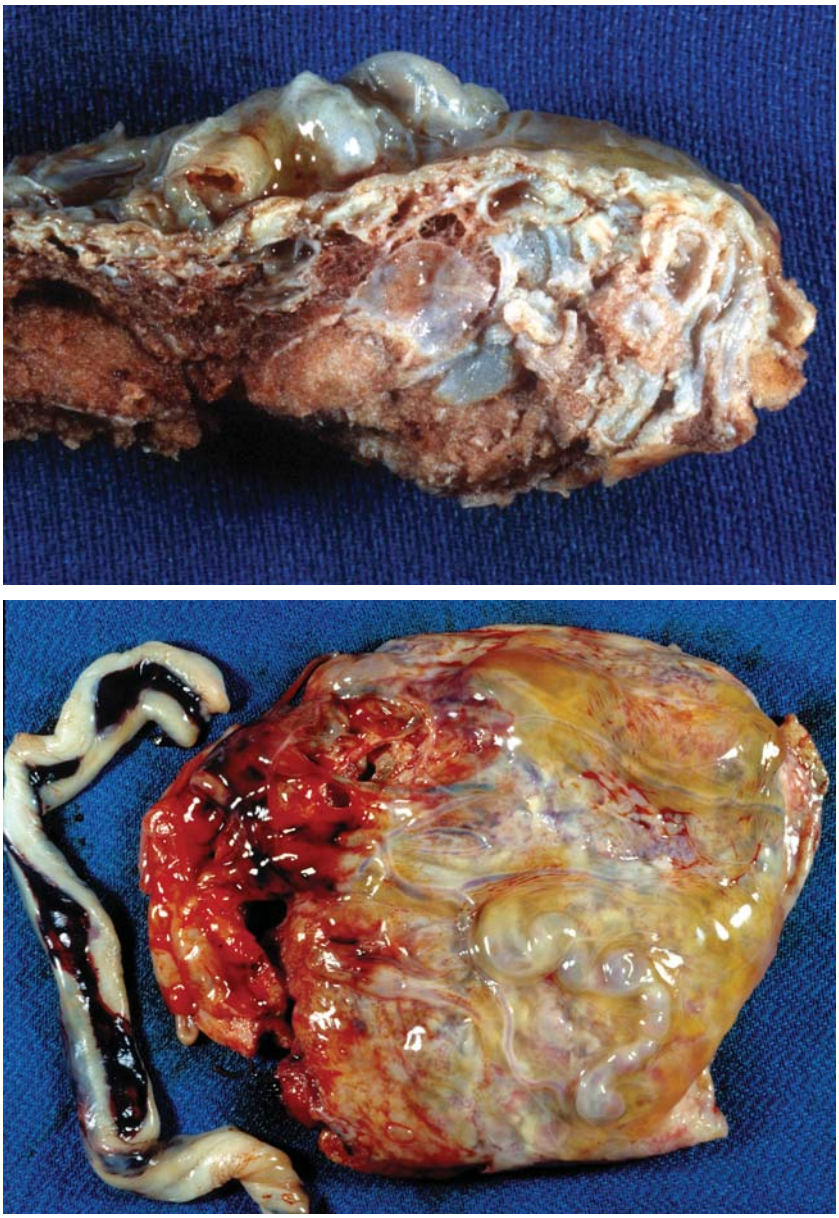


Figure 5.44. (**A**) Mesenchymal dysplasia is typically seen under the chorionic plate and will extend into the parenchyma as shown in this fixed placeenta. There are dilated villi and vessels in an irregular arrangement. (**B**) On the fetal surface of this fresh placenta, one sees dilated serpiginous vessels which are often thrombosed.

Inflammatory Villous Lesions

Infections reaching the infant from the mother's bloodstream will traverse the villi. Examples of this include rubella, cytomegalovirus, and syphilis. Usually no specific infectious gross lesions are identifiable, although the placenta may be hydropic or unusually firm and fibrotic. *Listeria monocytogenes* typically causes grossly visible necrotizing abscesses (Figure 5.45). Rarely other infectious lesions are identified

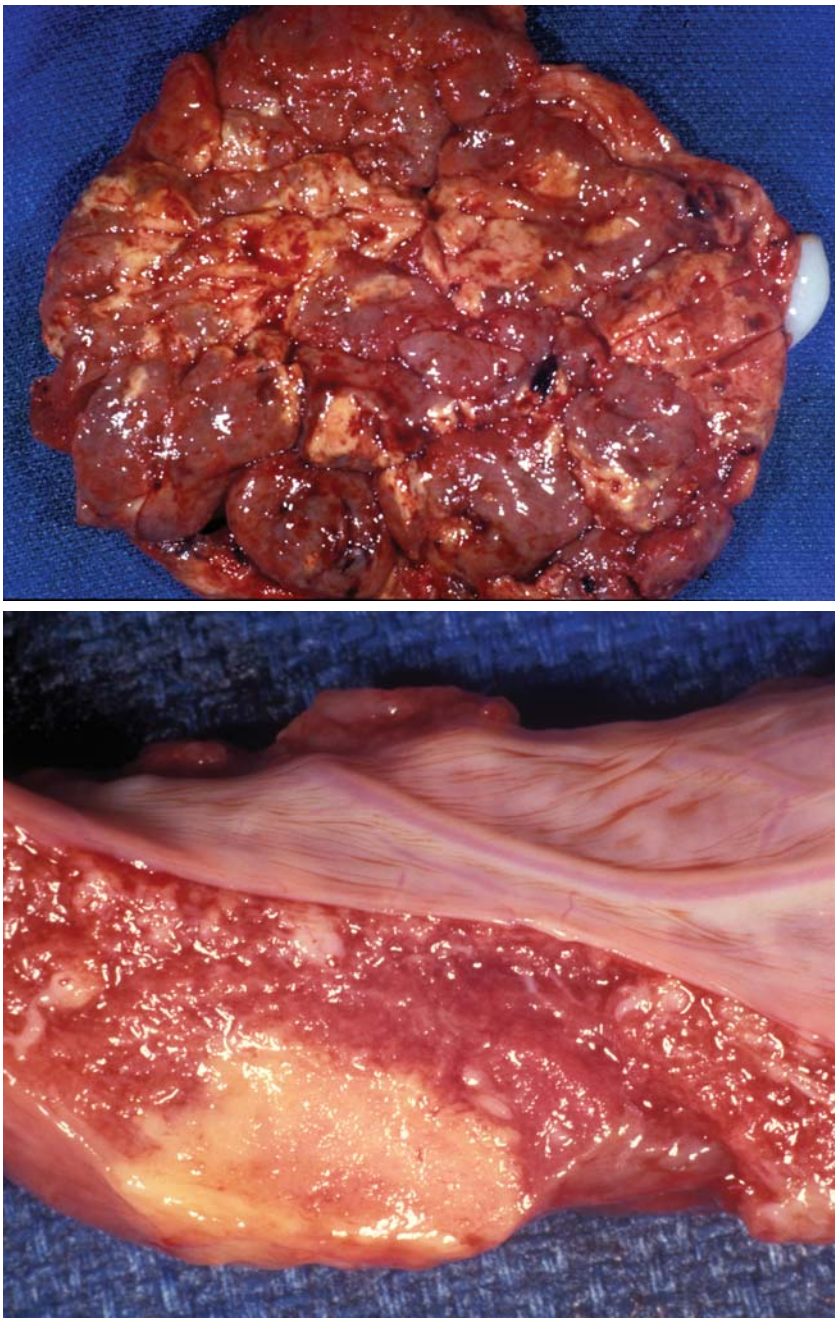


Figure 5.45. (**A**) The maternal surface of a 26-week placenta infected with listeria shows numerous yellow-white lesions, reminiscent of infarcts. The villous tissue, however, appear pale and immature, unusual when there is early severe vascular disease. This suggests a different process. The areas are actually abscesses. (**B**) Cross-section of one abscess also suggests infarction. Smaller lesions dispersed diffusely in the villi also occur. Listeria is usually associated with severe chorioamnionitis, and the fetal surface here is opaque.

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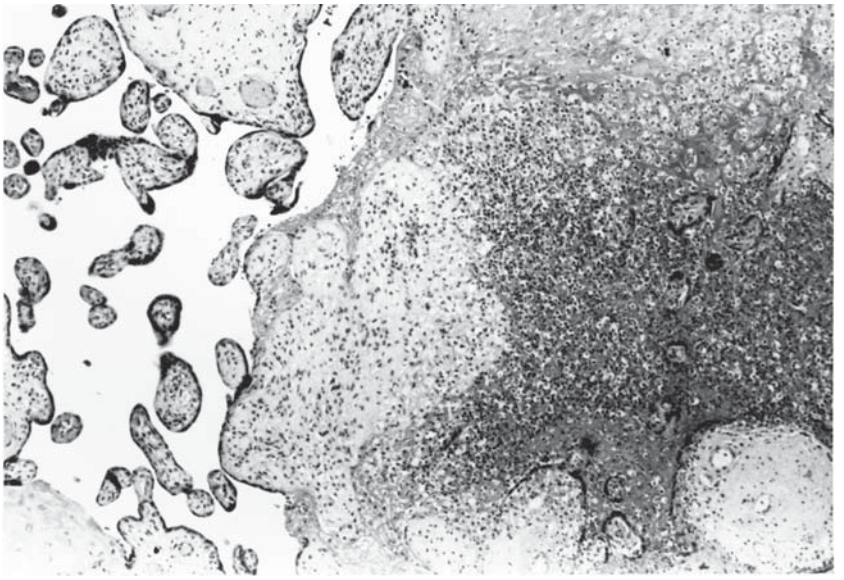
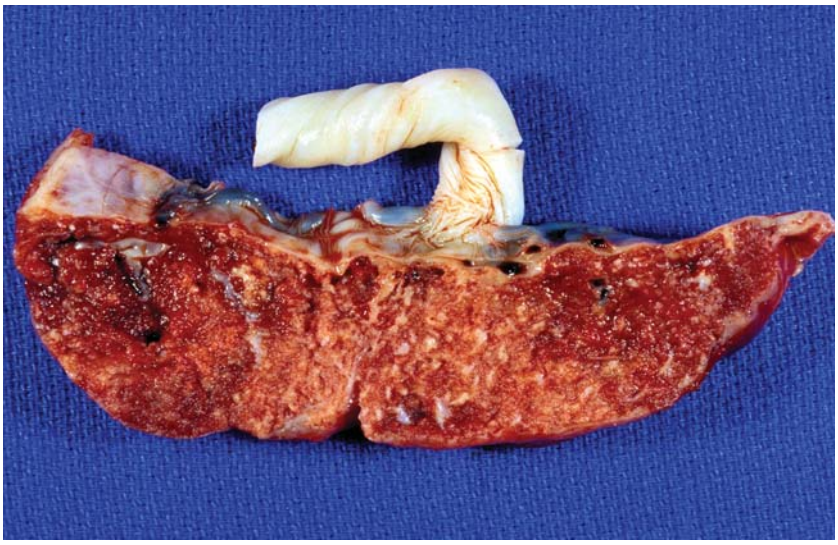


C

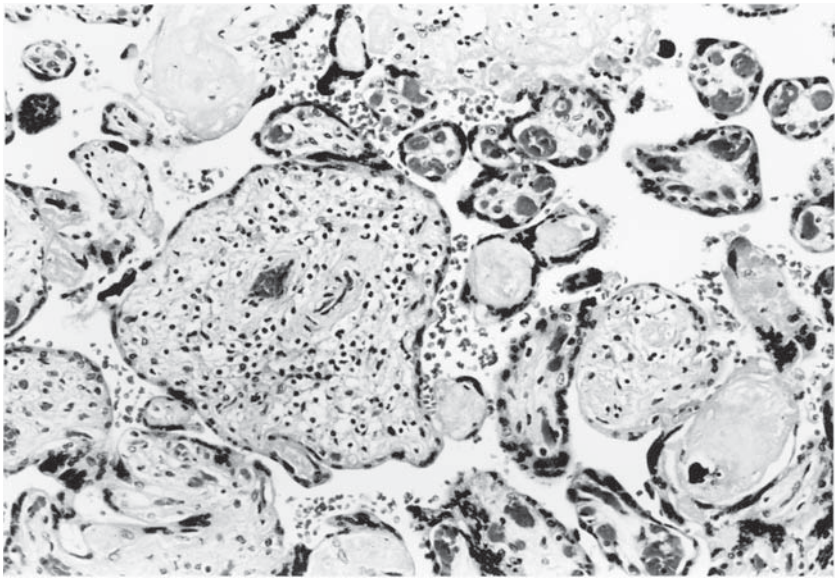
Figure 5.45 (Continued). (**C**) Microscopy of these lesions shows extensive acute inflammation. There is necrosis and some villous ghosts, contributing to the infarctive appearance.

Figure 5.46. Cross-sections of a placenta occasionally reveal round, soft yellow lesions only a few millimeters wide. Such areas may be small abscesses and should be examined microscopically. Early lesions of listeria will have this appearance. They may also be seen with maternal septicemia. The lesions shown in this fixed placenta were histologically granulomatous and occurred in a woman with HIV and disseminated tuberculosis. Acid-fast bacteria were abundant.

in the villous tissue (Figure 5.46). Much of the villous inflammatory disease identified histologically is nonspecific villitis, most likely not a lesion of infectious origin (Figure 5.47).



A



B

Figure 5.47. (**A**) Nonspecific villous inflammation (villitis of unknown etiology) is not usually identifiable grossly. Occasionally placentas with extensive disease will have visible abnormalities with features of avascular villi (see Figure 5.36). They often are somewhat yellow color, as shown here. Increased fibrin deposition is common. (**B**) On histology the placenta showed nonspecific inflammatory changes involving half the villi. Histology of nonspecific villitis shows villi enlarged with inflammatory cells (lymphocytes) admixed with normal villi. The fetal vasculature is obliterated in areas, which leads to the gross appearance. Fibrin deposition and villous agglutination may also be features. Such villitis is associated with a variable degree of growth restriction and can be recurrent.

Histologic Study

While careful examination of gross placental lesions is usually diagnostic, some will remain enigmas until microscopy is done (Figure 5.42, Figure 5.45). In placentas with extensive villous lesions and those placentas associated with fetal or maternal disease, histologic sectioning should include a few examples of the gross processes. Isolated infarcts or thrombi do not require further study, particularly in term placentas.

6

Multiple Gestations

Today in the United States, at least one in 100 births is a multiple gestation and the examination of these placentas is one of the most important aspects of gross placental pathology. Twins account for a disproportionate percentage of perinatal morbidity and mortality and have significantly higher rates than singletons. Placentas of multiple gestations demonstrate all the abnormalities seen in singletons, as well as their own special pathology. While most of the following discussion relates to twins, the same principles are used when evaluating triplet and quadruplet placentas. Multiple births have become more common with assisted reproductive techniques, but refinements of procedure have fortunately decreased the number of higher order births currently conceived. Special twin placenta report forms are useful in examination (Appendix A-2).

Chorionicity

Determining the chorionicity of a twin placenta is the most important step in its examination (Figure 6.1). "Dichorionic" means two placentas have formed, while "monochorionic" indicates a single shared placenta. Any gestation arising from two separate fertilized eggs will be dichorionic, as each conception forms its own placenta with all its components. These placentas may be totally separate; however limitations of space in the uterus frequently lead to "fusion" and a single disk. For practical purposes, there is no connection of the circulations in such placentas.

Monochorionic placentas occur only in monozygotic or "identical" twins. The fertilized egg splits early in gestation and each portion continues to develop separately. Splits occurring before three days of development, while all the cells of the conceptus are still undifferentiated, lead to gestations with totally separate placentas. At about three days, some cells become developmentally committed as trophoblast and can no longer split. This leads to two separate embryos and amnions developing within a single chorion. Later splits are unusual and lead to twins in a single amniotic sac (monoamnionic) and finally conjoined twins.

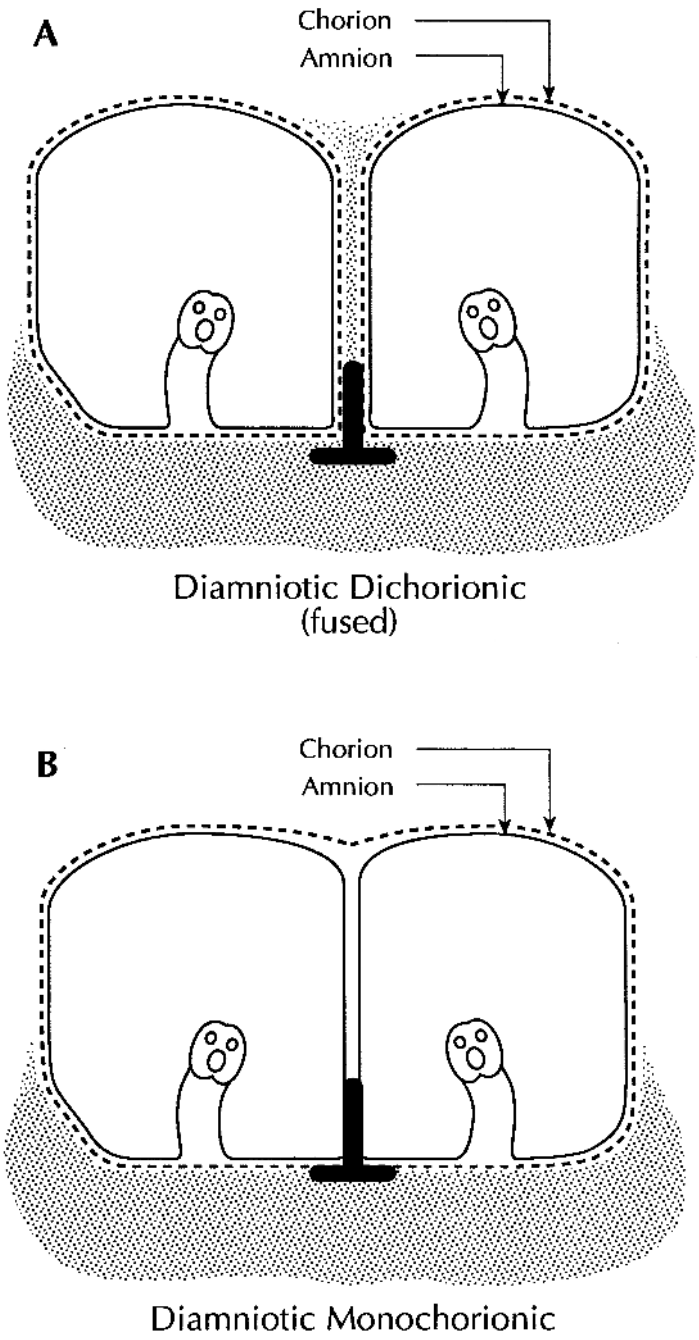


Figure 6.1. Diagrammatic views of the types of fused twin placentas with two amniotic sacs. "T" sections are taken from the point where the dividing membranes meet the fetal surface. (**A**) The dichorionic placenta has two sacs each enclosed by amnion and chorion. There is chorionic tissue (stipples) in the dividing membranes, forming a ridge on the surface. (**B**) The monochorionic placenta shows no chorionic material in the dividing membranes and the chorion forms a continuous plate on the surface of the placenta. The dividing membranes consist of only two amnions.

Two-thirds of monozygotic twins are monochorionic, and the remainder dichorionic.

Like-sexed monozygotic dichorionic twins cannot be differentiated from like-sexed dizygotic dichorionic twins by placental exam. Only genetic testing will definitively distinguish them. In the United States at least 80% of like-sexed dichorionic twins are dizygotic, based on the incidence of twin types. The incidence of monozygotic twins had been constant throughout the world at about 1/300 births. Assisted reproductive techniques have been found to double the rate of monozygotic twins. The incidence of dizygotic twins is quite variable in different populations around the world and this is the type of twinning that is familial.

Examination of Twin Placenta

Placentas received with totally separate disks are virtually always dichorionic, even when their reconstructed morphology suggests they were originally a single disc. These are examined as one would singleton placentas, perhaps with the addition of some dividing membranes if present. Minimally fused placentas are also usually dichorionic. The dividing membranes are similar in both fused and separate dichorionic placentas and gross determination of the chorionicity is quite simple. The dividing membranes are evaluated for thickness and opacity. Dichorionic membranes are relatively thick and opaque (Figure 6.2, Figure 6.3), and there is a ridge where the dividing membranes meet the fetal surface (Figure 6.4). If one tries to completely remove dichorionic dividing

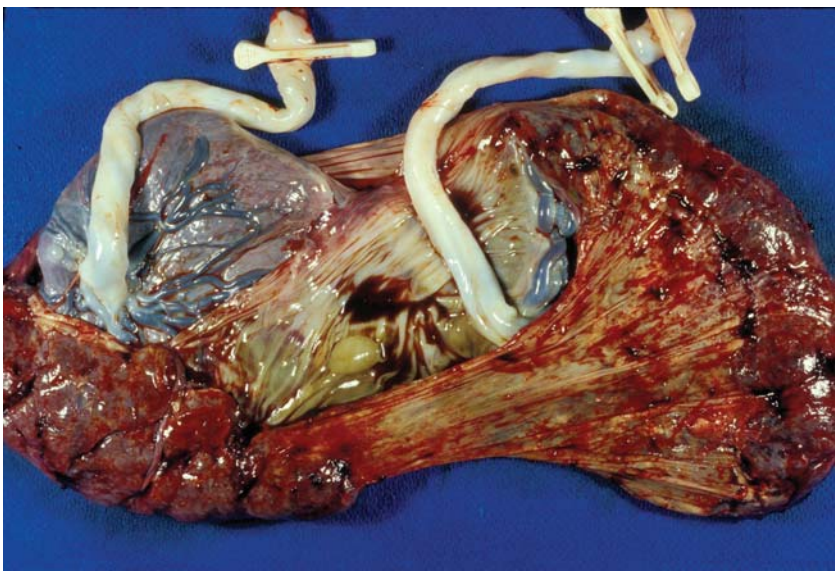


Figure 6.2. This near term dichorionic twin placenta has two separate disks connected by membranes. A draped piece of thick, dividing membranes can be seen between the cords. Note there is fresh meconium on the dividing membranes on the side with two clamps.

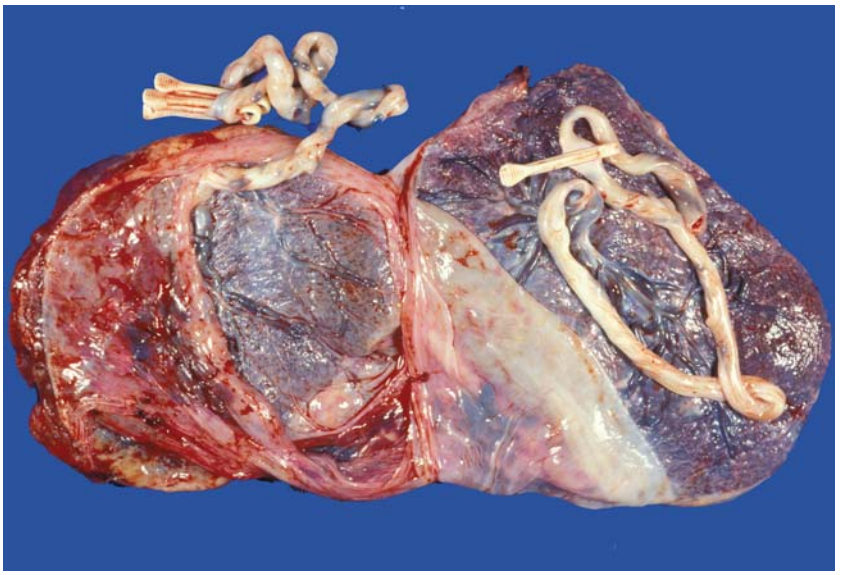


Figure 6.3. This placenta has two separate disks. There has been unequal chorionic "fusion" and the dividing membranes meet the fetal surface overlying the placenta of A with 1 clamp. Such lines are common on the surface of dichorionic placentas. These placentas can be manually separated with some superficial disruption.

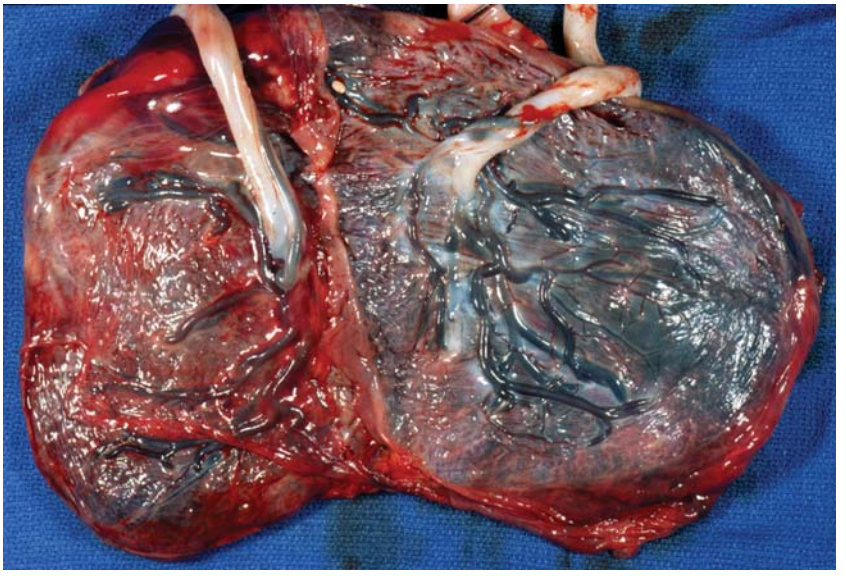


Figure 6.4. This dichorionic placenta has a "fused" disk. The dividing membranes have been largely removed. Note the ridge of chorionic tissue between the cords where the membranes had met the surface, diagnostic of a dichorionic placenta. Separation of the two placentas occurs along this ridge, and can usually be done with traction on each side. The vessels of these placentas do not connect. Note the yolk sac remnant at 12 o'clock.

membranes by separating the layers, the surface will be disrupted and the placentas will separate. In contrast, monochorionic placentas have nearly transparent membranes and are easily removed leaving a continuous monochorionic plate. No ridge is seen (Figure 6.5, Figure 6.6).

Chorionicity can be histologically confirmed in two ways. "T" sections include dividing membranes at a point where they reach the placental surface (Figure 6.1). Such sections are readily made on fixed dichorionic placentas; however in monochorionic ones it is difficult to keep the amnions intact. A roll of the dividing membranes can be made similar to what is done with the peripheral membranes. The dividing membrane is composed of 3 to 4 layers in dichorionic twins, and only two layers in monochorionic placentas (Figure 6.7).

Monochorionic placentas virtually always show one or more vascular anastomoses (Figure 6.8). These vascular anastomoses lead to the specific problems of monozygotic twins and it is important to document them. Diagrams are useful in complicated cases. Arteries always pass over veins. By visually following large superficial vessels one will identify many of the vascular connections between the two sides and determine sites of likely deep anastomoses. Once the placenta is fixed, this is all that will be possible. In fresh placentas, a small syringe can be used to inject a vessel by entering it proximal to the presumed point of

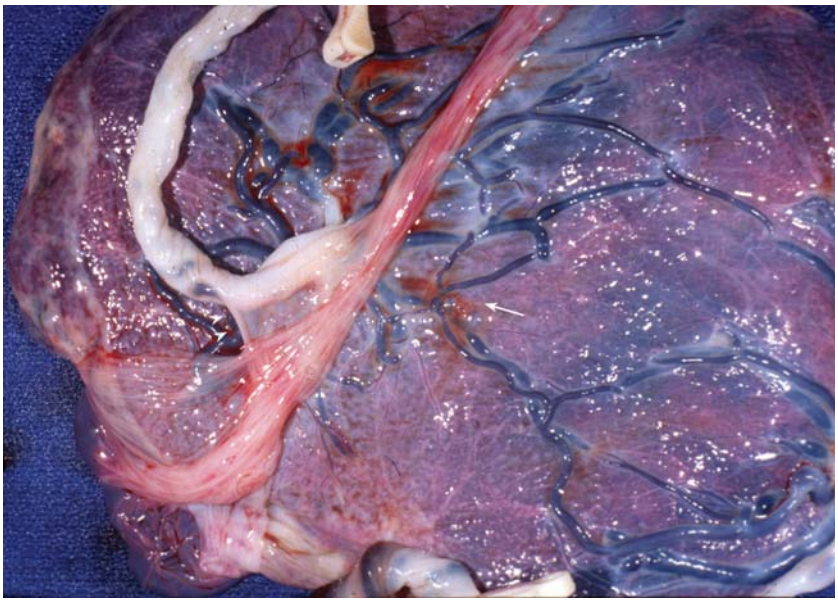


Figure 6.5. The extremely thin and delicate dividing membranes are folded on the surface of this monochorionic placenta. Note how little substance they have compared to those is Figure 6.2. Vessels dispersing from the cords can be seen to have complicated connections (*arrow*). In humans, only monochorionic placentas have vascular anastomoses. One cord shows a web to the dividing membranes (*arrowheads*).

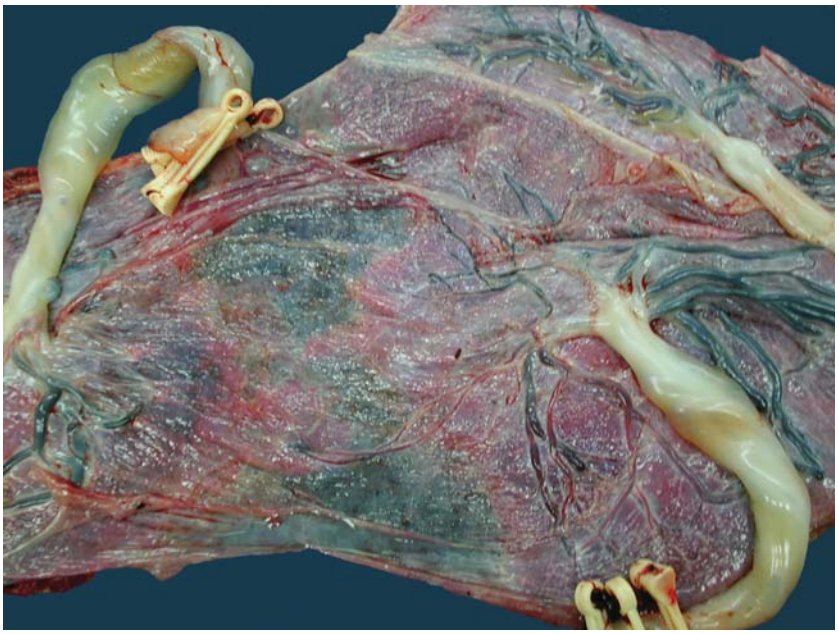
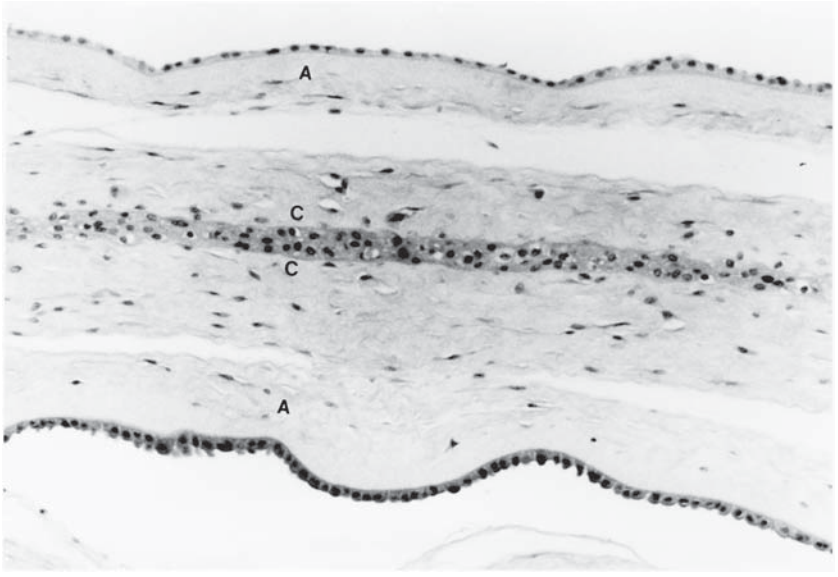


Figure 6.6. The dividing membranes of a monochorionic placenta can be readily separated, leaving a smooth, continuous chorionic surface between the two cord insertions. This triplet placenta had three amnions and 2 chorions. The amnions have been removed leaving a continuous plate between the monochoronic set and a ridge to the dichorionic triplet (upper right). In sectioning the dividing membranes in higher multiples, there may be several rolls made. A consistent means of submitting these should be adopted, such as A-B in A, B-C in B, and C-A in C.



A

Figure 6.7. (**A**) Microscopic view of dividing membranes in a roll from a dichorionic twin gestation shows they are composed of amnion from each twin containing epithelial cells and attached connective tissue (A) and chorion from each in which the two chorionic layers may fuse (**C**). Any chorionic tissue in the dividing membranes indicates a dichorionic placenta.

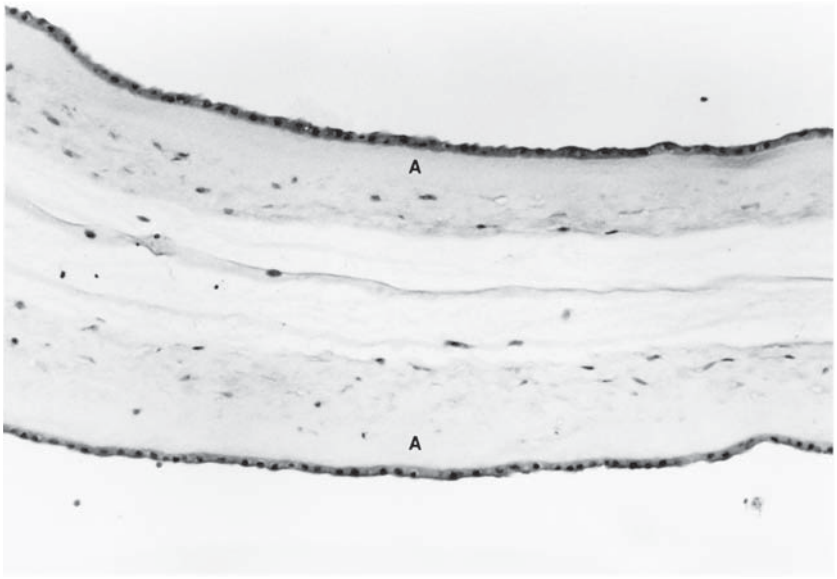


Figure 6.7. (**B**) Dividing membranes of a monochorionic gestation only show two layers of amnion (A).

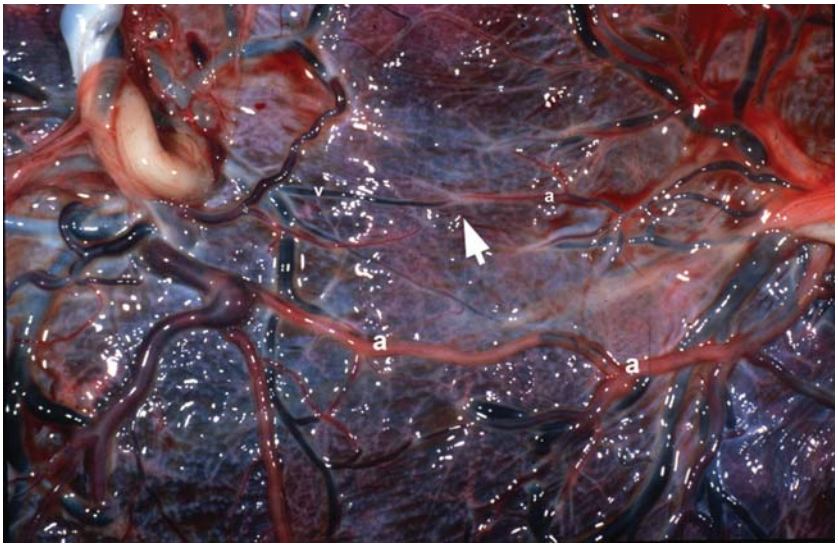


Figure 6.8. Vascular anastomoses in a monochorionic placenta are shown after removal of the amnions. The lower anastomosis shows large arteries ("a") from each cord fusing in the center. The vessels, clear from injected water, are recognized as arteries because they pass over other vessels. Injection is usually not necessary to identify such large connections. Above this (*arrow*) is an area suggestive of a deep artery to vein connection. Arteries and veins usually run together as pairs. Here, an artery (a) from one cord ends without a parallel returning vessel. A similar vein (v) ends just adjacent to it. While such anastomoses are important and most implicated in transfusion syndrome, they are difficult to inject because of pressure or disruption in the circuit. Recognition of their usual gross morphology is thus important.

anastomosis and manually occluding backflow. The water, milk, air or dye may be seen crossing to the other side. Small deep anastomoses are most difficult to identify, and injection is frequently not be successful due to disruption or incomplete filling.

What now remains to be done is the usual evaluation of the cord, membranes, and villous tissue. A single placental disk is measured overall. Fused dichorionic placentas can usually be separated manually with traction starting at the edge where the dividing membranes reach the surface. They are then examined as singletons. Monochorionic placentas, however, cannot be separated by traction and require cutting. This is done along the approximate line where each circulation ends. The distribution of veins can be used as there are fewer venous anastomoses than arterial ones. A visual assessment of the percentage of the placentas belonging to each twin is also used. Division of the disks is accurate in dichorionic placentas. The weight or size of each monochorionic portion is at best an estimate since there is considerable deep overlap. Differences between the sides such as villous color should be noted. Tissue from each placental portion should be placed in its own container. Hopefully the cords have been labeled. If not, they should be arbitrarily designated and the materials kept separate. The usual routine placental blocks are submitted along with dividing membranes if present. In monochorionic placentas, blocks should contain villous tissue clearly from the circulatory region of each twin. Sections of the transitional zone may highlight differences in villous structure.

Problems Unique to Monochorionic Twins

The vascular anastomoses virtually always present in monochorionic placentas cause special problems. Unbalanced cross-circulation can lead to the transfusion syndrome. In chronic cases the classic presentation is an anemic, growth-retarded donor twin with oligohydramnios and a larger, plethoric recipient with polyhydramnios (Figure 6.9). Hydrops may occur in either infant. The donor usually has a pale placenta from anemia while the recipient's placenta is deep red and congested (Figure 6.10). There may be microscopic differences in villous structure and maturation. These are usually subtle, even in clear-cut chronic transfusions. Acute transfusion syndromes also occur. One fetus can bleed through the anastomoses into the placenta of the other when pressures drop after the first is delivered or dies. At times this can reverse the gross appearance of a chronic transfusion (Figure 6.11). Very premature delivery is common in severe chronic transfusion syndromes, often occurring in the second trimester. Death of both twins is common (Figure 6.12). If only one twin dies, the chronic transfusion will stop, however there is about a 20% risk of vascular disruptive anomalies (e.g. porencephalic cysts, intestinal atresias) in the surviving infant (Figure 6.13). It is believed that circulatory changes similar to those in seen acute transfusion syndrome

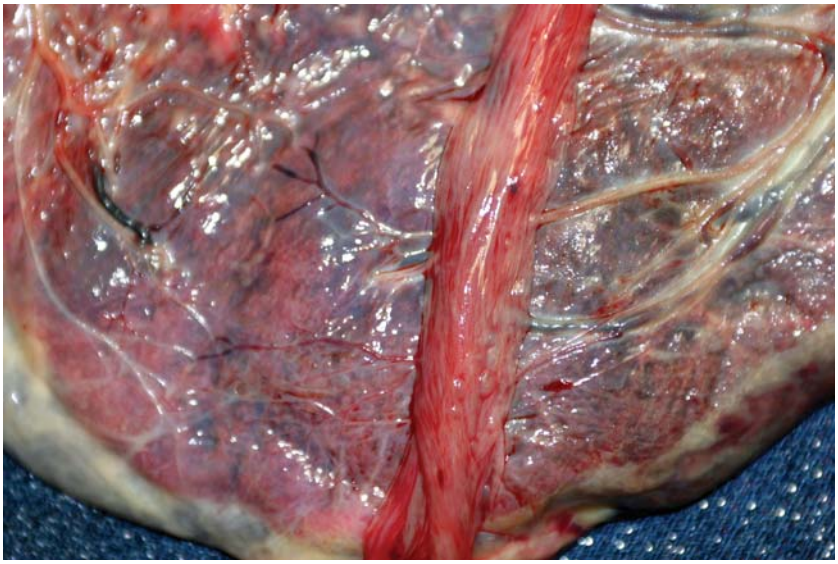


Figure 6.9. This monochorionic placenta is from a set of twins with well-developed chronic twin-twin transfusion syndrome. The placenta on the left is quite shiny and its sac had polyhydramnios. The surface on the right is dull with slight nodularity. This is amnion nodosum in the sac with minimal fluid.

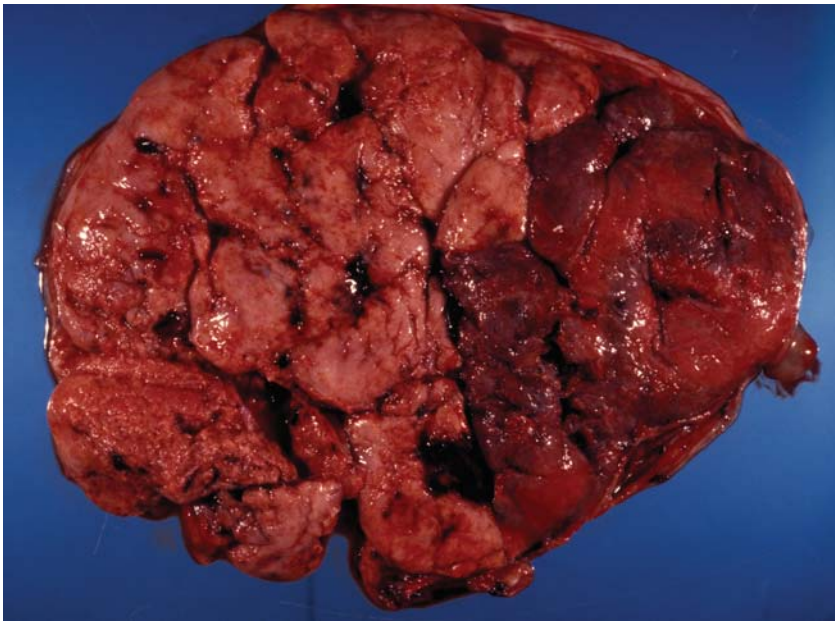


Figure 6.10. The maternal surface of this monochorionic placenta was from twins with severe chronic transfusion syndrome. There is a marked difference in color between the two sides with the paler but larger portion associated with the anemic donor twin. Such a striking difference is rare.

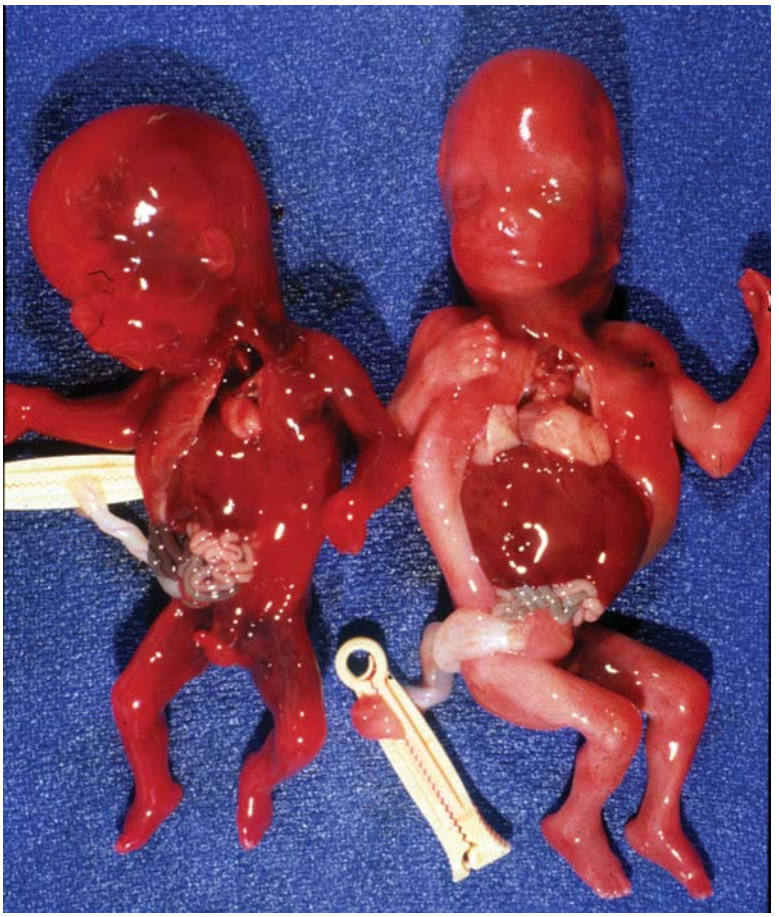


Figure 6.11. These two 17 week fetuses show evidence of both acute and chronic transfusion syndrome. The larger fetus had a hypertrophied heart, evidence of recipient status in chronic transfusion syndrome. It is, however, quite pale, having acutely lost most of its blood volume through an anastomosis into the smaller twin (chronic donor, acute recipient) who died first.

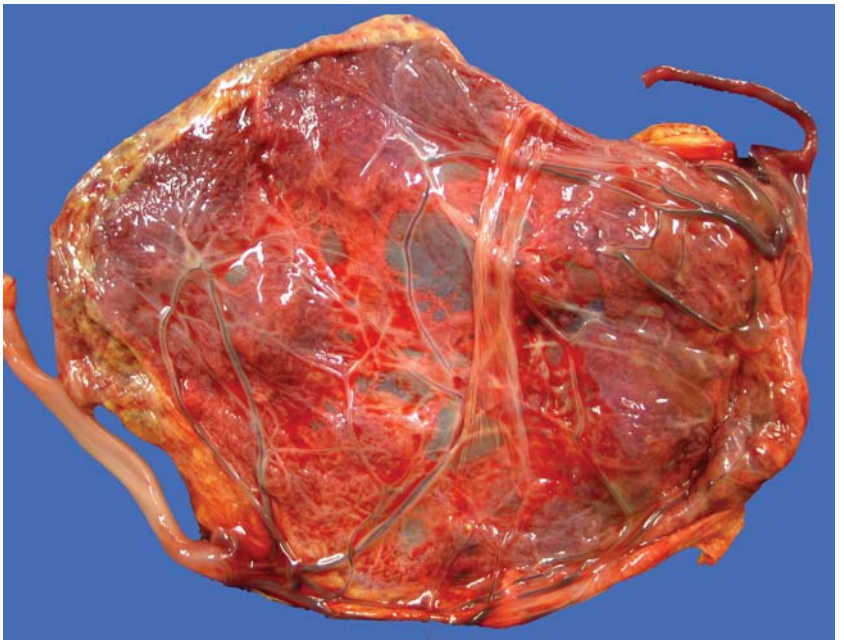


Figure 6.12. Intrauterine death of both twins occurred in this preterm pregnancy. The placenta is monochorionic and both cords have marginal to velamentous insertions. The fetus on the right, associated with the hemolytic cord and surface, died first. Its placenta was congested with blood, lost by the other twin through vascular anastomoses.

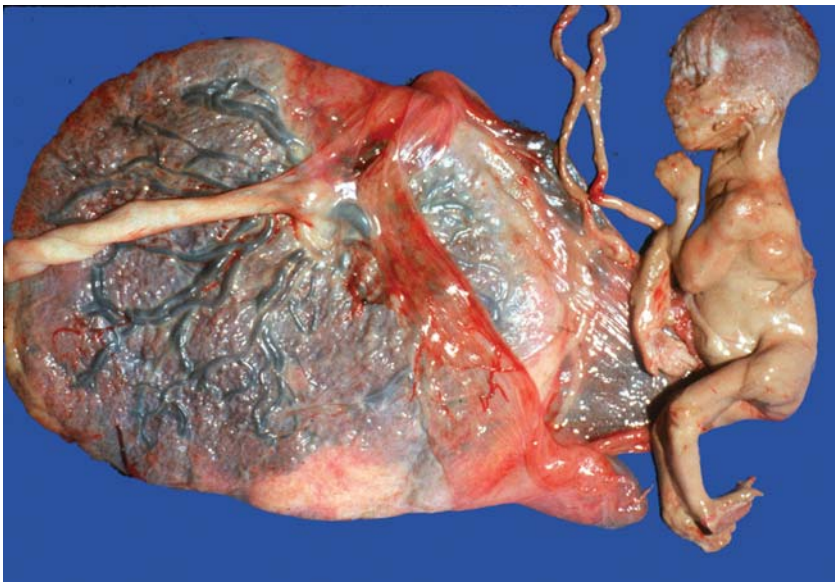


Figure 6.13. Death of one twin at 19 weeks led to the formation of a fetus papyraceous in this term pregnancy. Morphology was adequately preserved to permit the histologic confirmation of the dividing membranes as monochorionic. While the etiology of the death of the infant is not fully determinable at this time, transfusion syndrome is likely. The surviving twin was at increased risk for vascular disruptive anomalies, but was uninvolved. The risk for disruption seems to become greater as the gestational age at fetal death increases.

occur around the time of death and cause damage at that time from anemia and hypovolemia. The incidence of disruptions in the survivor does not seem to increase with long duration of the pregnancy after the demise.

A small portion of monochorionic twin placentas entail relatively late splits in the conceptus. Monoamniotic pregnancies are usually diagnosed prenatally by ultrasound. Numerous large anastomoses typically occur in such placentas, and chronic transfusion syndrome is rarely a problem. Cord entanglement leads to very high morbidity and mortality. A monoamniotic state should only be diagnosed if there is a layer of amnion covering the fetal surface between the cords (Figure 6.14). Most monochorionic twin placentas which apparently lack dividing membranes are actually disrupted diamniotic monochorionic placentas. A particular form of vascular anastomoses in a monochorionic placenta permits the development of acardiac twins. Such fetuses are passively perfused by their co-twin and lack cardiac development from the circulatory reversal. External and internal development is strikingly abnormal (Figure 6.15). Occasionally placentas are found which show intermediate forms between the classic configurations (Figure 6.16).

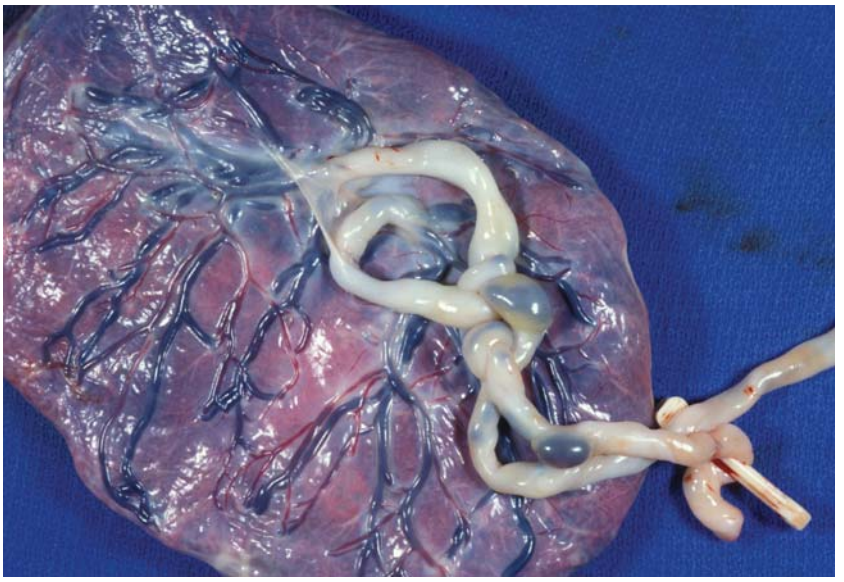
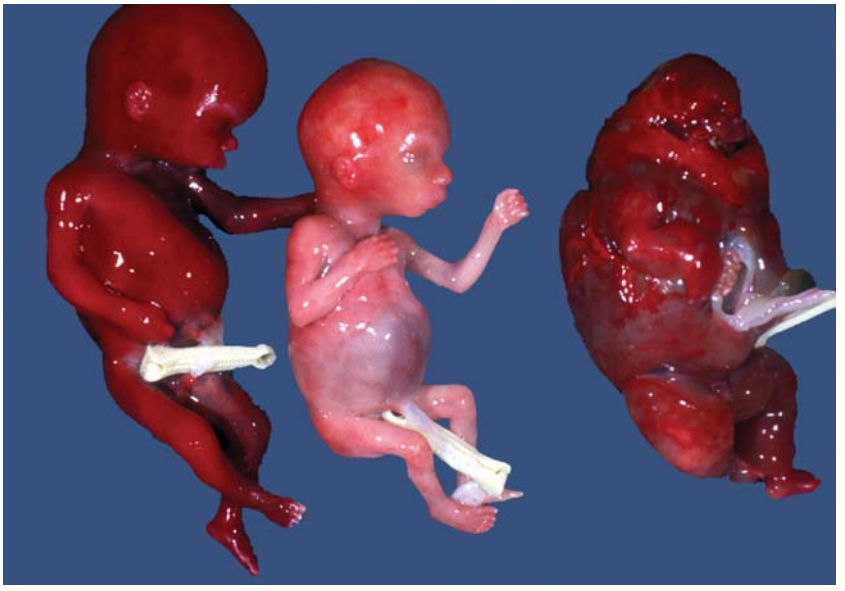
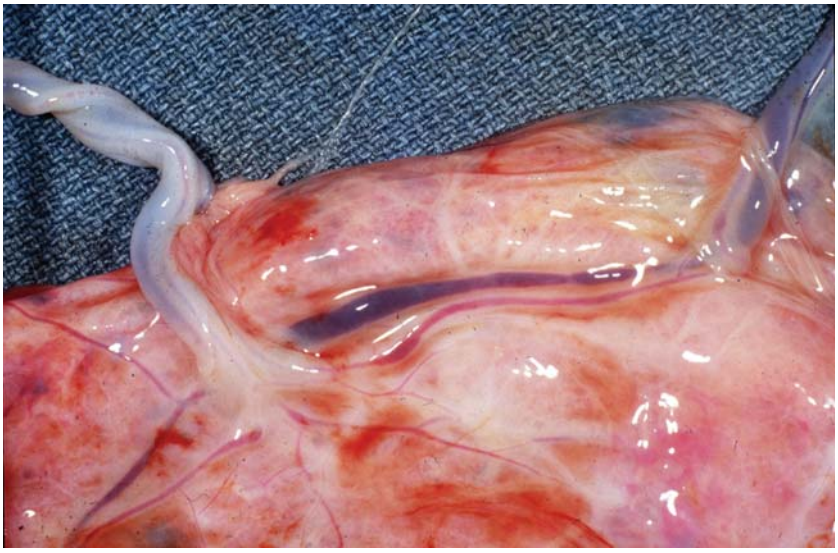


Figure 6.14. This monoamniotic placenta shows a common finding in such twins-entanglement of the cords with knotting. Mortality is said to be 50% in monoamniotic twins. Much of this cord-associated mortality occurs early in gestation. Limitation of space in the uterus helps prevent the necessary tightening after 30 weeks. Large vascular anastomoses are usually present in monoamniotic placentas and chronic transfusion syndrome is uncommon. These infants had no apparent problems and were delivered near term.



A

Figure 6.15. Another complication of monochorionic gestations is the formation of "acardiac twins." These are incompletely developed and may lack a heart and other vital organs. (**A**) In this set of monochorionic triplets, the small pale fetus (middle) was the donor to the larger normally formed plethoric twin as well as the pump twin for the acardiac.



B

Figure 6.15. (**B**) Single artery to artery and vein to vein anastomoses which were associated with the acardiac. These permit reversed circulation to occur through one twin leading to its abnormal development.

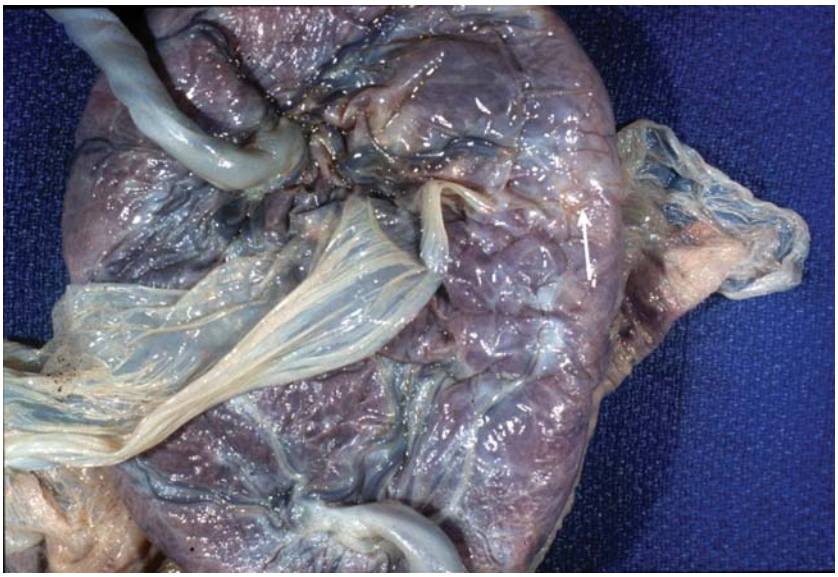


Figure 6.16. The dividing membrane is incomplete in this diamnionic monochorionic placenta. It is absent near 3 o'clock. This is an amniotic "plica." The origin of these is not always clear. Split of this conceptus may have occurred slightly earlier than in a true monoamniotic placenta, leading to partial formation of the amnion. It has also been suggested that rupture of the amnion in a diamnionic monochorionic placenta could lead to this configuration. Such transition stages are uncommon. (Reproduced with permission from Gilbert WM, Davis SE, Kaplan C, et al: Morbidity associated with prenatal disruption of the dividing membrane in twin gestations. Obstet Gynecol 1991;78:623–630).

Twin Assymetry

Differences between twins are common in both mono and dichorionic placentas and are often not related to the special aspects of monochorionicity (Figure 6.17). Abnormal cord insertions and single umbilical arteries are far more common (Figure 6.18). Differences in placental size

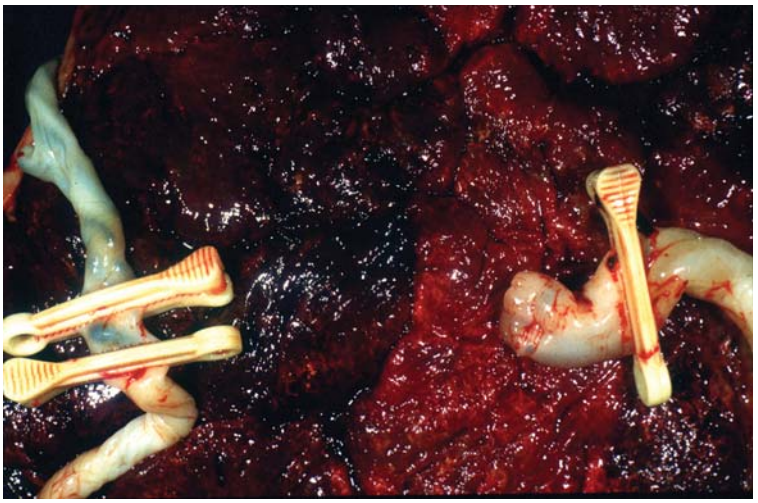


Figure 6.17. There is a slight difference in color on the maternal surface between the areas belonging to each twin. This is often due to differences in blood volume in the two sectors. While this may indicate transfusion between monochorionic twins, it is often seen in dichorionic twins due to differences in time to cord clamping, height of the infant after delivery or draining of blood from the placenta.

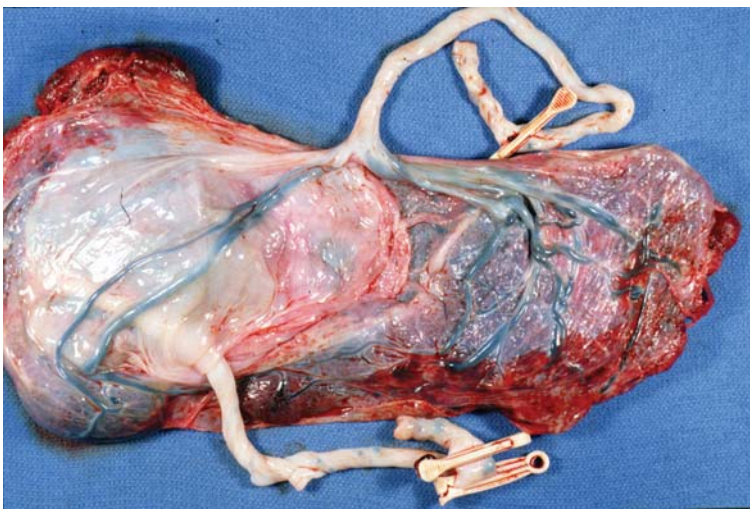


Figure 6.18. Cord abnormalities are very common in multiple gestations, and may contribute to asymmetric infants. A complex velamentous cord insertion is present here. The vessels of one cord traverse the dividing membranes to placental tissue on the opposite side of the other disk. Vessels within the dividing membranes only occur in dichorionic placentas. Dividing membrane insertions seem particularly prone to problems including compression and thrombosis.

can be associated with growth retardation (Figure 6.19). This is generally due to limitations of uterine space for placentation. Abnormal outlines and succenturiate lobes are frequent. Other pathologic processes such as pre-eclampsia or membrane rupture may differentially affect the two placentas (Figure 6.20).

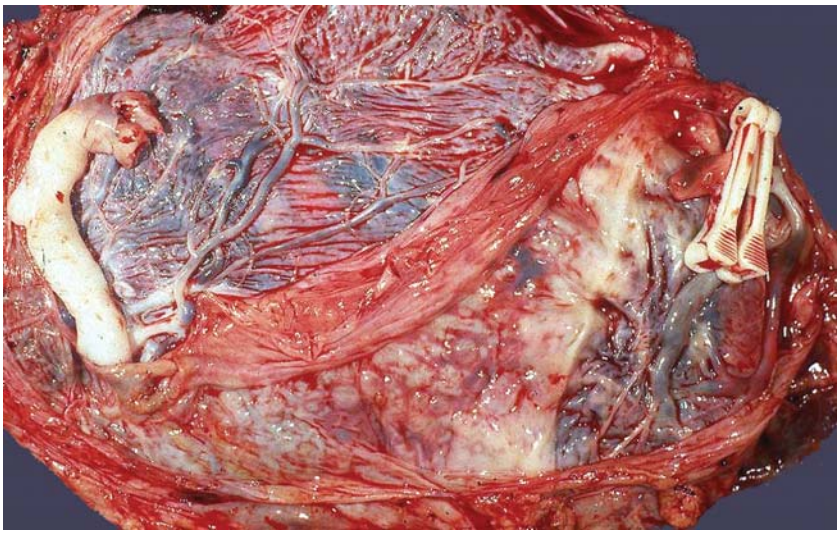


Figure 6.19. This dichorionic placenta (note prominent ridge) shows a marked difference between the sizes of the two placental portions. The smaller placenta was associated with a severely growth-retarded infant. Such discrepancies may be due to unequal placentation caused by problems of space in the uterus or by a process affecting only one infant (e.g., chromosomal aneuploidy, vascular disease). Similar inequalities occur in monochorionic twins as well.

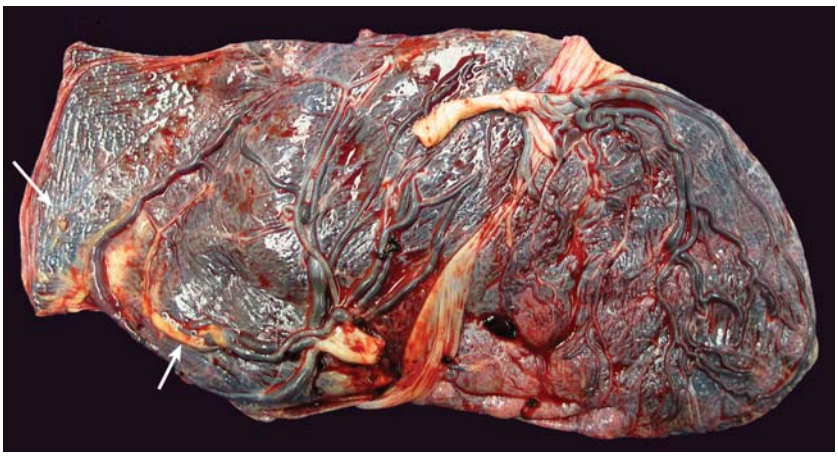


Figure 6.20. Amnion nodosum is present on the surface of one twin (*arrows*). There was prolonged rupture of the membranes in one sac of this dichorionic placenta. There are extensive unruptured velamentous vessels.

Higher Multiple Births

When examining the placentas of higher multiple births the same basic concepts used in twins apply. The steps of examining the dividing membranes and making rolls will need to be done several times, once for each pair. These placentas are often quite disrupted (Figure 6.21) and other abnormalities are frequently seen (Figure 6.22).

In multiple gestations, any fetus which dies is retained as long as the pregnancy continues, leading to a compressed "fetus papyraceous." These

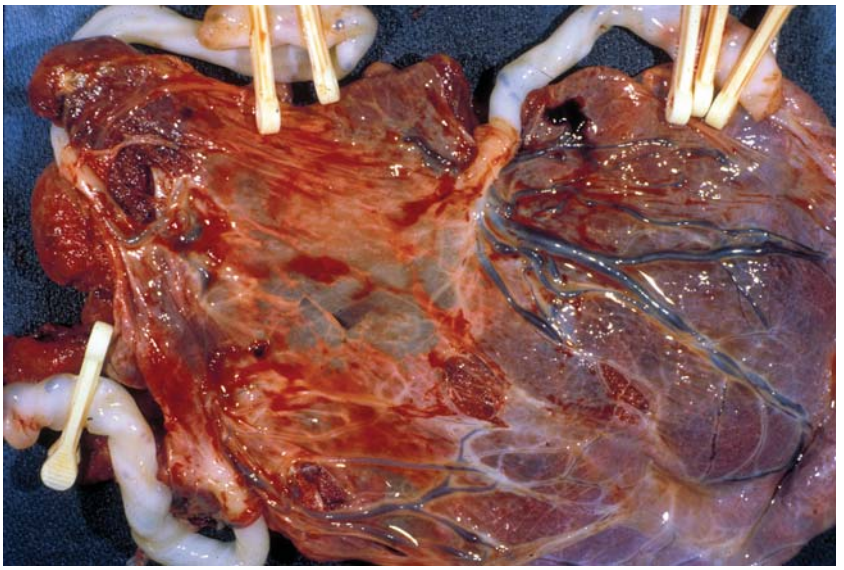


Figure 6.21. Although this triplet placenta is rather disrupted, one can still identify that this is a monochorionic set. There is one continuous chorionic plate with three cords. Even disrupted placentas should be carefully examined as there is often much that can still be identified about their gross morphology.

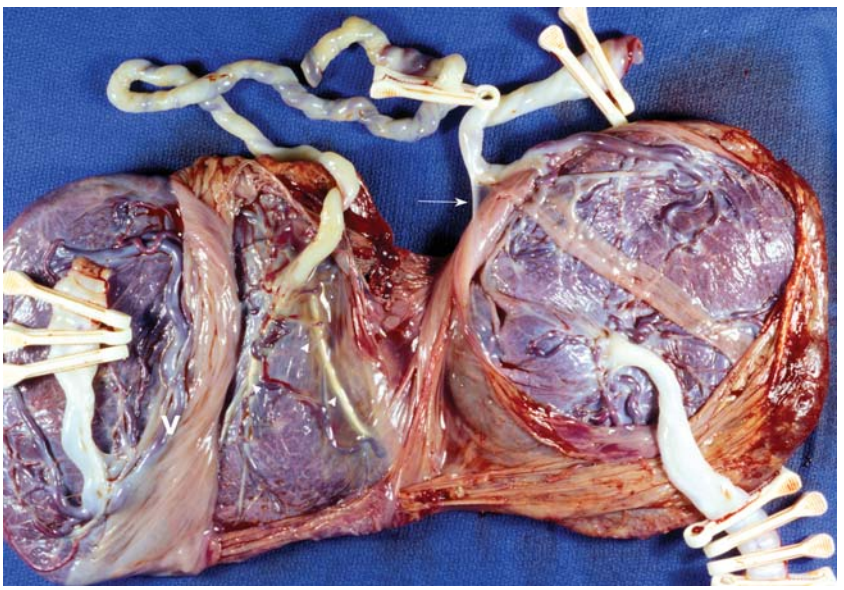


Figure 6.22. This is from a trichorionic quadruplet pregnancy. There are two separate disks. One belongs to the dichorionic set of A and C and the other to the monochorionic set B and D. A shows a white surface vein thrombosis, B has a velamentous cord with a small web (*arrow*), and C's cord inserts velamentously into the dividing membranes (V).

occur in both mono and multichorionic gestations, and chorionicity can usually be determined. Although some result from transfusion syndrome, other etiologies include anomalies, cord problems, and reductions of higher multiple births (Figure 6.23, Figure 6.24).

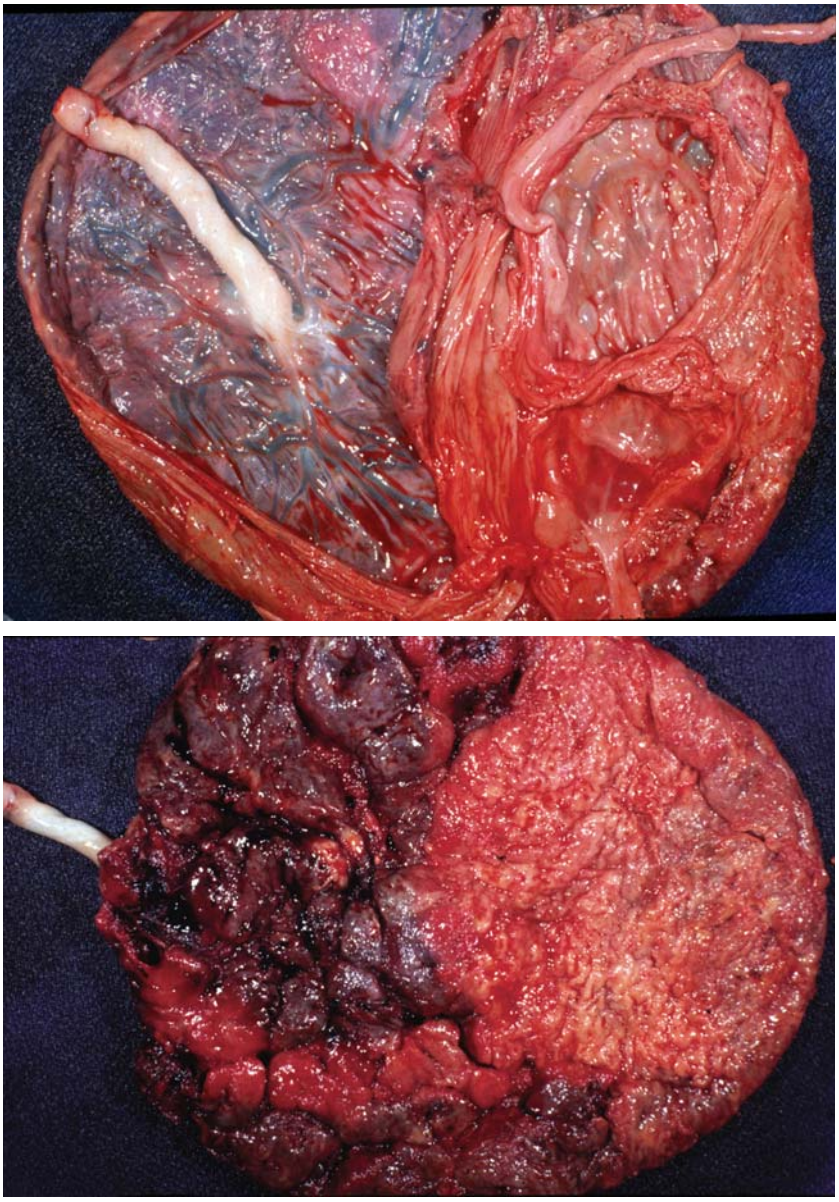


Figure 6.23. (**A**) Two of three fetuses were lost in this naturally occurring set of triplets. The surviving infant was female, while the two demises were male. Detailed examination of the dividing membranes showed them to be monochorionic and death was probably due to transfusion syndrome. These were biovular triplets, with split of one egg, the most common spontaneous type. (**B**) Maternal side of this placenta shows the extreme atrophy of the villous tissue belonging to the monochorionic twins (right). Marked changes of fetal demise, including avascular villi and extensive fibrin deposition, will be present with extremely long retention as occurred here.

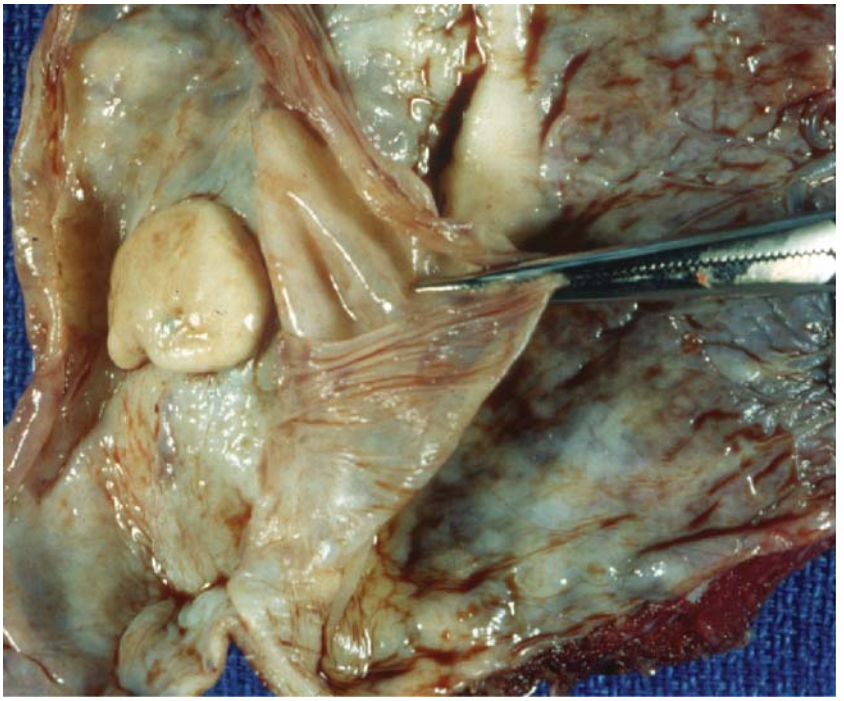


Figure 6.24. With assisted fertilization techniques there is often early loss of one or more conceptions, either spontaneously or through intervention. In this *in vitro* fertilization pregnancy, quintuplets were conceived. Three of the five were reduced at nine weeks. One fetus papyraceous is shown at the edge of a portion of the fixed placenta. Two others were present. Careful examination is necessary to identify these, as they may resemble plaques of fibrin or retromembranous hemorrhage. All five conceptions had separate chorions. The resulting dichorionic pair delivered at 35 weeks.

Selected References

Since the first edition of this atlas was published, many excellent references have been written. The chapters on the placenta in the current texts in surgical and pediatric pathology describe the microscopic pathology and discuss some of the clinical implications of the gross processes than previously. Several new monographs give significantly more detail. Individuals wishing to further pursue the original references will find them cited in these works.

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Weidner N, Cote RJ, Suster S, Weiss LM, eds. *Modern Surgical Pathology.* Philadelphia, Saunders, 2003.
Chapter 40. Gestational Pathology by Cynthia G. Kaplan

Wigglesworth JS, Singer DB, eds. *Textbook of Fetal and Perinatal Pathology*, 2nd ed. Malden, Massachusetts, Blackwell Scientific, 1998.
Chapter 7. Pathology of the placenta by D. Ian Rushton
Chapter 8. Pathology of multiple pregnancy by Virginia J. Baldwin

Appendix A

Sample Report Forms

A-1 SINGLETON REPORT FORM

S- NAME:

History:

Received fresh is a ____ gram placenta with a ____ × ____ cm 3 vessel left twisted (inserted ____cm/marginal/velamentous/furcate) cord with a ____ cm amniotic web from the margin. Membranes are (incomplete/essentially complete) and ruptured ____ cm from the placental margin. Membrane insertion is (at the margin/ % circummarginate/circumvallate with a rim to ____ cm). Subchorionic fibrin is (minimal/slight/moderate/abundant). There is (opacity/green coloration/no unusual coloration) of the fetal surface. The placental disk is ____ × ____ × ____ cm approximate greatest dimensions. The maternal surface is (apparently complete/disrupted focally). There is (no/slight/moderate/abundant) calcification. On cut section, color and consistency are unremarkable.
(No) other gross lesions:
retromembranous/retroplacental hemorrhage
intervillous thrombus
succenturiate lobe
marginal/central infarct

Microscopic performed. Gross only.

DIAGNOSIS:
Placenta, delivery~~No~~ pathologic diagnosis (NPD)
Immaturity
Ischemic change (terminal villous hypoplasia)
Subchorionic intervillositis/chorionitis/chorioamnionitis
Retroplacental/marginal hemorrhage
Intervillous thrombus
(Marginal) infarct
Succenturiate lobe

Fetal membranes, delivery~~NP~~D
Acute inflammation/chorioamnionitis
Meconium pigmentation
Retromembranous hemorrhage
Circumvallate/circummarginate

Umbilical cord, delivery~~NP~~D
Marginal/velamentous insertion
Acute phlebitis/vasculitis/funisitis

A-2 TWIN REPORT FORM

S- Name:

History:

A (1 clamp) male/female grams B(2 clamps) male/female grams

Received fresh is a diamniotic di/mono chorionic twin placenta with (separate/fused) disks. Cords are (unlabeled and arbitrarily designated/labeled with 1 and 2 clamps). Overall the placenta is ____ × ____ × ____ cm. Injection studies are performed revealing artery-to-artery and artery-to-vein anastomosis from ____ to ____. The placentas are divided (along the approximate vascular plane).

I (____ clamp) is ____ grams and ____ × ____ × ____ cm with a ____ × ____ cm 3 vessel left twisted (central/eccentric/marginal/velamentous) cord. Membranes are (incomplete/ruptured ____ cm from the margin). There is (opacity/green staining/no unusual color) of the fetal surface. Maternal side is (apparently complete/disrupted focally). (No/slight/moderate) calcification. No other gross lesions.

II (____ clamps) is ____ grams and ____ × ____ × ____ cm with a ____ × ____ cm 3 vessel left twisted (central/eccentric/marginal/velamentous) cord. Membranes are (incomplete/ruptured cm. from the margin). There is (opacity/green staining/no unusual color) of the fetal surface. Maternal side is (apparently complete/disrupted focally). (No/slight/moderate) calcification. (No) other gross lesions.

Representative sections (including dividing membranes).

DIAGNOSIS:
Placenta, delivery~~T~~wins, dichorionic/Twins, monochorionic (identical)
Immaturity
Ischemic change (terminal villous hypoplasia)
Subchorionic intervillositis/chorionitis/chorioamnionitis

Fetal membranes, delivery~~N~~PD
Acute inflammation/chorioamnionitis

Umbilical cord, delivery~~N~~PD
Marginal/velamentous insertion
Single artery
Acute phlebitis/vasculitis/funisitis

Note: Although like-sexed dichorionic twins may be mono or dizygotic, at least 80% are dizygotic.

Appendix B

Normal Values for Placentas

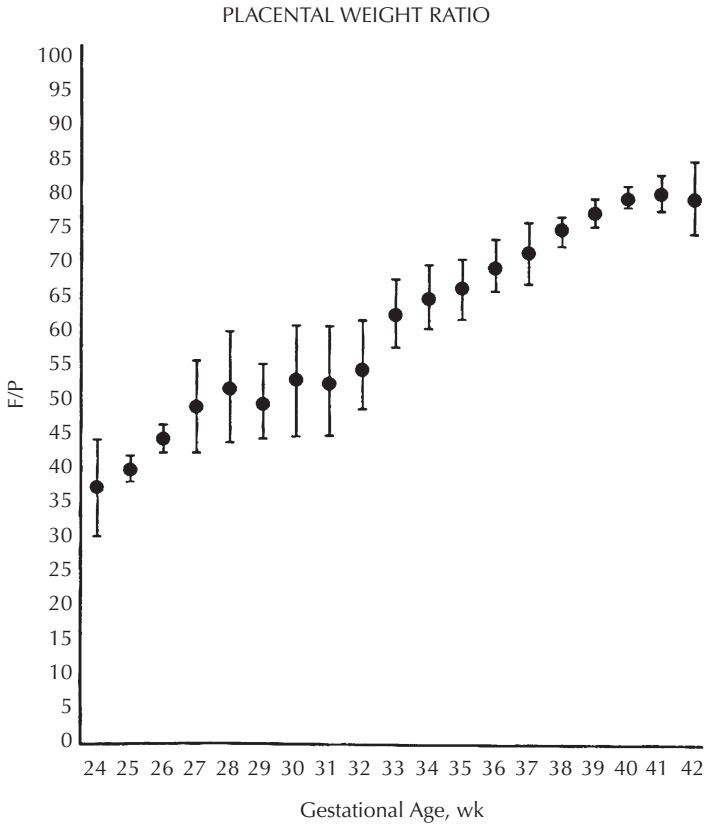

Figure B.1. Mean fetoplacental weight ratios with 95% confidence limits by gestational age for normally grown infants. (From Molteni RA, Stys DJ, Battaglia FC: Relationship of fetal and placental weight in human beings: Fetal/placental weight ratios at various gestational ages and birth weight distribution. J Reprod Med 1978;21:327.)

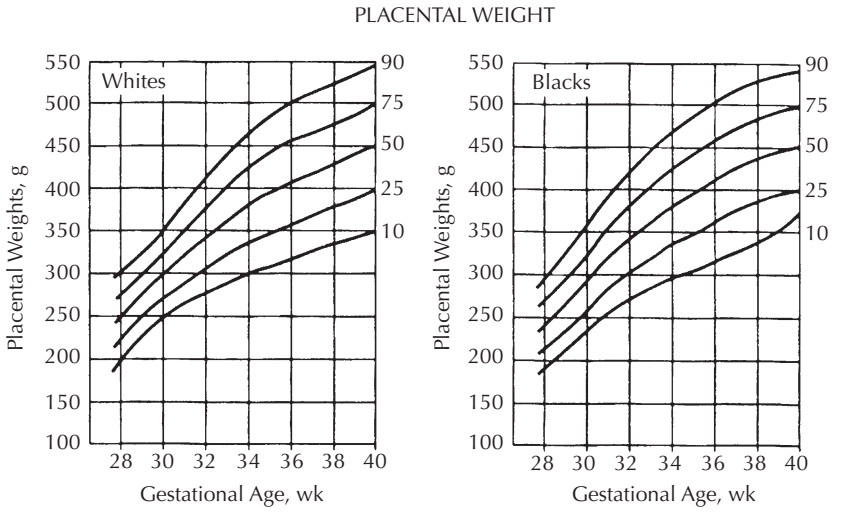

Figure B.2. Placental growth curves for whites and blacks (from Naeye RL: Do placental weights have clinical significance? (From Hum Pathol 1987;18:387–391.)

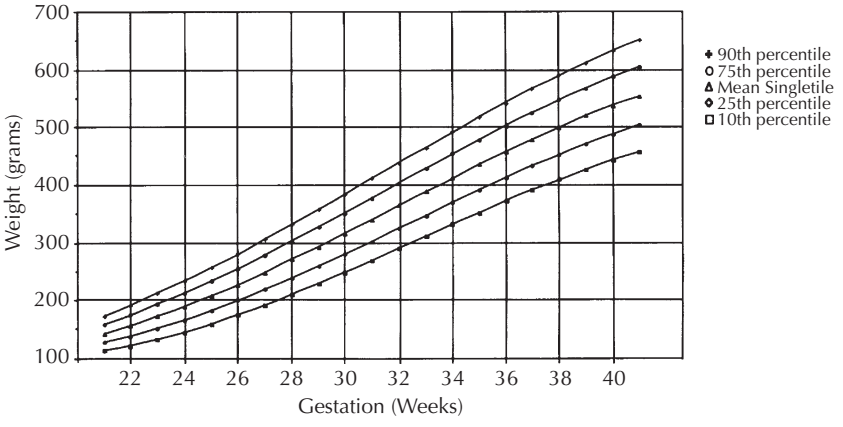

Figure B.3. Mean weights and percentiles for singleton placentas. (From Pinar H, Sung CJ, Oyer CE, Singer DB. References values for singleton and twin placental weights. Pediatr Pathol Lab Med 1996; 16:903.)

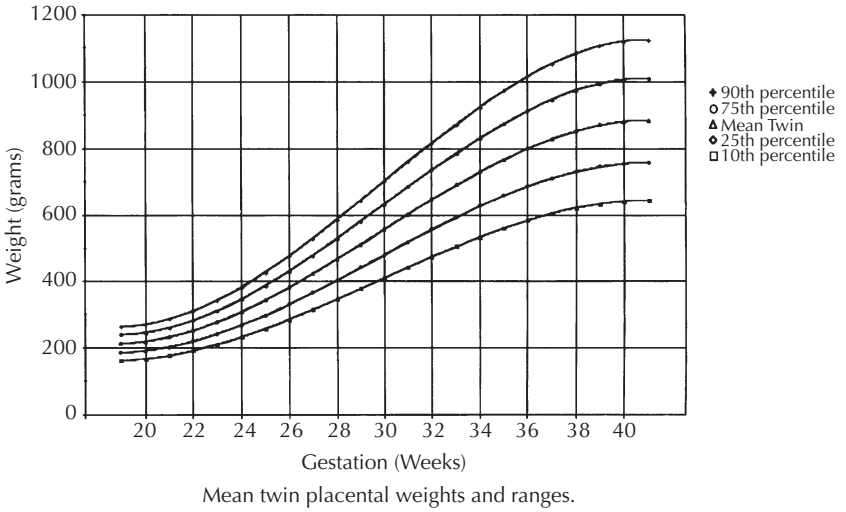

Figure B.4. Mean weights and percentiles for twin placentas. (From Pinar H, Sung CJ, Oyer CE, Singer DB. References values for singleton and twin placental weights. Pediatr Pathol Lab Med 1996;16:903.)

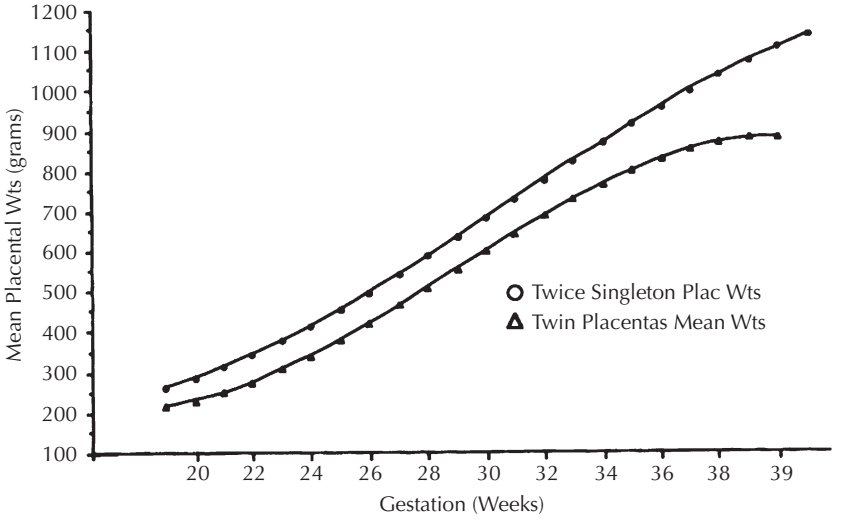

Figure B.5. Comparison of twin and singleton placental weights by gestational. (From Pinar H, Sung CJ, Oyer CE, Singer DB. References values for singleton and twin placental weights. Pediatr Pathol Lab Med 1996;16:903.)

UMBILICAL CORD LENGTH

Gestational age, wk	n	Umbilical Cord Length, cm
20 to 21	16	32.4 ± 8.6
22 to 23	27	36.4 ± 9.0
24 to 25	38	40.1 ± 10.1
26 to 27	59	42.5 ± 11.3
28 to 29	80	45.0 ± 9.7
30 to 31	113	47.6 ± 11.3
32 to 33	337	50.2 ± 12.1
34 to 35	857	52.5 ± 11.2
36 to 37	3153	55.6 ± 12.6
38 to 39	10083	57.4 ± 12.6
40 to 41	13841	59.6 ± 12.6
42 to 43	4797	60.3 ± 12.7
44 to 45	1450	60.4 ± 12.7
46 to 47	492	60.5 ± 13.0

Figure B.6. Umbilical cord length at various gestational ages. (From Naeye RL: Umbilical cord length: Clinical significance. J Pediatr 1985;107:278–281.)

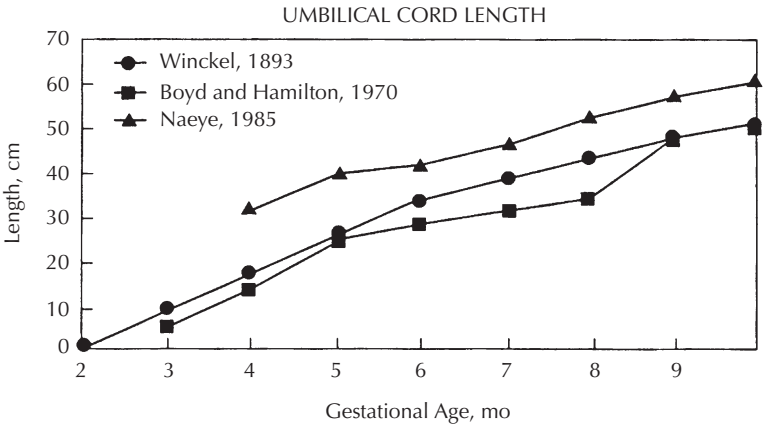

Figure B.7. Comparison of published cord lengths. (From Benirschke K, Kaufmann P. Pathology of the Human Placenta. New York, Springer, 1999; p. 349.)

Index