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# Cord abnormalities, structural lesions, and cord “accidents”

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## KEYWORDS

Umbilical cord;  
 Cord accident;  
 Neurologic injury;  
 Cerebral palsy

As the umbilical cord is the lifeline of the fetus, obstruction or disruption of blood flow through the umbilical vessels can lead to severe fetal compromise. Obstruction is usually mechanical in nature and is associated with compression of the umbilical cord and umbilical vessels. Disruption of umbilical or fetal vessels is usually traumatic in origin. These conditions have in common a loss of blood flow to the fetus and an association with adverse perinatal outcome.

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Conditions such as abnormal cord length, abnormal coiling, knots, entanglements, constrictions, prolapse and velamentous vessels may lead to cord compression and subsequent diminished blood flow in umbilical vessels. The umbilical vessels may be compressed by fetal parts, against the cervix or by an abnormal configuration of the cord itself. Not surprisingly, these conditions have been associated with fetal demise and adverse perinatal outcome.<sup>1-4</sup> Disruption of the umbilical cord or fetal vessels is usually traumatic in nature and is associated with some degree of fetal hemorrhage. Vascular disruption may occur when excessive traction is used on a short cord<sup>5</sup> or on a placenta with abnormal adherence to the uterus due to a placenta accreta. Disruption may also occur from pathologic processes rendering the cord more friable such as necrotizing funisitis,<sup>6</sup> meconium associated damage,<sup>7</sup> aneurysms<sup>8</sup> and hemangiomas<sup>8</sup> or from direct trauma due to fetal blood sampling or amniocentesis.<sup>4</sup> If large vessels are disrupted, severe fetal hemorrhage can develop relatively quickly, with the potential for acute hypovolemia and circulatory collapse, while hemorrhage from small vessels tends to be more chronic but still may be quite significant. These conditions have also been associated with demise and significant neurologic damage.<sup>4-9</sup>

## Cord compression: General considerations

Mechanical obstruction of blood flow through the umbilical cord may occur secondary to any type of force that compresses umbilical vessels.<sup>1-9</sup> The fetus itself may compress the cord when there are cord entanglements, membranous vessels, and cord prolapse. Compression may arise from an abnormal configuration of the cord such as knots, abnormal coiling, abnormal length, or constrictions. Often these structural abnormalities are linked; for example, entanglements and knots are frequently seen in long cords and excessive coiling is often seen with constrictions. These conditions are generally present for many weeks or months and so may cause chronic obstruction of blood flow. However, acute obstruction is also possible when there is an acute progression at or near the time of delivery. This is the case when a true knot or entanglement tightens as the infant descends down the birth canal or when membranous vessels become compressed after membranes rupture and there is loss of the cushioning effect of the amniotic fluid. If obstruction is

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complete, fetal death will be the eventual result, whereas lesser degrees of obstruction can lead to severe neurologic injury.<sup>2,4,9-13</sup> This is consistent with animal studies in which fetal lambs subjected to intermittent partial cord occlusion develop cerebral necrosis and serious fetal neurologic damage.<sup>14</sup> Chronic partial obstruction can also lead to fetal growth restriction. Abnormally coiled cords, abnormally short or long cords, velamentous cord insertions, constrictions, true knots, cord entanglement, and cord prolapse have all been associated with an increased risk of fetal demise, neurologic injury, or abnormal developmental outcome.<sup>1,2,5,6,8-11,13</sup> With the exception of cord entanglement and prolapse, these lesions are easily diagnosed by gross examination of the placenta.

In acute compression, the umbilical vein, being more distensible, will be compressed initially and to a greater degree than the arteries. This leads to vascular congestion in the placenta, and if severe, to hypovolemia and anemia in the fetus. Doppler studies have confirmed that cord obstruction and compression cause impeded venous return.<sup>15</sup> Decreased venous return of oxygenated blood from the placenta will result in distension of the umbilical vessels, particularly the vein, tributaries of the umbilical vein in the chorionic plate, and the villous capillaries. Direct compression of the cord by fetal parts or the cervix may also cause nonspecific damage and degenerative change of Wharton's jelly and the umbilical vessels. Rarely, severe acute compression results in hemorrhage, thrombosis, and even rupture of the cord. Although the above findings are visible on microscopic examination, they are nonspecific and therefore do not enable the definitive diagnosis of cord compression, per se, or indicate the underlying cause of the compression.

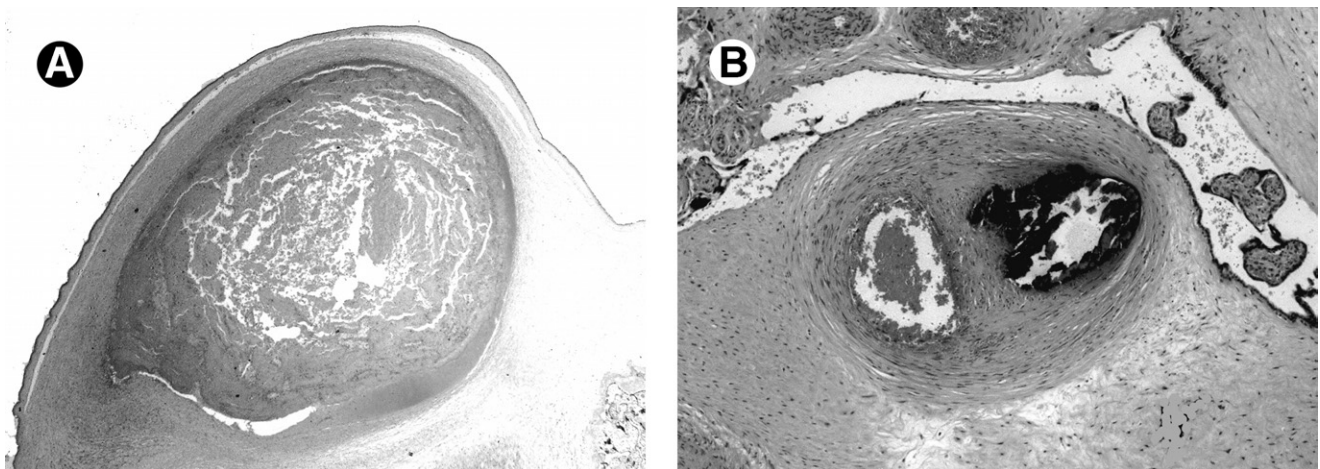
Chronic cord compression develops from the same mechanical forces that lead to acute compression; however, the pathologic changes are more clearly delineated. Chronic obstruction of blood flow through the venous circulation initially leads to venous stasis and may ultimately lead to endothelial damage and subsequent fetal vascular thrombo-

sis, further embarrassing blood supply to the fetus. Thrombi in umbilical vessels and fetal circulation can occur secondary to any process associated with cord compression or decreased venous return. The above described cord abnormalities have not only been associated with poor outcome, but with fetal thrombosis, and fetal thrombosis has itself been associated with poor outcome and pathologic lesions in the brain.<sup>9,10,16,17</sup>

Thrombosis in umbilical vessels can be identified by careful gross examination of the placenta. Recent thrombi appear as dark, clotted blood within the vessel, whereas older thrombi may be visible as white streaks in the vessels, which is due to the presence of calcification. Although calcification of the umbilical cord has classically been associated with acute necrotizing funisitis and syphilis infection, it is more commonly due to thrombosis. Venous thrombosis is more common than arterial thrombosis, but the latter is more often lethal.<sup>17</sup> The appearance of thrombi in the cord is often subtle and difficult to identify by external examination. Therefore, serial sectioning is recommended in all areas of cord discoloration. Areas of previous cord clamping should be avoided, as these are associated with artifactual hemorrhage and disruption. Often, only the vague impression of a clamp is visible, so careful gross inspection is necessary to rule this out. Thrombi in umbilical vessels are much less common than those in the large vessels of the chorionic plate and its tributaries. On microscopic examination, recent thrombi can be occlusive or nonocclusive and contain primarily fibrin and clotted blood (Figure 1A). More remote thrombi may show organization in the form of intramural calcification, a finding indicative of duration of many weeks (Figure 1B).

### Umbilical cord coiling and constriction

The umbilical cord is usually twisted or coiled counterclockwise, to the left, with a left to right ratio of about 7:1.<sup>4</sup>



**Figure 1** Fetal thrombotic vasculopathy. (A) Histologic section of a large tributary of an umbilical vessel with a recent occlusive thrombus consisting mostly of fibrin. H&E; original magnification 4 $\times$ . (B) Small fetal stem vessel with calcified mural thrombus indicative of a longstanding event. H&E; original magnification 40 $\times$ .

The direction of coiling does not appear to be associated with handedness but some have found a deleterious effect of right coiling in its association with placenta previa and perinatal hemorrhage.<sup>18</sup> The average number of coils in the entire length of cord is about 40, with approximately 0.2 coils per 1 cm of cord. The latter is referred to as the coiling index.<sup>2</sup> Coiling is established early in gestation and can be seen by sonography as early as the 9th week. The origin of umbilical cord coiling has long been debated, but some data suggest that it is due, at least in part, to fetal rotation and activity. Thus, the lack of coiling may partially reflect fetal inactivity or possible neurologic abnormalities,<sup>19</sup> whereas marked coiling may reflect fetal hyperactivity.<sup>4</sup> Other theories of the origin of coiling include differential vascular growth, fetal hemodynamic forces, and the configuration of the muscular fibers in the umbilical vessels.<sup>20</sup> Absent or minimal coiling is uncommon, but when present, it has an ominous prognosis, as it is associated with fetal distress, fetal anomalies, chromosomal errors, and increased fetal and perinatal mortality.<sup>2,19-21</sup> Similarly, excessive coiling has been associated with preterm labor, fetal demise, low umbilical arterial pH, fetal asphyxia, and chronic fetal hypoxia (Figure 2).<sup>2,19-21</sup> Excessive coiling is also seen more frequently in cords with constrictions and those of excessive length, both of which are also associated with adverse outcome.<sup>2,3,10</sup> Regardless of the etiology, excessive coiling has the potential for obstruction of blood flow through the umbilical vessels. As with other types of mechanical obstruction, the presence of associated thrombosis in the umbilical vessels and in the fetal circulation may reflect lesions of significance for fetal or neonatal outcome.

Significant reductions in the diameter of the umbilical cord are referred to by various terms such as constriction, stricture, torsion, and coarctation. When present, they are most frequently found at the insertion of the cord into the



**Figure 2** Second trimester fetal demise due to excessively coiled umbilical cord. There is marked congestion throughout the cord and narrowing near the insertion site into the fetal abdomen. Reprinted with permission.<sup>8</sup>

abdominal surface of the fetus. They are seen more commonly in long and markedly coiled cords.<sup>21</sup> Obstruction of blood flow occurs by the same mechanism as with excessive coiling. Some authors have been skeptical about the significance of this lesion. They have suggested that it is merely a secondary phenomenon associated with fetal demise, due to gradually diminishing Wharton's jelly at the fetal end of the cord,<sup>22</sup> or due to a primary deficiency of Wharton's jelly.<sup>23</sup> The latter explanation may be operative in certain cases in which there have been multiple deaths due to cord torsion occurring in families<sup>23</sup> and in women who have had a recurrence in subsequent pregnancies.<sup>24</sup> On the other hand, if constrictions were solely artifacts, they would be seen in the majority of fetal demises, which is not the case. Furthermore, one often sees congestion on one side of the constriction and thrombosis of umbilical vessels. This is proof, at least in those cases, that it is not an artifact. However, because constrictions often occur in macerated fetuses, the demonstration of thrombi is hampered, particularly since clotting is not well developed in immature fetuses. There have been many publications demonstrating the poor outcome of umbilical cord stricture. The most common adverse outcome has been fetal demise, but cord constrictions have also been implicated in fetal growth restriction and fetal intolerance to labor.<sup>2,4,11</sup>

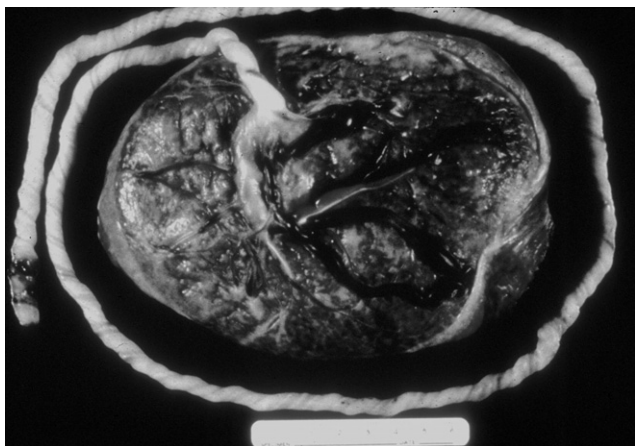
### Abnormal cord length

The umbilical cord is, on the average, 55 to 61 cm in length at term, which is sufficient length for a vaginal delivery to be accomplished with a fundal implantation of the placenta.<sup>25,26</sup> Thus, as suggested by Leonardo da Vinci, the umbilical cord is usually the same length as the baby. The cord grows and lengthens throughout gestation, although growth slows after 28 weeks. At 6 weeks postconception, the cord has a mean length of about 0.5 cm, by the 4th month it averages between 16 and 18 cm, and by the 6th month to between 33 and 35 cm.<sup>4</sup> There are standard curves of cord length from 34 to 43 weeks gestation.<sup>25</sup> When cord entanglement is present, the cord is usually longer. Therefore, when there is one cord looped around the neck, a nuchal cord, the average length is 76.5 cm, and when there are two nuchal cords, the average is 93.5 cm.<sup>26</sup> It is interesting to note that the cord can shrink up to 7 cm in length in the first few hours following delivery.<sup>4</sup> This is one of the reasons that accurate measurement of the entire length of the cord at birth is optimal. In practice, however, this must be done by the delivering physician and attempts to convince the latter of the importance of such measurements have generally failed.

As with umbilical cord coiling, cord length appears to correlate with fetal activity in utero. Thus, short cords are present in conditions where there is intrauterine constraint of fetal movement, such as uterine anomalies, amniotic bands, and ectopic pregnancies,<sup>5</sup> or when there is decreased

movement of the fetus, such as neurologic conditions, skeletal dysplasia,<sup>27</sup> and other fetal anomalies. The relationship between long cords and excessive fetal movements is more difficult to assess because of the lack of data on prenatal movements and follow up on infants with long cords to ascertain whether they are “hyperactive” in later life as suggested by some.<sup>28</sup> Experimental studies have supported the association of fetal movement with cord length in that animals exposed to physical constraint or drugs that lead to decreased movement develop short cords, whereas those without constraint develop longer cords.<sup>29,30</sup> There also appears to be a genetic component since mothers with a history of an excessively long cord are at increased risk of a second long cord in subsequent pregnancies.<sup>3</sup> The issue is thus complex.

There is no consensus on the minimum length for a diagnosis of an excessively long cord with definitions ranging from 70 to 90 cm. This inconsistency is due in part to the lack of accurate measurement of cord length at the time of delivery and the fact that the entire umbilical cord is not submitted for pathologic examination. Pathologists are then left with a cord length of “at least” a certain measurement rather than the true measurement. Excessively long cords are present in 3.95% of placentas.<sup>3</sup> Right-coiling, excessive coiling, true knots, single umbilical artery, and cord entanglements are more common in long cords.<sup>3</sup> It has been proposed that excessively long and coiled cords would require greater perfusion pressure due to increased resistance to flow, but this has not been confirmed by direct experiments. This theory is supported by the fact that long cords are associated with histologic abnormalities consistent with obstruction of venous return from the placenta such as villous capillary congestion and fetal vascular thrombosis (Figure 3)<sup>3,31</sup> and studies that have shown that cardiac enlargement and hypertrophy are seen in infants with long cords.<sup>3,32</sup> Evidence of intrauterine hypoxia (chorangiosis, increased



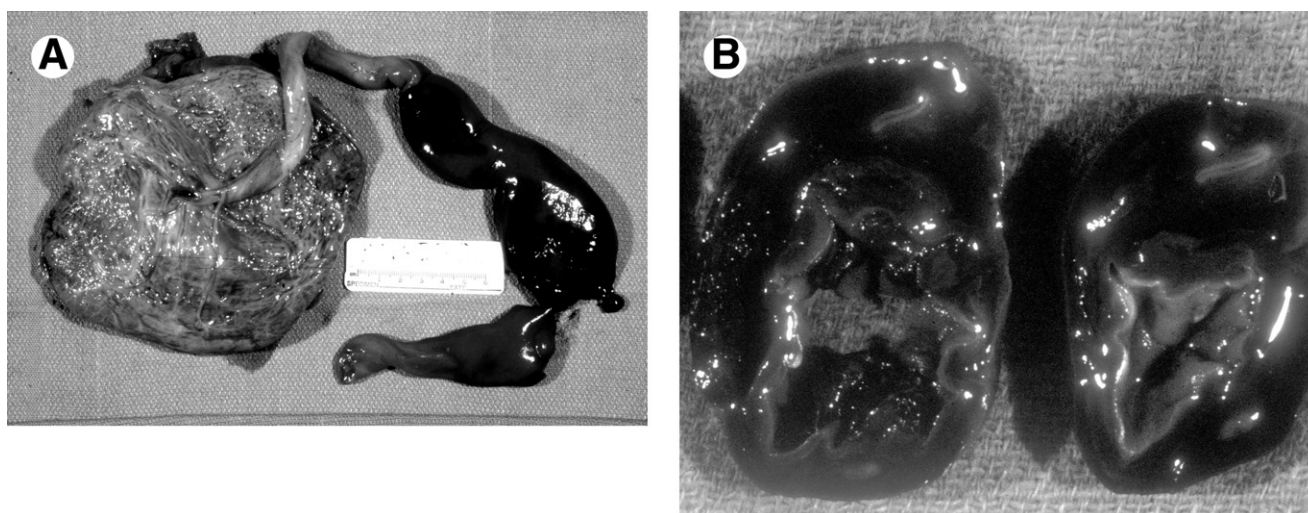
**Figure 3** Term placenta with excessively long and coiled umbilical cord. Note the white streak in the center of the specimen representing a thrombus in a fetal surface vessel. Reprinted with permission.<sup>8</sup>

nucleated red blood cells) is also seen with increased frequency in placentas with long cords,<sup>3</sup> and growth restriction, intrauterine demise, and neonatal coagulation disorders are all seen with increased frequency in long cords. Long cords have been implicated in cerebral degenerative changes, and are associated with a significant increase in brain imaging abnormalities, neurologic injury, and poor neurologic outcome.<sup>3,9,10,16,21,31</sup>

The definition of what constitutes an excessively short cord is also not well defined, with figures reported anywhere from 32 to 40 cm at term. The incidence of short cords is less than long cords, being around 2% of placentas at term.<sup>4</sup> There is a practical reason for defining short cords at this length as it has been shown that a cord less than 32 cm in length will not allow vaginal delivery from a vertex presentation.<sup>26</sup> Excessively short cords correlate well with a variety of fetal and neonatal complications and CNS problems<sup>33</sup> as well as with depressed intelligence quotient (IQ) values.<sup>4</sup> The essential question, though, is whether the short length is due to prenatal CNS problems or whether the CNS problems resulted from complications that ensued from delivery of an infant with a short cord. Short cords, especially those less than 15 cm, have a strong association with fetal anomalies, particularly abdominal wall defects, spinal and limb deformities, and a number of other malformations. The complications associated with short cords are also associated with “relatively” short cords that are created by cord entanglements. Cord rupture or premature separation of the cord from the placenta during delivery may result in significant fetal bleeding<sup>4</sup> and then serious neurologic sequelae or death may be the result (Figure 4). Premature detachment of the placenta (abruption) can also occur due to increased traction on the cord during delivery.<sup>34</sup> Unfortunately, the diagnosis of a short cord can almost never be made on pathologic examination since the amount of cord submitted for examination is so variable. Occasionally, the clinical history submitted with specimen may indicate that a short cord was present, but generally, a measurement has not been made. Nevertheless, since the potential neurologic sequel of short cords is often due to fetal hemorrhage, diagnosis of the associated findings of hemorrhage in the cord or placenta, anemia, fetal anomalies, or placental abruption is essential in potentially explaining adverse outcome.

### Cord entanglement, true knots, and cord prolapse

The most common type of cord entanglement is a nuchal cord in which the cord is looped around the fetal neck, but entanglements with the extremities or the body also occur. Nuchal cords are quite common, with an incidence of 15% to 20%. They may encircle the neck in an unlocked or locked pattern, and the latter is considered to



**Figure 4** Short cord with hematoma and rupture. (A) Term placenta with an excessively short umbilical cord. Note the large, recent hematoma with an obvious fusiform shape and rupture of the cord at the right of the figure. Reprinted with permission.<sup>8</sup> (B) Cut section of the umbilical cord in the area of hematoma showing a markedly dilated vein with thinning of the wall and fresh blood in Wharton's jelly completely compressing the umbilical arteries.

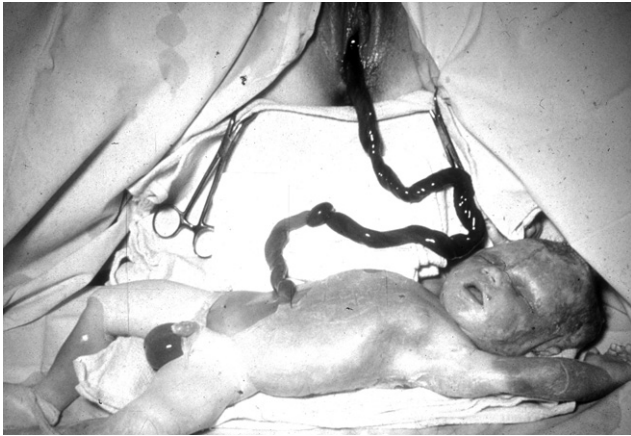
have more severe consequences to fetal outcome.<sup>35</sup> Infrequently, multiple loops of cord may become wrapped around the neck and up to eight loops have been reported.<sup>4</sup> As might be expected, cord entanglements of any kind are more common with long cords.<sup>3,36</sup> Entanglements have been found as early as 10 weeks gestation by sonography, but some of these early cord entanglements resolve by term.<sup>37</sup>

Cord entanglements may lead to cord compression with the changes previously described. Most cord entanglements do not lead to adverse outcomes, probably because they are somewhat loose. Some entanglements may become tighter after membrane rupture and when the infant descends down the birth canal. If one looks only at tight entanglements, perinatal complications are increased, as are low Apgar scores and frequency of stillbirths.<sup>13</sup> Nuchal cords have been associated with fetal growth restriction, suggesting that entanglements and their associated cord compression are longstanding prenatal events.<sup>38</sup> Neonates with nuchal cords are significantly more anemic than controls, presumably because of decreased venous return from compression of the umbilical vein,<sup>39</sup> and tight nuchal cords may be so severe as to lead to hypovolemic shock of the neonate.<sup>40</sup> Importantly, there is a statistically significant correlation between the presence of a tight nuchal cord at delivery and cerebral palsy.<sup>41,42</sup>

True knots should be distinguished from false knots, which should not be called knots at all. False knots are anomalies that develop from looping or local redundancies of the umbilical vessels, primarily the umbilical vein. Sometimes focal varicosities of the veins or perivascular accumulations of connective tissue result in a similar gross appearance. Unlike true knots, these structures have absolutely no clinical importance. Like cord entanglements, knots may be tight or loose and may

acutely tighten with fetal movement or with fetal descent during delivery. Knots cause compression of Wharton's jelly, and those present for an extended period will retain their curled configuration when untied. Venous distension and vascular congestion distal to the knot is a characteristic finding in tight knots of clinical significance (Figure 5). The associated venous stasis often results in thrombosis of placental surface veins as well. The incidence of true knots is reported to be from 0.4% to 1.2%,<sup>4</sup> but the frequency is higher with polyhydramnios and with long or excessively coiled cords.<sup>3,4,8</sup> In monoamniotic–monochorionic twins, complex knots and entanglements of the two cords are especially frequent and are associated with significant morbidity and mortality. Multiple or compound knots have also been described in singletons. Although not all true knots lead to perinatal problems or adverse outcome, they have been associated with signs of fetal distress and fetal hypoxia, perinatal mortality, and long-term neurological damage.<sup>4,42</sup>

Cord prolapse is a clinical diagnosis made when the umbilical cord precedes the presenting fetal part during labor and delivery. Hence, the cord may be acutely compressed between the fetal head and the cervix as the fetus descends down the birth canal. Risk factors for cord prolapse include abnormal fetal presentations, preterm labor, multiparity, multiple gestation, low birth weight, obstetric manipulation, polyhydramnios, abruption, placenta previa, and excessively long cords.<sup>43</sup> Although prolapse is relatively uncommon, occurring in less than 1% of deliveries, the perinatal mortality is estimated to be 10% to 13%.<sup>4</sup> Therefore, prenatal diagnosis by ultrasound examination is essential. Pathologic findings are nonspecific, showing only acute congestion, distension of the umbilical vein, and in some cases, localized damage to the umbilical cord at the site of the compression. Cord



**Figure 5** Fetal demise due to a tight true knot in the umbilical cord. Note the marked congestion on the placental side of the knot indicating obstruction of venous return from the placenta. Reprinted with permission.<sup>4</sup>

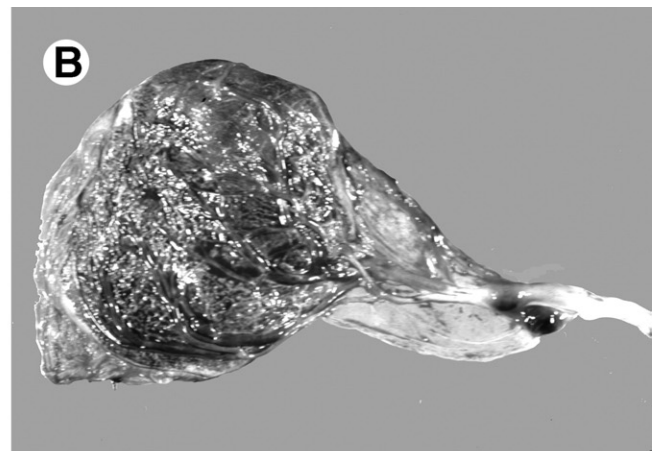
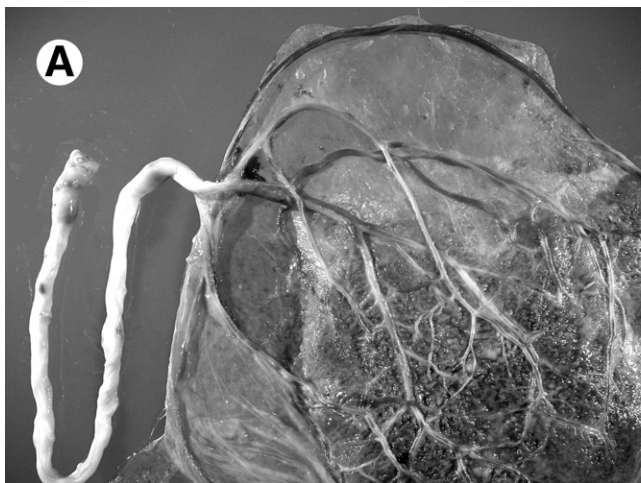
prolapse is considered an obstetric emergency as cord obstruction can lead to fetal death or neurologic damage relatively quickly.

### Velamentous vessels

The umbilical cord normally inserts into the fetal surface of the placenta at or near the center. In about 7% of term placentas, the cord inserts marginally, and in about 1%, it inserts into the membranes, a velamentous insertion.<sup>4,8</sup> Both marginal and velamentous insertions are more common in twins. Velamentous vessels run within the free membranes without the protection of Wharton's jelly and are thus susceptible to thrombosis, compression, disruption, or other trauma, particularly after membrane rupture when the added

protection afforded by the amniotic fluid is lost (Figure 6). A velamentous cord may insert within a few centimeters of the placental margin or far away from it. Close insertion is much more common than the extreme situation, when the cord inserts at the apex of the membranous sac. In the latter configuration, the long membranous course of the vessels makes them even more vulnerable to injury. Membranous vessels are not reserved to a velamentous cord insertion as membranous vessels may branch away from the chorionic plate in marginally inserted cords and they have the same potential for serious injury. The same is true of membranous vessels coursing between lobes in a bilobed placenta or vessels supplying a succenturiate lobe. Furcate cord insertion is a rare abnormality in which the umbilical vessels separate from the cord substance before reaching the surface of the placenta. Like a velamentous insertion, these vessels have lost the protection afforded by Wharton's jelly and are prone to thrombosis and injury.

In vasa previa, velamentous vessels cross the cervical os, preceding the presenting fetal part, and may be disrupted if a vaginal delivery is attempted. Depending on the size of the velamentous vessels and the extent of the subsequent fetal hemorrhage, fetal death from exsanguination may result or serious neurologic injury may ensue in the infants who survive. Hemorrhage from ruptured velamentous vessels is uncommon, occurring in about 1 in 50 velamentous cord insertions, but if rupture does occur, the mortality rate is estimated to be from 58% to 73%.<sup>44</sup> Other consequences of this condition include fetal distress and hypoxia from compression of the vessels during labor<sup>45</sup> and neonatal thrombocytopenia. Thrombosis of velamentous vessels has been associated with neonatal purpura and fetal death. Abnormal cord insertions have also been associated with abnormal fetal heart rate tracings, fetal growth restriction, low birth weight, and low Apgar scores.<sup>4,46,47</sup>



**Figure 6** Velamentous insertion of the umbilical cord. (A) Note the presence of vessels coursing through the membranes without support of Wharton's jelly. All membranous vessels were intact but presumed compression occurred during labor and delivery, necessitating a cesarean section for "non reassuring fetal status." (B) Velamentous insertion associated with a thrombus in a velamentous vessel. Reprinted with permission.<sup>8</sup>

Examination of the placenta is essential to document the type of cord insertion and the presence of velamentous vessels. It is extremely helpful when the suspicion of ruptured velamentous vessels is communicated to the pathologist before examination. However, this is often not done, so extra care must be taken to preserve the pathologic findings in every placenta with velamentous vessels. The presence of membranous vessels, the distance that they course through the membranes, and evidence of thrombosis, disruption, and hemorrhage into adjacent membranes should all be noted. Study of the histology of velamentous vessels<sup>4</sup> have shown that they are firmly attached to the chorion by collagenous fibers, which explains why the vessels rupture so easily when the chorion is disrupted. Microscopic examination can confirm the presence of velamentous vessels and identify thrombosis or disruption with associated hemorrhage. When significant fetal hemorrhage has occurred no matter what the cause, the placental parenchyma will be pale and the villous capillaries will appear relatively bloodless on histologic section. It is important to note that bleeding or thrombosis in velamentous vessels does not necessarily only occur acutely, and in some cases, thrombosed or disrupted vessels may be seen associated with hemosiderin-laden macrophages, which is evidence of previous rupture and perhaps chronicity.

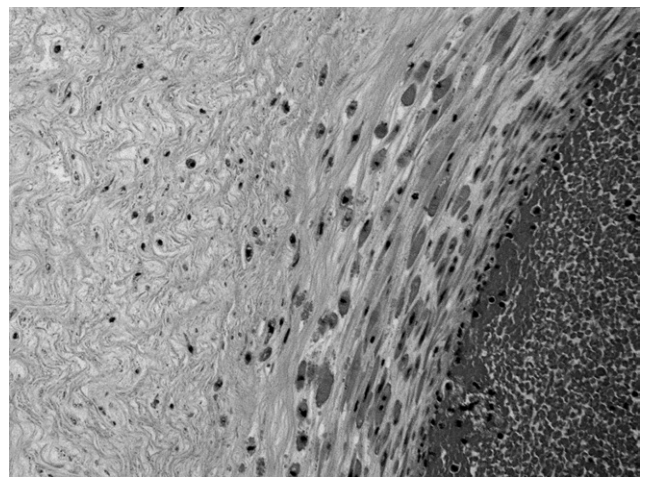
## Meconium

Discharge of meconium, the intestinal content of the fetus, into the amniotic fluid is a relatively common event, especially in term or post term infants. In most cases, it does not lead to significant problems. In a small percentage of cases, meconium is aspirated by the fetus and then meconium aspiration syndrome may develop, a condition associated with significant neonatal morbidity and mortality. It is often suggested, particularly in legal cases, that meconium discharge is indicative of fetal distress. Although it is true that meconium discharge may be a response to fetal distress and/or hypoxia, it often occurs in babies with no evidence of distress or poor outcome. Furthermore, term babies with other evidence of in utero distress and babies who die in utero do not always show evidence of meconium discharge. Thus, the notion that its presence is always indicative of prior distress is unfounded, particularly in term babies.

Meconium is a noxious material, containing bile salts, cholic acid, enzymes, and other compounds.<sup>48</sup> If meconium is present in the amniotic fluid for a sustained period, it damages the amnion, the umbilical cord, and fetal vessels. Initially, within a few hours of meconium exposure, the fetal membranes and surface are stained green on gross examination. Edema is often present as well, giving the membranes a slimy appearance. Microscopically, there is degenerative change of the amniotic epithelium of the fetal membranes and chorionic plate, manifesting as piling up of the epithelial cells, vacuolation, loss of epithelial cells, and

necrosis associated with the presence of pigment-filled macrophages.<sup>48,49</sup> In vitro studies have suggested that it takes 1 hour for macrophages to appear in the amnion and 3 hours for them to appear in the chorion, but this may not be a true estimation of what happens in vivo.<sup>49</sup> One must be cognizant of the fact that meconium pigment does not survive exposure to light and so the pigment will fade in glass slides left exposed to ambient light.<sup>50</sup> A longer period of meconium exposure is required for gross staining of the umbilical cord. In the umbilical cord, meconium-filled macrophages may be difficult to identify due to the paucity of macrophages. After 12 to 16 hours or more, there may be additional damage manifesting as necrosis of the vascular smooth muscle of umbilical vessels and their ramifications on the placental surface.<sup>48</sup> This myonecrosis most commonly involves the arteries, most probably because they are closer to the surface. The muscle fibers, which are normally spindled, round up and the cytoplasm takes on a deeper eosinophilia (Figure 7). The nuclei may become pyknotic and eventually disappear completely. Rarely, umbilical arteries can become completely detached from the cord due to damage to the amnion and Wharton's jelly or the cord may become ulcerated due to meconium exposure.<sup>51</sup> Meconium toxicity has been held responsible for these types of tissue damage, even though the exact toxic moiety in meconium is not known.

Not only does meconium cause damage to the tissues of the placenta, but also in vitro studies have shown that meconium causes vasoconstriction of umbilical vessels.<sup>7,52</sup> The vasoconstrictive effect of cholic acids, a component of meconium, has been demonstrated as well.<sup>53</sup> It is possible that vasoconstriction may also be mediated by interleukin-1, as the latter has been demonstrated to be present in meconium staining,<sup>54</sup> and a similar mechanism is proposed for



**Figure 7** High power view of an umbilical artery associated with meconium discharge of many hours duration. Note the paucity of muscle fibers. The remaining fibers are abnormal in that many show “rounding up” and deepening eosinophilia of the cytoplasm with pyknotic nuclei. Some fibers show further degeneration with karyorrhexis and complete loss of the nucleus. H&E; original magnification 20 $\times$ .



vasoconstriction due to bacterial products in the setting of an ascending infection.<sup>55</sup> This vasoconstrictive effect is more likely to occur with long-standing meconium exposure. If the vein is involved, there may be decreased venous return of oxygenated blood from the placenta, or, if the arteries are involved, there may be decreased blood flow to the placenta. Since vasoconstriction compromises blood flow, it is not unexpected that meconium-associated myonecrosis has been linked to fetal distress, cerebral hypoperfusion, and a significant risk of neurologic injury and cerebral palsy.<sup>1,56</sup> Arterial necrosis with ulceration of the umbilical cord has been described in association with meconium discharge in infants suffering from hypoxic ischemic encephalopathy.<sup>57</sup>

### Miscellaneous cord lesions

In an abnormally thin cord, there is a lack of Wharton's jelly and decreased water content, making vascular compression a greater possibility. Thin cords are often seen in growth-restricted infants. Cords with a single umbilical artery also have a smaller diameter, and these cords are associated with an increased risk of other cord complications<sup>58</sup> such as velamentous insertion and with fetal demise, growth restriction, and prematurity. Fetal growth restriction and prematurity are themselves associated with an increased risk of neurologic injury.

Hematomas of the umbilical cord have been reported to have a fetal mortality of up to 50% and may be the cause of severe neurologic injury.<sup>4</sup> In large hematomas, morbidity and mortality may be due to blood loss, but in smaller lesions, adverse outcome may be secondary to compression of the umbilical vessels by the hematoma.<sup>4</sup> Grossly, cord hematomas appear as an elongated, fusiform swelling of the cord with dark red discoloration and engorgement of blood (Figure 5). Usually the cut section of the cord will show hemorrhage throughout. Hematomas may develop due to trauma and thus are associated with short cords, long cords, velamentous insertions, and cord entanglements. They may also be caused by inherent abnormalities of the umbilical vessels, such as aneurysms or hemangiomas that rupture and bleed. Unfortunately, in many cases, the primary cause is unknown.

Aneurysms of the umbilical vessels, usually the vein, have been described. Elastic stains have shown that the elastic fibers of such veins are focally deficient. Aneurysmal dilatations of umbilical vessels may compress other umbilical vessels or cause a cord rupture or hematoma. Thus, aneurysmal thinning may lead to death or neurologic injury.<sup>59-61</sup> Fetal growth restriction has also been described in this condition. Aneurysms have been associated with abnormal cord insertion, single umbilical artery, and other miscellaneous placental anomalies.<sup>4</sup>

Hemangiomas appear histologically similar to those described elsewhere in the body, and hemangiomas of the cord

may coexist with similar lesions in the fetus.<sup>62</sup> They are most common at the placental end of the cord, arising from one or more umbilical vessels.<sup>63</sup> Prenatal diagnosis may be sometimes made by sonography. These tumors are never malignant, but fetal death is frequent if the tumor is large. Much of the adverse outcome is dependent on rupture and secondary hemorrhage or hematoma formation. Hemangiomas up to 18 cm in length, 14 cm in diameter, and weighing up to 900 g<sup>4</sup> have been described.<sup>4</sup> In some, myxoma-like Wharton's jelly is present within the tumor,<sup>59</sup> and in these cases, the tumor is designated an angiomyxoma. Unlike chorangiomas within the placental parenchyma, angiomas of the cord are usually not associated with hydramnios or hydrops. There is, however, an elevation in maternal serum alpha-fetoprotein in some cases.

Trauma to the umbilical cord is an important cause of fetal hemorrhage leading to perinatal death or neurologic injury. Trauma may result from cordocentesis, amniocentesis, and fetal transfusion when there is direct damage to the cord or occasionally by direct needle puncture of the fetus. In the latter case, the fetus may show scars as evidence of previous trauma. As in other cases of hemorrhage from fetal or umbilical vessels, blood will often be present in the amniotic fluid and the fluid will take on a port wine color. Examination of the placenta will show hemorrhage and/or hematoma surrounding the area of trauma. In very acute hemorrhage, there will be no staining but extravasated fresh blood may be visible in the site of the trauma although the actual site of trauma may be quite difficult to identify. If the injury is subacute, there may be hemolysis of the extravasated blood causing a reddish discoloration of the umbilical cord and fetal surfaces of the placenta. With more remote hemorrhage, the site of trauma will show organizing clot and hemosiderin deposition and eventually the fetal surface of the placenta may become stained yellow to brown. On microscopic examination, hemosiderin-laden macrophages will be present and the progressive organization of the hematoma can give an estimation of the timing of the traumatic event. It must be cautioned, however, that sub-amniotic fresh blood is commonly found in placentas and is often iatrogenic. It may be the result of excessive traction on the cord during delivery of the placenta or, due to removal of blood from placental surface vessels for pH determination or for donation of fetal stem cells.

Cord rupture is, fortunately, a rare event. Fetal hemorrhage and severe anemia are the result with a significant risk of neurologic injury in those infants who survive. There are several underlying causes of cord rupture. An excessively short cord may avulse from the placenta during descent of the fetus during vaginal delivery.<sup>64</sup> A long cord, if wound multiple times around the neck or the body, may be "relatively" short, and result in rupture from the same mechanism. Velamentous cord insertions are probably the most frequent antecedent events. Meconium-induced myonecrosis of umbilical vessels on rare occasion has led to ulceration and rupture of the cord.<sup>50</sup> Rupture can also develop

due to severe necrotizing funisitis.<sup>6</sup> Spontaneous rupture is a very uncommon event. All these etiologies are rare, and careful pathologic examination is necessary to document the specific underlying lesion as well as confirm that the rupture is not a post delivery event. The cord will rupture most often at the site of its placental attachment and this will be the most common site of hemorrhage or hematoma formation.<sup>65</sup> As with other types of fetal hemorrhage, the placenta will often be pale, reflective of the severe fetal anemia.

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