Gross Evaluation and Normal Histology of Umbilical Cord

**TERMINOLOGY**

**Synonyms**
- Omphalomesenteric duct = vitelline duct
- Allantois = urachus = median umbilical ligament

**GROSS EVALUATION**

**Gross Inspection of Cord**
- Very important aspect of placental examination
- Abnormalities associated with fetal morbidity and mortality
  - Tight knots
  - Umbilical cord prolapse through or into cervix
  - Velamentous cord ± vasa previa
  - Abnormal cord length
  - Abnormal cord coiling, hypercoiling or hypocoiling
  - Hematoma/hemorrhage
  - Thrombosis
  - Hemangioma
  - Cord entanglement around neck or body
  - Cord entanglement between monoamniotic twins
- Every exam should document
  - Color, normally white
    - Green-brown discoloration with meconium staining
    - Yellow discoloration with meconium or inflammation
    - Red-brown discoloration after fetal demise
    - Discolored stripe may indicate thrombus
  - Total length
  - Diameter
  - Coiling
    - Count number of coils in total length to determine if undercoiled or overcoiled
  - Cord insertion site, distance from insertion to edge of placental disc
  - Presence of amniotic web
    - Extension of amnion from cord to chorionic plate tethers cord
    - May limit fetal mobility
    - Often mistaken for marginal or velamentous insertion on ultrasounds
- Document abnormalities with gross photograph

**Umbilical Cord Length**
- Reference values for cord length are established for fresh cord at gross exam
  - > 70 cm at term considered excessively long
    - Fetal heart failure due to increased work of moving blood through long umbilical cord
    - Increased risk of cord wrapping around neck, body, or limbs, with potential effects on circulation through affected body part as well as through cord
    - Associated with increased fetal activity, male gender, increased maternal height, BMI and parity
  - < 35 cm at term considered short (clinical correlation necessary)
    - Associated with decreased fetal movement
    - Increased risk of premature placental separation or cord avulsion
    - Cord length shortens in fresh state approximately 3% in first 2 hours after delivery
    - Formalin fixation leads to further shortening of approximately 12% at 24-48 hours

*(Left) The umbilical vessels may have varicosities, commonly called “false knots,” that usually arise from the vein. They are of little clinical significance. Rarely, they may contain thrombi. (Right) The umbilical cord is composed of myofibroblasts, found near the vessels and collagen fibers. Wharton substance is found between the cellular components. This includes fibroblasts, macrophages and mast cells. Mast cells produce heparin-like substances to prevent thrombosis. The cord has no lymphatics or nerves.*
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Umbilical Cord Diameter
- Length of cord received in pathology is usually < true total length, as segments may be sent from delivery room for blood gas analysis, cord blood banking, cytogenetics or cultures
- Reference values for cord diameter on fresh cord
  - Cord diameter measured from slides will be approximately 0.1-0.2 cm smaller due to shrinkage with fixation and processing
  - Thick cords (> 3 cm fresh) associated with large placenta, fetal macrosomia and hydrops
    - Usually due to increased volume of Wharton substance, may be secondary to increased umbilical vessel size
  - Thin cords (< 8 mm measured off slides) associated with prematurity, postmaturity, fetal growth restriction, decreased uteroplacental blood flow, and oligohydramnios
    - Thinning usually due to decreased volume of Wharton substance or single umbilical artery
    - Usually has wrinkled cord surface
  - Fetal end of cord is usually thicker than placental end

Umbilical Cord Coiling
- Helical coiling of umbilical arteries around vein
  - Coiling protects vessels from compression
  - 75% coil counterclockwise, leftward
- Average number of coils is reported as coiling index
- Normal coiling ranges 1-3 twists per 10 cm of length
- Hypercoiled cords noted in 20%
  - May be associated with increased vascular resistance to blood flow through cord with increased afterload on fetal heart, torsions or strictures, further compromise flow
  - Chorionic plate and stem vessels may show thrombi
  - Hemodynamic effect of hypercoiling more severe in small-caliber arteries and excessively long cords
- Hypocoiled cords noted in 7.5%
  - May be more susceptible to kinking and acute obstruction of fetal blood flow
  - Associated with aneuploidy and single umbilical artery, meconium staining
  - Flat cords may be associated with nuchal or body wraps

Umbilical Cord Insertion
- Insertion is defined as point where cord vessels branch and are no longer covered with Wharton substance
- "Normal" cord insertion
  - Insertion within central 2/3 of disc (paracentral or eccentric insertion most common)
  - Peripheral cord insertion, may be less efficient
    - Insertion within 3 cm of disc edge
  - Marginal cord insertion, less efficient
    - Insertion within 1 cm of disc edge
  - Velamentous cord insertion, less efficient
    - Insertion in membranes of placenta
    - Vessels coursing through membranes to disc are at risk for compression or disruption
      - No protection from compression by Wharton substance
      - Can tear if near site of membrane rupture
- "Normal" cord insertion
  - Umbilical vessels branch before cord inserts onto placental surface
    - No protection by Wharton substance along branched segments
    - Increased risk of compression, thrombi, tearing

HISTOLOGIC COMPONENTS

Amniotic Epithelium
- Low cuboidal epithelium
- May become squamous, especially near term and near placental insertion site
- Skin covered component at fetal abdomen will have dermal appendages
- Tightly adherent to underlying connective tissue, unlike amnion of membranes

Umbilical Arteries
- 99% have 2 umbilical arteries
- Derived from allantoic vessels accompanying allantoic duct
- Continuation of internal iliac arteries in fetus
- Brings deoxygenated blood from fetus to placenta
- Thick, muscular vessels with 50-60 smooth muscle layers
  - No internal elastic lamina, but scant elastic fibers in wall
  - Smooth muscle arranged in helical bundles, allows for greater contractility
- Arteries frequently anastomose within 2-3 cm of cord insertion onto placental disc (Hyrtl anastomosis)
  - Equalizes pressure and ensures supply of blood throughout placenta if 1 umbilical artery is thrombosed
  - Various patterns of anastomosis, including varying length of fusion, or ≥ 1 communicating branch
- Single umbilical artery, 1% at term
  - Either left or right UA may be absent, more commonly left
  - More common in Caucasians
  - May see atrophic remnant of 2nd umbilical artery
  - More frequent in twins, usually in smaller twin when growth is discrepant
  - 20% have additional malformations with significant morbidity and mortality
    - Abnormal karyotype and multiple malformations are more common when left umbilical artery is missing
    - Associated with changes of fetal vascular malperfusion in small-for-gestational-age-growth fetus
  - Discordant size, > 0.1-cm difference in arteries
    - Similar associations as single umbilical artery
  - No vasa vasorum, thrombosis results in vessel necrosis

Umbilical Vein
- Paired in early gestation, singular with regression of right umbilical vein by 2nd month
  - Persistence of right umbilical vein is cause of true supernumerary vessels in < 1% of cords
    - Discern true supernumerary vessel from sectioning through varicosity with additional sections
  - Returns oxygenated blood from placenta to fetus
  - Derived from allantoic vessels accompanying allantoic duct
Gross Evaluation and Normal Histology of Umbilical Cord

Overview of Gross and Microscopic Changes

- Thin, muscular vessel with 30-40 layers, less well organized than arteries and less able to constrict
- Well-developed internal elastic lamina
- External diameter of vein is usually twice that of arteries
- No vasa vorum, thrombosis results in vessel necrosis

**Wharton Substance**
- Mucoid extracellular ground substance protecting umbilical vessels from compression
- Rich in hyaluronic acid, chondroitin sulfate and collagen
- Scattered stellate myofibroblast-like cells, more concentrated toward vessels
- Scattered heparin producing mast cells and macrophages
- Derived from extraembryonic mesoderm
- Liquefies under pressure
  - Cystic degeneration seen in hydrops and with omphalocele
- No lymphatics or nerves are present in umbilical cord

**Vestigial Remnants**
- Present in 23% of cords
- Allantoic duct remnant, most common (63%)
  - Located between umbilical arteries
  - Lined by flattened, cuboidal or transitional-like urothelium, with occasional mucin-producing cells
  - Surrounded by concentric dense connective tissue, rarely smooth muscle
  - Frequently contains eosinophilic or calcified debris
  - May contain urine if urachus is patent
- Vitelline vessel remnants (30%)
  - May accompany omphalomesentric duct remnant
  - Lined by simple endothelium, with thin muscular wall
  - Variable number of channels
    - Commonly paired at fetal end of cord
    - May be singular at placental end of cord, continuing onto chorionic plate and yolk sac
  - May be associated with proliferation of small capillaries, so-called “hemangioma”
- Omphalomesentric duct remnant, least common (7%)
  - Usually present at periphery of cord
  - Lined by various endodermal epithelia, typically small intestinal type (rarely gastric, hepatic, pancreatic)
  - Commonly has smooth muscle coat
  - May be cystic, contain eosinophilic or rarely meconium-like material
  - May be associated with other anomalies of persistent duct, such as Meckel diverticulum

**ARTIFACTS, SPONTANEOUS AND IATROGENIC LESIONS**

**Gross Artifacts**
- Hematomas
  - Usually due to clamping of cord during delivery of placenta
    - Usually disruption of thinner umbilical vein and extension of blood along perivascular spaces
    - Look for parallel clamp marks on cord surface
  - Small fresh hemorrhages may be due to cord blood sampling for gas analysis
- Changes should not be confused with hemorrhages that occur before delivery
- Avulsion of cord usually occurs with delivery of placenta after birth
  - Communicate with obstetric team if timing of avulsion is uncertain

**Microscopic Artifacts**
- Inclusion “cyst” of amnion
  - Usually not true cyst but artifact due to tangential sectioning through spiral of cord
- Loss of 2nd umbilical artery due to incomplete sectioning
  - Section taken in area of Hyrtl anastamosis, close to placental end of cord
  - > 3 vessels on section
  - Section taken in area of excessive coiling or varicosity of vessels, false knots

**Umbilical Cord Rupture or Avulsion**
- Rupture of cord prior to delivery of infant
  - Presents with bloody amniotic fluid and fetal distress
  - Associated with precipitous or uncontrolled delivery
  - Associated with short cords
- Avulsion of cord, partial or complete
  - True avulsion in utero is exceedingly rare
    - Increased risk with velamentous, marginal or furcate insertion
    - May be associated with vascular ectasia or focal segmental thinning of umbilical vessels
    - Rare complication of intrauterine pressure catheter
  - Presents with bloody amniotic fluid and fetal distress
    - Blood extravasates into Wharton substance and into subamniotic space on chorionic plate

**Umbilical Cord Hematoma**
- Small hemorrhages may be due to excessive coiling, entanglement of cord around fetal body, knots or thrombi
- Small hemorrhages may be complication of amniocentesis or cordocentesis
- Spontaneous hematomas are usually large, fusiform, and near fetal abdomen
- Rare complication of forceps delivery

**SELECTED REFERENCES**

### Gross Evaluation and Normal Histology of Umbilical Cord

#### Umbilical Cord Diameter (cm)

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<th>Gestational Age (Completed Weeks)</th>
<th>10th Percentile</th>
<th>50th Percentile</th>
<th>90th Percentile</th>
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Umbilical cord diameter (UCD) percentiles and mean and standard deviation of the cohort (N = 497) are shown. UCD was calculated using the formula: \( UCD = 2x \sqrt{(weight/\pi \times length)} \). The substitution of weight in place of volume was used after showing that umbilical cord volume was similar to weight \((p < 0.001; r = 0.997; y = 1.071x - 0.644)\).


#### Umbilical Cord Length at Various Gestational Ages

<table>
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<th>Gestational Age (Weeks)</th>
<th>N</th>
<th>Umbilical Cord Length (cm)</th>
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<td>20-21</td>
<td>16</td>
<td>32.4 ± 8.6</td>
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<td>42-43</td>
<td>4,797</td>
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Data represent mean ± 1 standard deviation of cord length in fresh state after birth. Shortening occurs in fresh state and with formalin fixation.

**Overview of Gross and Microscopic Changes**

*(Left)* Gross exam includes close inspection of the surface. The small, white plaques on the cord surface are foci of peripheral funisitis. The lesion is nearly pathognomonic for candidal infection of the amniotic fluid. *(Right)* This segment of cord is hypocoiled. Vitelline vessels may be visible on gross inspection. They are a remnant vasculature that accompanied the omphalomesenteric duct in early development. They are often paired on the fetal end of the cord.

*(Left)* True knots can be loose or tight. The lack of congestion on either side of this knot indicates that it is not a tight knot and may have had little clinical significance. The wrinkled cord surface indicates the loss of Wharton substance. *(Right)* Coiling index refers to the number of 360° coils made by the umbilical arteries (blue) around the umbilical vein (red). Normal coiling ranges from 1-3 per 10 cm length of cord. Both overcoiling (top) and undercoiling (bottom) have been associated with adverse outcome.

*(Left)* The cause of overcoiling is unknown. The cords of these monochorionic twins are discrepant for coiling index and direction. *(Right)* The discoloration of the cord is an indication of prolonged fetal demise. The area of torsion is toward the fetal end of the cord, and the dilated area is toward the placental end.
Overview of Gross and Microscopic Changes

**Gross Evaluation and Normal Histology of Umbilical Cord**

*Left* This hypercoiled cord led to 2nd-trimester fetal demise. Mathematical modeling suggests that excessive coiling increases resistance to blood flow. Excessive length and hypercoiling increase the work required for placental perfusion. The hypercoiling is often difficult to appreciate. *Right* This undercoiled cord is from a case of severe, chronic meconium exposure and intrauterine fetal demise. Undercoiled cords are more susceptible to acute occlusion from kinking.

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**Umbilical Vein Thrombus**

*Left* Gross image shows a thrombus of the umbilical vein near the cord insertion. Note the smaller diameter of the 2 umbilical arteries. The white discoloration of the proximal chorionic plate vein indicates extension of the thrombus. *Right* These cross sections of the cord show loss of the muscularis of one of the umbilical arteries due to longstanding thrombosis.

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**Umbilical Artery Thrombus**

*Left* Hypercoiled Umbilical Cord

*Right* Undercoiled Umbilical Cord

*Left* This hypercoiled cord led to 2nd-trimester fetal demise. Mathematical modeling suggests that excessive coiling increases resistance to blood flow. Excessive length and hypercoiling increase the work required for placental perfusion. The hypercoiling is often difficult to appreciate. *Right* This undercoiled cord is from a case of severe, chronic meconium exposure and intrauterine fetal demise. Undercoiled cords are more susceptible to acute occlusion from kinking.

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**Umbilical Cord Hematoma**

*Left* Hemorrhage within the cord substance may be spontaneous, iatrogenic, or an artifact of delivery. The cord should be carefully inspected for clamp marks near the lesion. *Right* While the amount of blood that the fetus can lose in a cord hematoma is limited, the pressure may occlude flow through the remaining intact vessels.
Overview of Gross and Microscopic Changes

Central and eccentric cord insertions are most common. Marginal, velamentous, and furcate are more often associated with pathology. Velamentous and furcate cords leave vessels vulnerable to injury. Marginal insertion may be less efficient for perfusion. (Right) Cords that insert at the margin, or within 1 cm of the margin, are deemed marginal. Marginal cord insertion is associated with magistral chorionic plate vasculature. There are few artery/vein pairs, which show little decrease in diameter or branching.

Gross Evaluation and Normal Histology of Umbilical Cord

(Umbilical Cord Insertion) Central, Eccentric, Marginal, and Furcate Cord Insertions

(Velamentous Cord Insertion) Gross image shows vulnerable vessels in a velamentous insertion. Inspect closely for tears or thrombi and measure the length of the unprotected intramembranous vessels. All velamentous cord insertions are also furcate. (Right) Cords that insert at the disc margin frequently have vessels that may course through the membranes. These are also vulnerable to compression or tearing as in velamentous cord insertion.

(Furcate Cord Insertion) In furcate cord insertion, the umbilical vessels branch like the tines of a fork before the cord inserts on the chorionic plate. Such vessels are vulnerable to compression or tearing. Tearing may be the source of subamniotic hemorrhage. Not all furcate cords are velamentous. (Right) In the amniotic web of the umbilical cord, an extension of amniotic membranes tethers the cord to the chorionic plate. This may limit cord mobility and cause the cord to be functionally short. Tearing of the web may result in subamniotic hemorrhage.
Overview of Gross and Microscopic Changes

1. **Gross Evaluation and Normal Histology of Umbilical Cord**

   - **Early 2nd-Trimester Cord**
   - **Single Umbilical Artery**

   (Left) The thicker umbilical arteries are easily distinguished from the thinner-walled vein in this 15-week gestation cord. The loose stroma has an immature appearance. The umbilical vein is usually 2x the diameter of an artery but thinner walled. (Right) A single umbilical artery should be confirmed microscopically. There is 1 umbilical artery and 1 umbilical vein present. This common anomaly has little clinical significance in the vast majority of newborns.

2. **Umbilical Vein**

   - **Umbilical Vein Elastin Stain**

   (Left) In contrast to the umbilical arteries, a vague resemblance to separate longitudinal and circular layers can be seen in the umbilical vein. The vein has limited ability to contract if damaged. (Right) The umbilical vein has an internal elastic lamina.

3. **Umbilical Artery**

   - **Umbilical Artery Elastin**

   (Left) The muscle of the umbilical arteries consists of crossing spiral bundles of smooth muscle. The inner layers often appear less organized, and may bulge into the lumen. The artery has more ability to contract, limiting bleeding. Desmin expression is often limited to the outer, more differentiated-appearing layers. (Right) The umbilical arteries lack a well-developed internal elastic lamina but have scattered circumferential elastic staining in the inner muscular layers.
Overview of Gross and Microscopic Changes

**Gross Evaluation and Normal Histology of Umbilical Cord**

(Left) The cord increases in diameter throughout gestation from growth of the vessels and increase in Wharton substance. This 2nd-trimester cord shows spindled fibroblasts and few delicate collagen fibers. This connective tissue floats in a hyaluronic acid and proteoglycan-rich matrix termed "ground substance."

(Right) The normal cord has variable amounts of fluid in the extracellular matrix. The blue staining of the hyaluronic acid component may be seen with certain hematoxylin and eosin stains.

(Left) Squamous metaplasia is a feature of a mature cord and is most often seen at the placental end of the cord. This section came from the placental end of the cord. The 2 umbilical arteries on this section share a muscular wall. Sections from 1 side of this will have only 1 artery and the other side 2 arteries.

(Right) Pseudocysts may form in areas of large accumulations of Wharton substance. There is no epithelial or endothelial lining, only condensed spindle cells. These are common near the fetal abdomen in association with omphalocele.

(Left) Pseudocysts are gathered by amnion into the body stalk. Paired allantoic arteries, initially paired allantoic veins (2nd vein regresses) with allantoic duct (not shown), vitelline duct and vitelline vessels. The latter 3 structures can be seen as vestigial remnants in the mature cord.
Gross Evaluation and Normal Histology of Umbilical Cord

Omphalomesenteric Duct Remnant

Omphalomesenteric duct remnants are typically present at the periphery and may have a smooth muscle layer. Various types of endodermal tissue may be seen, but typically they are lined by a cuboidal to low columnar epithelium, with occasional goblet cells.

(Right) This omphalomesenteric duct remnant has a smooth muscle coat and well-differentiated intestinal-type mucosa.

Capillary Proliferation (Hemangioma) Associated With Vitelline Vessel Remnants

Vitelline vessel remnants are usually found paired on the fetal end of the cord. They may have an associated capillary proliferation as seen in this image.

(Right) Vitelline vessels once communicated with the embryonic yolk sac, the primary source of hematopoiesis in the early embryo. Remnants in the mature cord may also feature extramedullary hematopoiesis as seen here.

Allantoic Remnant

Allantoic remnants are usually located between the 2 umbilical arteries. The epithelium is typically cuboidal or transitional. They are usually of no clinical significance.

(Right) The allantoic remnant occasionally shows a patent lumen. Rarely, large patent allantoic remnants communicate with a persistent urachus in the fetus. Urination into the cord may occur.