PLACENTAL EXAMINATION IN THE INTRAUTERINE FETAL DEATH

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Sampling and Definitions of Placental Lesions Amsterdam Placental Workshop Group Consensus Statement Khong et al.

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Pathology of the placenta, cord, or membranes is attributed as a cause or contributory to stillbirth in 11% to 65% of cases.

Especially stillbirth cases may easily undergo medico-legal litigation and placental examination may become fundamental in assessing the liability of the whole medical assistance.

Placental gross description, sampling specifications, pathologic terminologies, and diagnostic criteria represent a critically needed systematic approach.

Placental Weight

Description of the placenta should include the placental weight trimmed of extraplacental membranes and umbilical cord, and notation of whether the placenta was fresh or fixed when measured.

Fixation of the placenta will affect its weight, with an increase of 3% to 6%.

The placental weight is a surrogate for placental function, and fetoplacental weight ratio has been suggested as a possible indicator of adequacy of placental reserve capacity in fetal growth restriction (FGR).

Appendix 2C

FETAL-PLACENTA WEIGHT RATIO PERCENTILES BY GESTATIONAL AGE[a]

Gestational Age (weeks)	N[b]	Mean	SD	Percentile 3	5	10	25	50	75	90	95	97
22	19	2.9	0.8		1.0	1.0	2.0	2.4	3.6	3.9	4.3	
23	16	3.3	0.7				2.4	2.9	3.6	4.5		
24	16	3.4	1.0				2.0	2.6	4.0	4.6		
25	26	4.0	1.4		1.7	2.3	3.2	3.8	4.6	6.0	7.4	
26	22	4.1	1.2		2.1	2.8	3.4	3.7	4.8	5.2	7.7	
27	22	4.5	1.1		2.6	3.0	3.3	3.6	4.5	6.0	7.1	
28	41	4.8	1.0	2.3	2.5	3.6	3.9	4.2	4.7	6.5	6.6	6.9
29	37	5.2	1.4	1.9	2.5	3.7	4.4	5.0	5.7	7.5	8.0	9.2
30	42	5.2	1.1	2.7	3.1	3.6	4.5	5.1	5.8	6.8	6.9	7.6
31	57	5.5	1.1	3.3	4.1	4.4	4.7	5.4	6.2	6.9	7.3	8.2
32	69	5.9	1.2	3.2	4.1	4.4	5.0	5.8	6.8	7.7	7.9	8.4
33	117	6.0	1.1	4.3	4.5	4.7	5.2	6.0	6.6	7.7	8.2	8.7
34	160	6.2	1.0	4.4	4.7	5.0	5.5	6.1	6.7	7.5	7.9	8.2
35	260	6.4	1.2	4.5	4.7	5.0	5.6	6.3	7.2	8.0	8.6	9.1
36	538	6.6	1.1	4.8	4.9	5.3	5.8	6.4	7.3	8.1	8.4	8.8
37	1103	6.8	1.1	4.9	5.1	5.4	6.0	6.7	7.4	8.2	8.8	9.1
38	2469	6.9	1.1	5.1	5.2	5.6	6.1	6.8	7.5	8.3	8.9	9.2
39	3932	7.1	1.1	5.2	5.4	5.7	6.3	7.0	7.7	8.5	9.1	9.4
40	4114	7.2	1.1	5.3	5.5	5.8	6.4	7.1	7.9	8.6	9.1	9.5
41	1982	7.2	1.1	5.4	5.6	5.9	6.5	7.1	7.8	8.6	9.1	9.4
42	321	7.1	1.1	5.3	5.5	5.9	6.4	7.1	7.8	8.5	8.9	9.1

[a]Data derived from reference 2 with assistance from biostatistician Jane McCall.
[b]Number of placentas at each placental age; SD = standard deviation.

Appendix 2A

PERCENTILES, MEANS, AND STANDARD DEVIATIONS FOR PLACENTAL WEIGHTS BY GESTATIONAL AGE[a]

Gestational Age (weeks)	N[b]	Mean	SD	Percentile 3	5	10	25	50	75	90	95	97
22	19	189	89		99	107	130	166	206	285	499	
23	16	190	41			127	168	188	208	262		
24	16	190	42			128	157	192	222	252		
25	26	197	70		105	128	153	184	216	299	400	
26	22	226	100		107	138	179	200	259	281	570	
27	22	240	77		119	130	166	242	310	332	381	
28	41	223	66	103	128	140	173	214	261	321	361	371
29	37	269	96	124	135	161	214	252	309	352	496	629
30	42	324	88	185	190	208	269	316	374	433	502	570
31	57	314	105	142	152	175	246	313	360	417	479	579
32	69	325	77	161	214	241	275	318	377	436	461	465
33	117	351	83	190	224	252	286	352	413	446	475	504
34	160	381	84	221	260	283	322	382	430	479	527	558
35	260	411	99	232	250	291	344	401	471	544	600	626
36	538	447	110	270	291	320	369	440	508	580	628	679
37	1103	467	107	303	324	349	390	452	531	607	660	692
38	2469	493	103	320	335	365	420	484	560	629	675	706
39	3932	500	103	330	350	379	426	490	564	635	683	713
40	4114	510	100	340	360	390	440	501	572	643	685	715
41	1982	524	100	358	379	403	452	515	583	655	705	738
42	321	532	99	370	388	412	460	525	592	658	700	771

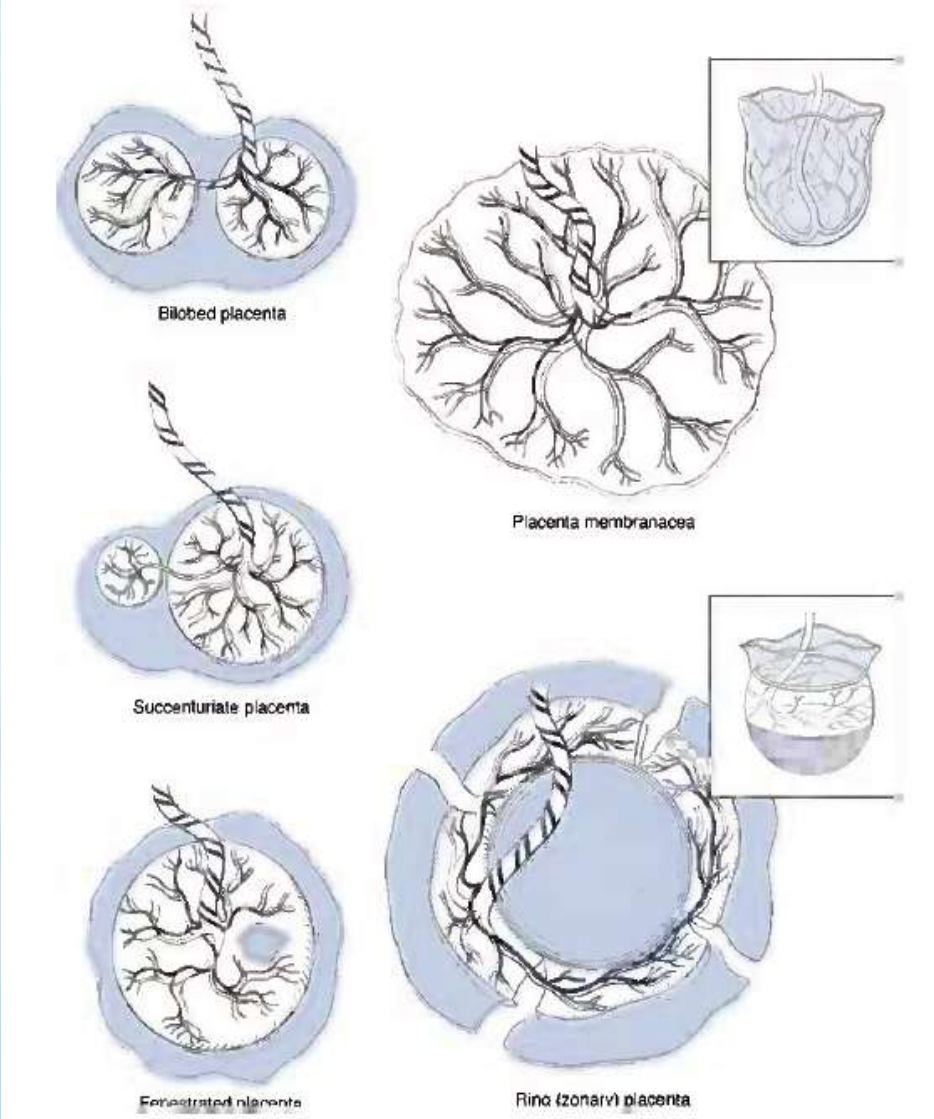
[a]Data derived from reference 2 with assistance from biostatistician Jane McCall.
[b]Number of placentas at each placental age; SD = standard deviation.

Placental Disk Dimensions

The placenta should be measured in three dimensions: the maximal linear dimension (length), the greatest dimension of the axis perpendicular to this linear measurement (width), and the mural minimal and maximal thickness.

Measuring the placental dimensions will also allow further refinement of determining the functional reserve of the placenta by correlation of size of any lesions with the overall dimensions of the placenta.

Placental disk shape



There are **always** membranous vessels connecting the villous tissue between lobes. These membranous vessels, being devoid of the protection of Wharton's jelly, are susceptible to damage from *compression*, *rupture*, *or thrombosis*.

Umbilical Cord

Description of the umbilical cord should include:

- number of vessels
- average diameter of the cord
- length
- site of insertion in relation to the center/margin of the placenta
- strictures
- coiling

Cord diameter

The diameter of the cord is predominantly due to the water content of Wharton's jelly and is usually reflective of the fluid status of the fetus. The diameter increases slowly throughout gestation and then declines slightly in the last few weeks before full maturity. The average cord diameter at term varies from about 1.2 to 1.7 cm. An increased cord diameter is usually due to **edema.**

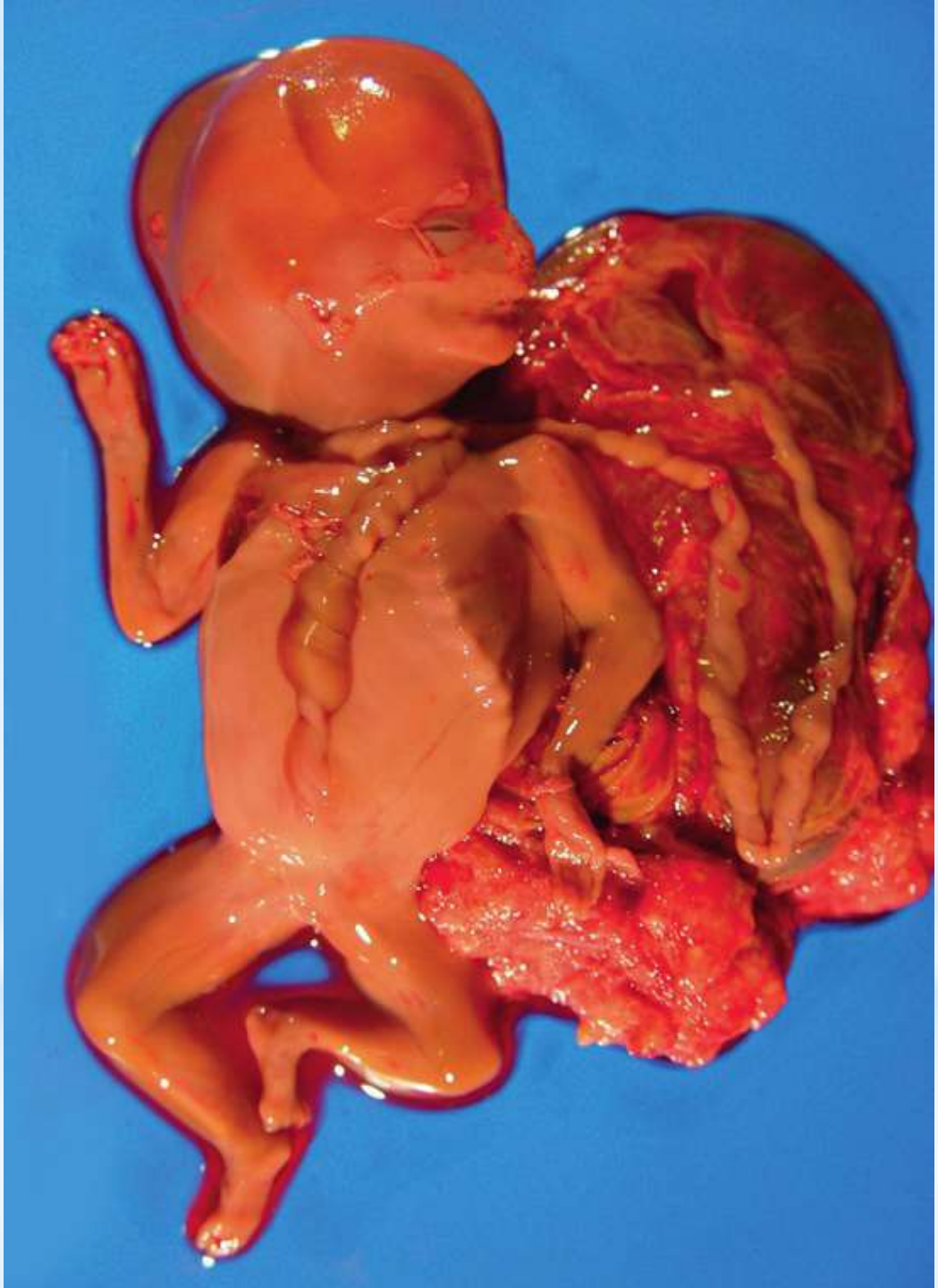
Thus, very thin cords can be thought of as relative "dehydration" and thick cords as a manifestation of increased fluid, which is why the latter is associated with hydramnios and hydrops.

Cord Length

* Short cords: less than 35 cm, as this is the minimum length needed to allow a vaginal delivery with a fundal placental implantation.
* Long cords are considered to be those greater than 70–80 cm.

* Short cords are associated with placental abruptio, cord hemorrhage, cord hematoma, cord rupture.

* Abnormally long cords can be associated with cord entanglement, cord prolapse, true knots, excessive coiling, constriction, and thrombosis.



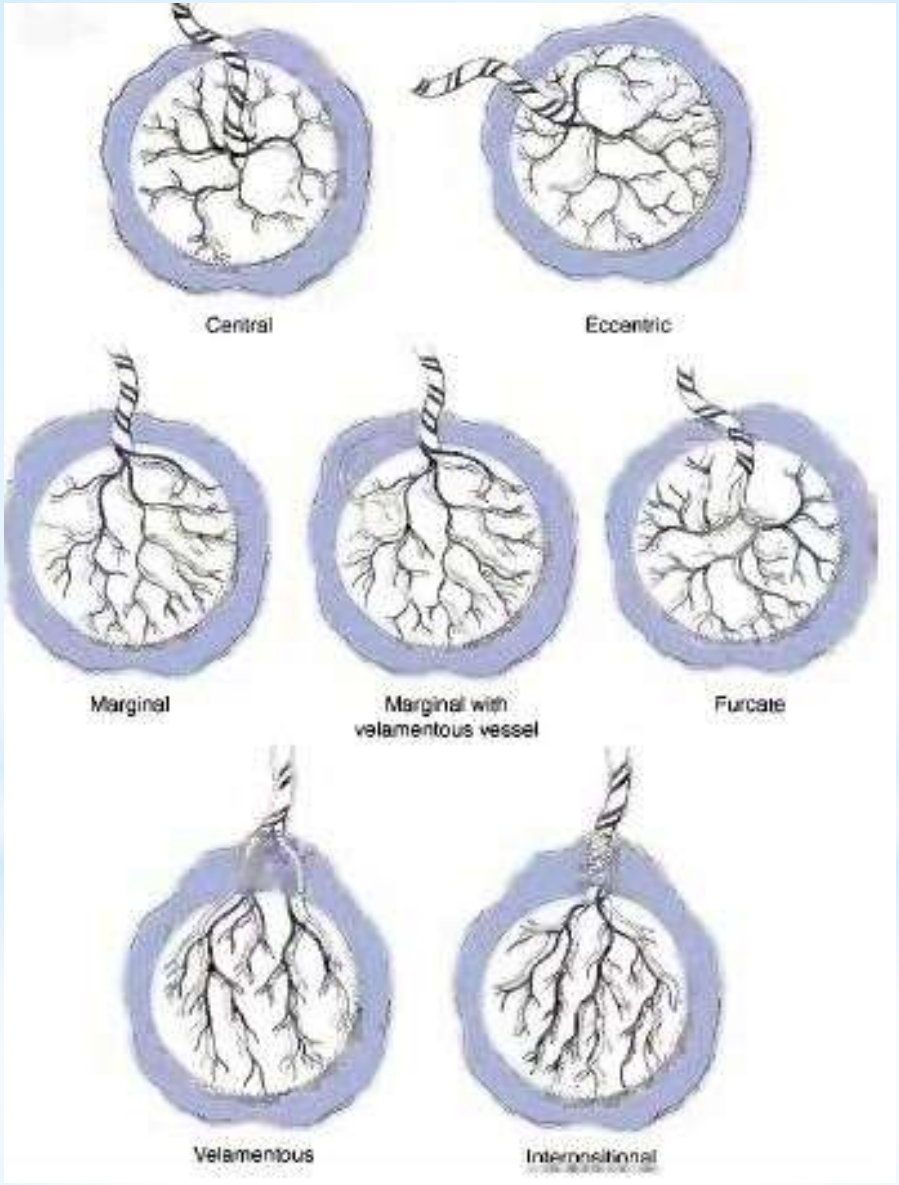
True knots of the umbilical cord may be loose or tight.

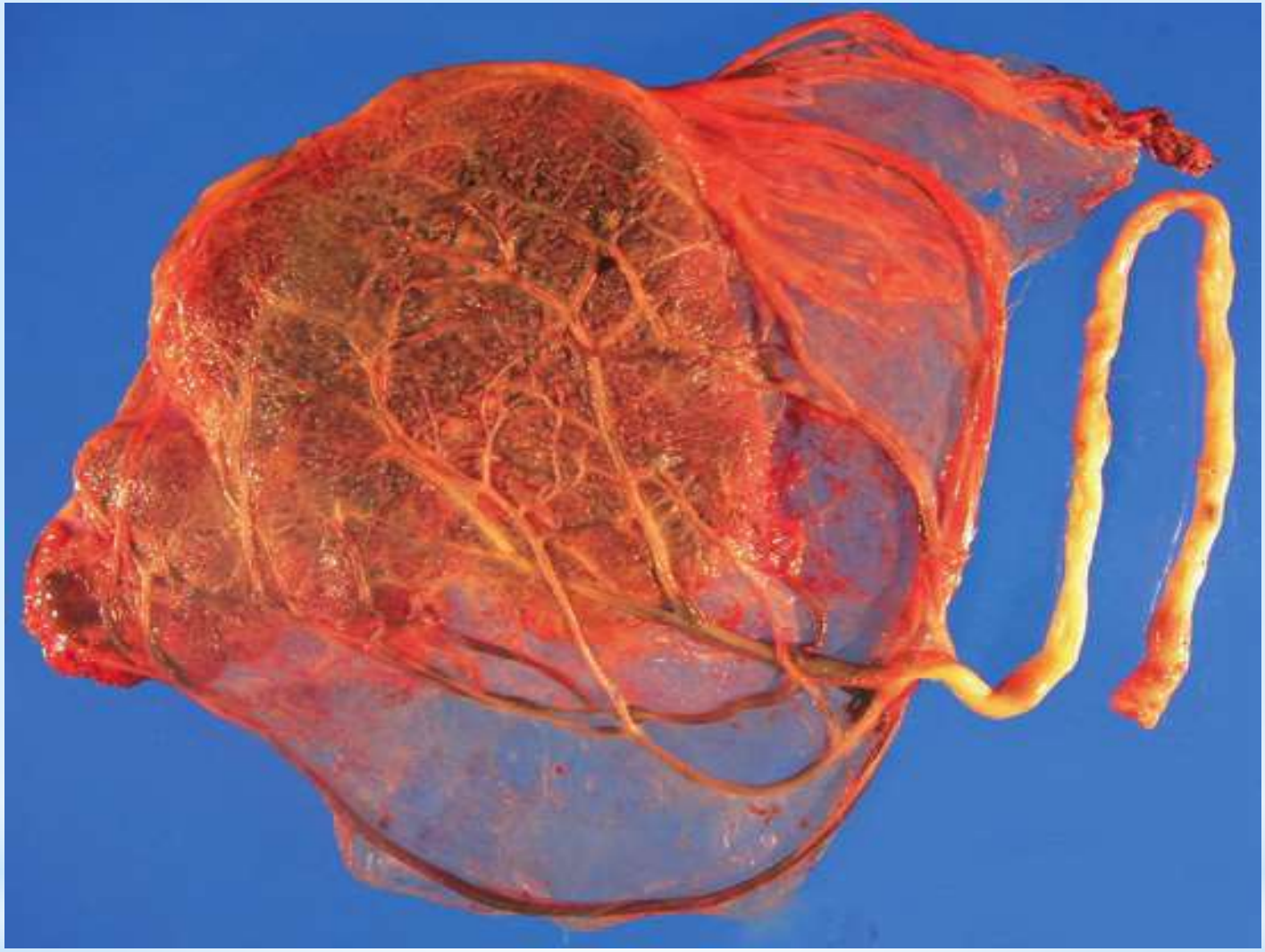
Tight true knots cause compression of Wharton's jelly at the site of knotting, congestion on the placental side of the knot (due to decreased venous return to the placenta), and tendency of the unknotted cord to curl (if the knot has been present for a period of time).

In clinically significant knots, the venous stasis that occurs often results in thrombosis of placental surface veins or even umbilical vein thrombosis.

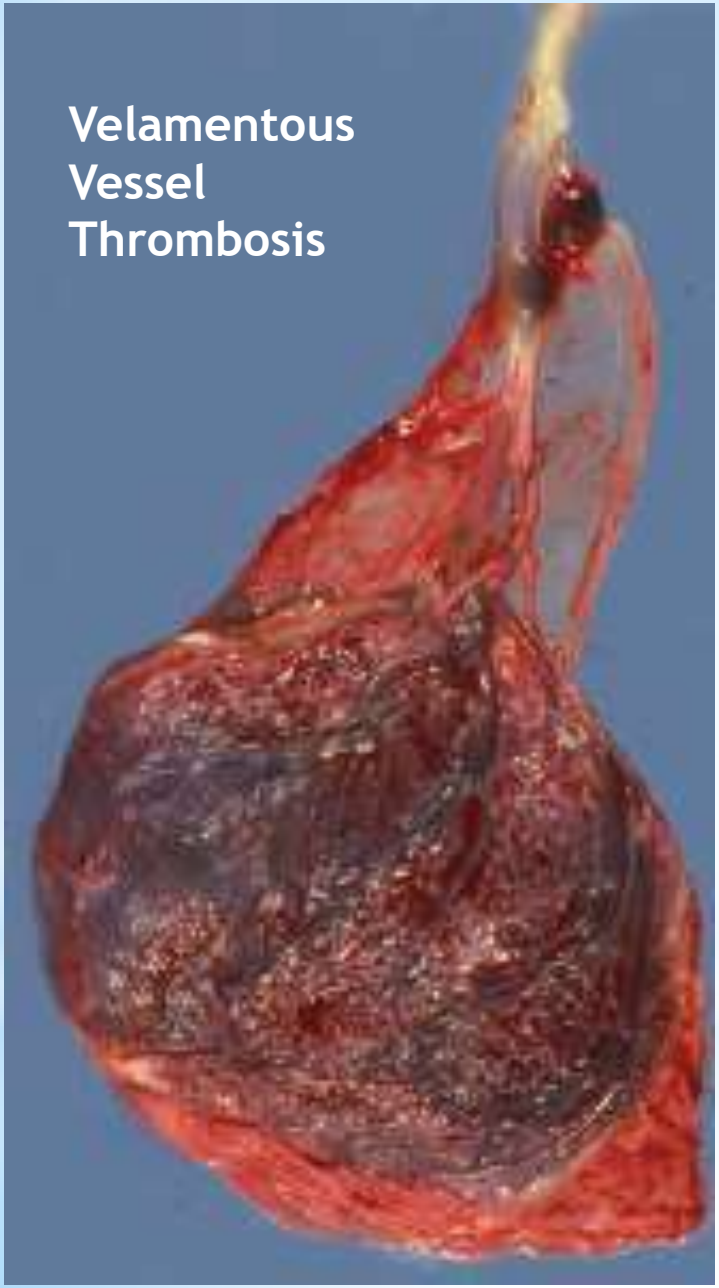
Mural thrombosis or complete occlusion may be found, and calcifications may occur in long standing thrombosis.

Site of insertion

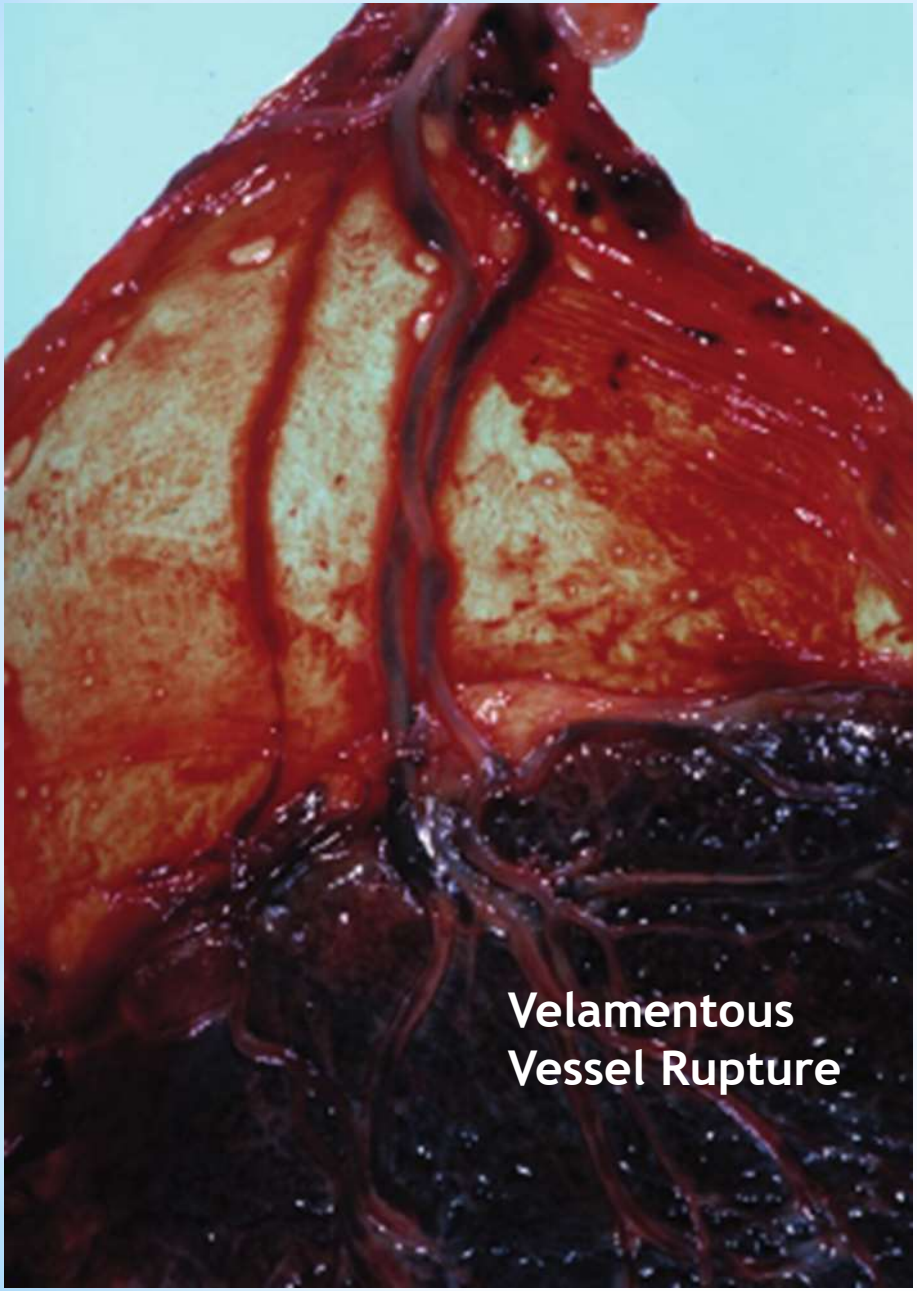




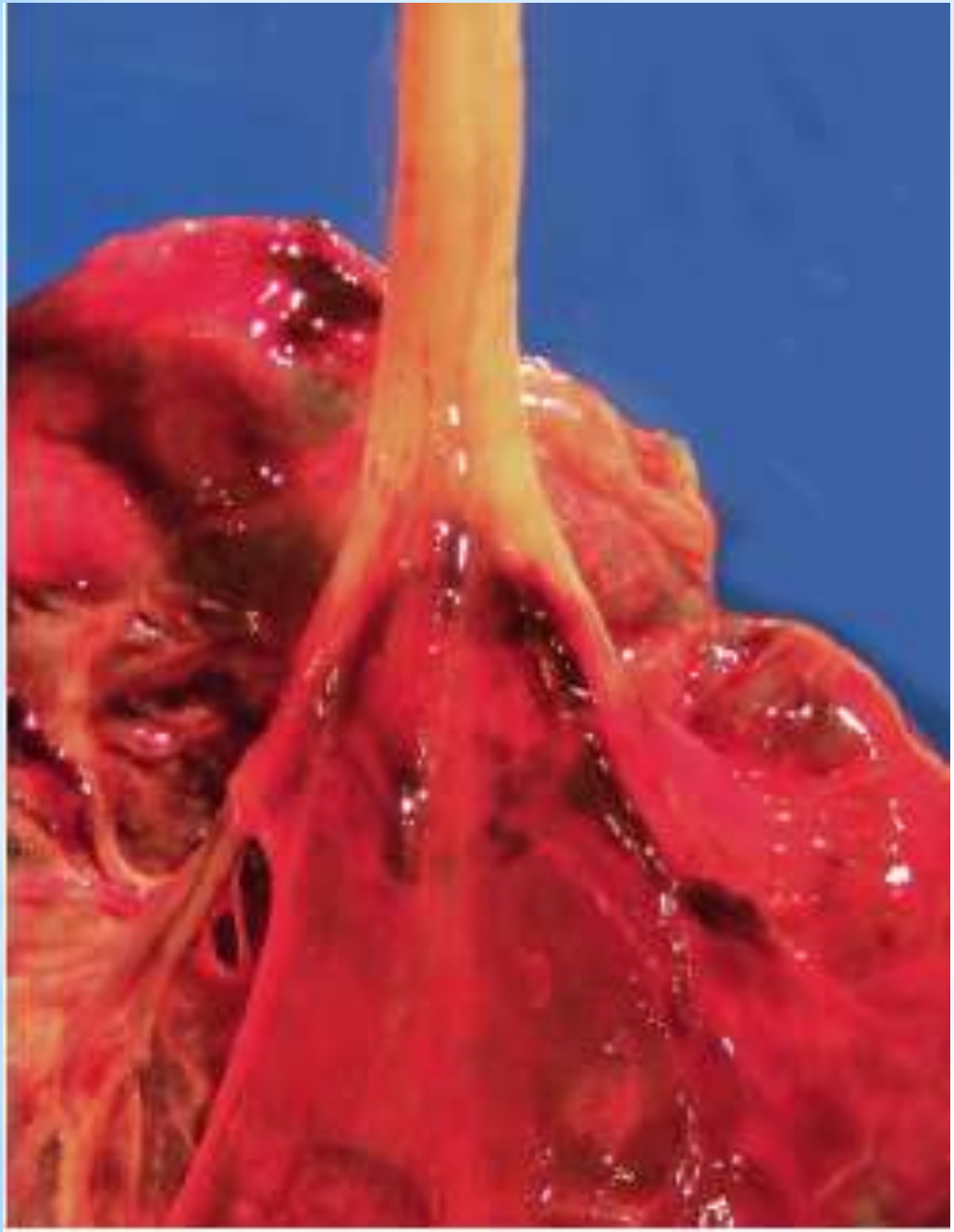
Velamentous insertion of umbilical cord. Note that the cord inserts relatively close to the placental margin but the course of the velamentous vessels is long as they branch out around the placental disk.



Velamentous vessels are susceptible to compression by fetal parts, resulting in obstruction of blood flow.

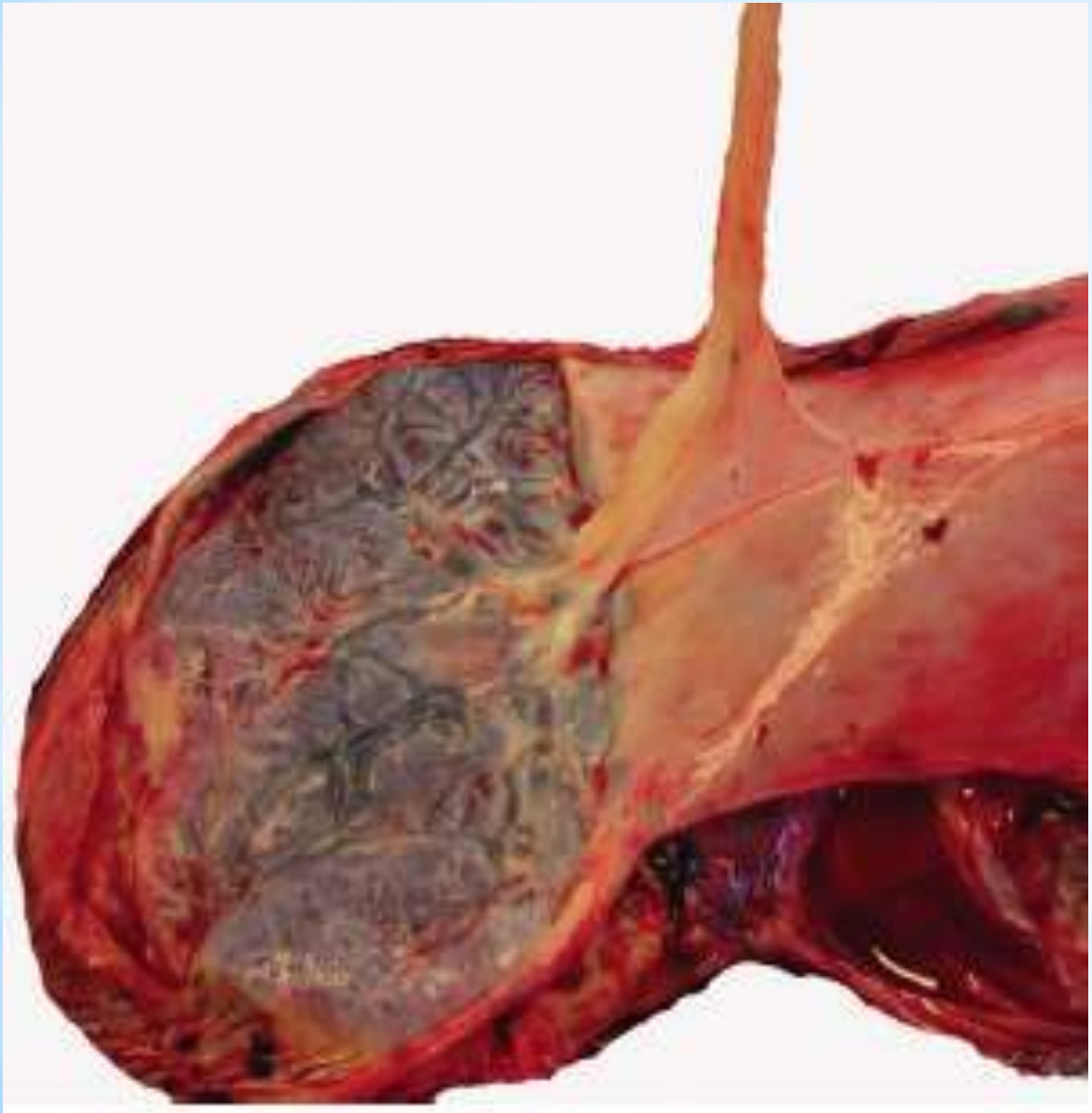


One of most serious complications of velamentous vessels is **vasa previa** in which membranous vessels are present over the internal cervical os. In this situation, membranous vessels may be disrupted by the exiting fetal head. *Exsanguination* from ruptured membranous vessels can proceed within minutes.



Furcate insertion of the umbilical cord.

This is a rare abnormality in which the *umbilical vessels split and separate from the cord substance prior to reaching the surface* of the placenta. They may lose the protection afforded by Wharton's jelly and are thus *prone to thrombosis and injury.*



Interpositional insertion of umbilical cord.
The cord does not divide but actually runs within the membranes before inserting onto the placental surface. The membranous portion of the cord has not lost the protection of Wharton's jelly..

Coiling

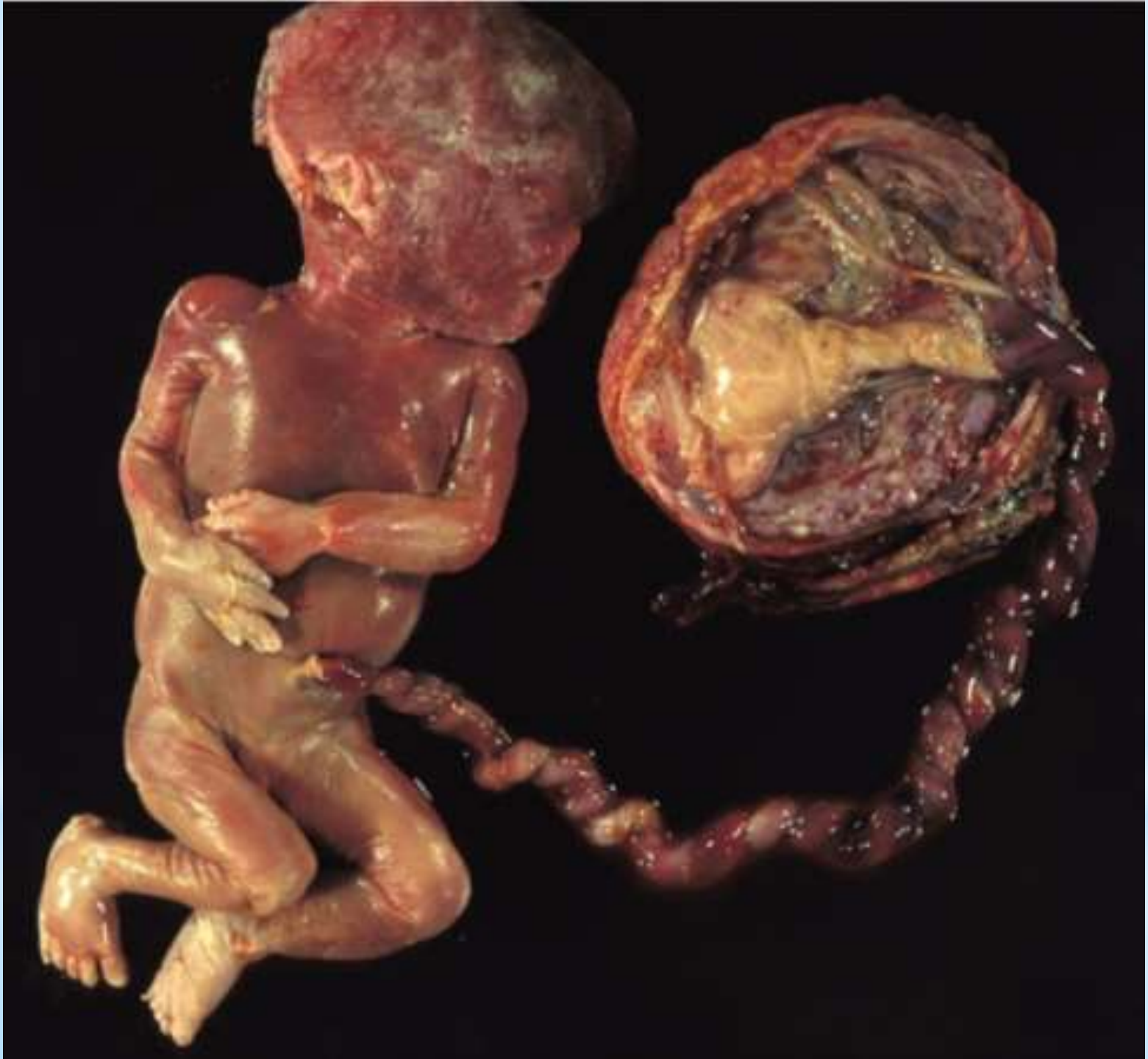
* The umbilical cord is usually **coiled**, **twisted**, **or spiraled**, more commonly in a counterclockwise direction (a “left” twist) in a ratio of about 4:1.
* The **coiling index** has been used to evaluate the degree of twisting, defined as *the number of coils divided by length of cord*. The average coiling index is 0.21/cm or one complete spiral for approximately 5 cm of cord.
* **Noncoiled**
* **Hypocoiled**
* **Hypercoiled**
* Twisting of the cord is thought to be the result of fetal activity.
* Lack of coiling may then reflect fetal inactivity, and this concept is supported by the fact that coiling is reduced in cases of restriction of fetal movement due to intrauterine constraint from uterine anomalies or amnionic bands, anomalies that restrict fetal movement such as skeletal dysplasias, and diminished fetal movement resulting from central nervous system (CNS) disturbances.

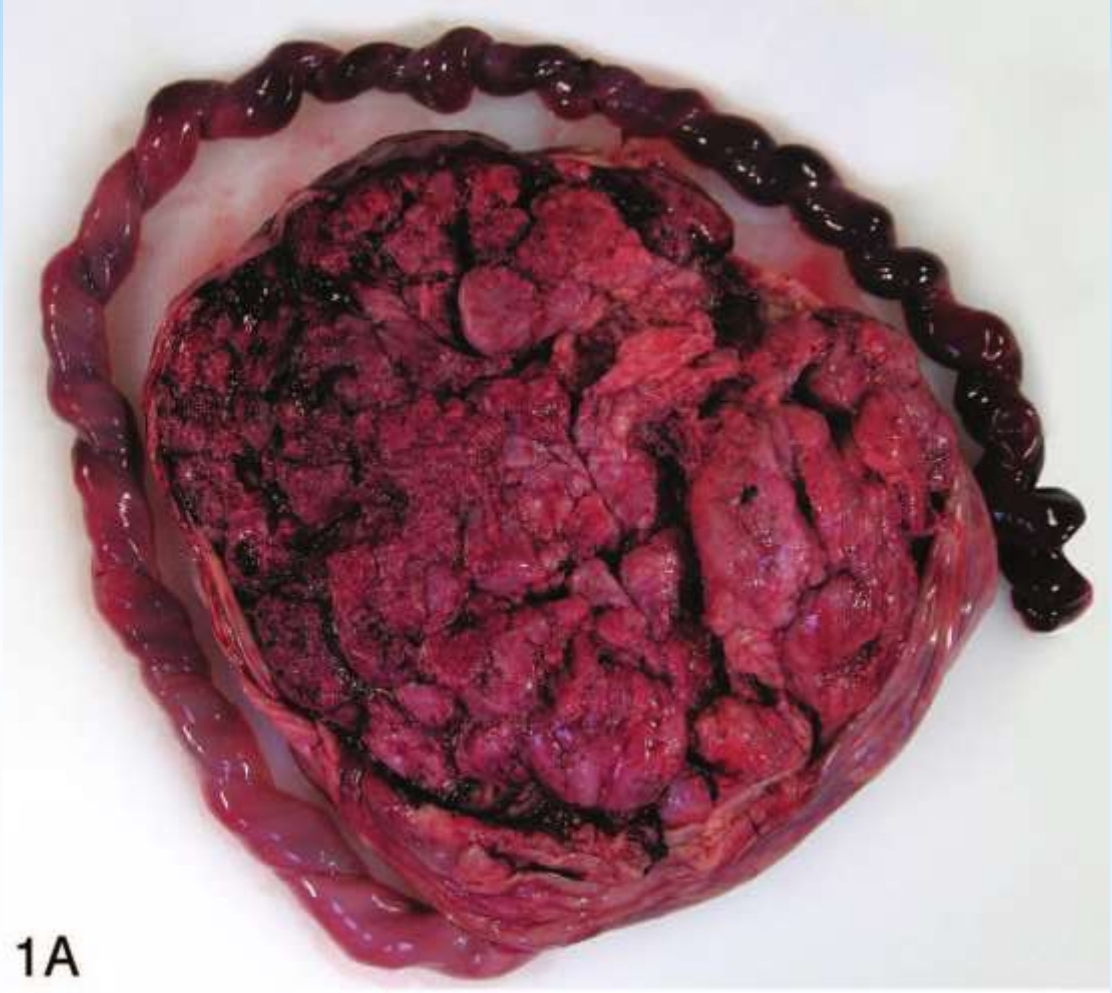
Hypocoiling and hypercoiling are both associated with adverse perinatal outcome.

Hypercoiling and constrictions are often seen together and have a strong correlation with fetal demise due to mechanical obstruction of blood flow through the cord (thrombosis).

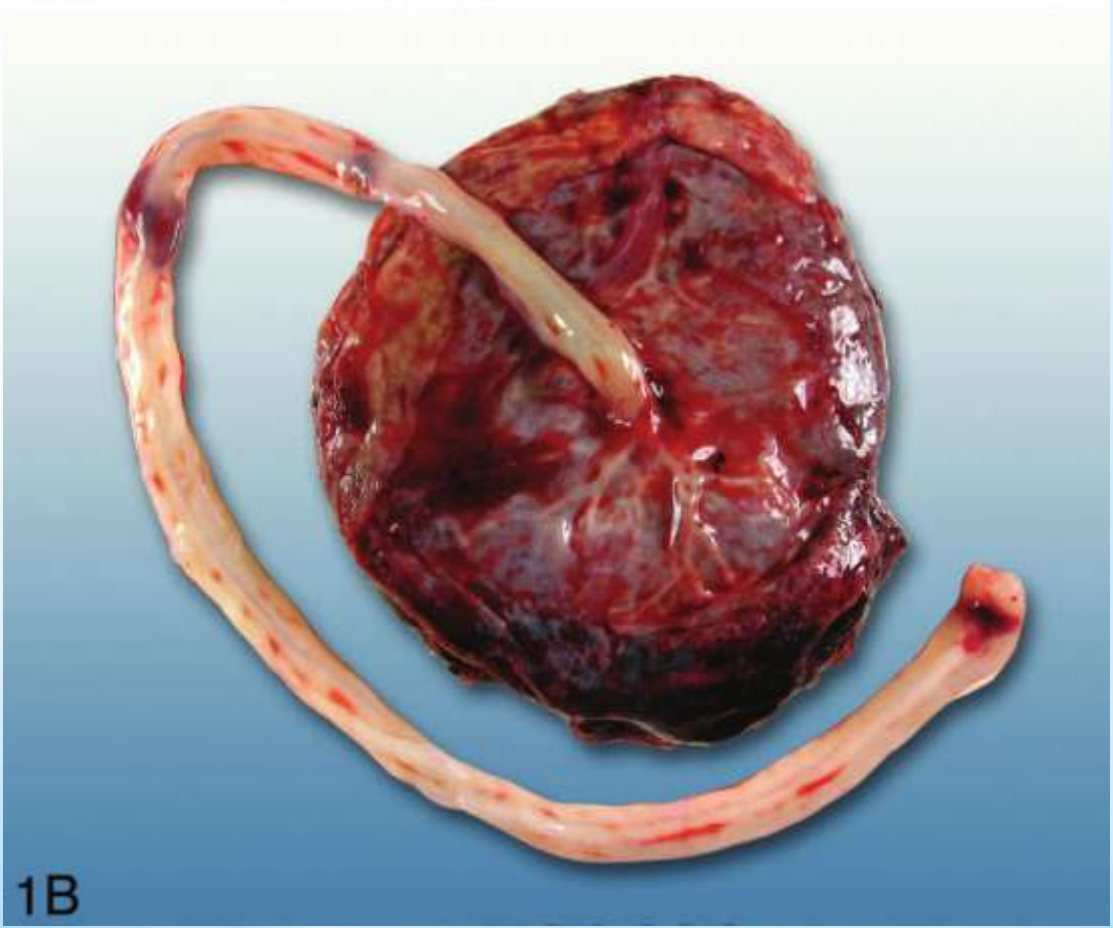
If a stricture is present in the setting of a fetal demise and there is evidence of venous obstruction, such as thrombosis, the constriction can be considered the cause of death.

If supporting histologic findings are not present, the constriction may be suggested as a cause of demise.





1A

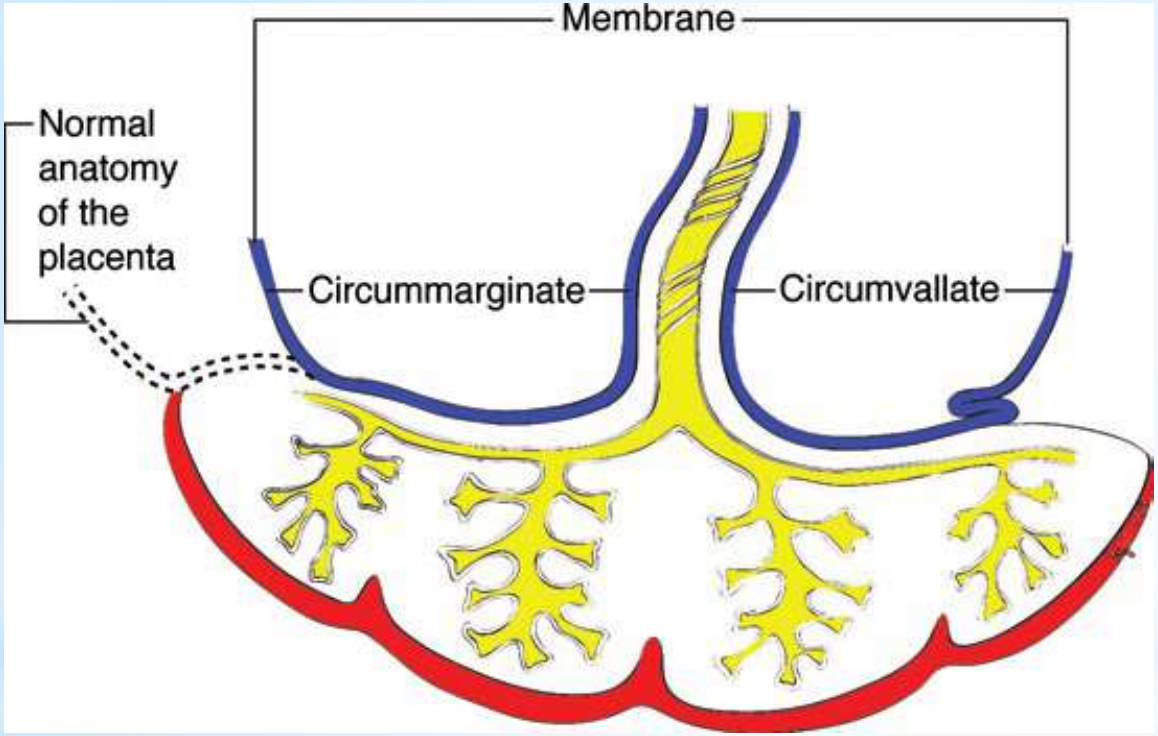


1B

Membranes

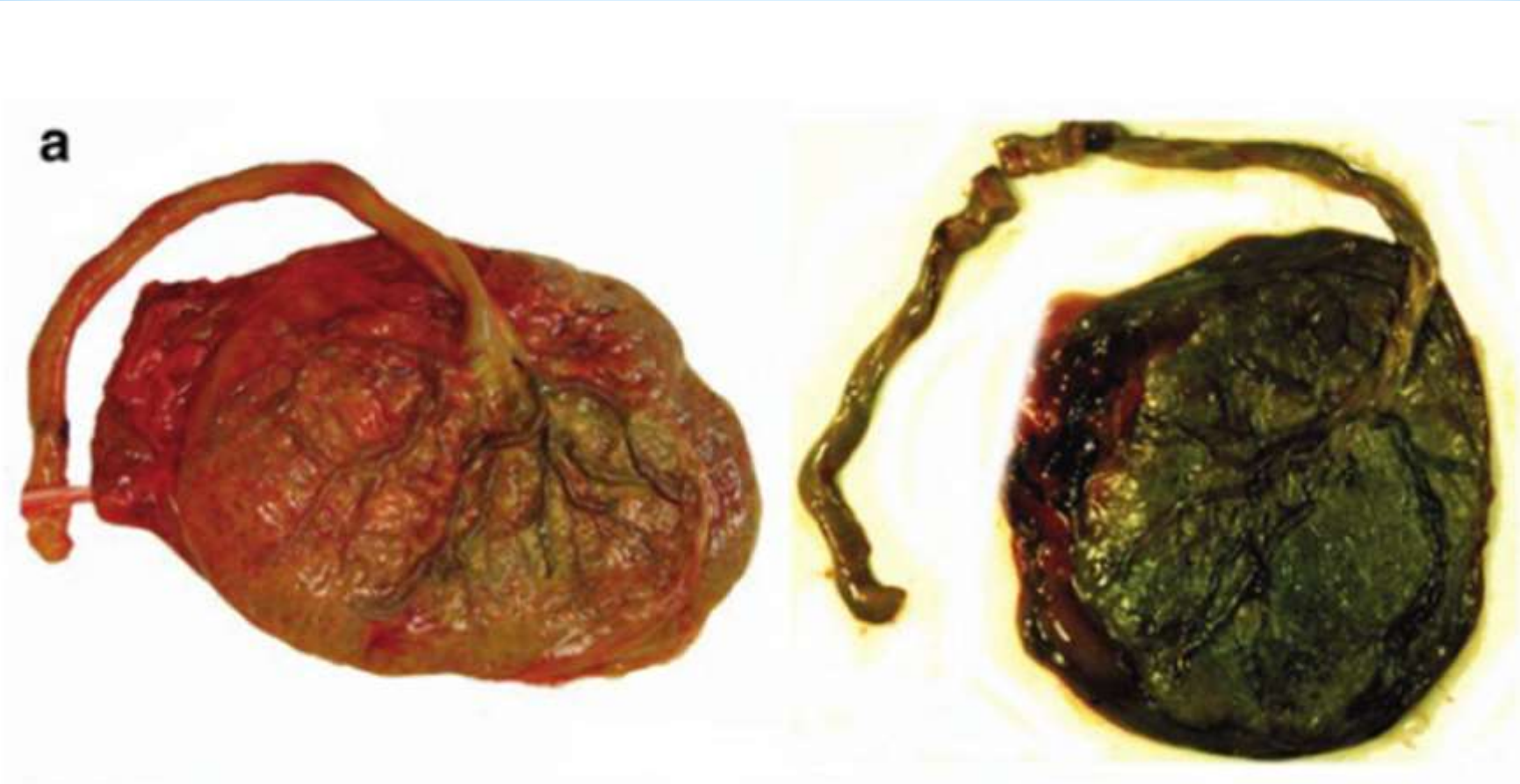
- Insertion
- Pigments:
  - Meconium
  - Hemosiderin

Circumvallate and Circummarginate Placentas

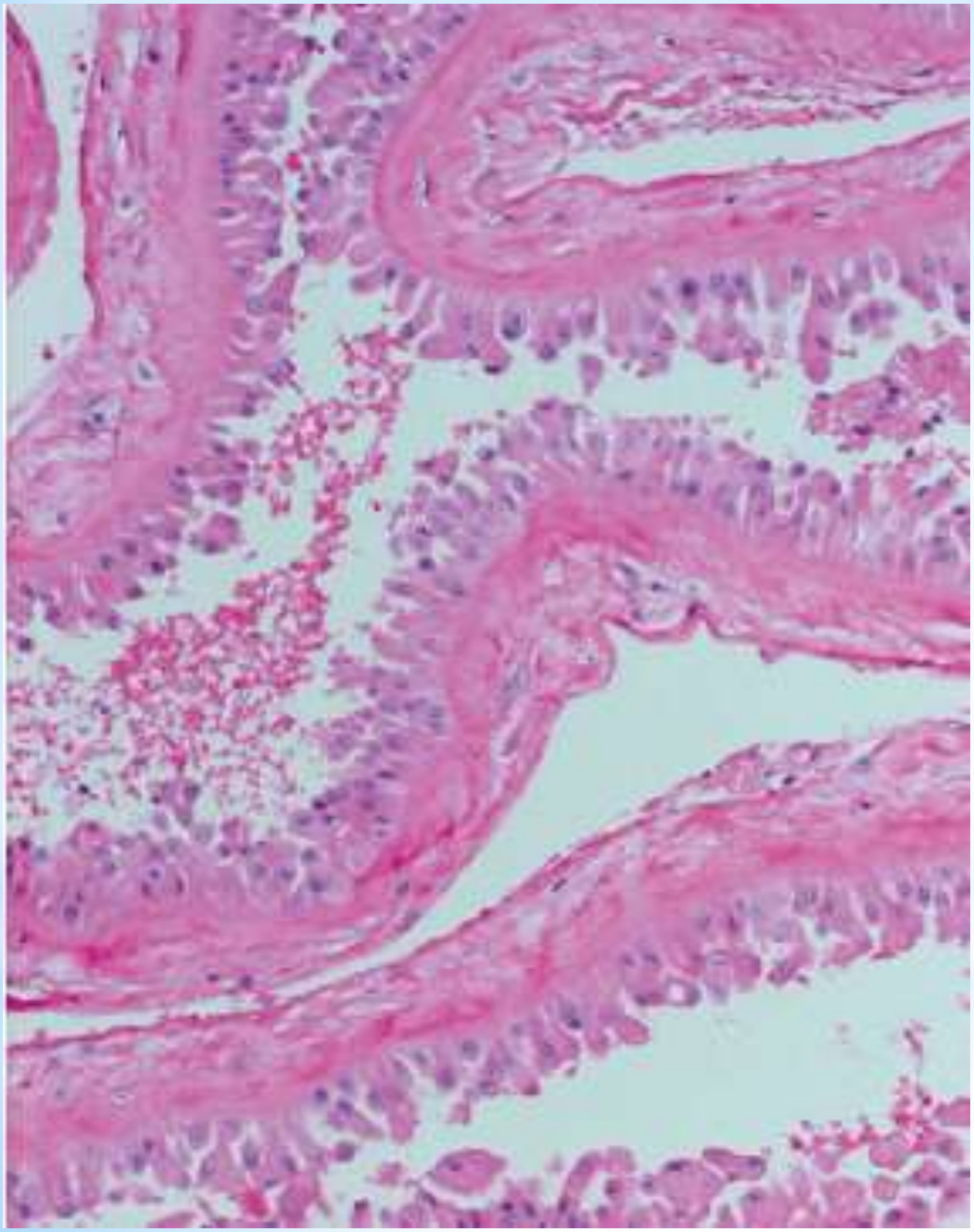


The incidence of circumvallation is from 1.0 to 6.5% and the incidence of circummargination is up to 25% of placentas. The most common complications of **circumvallation** are antenatal bleeding and premature delivery.
Additional, uncommon associations include premature membrane rupture, oligohydramnios, non-reassuring fetal status, abruption, perinatal or **intrauterine death**, congenital anomalies, single umbilical artery, and intrauterine growth restriction. Cases with **extensive hemorrhage and marginal hematomas** may lead to significant clinical bleeding.

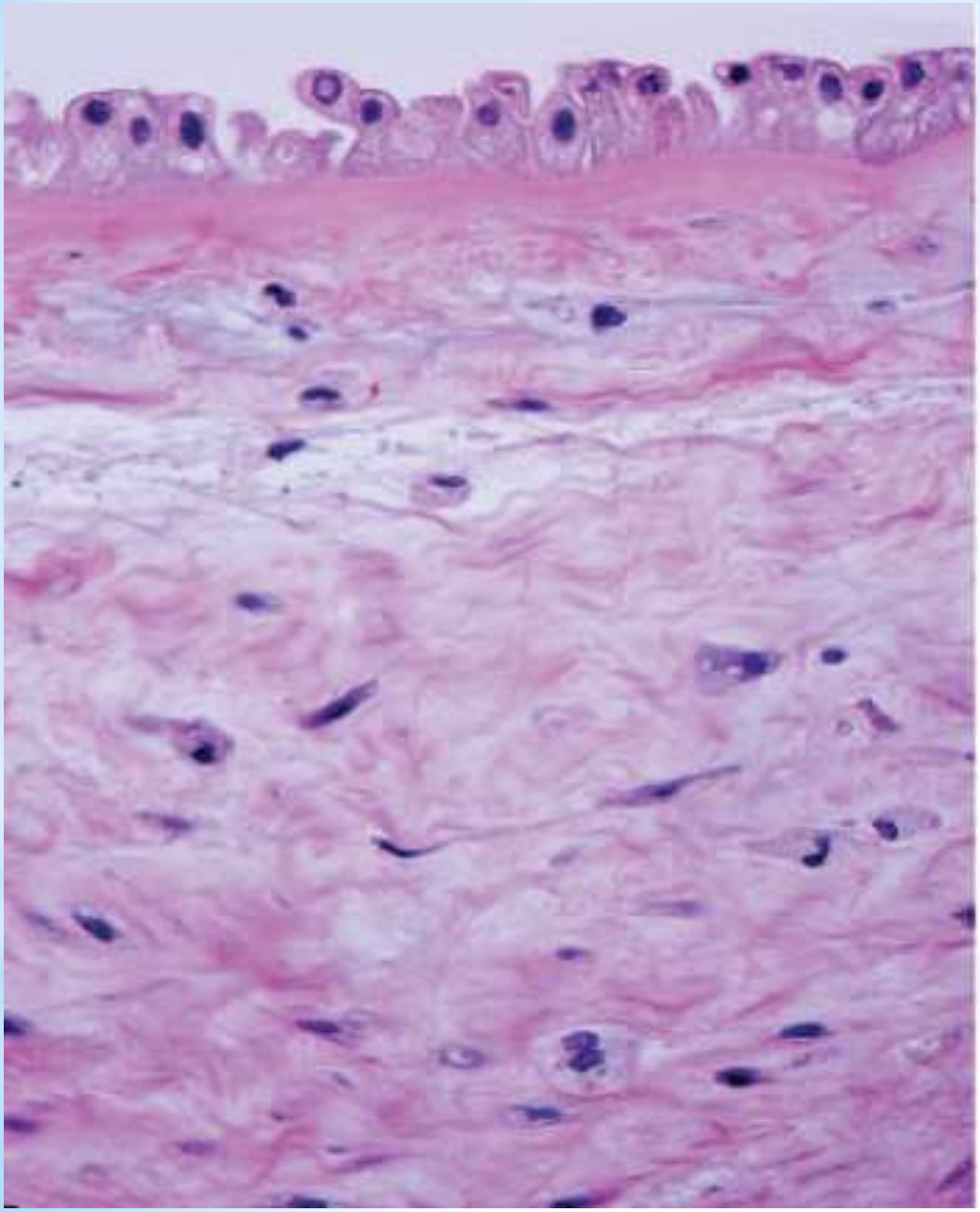
Circummarginate and circumvallate membrane insertion.
In both, the fetal membranes do not insert at the edge of the placenta but rather at some point inwards. In circumvallation there is a plication of the membranes evident as a fibrin ridge on gross examination. In circummargination, the membrane insertion is flat and a ridge is not present.



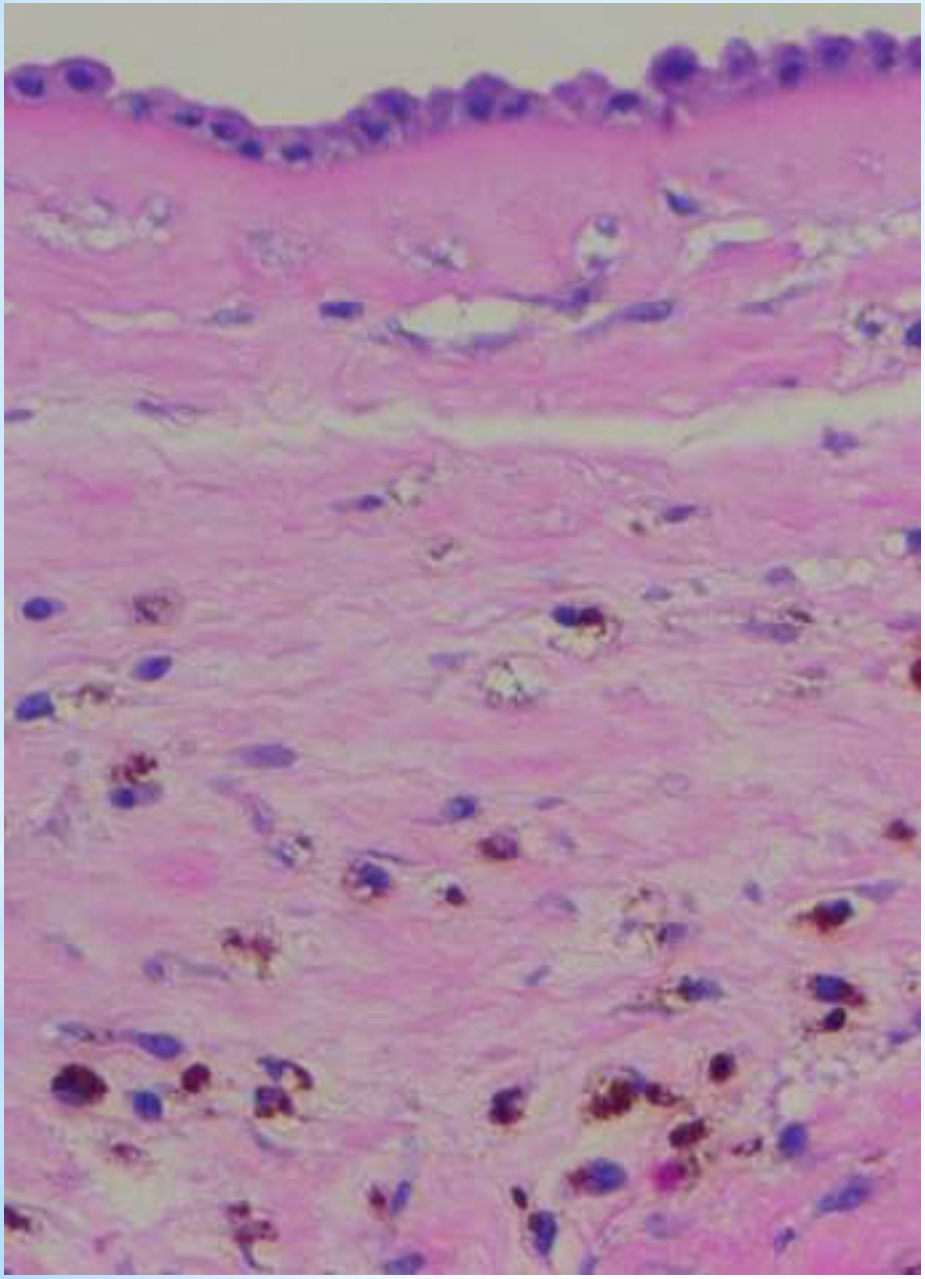
When meconium is discharged before parturition, *the baby and placenta may be meconium-stained and deeply green*.



Meconium induced degenerative change of the amnion. Note the piling up of the epithelium.



Meconium laden macrophages within the amnion and chorion.



Hemosiderin laden macrophages in the fetal membranes showing yellow-brown particulate material. The nature of this pigment must be confirmed with iron stain.

Maternal Vascular Malperfusion of the placental bed

Pathology of the uteroplacental circulation, beginning with maladaptation of placental bed spiral arteries, leads to reduced perfusion of the intervillous space.

Placental features considered to be indicative of MVM include both gross and microscopic findings.

Gross findings include infarction and retroplacental hemorrhage.

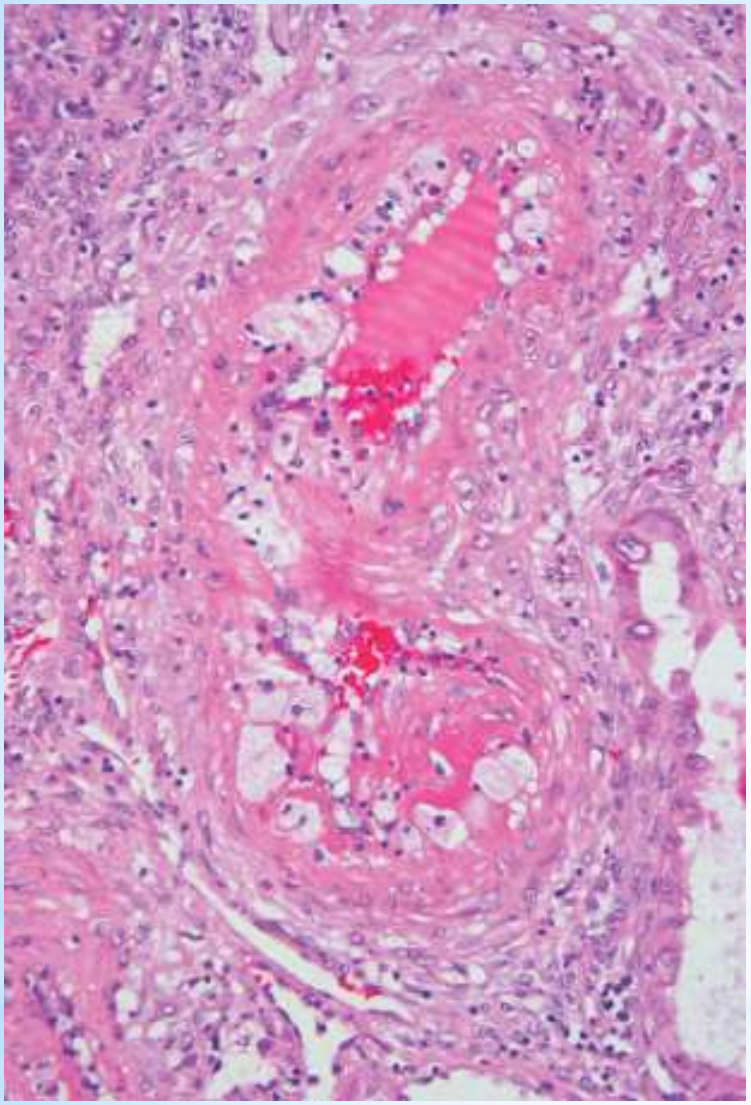
Microscopic findings include abnormalities of decidual arteries (decidual arteriopathy) and of villous development (distal villous hypoplasia, accelerated villous maturation).

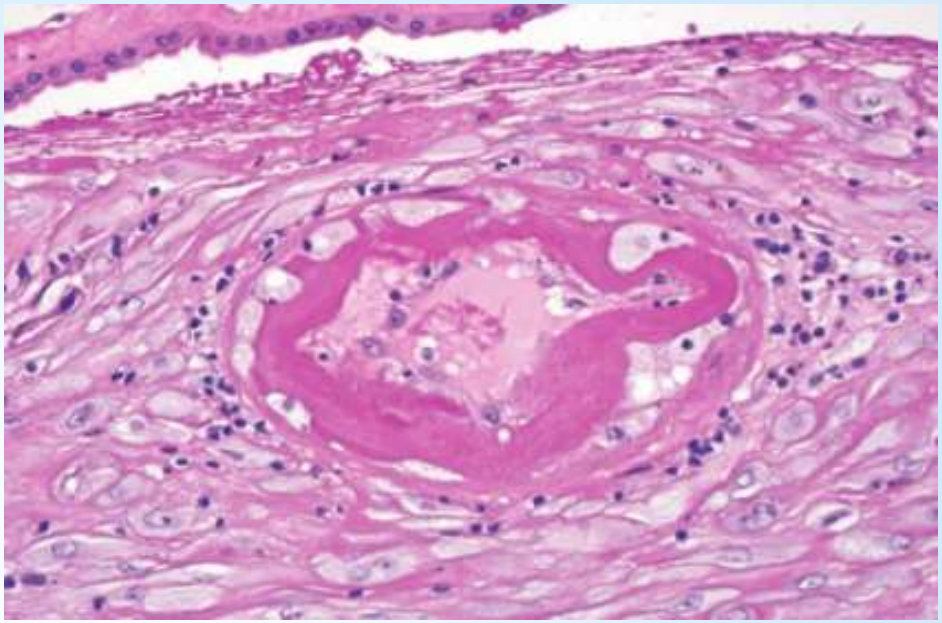
Decidual Arteriopathy

These lesions are the underlying cause of the other placental changes such as infarcts and abruptios.
The location should be stated as whether it is in the membrane roll or basal plate or both.

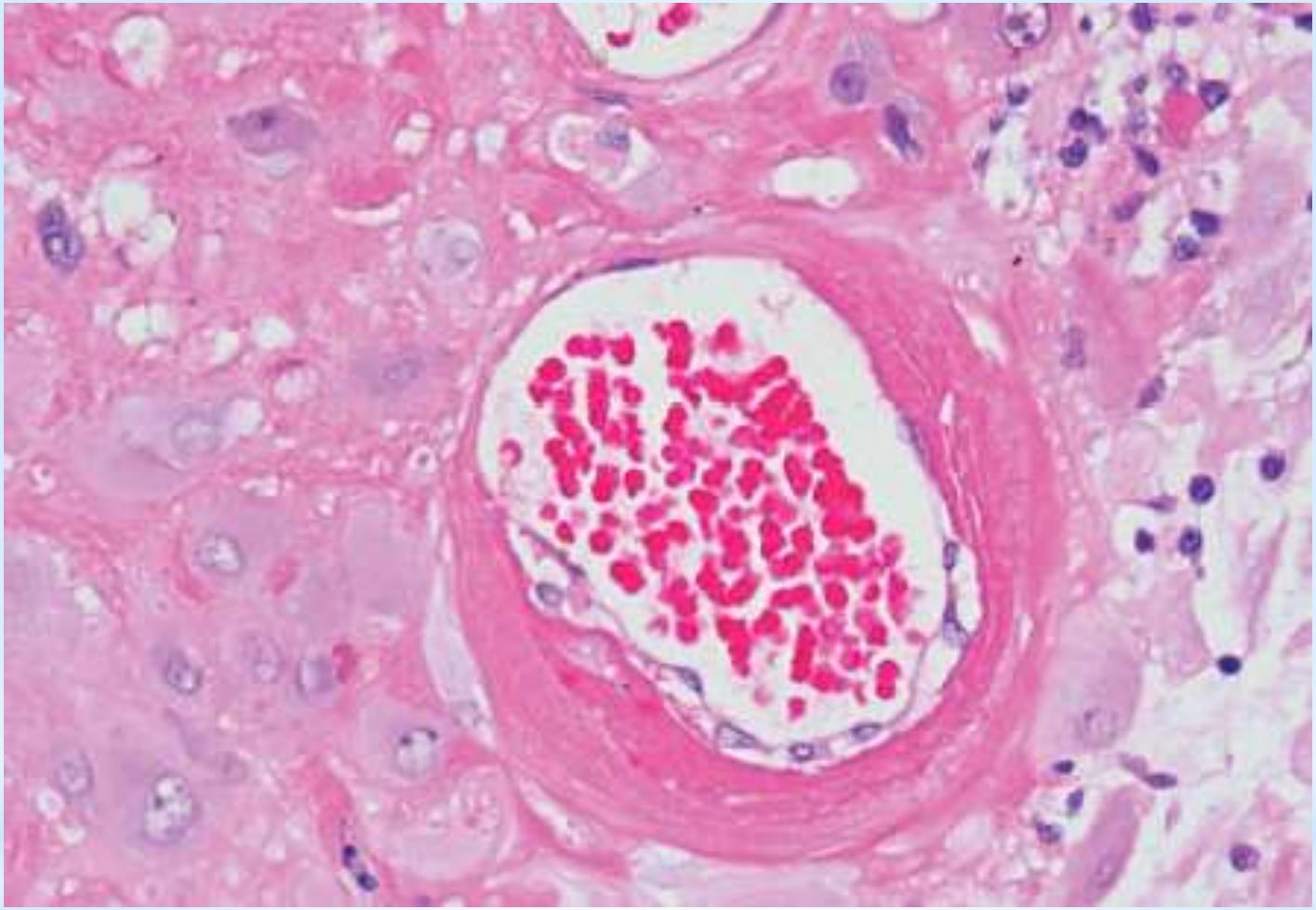
The lesions include:

- acute atherosis
- fibrinoid necrosis with or without foam cells
- mural hypertrophy
- chronic perivasculitis
- absence of spiral artery remodeling
- arterial thrombosis
- persistence of intramural endovascular trophoblast in the third trimester

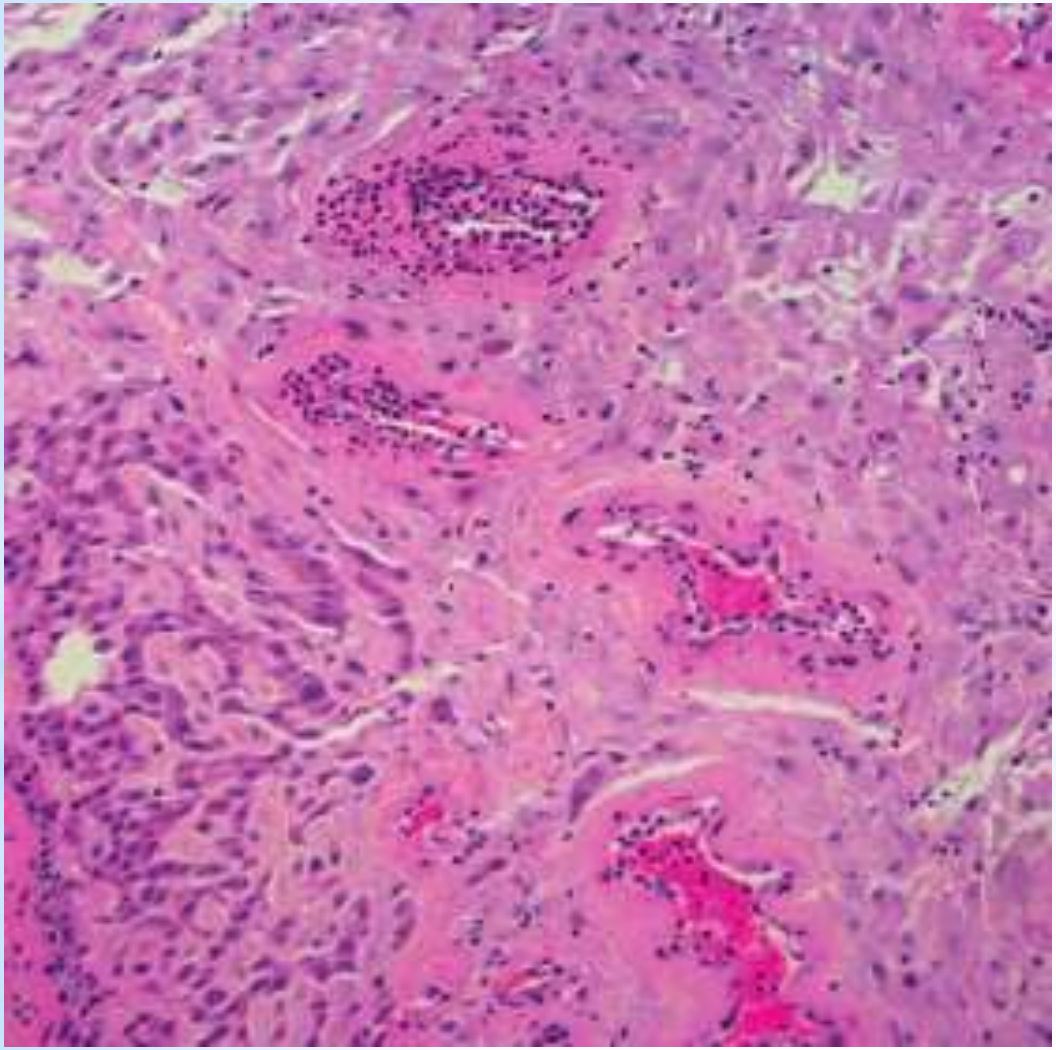




Atherosis in decidual arterioles. The vessel wall has been replaced by fibrin, the intima replaced by cholesterol laden macrophages, and there is early mural thrombosis.



Fibrinoid necrosis of small maternal artery without an accompanying lipophage or lymphocytic component.

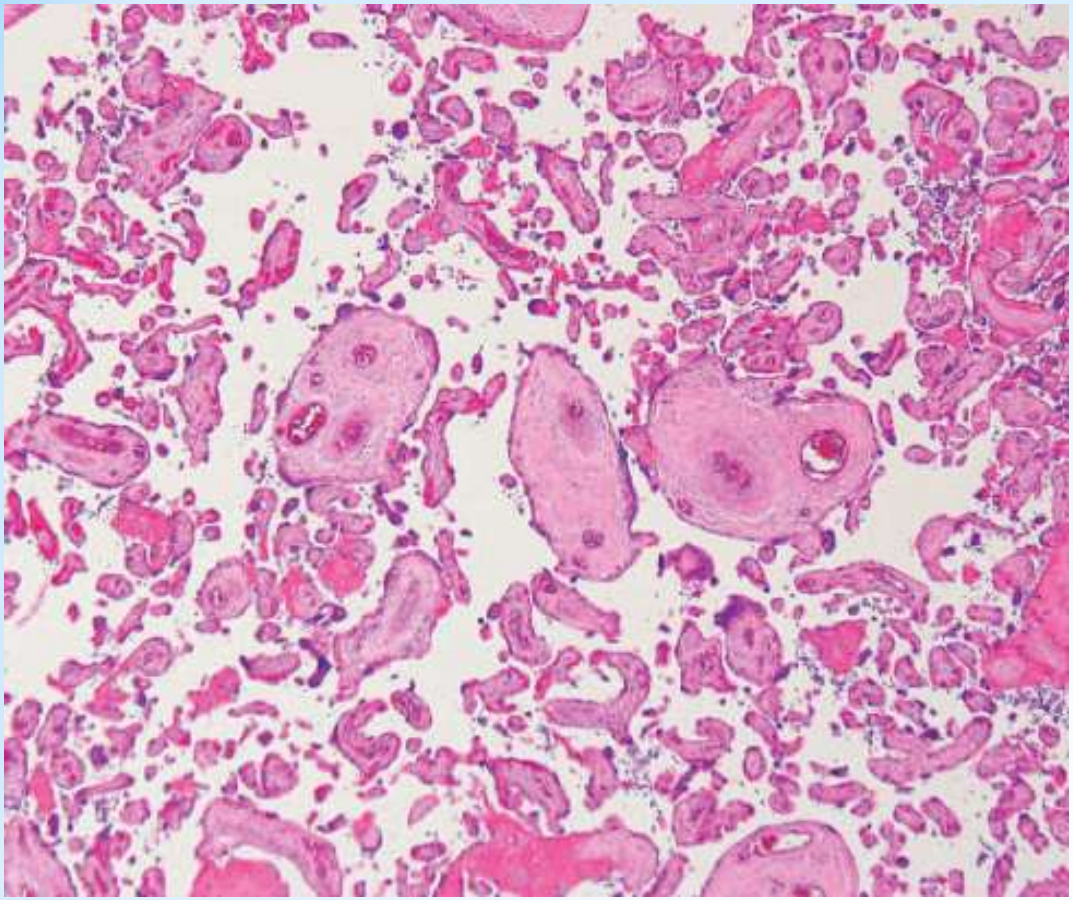


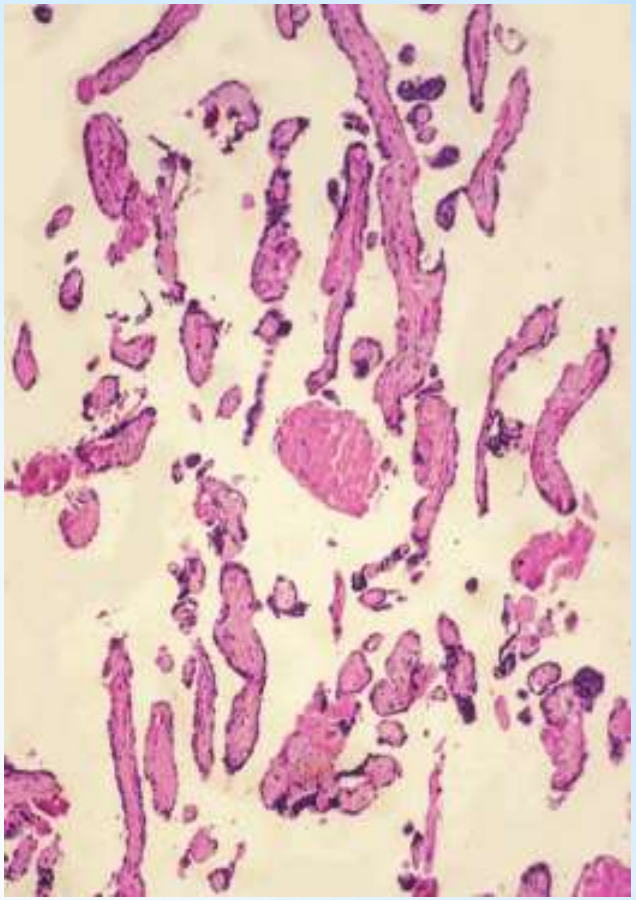
Lymphocytic decidual perivasculitis and mural hypertrophy

Distal Villous Hypoplasia

Distal villous hypoplasia (DVH) is defined as the paucity of villi in relation to the surrounding stem villi. The villi are thin and relatively elongated-appearing.

The diagnosis should Be made when the features are seen in the lower two-third (retrodecidual) and involve at least 30% of 1 full-thickness parenchymal slide.



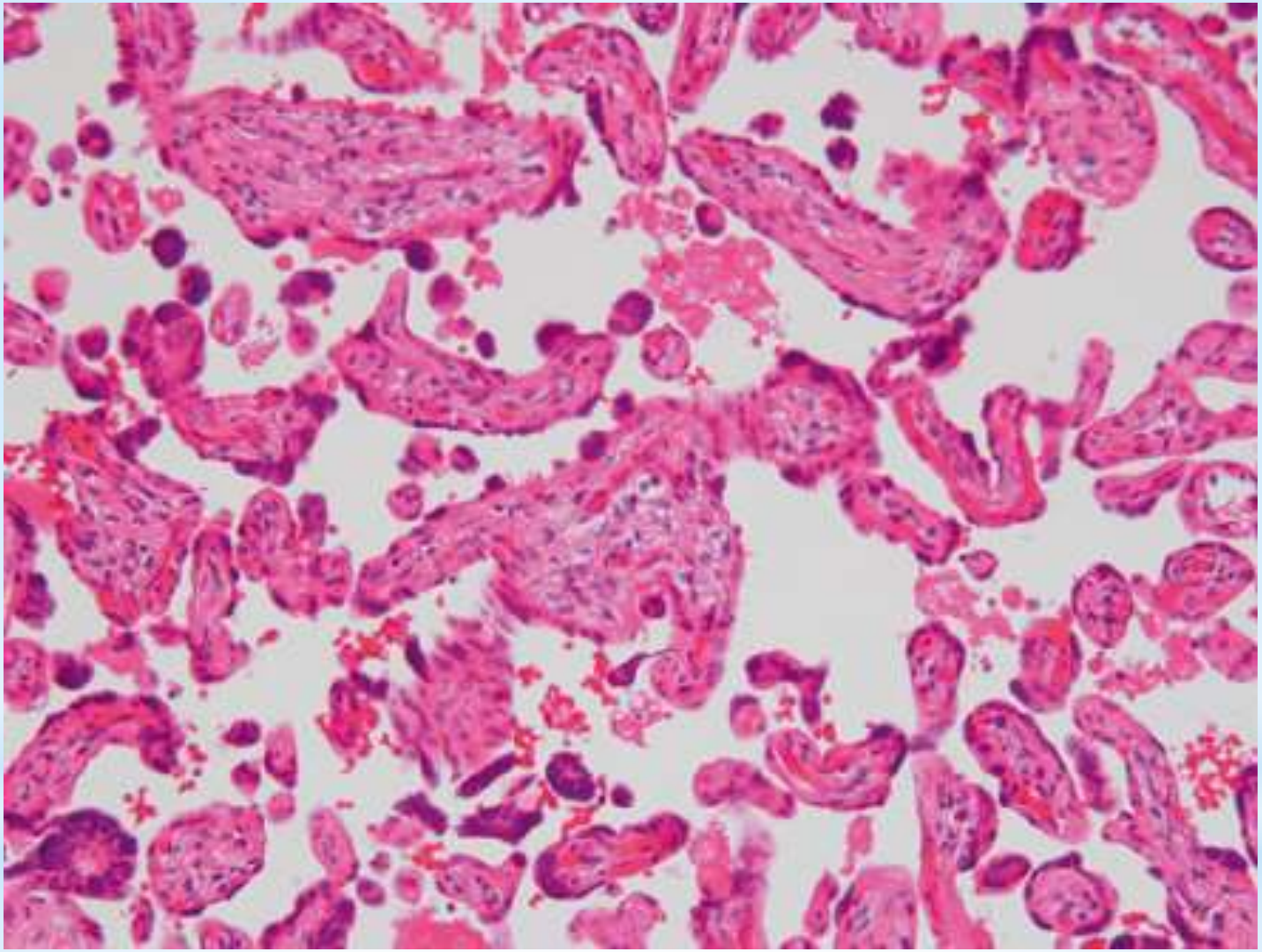


In DVH there is a predominance of small villous calibers and filiform longitudinal profiles and an unusually wide intervillous space.

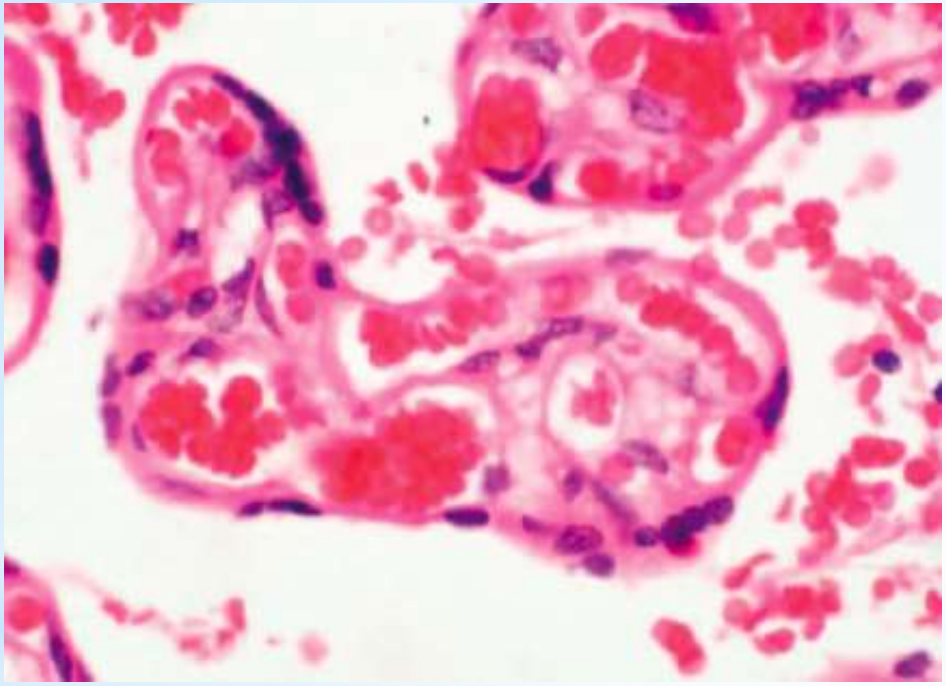
Accelerated Villous Maturation

Accelerated villous maturation is defined as the presence of small or short hypermature villi for gestational period, usually accompanied by an increase in syncytial knots.

It may be difficult to recognize in a term placenta, but it is a reproducible pattern to diagnose prior to term. It is diagnosed by identifying a diffuse pattern of term-appearing villi with increased syncytial knots and intervillous fibrin, usually alternating with areas of villous paucity.

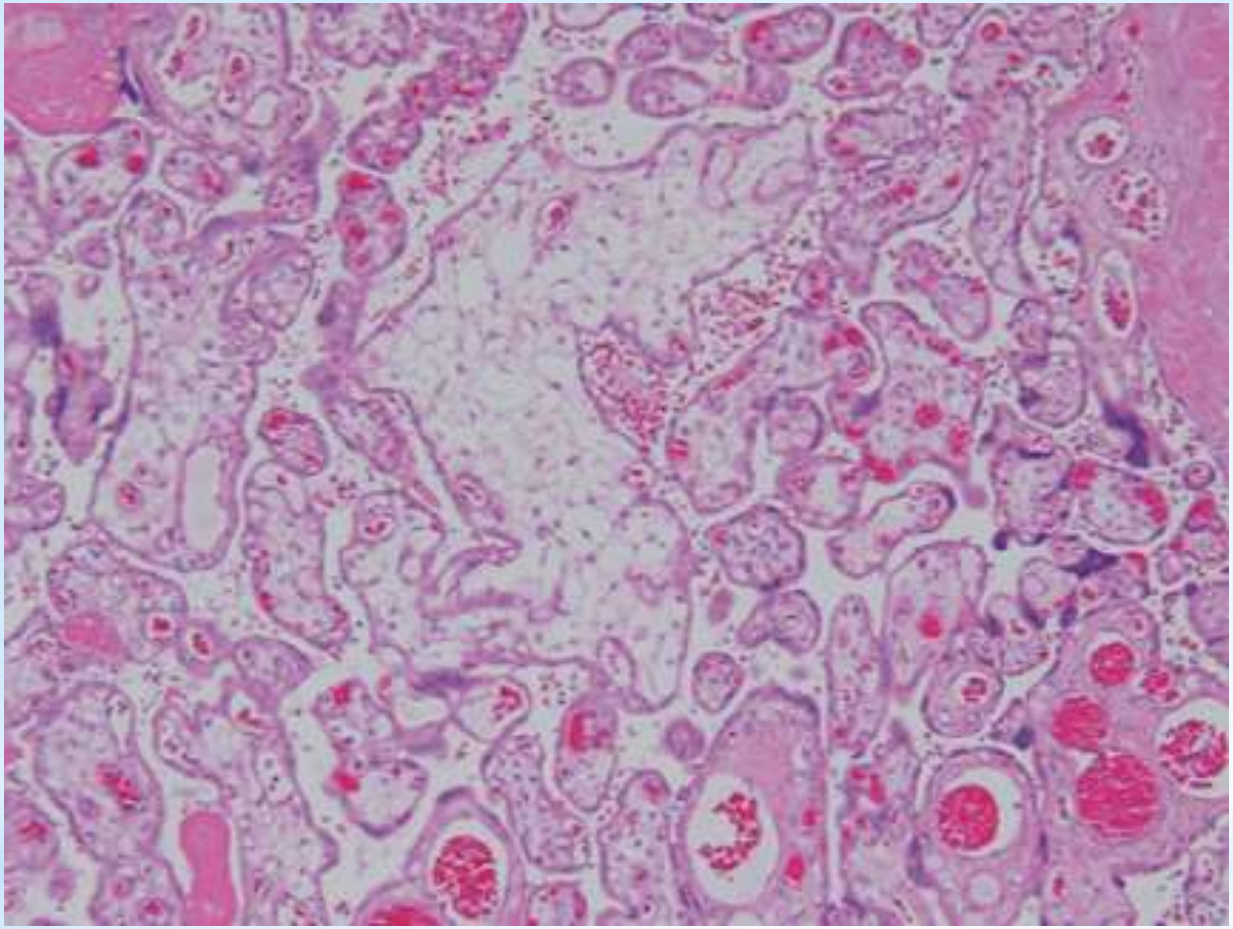


Delayed Villous Maturation

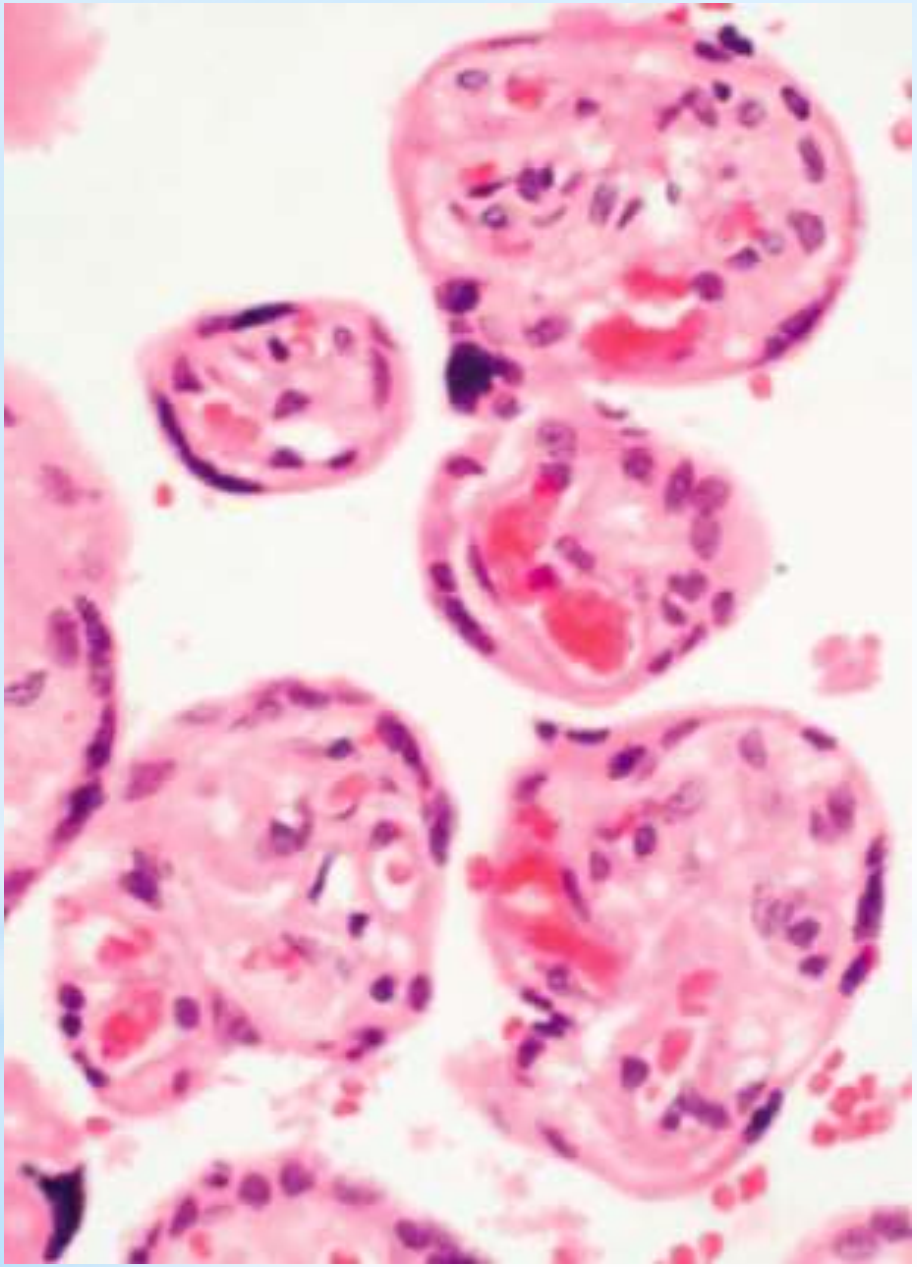


Terminal villi: abundance of vasculo-syncytial membranes.

Vasculo-syncytial membranes are composed of fetal capillary walls located near the trophoblast basement membrane and a thin layer of trophoblast cytoplasm and facilitate optimal gas exchange.



On low-power magnification, the villi are enlarged with increased stromal cellularity and extracellular matrix.



On higher-power magnification, many capillaries are not peripherally located, resulting in a decrease in VSM. The villous trophoblast surrounding the villous appears thickened and hypercellular.

Fetal Vascular Malperfusion

The lesions are likely to be due to obstruction in fetal blood flow (eg, umbilical cord lesions, hypercoagulability, complications of fetal cardiac dysfunction).
Findings consistent with FVM are *thrombosis, segmental avascular villi, and villous stromalvascular karyorrhexis*.

Thrombosis would be considered to be a premortem process.

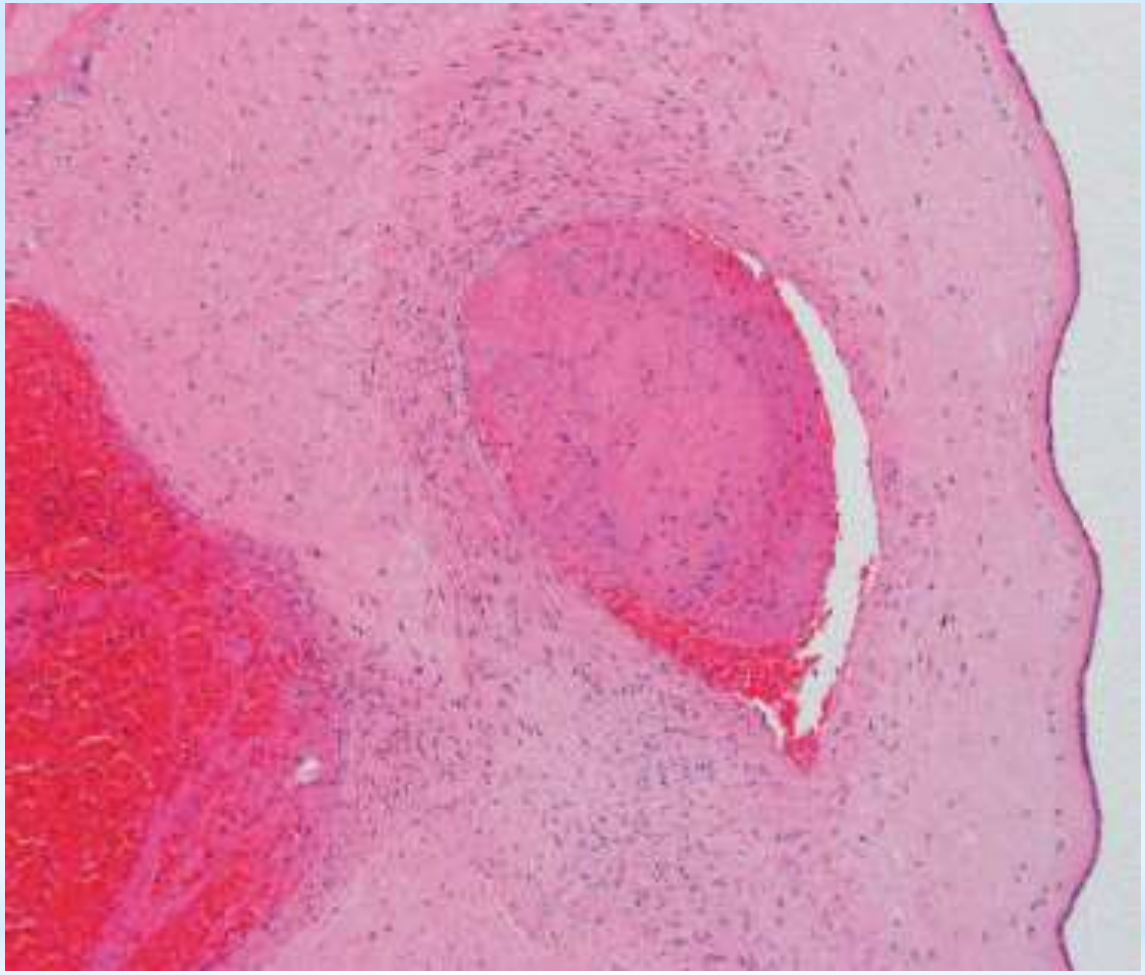
Low Grade FVM

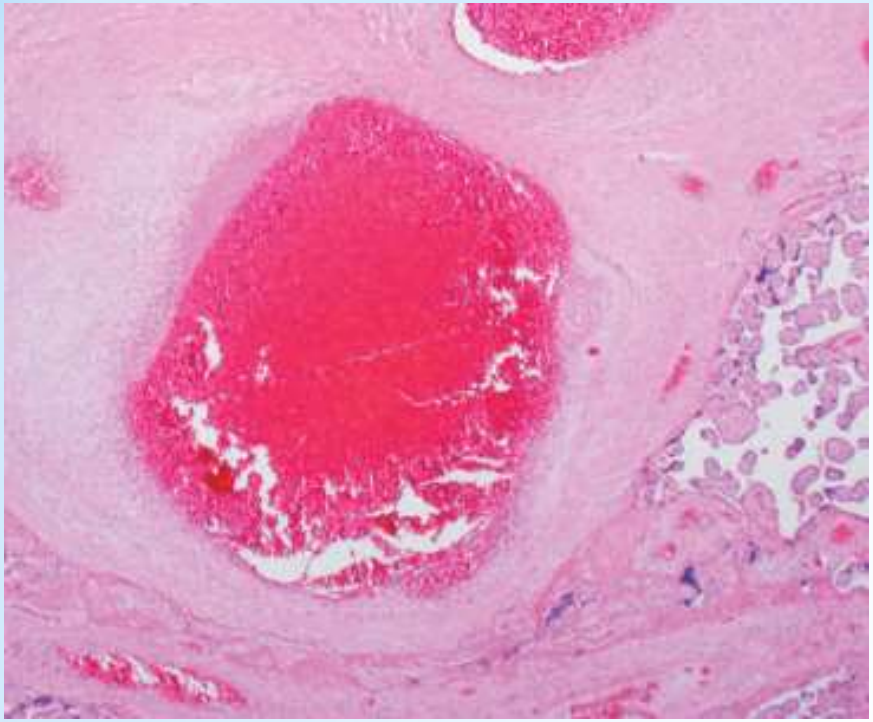
This is segmental FVM with thrombotic occlusion of chorionic or stem villous resulting in complete blood flow impairment to the villi downstream.

High Grade FVM

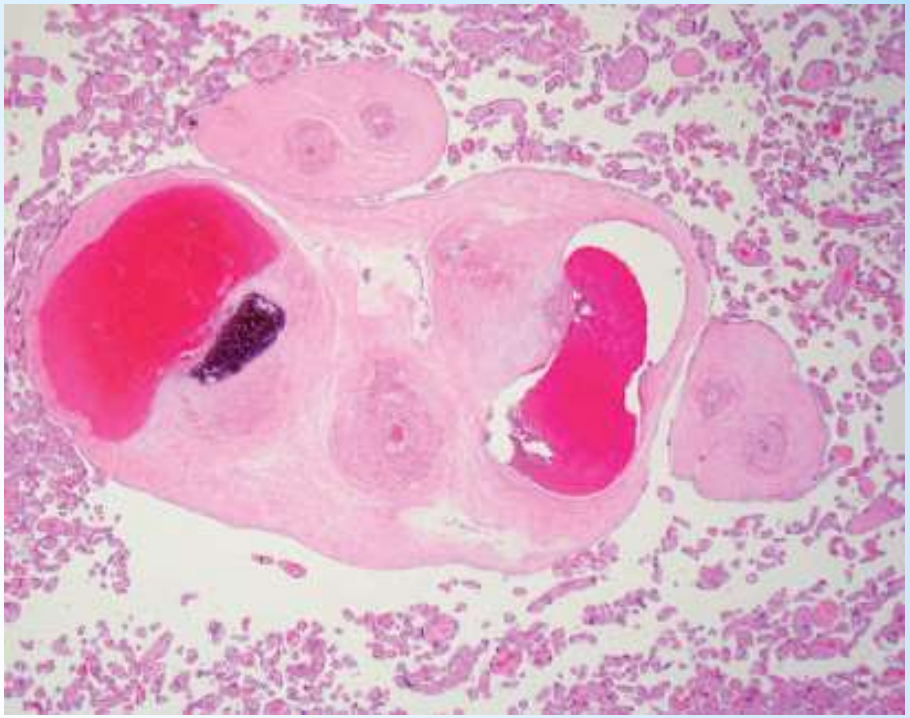
This is global FVM, indicating partially obstructed umbilical blood flow with the finding of more than one focus of avascular villi (a cumulative assessment of >45 avascular villi over 3 sections examined or an average of >15 villi per section) with or without thrombus, or 2 or more occlusive or nonocclusive thrombi in chorionic plate or major stem villi, or multiple nonocclusive thrombi.

The obstruction is partial or intermittent, but the lesions can be distributed over much of the placenta.

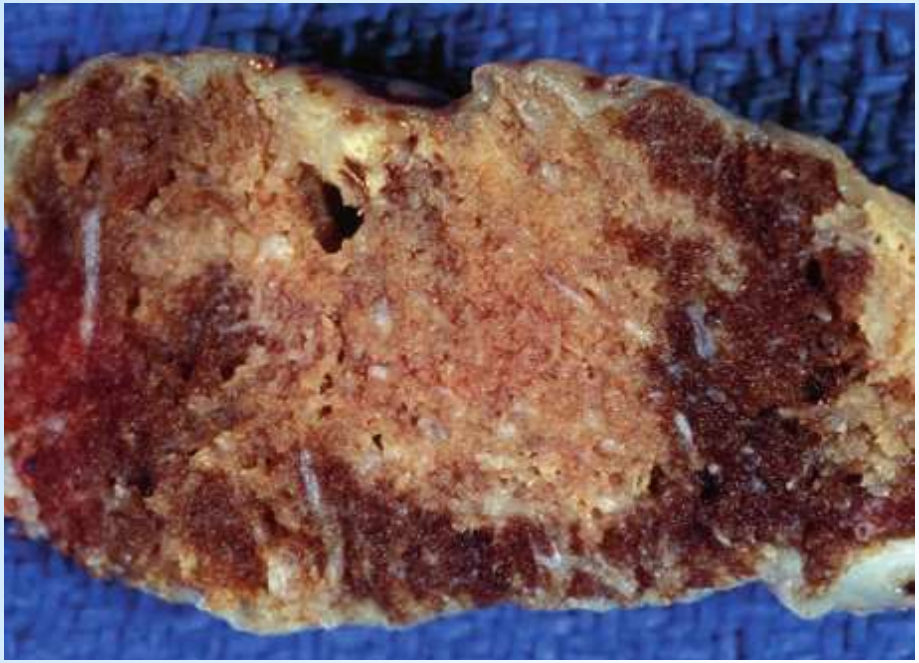




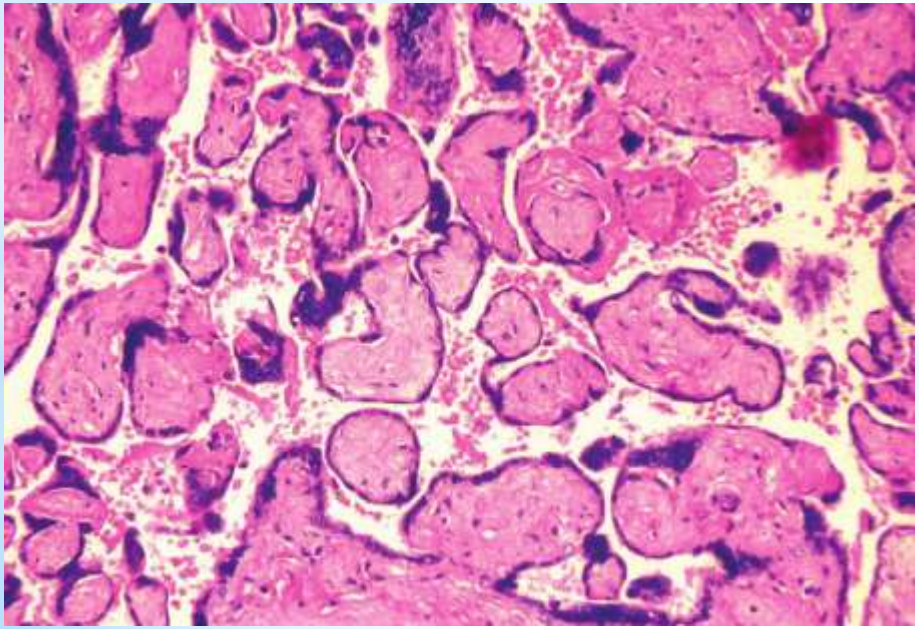
Intramural fibrin deposition in a large main stem vessel.



Intramural fibrin deposition and calcification, indicating remoteness of lesion, within a wall of a large fetal vessel.



Cross section of placenta with large focus of avascular villi.
Note the pallor of the lesion and the irregular border.



Microscopic section of a focus of avascular villi with hyaline stroma, devoid of vessels.

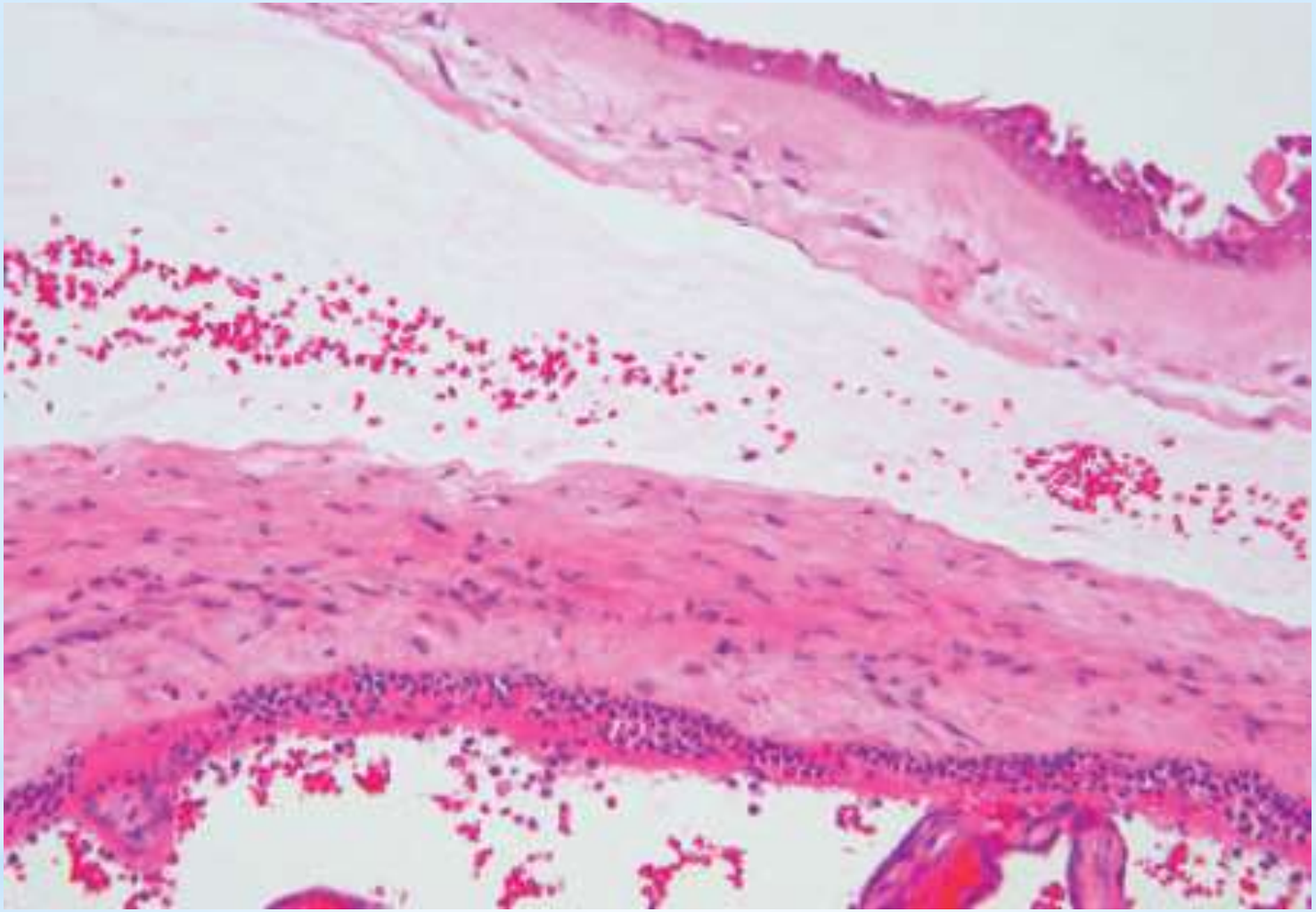
Ascending Intrauterine Infection

Histologic chorioamnionitis may not be equivalent to clinical chorioamnionitis.

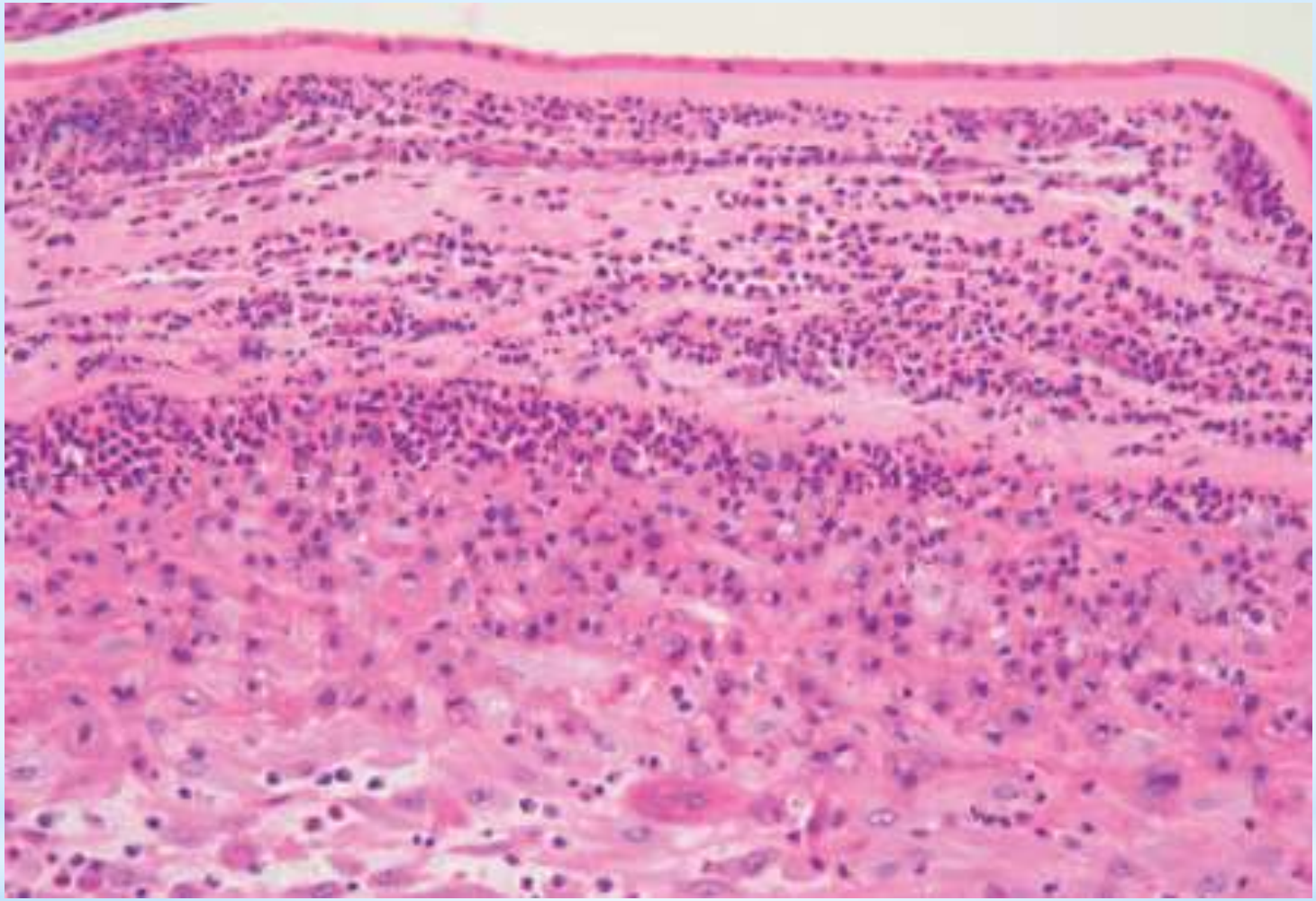
The topography and constituents of the inflammatory response should be documented (acute or chronic).

Staging and Grading of the Maternal and Fetal Inflammatory Responses in Ascending Intrauterine Infection	
Maternal Inflammatory Response	
Stage 1—acute subchorionitis or chorionitis Stage 2—acute chorioamnionitis: polymorphonuclear leukocytes extend into fibrous chorion and/or amnion Stage 3—necrotizing chorioamnionitis: karyorrhexis of polymorphonuclear leukocytes, amniocyte necrosis, and/or amnion basement membrane hypereosinophilia	Grade 1—not severe as defined Grade 2—severe: confluent polymorphonuclear leukocytes or with subchorionic microabscesses
Fetal Inflammatory Response	
Stage 1—chorionic vasculitis or umbilical phlebitis Stage 2—involvement of the umbilical vein and one or more umbilical arteries Stage 3—necrotizing funisitis	Grade 1—not severe as defined Grade 2—severe: near-confluent intramural polymorphonuclear leukocytes with attenuation of vascular smooth muscle

Which fetal vessels show an inflammatory response should be specified. Evidence suggests a difference in cytokine levels between umbilical arteritis and umbilical phlebitis, and a correlation between cytokine levels and the number of vessels involved. Higher rates of adverse neonatal outcomes have been reported in neonates with umbilical arteritis compared with those without.



Subchorionitis



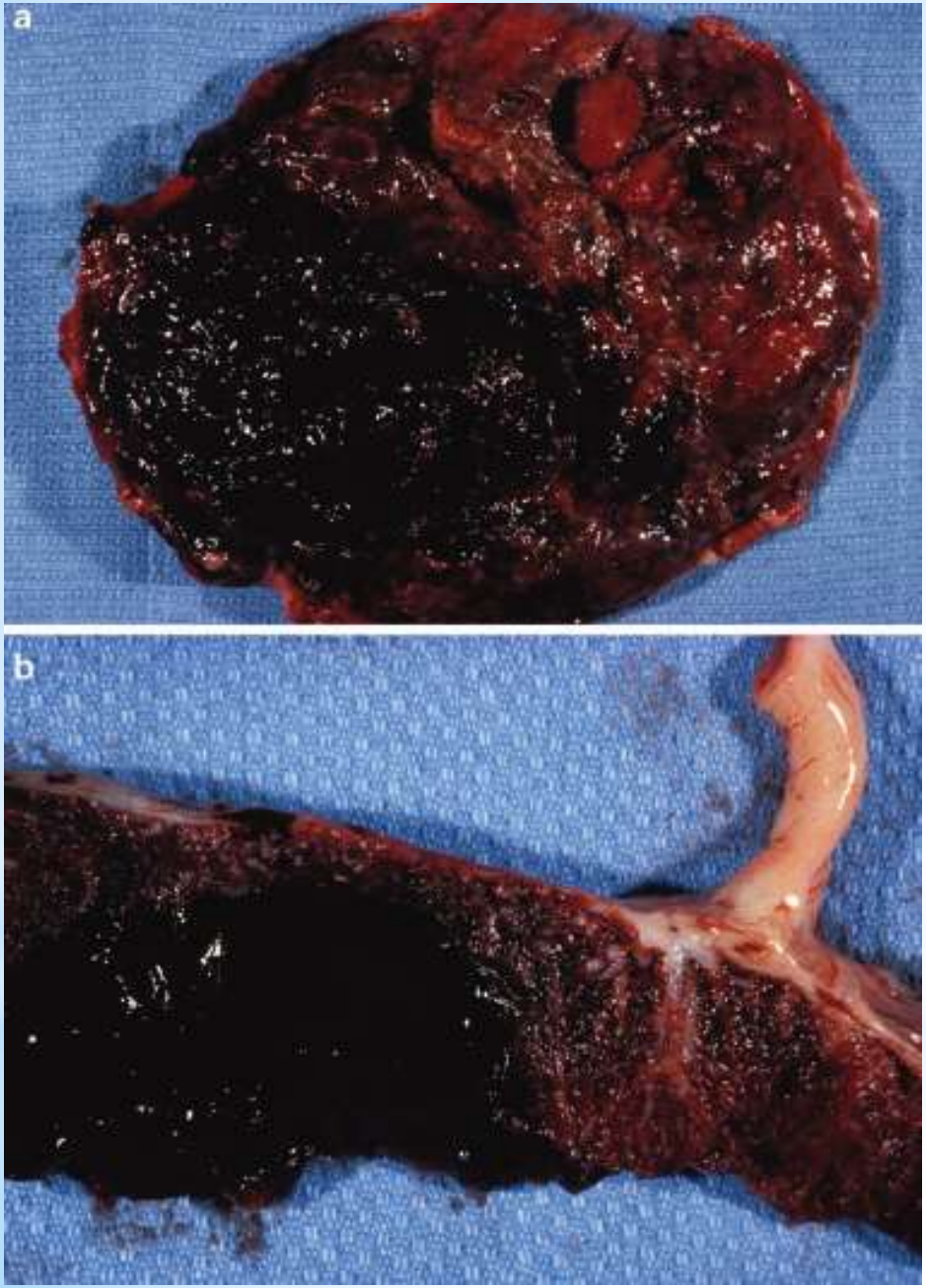
Acute chorioamnionitis: stage 2, grade 2

Abruptio Placentae

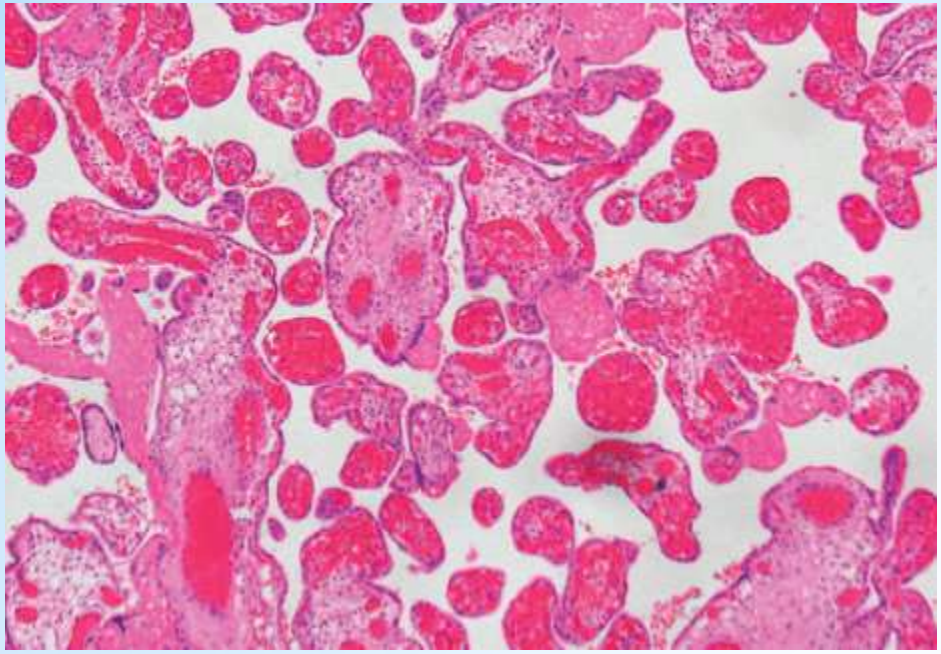
Abruptio placentae is defined as detachment of the placenta from its decidual seat.

Placental abruption is a clinical diagnosis and the correct descriptor for the pathologic finding is retroplacental hemorrhage or retroplacental hematoma.

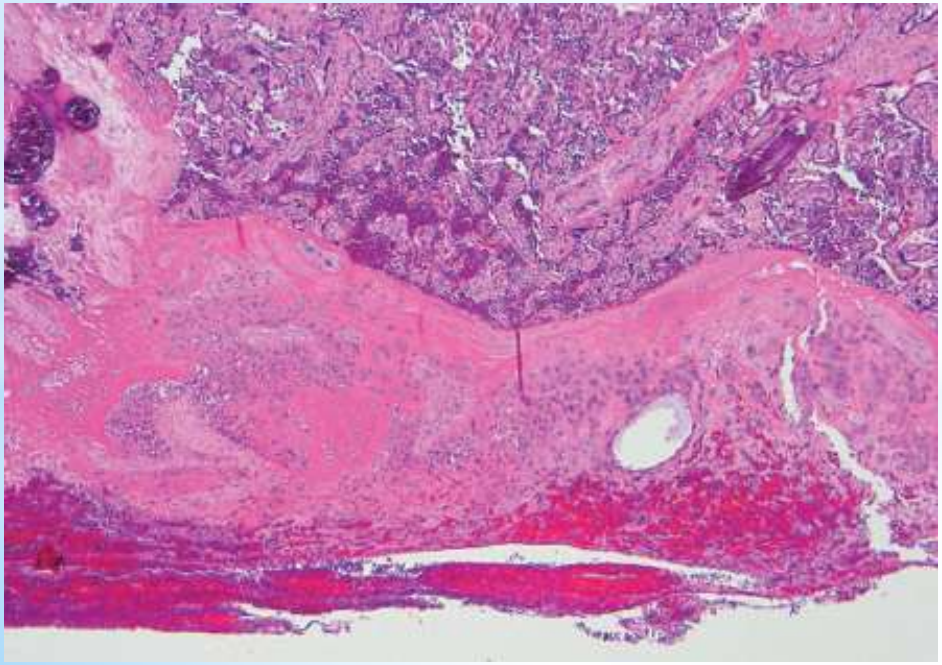
Here, the hemorrhage begins with the decidual vascular lesions described, specifically, lesions of the decidual arterioles lead to necrosis and subsequent venous hemorrhage. Pathologically, this results in a retroplacental hematoma. The hematoma pulls the placenta away from the uterus, and, ultimately, the villous tissue underlying the hematoma will become infarcted, as it has lost its blood supply.



(**a**) Maternal surface of the placenta with a retroplacental hematoma showing recent adherent blood clot. (**b**) Cross section of the placenta shows that the recent blood clot compresses the underlying villous tissue, which shows no alteration.



Intravillous hemorrhage accompanying retroplacental hemorrhage.



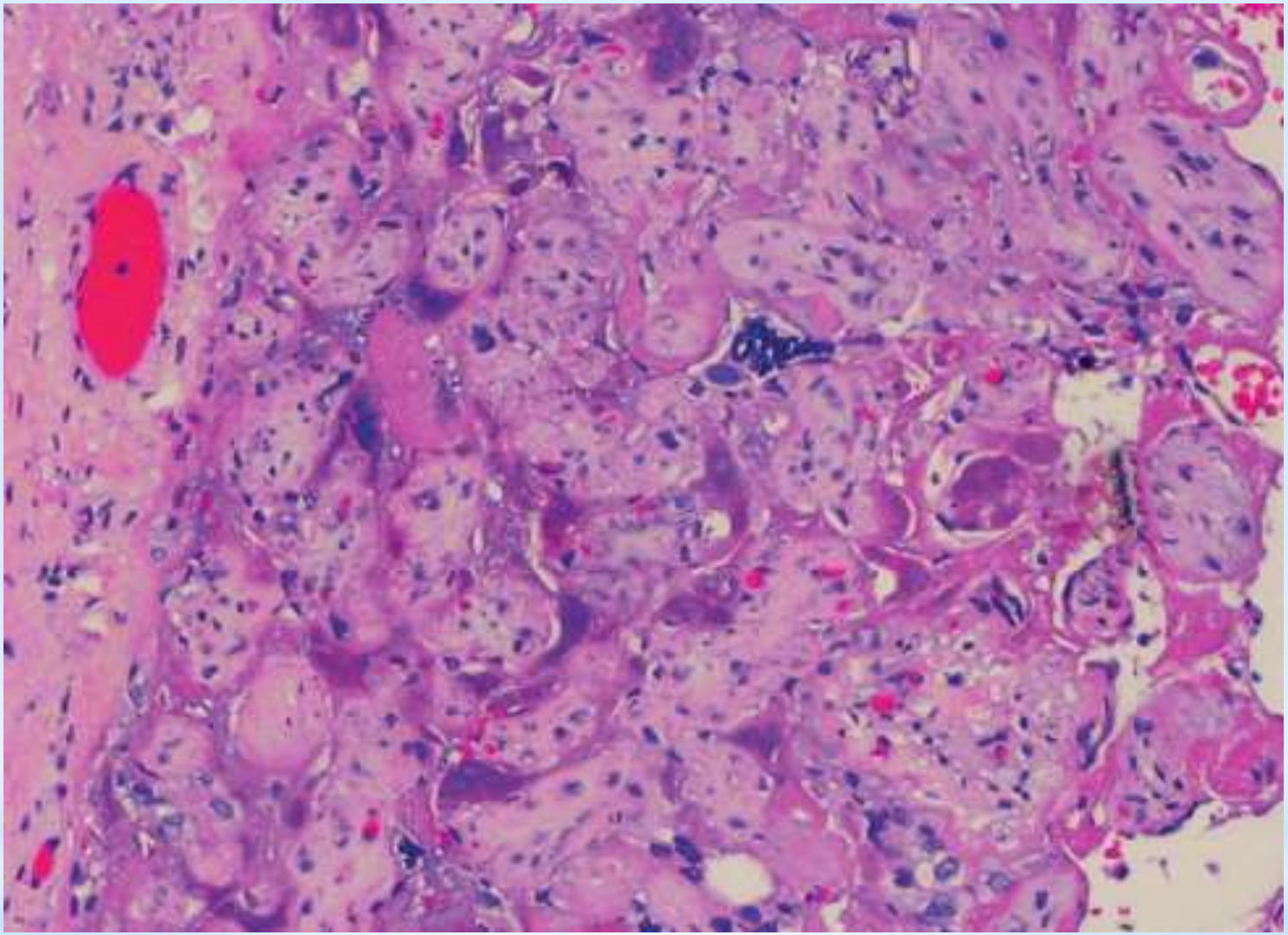
Dissection of the basal plate in retroplacental hemorrhage. There is congestion of the intervillous space immediately above the Hemorrhage.

Placental infarcts

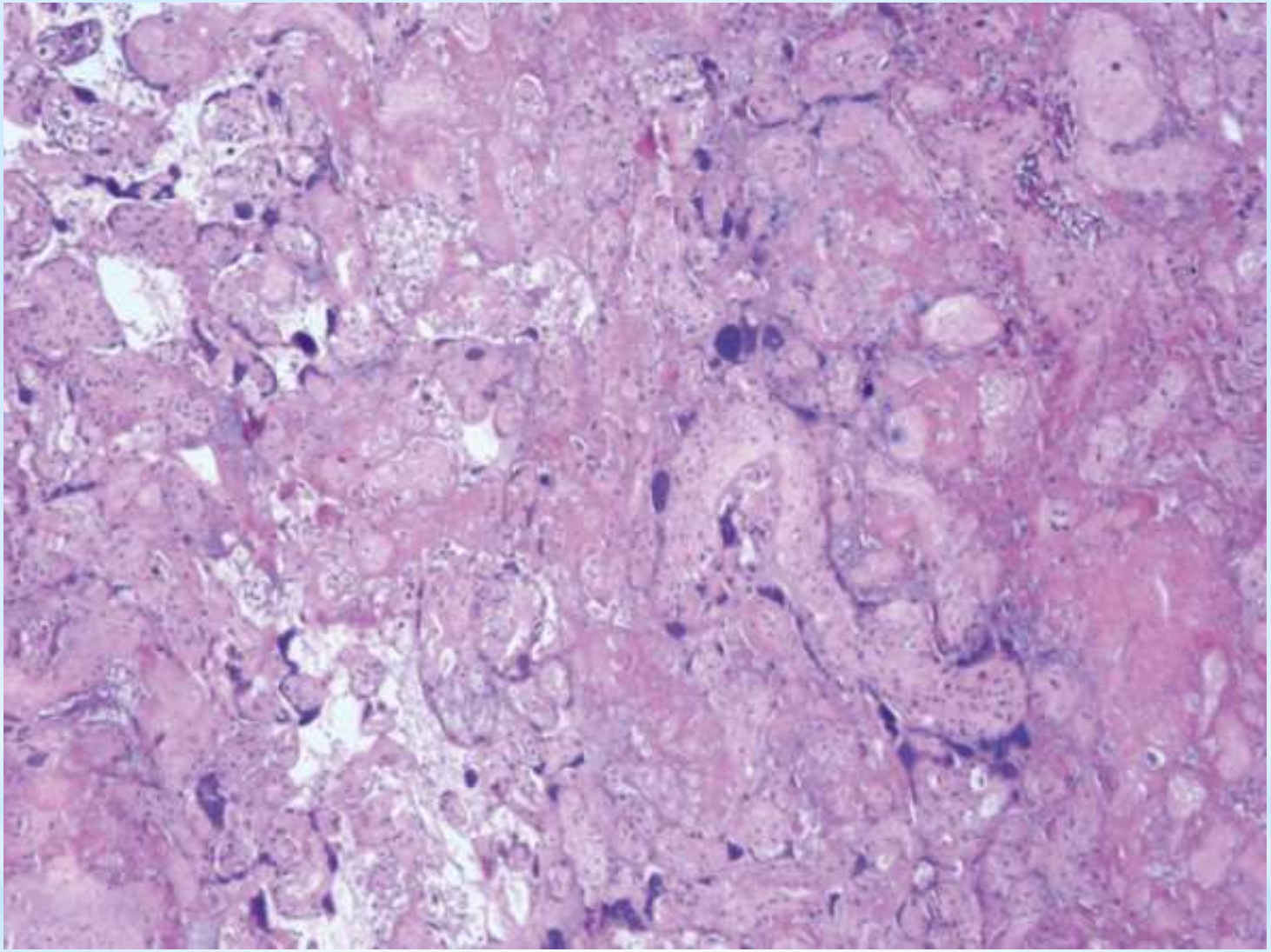
They represent villous tissue that has died because of deficient intervillous (maternal) circulation.

* Old
* Intermediate
* Recent

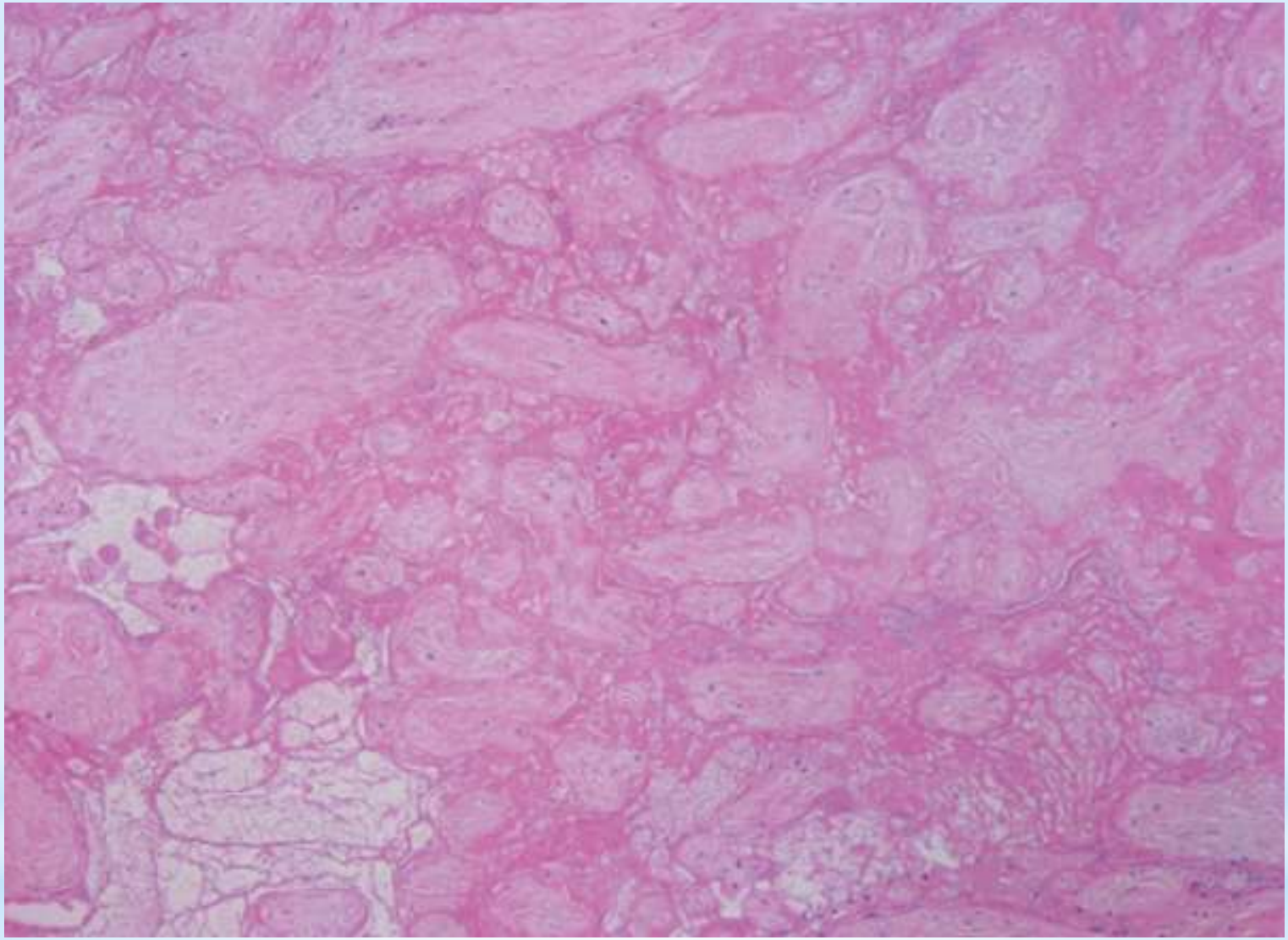
Older infarcts appear tan colored, whereas the fresher ones appear red and congested.



Early infarct with ischemic change, collapse of villi, and loss of the intervillous space and smudging of the trophoblastic nuclei.



Intermediate age infarct with smudging and karyorrhexis of trophoblastic nuclei. Focally there is loss of the basophilic staining of the nuclei.



Old infarct with ghost-like villi showing virtually no basophilic staining. The villous are collapsed on one another with a thin layer of fibrinoid interposed.

The number of infarcts, and more importantly, ***the percentage of the placental mass involved***, has important clinical significance for the fetus. It has been stated that a minimum of 190 g placental tissue, in a term placenta, is needed for fetal survival. Thus, large infarcts, or multiple small infarcts involving a substantial portion of the placenta may be fatal. Usually, infarcts involving less than 10% of the placental parenchyma do not affect oxygenation per se. However, the higher percentage of involvement of villous tissue, the less placental reserves exist, which can ultimately affect fetal outcome if additional problems arise.

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