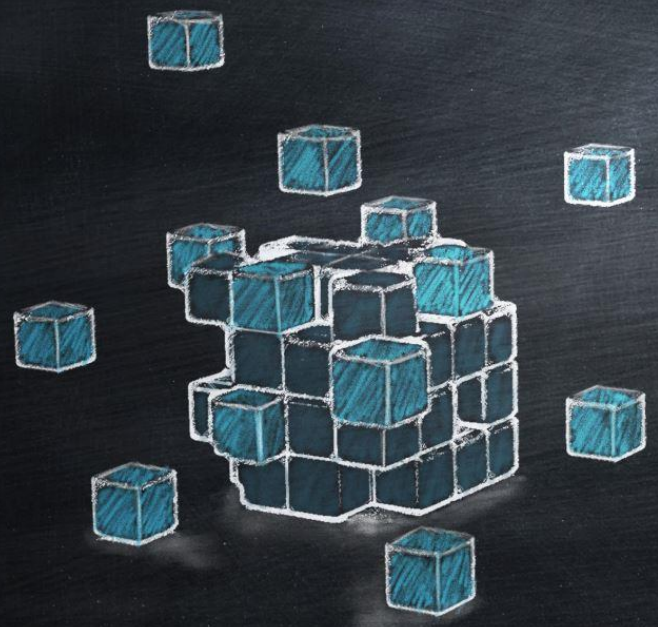


PLACENTAL EVALUATION

IN CLINICAL PRACTICE

Marcella Baldewijns
Afdeling Pathologie
UZ Leuven

CONTENT

1. Placental evaluation: IUGR
2. Placental evaluation in stillbirth: pre-mortem changes
3. Placental evaluation in stillbirth: post-mortem changes
4. Placenta quiz

1. PLACENTAL EVALUATION: IUGR

ADEQUATE FETAL GROWTH DEPENDS ON ADEQUATE SUPPLY OF OXYGEN AND NUTRIENTS TO FETUS

IUGR

- Maternal factors
- Fetal factors
- Placental factors

Fetal growth is dependent upon adequate maternal-placental blood flow,

placental-fetal blood flow,

and villous permeability

- maternal vascular malperfusion
- fetal vascular malperfusion
- high-grade chronic villitis
- massive perivillous fibrin
- chronic histiocytic intervillositis
- chronic abruption

FETAL AND PLACENTAL WEIGHT

- Low fetal body weight percentile
- Low placental weight percentile
- Fetal:placental weight ratio: Increases with ↑ GA = ~ 7:1 at term

ratio > 9-10:1 suggests placental insufficiency

CASE 1

G1, 26w

IUGR (male 504 g)

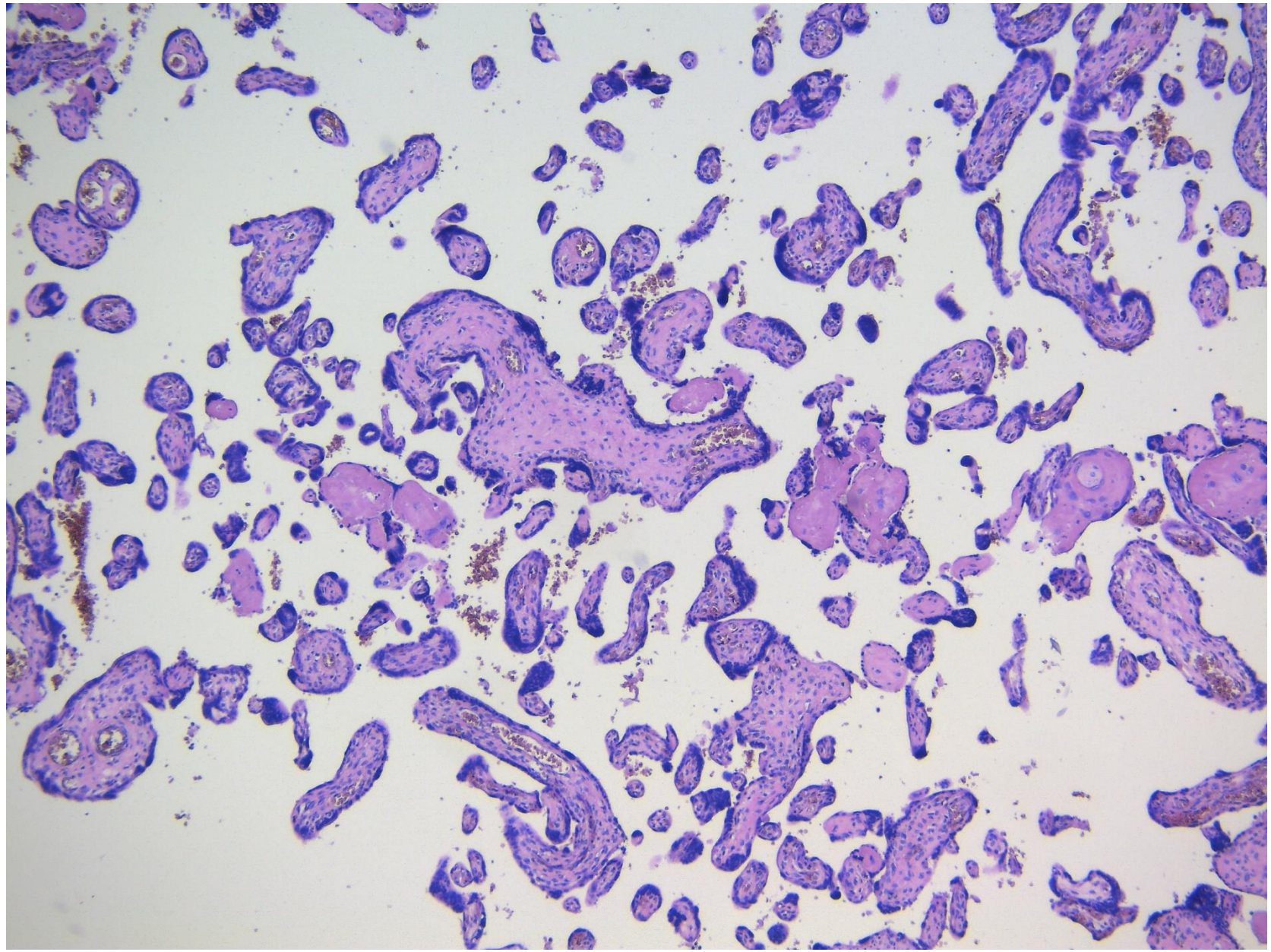
sectio because of

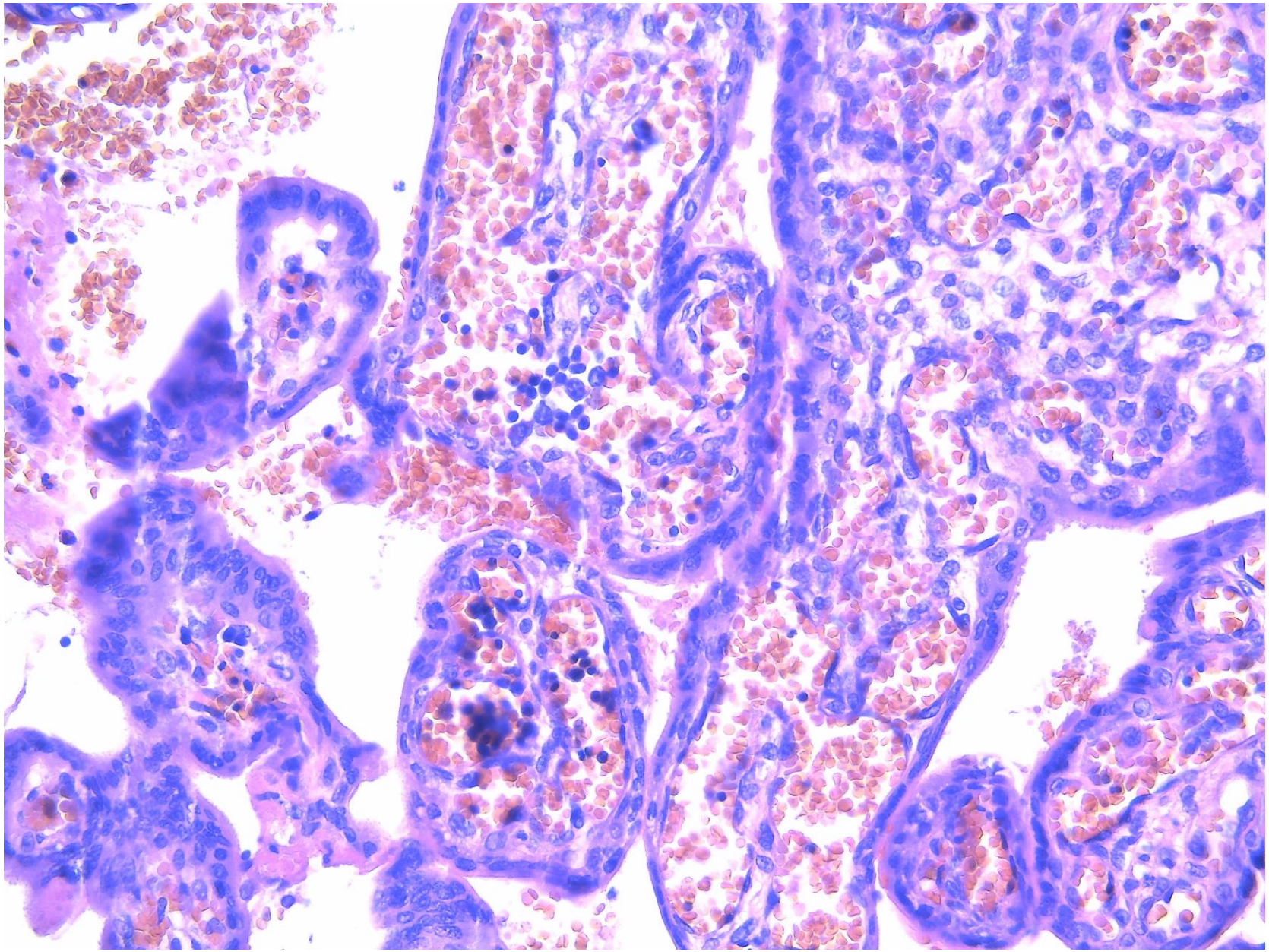
abnormal CTG

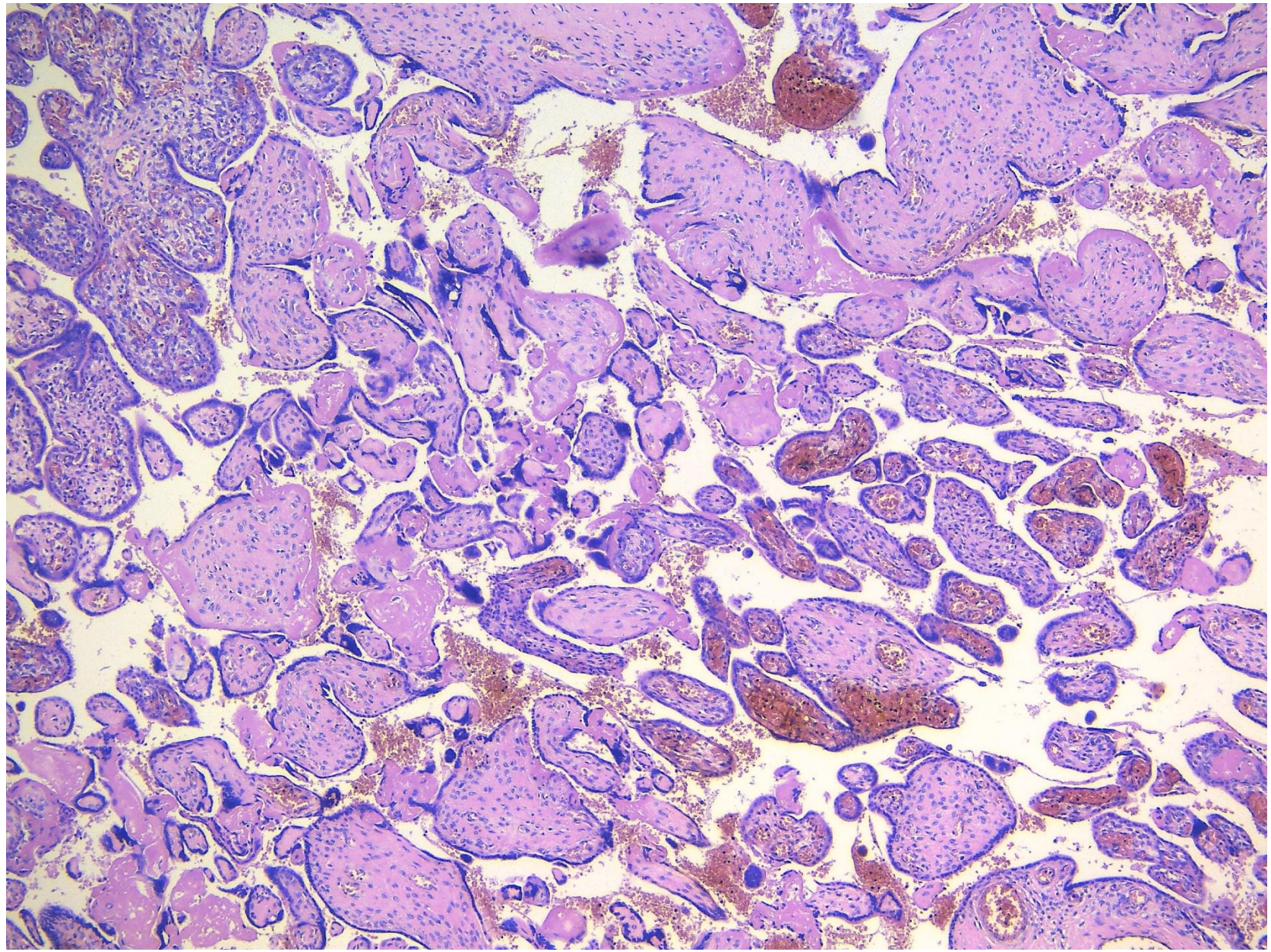
MACROSCOPY:

Placental weight: P3-P10

No other abnormalities







CASE 1

G1, AD 26w

IUGR (male 504 g)

sectio because of abnormal CTG

Conclusion:

Placenta, 26 weeks of gestation:

- Low placental weight (P3 en P10) in correlation with gestational age
- Other placental findings: features of maternal vascular malperfusion and fetal vascular malperfusion.
- Increased presence of nucleated red blood cells and erythroblasts in fetal vessels probably due to fetal stress/hypoxia which can occur in conditions of severe maternal vascular malperfusion

CASE 2

Partus per sectio at 33w.

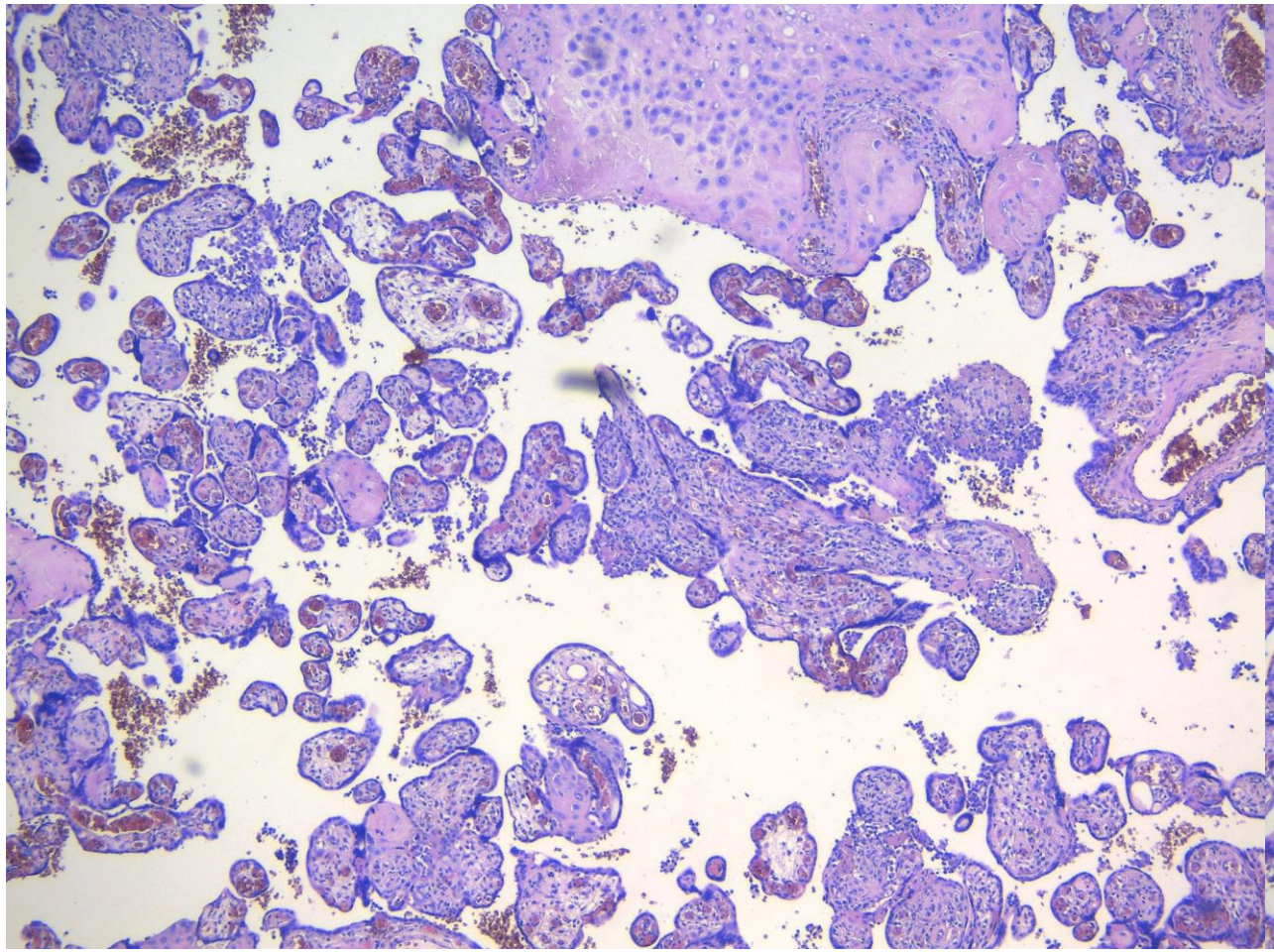
Severe IUGR

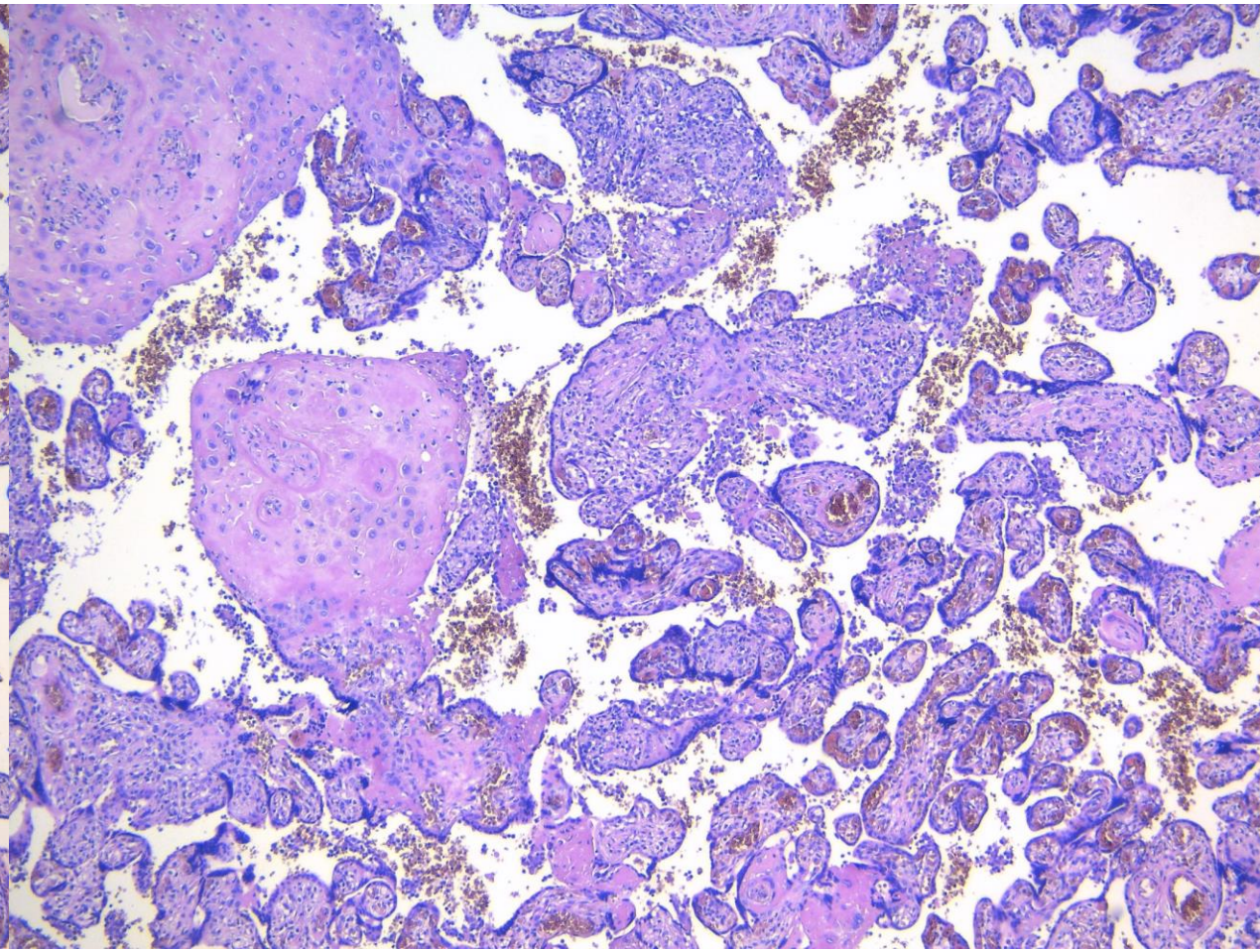
Abnormal dopplers.

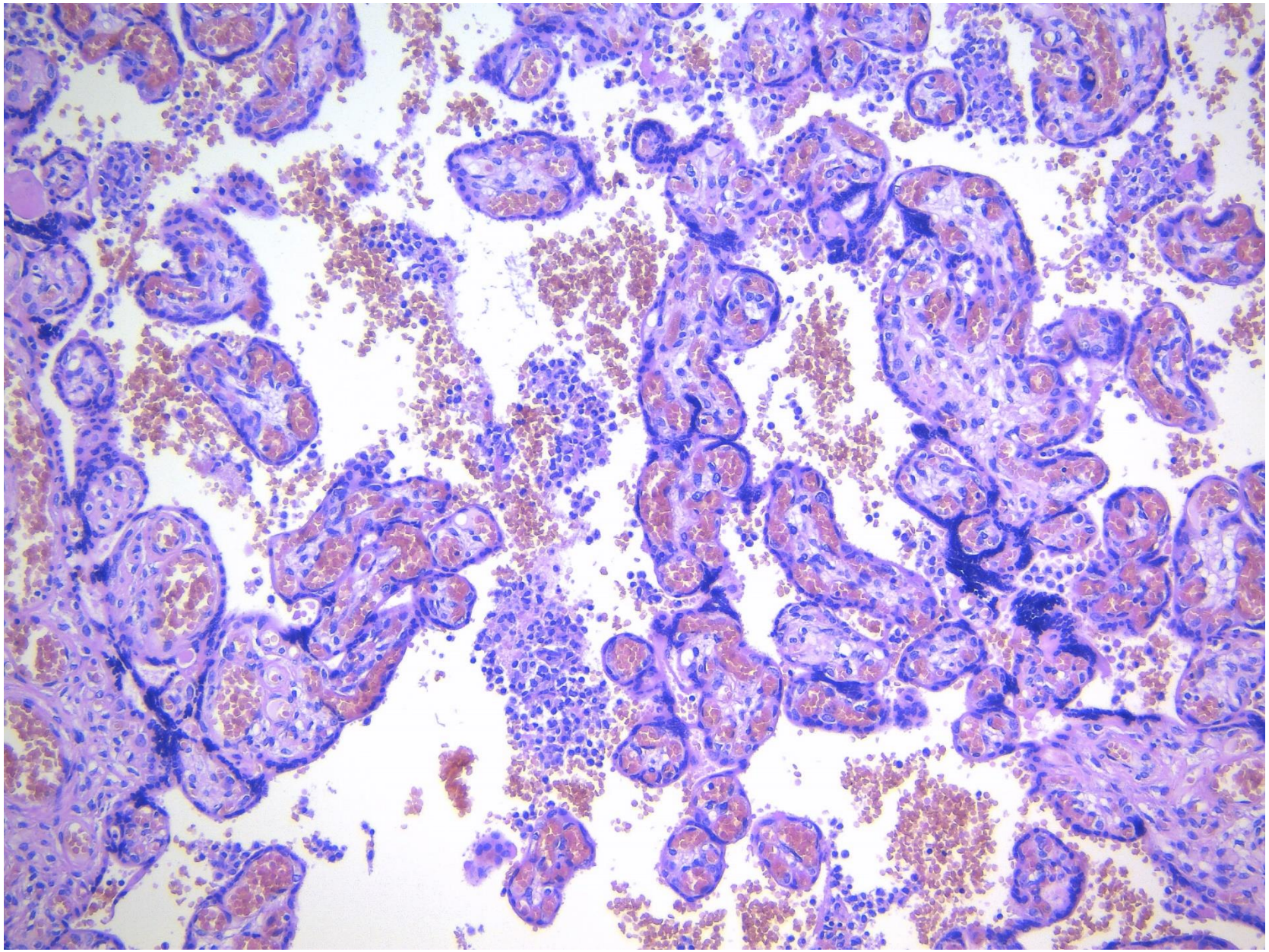
MACROSCOPY:

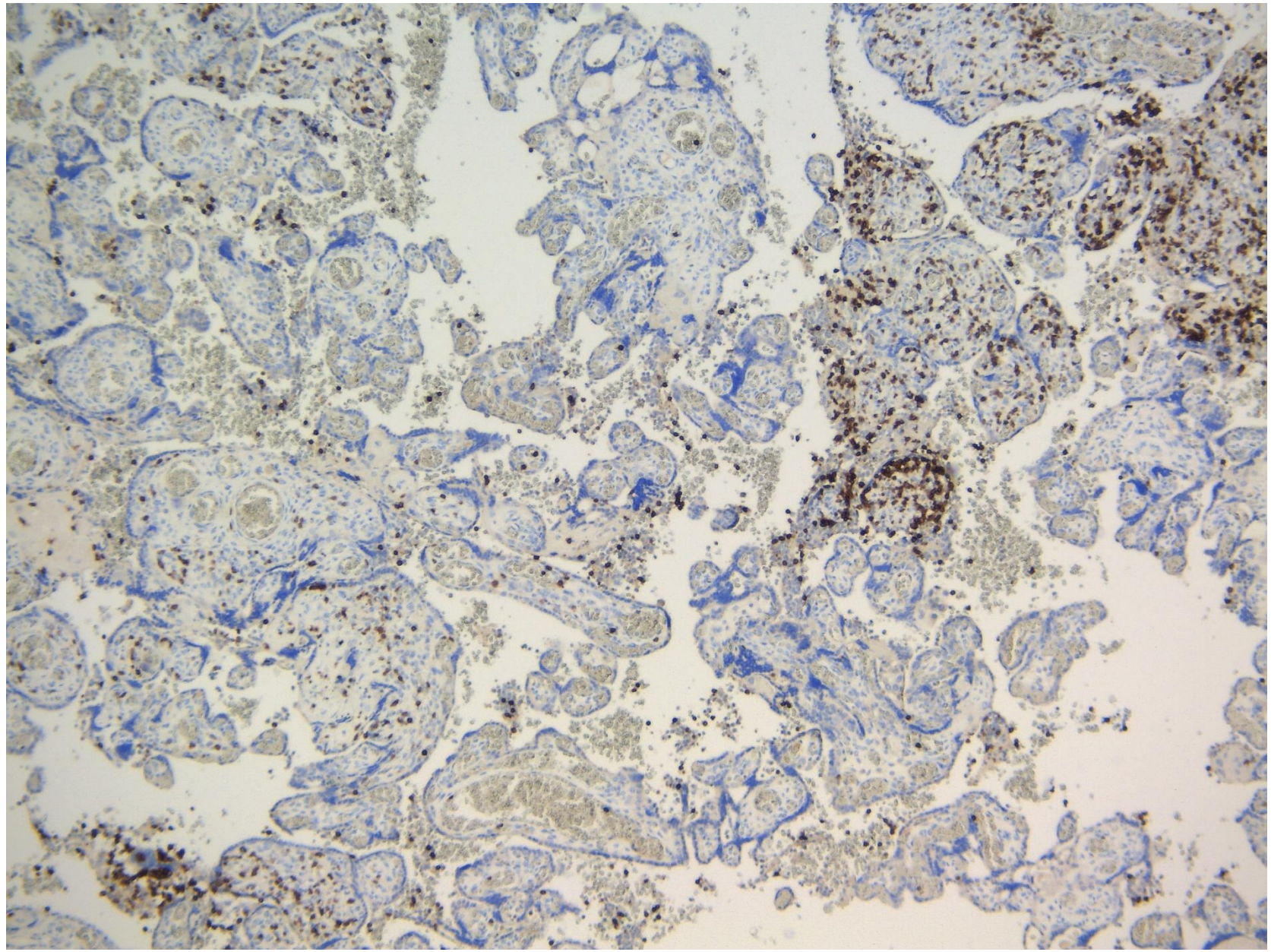
333 gr (P10 - P25)

No visible lesions









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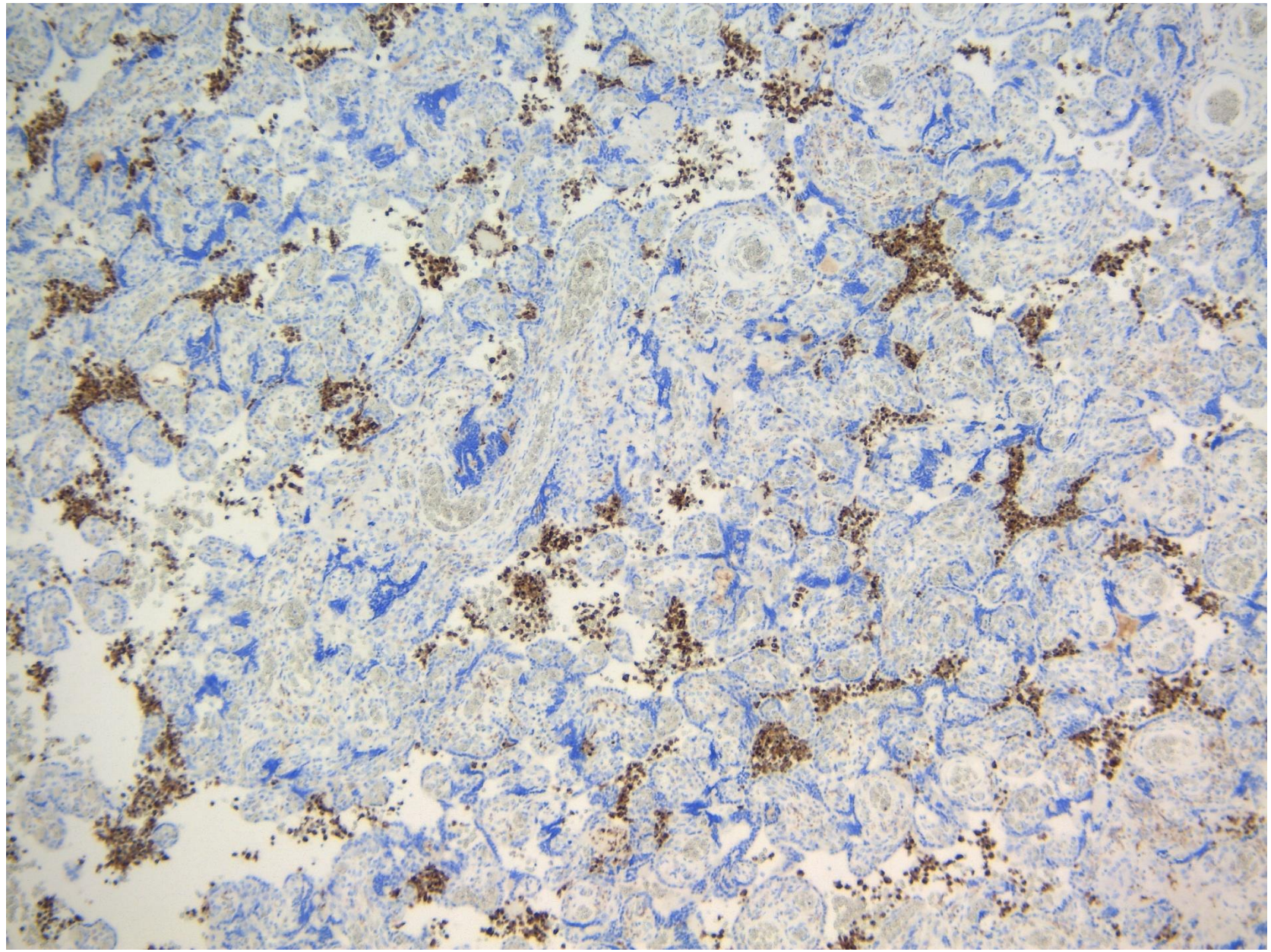


CD68

CASE 2

Partus per sectio at 33w.

Severe IUGR

Abnormal dopplers.

Conclusion:

- high grade chronic villitis of unknown etiology with signs of a chronic histiocytic intervillositis and chronic deciduitis

2. PLACENTAL EVALUATION: STILLBIRTH

PREMORTEM CHANGES

1ST TRIMESTER PREGNANCY LOSS

(UP TO 13 WEEKS OF GESTATION)
10-20% RESULT IN PREGNANCY LOSS

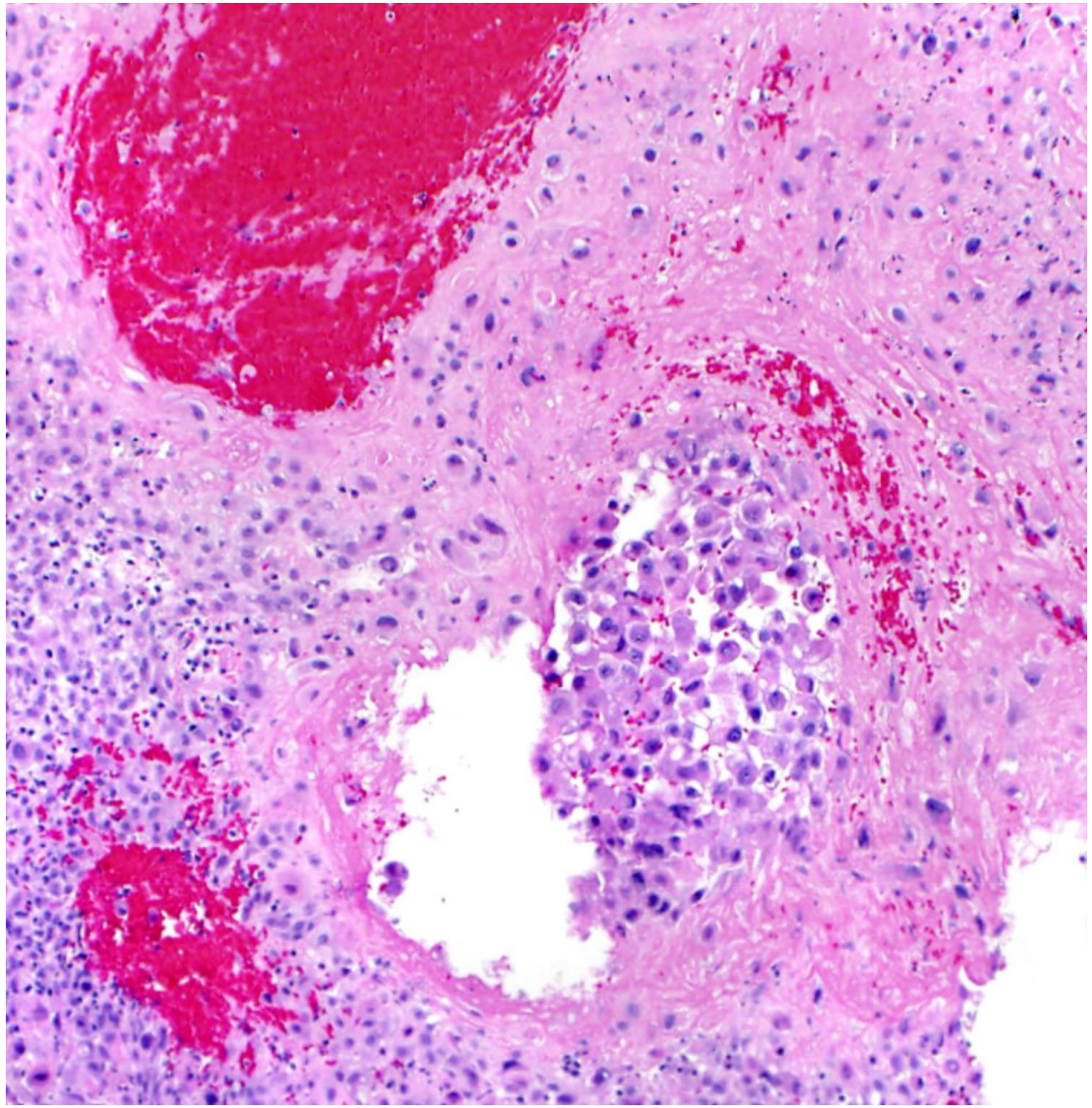
40-70% **CHROMOSOMAL** ABNORMALITIES

MATERNAL:
- AUTOIMMUNE DISORDERS
- ENDOCRINOPATHY (I.E., DIABETES, OBESITY, LUTEAL-PHASE DEFECTS, POLYCYSTIC OVARY SYNDROME)
- THROMBOPHILIA
- SEVERE ACUTE ILLNESS (E.G., PNEUMONIA, APPENDICITIS)
- INFECTION (RARE): *LISTERIA*, *TOXOPLASMA*, HERPES SIMPLEX VIRUS, COXSACKIEVIRUS, CYTOMEGALOVIRUS
- UTERINE ANOMALIES (INTRAUTERINE ADHESIONS, UTERINE SEPTUM, AND LEIOMYOMATA)
- TERATOGEN EXPOSURE AND SMOKING/DRUG USE

1ST TRIMESTER PREGNANCY LOST:

PLACENTAL EVALUATION

1. Confirming Intrauterine Pregnancy
2. Implantation site decidua and maternal vessels



Normal invasive trophoblast

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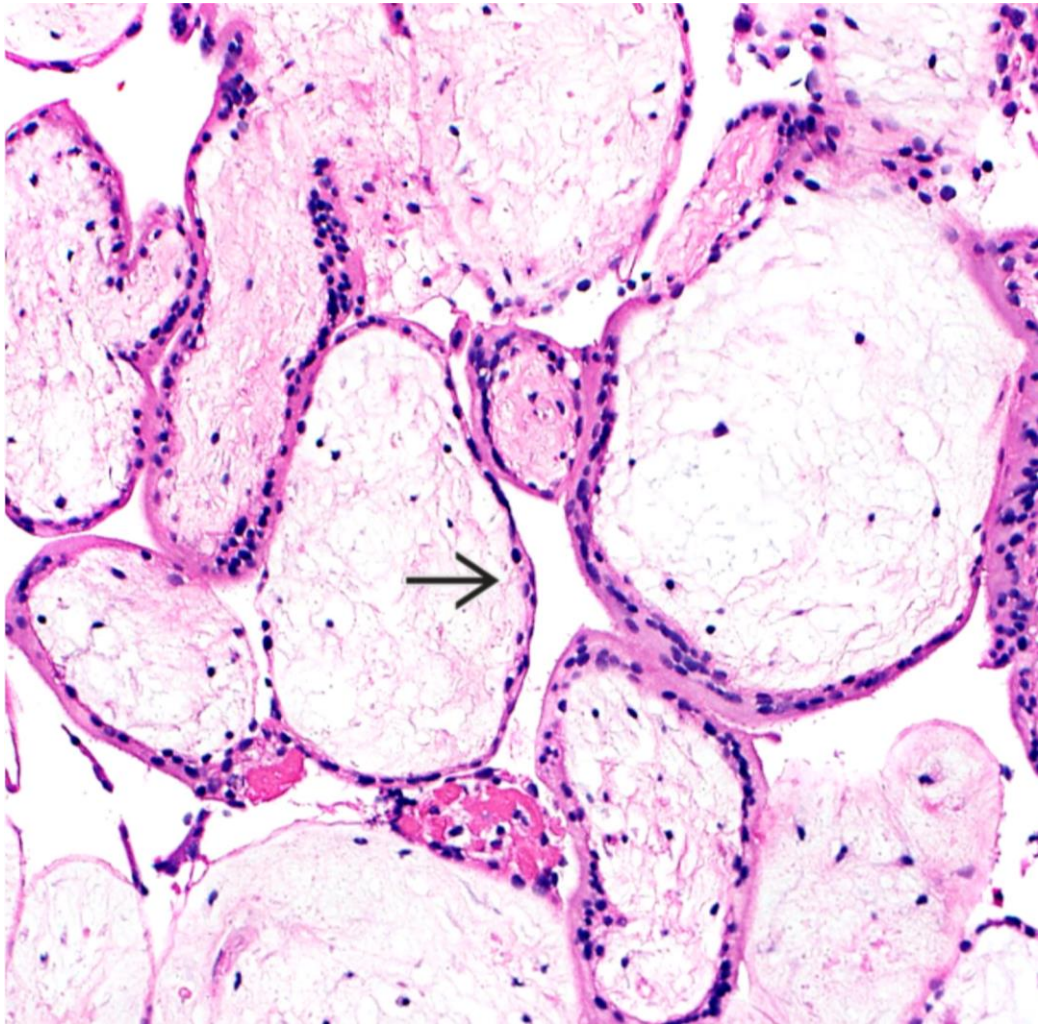
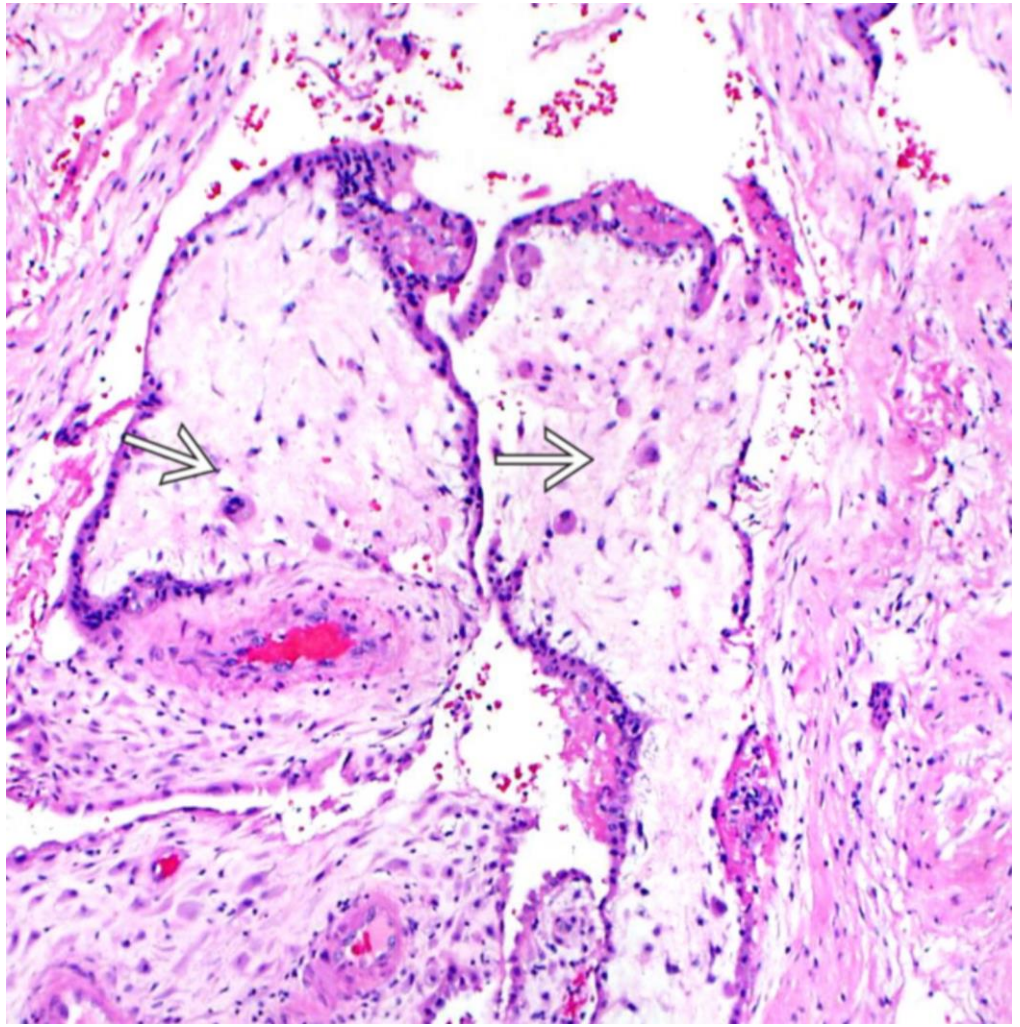
1ST TRIMESTER PREGNANCY LOST:

PLACENTAL EVALUATION

1. Confirming Intrauterine Pregnancy
2. Implantation site decidua and maternal vessels
3. Distinguishing Hydropic Degeneration From Hydatidiform Mole
4. Villous Changes in Pregnancy Loss With abnormal Karyotype



Hydropic degeneration



Intermediate trophoblasts in the villous stroma

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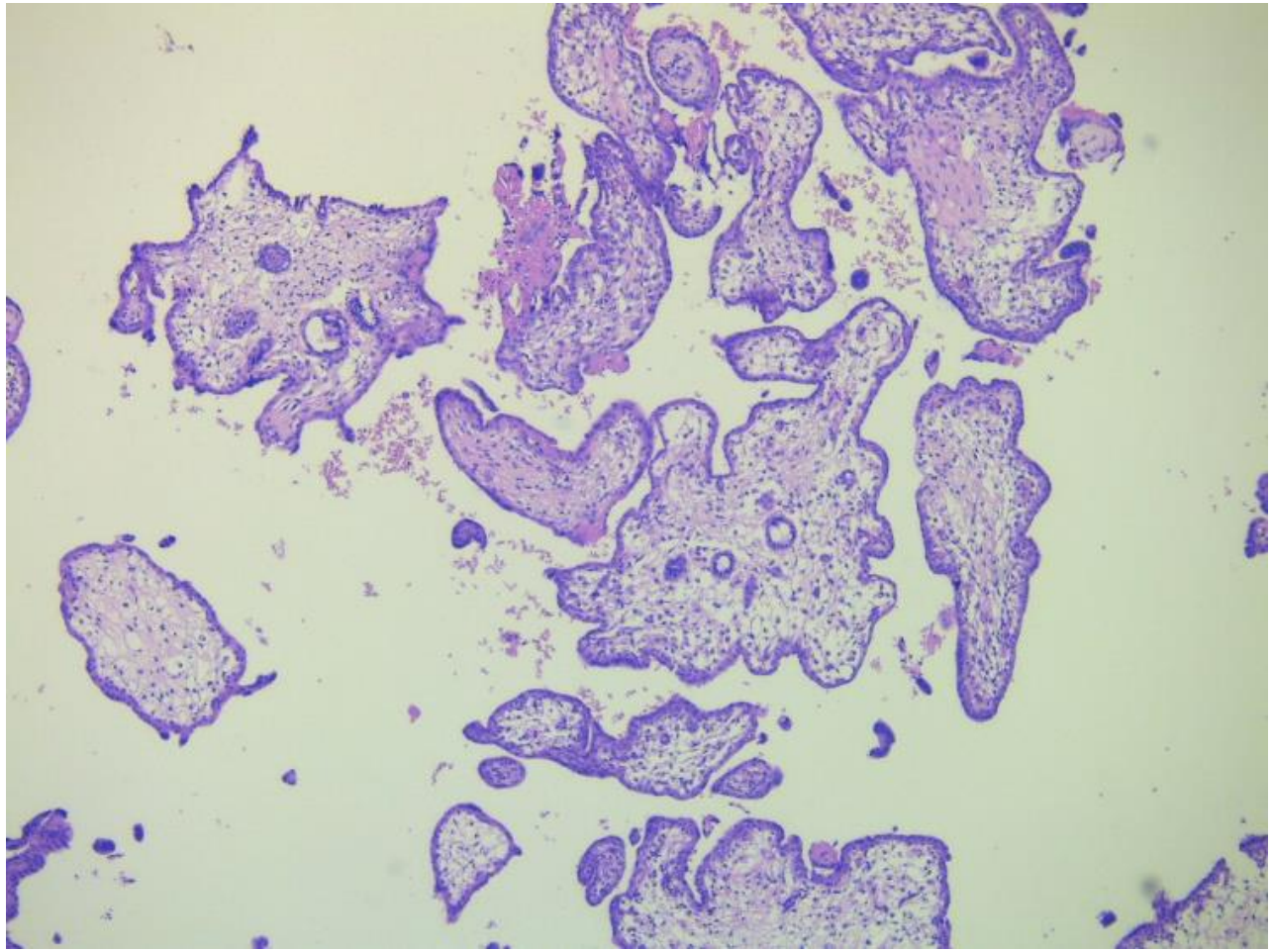
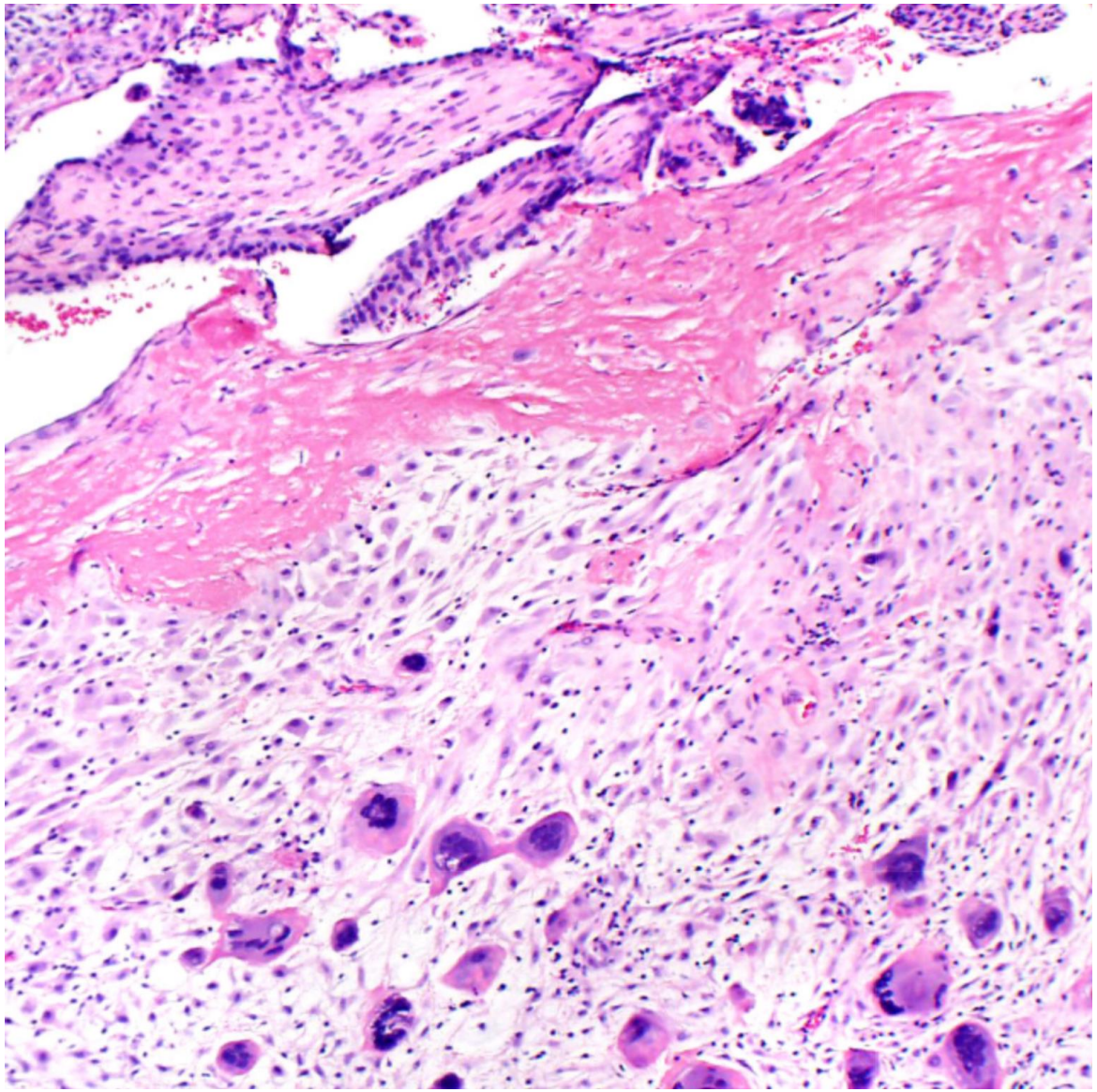


Dysmorphic villi with trophoblast inclusions



multinucleated invasive trophoblasts at the implantation site

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1ST TRIMESTER PREGNANCY LOST:

PLACENTAL EVALUATION

1. Confirming Intrauterine Pregnancy
2. Implantation site decidua and maternal vessels
3. Distinguishing Hydropic Degeneration From Hydatidiform Mole
4. Villous Changes in Pregnancy Loss With abnormal Karyotype
5. Chronic histiocytic intervillositis
6. Embryo

2ND TRIMESTER PREGNANCY LOSS

(13 WEEKS -27 WEEKS OF GESTATION)
IUFD IS RELATIVELY UNCOMMON IN 2ND TRIMESTER (1-5%)

1. 24% CHROMOSOMAL ABNORMALITIES
2. INFECTIONS: .

   ASCENDING INFECTION: **40-60%** OF 2ND-TRIMESTER FETAL DEATHS

   (GROUP B *STREPTOCOCCUS*, *NEISSERIA GONORRHOEAE*, *GARDNERELLA* SPP., *MYCOPLASMA/UREAPLASMA*, *FUSOBACTERIUM* SPP.)

   HEMATOGENOUS *(TORCH)*

3. PLACENTAL INSUFFICIENCY: MVM/ FMH/FVM/CHRONIC ABRUPTION
4. MATERNAL

2ND TRIMESTER PREGNANCY LOSS:

PLACENTAL EVALUATION

- Look for evidence of **amniotic fluid infection**
- Look for fetal thrombi and organizing changes of **fetal vascular malperfusion**
- Look for changes of **uteroplacental malperfusion**
- Look for **villous parenchymal processes**
- Look for evidence of **hematogenous infection**

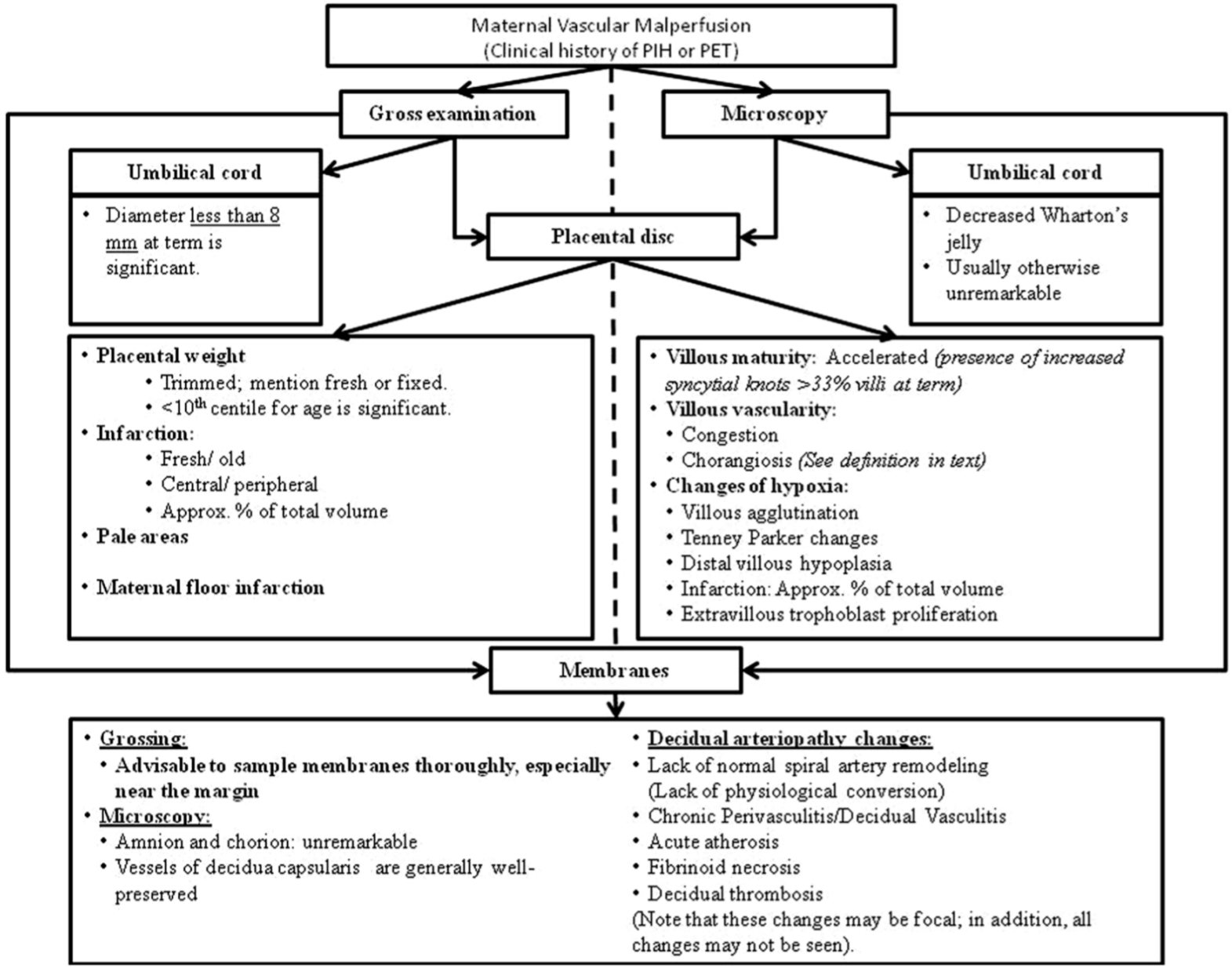

Fig. 3 Pathological changes in maternal vascular malperfusion (MVM). *PIH* Pregnancy induced hypertension; *PET* Pre eclamptic toxemia

Box 3.1 List of Recognisable Placental Conditions that May Cause Recurrent Pregnancy Loss

Massive perivillous fibrin deposition.
Chronic histiocytic intervillositis.
Villitis of unknown aetiology (VUE).
Maternal vascular malperfusion.

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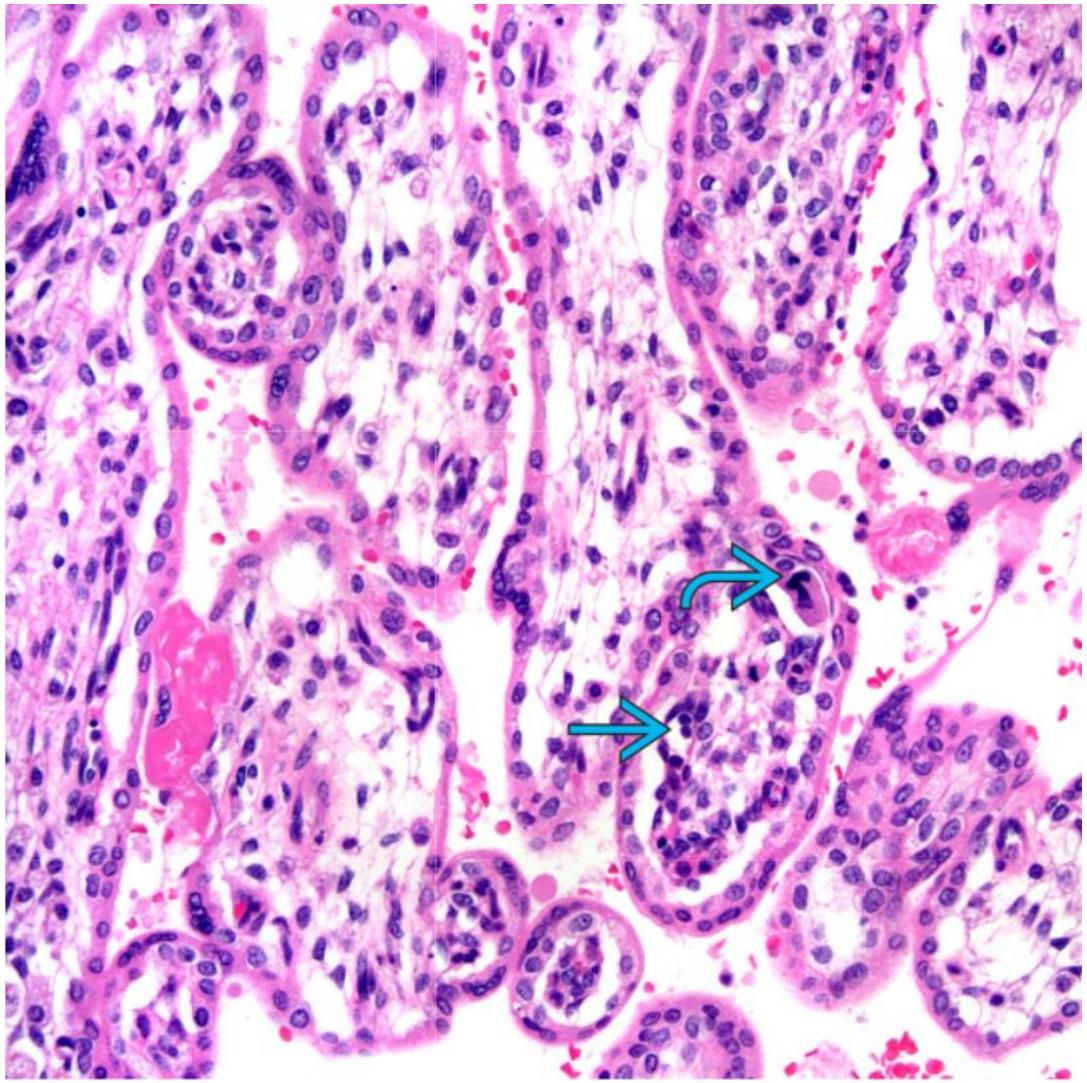
3RD TRIMESTER PREGNANCY LOSS

- Look for evidence of amniotic fluid infection
- Look for fetal thrombi and organizing changes of fetal vascular malperfusion
- Look for changes of uteroplacental malperfusion
- Look for villous parenchymal processes
- Look for evidence of hematogenous infection
- Look for evidence of **fetal-maternal hemorrhage**
- **Delayed villous maturation**



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fetal-maternal hemorrhage:

- hydropic pale placenta
- NRBC in fetal circulation and intervillous thrombi

DD. Fetal anemia due to hemolytic anemia, Parvo or CMV

Clinical diagnosis: Kleihauer-Betke or flowcytometry

3RD TRIMESTER PREGNANCY LOSS

- Look for evidence of amniotic fluid infection
- Look for fetal thrombi and organizing changes of fetal vascular malperfusion
- Look for changes of uteroplacental malperfusion
- Look for villous parenchymal processes
- Look for evidence of hematogenous infection
- Look for evidence of fetal-maternal hemorrhage
- **Delayed villous maturation**

Delayed villous maturation

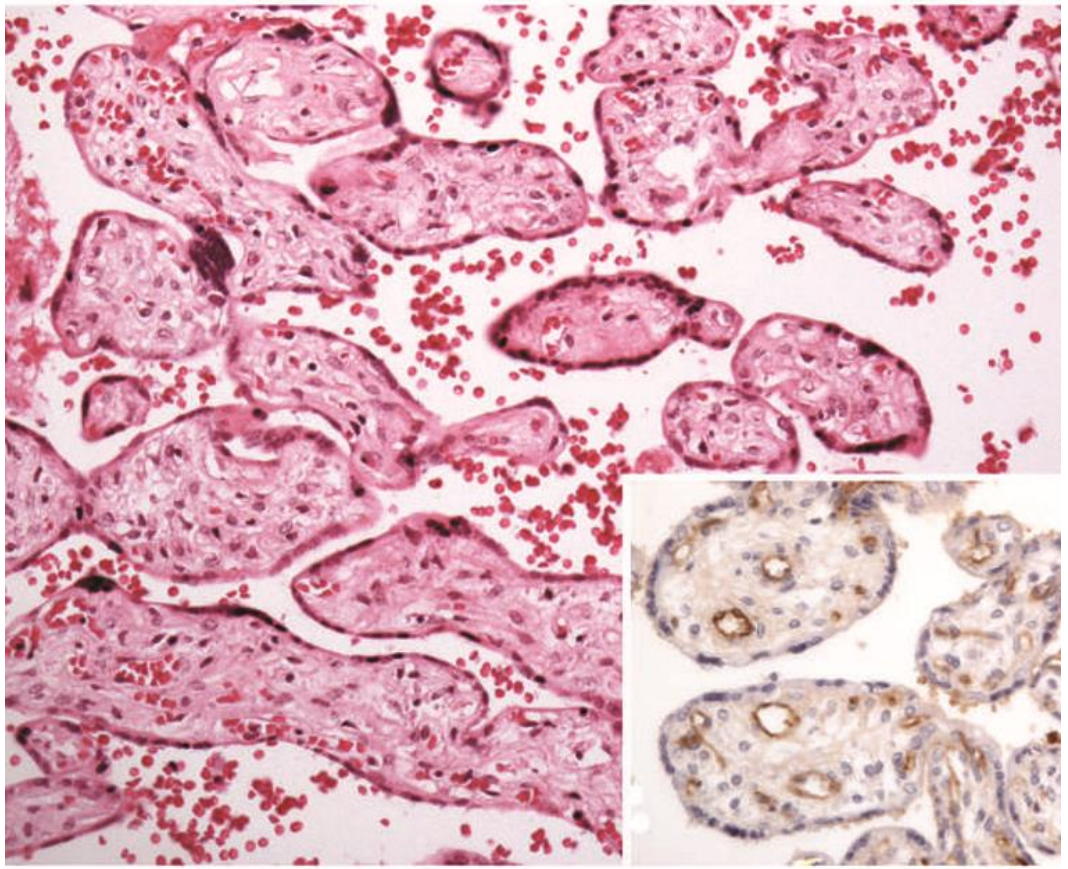
Increased risk of **fetal death at > 37 weeks**
Up to 5% risk of recurrent stillbirth

Areas of immature-appearing villi comprised of at least 10 abnormal villi demonstrating poor vasculosyncytial membrane formation, centrally placed capillaries, continuous cytotrophoblast (later third trimester)

At least 30% of parenchyma of at least 1 full-thickness slide should be involved

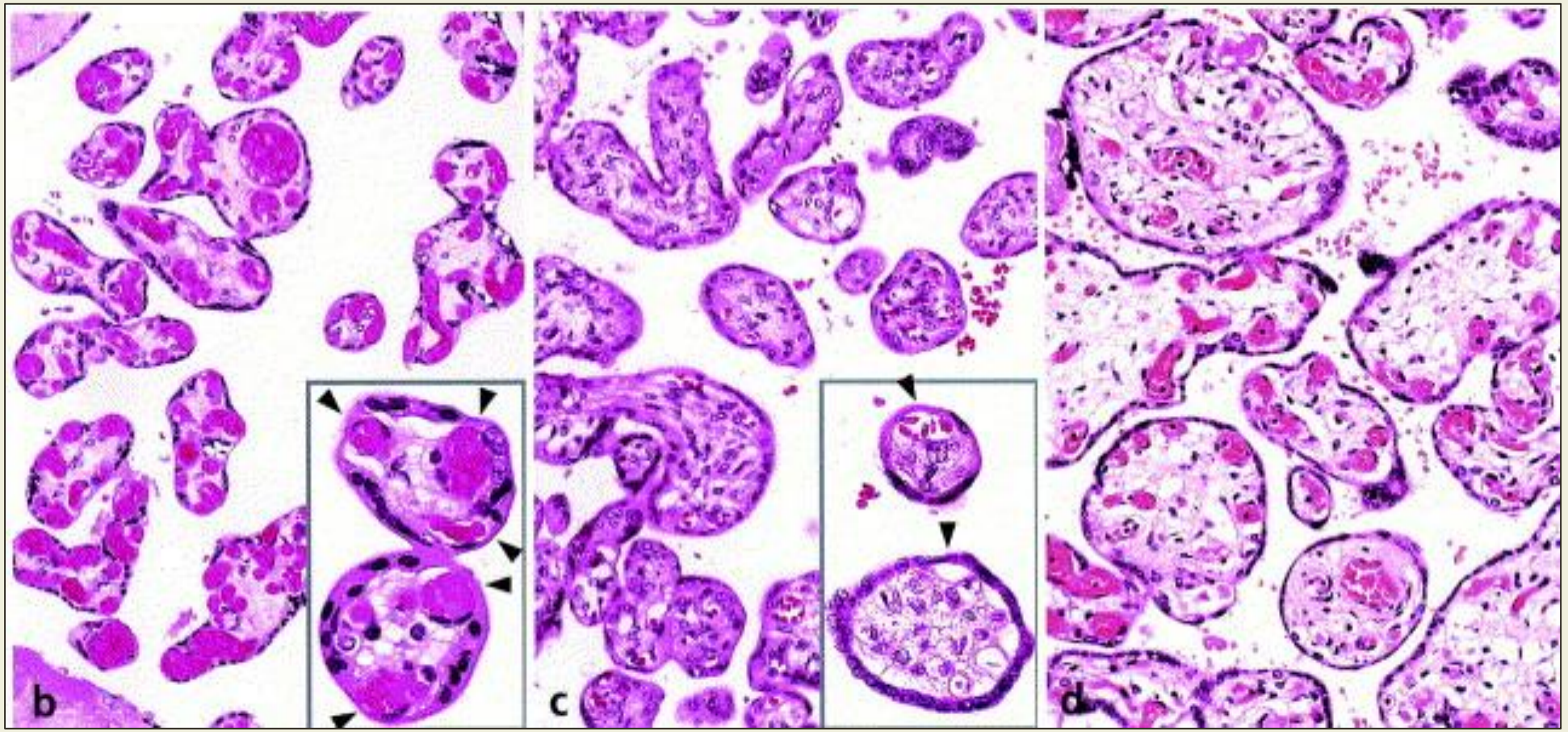
- associated with maternal diabetes, obesity, excessive weight gain in pregnancy
- Less commonly associated with chronic variable umbilical cord obstruction, fetal chromosomal abnormalities

May be clinically silent with lack of prenatal and US markers



Arch Pathol Lab Med—Vol 137, May 2013

Delayed villous maturation



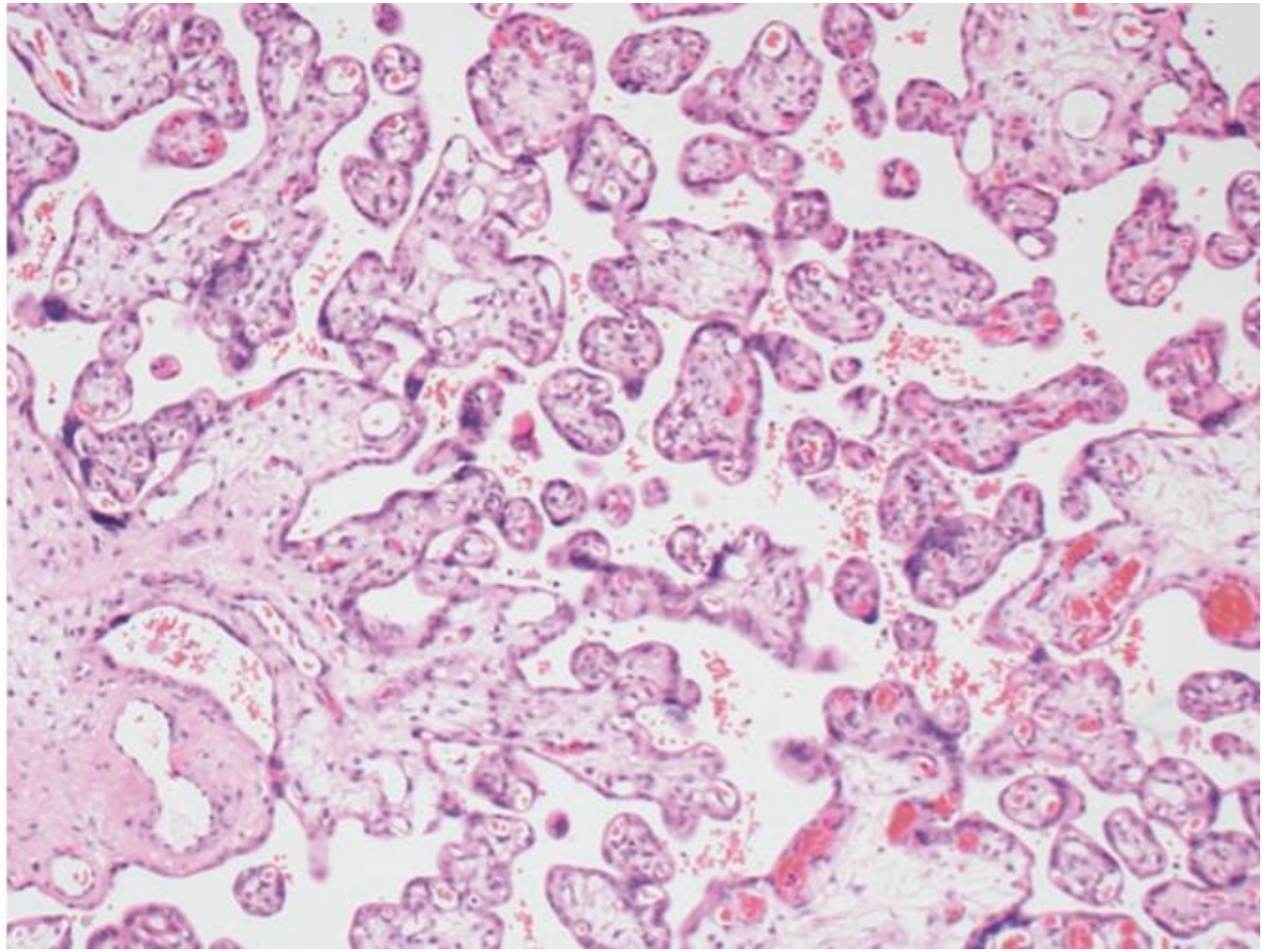
Normal a term

Pattern 1

Pattern 2

Stallmach et al. Obstet Gynecol 2001; 97: 505-9

Delayed villous maturation: Pattern 3



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3.PLACENTAL EVALUATION: STILLBIRTH

POSTMORTEM CHANGES

POSTMORTEM CHANGES

Consequences of….

Regardless of etiology

- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.

POSTMORTEM CHANGES

Consequences of….

- **1. Cessation of fetal blood flow**
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.

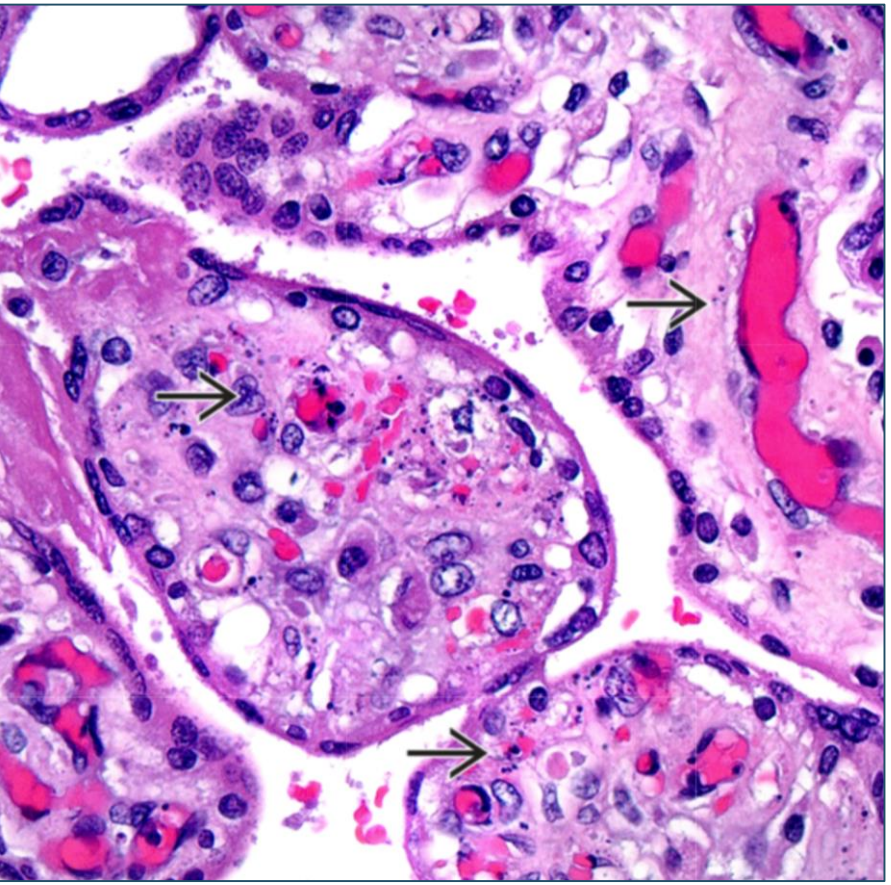
1. CESSATION OF FETAL BLOOD flOW

Villous capillary changes

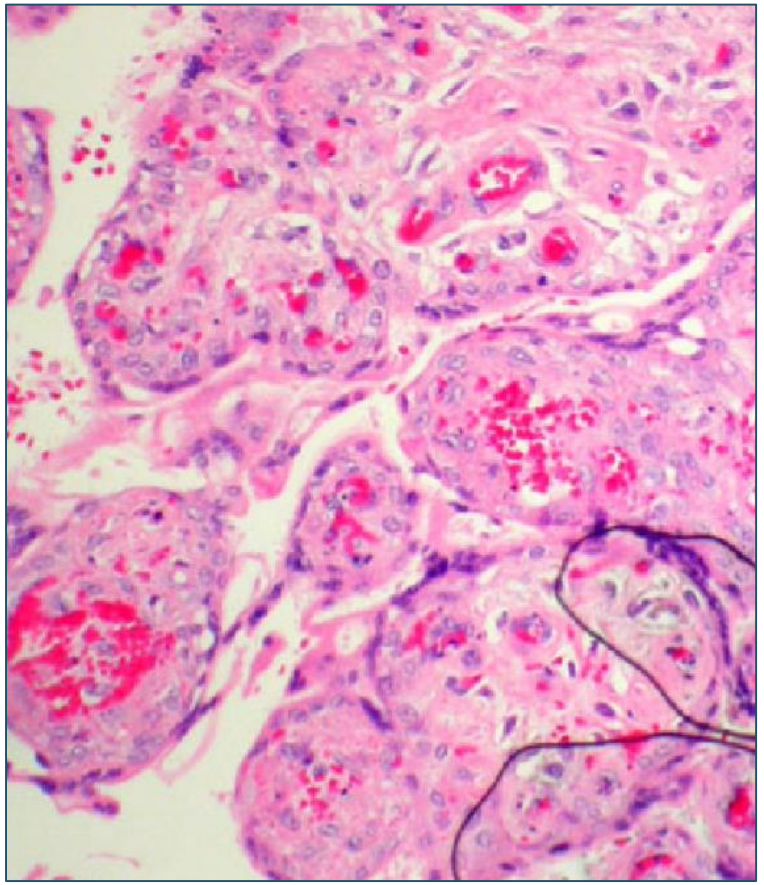
- Intravascular karyorrhexis
- Villous stromal-vascular karyorrhexis
- Extravasation of erythrocyte fragments into the villous stroma
- Villous capillaries involution→ avascular villi

Muscular (stem, chorionic) vessel changes

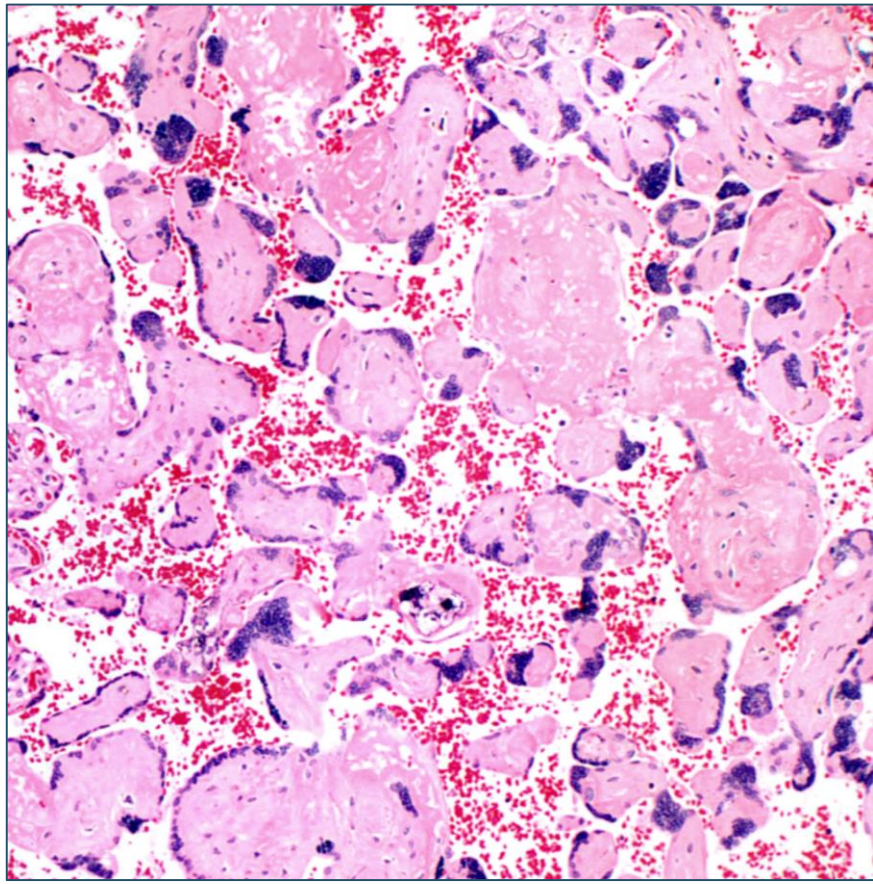
- Intravascular karyorrhexis → extravasation of erythrocytes into the peri-luminal mural wall
- Fibroblast ingrowth into the vessel lumen, resulting in luminal septation.
- Stem villous obliteration



→ karyorrhectic debris



extravasation of erythrocytes



avascular villi

FETAL CAPILLARY CHANGES

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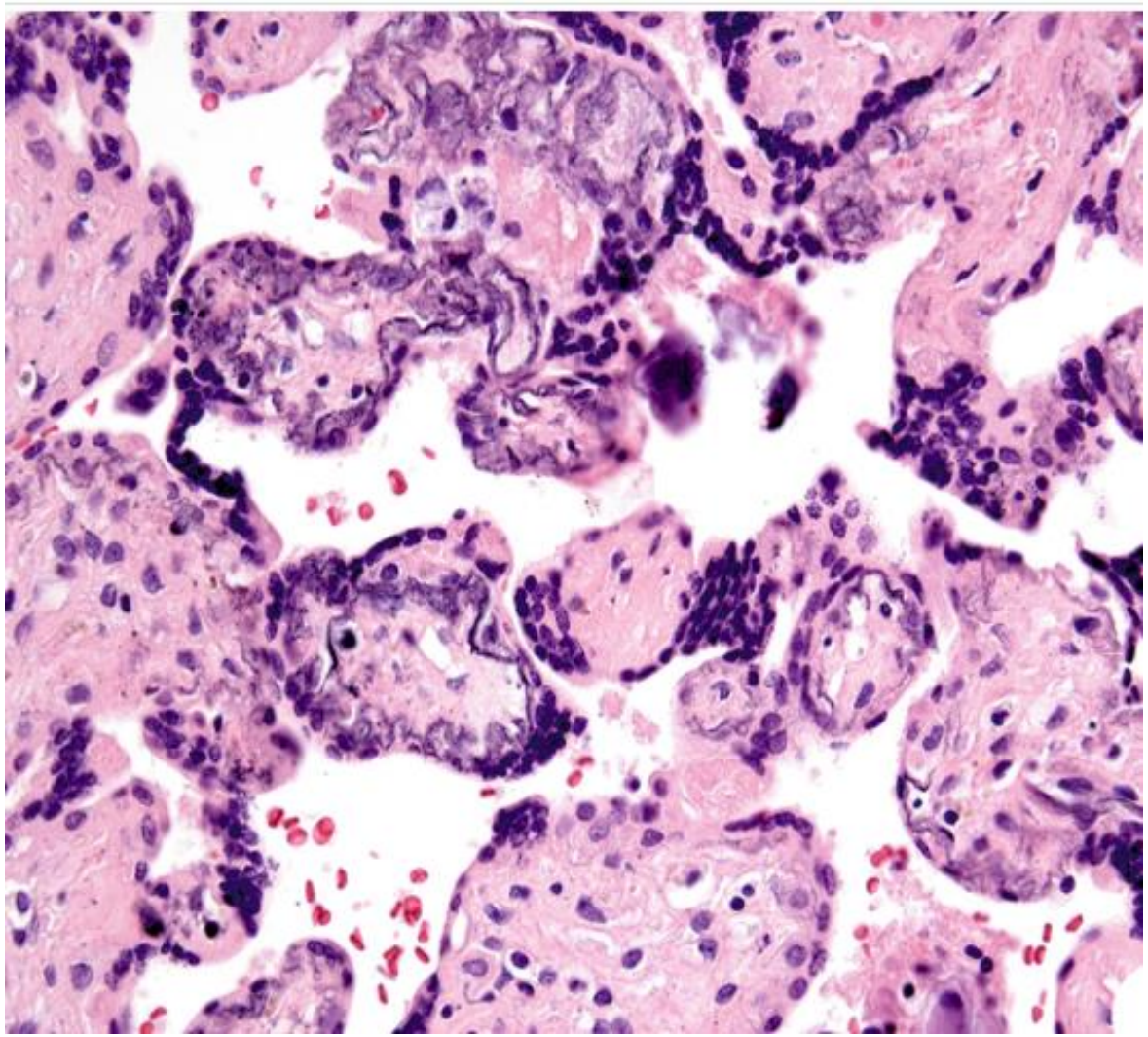
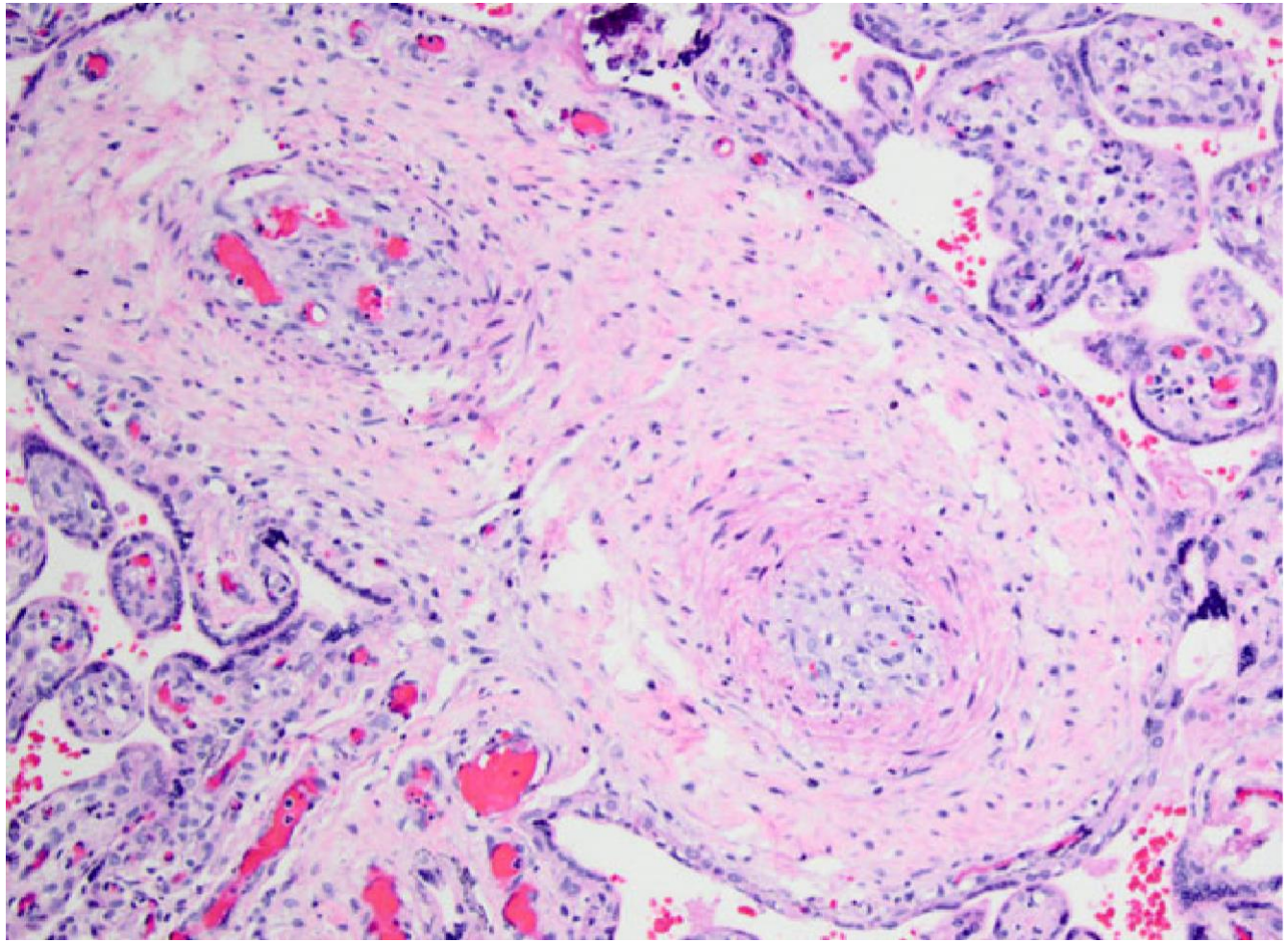


Calcification



MUSCULAR (STEM, CHORIONIC) VESSEL CHANGES

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POSTMORTEM CHANGES

Consequences of….

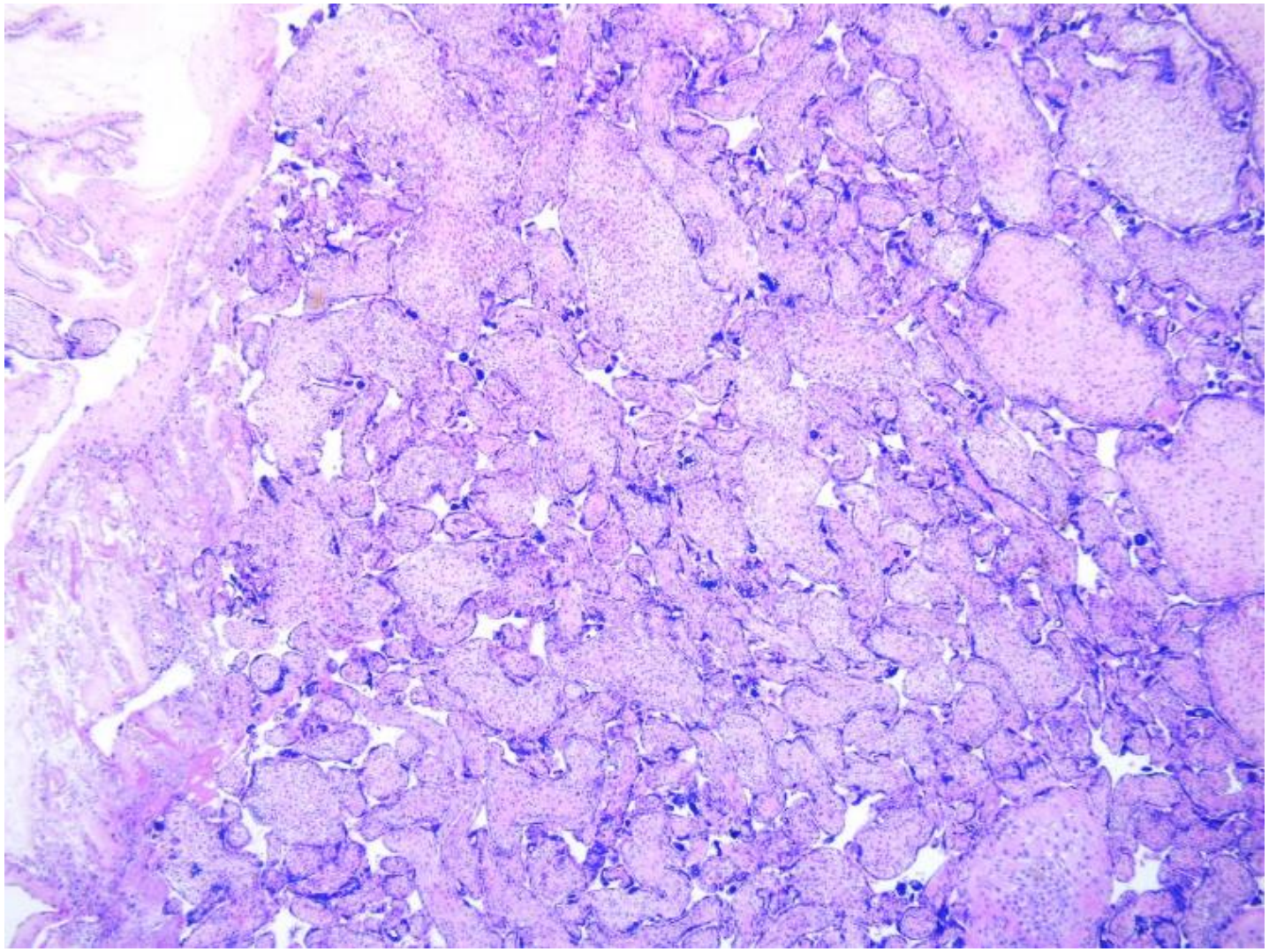
- 1. Cessation of fetal blood flow
- **2. Altered maternal perfusion**
- 3. Maternal inflammation to non-viable products of conception
- 4. Labor associated changes related to placental separation.

2. ALTERED MATERNAL PERFUSION

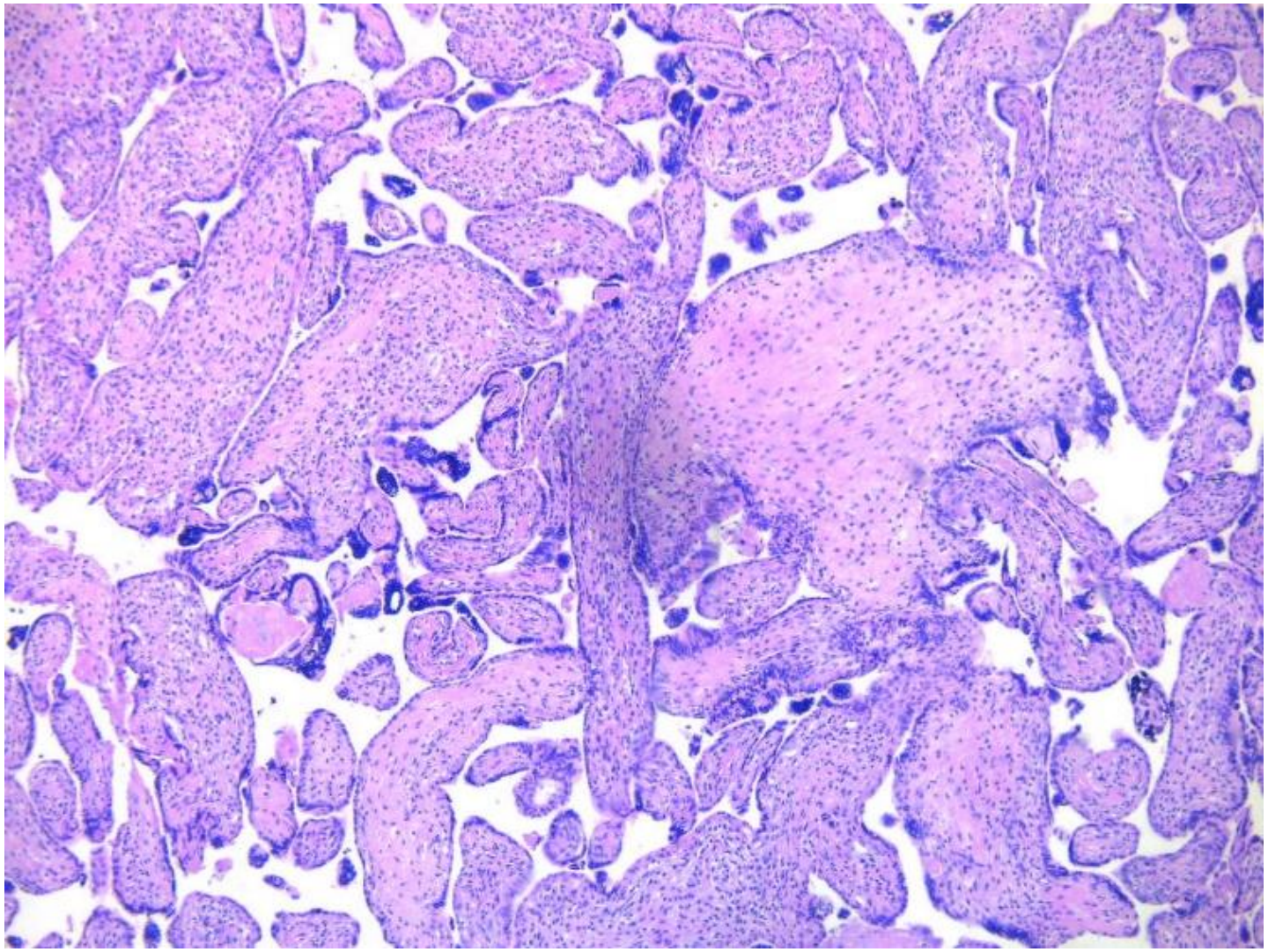
- Excessive syncytial knots diffusely
- Clustering of villi and obliteration of intervillous spaces
- Intervillous fibrin deposition (fine fibrine network)

---> excessive placental fibrosis (6 to 8 weeks)--->interpretation difficult

---> look at PATTERN of distribution of lesions



Mors in utero: 17 w AD



POSTMORTEM CHANGES

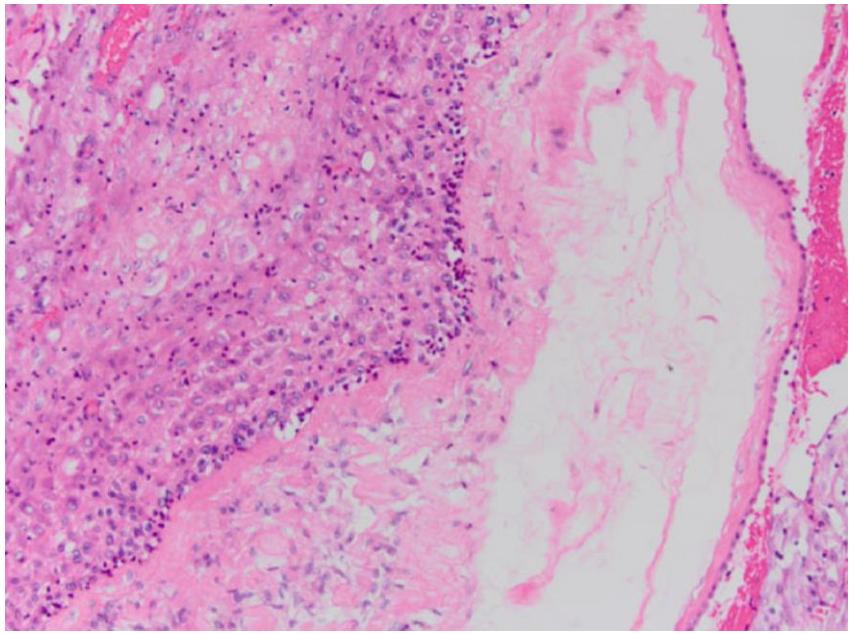
Consequences of….

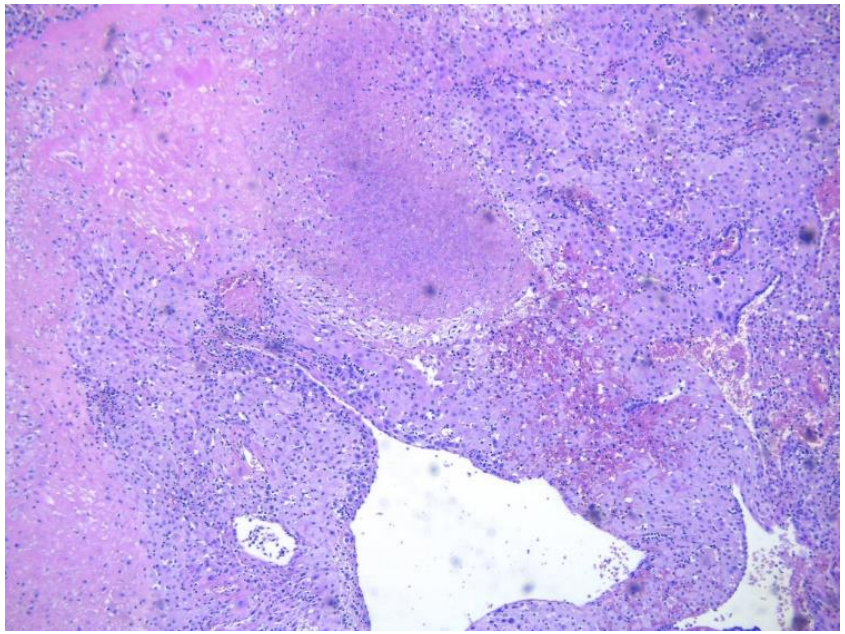
- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- **3. Maternal inflammation to non-viable products of conception**
- 4. Labor associated changes related to placental separation.

3. MATERNAL INflAMMATION TO NON-VIABLE PRODUCTS OF CONCEPTION

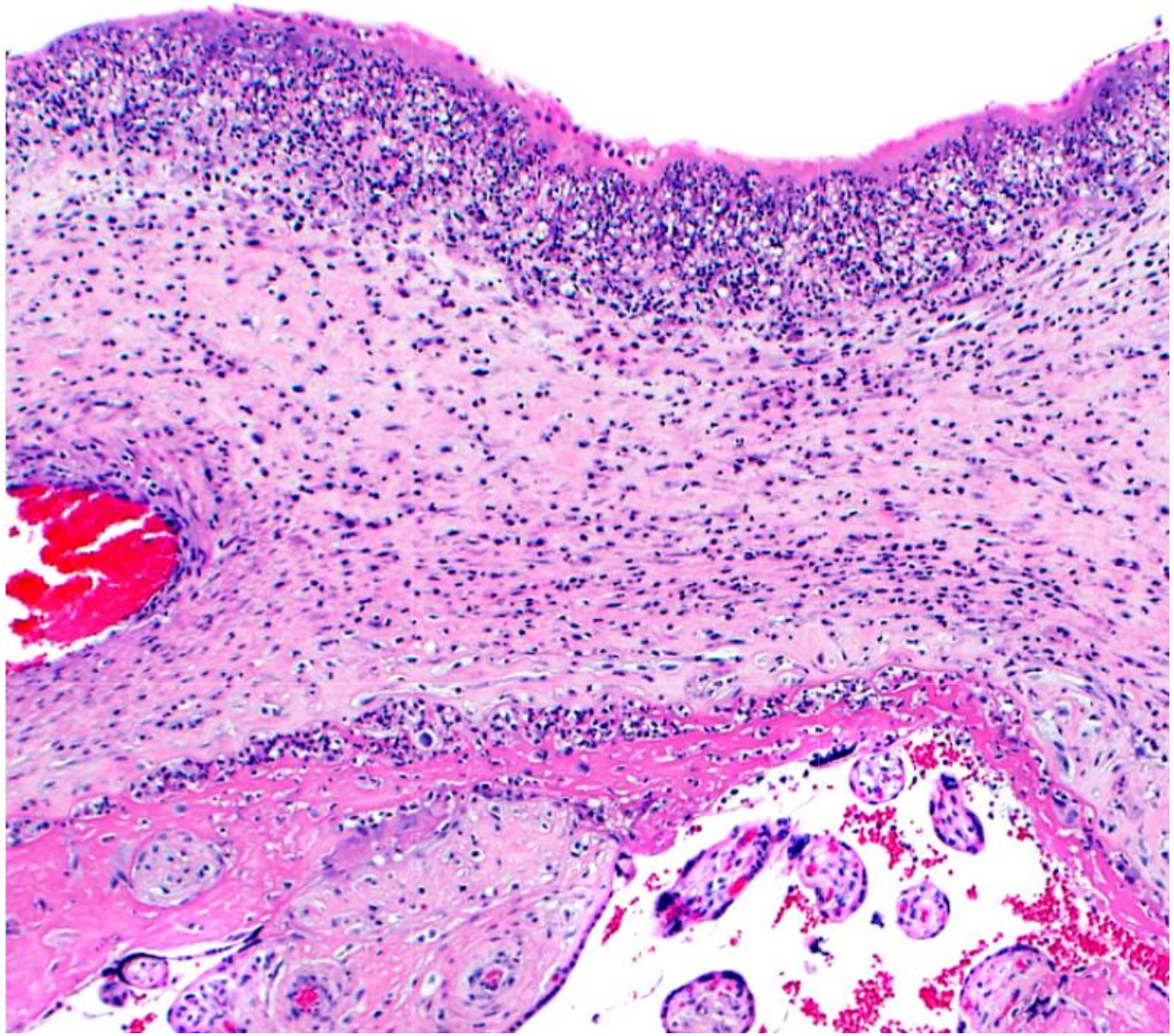
- maternal neutrophil migration into the extraplacental membranes

→ postmortem chorioamnionitis





Subacute necrotizing chorioamnionitis



POSTMORTEM CHANGES

Consequences of….

- 1. Cessation of fetal blood flow
- 2. Altered maternal perfusion
- 3. Maternal inflammation to non-viable products of conception
- **4. Labor associated changes related to placental separation.**

4. LABOR ASSOCIATED CHANGES RELATED TO PLACENTAL SEPARATION.

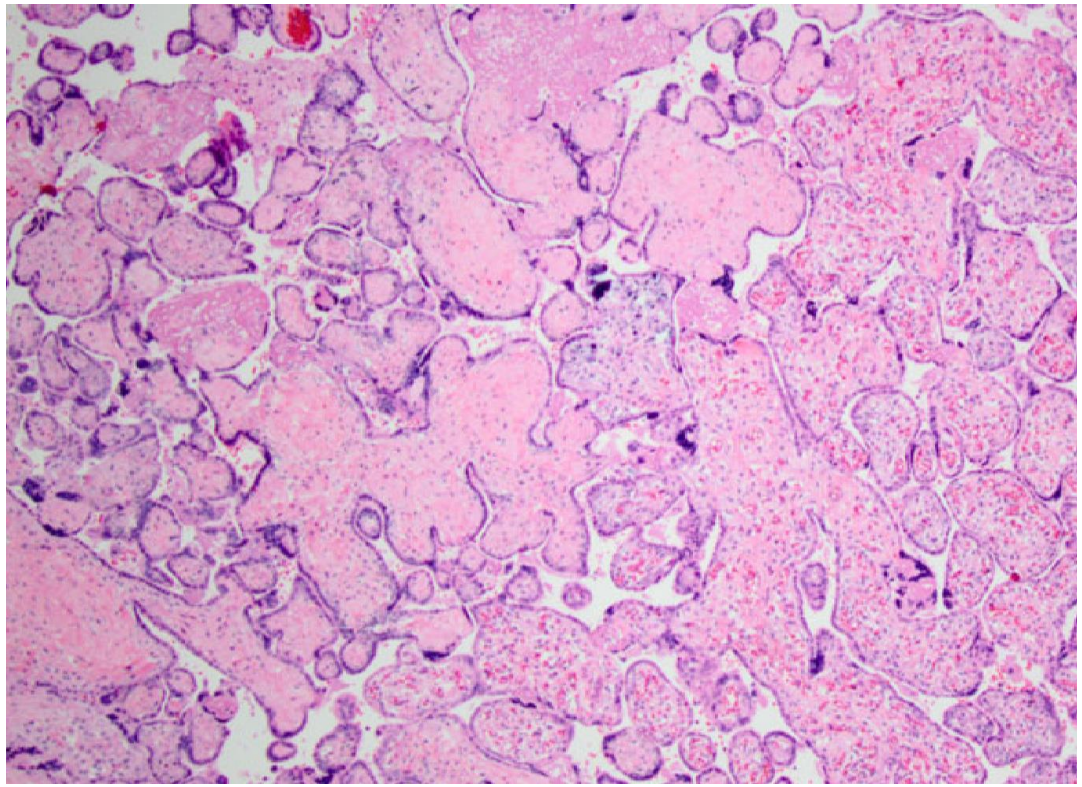
- features of placental abruption, with adherent retroplacental blood and microscopic recent placental infarction

Key: compare the temporal evolution of placental changes to the time fetal death

DIFFERENTIAL DIAGNOSES

Fetal vascular malperfusion

- **Temporal and spatial heterogeneity** to the patterns
- Demise to delivery interval



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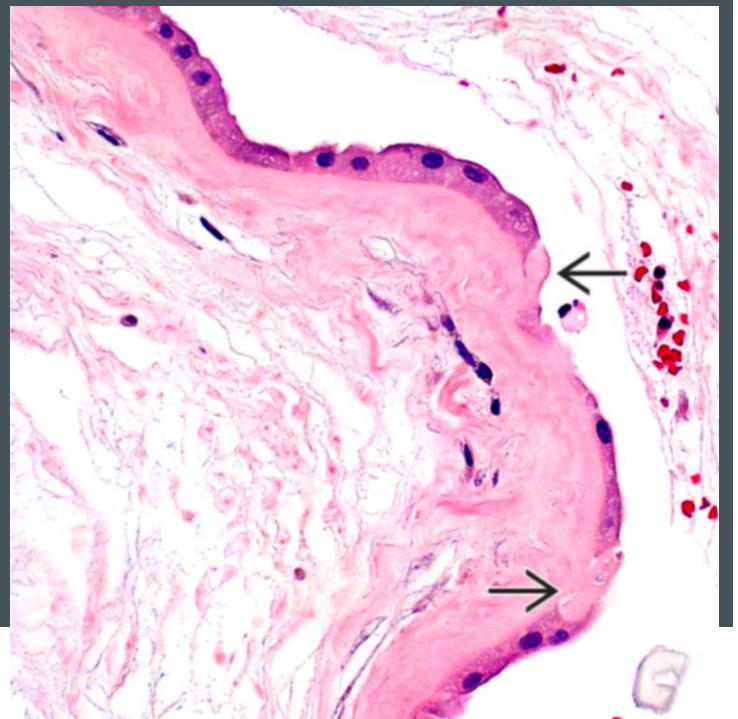
DIFFERENTIAL DIAGNOSIS

Maternal vascular pathologies

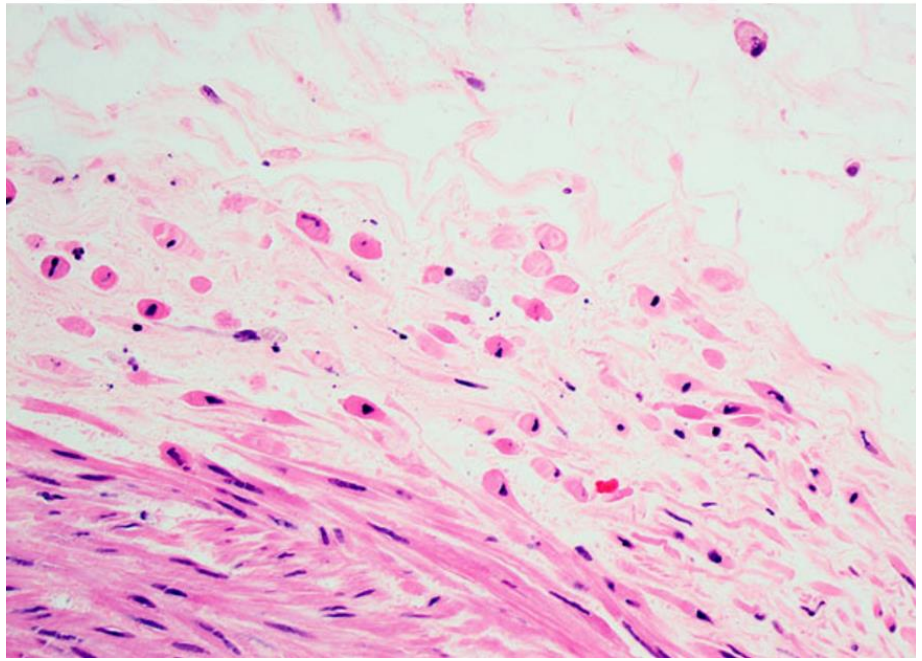
- Postmortem changes are diffuse and primary vasculary insufficiency is focal
- Comparison of demise-to-delivery interval

ASSOCIATED FINDINGS

Meconium



- Meconium is rarely released in response to fetal stress prior to the third trimester
- Third trimester: fetuses may release meconium in response to stimuli, including **hypoxia and infection**
- **meconium vascular necrosis**



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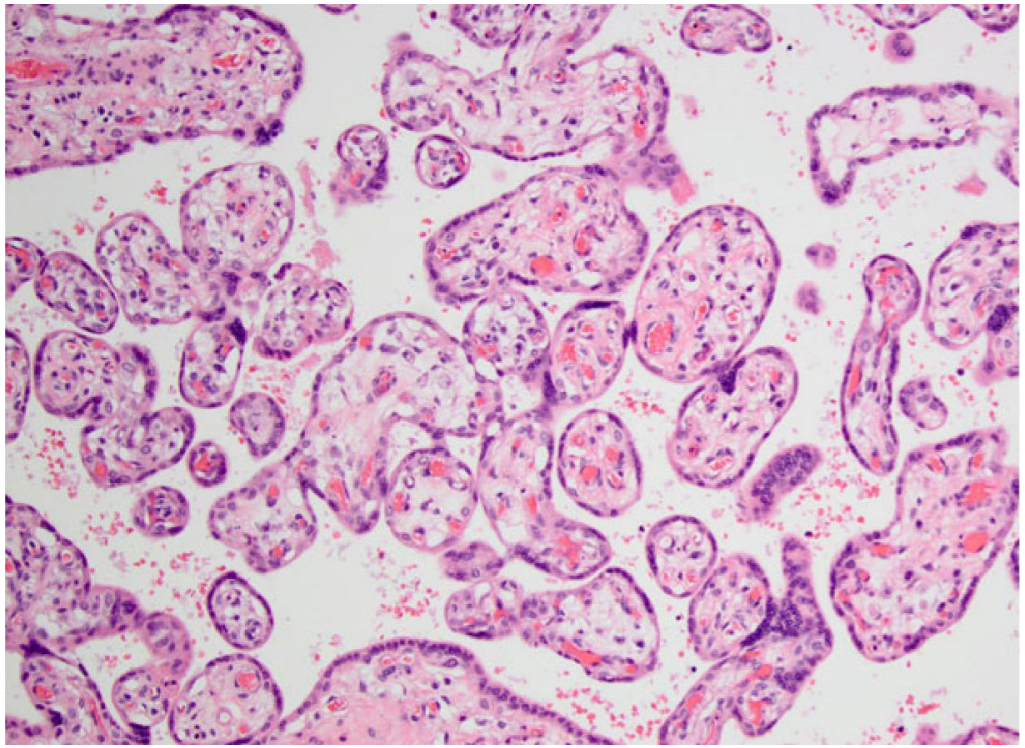
ASSOCIATED FINDINGS

Villous edema

- **nonspecific finding**, can be present in stillbirth placentas.
- more commonly in preterm placentas and in placentas with chorioamnionitis, acute and complete umbilical cord occlusion….



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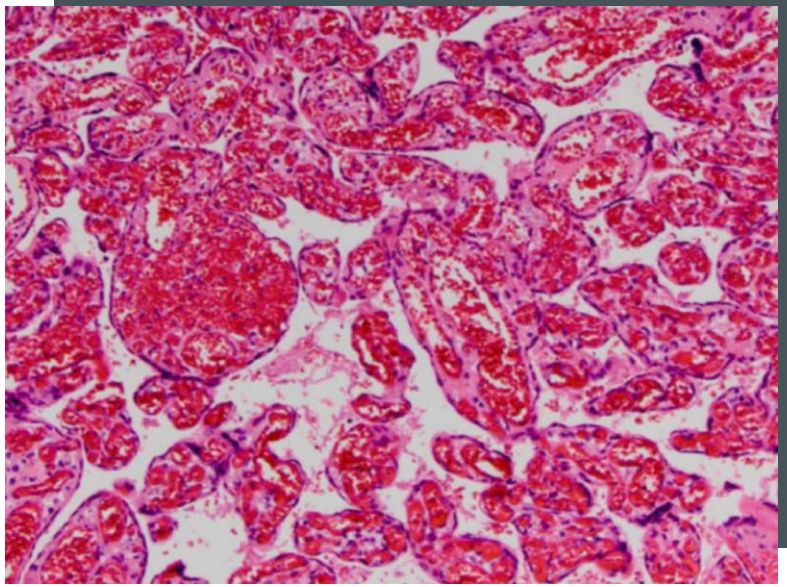
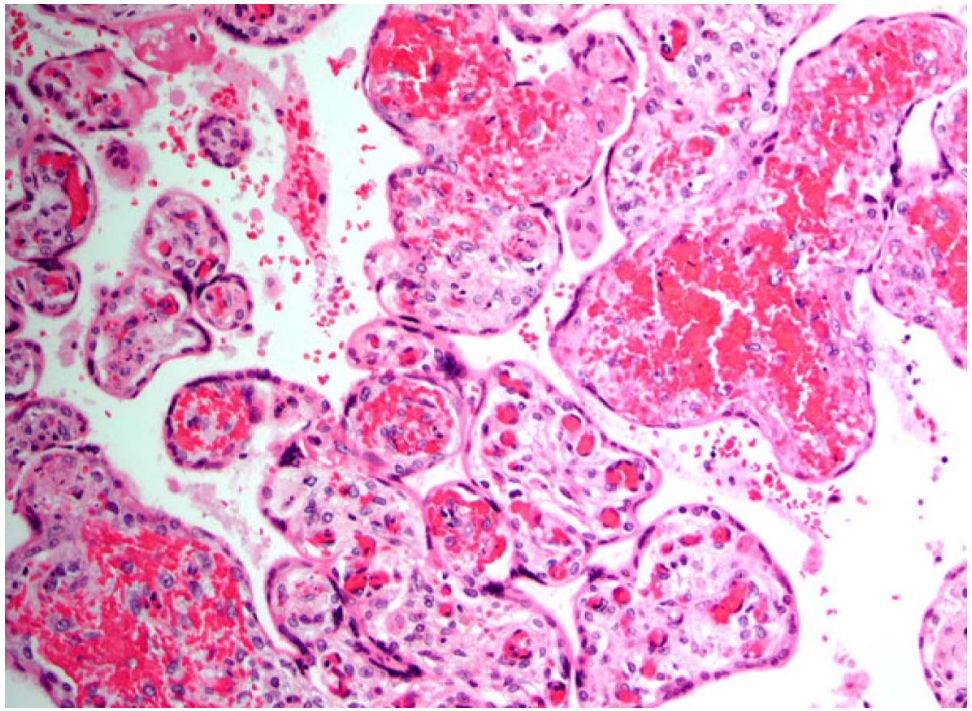
ASSOCIATED FINDINGS

Intravillous hemorrhage

- intact fetal red blood cell extravasation into the villous stroma
- acute cord prolapse
- placental–uterine separation
- DD. villous stromal-vascular karyorrhexis





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Estimation of In Utero Demise-to-Delivery Intervals				
Features	**Postdemise Interval**	**Sensitivity**	**Specificity**	**Positive Predictive Value**
Placental Histology				
Intravascular karyorrhexis in small villous vessels of several different regions	≥ 6 hours	94%	100%	1.000
Multifocal (10-25%) stem vessel luminal abnormalities	≥ 48 hours	94%	100%	1.000
Extensive (> 25%) stem vessel luminal abnormalities	≥ 2 weeks	78%	98%	0.875
Extensive (> 25% of terminal villi) avascular villi	≥ 2 weeks	100%	93%	0.750

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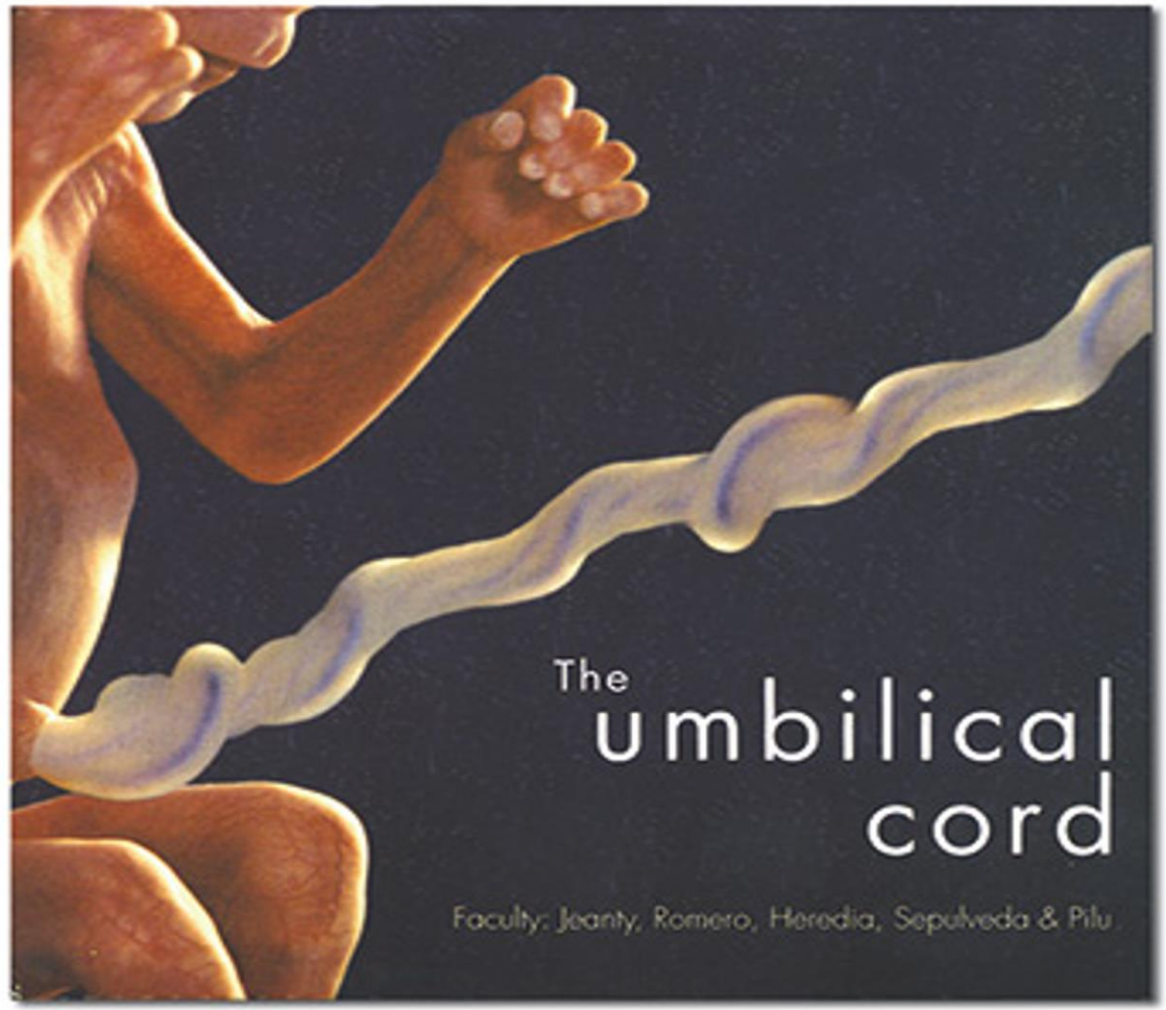
4. PLACENTA QUIZ

Q1 : How many coils are there?



Q 1: HOW MANY COILS ?

- A. 5
- B. 6
- C. 7
- D. 8

Q 1: HOW MANY COILS ?

- A. 5
- B. 6
- C. 7
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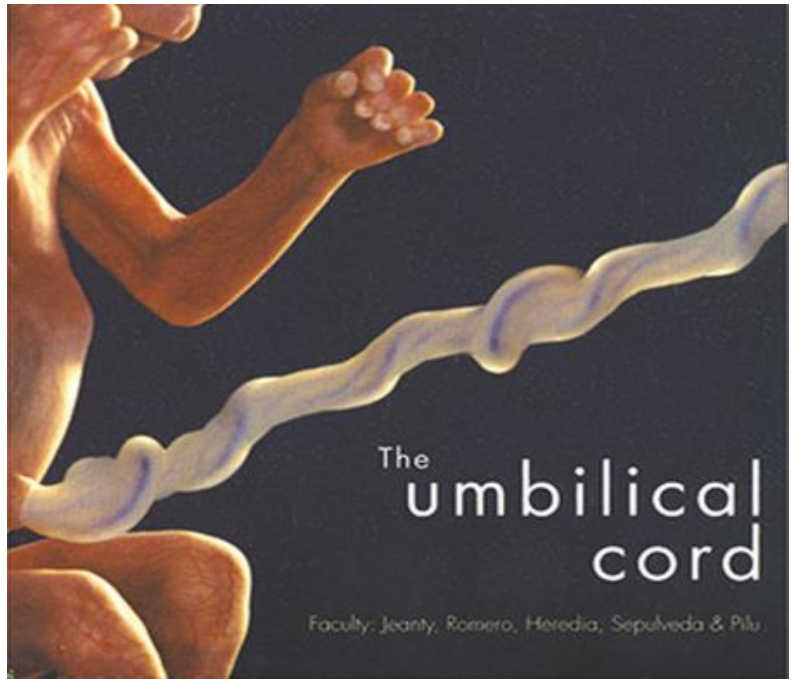
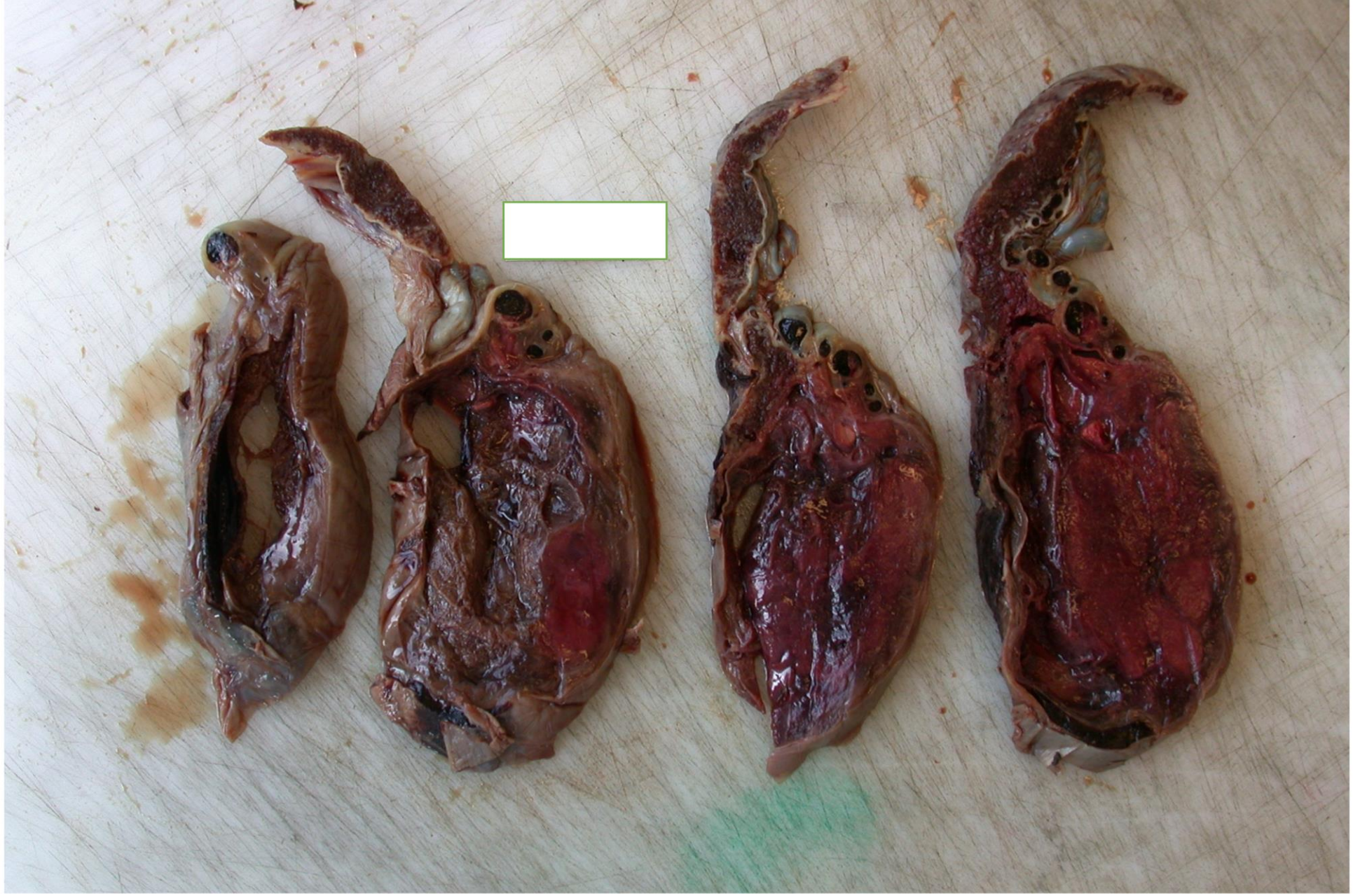


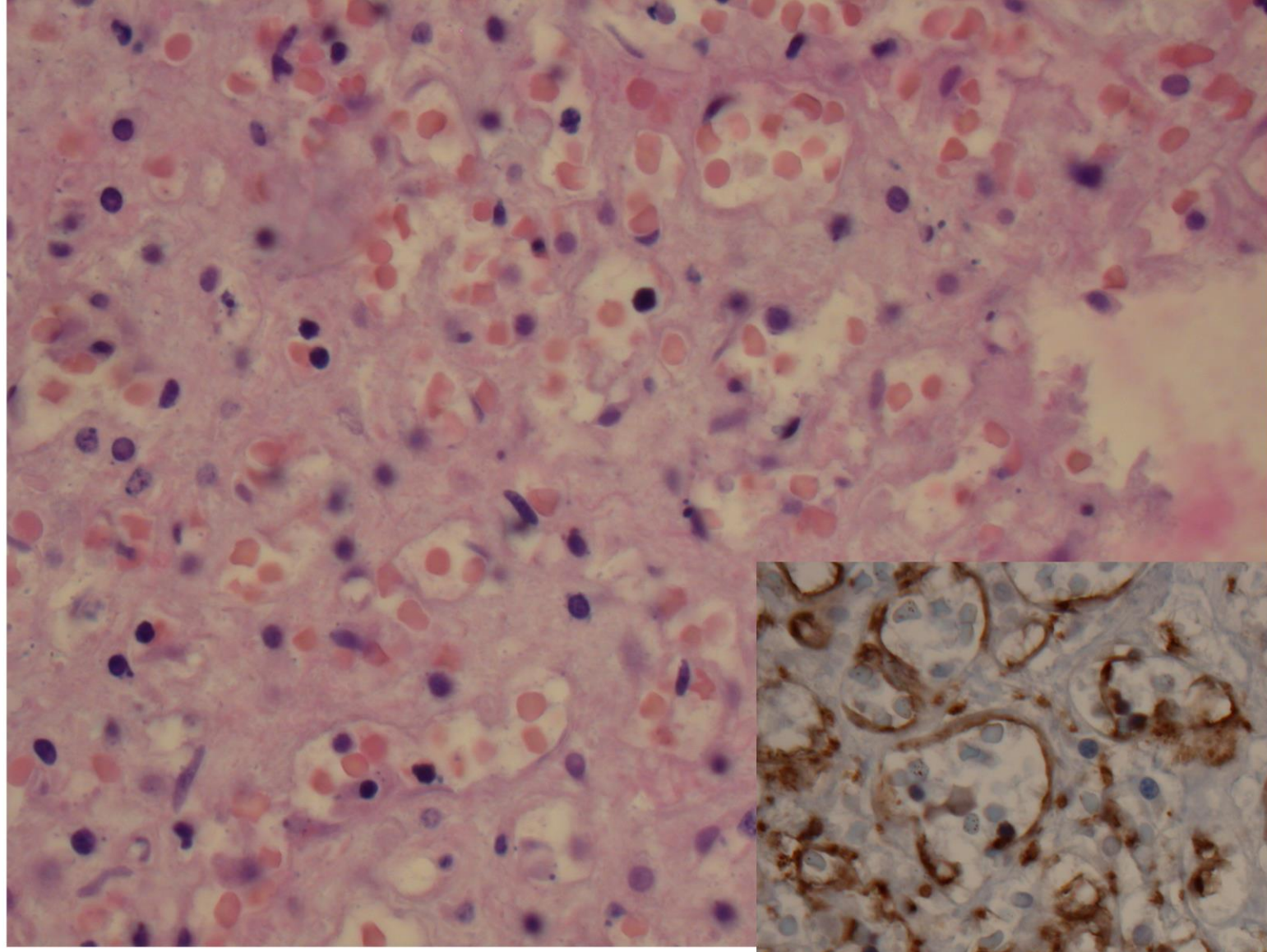
Q2 Clinical data

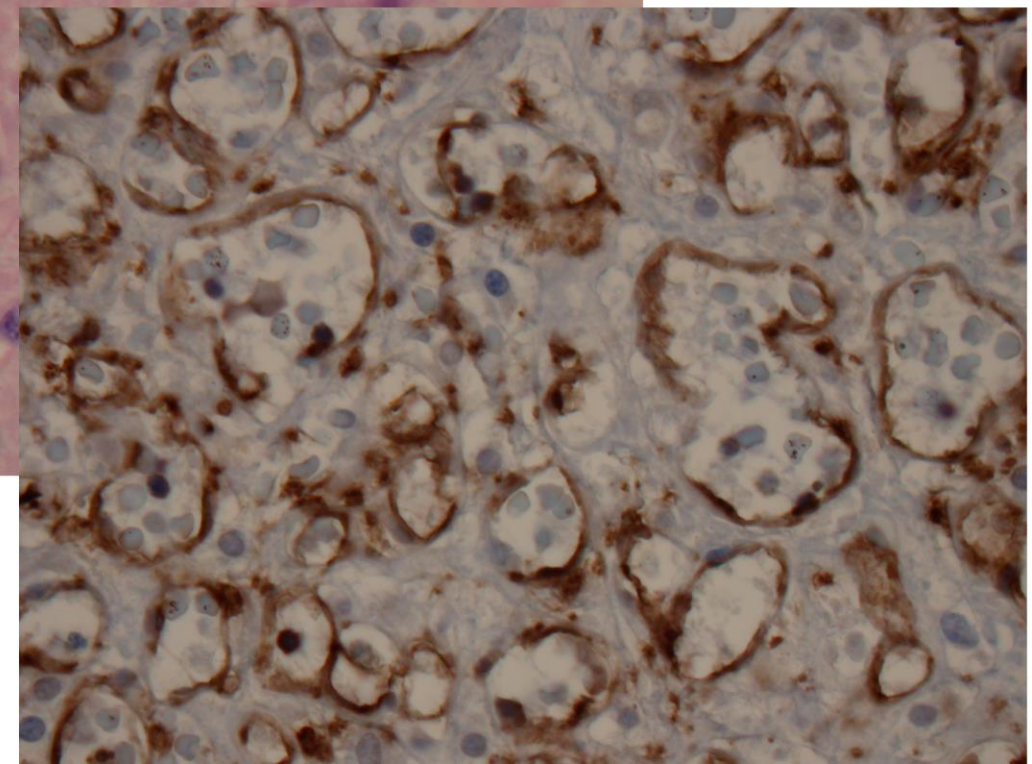
- Mother 35 yrs G1 P0.
- child 3000 gr
- placenta 710 gram (38 AD: > P90)

Macroscopy:

- RIP diameter 9 cm.







Q.2

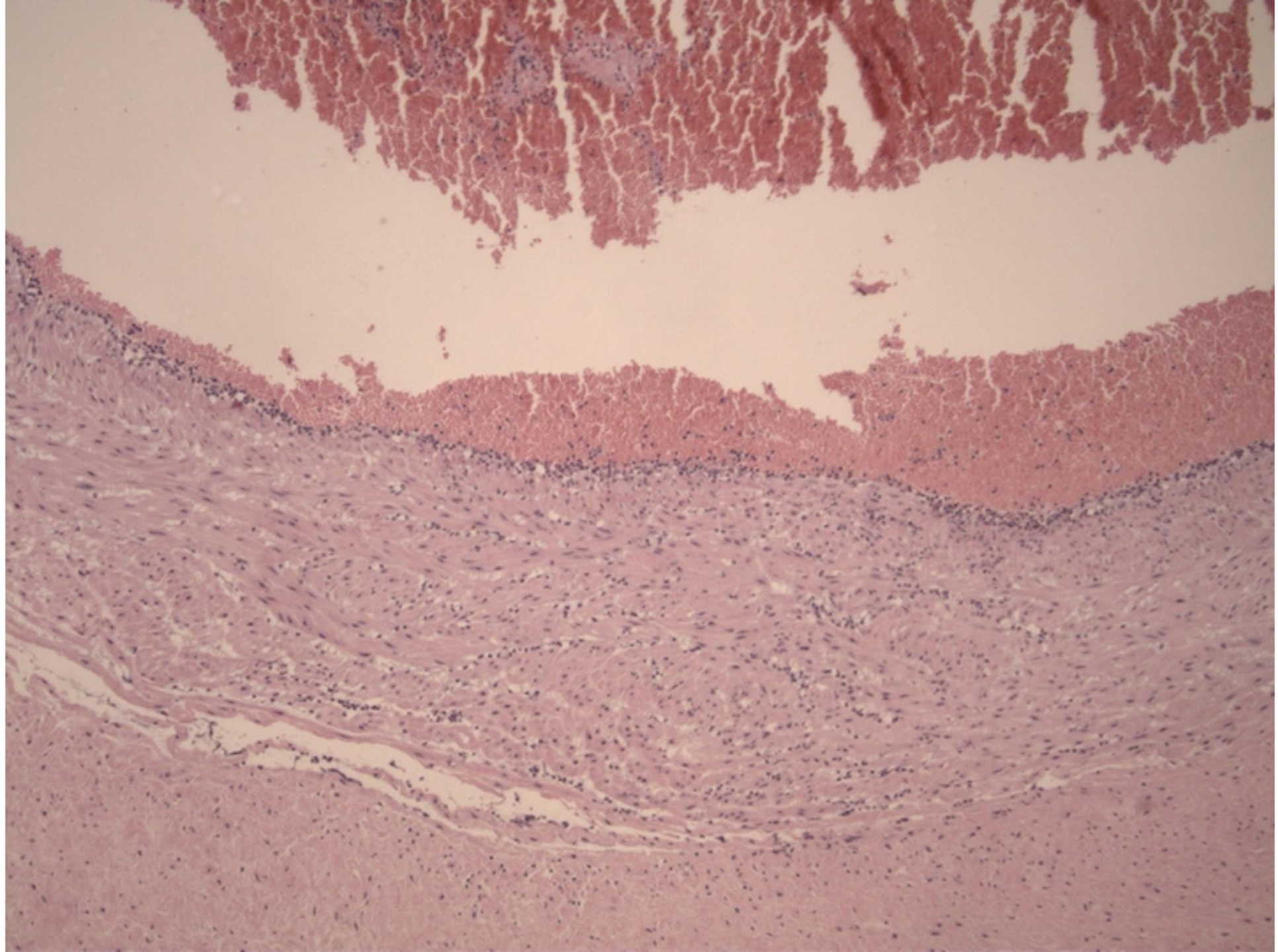
- A. Foetus Papyraceus
- B. Chorangioma
- C. Teratoma

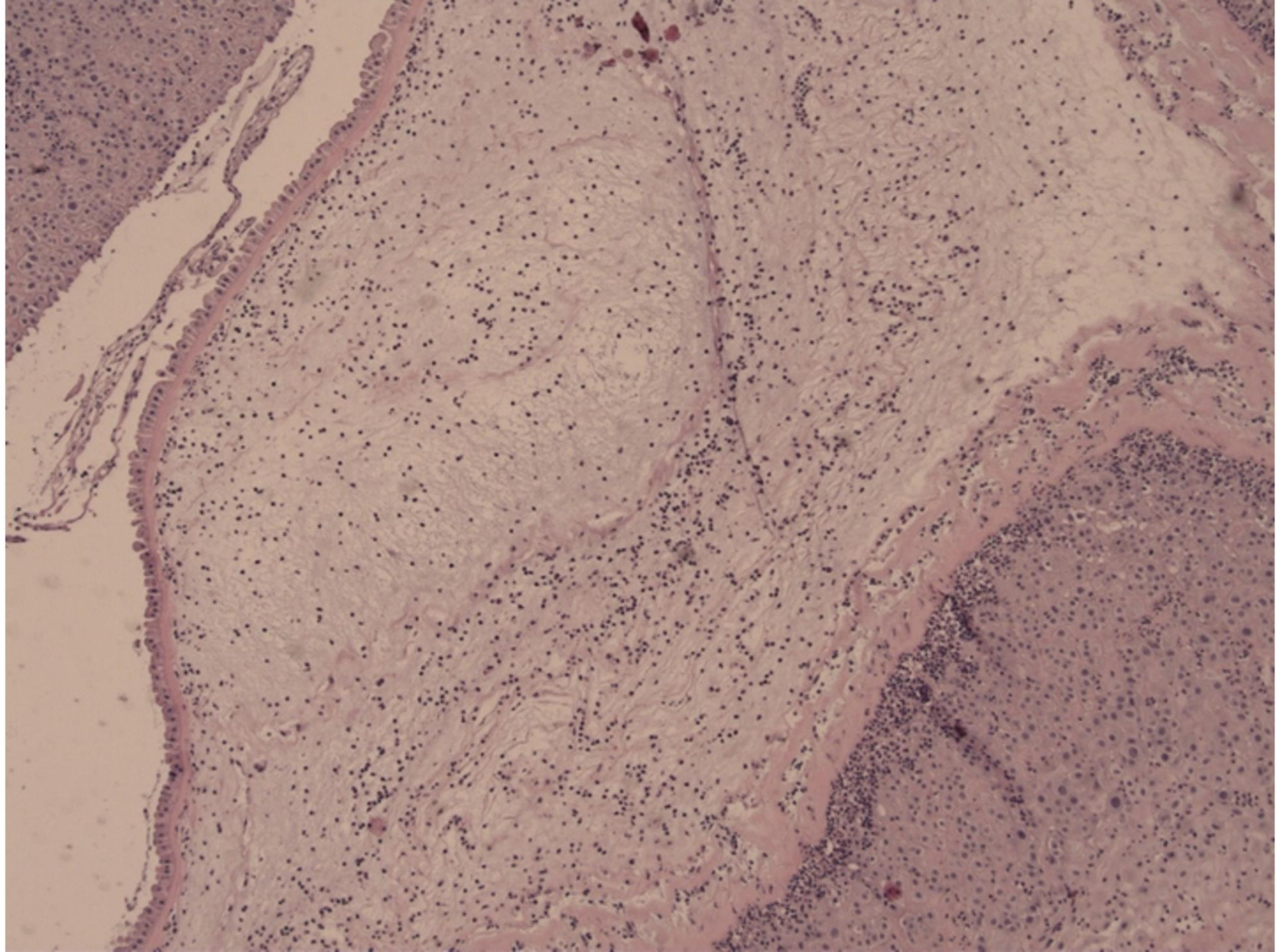
Q.2

- A. Foetus Papyraceus
- B. Chorangioma
- C. Teratoma

Q3 Clinical data

- G4P0
- AD 41+4
- Weight child 5060
- APGAR 4/6/8





Q3: REASON LOW APGAR ?

- A. Chorioamnionitis
- B. Meconium aspiration
- C. Chorioamnionitis and funiculitis

Q3 Reason low apgar’s?

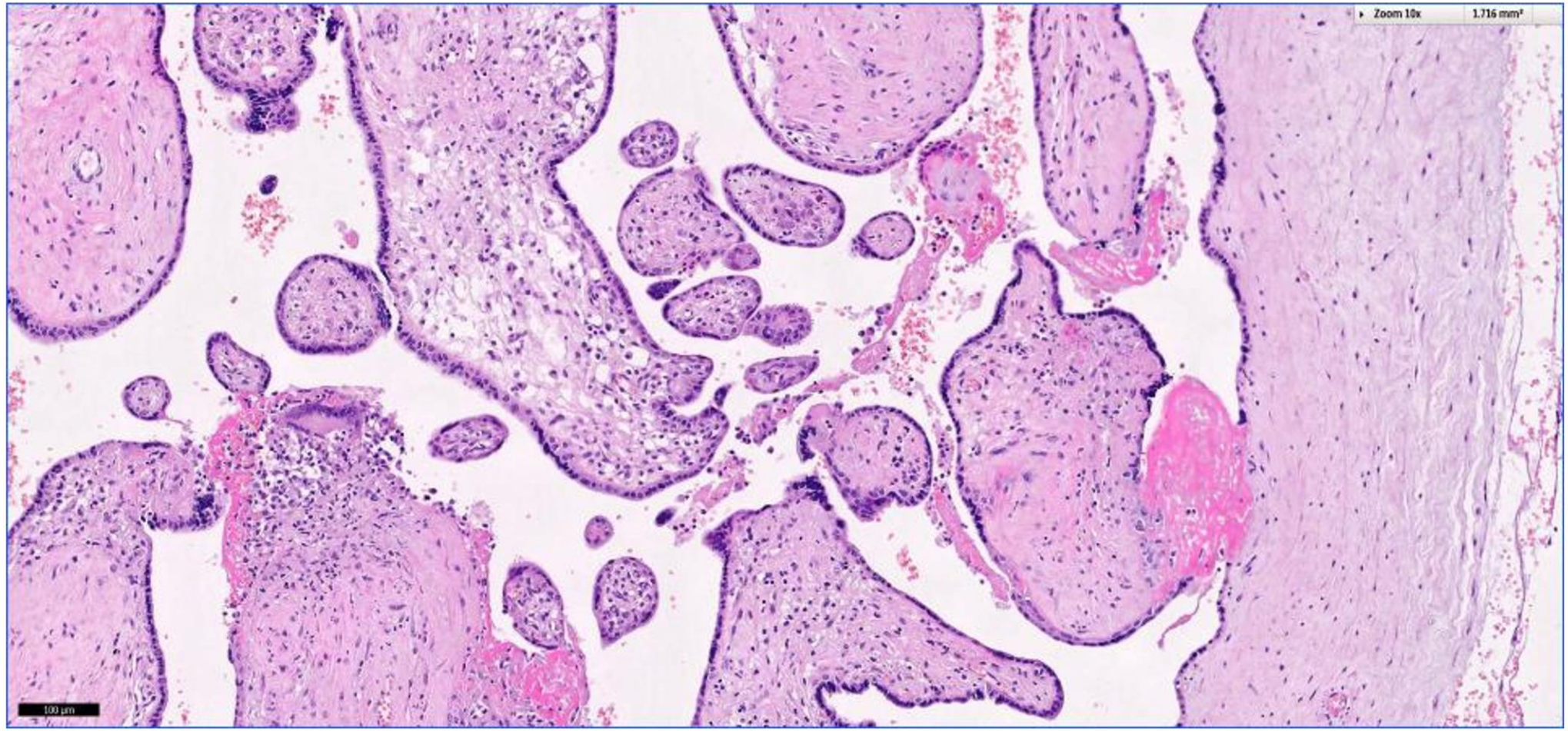
A. Chorioamnionitis
B. Meconium aspiration
C. Choriamnionitis with funiculitis
D. Don’t know

Q 4

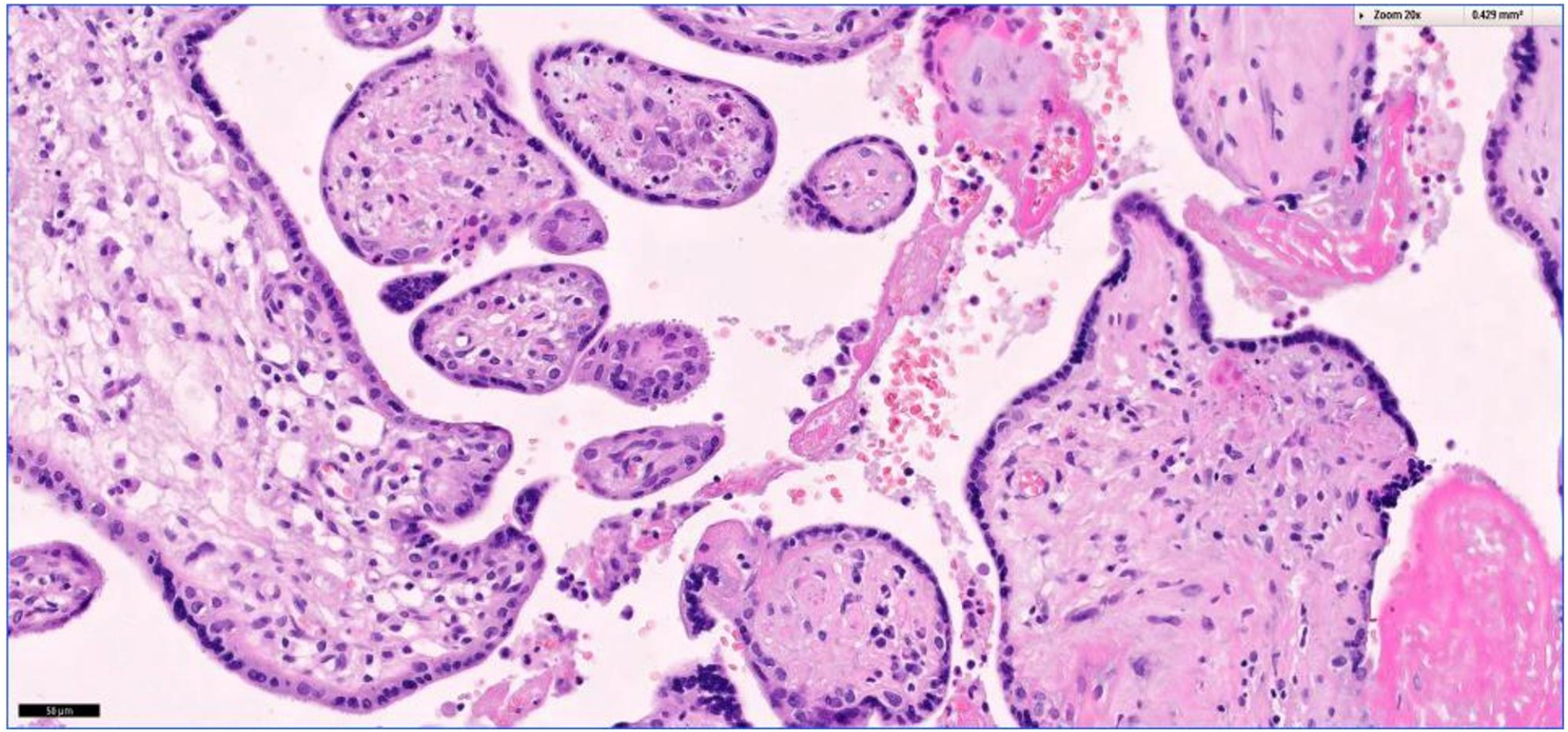
- GA 23+2 induction
- Multiple congenital anomalies at ultrasound
  - Hydrops fetalis, cerebral anomalies

- Placenta 460 g (>>p90)
- No lesions macroscopically

H&E 1x



H&E 20x



Diagnosis?

A. Acute villitis

B. Chronic villitis of unknown origin (VUE)

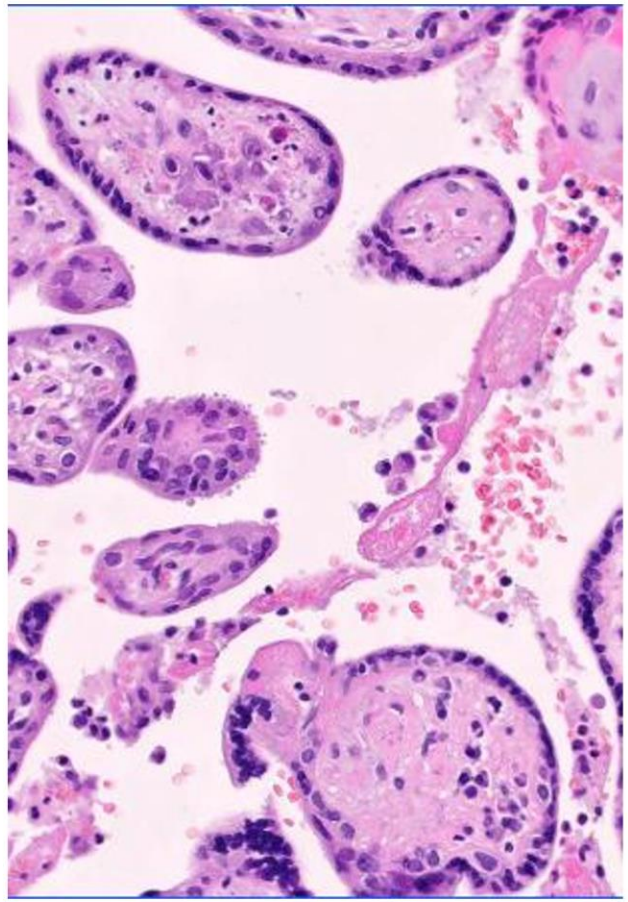
C. Chronic inflammation with plasmacells

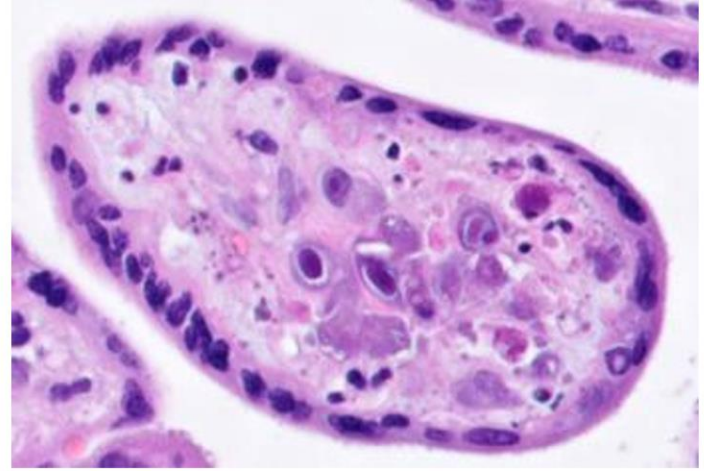
D. Viral induced villitis

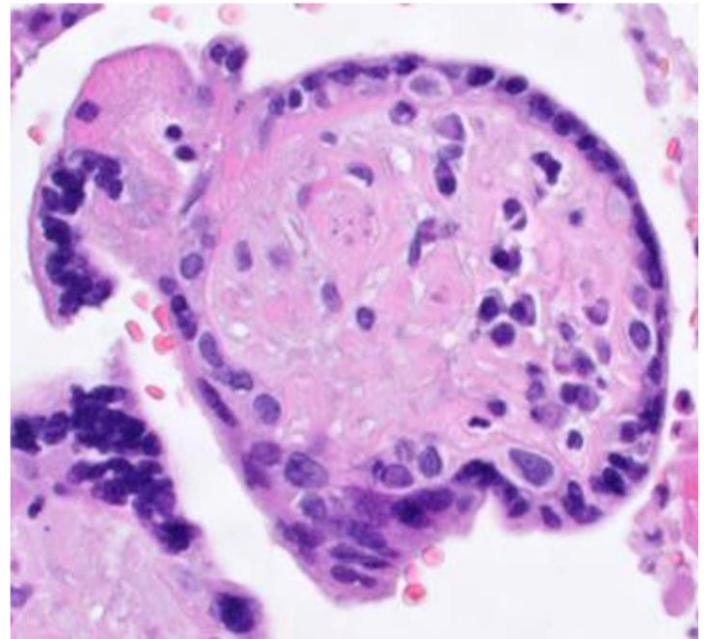
Answer: D

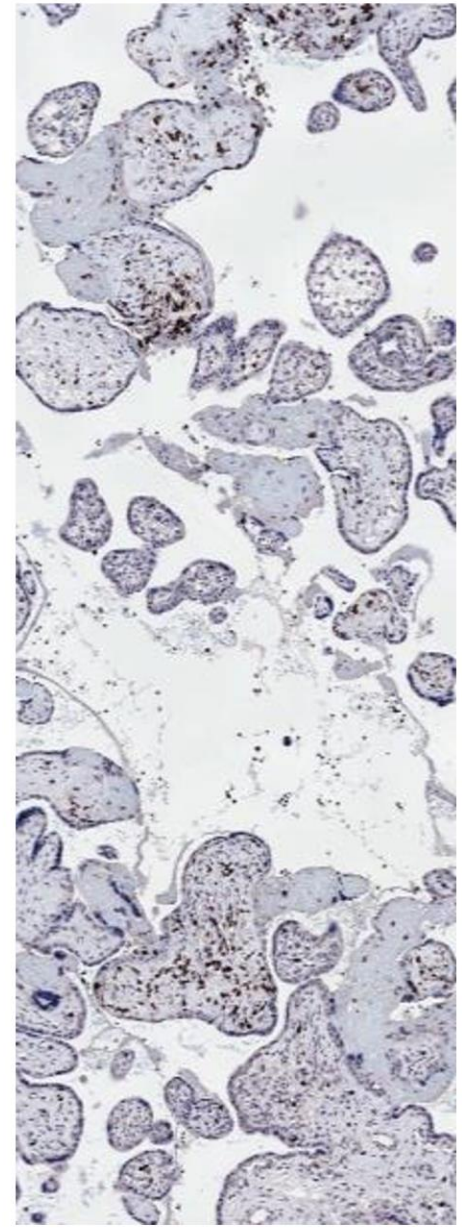
- Chronic villitis, CMV induced

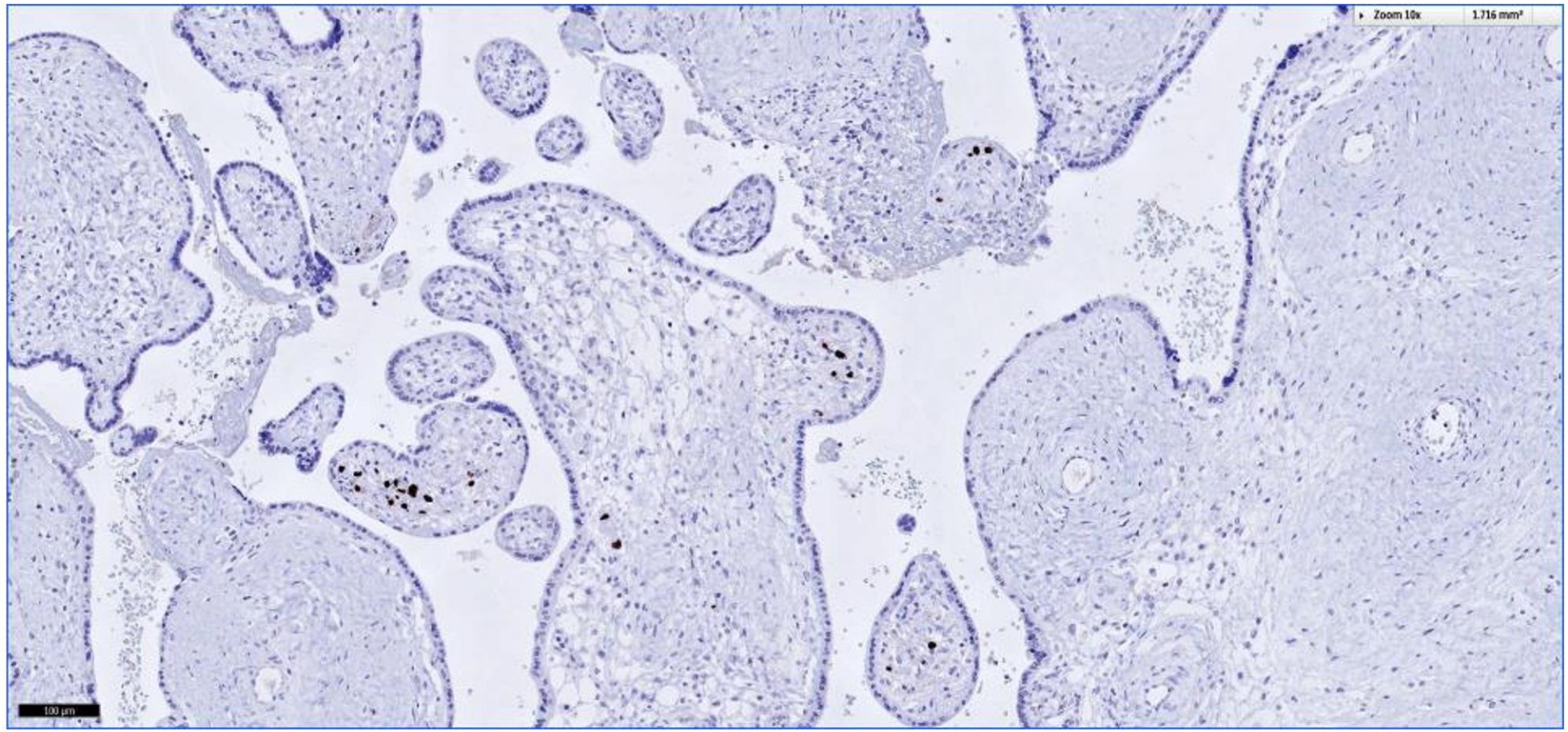
- Histology:
  - Lymfocytic villitis
  - Plasmacells
  - Iron deposition and calcifications
  - Viral changes
  - CMV +







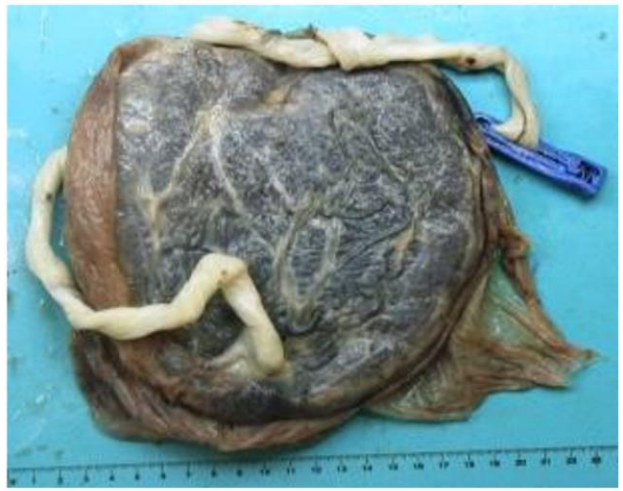


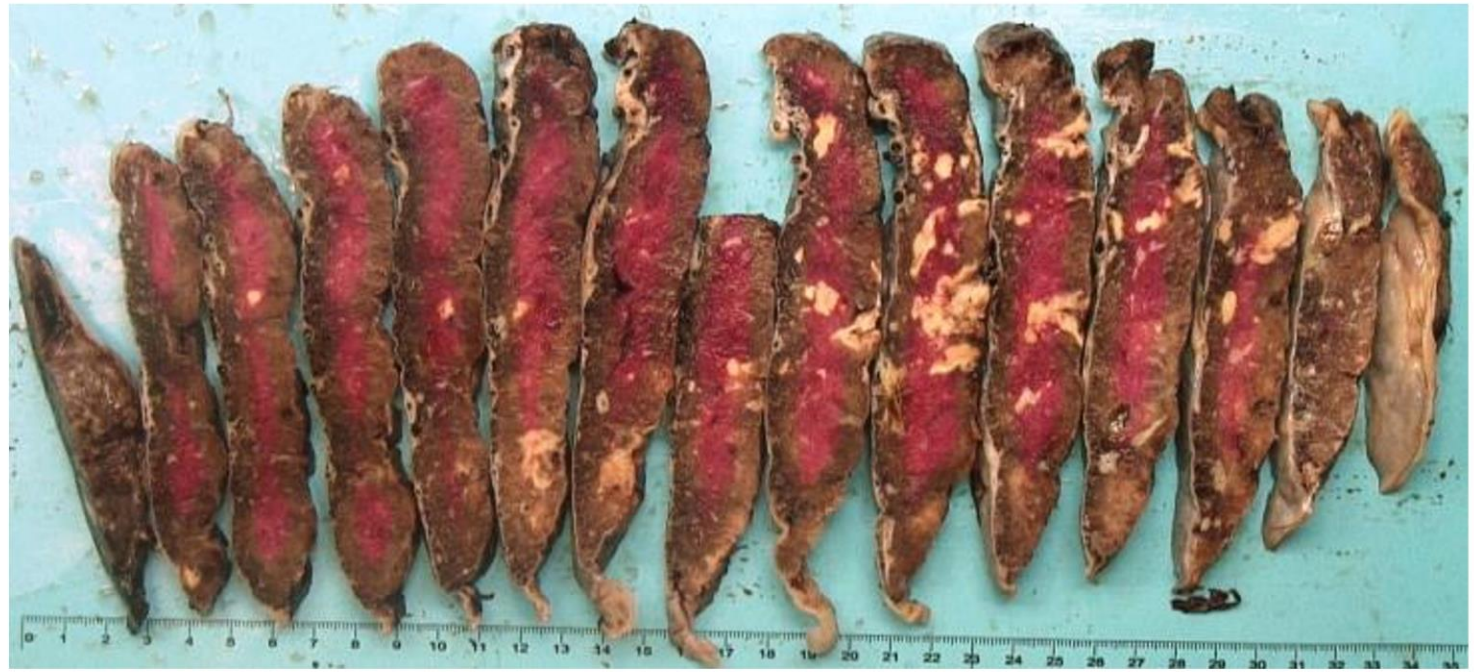

Zoom 10x
1.716 mm²
100 µm

Q5

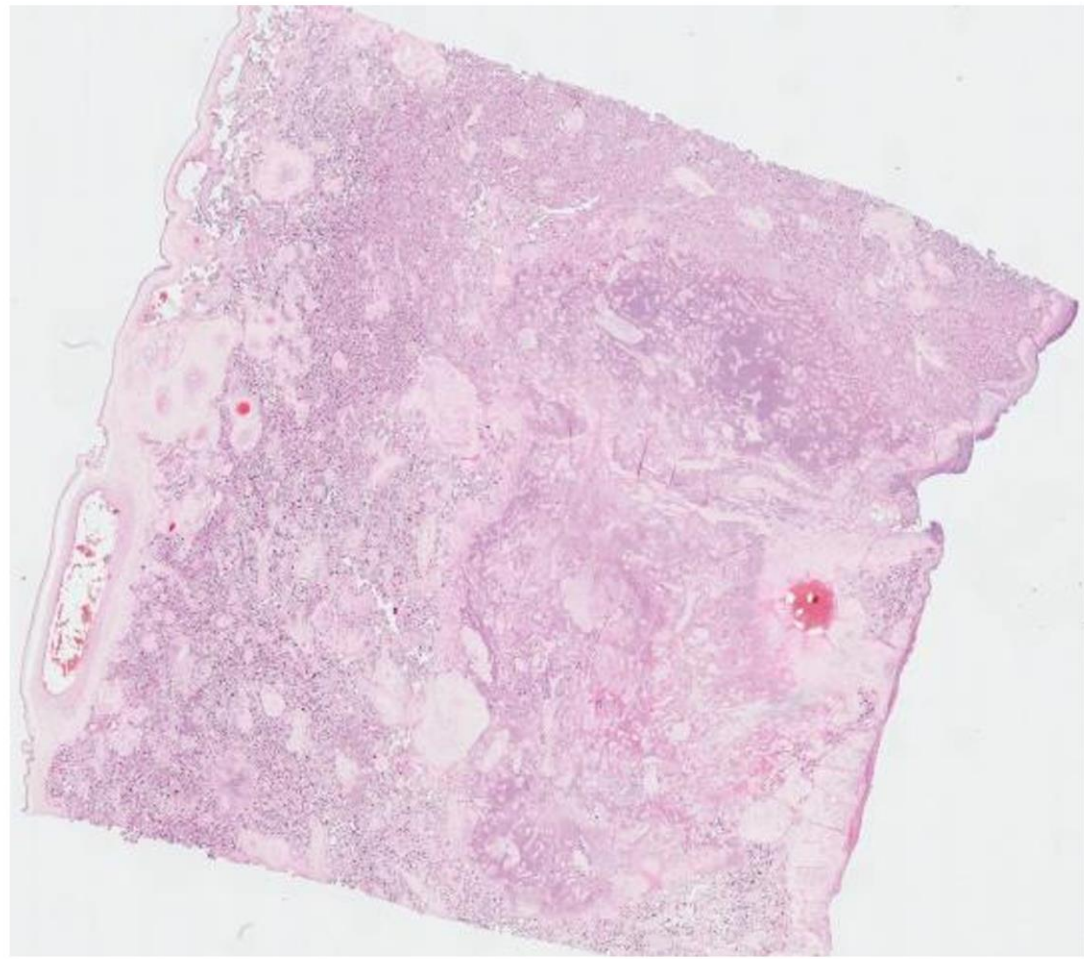
- GA 38+4, rupture of membranes >24h
- Intra-uterine growth restriction

- Placenta 334 g (<p10)

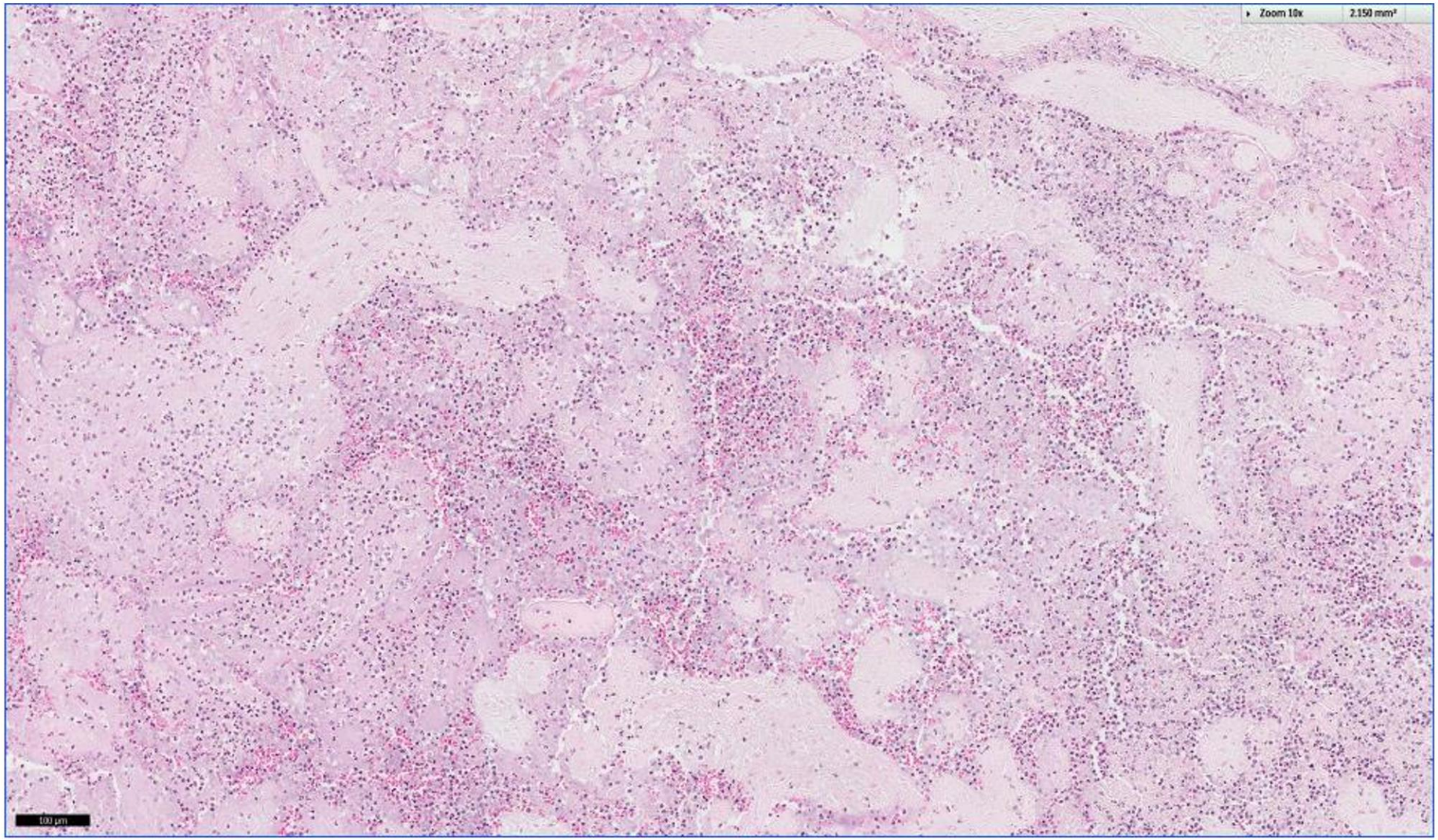




H&E 0,5x



H&E 10x



Diagnosis?

A. Infarction

B. Acute villitis

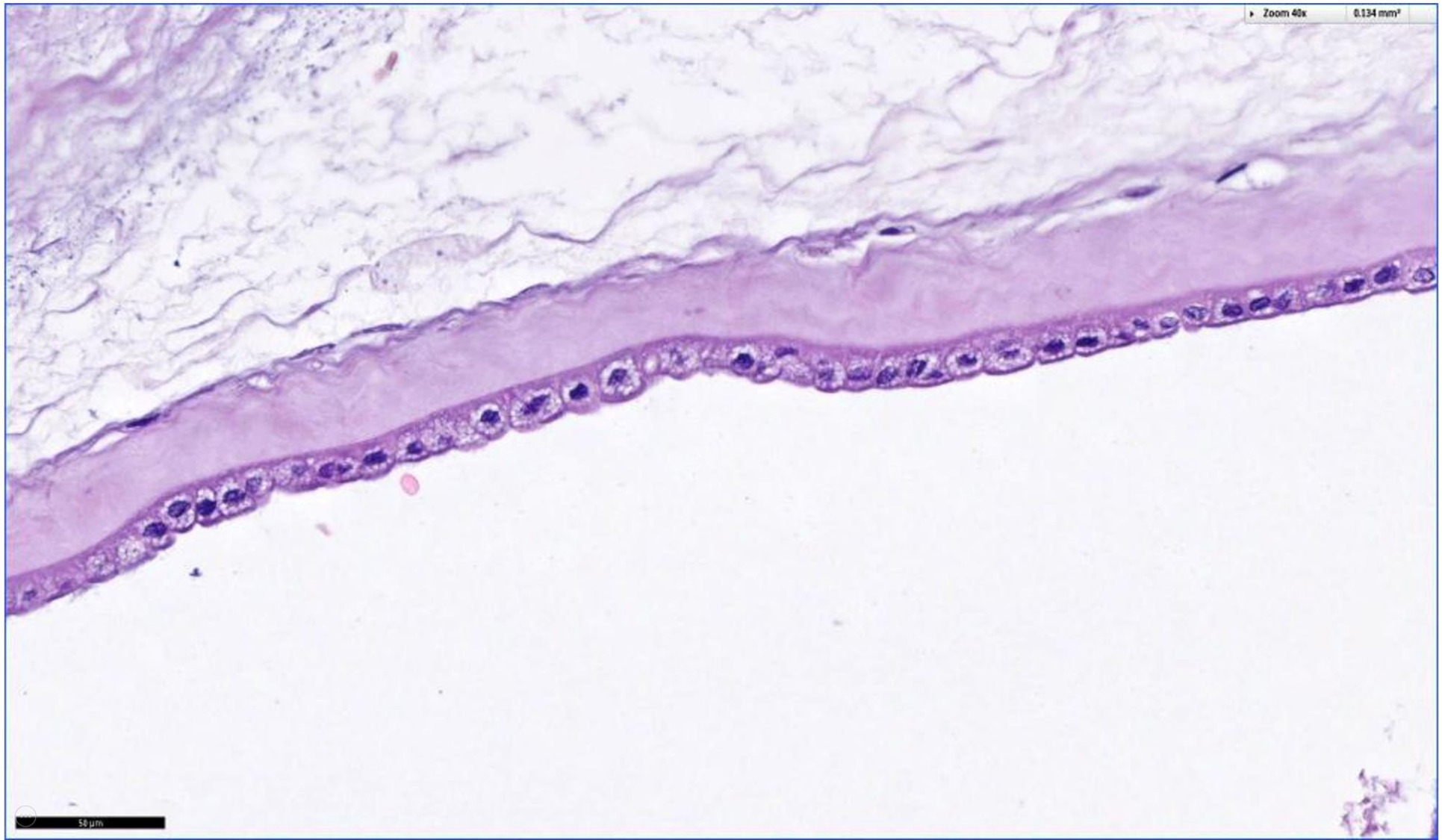
C. Intervillous abcesses

Answer: C

- Intervillous abcesses

- Associated with acute villitis and villous necrosis
- Micro-organisms:
  - Listeria monocytogenes, Staphylococcus, Escherichia coli, Campylobacter and Chlamydia
- This case showed some Gram positive cocci; possible listeriosis

Q6



Diagnosis?

A. Reactive changes due to meconium

B. Amnion nodosum

C. Vacuolation due to gastroschisis

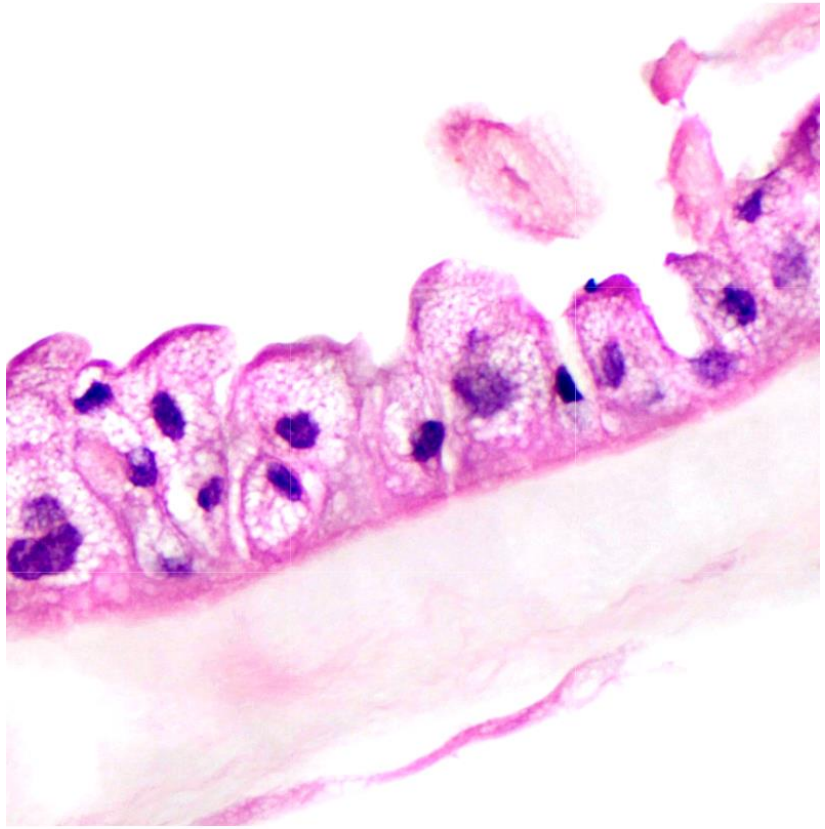
D. Vacuolation due to glycogen storage disease

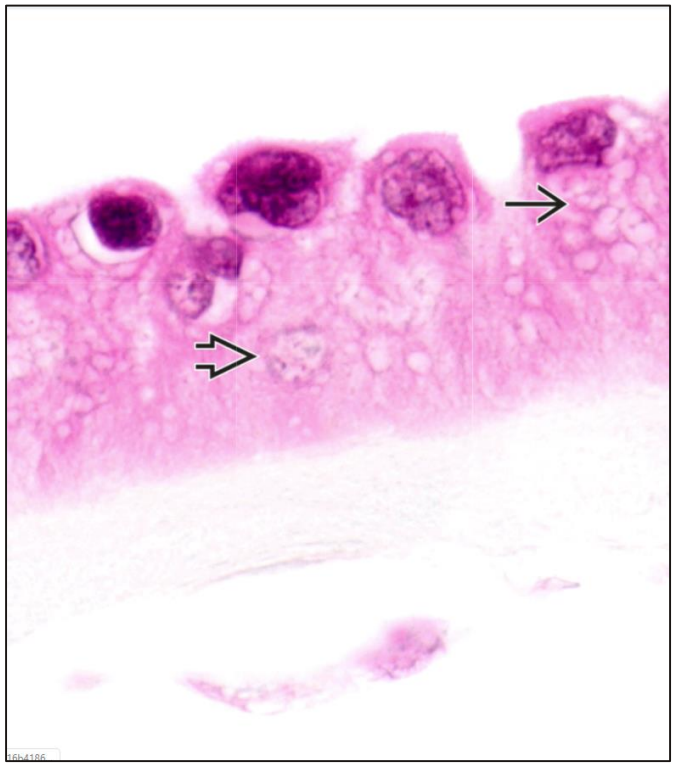
Answer: C

- Vacuolation due to gastroschisis

- Fine, uniform, extensive vacuolation
- Vacuoles contain lipid; origin is unknown

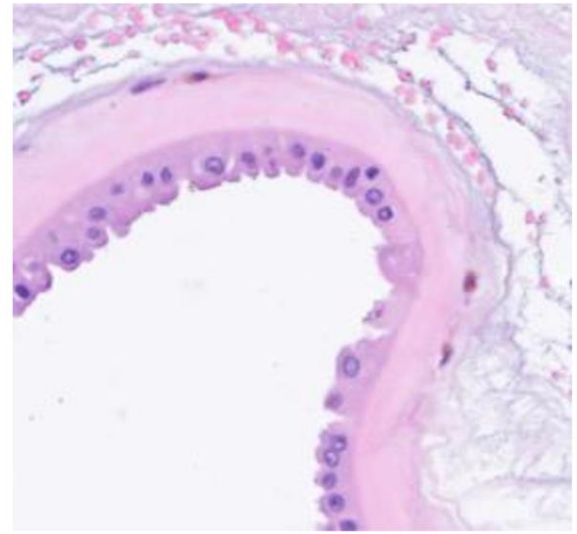
- Not found in combination with omphalocele





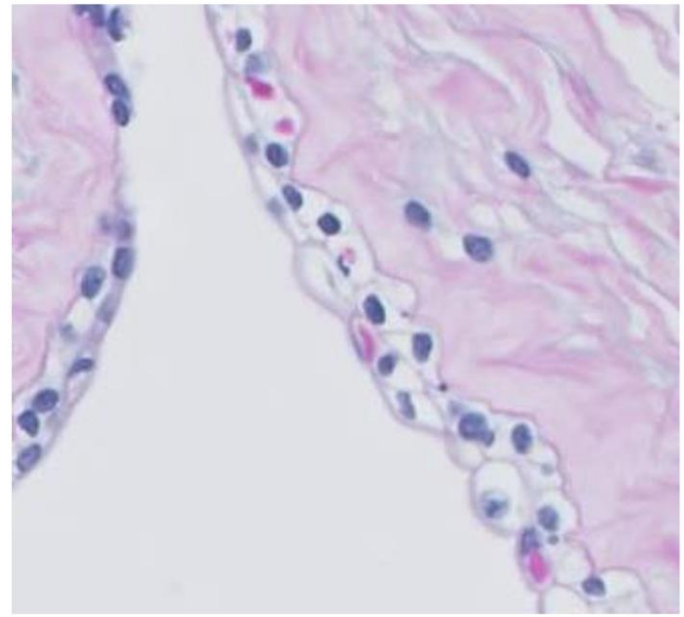
Meconium exposure: vacuolation is more coarse with greater variability

meconium pigment can be seen in some vacuoles

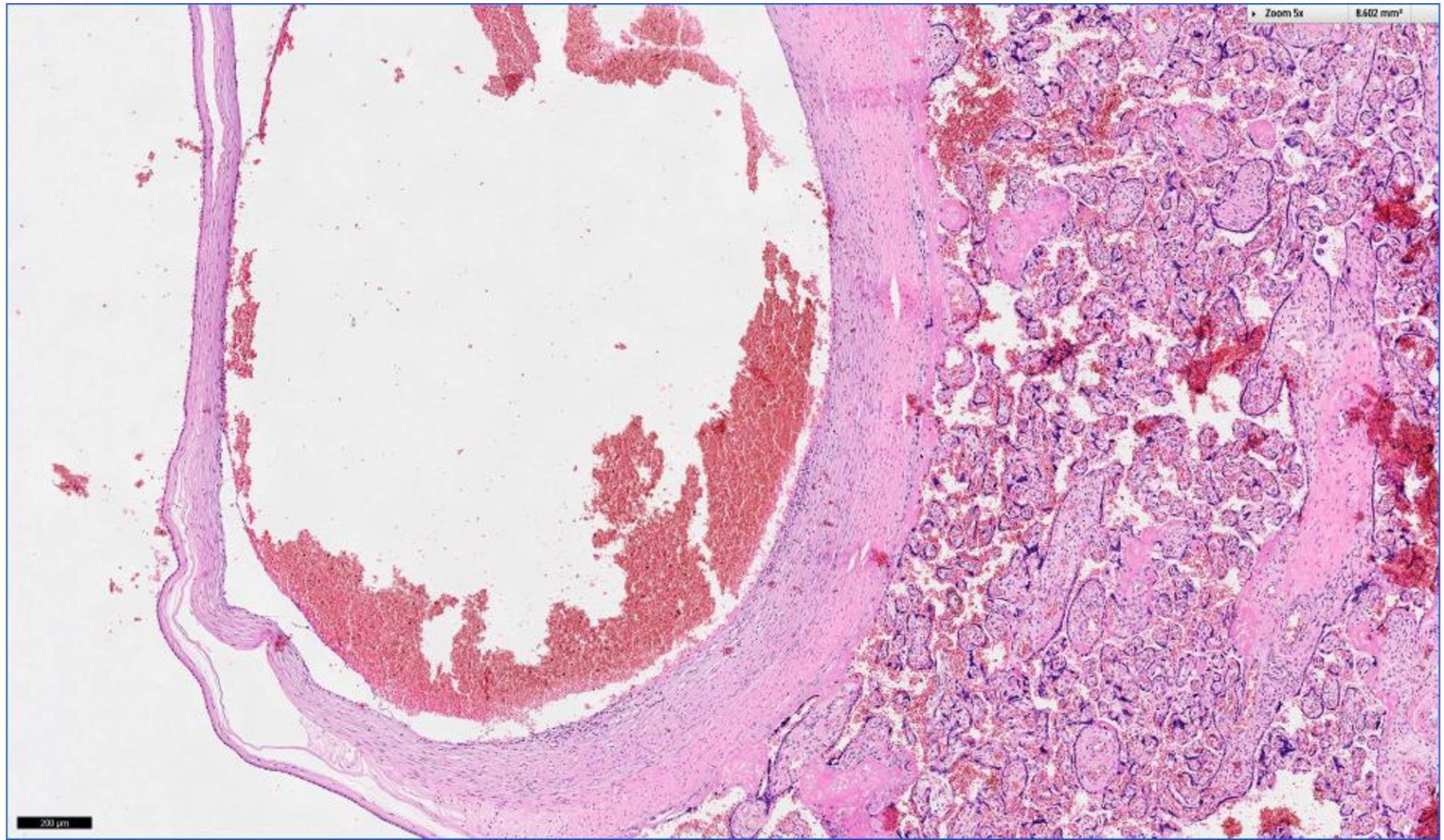


- Meconium:
  - Meconium-filled macrophages
  - Vacuolization, heaping up of cells, dissociation, necrosis

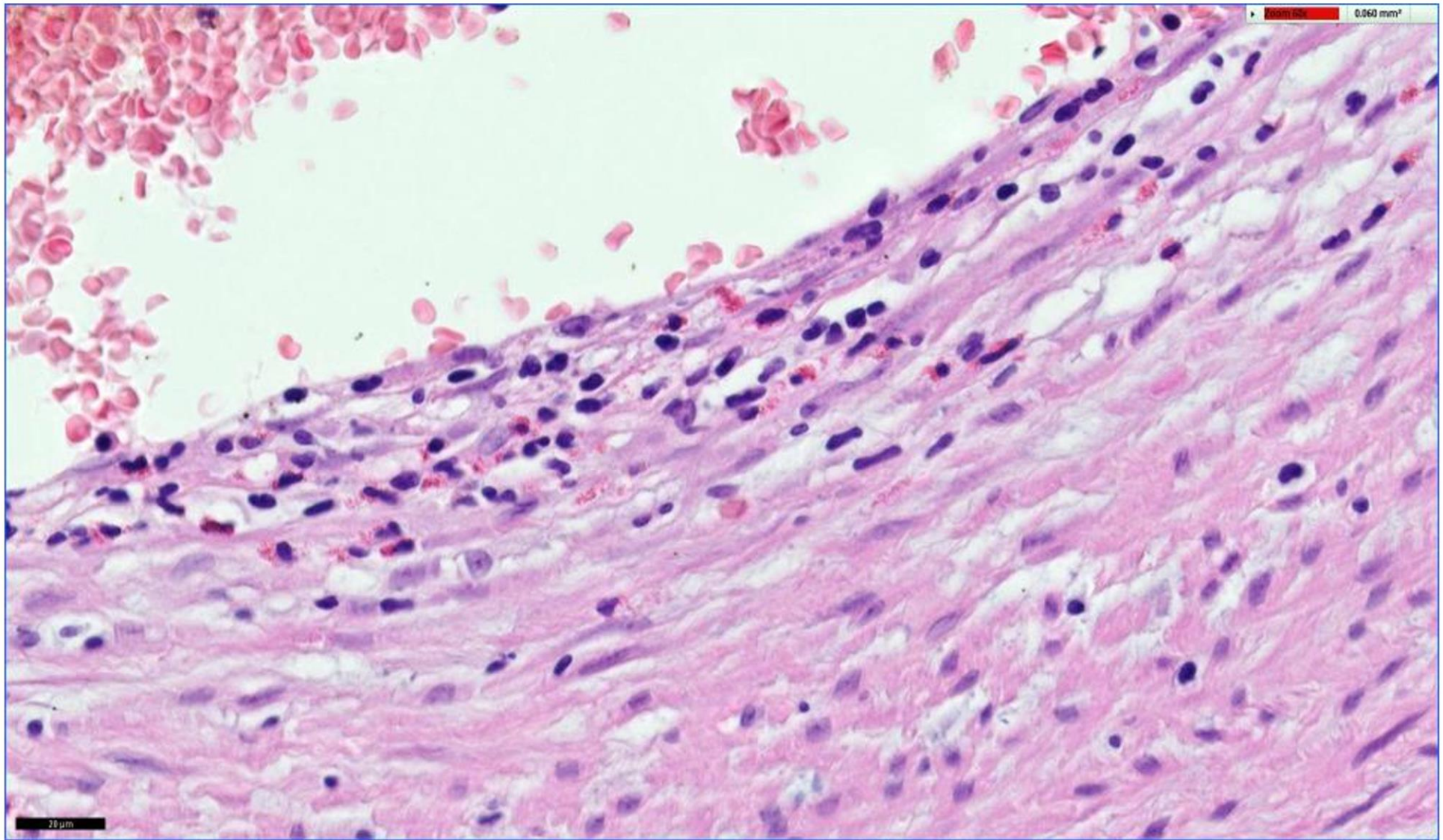
- Glycogen storage disease:
  - Vacuoles filled with glycogen-like material, PAS positive



Q8



H&E 60x



Diagnosis?

A. Eosinophilic vasculitis

B. Chronic vasculitis

C. Acute chorioamnionitis with fetal respons

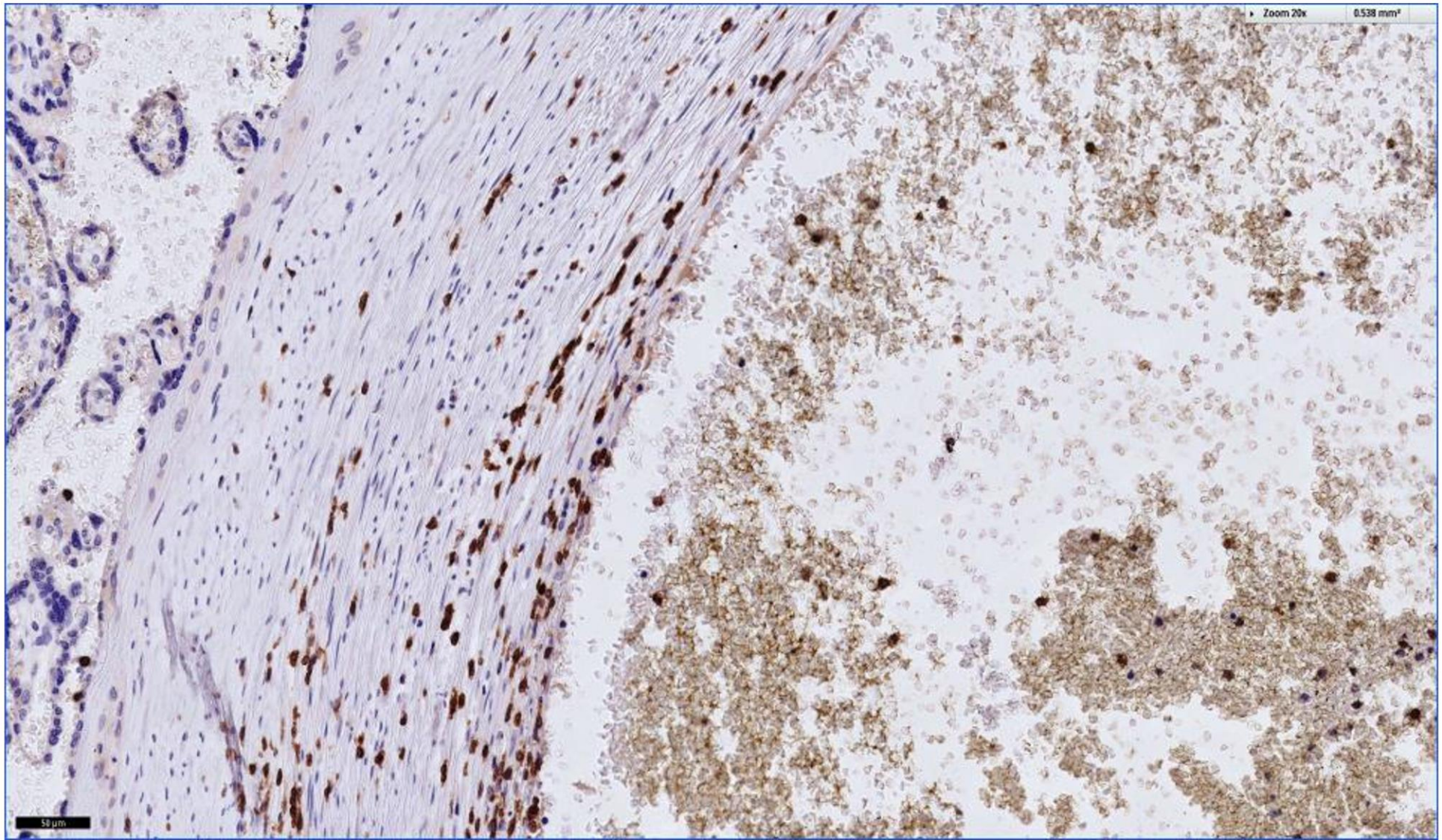
D. Subacute vasculitis

Answer: A

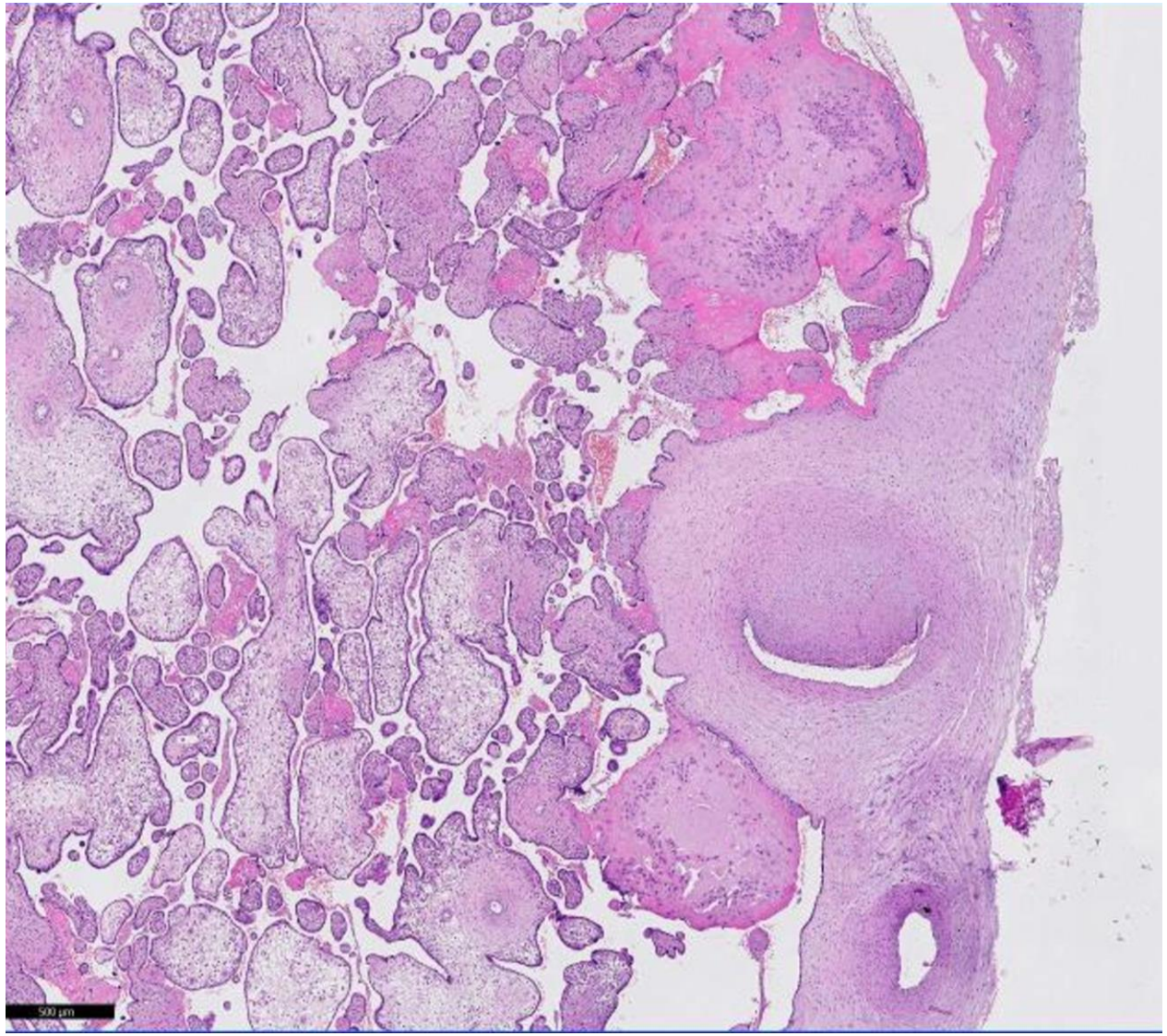
- Eosinophilic / T-cell vasculitis

- Fetal-derived chronic inflammatory infiltrate
- Eosinophils & small lymphocytes
- No neutrophils
- Incidence: 0,2%
- Associated with chronic villitis
- No specific clinical associations / consequences

CD3 20x

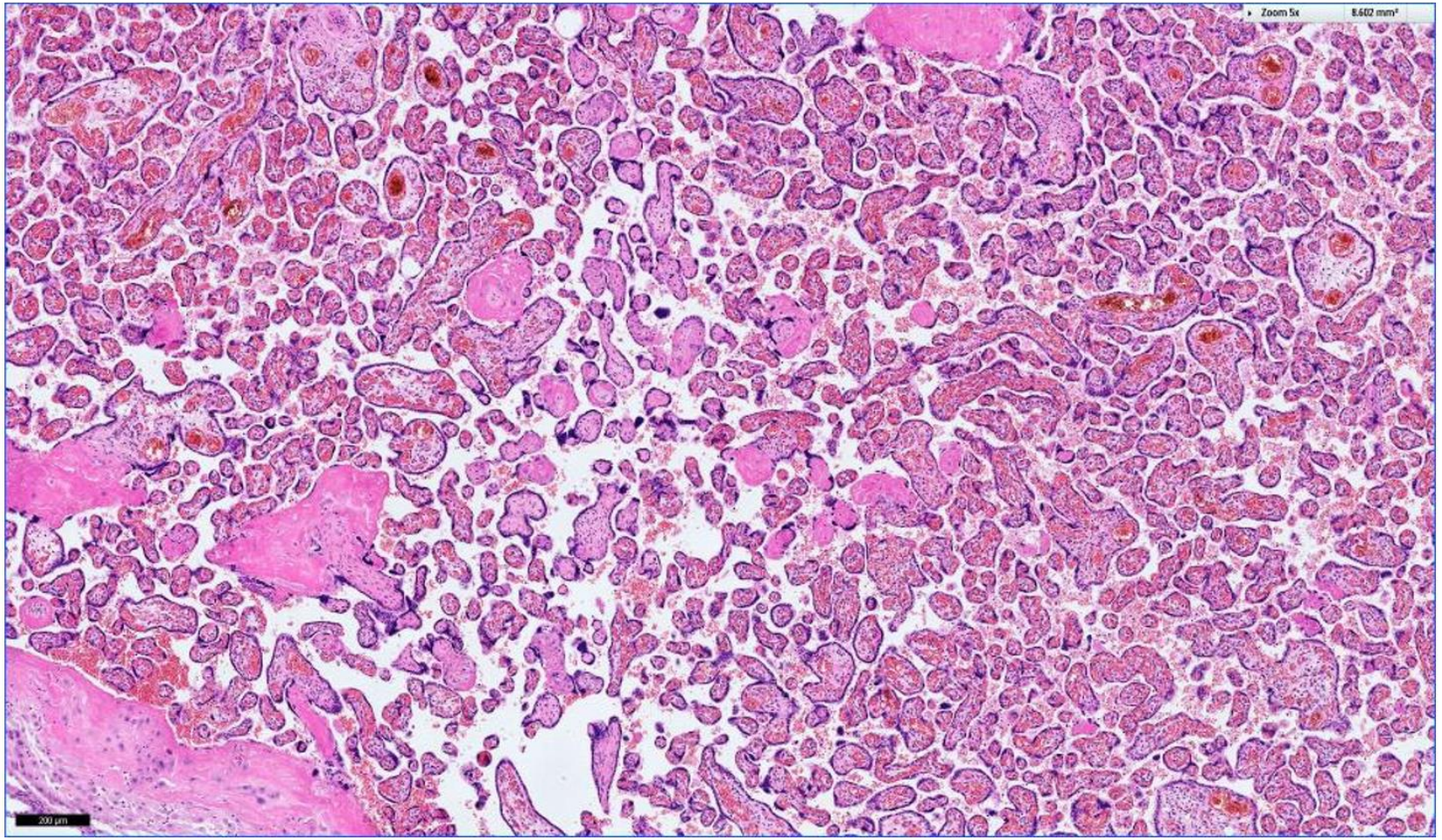


Q9 a term



Q9 a term

H&E 5x



Diagnosis?

A. Maternal vascular malperfusion

B. Fetal vascular malperfusion

C. Chronic villitis

Answer: B

- Fetal vascular malperfusion

- Obstruction in fetal blood flow
- Histology:
  - Thrombosis, segmental avascular villi, villous stromal-vascular karyorrhexis