Placenta: High Yield Pathology

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Disclosure

Author for UpToDate

Author for Cambridge University Press and the AFIP fascicles

Adapted clinical benefits of placental pathological examination (after Chang and Langston et al PMID f9167599)

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1. Provision of an audit of antenatal clinical judgement and management – perinatal review (provider)
2. Identification of etiologies and pathological processes contributing to or causing an adverse pregnancy outcome (provider,family)
3. Improved management of subsequent pregnancies by identification of conditions known to have recurrence risks or which may be either treatable or preventable (family,provider)
4. Identification of a pathological condition requiring timely clinical intervention (family, provider)
5. Understanding of antenatal and intrapartum events that contribute to long-term neonatal morbidity and adult diseases/disorders with early identification of such changes making possible early interventions and improvement in long-term outcome (family)
6. Assessment of factors contributing to poor outcome as a factual basis for resolving medicolegal issues
7. Understanding of antenatal and intrapartum events that contribute to long-term maternal morbidity such that interventions may improve outcome (family)

Placental pathology that redirects patient care

- Diagnosis or suspicion of a neonatal disease or syndrome
- Diagnosis of a pathology associated with poor obstetric outcomes that has a significant recurrence rate
- Findings that point to an unsuspected specific infection to mother or fetus/neonate

Spectrum of disorders involving increased intervillous fibrin/fibrinoid with significant recurrence risks

- Massive chronic intervillositis (chronic histiocytic intervillositis) [MCI]
- Maternal floor infarct [MFI]
- Massive perivillous fibrin [MPFD]

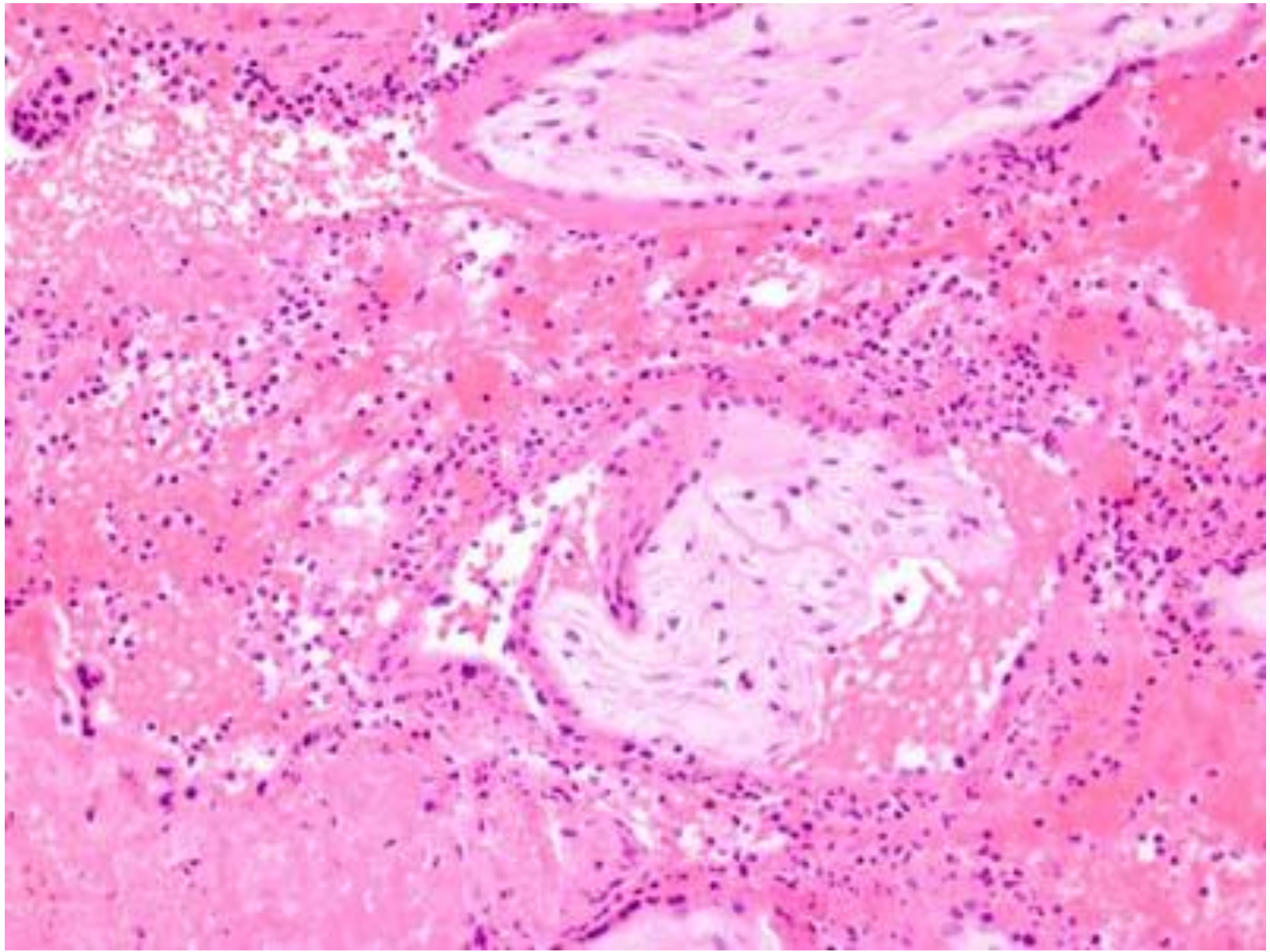
Massive Chronic Intervillositis

- Pregnancy losses at any gestational age but most common in first trimester
- Normal karyotype
- Recurrences reported
- Histology:
  - Maternal space filled with histiocytes and fibrin

Massive Chronic Intervillositis
aka Chronic Histiocytic Intervillositis

- Marked intervillositis of histiocytes
  - Lesser contribution of cd8+ T cells
- Admixed with fibrin
- With or without chronic villitis
  - Should be a minor component

Massive Chronic Intervillositis



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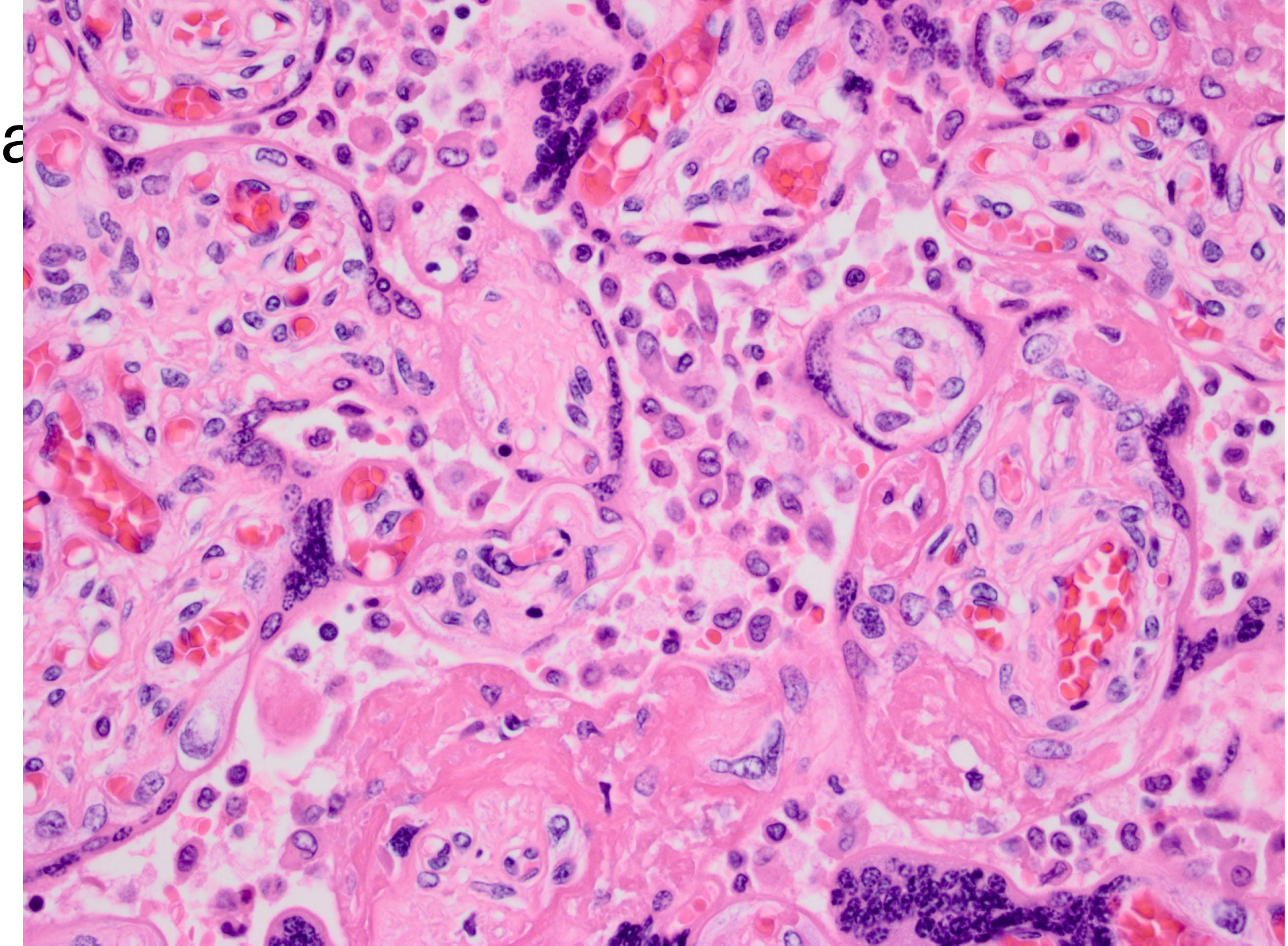

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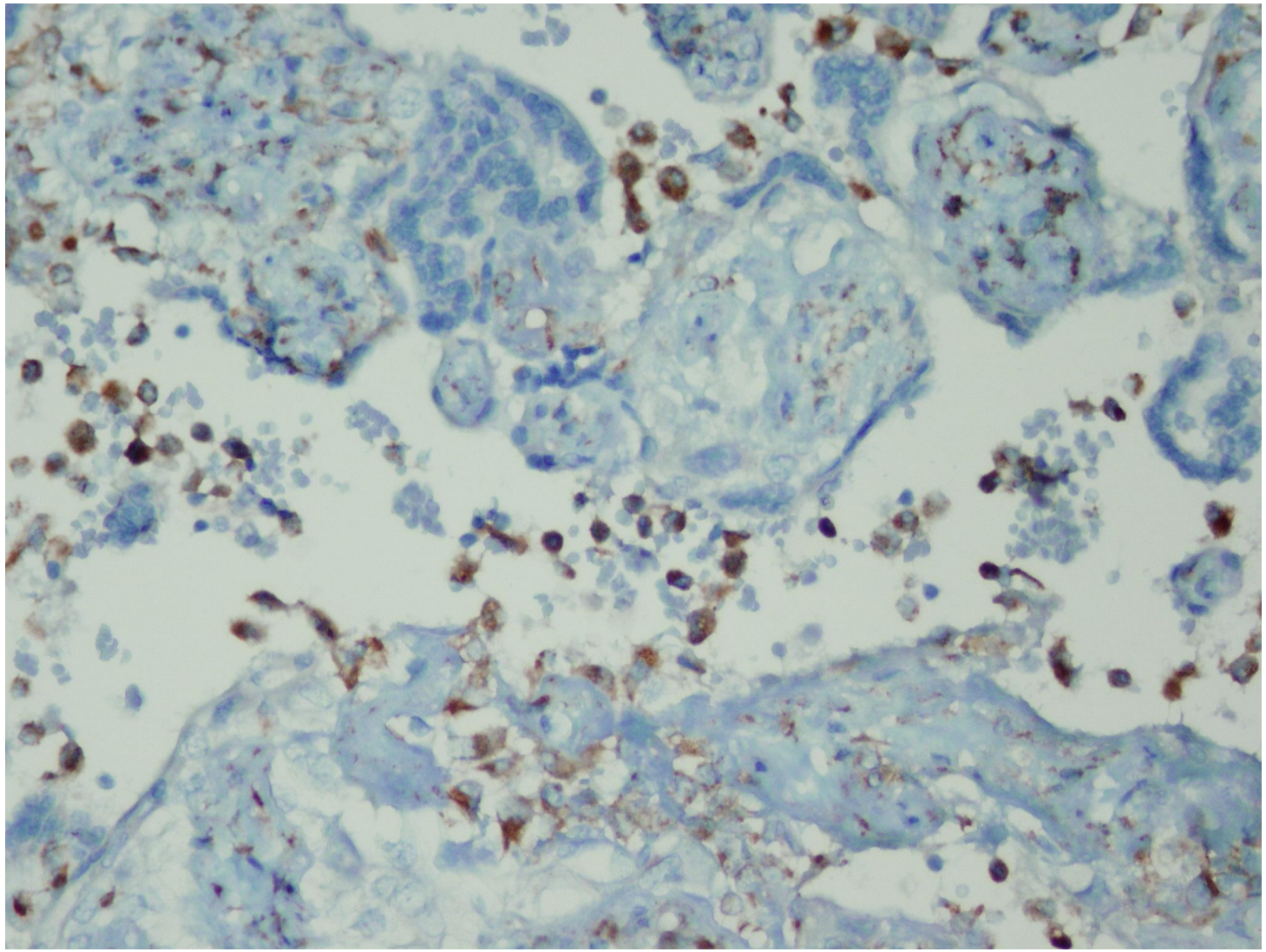
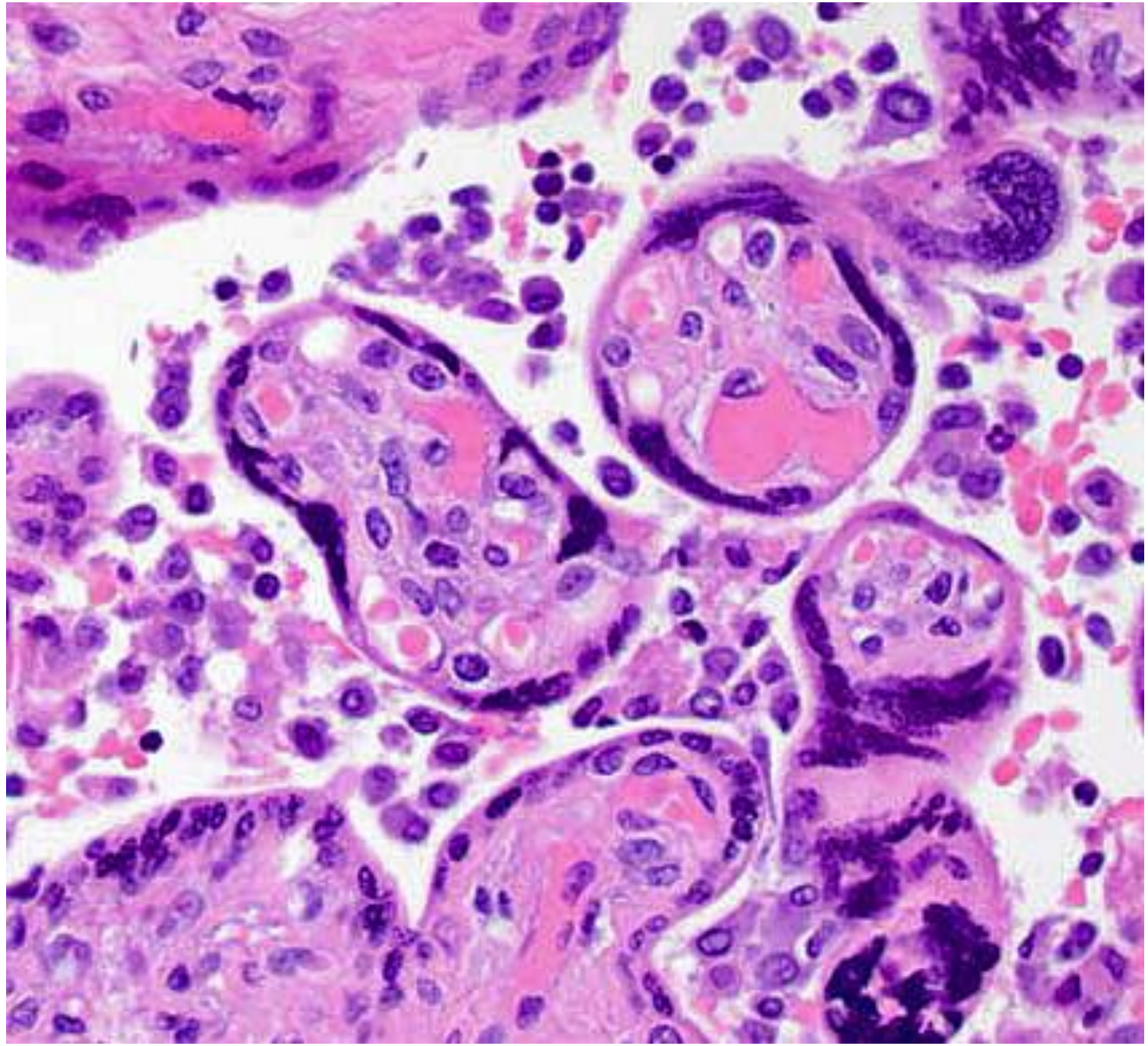
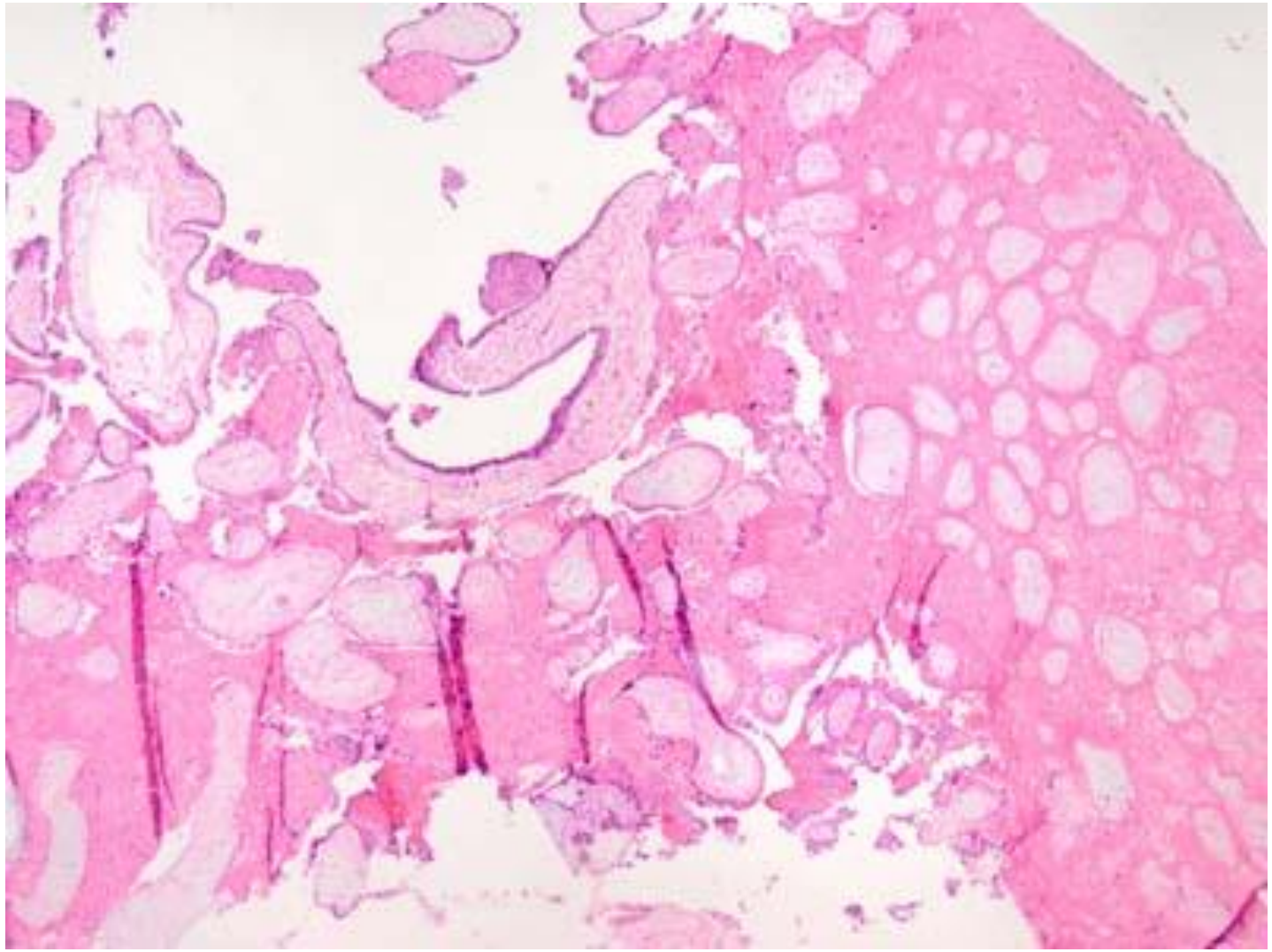
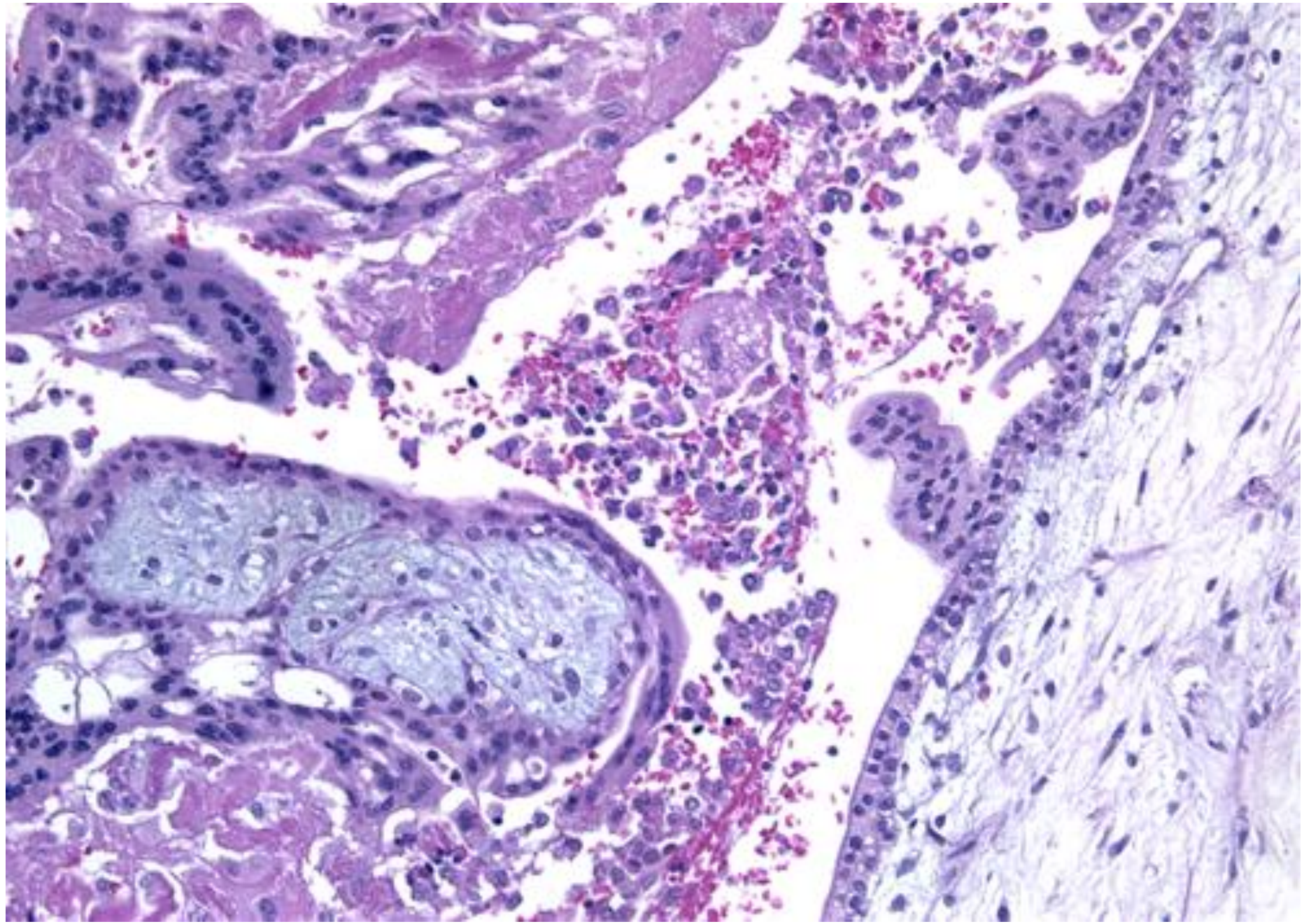




First trimester MCI





Massive Chronic Intervillositis

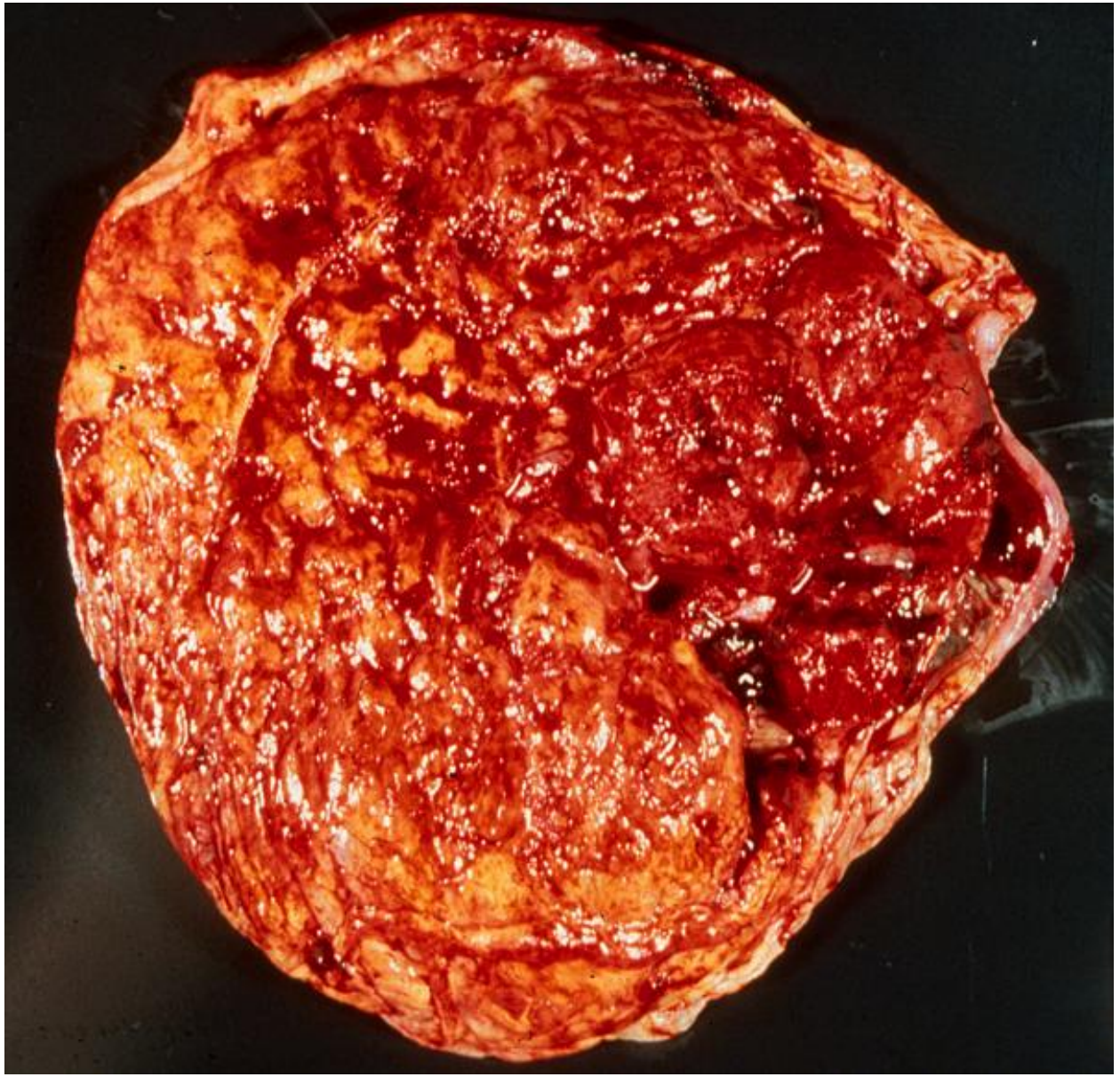
- Suspect when see clusters of histiocytes in the maternal space with or without admixed fibrin
- Often associated with elevated msAFP or Alk Phos
- Review ALL previous OB pathologies
- Recurrence risk 70-100% (one report says 18%)
- Some anecdotal treatment “successes” with a variety of Rx
  - IVIG, LMWH, ASA, Prednisone

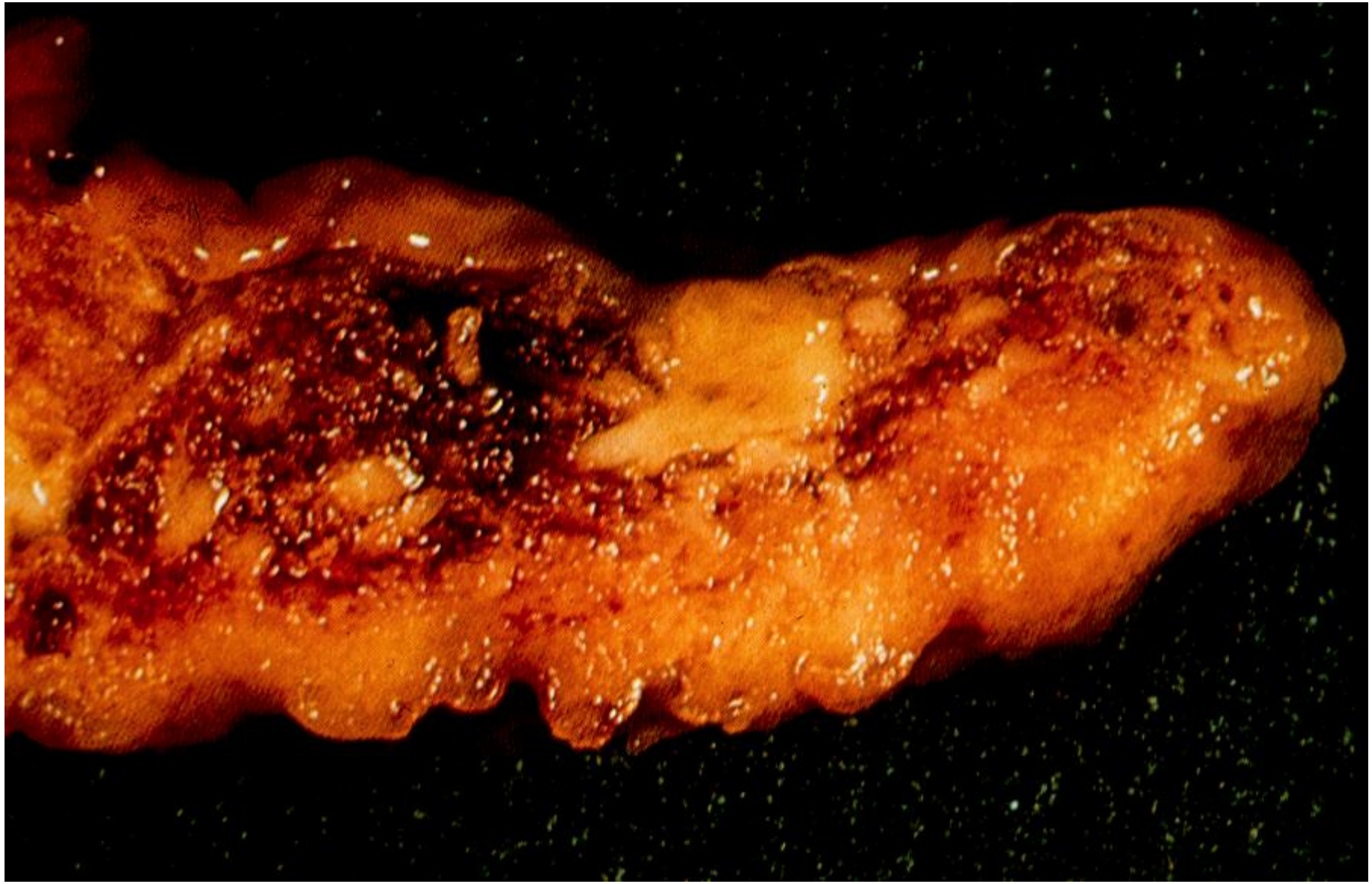
Maternal floor infarct

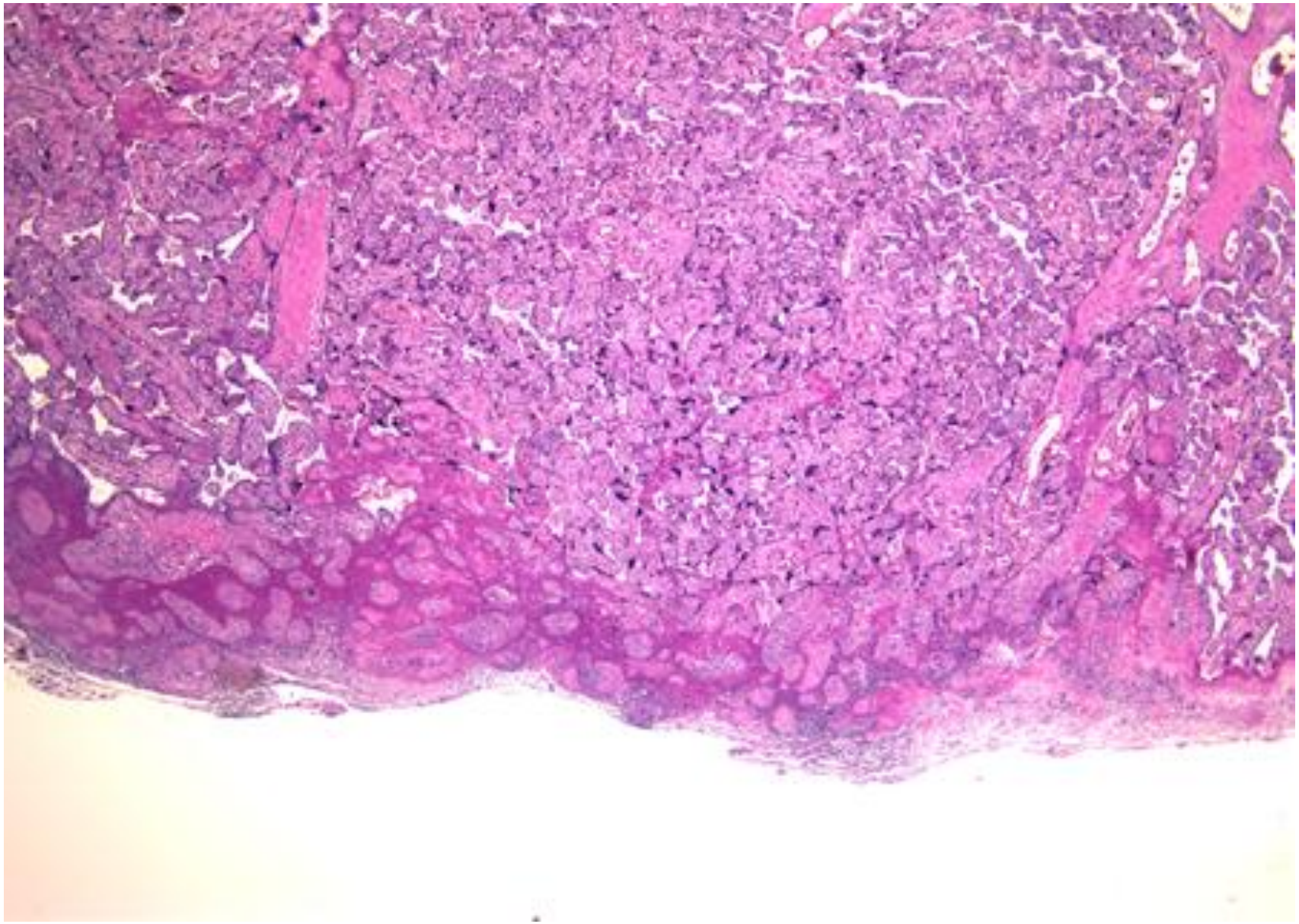
- Rare disorder associated with:
  - Miscarriage
  - IUGR (24-100%)
  - IUFD (13-50%)
  - Neonatal death
  - Renal tubular dysgenesis
  - Cerebral palsy and other neurocompromise
  - Recurrence (12-50%)
  - Elevated MSAFP

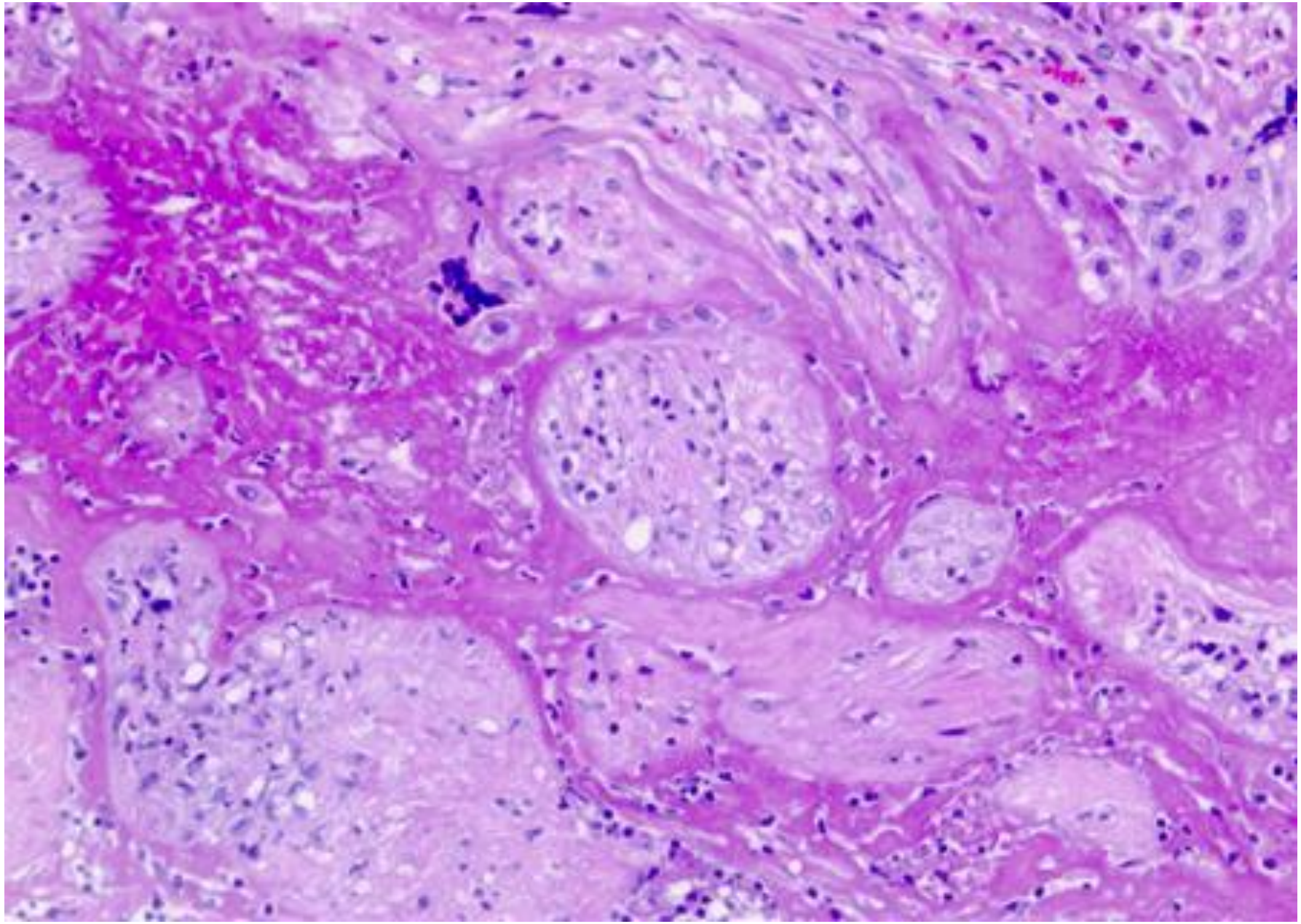
Diagnosis of MFI

- Diagnosis depends on gross and histologic exam
  - “orange rind” like maternal floor
  - Basal villi of entire maternal floor encased by perivillous fibrinoid of ≥ 3mm thick

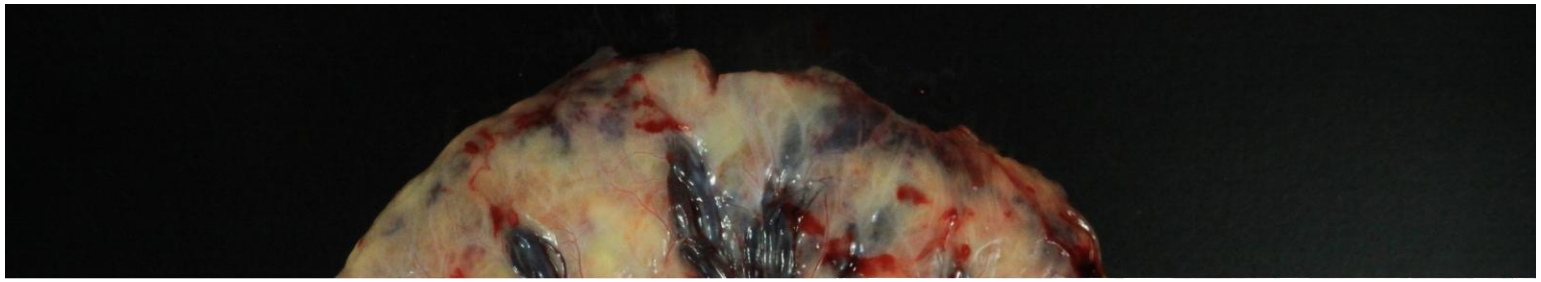


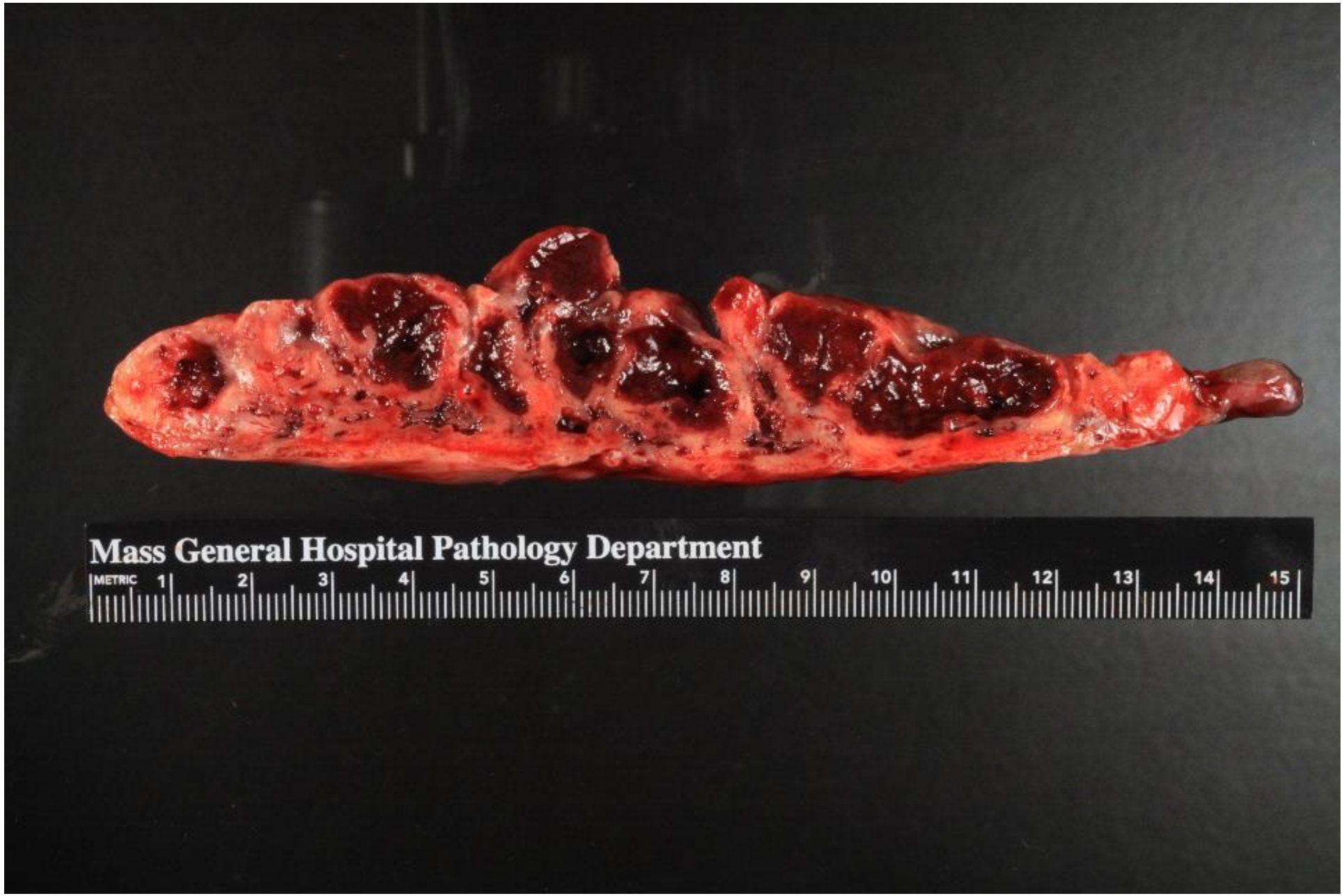






Massive Perivillous Fibrin Deposition




Mass General Hospital Pathology Department
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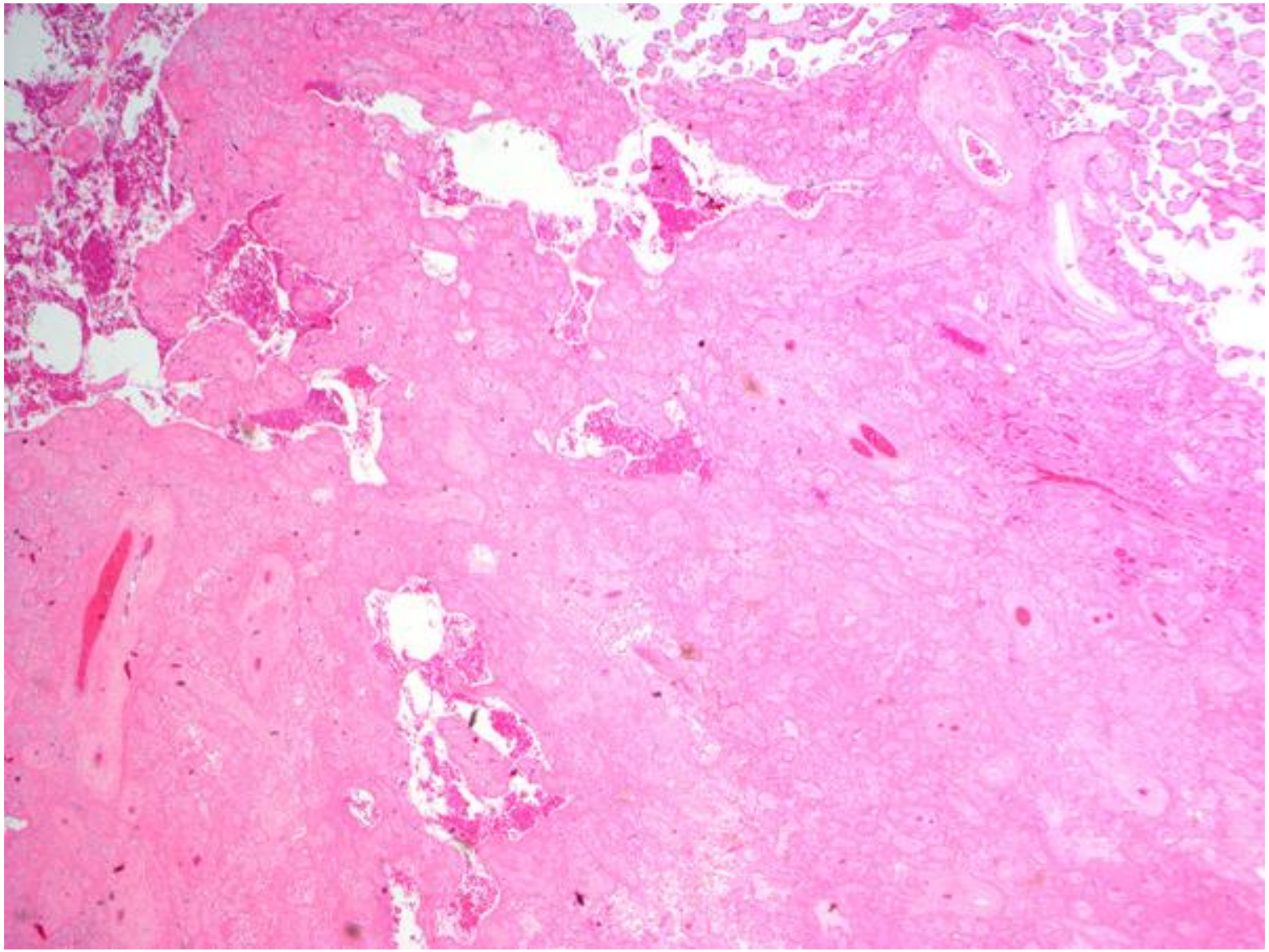
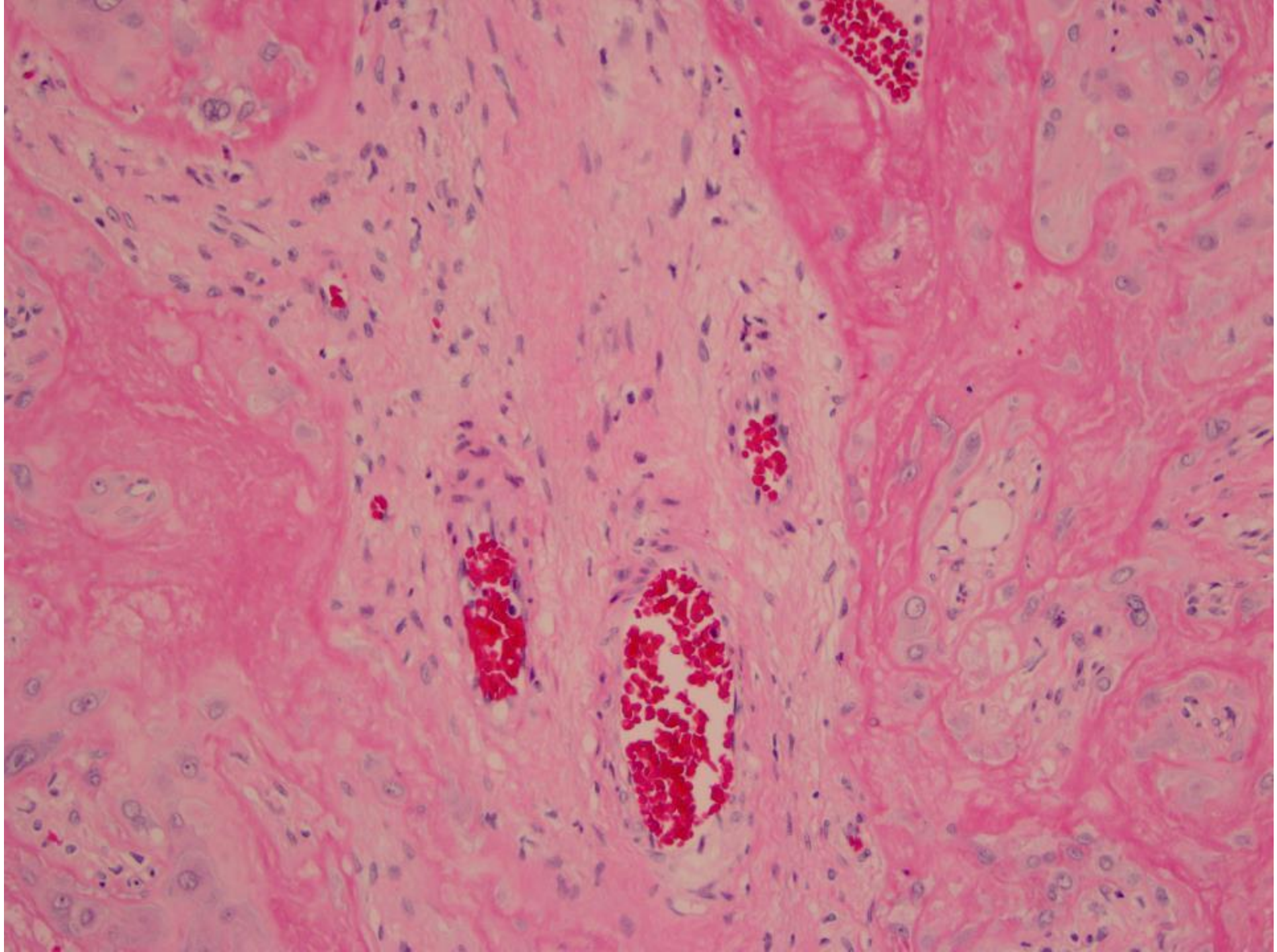
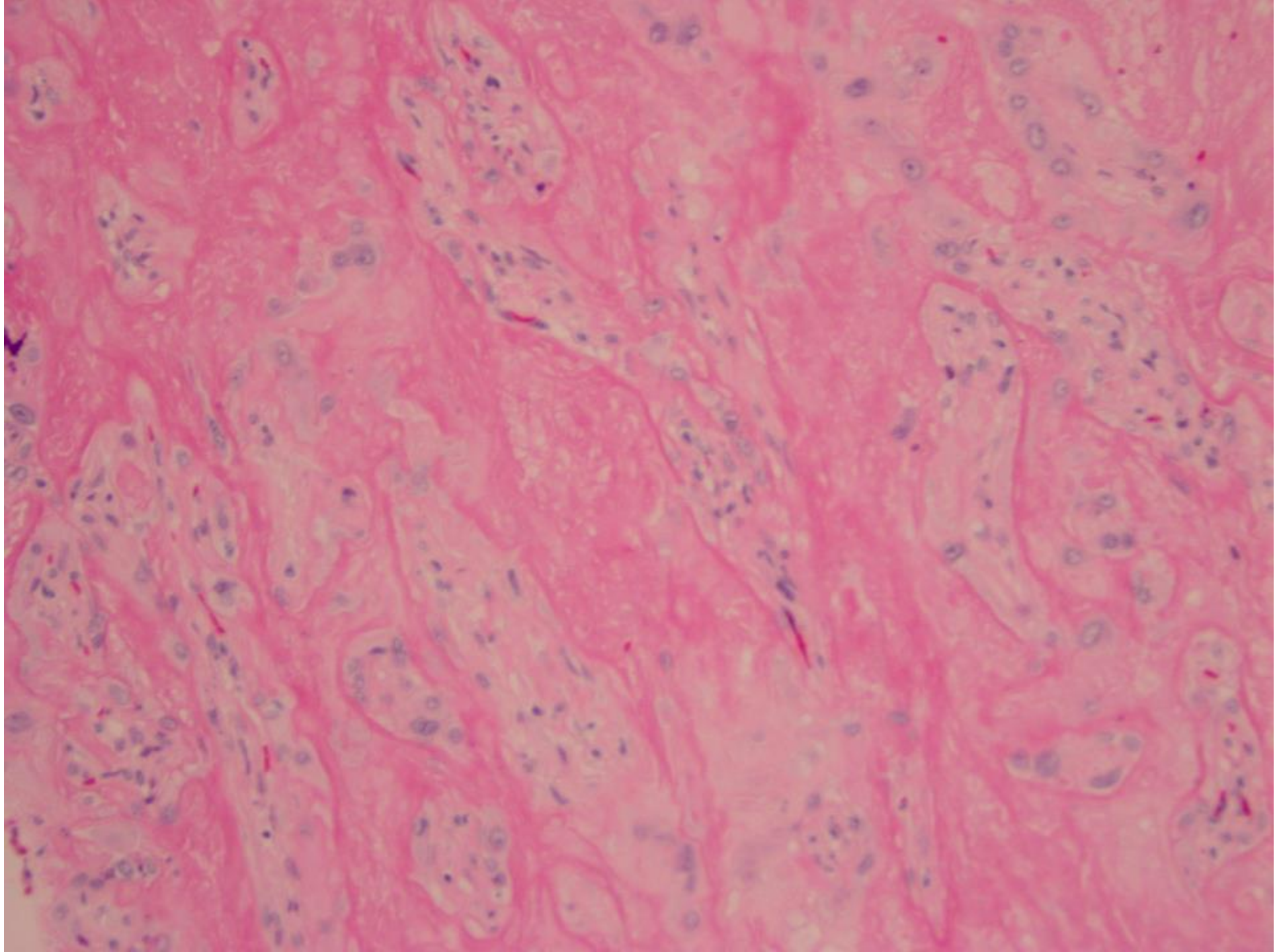
Massive Perivillous Fibrin Deposition







Review of MFI

Katzman and Genest, Pediat Dev Path 2002;5:159-164

- Over diagnosed – this is a *rare* diagnosis
  - 0.028-0.5%
- ~30% associated with IUGR
- Recurrence in 14% in 2-3rd trimester
- Recurrence at 50% in 1st trimester

Risk factors

- Antiphospholipid antibody syndrome
- Activated protein C resistance
- Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency heterozygosity
- Other “immune disorders” in mother
  - Polymyositis
  - Dematomyositis
  - Scleroderma
  - SLE

Etiology

- Rejection phenomena*
  - Associated with plasma cell deciduitis
  - maternal anti-HLA antibodies to fetal antigens
  - Evidence of antibody mediated complement activation on umbilical vein (c4d expression)
  - Elevation of maternal plasma CXCL-10
- Imbalance of pro-anti angiogenic factors**
  - Lower mean plasma concentration of PIGF from 20-30 weeks
  - Higher mean plasma concentration of sVEGFR from ~14 weeks
  - Higher mean sENG concentration
  - Lower mean PIGF/sVEGFR and PIGF/sENG from ~17 weeks

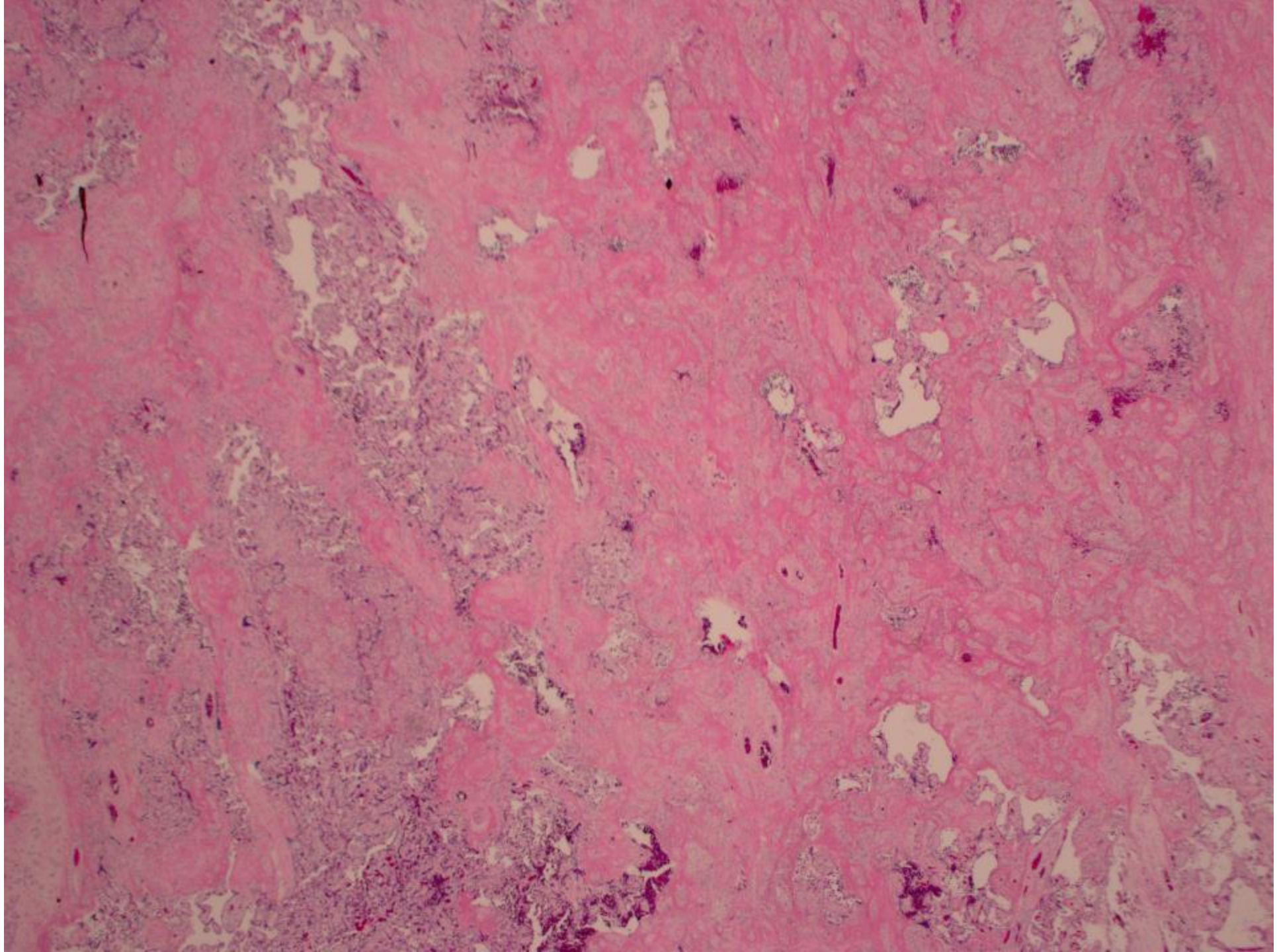
* Romero et al. Am J Reprod Immunol, 2013; 70:285-298
**Whitten et al. A J Ob GYN, 2013 310e1

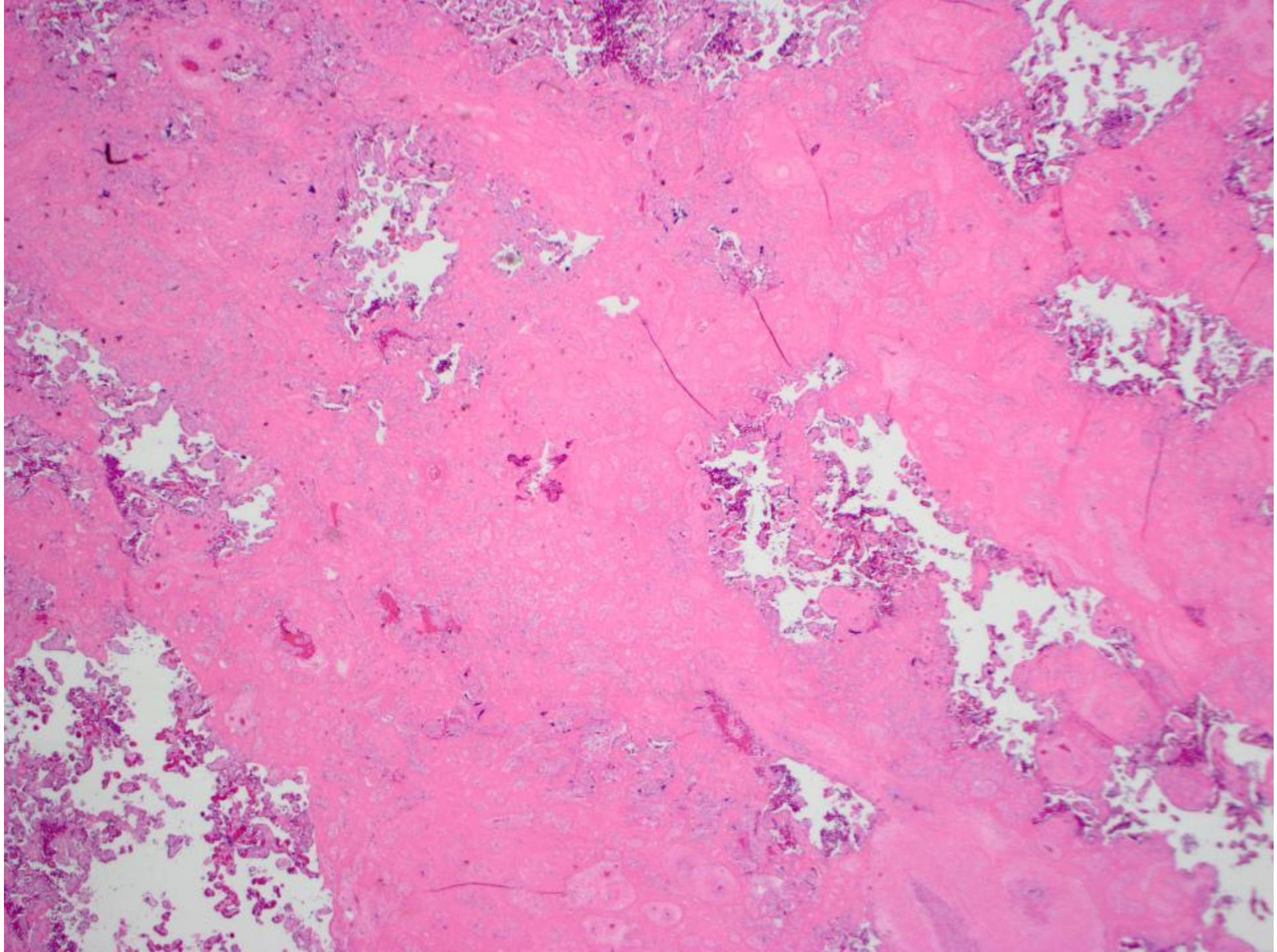
MFI/MPFD Differential Diagnosis

- Routine placental infarct
  - Villi touch each other without significant perivillous fibrin
- Marginal fibrin
  - Common at term
  - Circummarginate placentation
- Misoprostol treatment
  - Failed medical abortions

When is fibrin too much?

- When it is diagnosable grossly
- When it fills a slide from basal plate to chorionic plate – even focally
  - Nodular (>50% of villi encased on a slide)
  - Interlacing
- Preterm





How to report MFI/MCI/MPFD

- Note: This is a distinctive pathology of unclear etiology but with a definite recurrence risk. The pathology is associated with perinatal morbidity and mortality. Often the MS-AFP is elevated in this condition. The patient may benefit from consultation with a Maternal Fetal Medicine specialist.

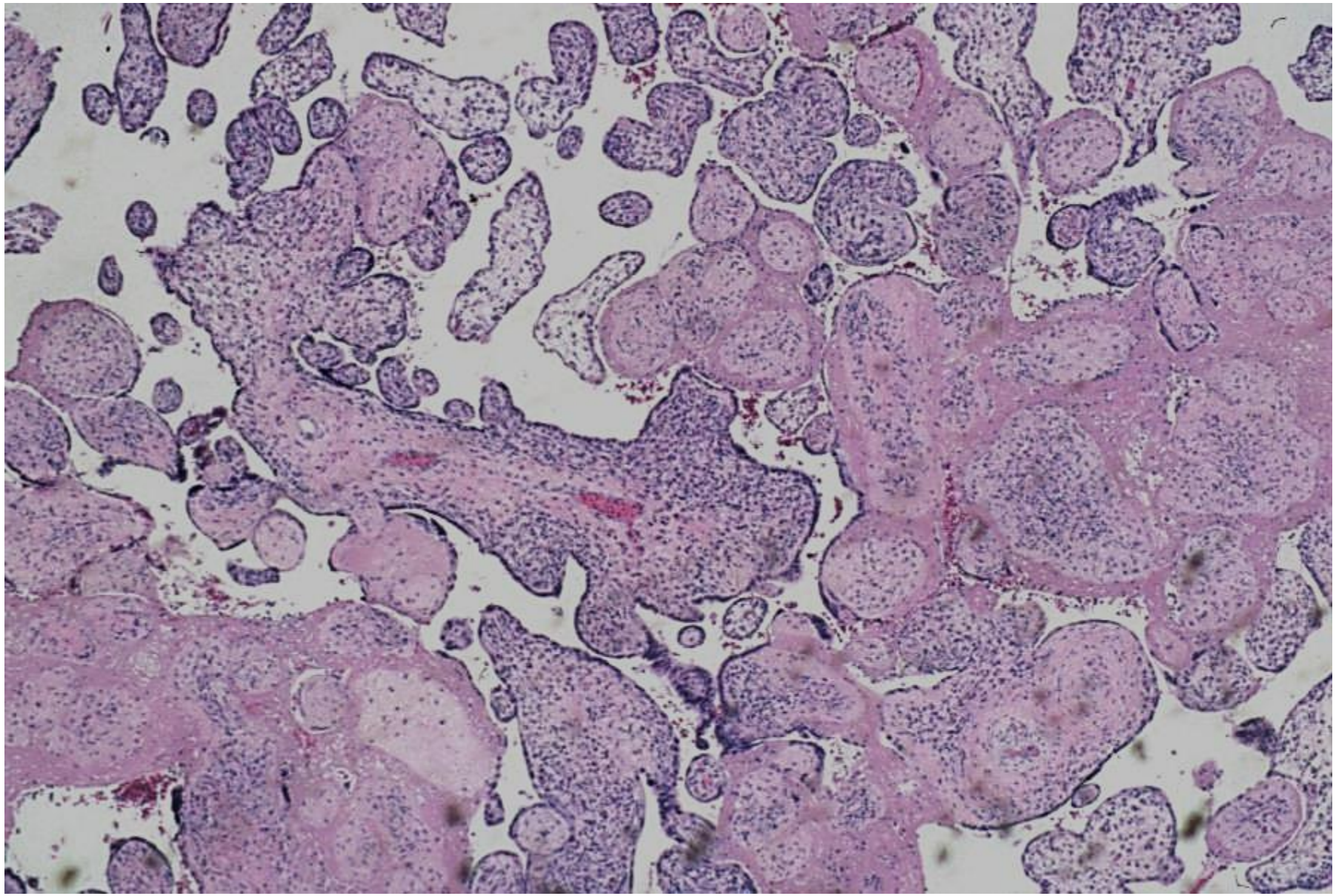
Diagnoses with distinct recurrence risk

- Massive chronic intervillositis
- Massive perivillous fibrin
- Maternal floor infarct
- Chronic villitis

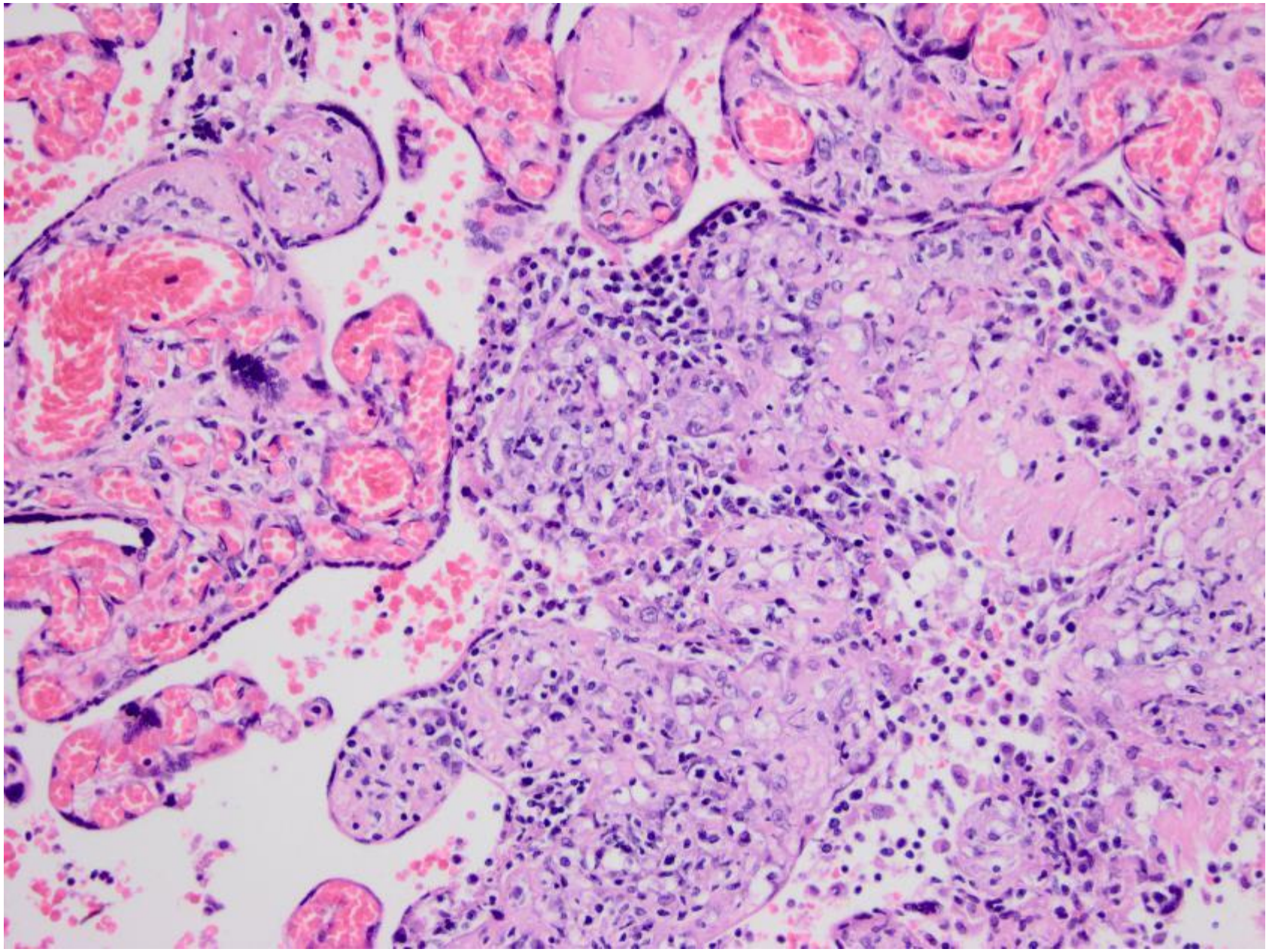
CHRONIC VILLITIS

- Maternal inflammatory infiltration of the chorionic villi.
- Associated with perinatal morbidity and mortality.
- Most are idiopathic (immunologically based) and can recur in future pregnancies.
- Small percentage are due to congenital infection, classically TORCH infections

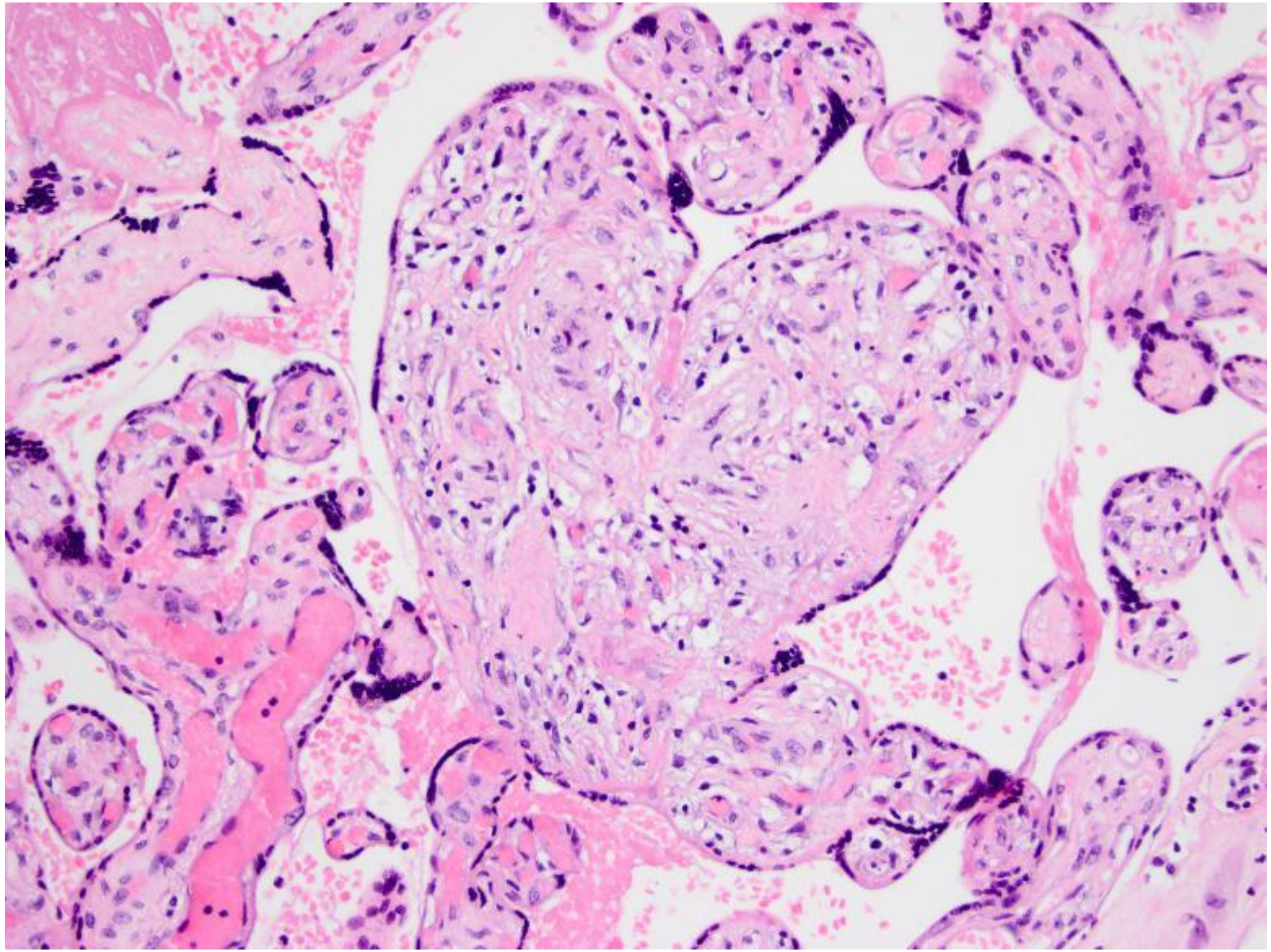
Chronic Villitis

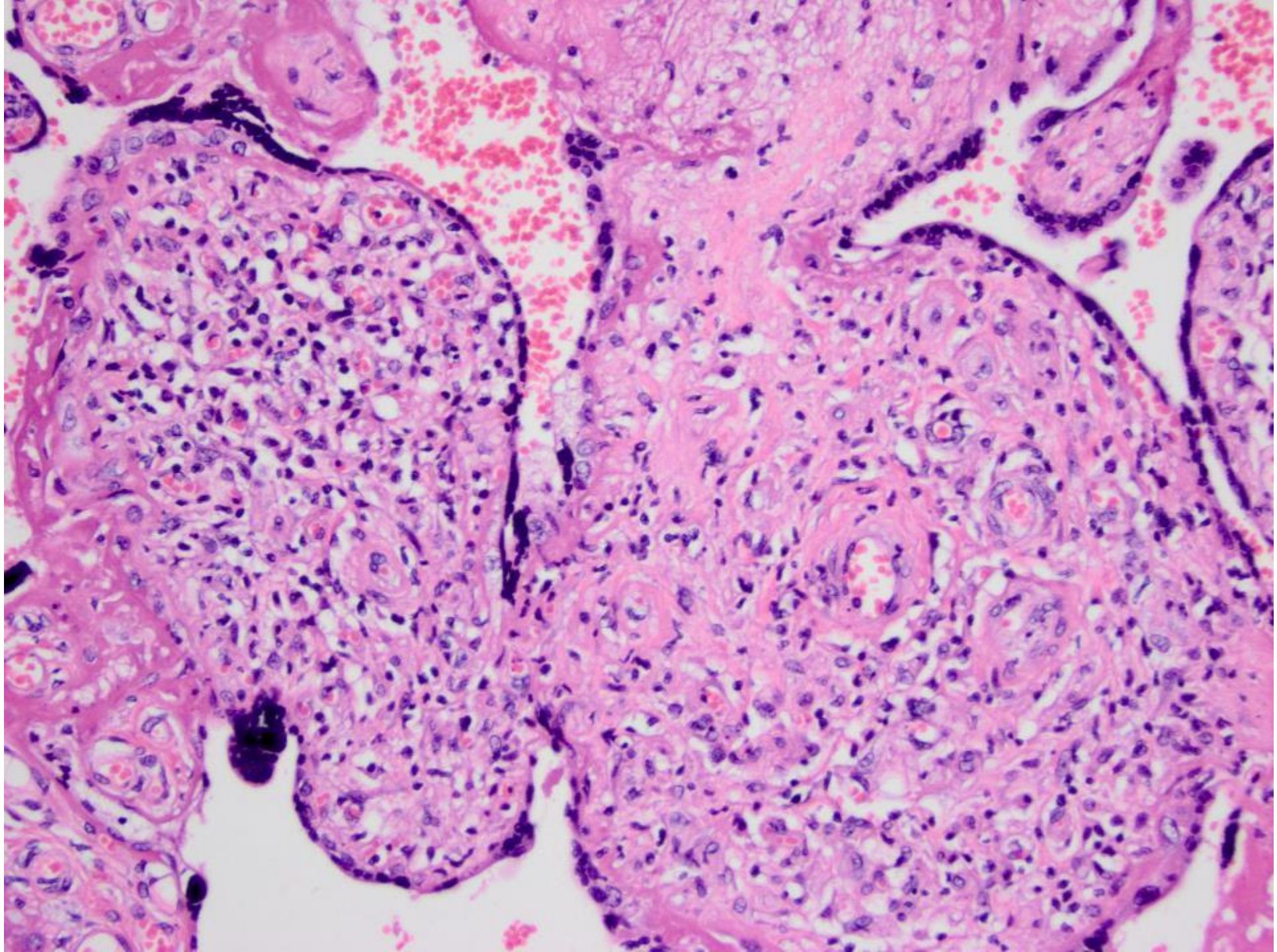


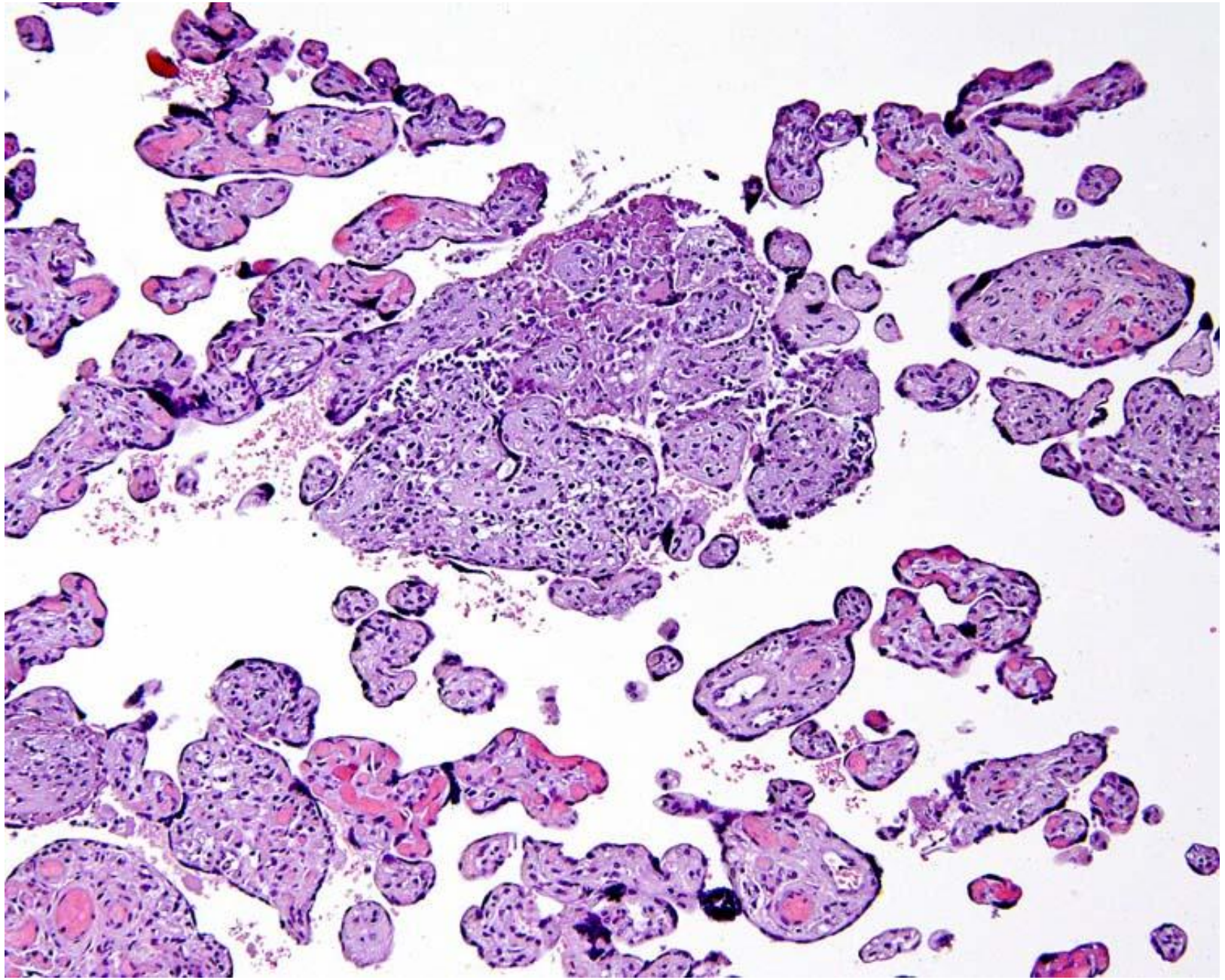
Chronic Villitis - cellular

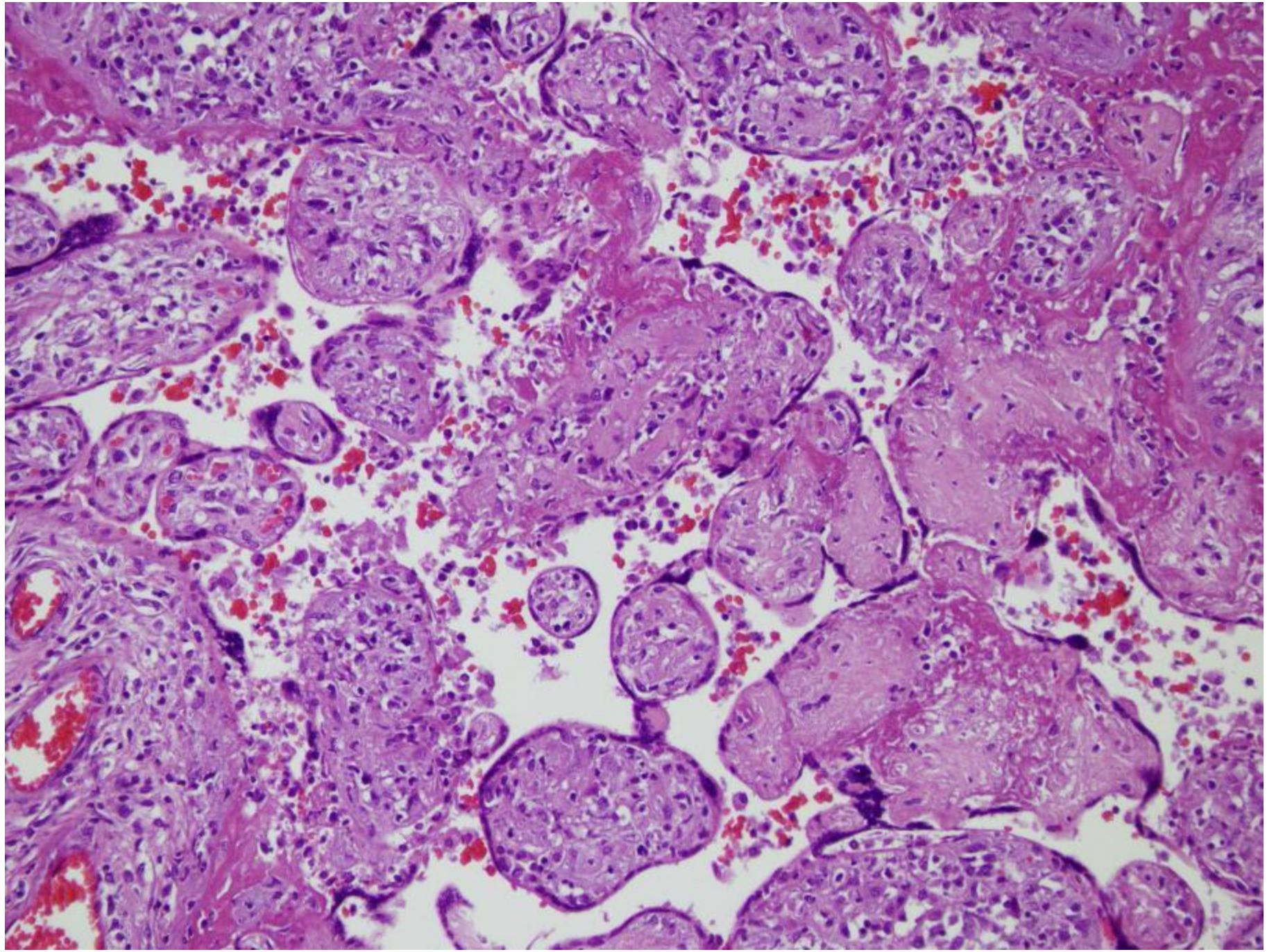


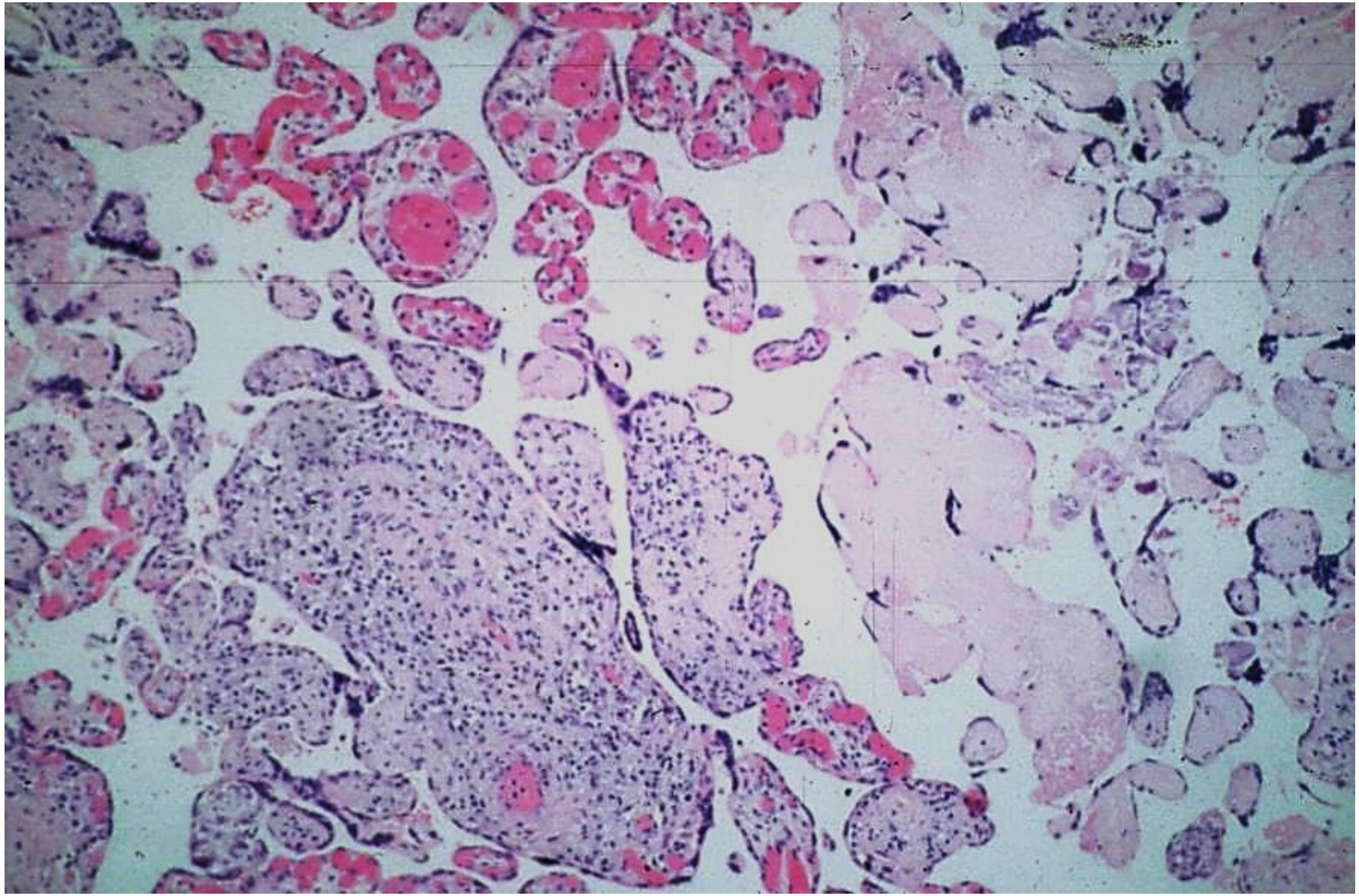
Chronic villitis – paucicellular

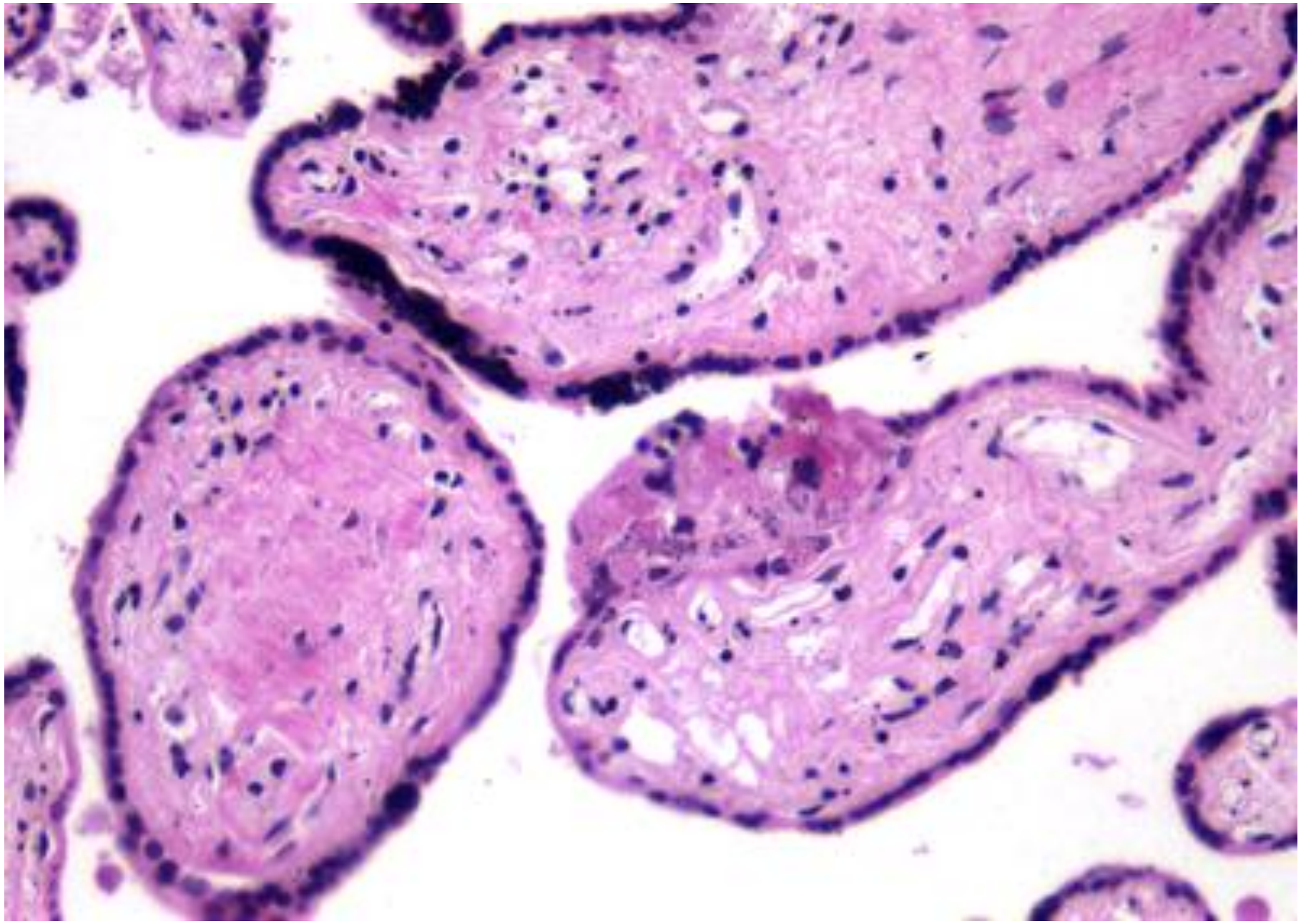












Etiology

- Infections (primarily viral)
- Rejection phenomena*
  - Associated with plasma cell deciduitis
  - maternal anti-HLA antibodies to fetal antigens
  - Evidence of antibody mediated complement activation on umbilical vein (c4d expression)
  - Elevation of maternal plasma CXCL-10
- Imbalance of pro-anti angiogenic factors**
  - Lower mean plasma concentration of PIGF from 20-30 weeks
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* Romero et al. Am J Reprod Immunol, 2013; 70:285-298

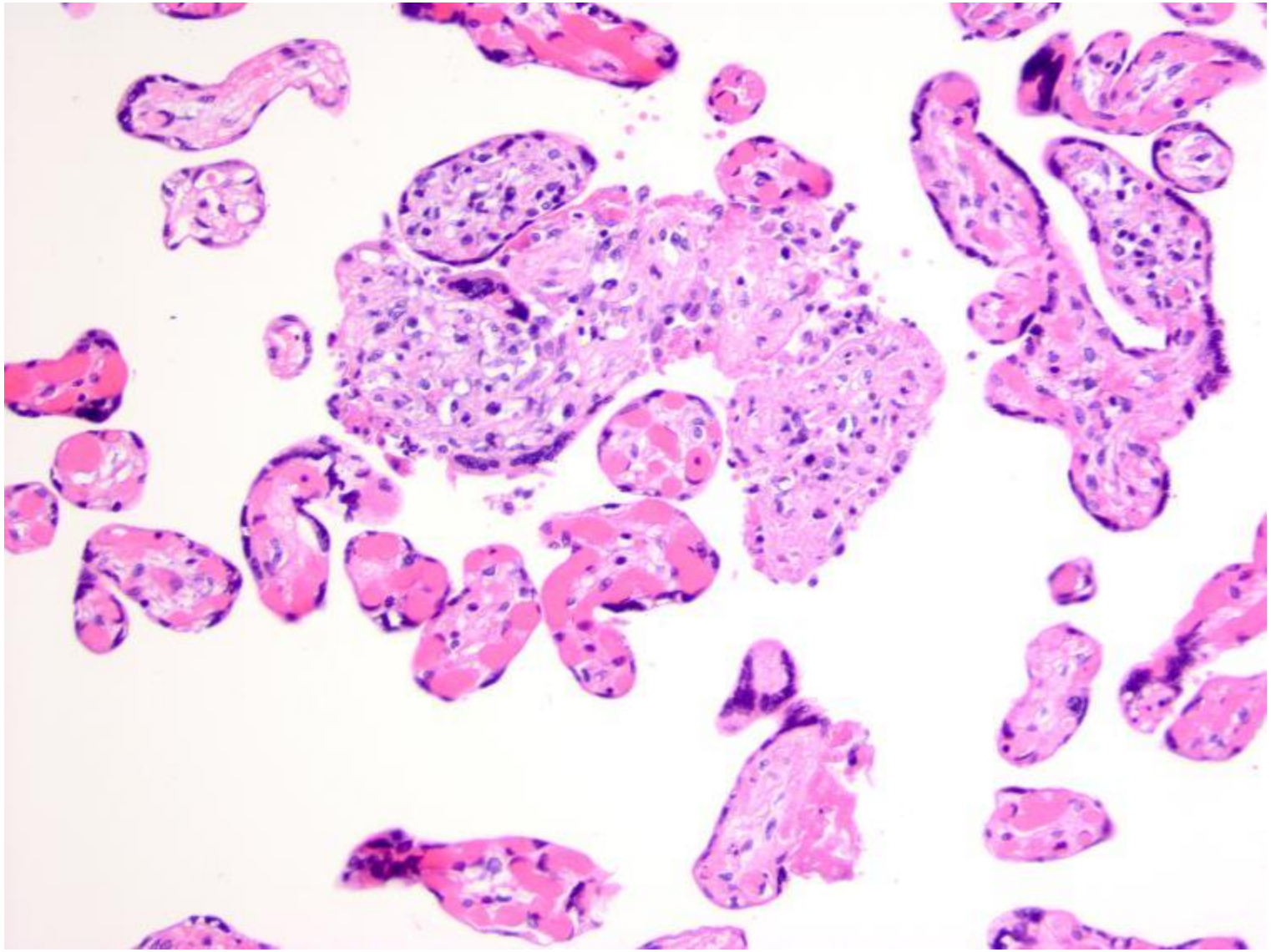
**Whitten et al. A J Ob GYN, 2013 310e1

Villitis of unknown etiology

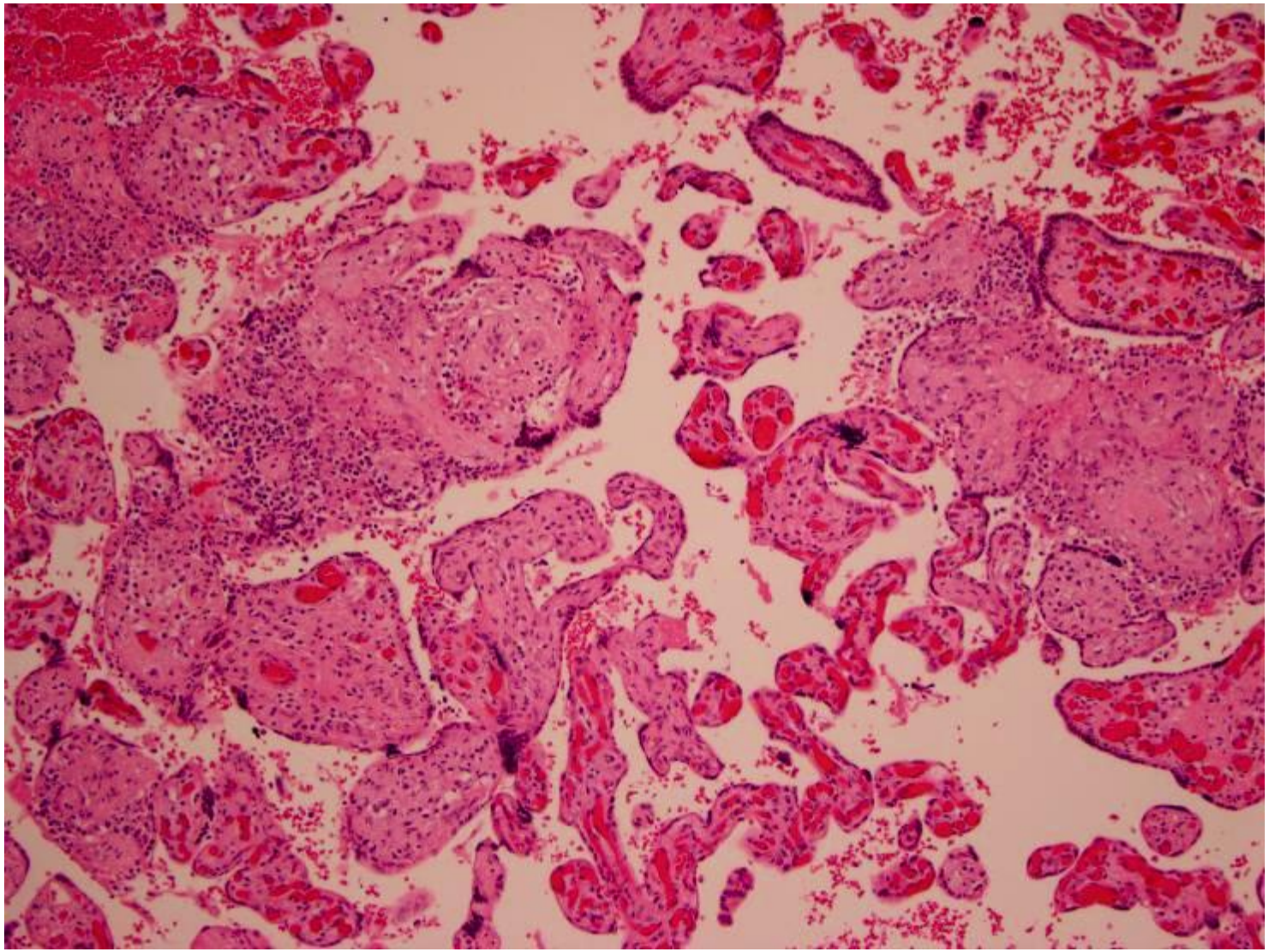
- Associations
  - IUGR
  - IUFD
  - Central pattern of CNS injury*
- Prevalence
  - ~5-15% of all placentas
- Recurrence
  - ~33% but those that recur often progress

* Harteman et al. J Pediatr. 2013;163(4):968-95.

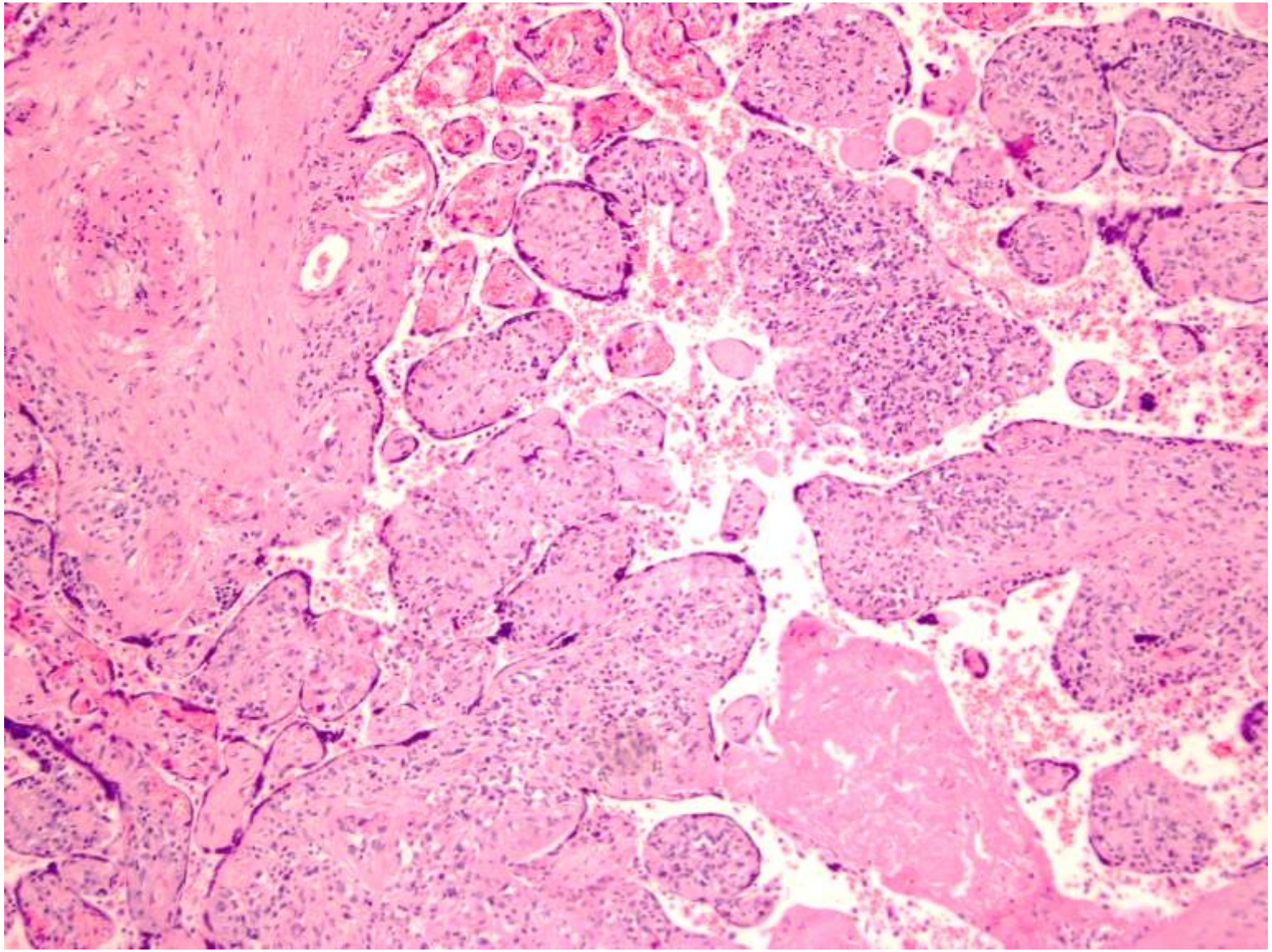
Focal chronic villitis



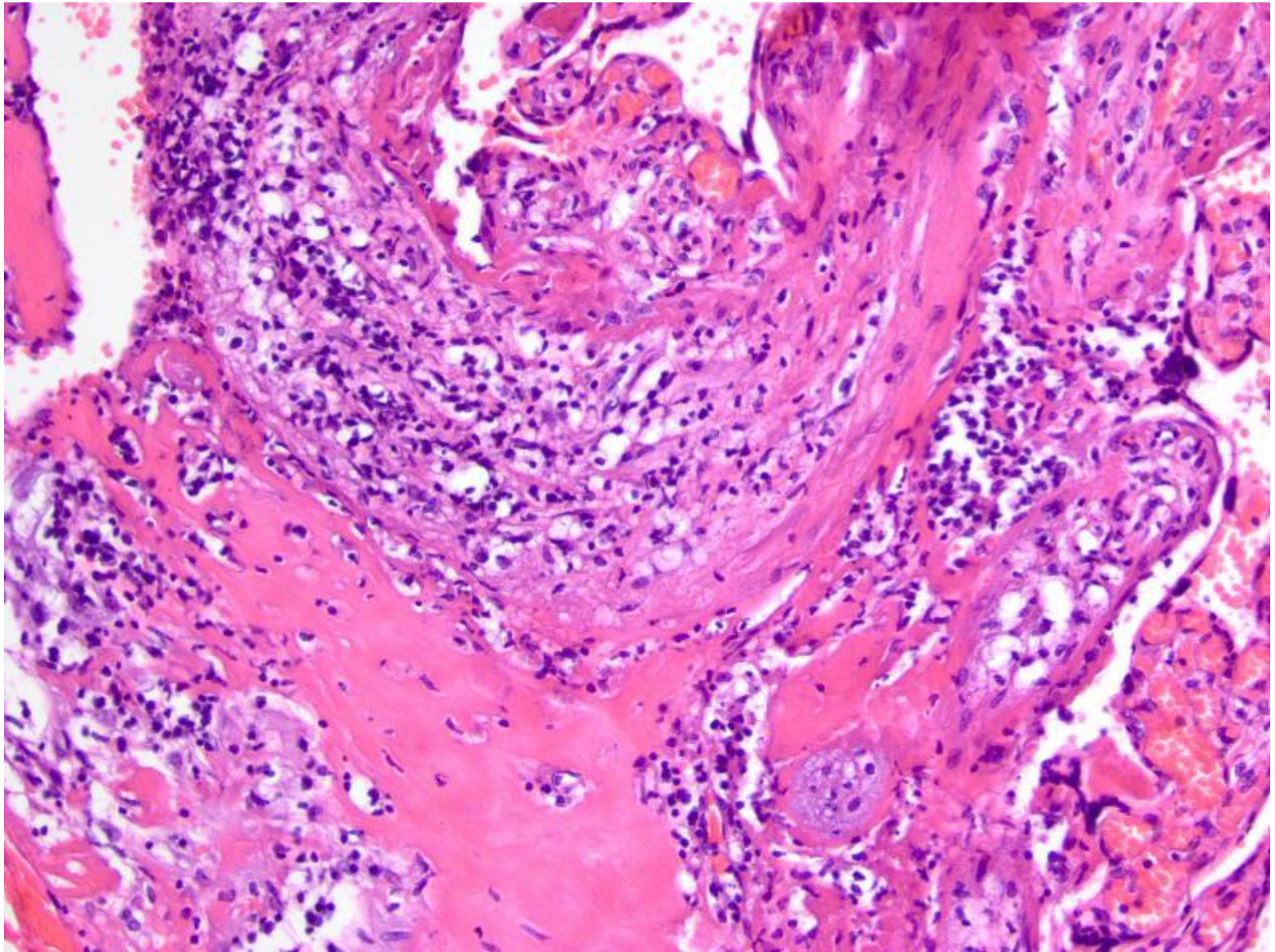
Patchy chronic villitis

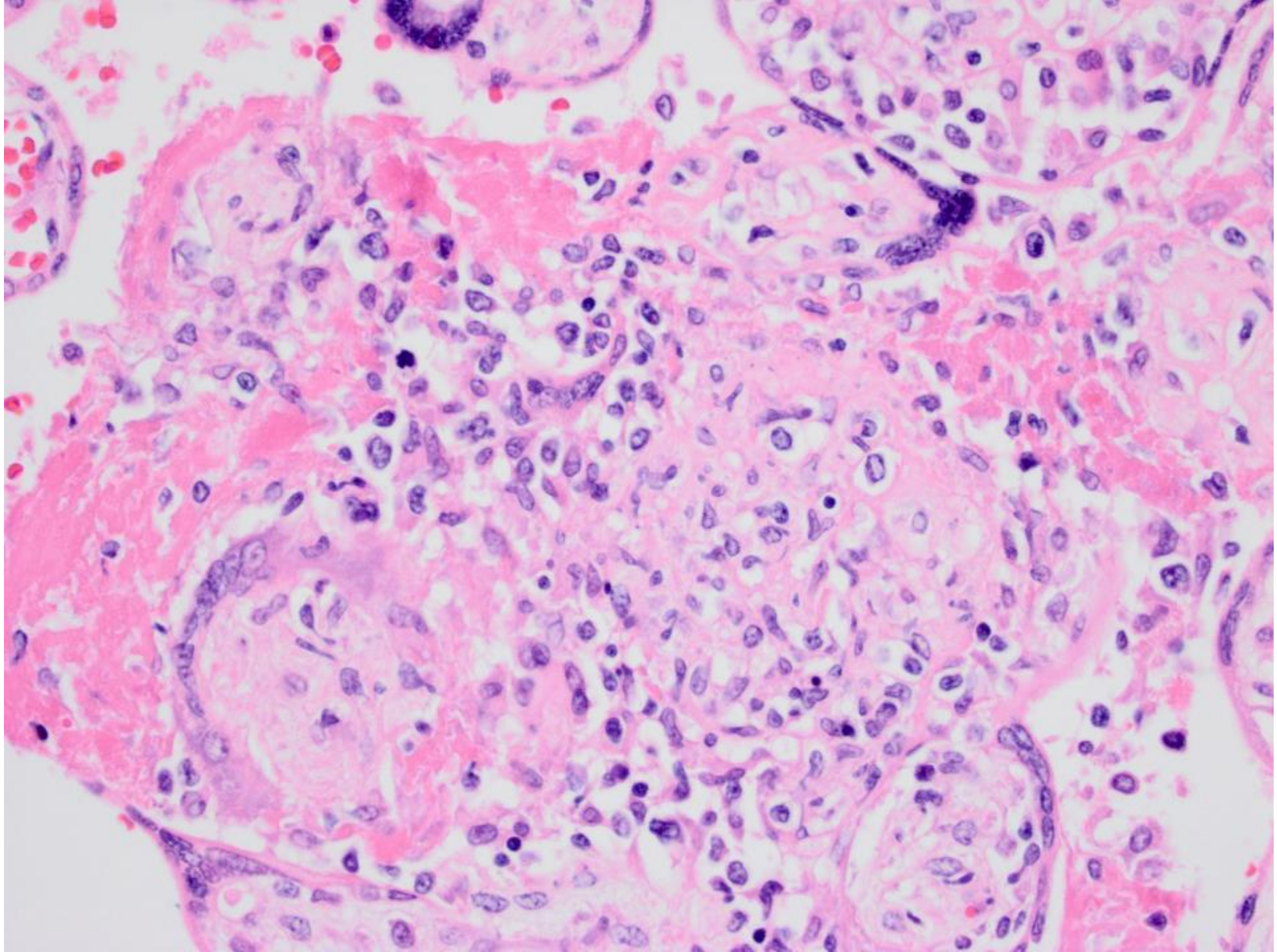


High Grade chronic villitis

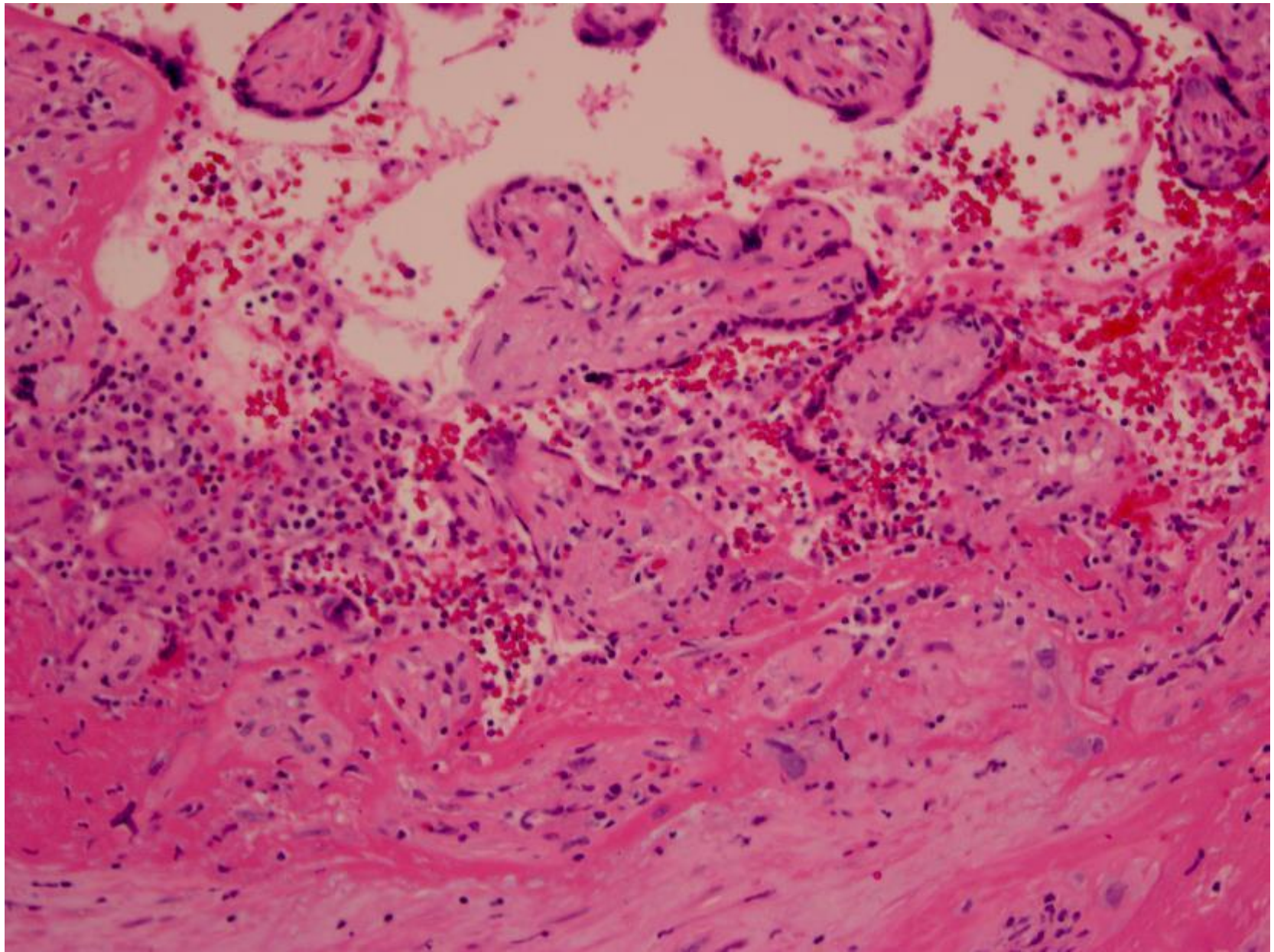


Villitis with intervillositis

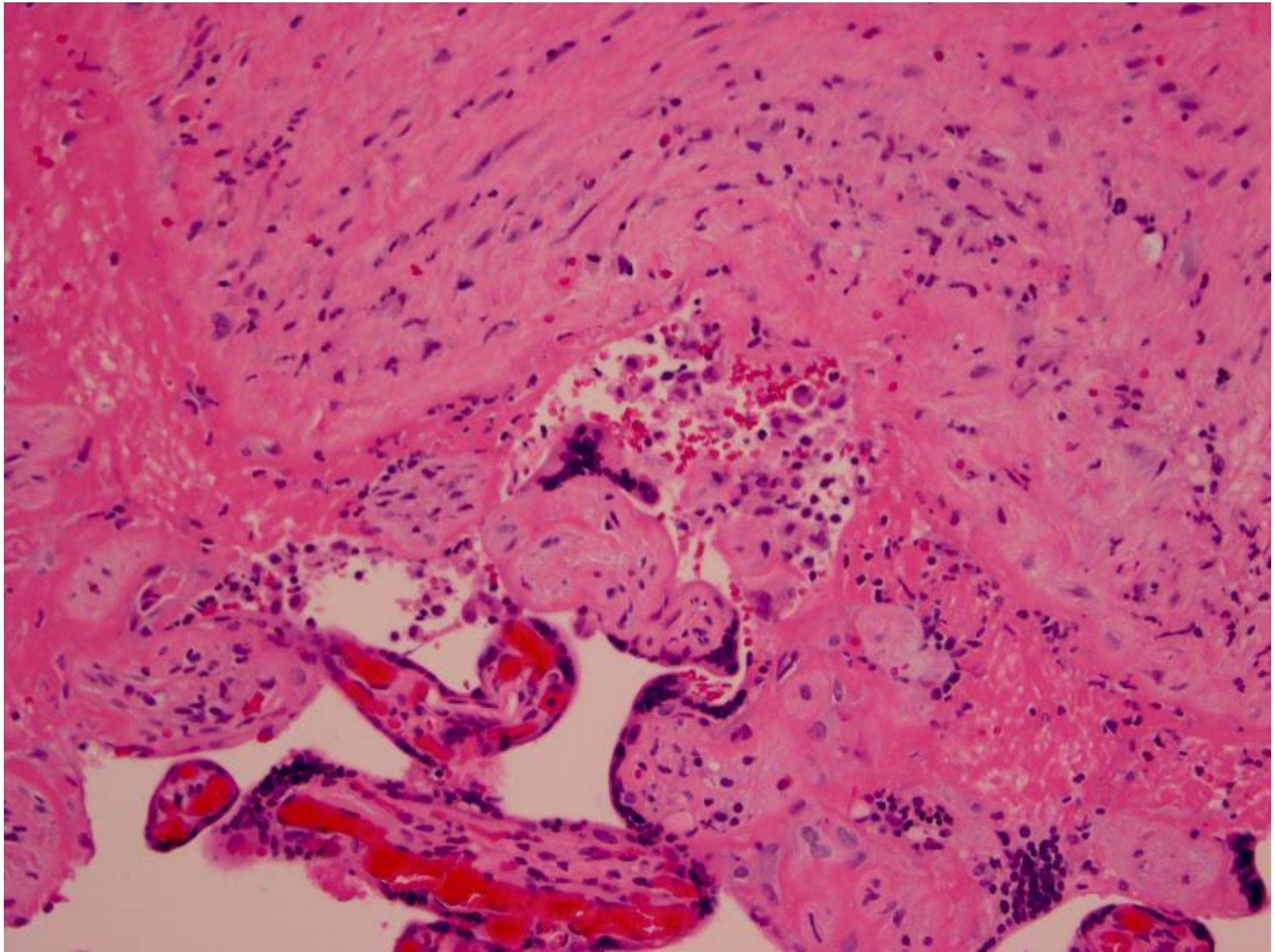




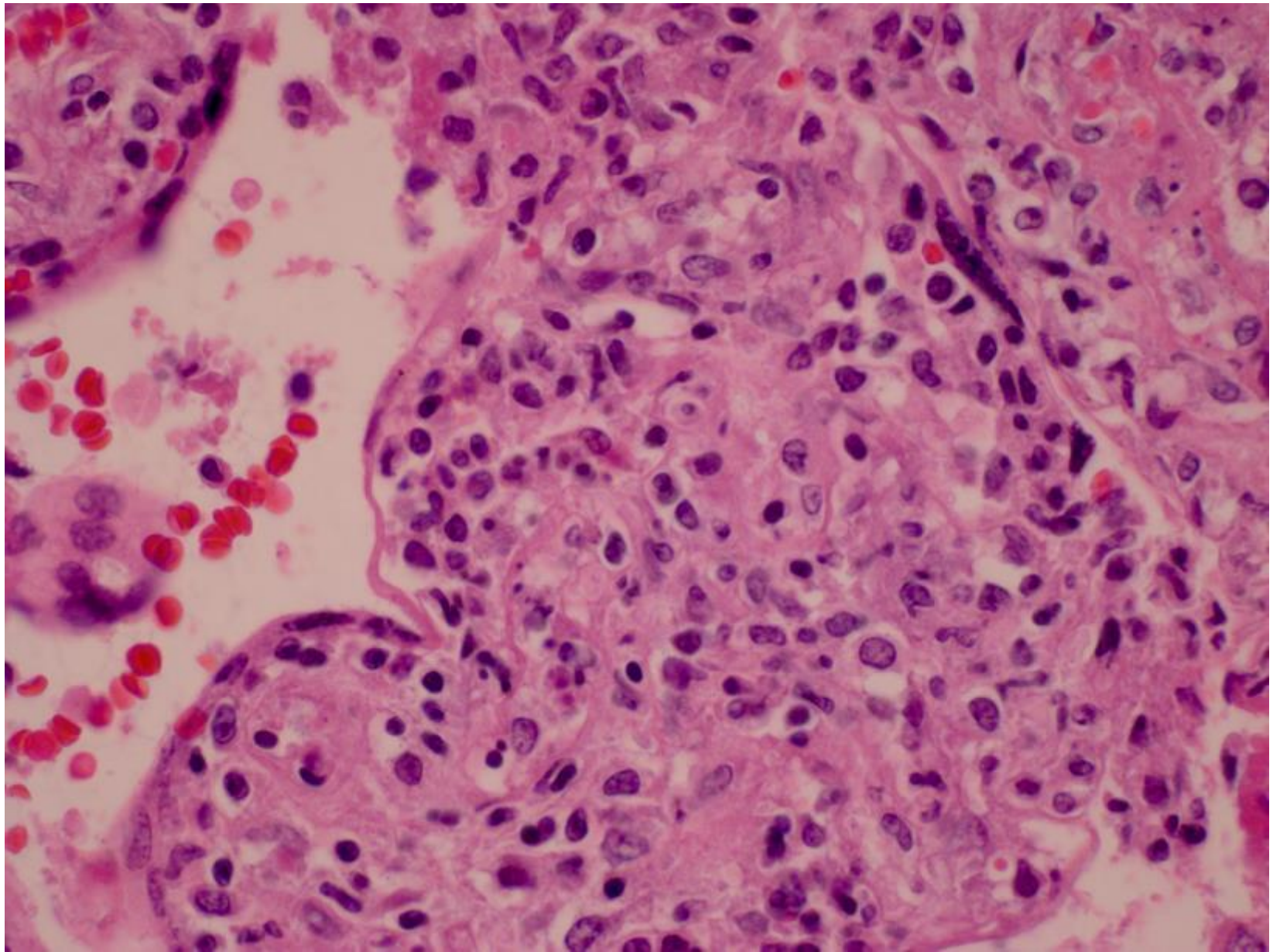
Interface basal plate involvement



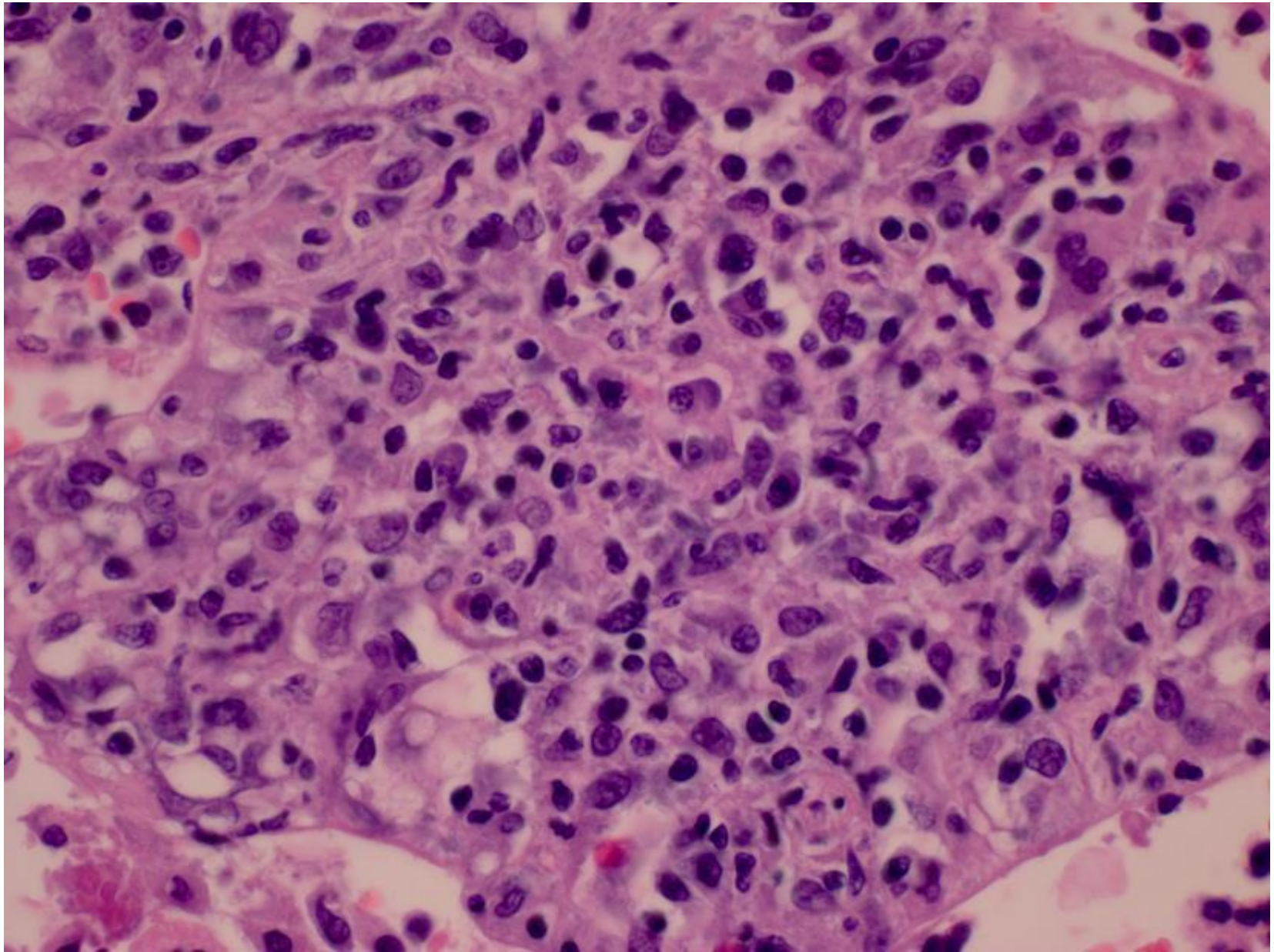
Interface chorionic plate involvement



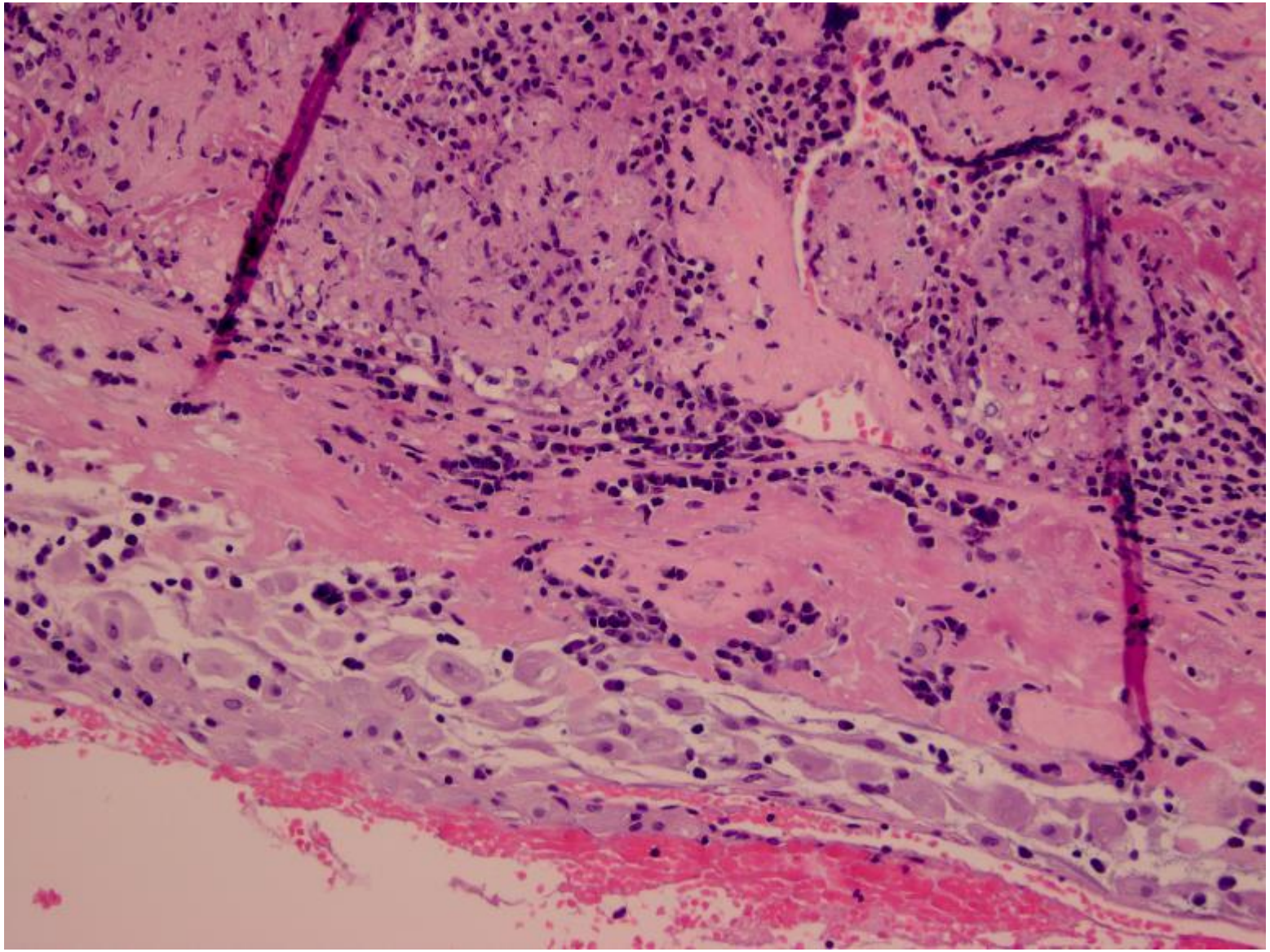
Usual type chronic villitis

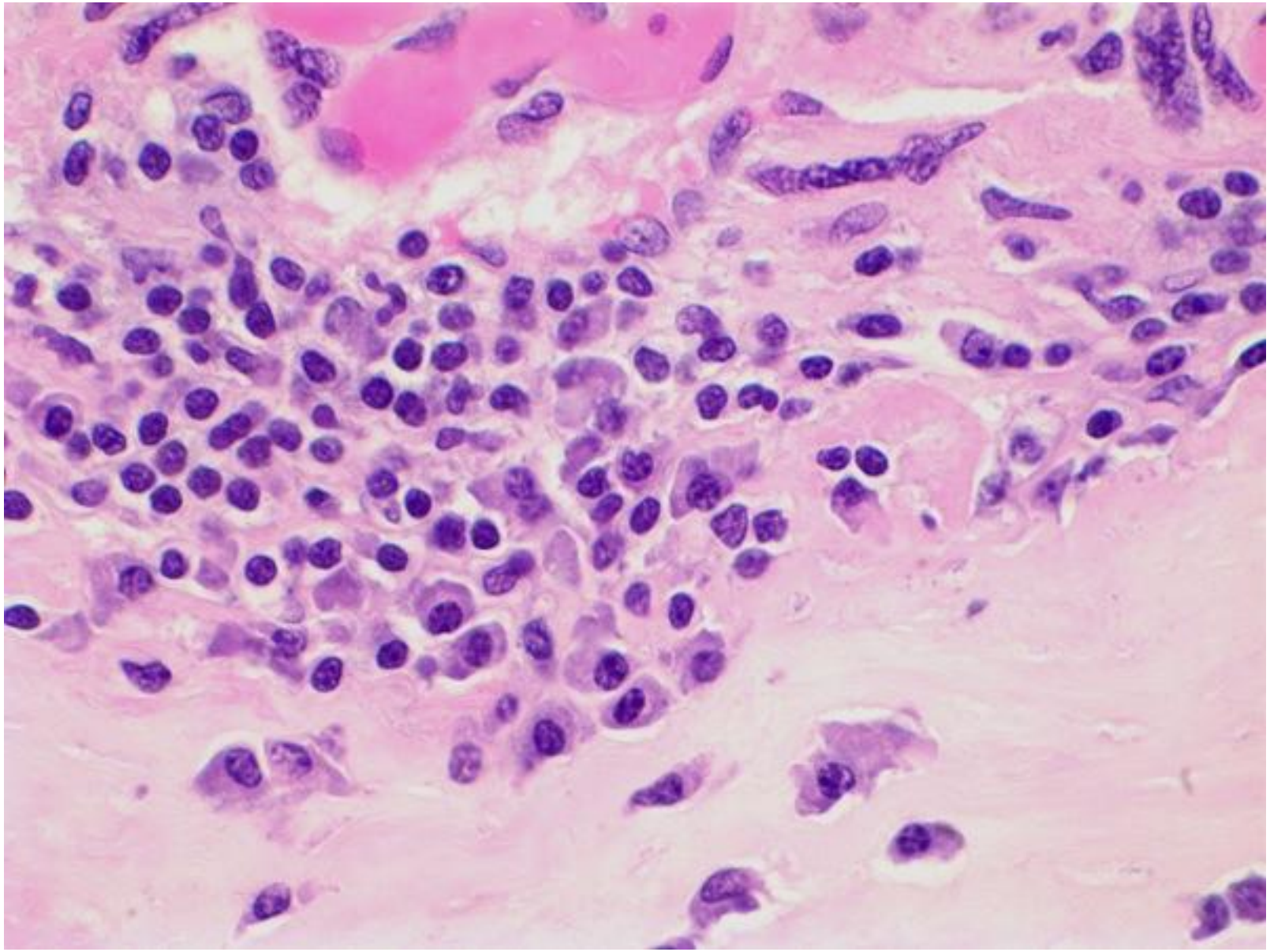


Plasma cell villitis

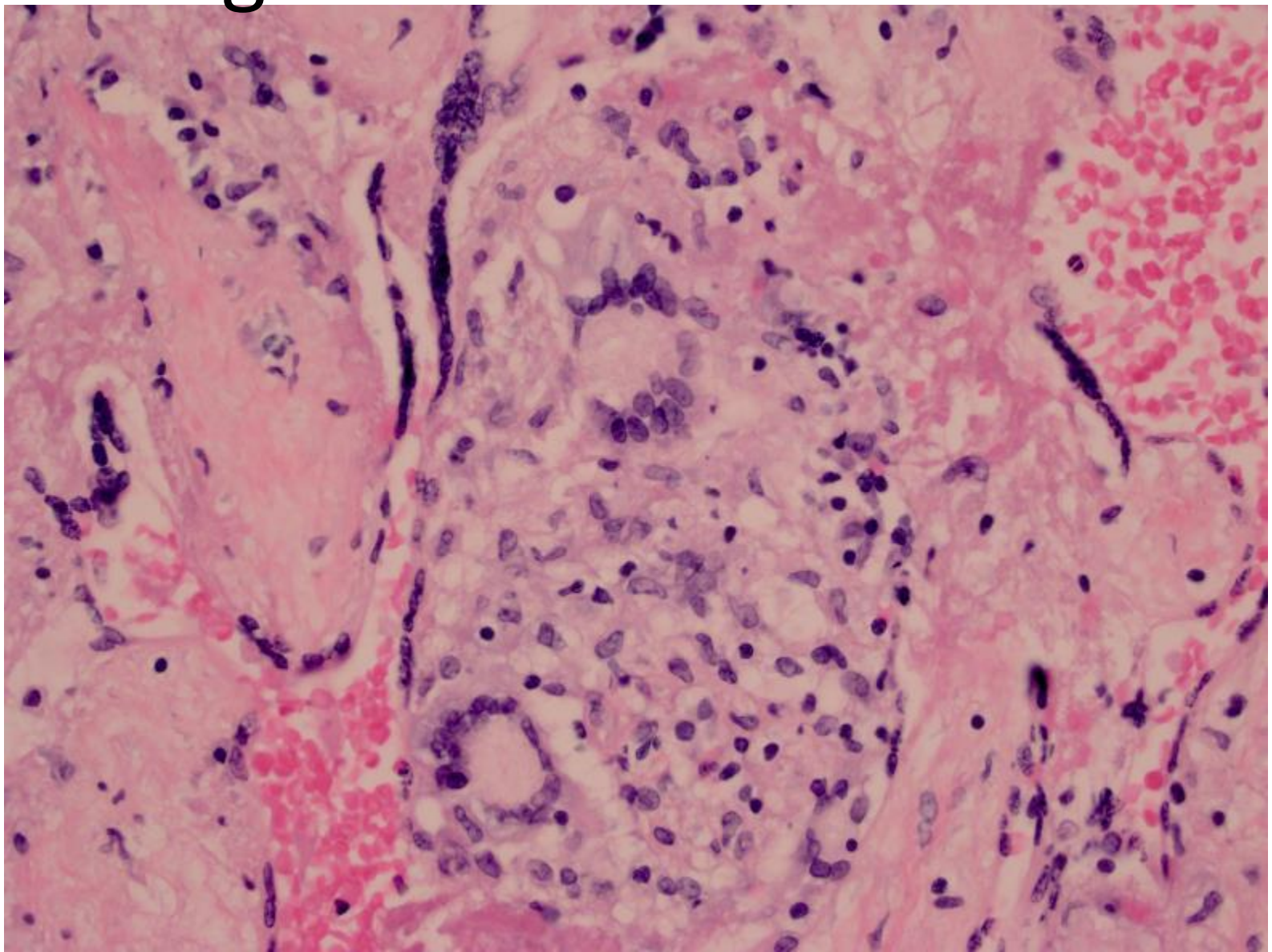


Basal villitis with plasma cell deciduitis

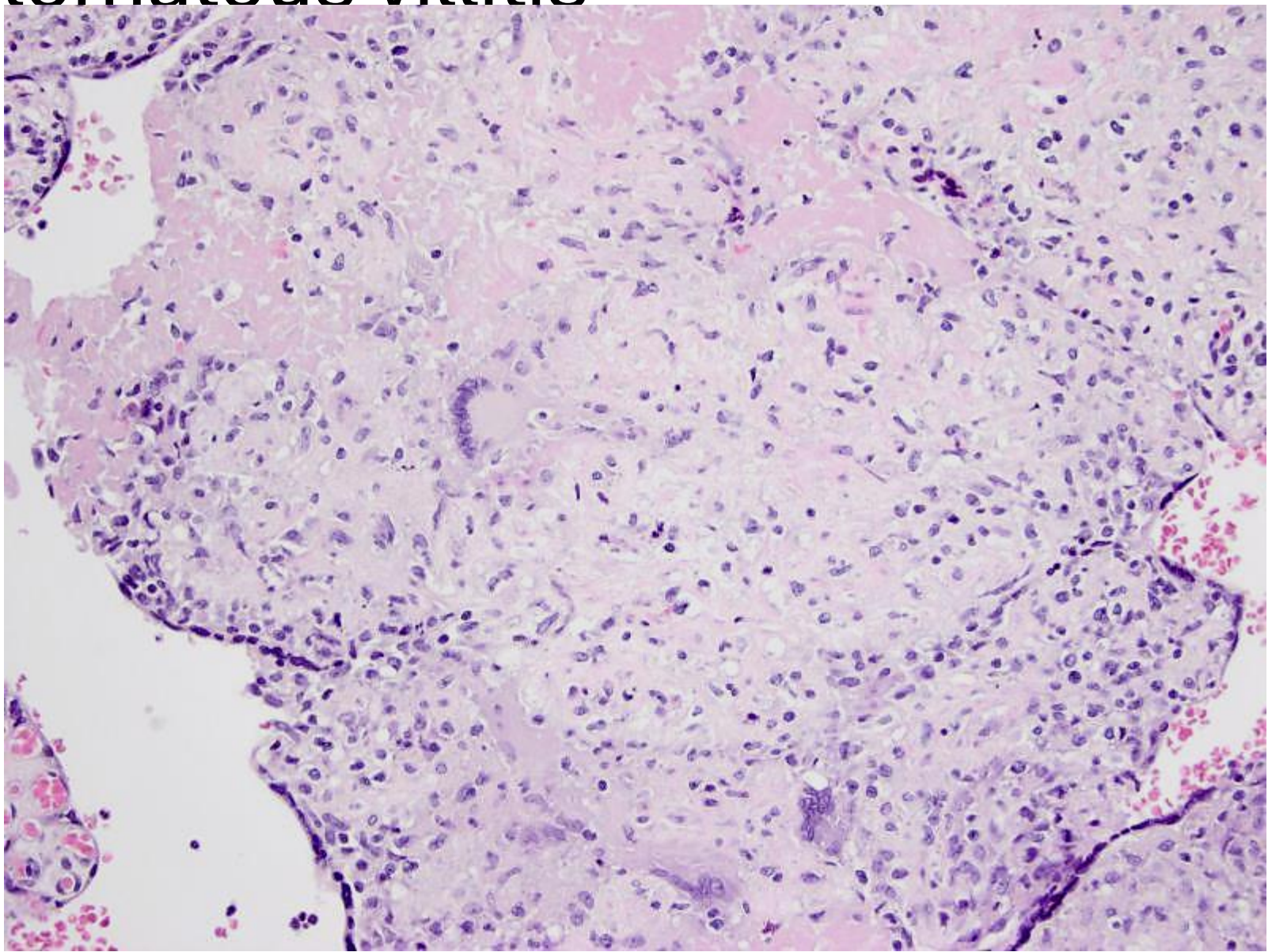




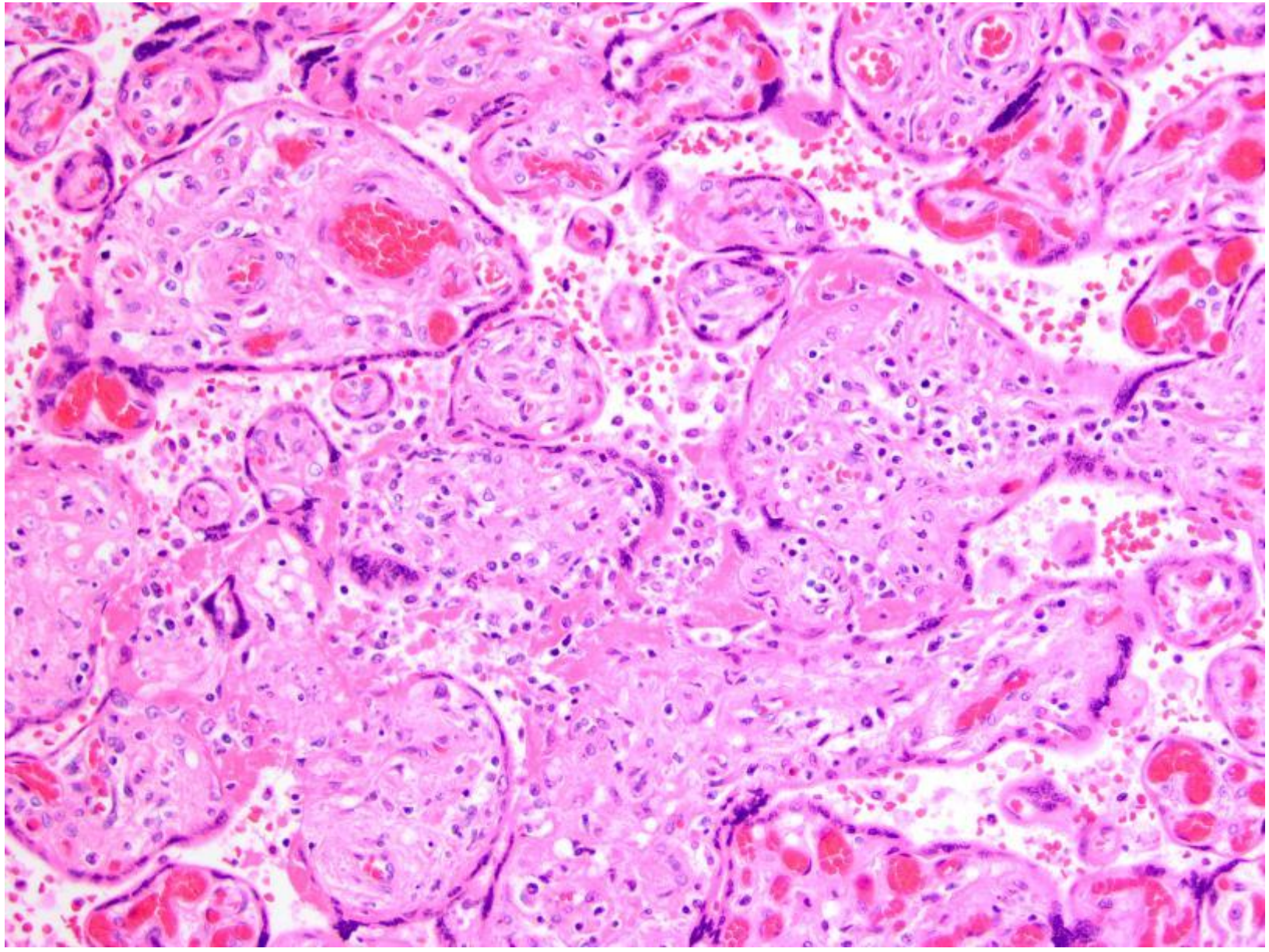
Giant cell or granulomatous villitis

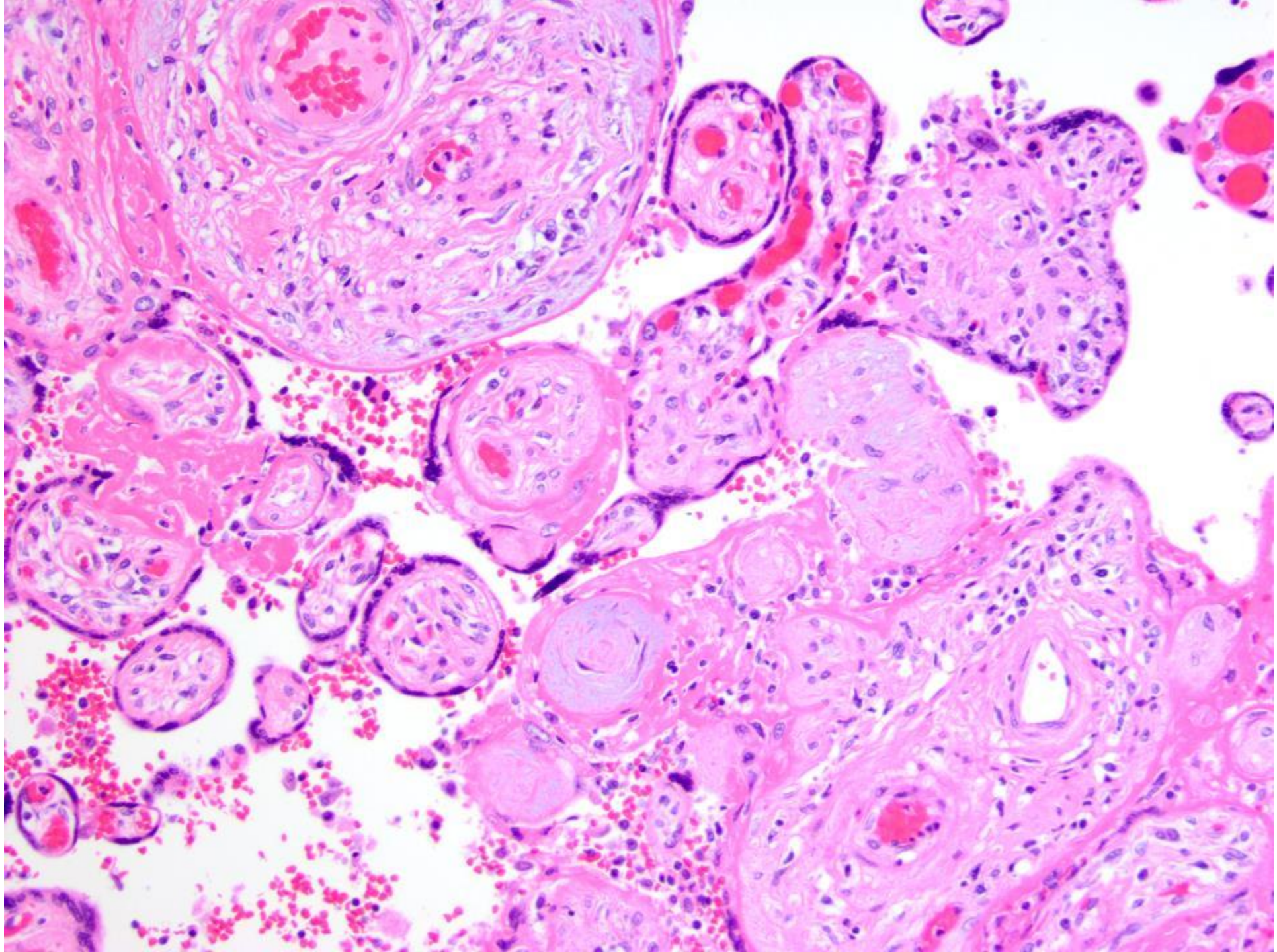


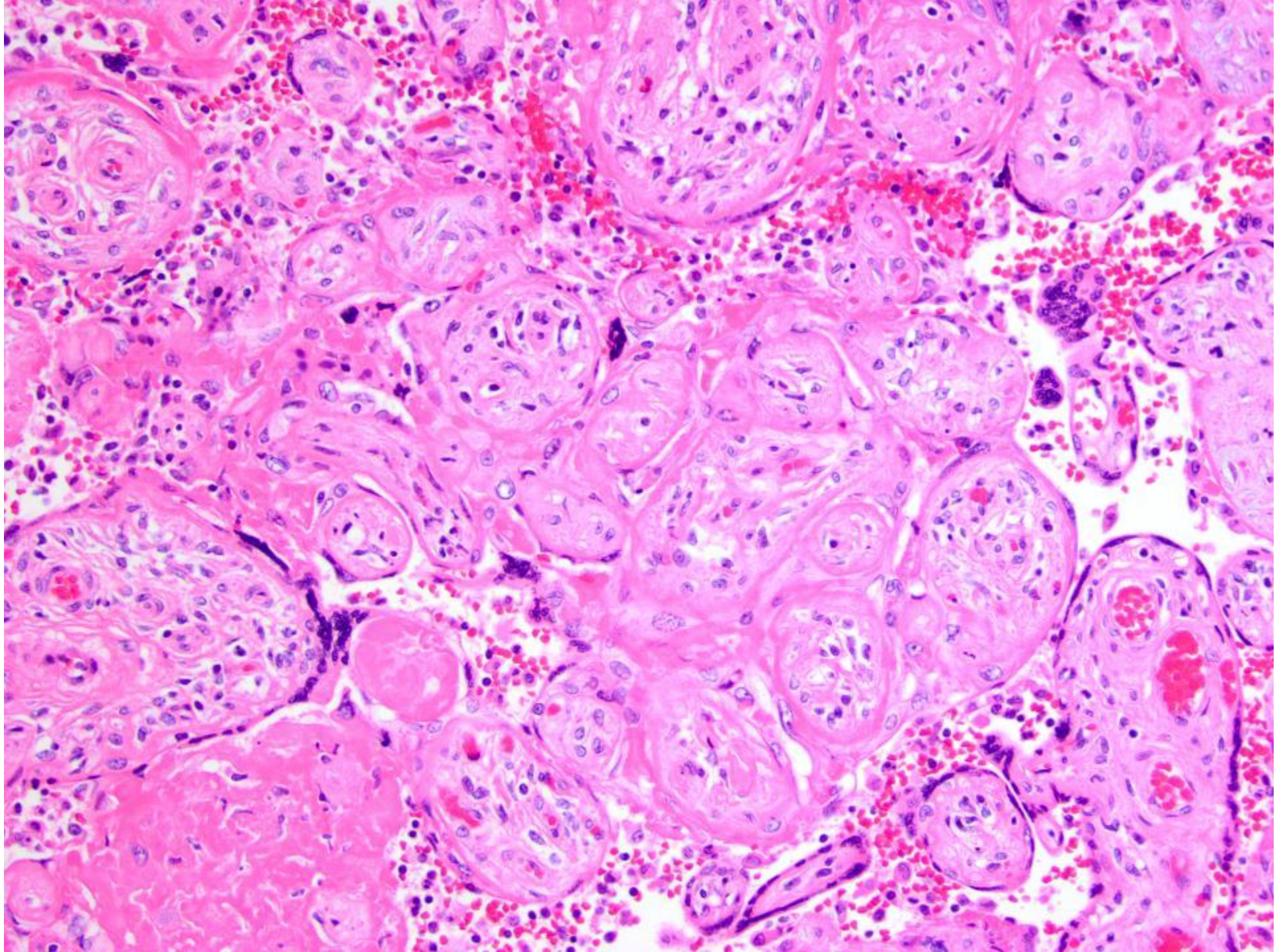
Granulomatous villitis

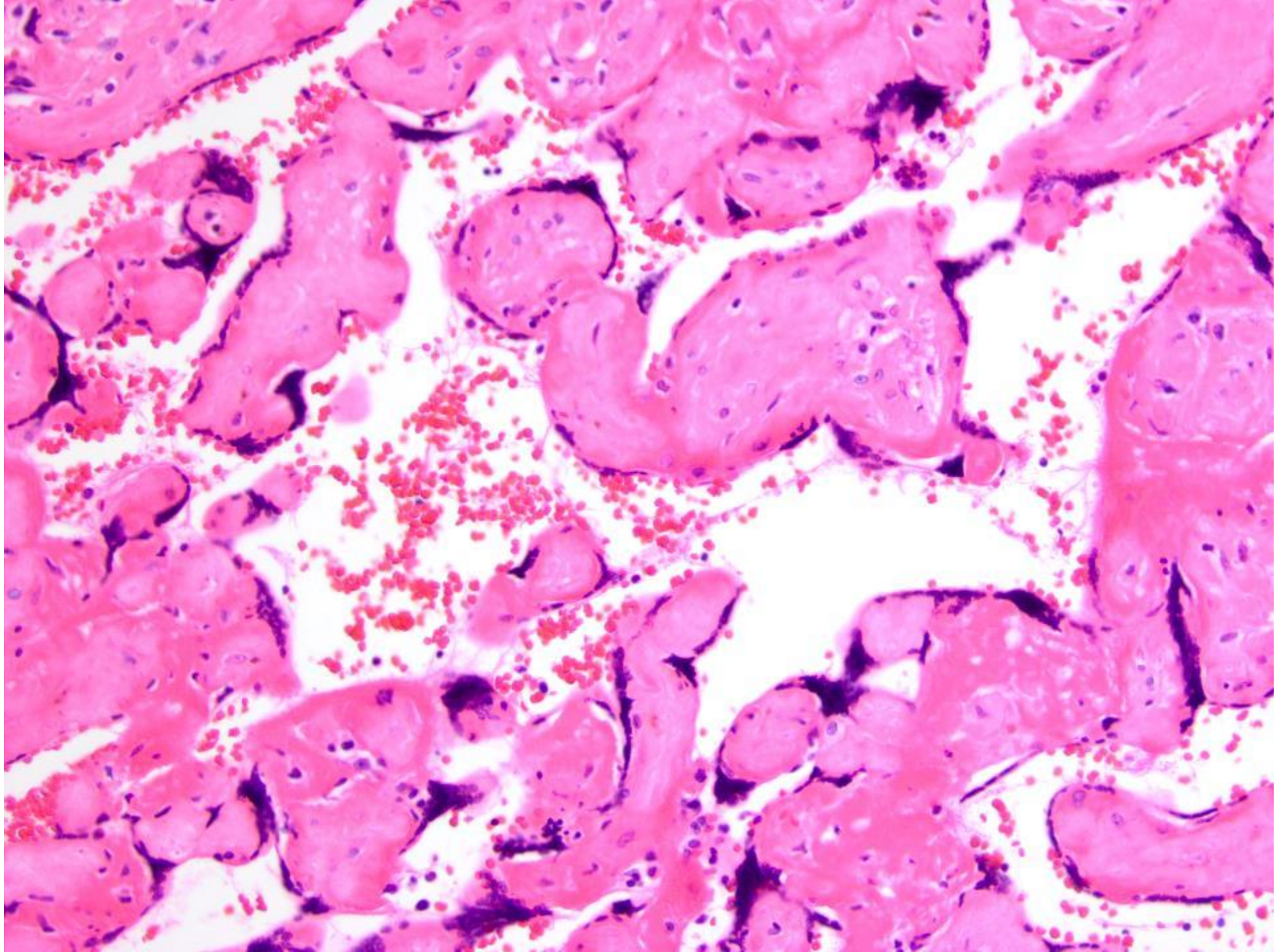


Obliterative villitis

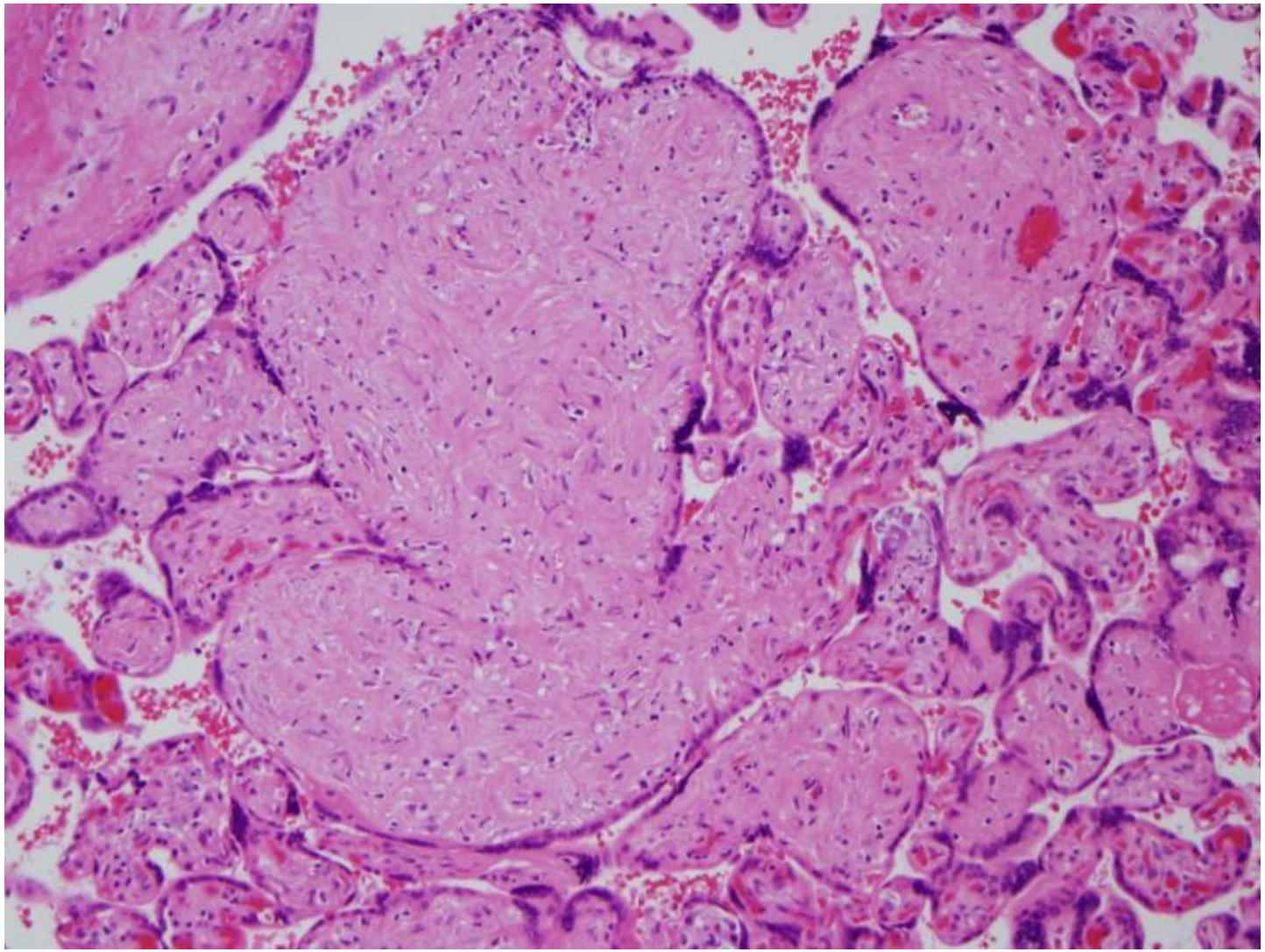


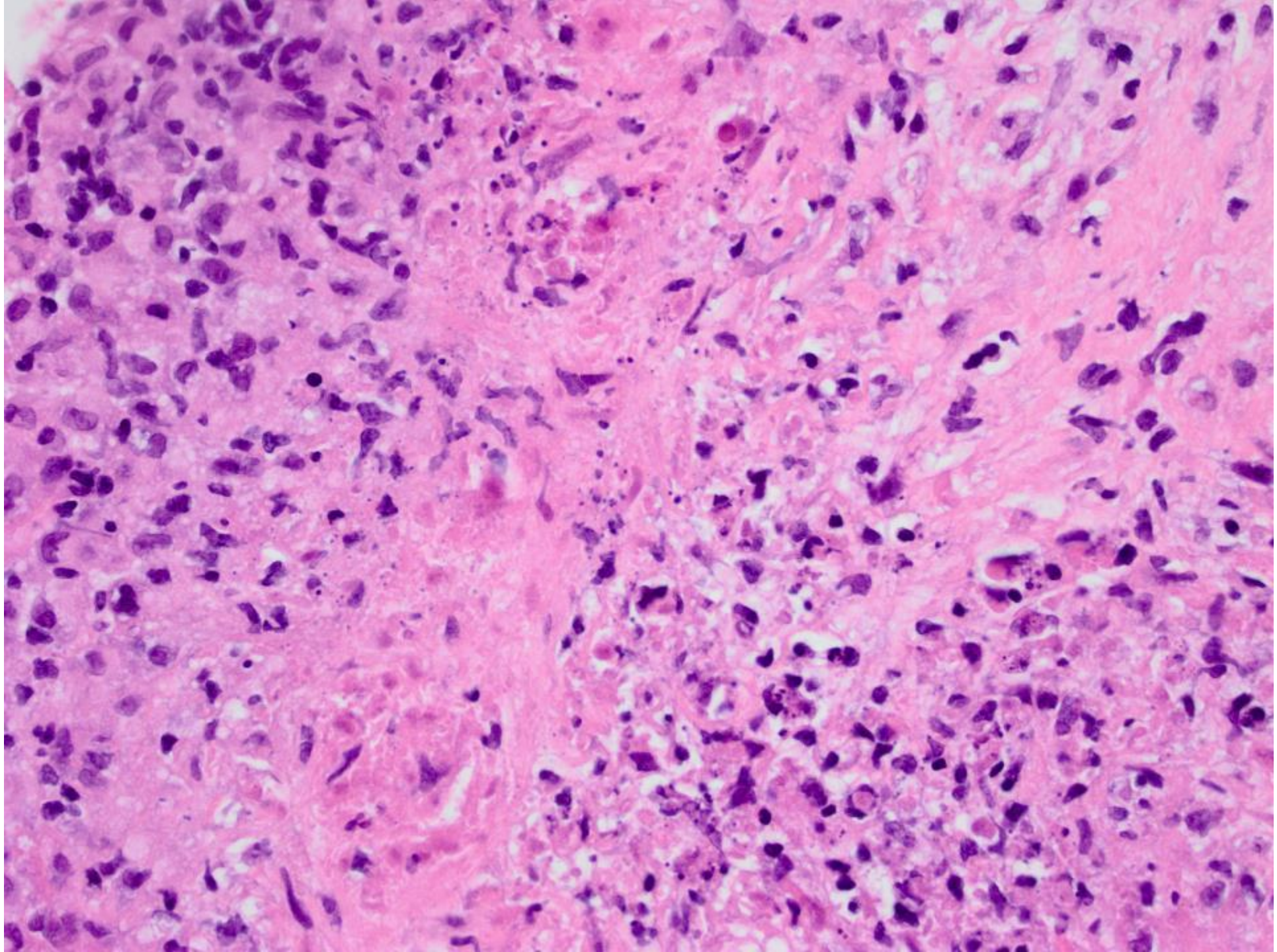






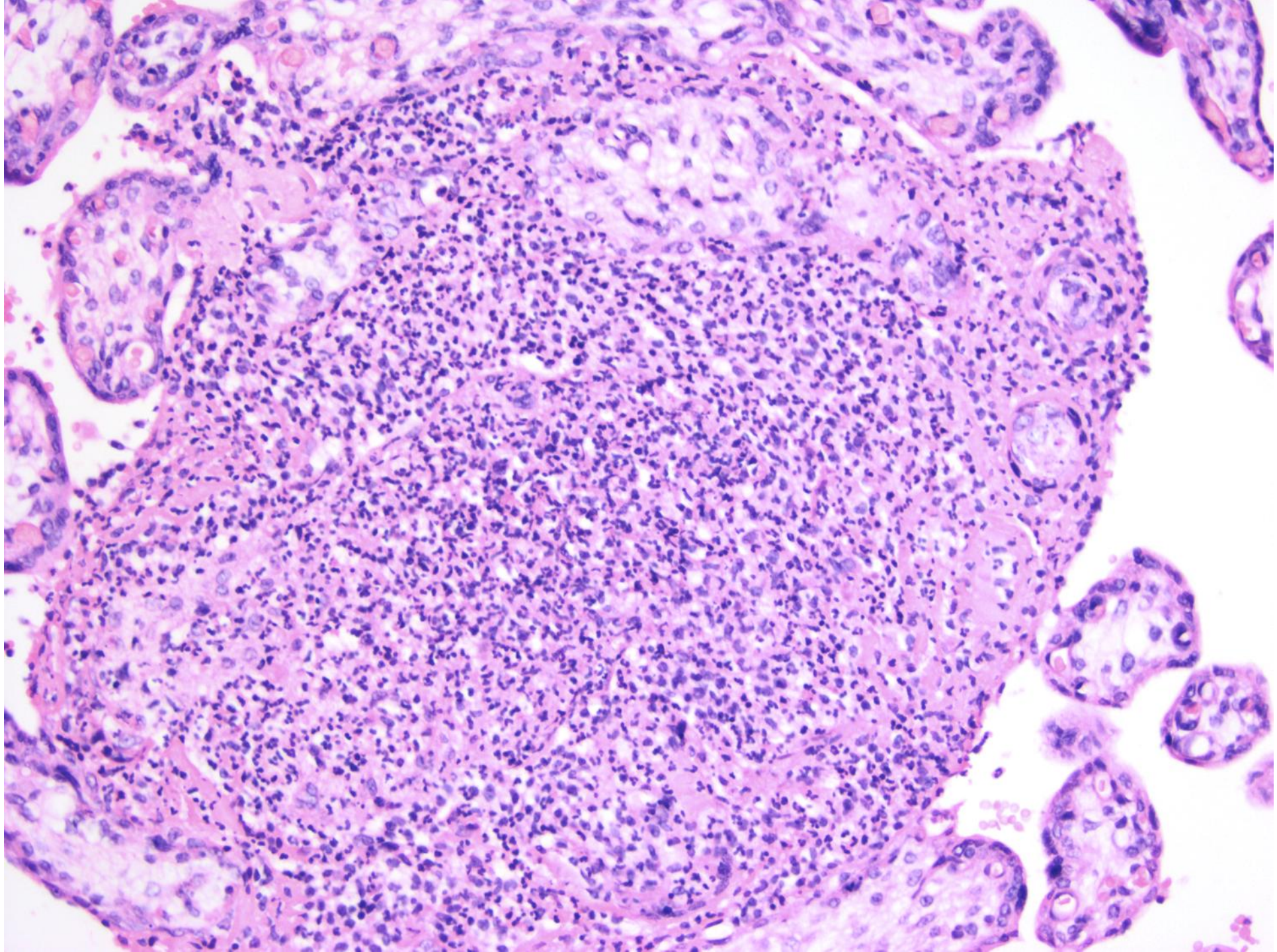
Stromal expansion with superficial necrosis

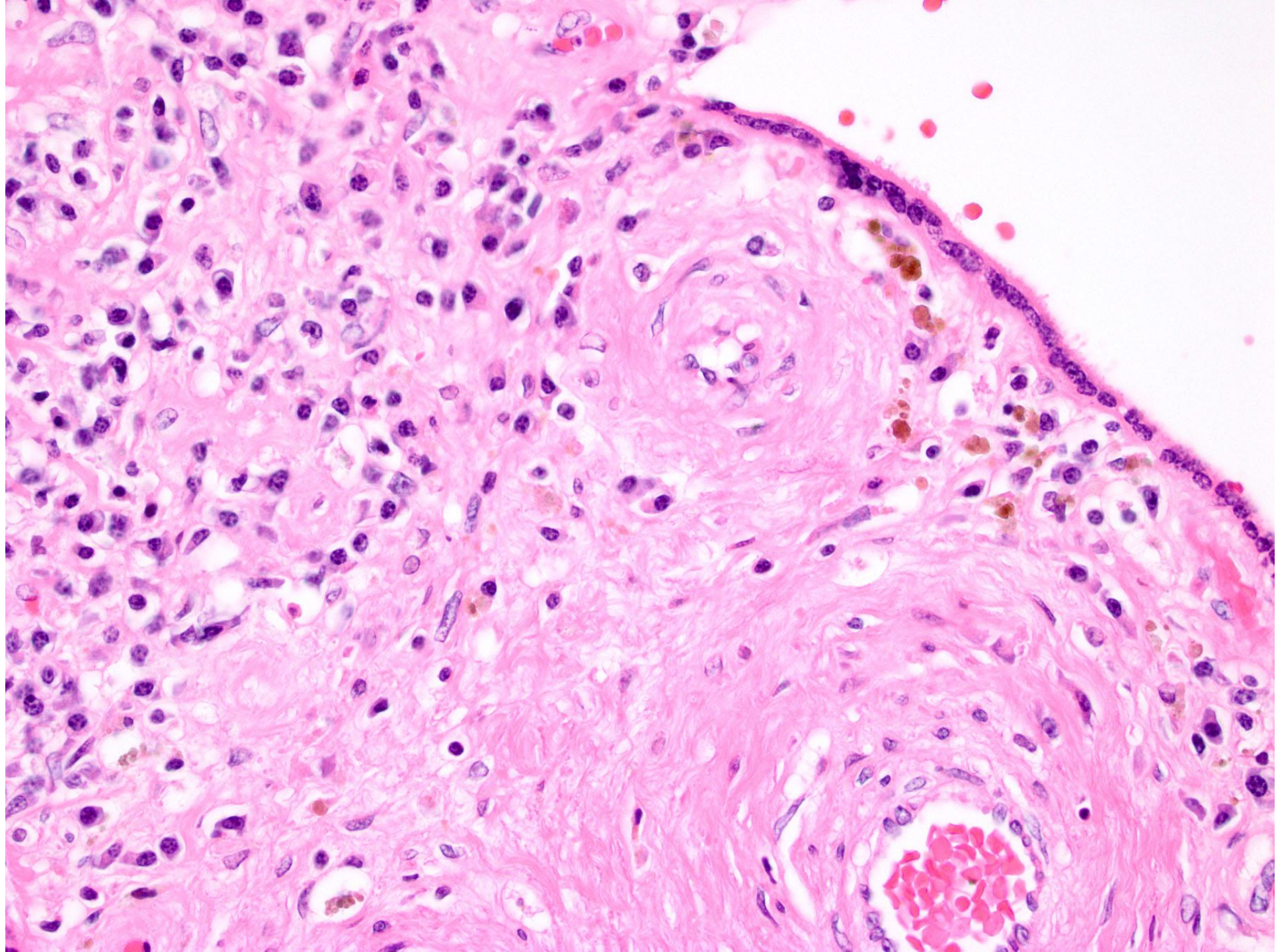


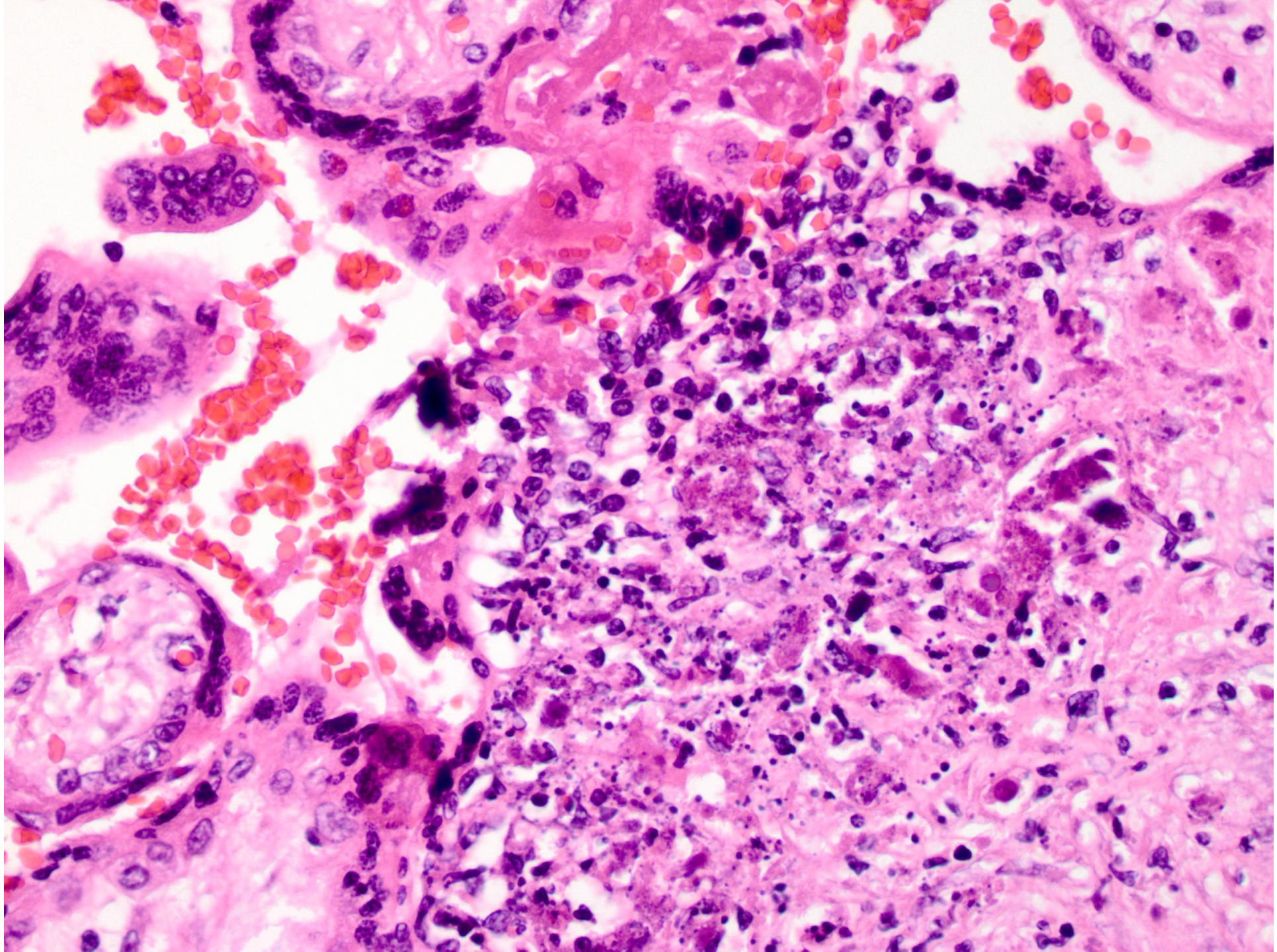


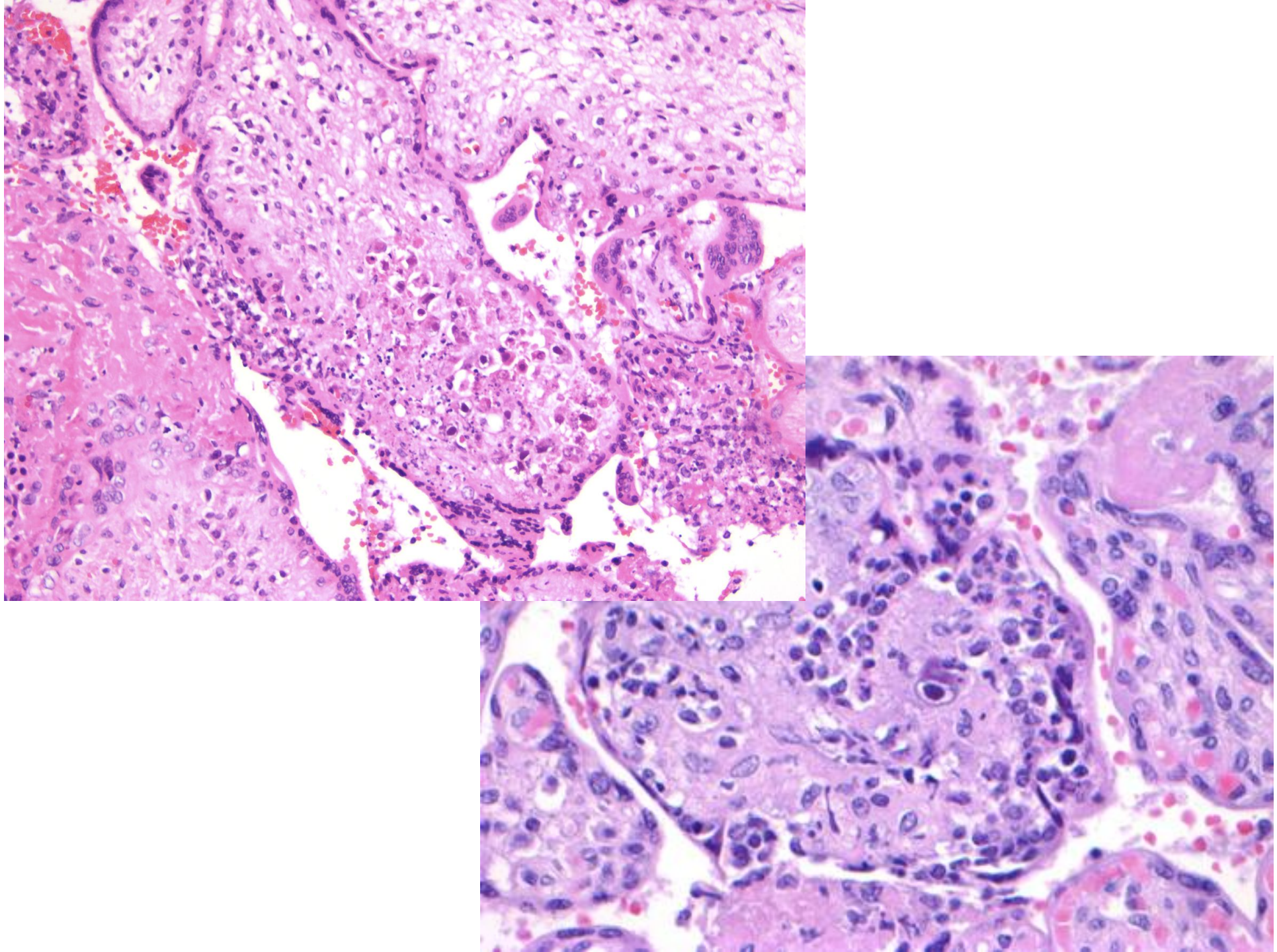
When to worry about chronic villitis

- Features suspicious for an infectious villitis
  - Preterm
  - Diffuse
  - Associated with stromal expansion
  - Plasma cells, neutrophils, giant cells
  - Hemosiderin
  - necrosis
  - normoblasts
- High grade villitis
- Recurrent villitis
- Villitis in a small placenta









Types of chronic villitis – how to report

- Describe geography
  - Focal
  - Patchy
  - Interface
  - diffuse
- Describe cell type
  - Granulomatous
  - Plasma cell
  - Usual type – mononuclear cells

Reporting Chronic Villitis

- Infectious chronic villitis
- Recurrent Chronic villitis
- Villitis of unknown etiology
  - Grade
    - High grade – multiple foci on more than one slide, more than 10 villi affected each focus
    - Low grade – more than one focus of at least 10 contiguous affected villi
    - Ungradeable
  - Associated pathology
    - Avascular villi (“obliterative villitis”)
    - Fibrin (?massive chronic intervillositis)
    - Chronic chorioamnionitis
    - Intervillositis (?massive chronic intervillositis)

How to report - NOTE

- Note: Most cases of chronic villitis are idiopathic and not infectious. In this case we see no findings to suspect an infectious etiology but this is best excluded clinically. The infections most commonly associated with chronic villitis are those of the TORCH class. Non-infectious chronic villitis (villitis of unknown etiology) is a common finding but has an increased association with perinatal morbidity. There is a small but definite recurrence risk.

Things that recur – relevance of perinatal pathology

- Indication for placental pathologic examination
  - History
    - IUGR, IUFD, Preterm Delivery
  - Current
    - Any of the above

- Recurrent SABs or infertility

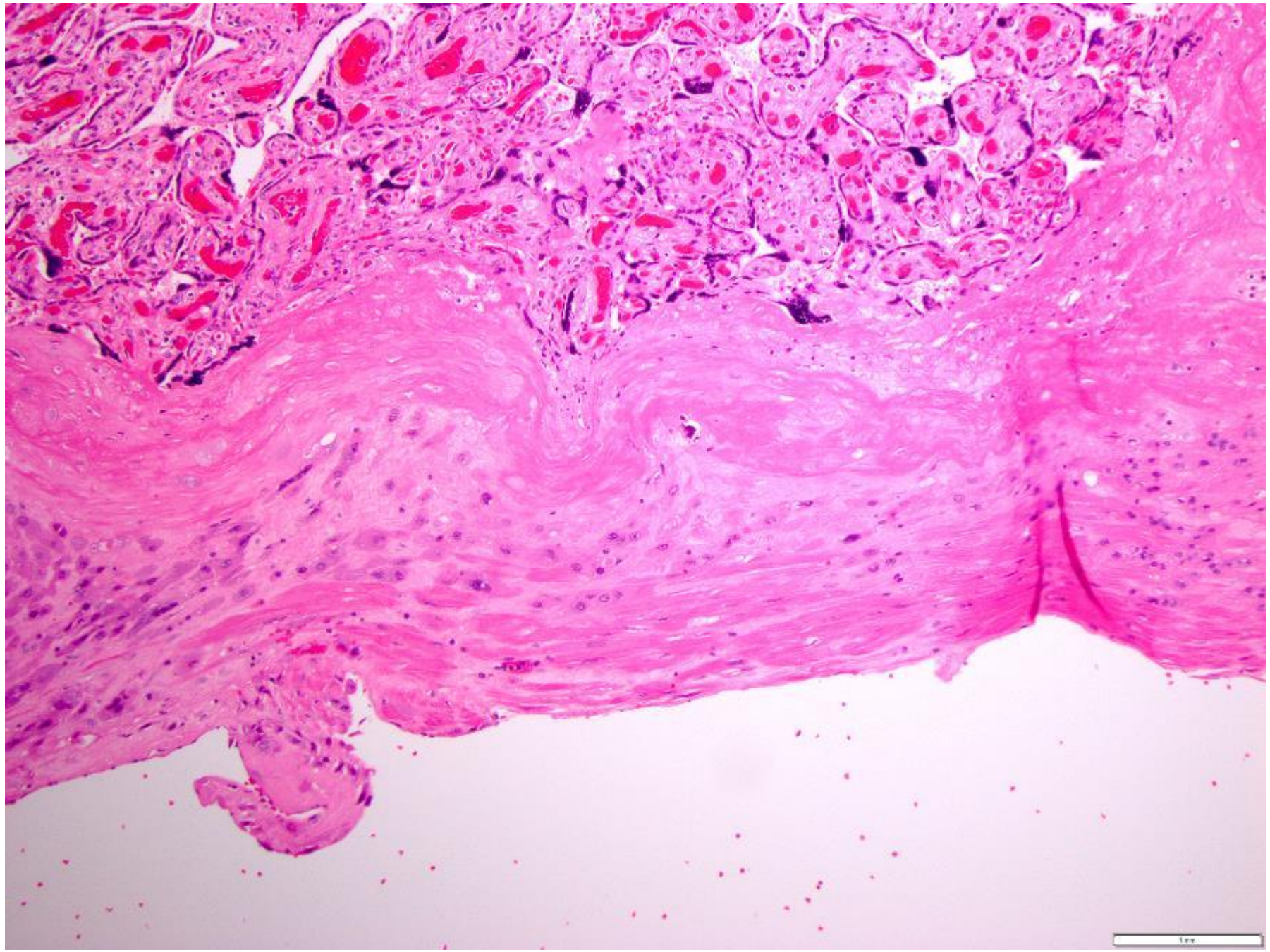
Adherent myometrial fibers

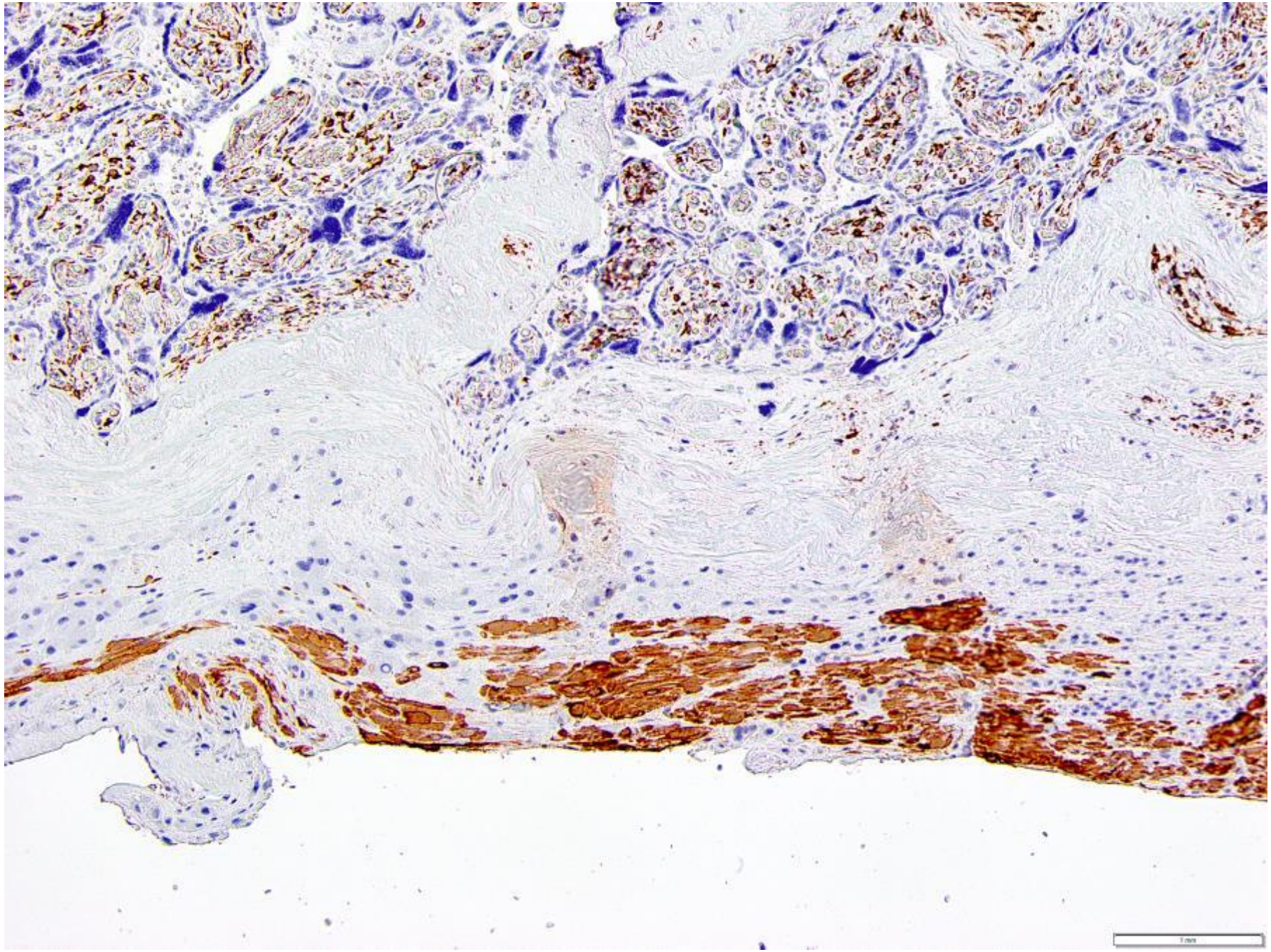
- Reported incidence widely variable from ~3% to 40%
- Can be staged - higher stages more associated with clinically significant placenta accreta spectrum (PAS) and risk for cretas in future pregnancies
  - Staging is based on presence and amount of decidual cells intervening between the villi and the myometrium

Staging

- **Stage 0 - no adherent myometrial fibers**
- **Stage 1 - adherent myometrial fibers with intervening decidua**
- **Stage 2 - adherent myometrial fibers without intervening decidua**

Hecht JL, Baergen R, Ernst LM, Katzman PJ, Jacques SM, Jauniaux E, Khong TY, Metlay LA, Qureshi F, Rabban JT, Roberts DJ, Shainker S, Heller DS. Classification and reporting guidelines for the pathology diagnosis of placenta accreta spectrum (PAS) disorders; recommendations from an expert panel. Modern Pathology, in press (2020)





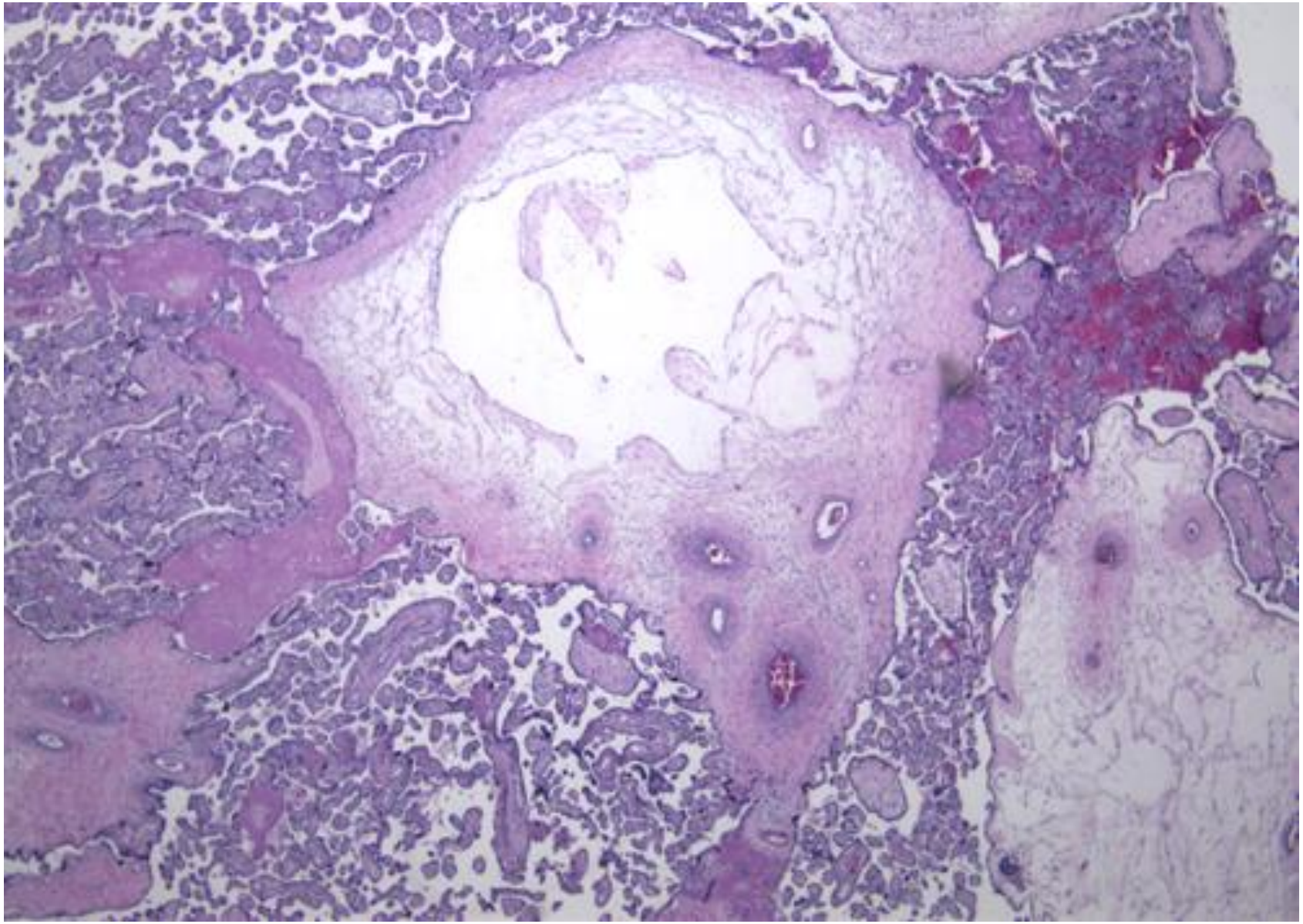
Adherent myometrial fibers, stage 2

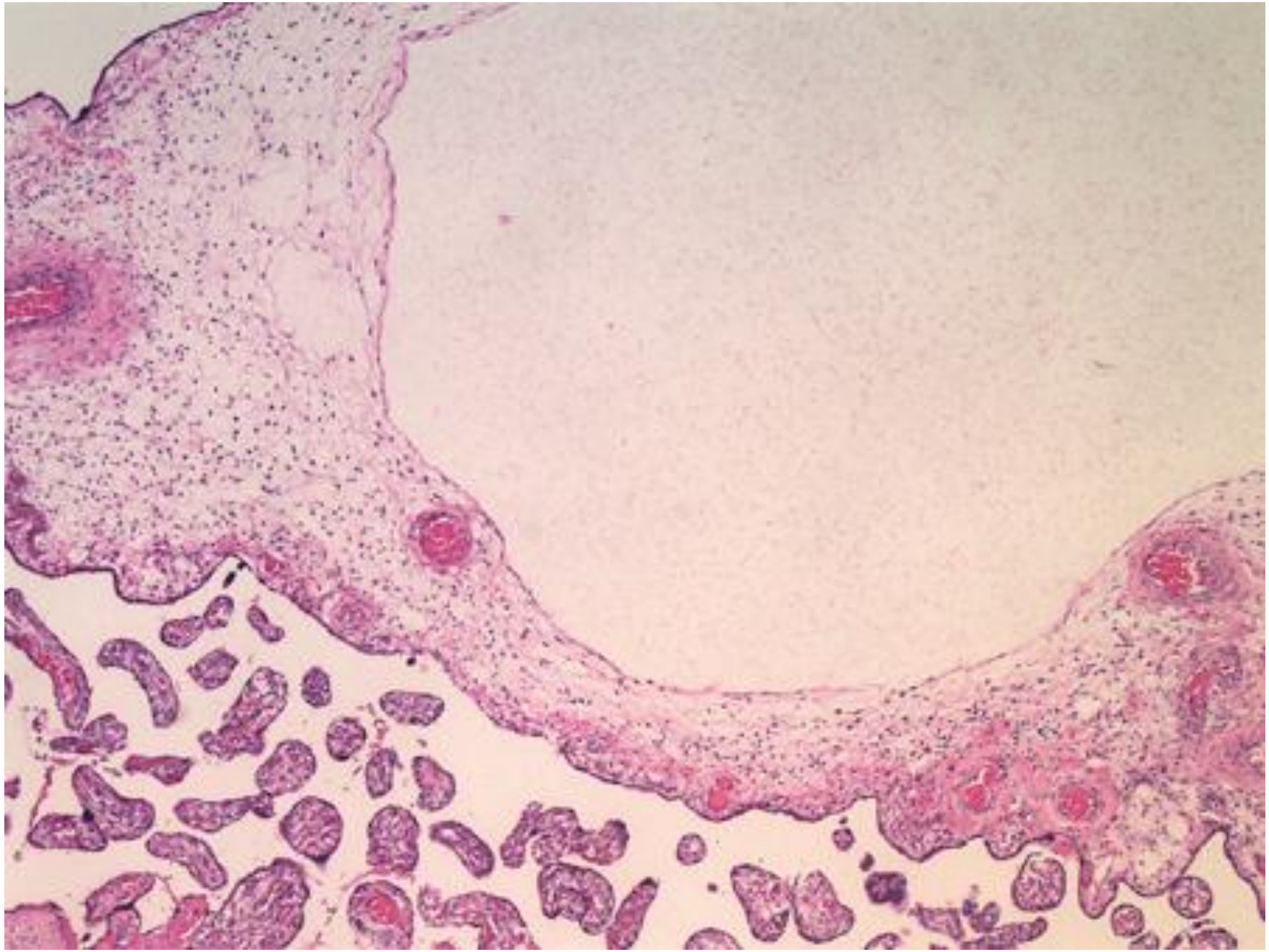
- Increase the risk of a truly morbidly adherent placenta in the next pregnancy
- More than 80% of clinically significant PAS had adherent myometrial fibers in their antecedent placentas

What the obstetrician needs to do with a diagnosis of adherent myometrial fibers

- Surveillance of future pregnancies for accreta or worse

Cystic placenta grossly with placentomegally





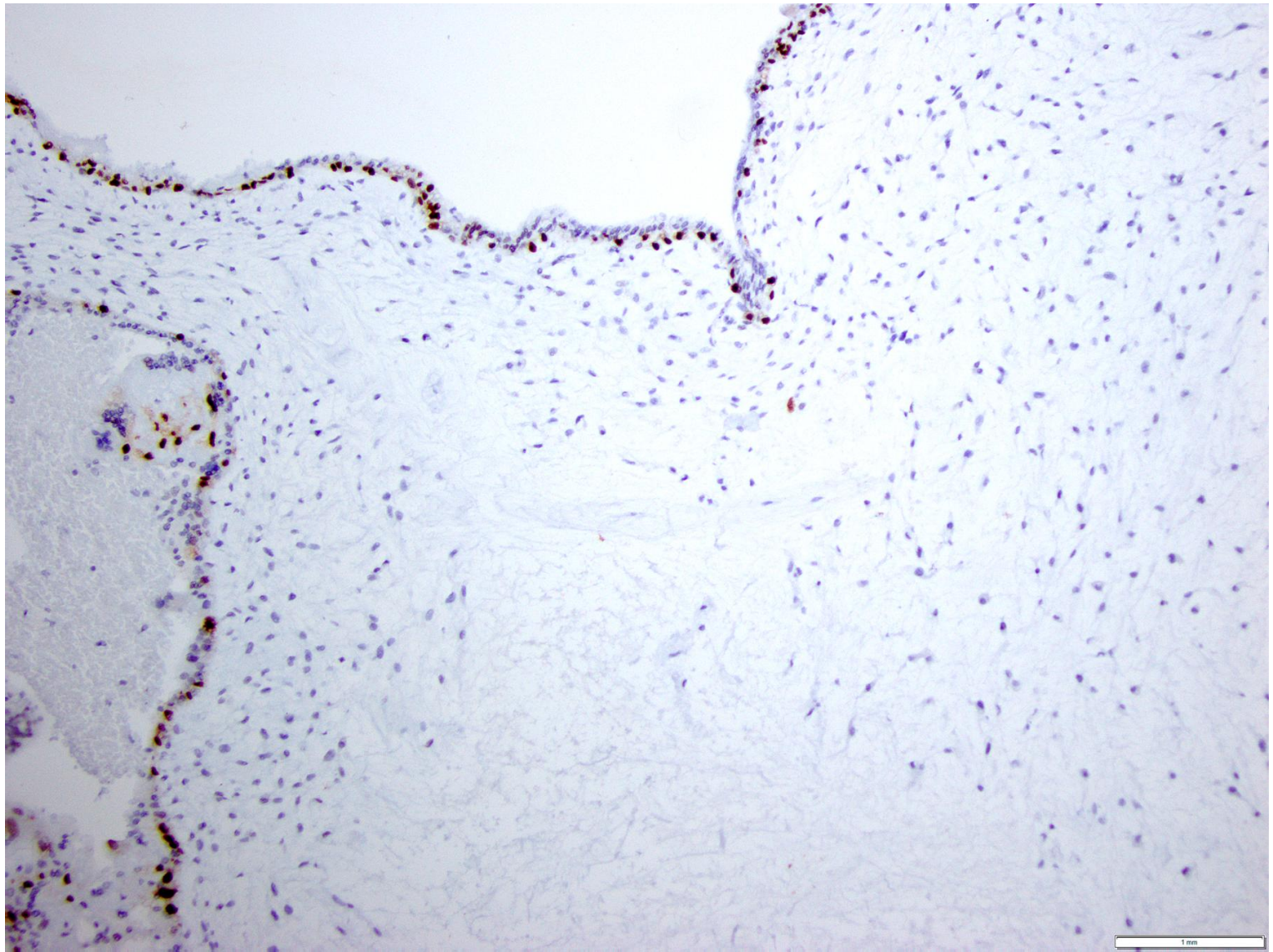
Placental Mesenchymal Dysplasia

- Placentomegaly
- Stem villi with cisternae
- Rope-like chorionic plate and stem villous vessels
- Chorionic vascular thrombi

Mesenchymal Dysplasia

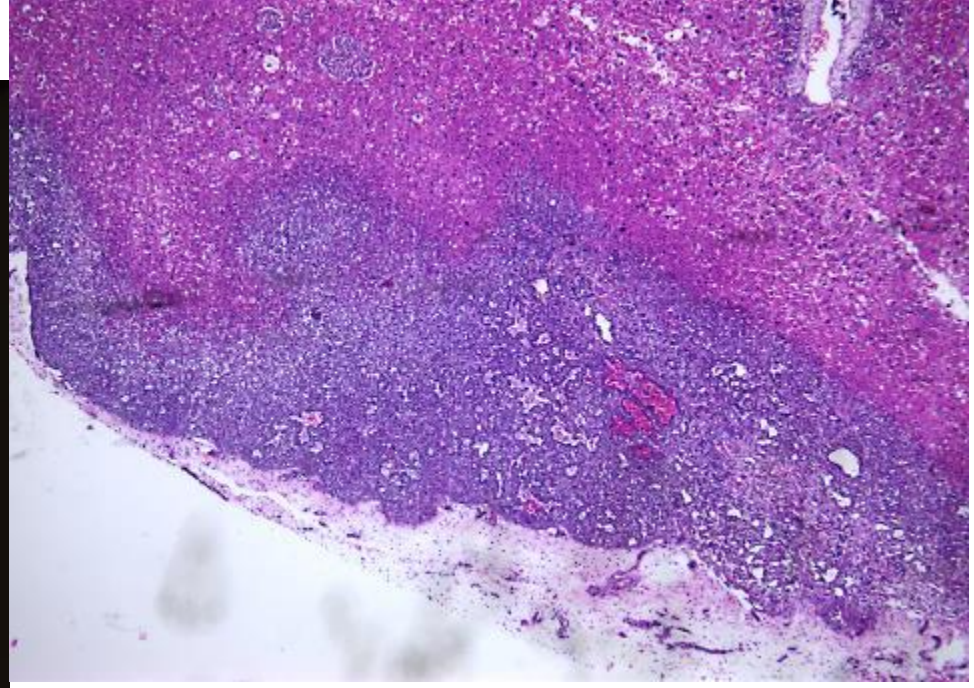
- Syndromic: Beckwith-Wiedemann
  - Neonatal phenotype may not be obvious
- Non-syndromic
  - Biparental/uniparental mosaic tissue contributions
    - Villous trophoblast is biparental
    - Villous stroma is androgenic (uniparental paternal)

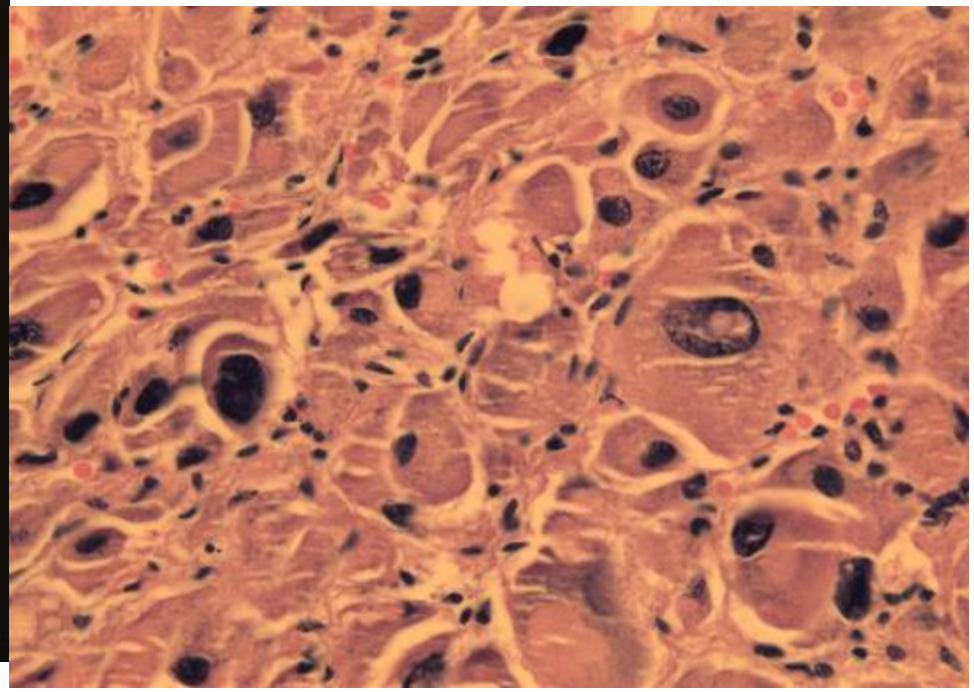
p57 in Mesenchymal Dysplasia



Beckwith-Wiedemann Syndrome

- Macrosomia
- Macroglossia
- Hemi-hypertrophy
- Congenital and pediatric neoplasms
- Placental mesenchymal dysplasia
- Incidence 1/13,700
- Extra paternal 11p





Benefits of the placental examination

- For the neonatologists/pediatricians and family – association with BWS and congenital/perinatal/pediatric tumors.
- For the obstetrician – documentation of the diagnosis for the US findings in the placenta and fetus.

References

- Books
  - Atlas of placental pathology : https://doi.org/10.55418/9781933477091
  - Placental and gestational pathology: doi.org/10.1017/9781316848616
  - Diagnostic placental pathology **ISBN-13:** 9780443116544
  - Survival guide to placental pathology Innovative Science Press

More References

- Manuscripts:

Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement
doi: 10.5858/arpa.2015-0225-CC

Four major patterns of placental injury: a stepwise guide for understanding and implementing the 2016 Amsterdam consensus
doi: 10.1038/s41379-021-00747-4

The Amsterdam Criteria and beyond: development of a Standardized Structured Reporting (SSR) tool for diagnosis of placental pathology
doi: 10.1007/s00428-025-04143-0

Criteria for placental examination for obstetrical and neonatal providers
doi: 10.1016/j.ajog.2022.12.017

THANKS for the opportunity to speak the importance of placental examination and for your attention and hospitality!