Molar Pregnancy and Gestational Trophoblastic Disease

Brad Quade, M.D., Ph.D.

Chief of Perinatal Pathology

BRIGHAM HEALTH
BWH BRIGHAM AND WOMEN'S HOSPITAL

DANA-FARBER CANCER INSTITUTE

HARVARD MEDICAL SCHOOL

Conflict of Interest Disclosure

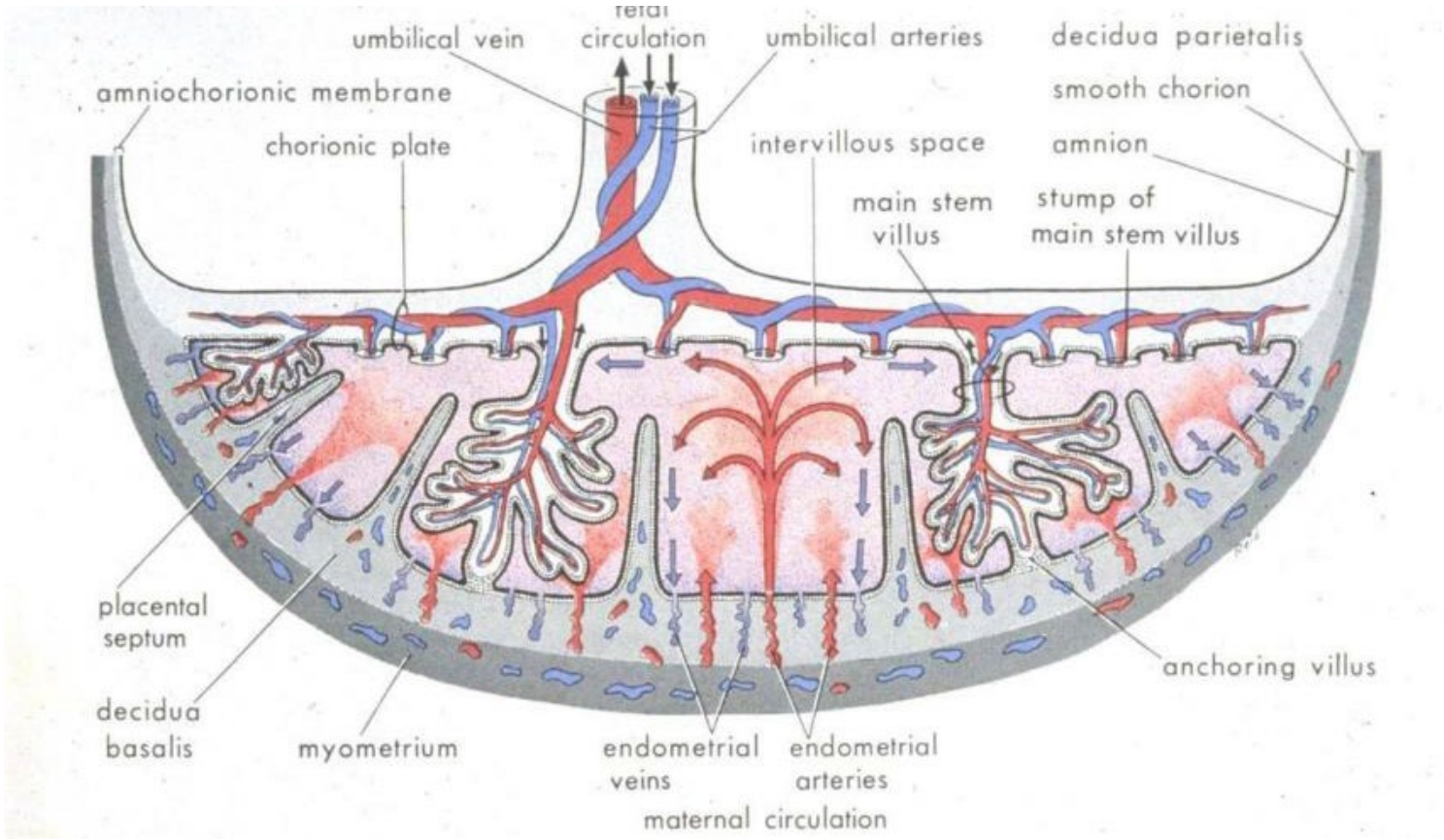
None

Goals

- **Molar Pregnancy and Gestational Trophoblastic Disease**
  - Highlight molar gestations in their pathobiological context
  - Define the histologic and genetic features that distinguish molar gestation from each other and their mimics
  - Provide a practical strategy for pathologic diagnosis that leverages your available ancillary tools

- ***Breaking News:*** **COVID-19 in Pregnancy**
  - Review the pathobiology of SARS-CoV-2 infection in the placenta and its clinical implications
  - Define the features of COVID-2 placentitis

Molar Pregnancy – Key Concepts

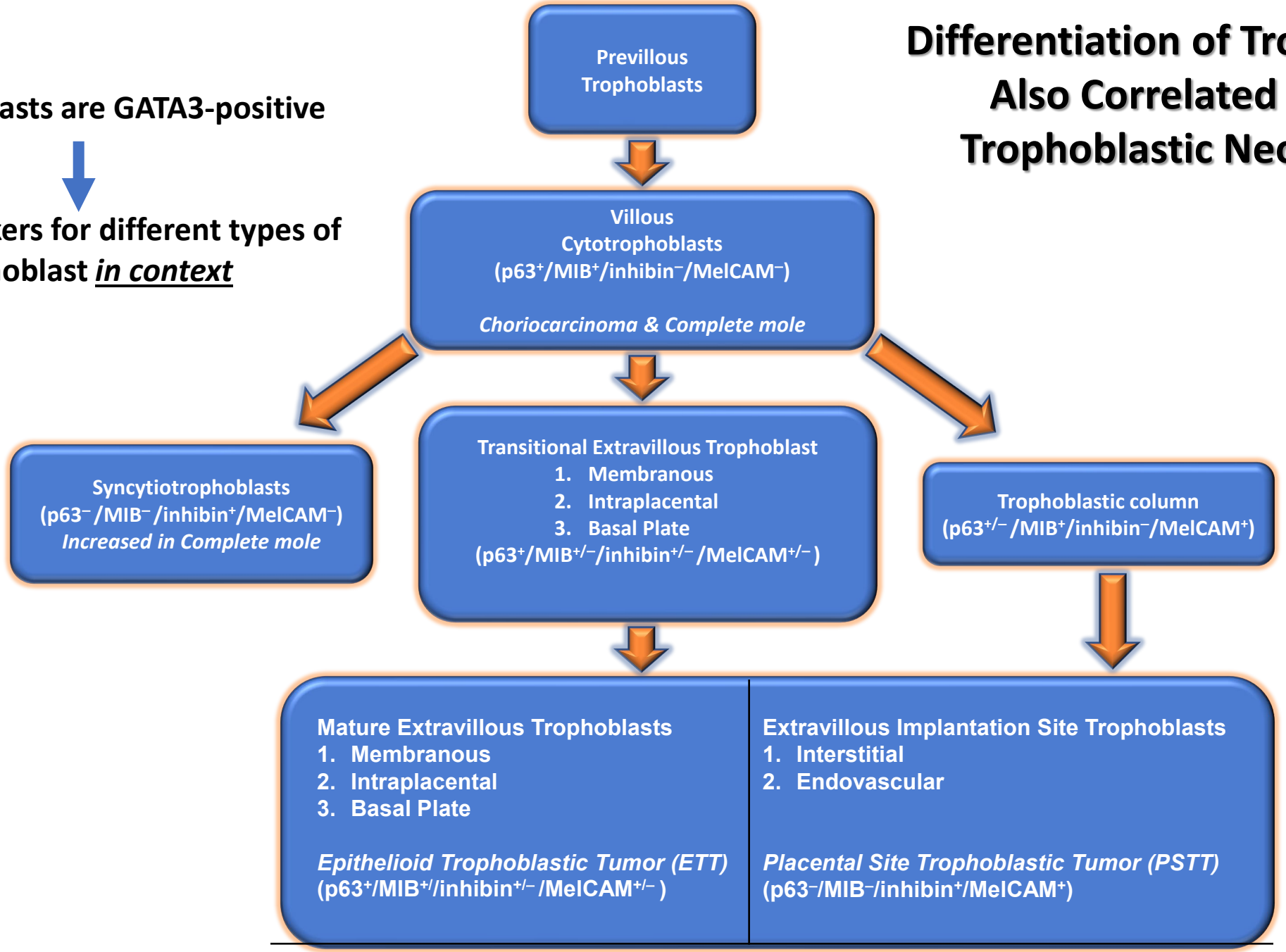


- Products of conception
- Genetically distinct from the host in which they reside
- Arise most frequently from genetic errors occurring in fertilization
- Like normal trophoblasts, invade tissue and blood vessels
- Nosologic organization begins with presence or absence of villi
- Phenotypes resemble cells constituting the normal placenta
- Must be considered in the spectrum of trophoplastic neoplasia

Differentiation of Trophoblast Also Correlated With Trophoblastic Neoplasia

All trophoblasts are GATA3-positive

Specific markers for different types of trophoblast *in context*



Nosology Of Trophoblast Neoplasia

Tumor	Fetus	Cyto-trophoblast	Syncytio-trophoblast	Intermediate (Implantation Site) Trophoblast	Chorionic Membrane Trophoblast	Villi	Biological Potential	Primary Differential Diagnosis	Typical Genetics
Partial Hydatidiform Mole	✓	✓	✓	✓	✓	✓	?	Aneuploidy (+18), Complete Mole +/- co-twin, Mesenchymal Dysplasia, Beckwith-Wiedemann Syndrome	3n with diandry (2p1m)
Complete Hydatidiform Mole		✓	✓	✓		✓	Invasive & Metastatic	Hydropic Abortus, Partial Mole	2n with diandry (2p)
Chorio-carcinoma	✓	✓	✓				Invasive & Metastatic	Other High Grade Neoplasm	Diploid, possibly diandric
Placental Site Trophoblast Tumor (PSTT)	✓			✓			Invasive & Metastatic to Lungs, pelvis, LNs (30-50%)	"Exaggerated" & Molar Implantation	46,XX
Epithelioid Trophoblast Tumor	✓				✓		Invasive	SCC of cervix ?De-diff. C	46,XX

Risk Factors For Trophoblastic Neoplasia

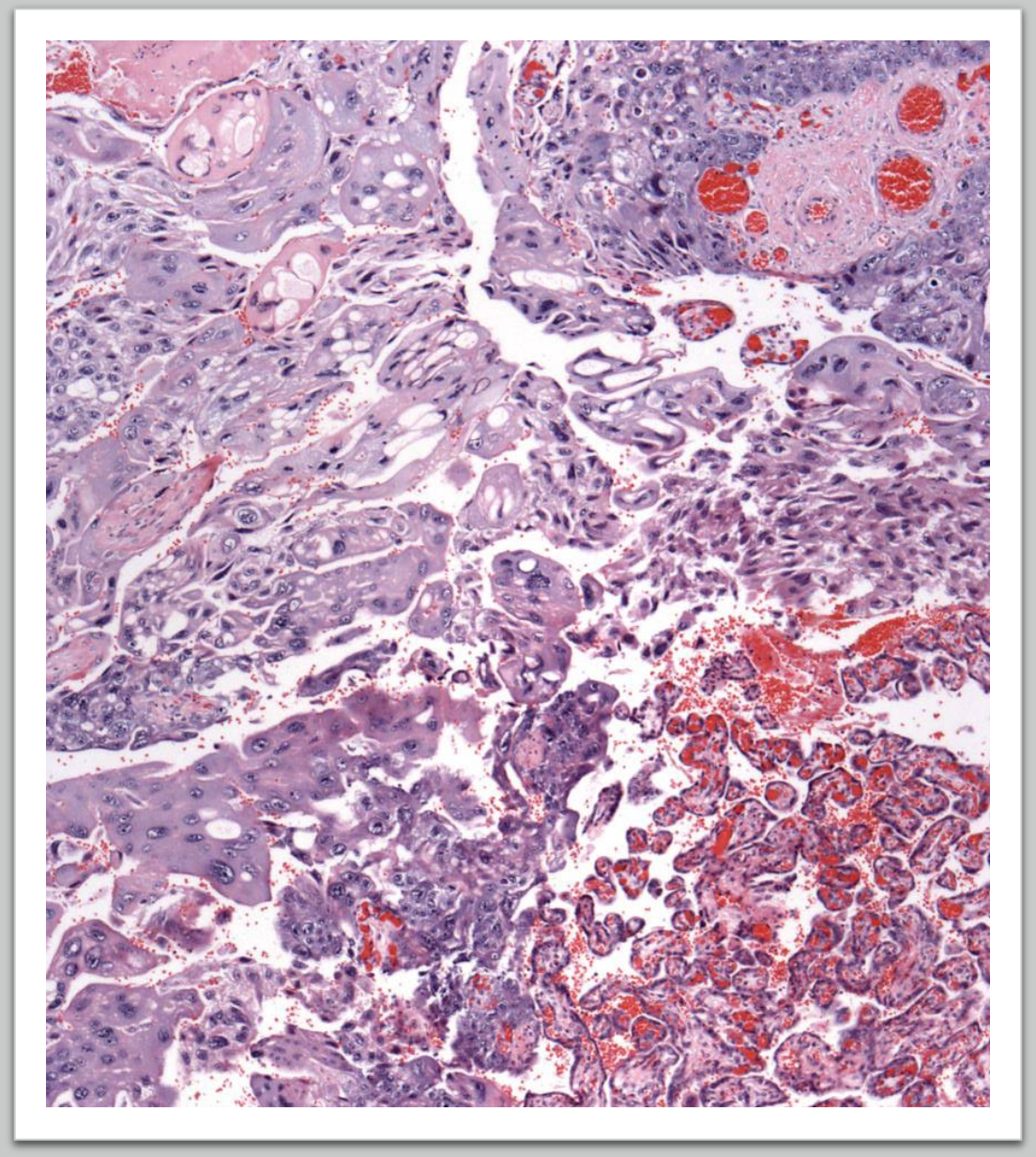
- Maternal Age
  - < 20 y/o RR = 1.5
  - >40 y/o RR = 5.2
- Race/Ethnicity
  - Indonesia Incidence = 1:85
  - Japan Incidence = 1:522
  - Sweden Incidence = 1:1560
  - USA Incidence = 1:1724
  - Asian women in the USA have a higher risk than other ethnic groups
- Prior Molar Pregnancy, especially >1
- Nulliparity
- Low socioeconomic status

(best studied in complete hydatidiform mole)

Choriocarcinoma (ChorioCA)

The Foundation Of Trophoblastic Neoplasia

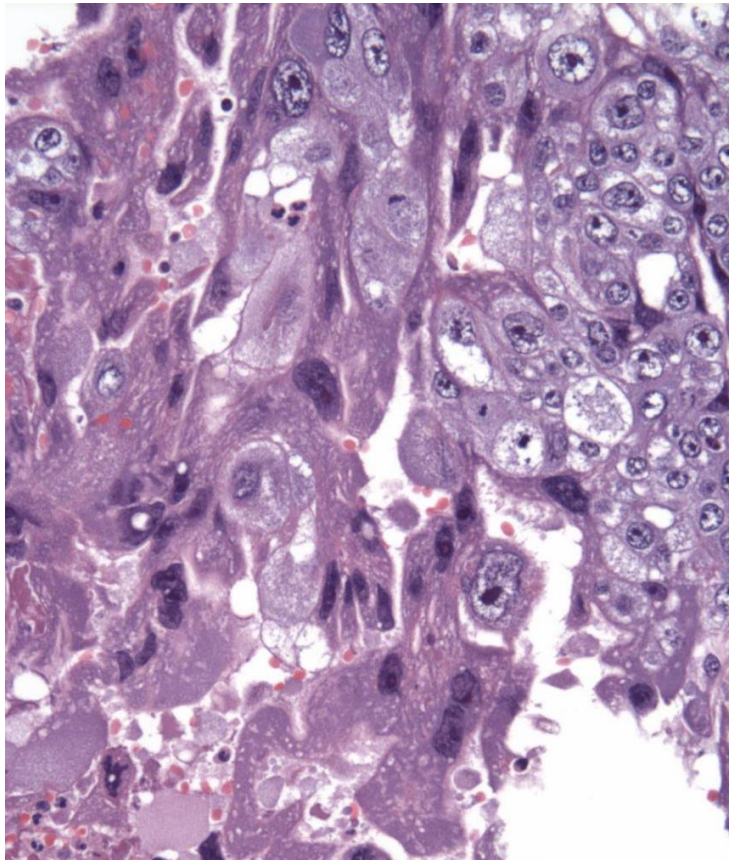
Image from engineeringbookspdf.com

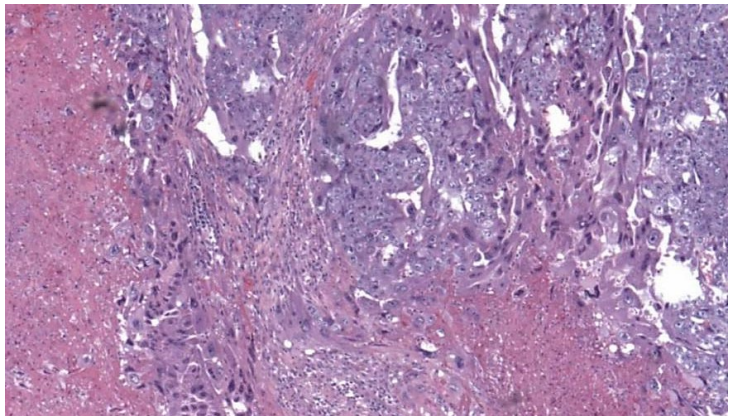


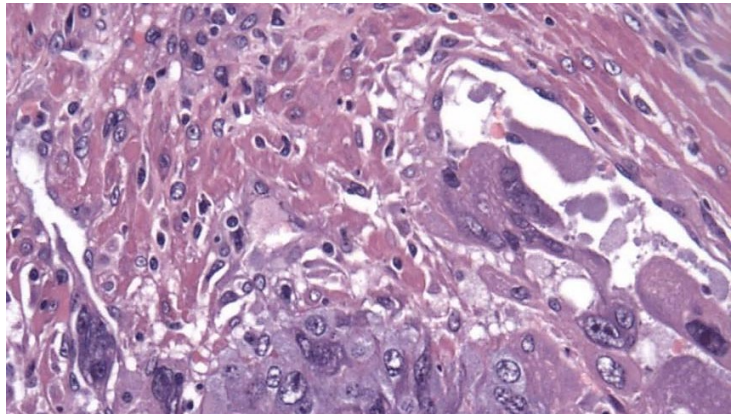
Choriocarcinoma – Clinical Context

- Gestational association:
  - 50% molar (complete >> partial)…but only 1 in 40 molar pregnancies
  - 25% spontaneous abortion
  - 2.5% ectopic gestation
  - 22.5% normal pregnancies (most often in 3rd trimester)
- Time Interval
  - Late -- many years (report of 14 yr)
  - Early -- concurrent (intraplacental choriocarcinoma)

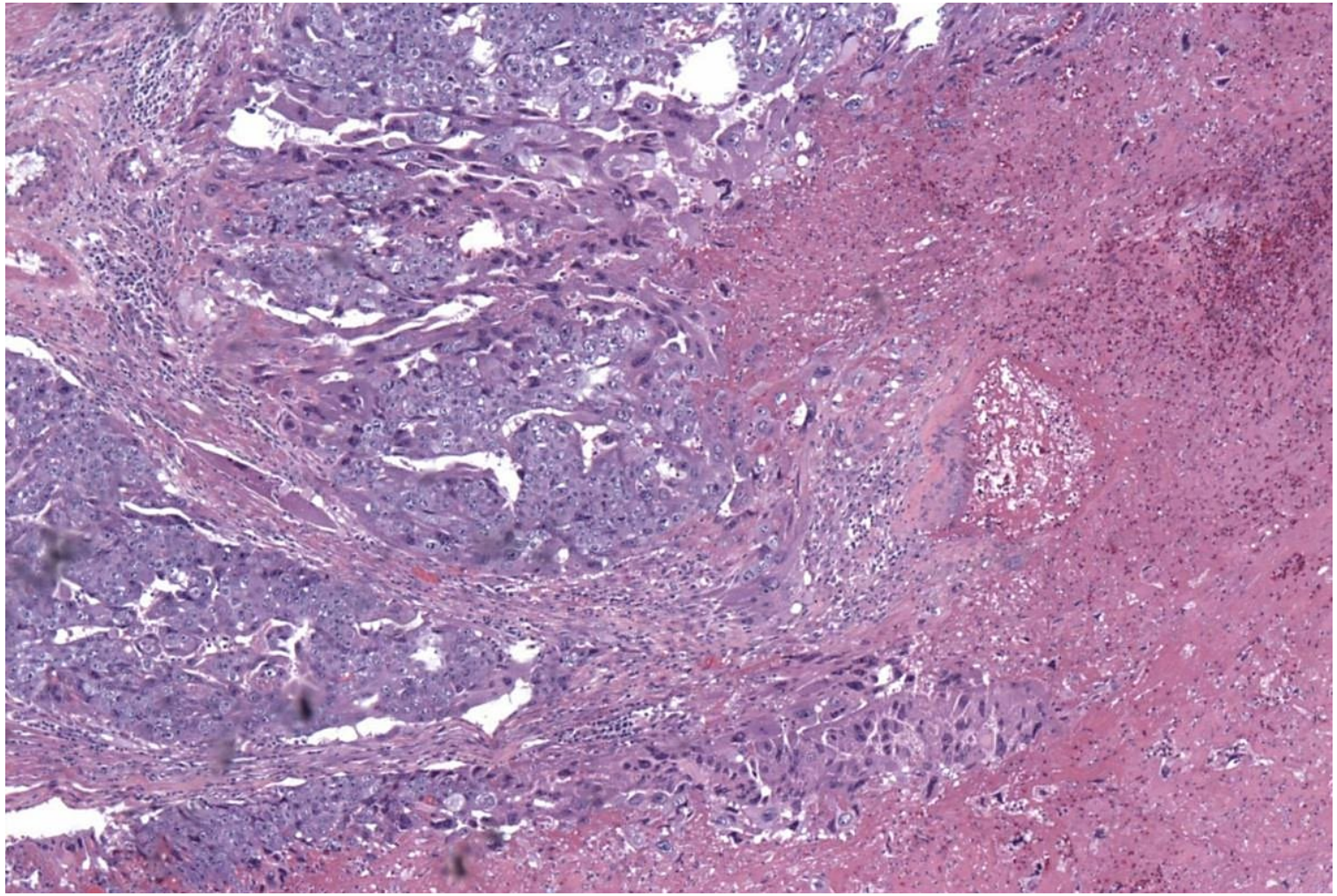
Choriocarcinoma- Diagnosis



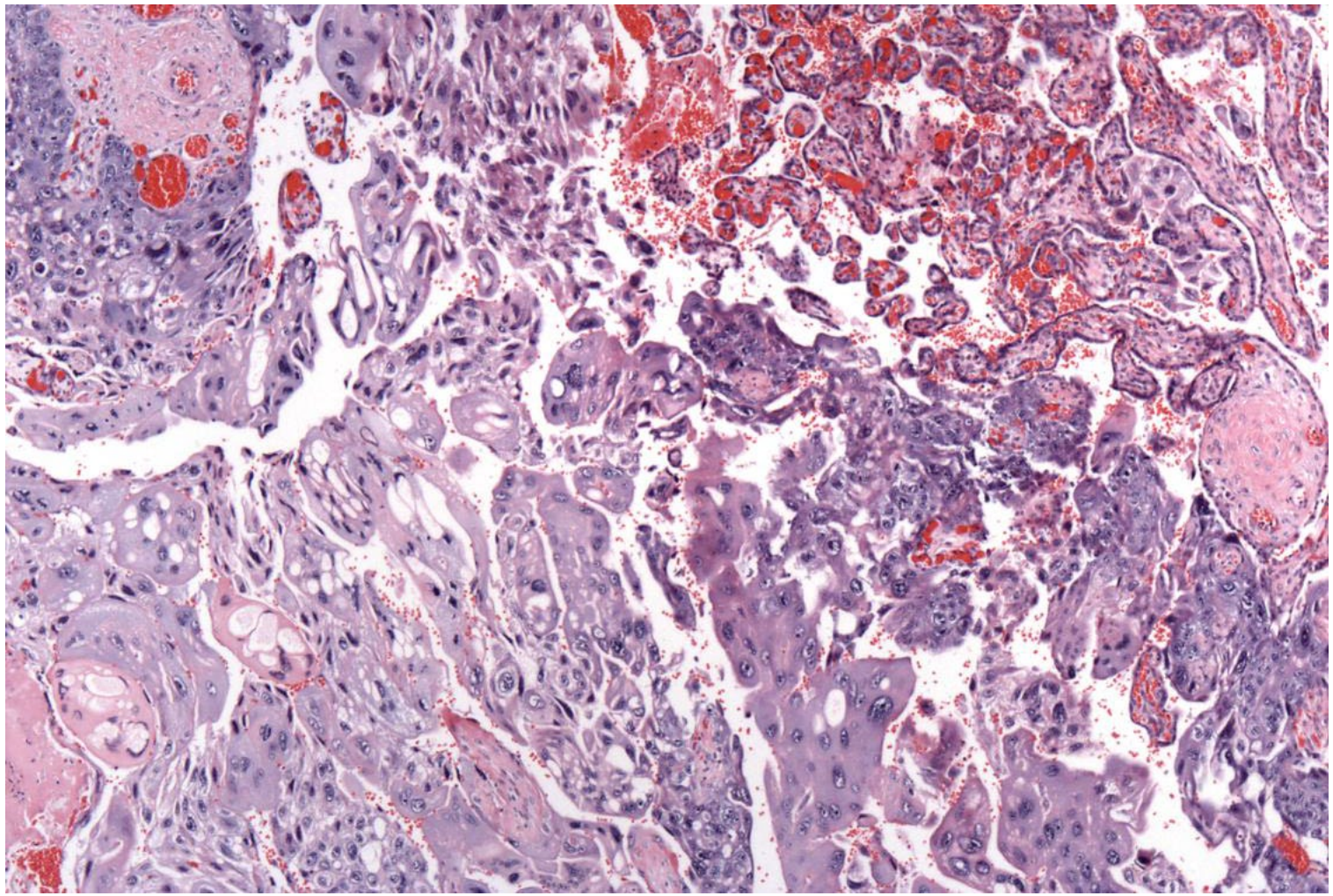




- **Gross features**
  - Hemorrhagic nodule(s)
  - Sampling of blood clot…particularly at the periphery
- **Histological features**
  - Biphasic (all cytokeratin +, GATA3)
    - Cytotrophoblasts and intermediate trophoblasts
    - Syncytiotrophoblasts (strong + for β-HCG, weak for HPL)
      - Caveat: may be infrequent in some tumors, possibly reduced following chemoTx
  - Hemorrhage and necrosis may predominate

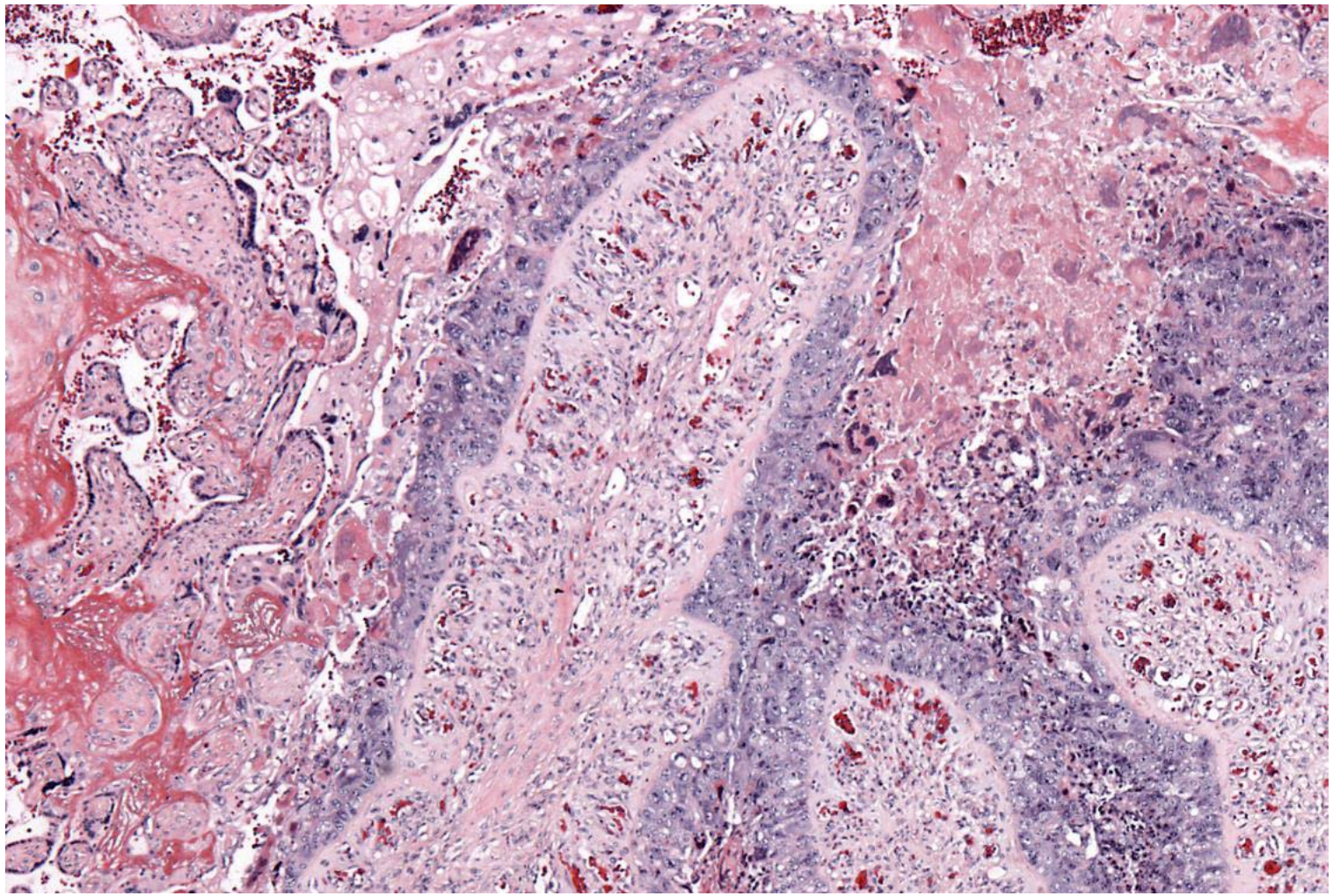


Choriocarcinoma with hemorrhagic necrosis



Choriocarcinoma During Pregnancy:

Intraplacental choriocarcinoma in term non-molar placenta



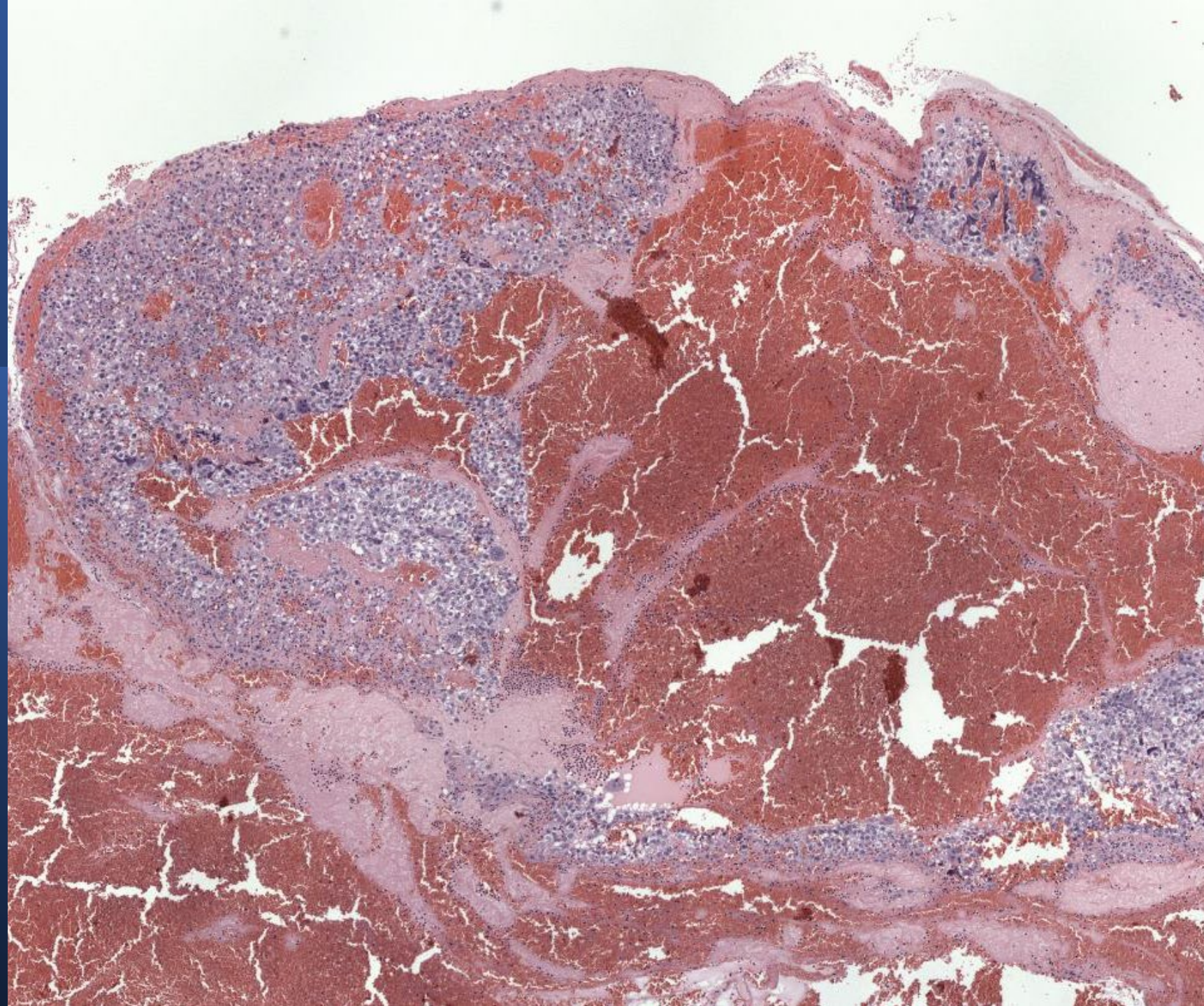
Intraplacental choriocarcinoma in term non-molar placenta

Choriocarcinoma

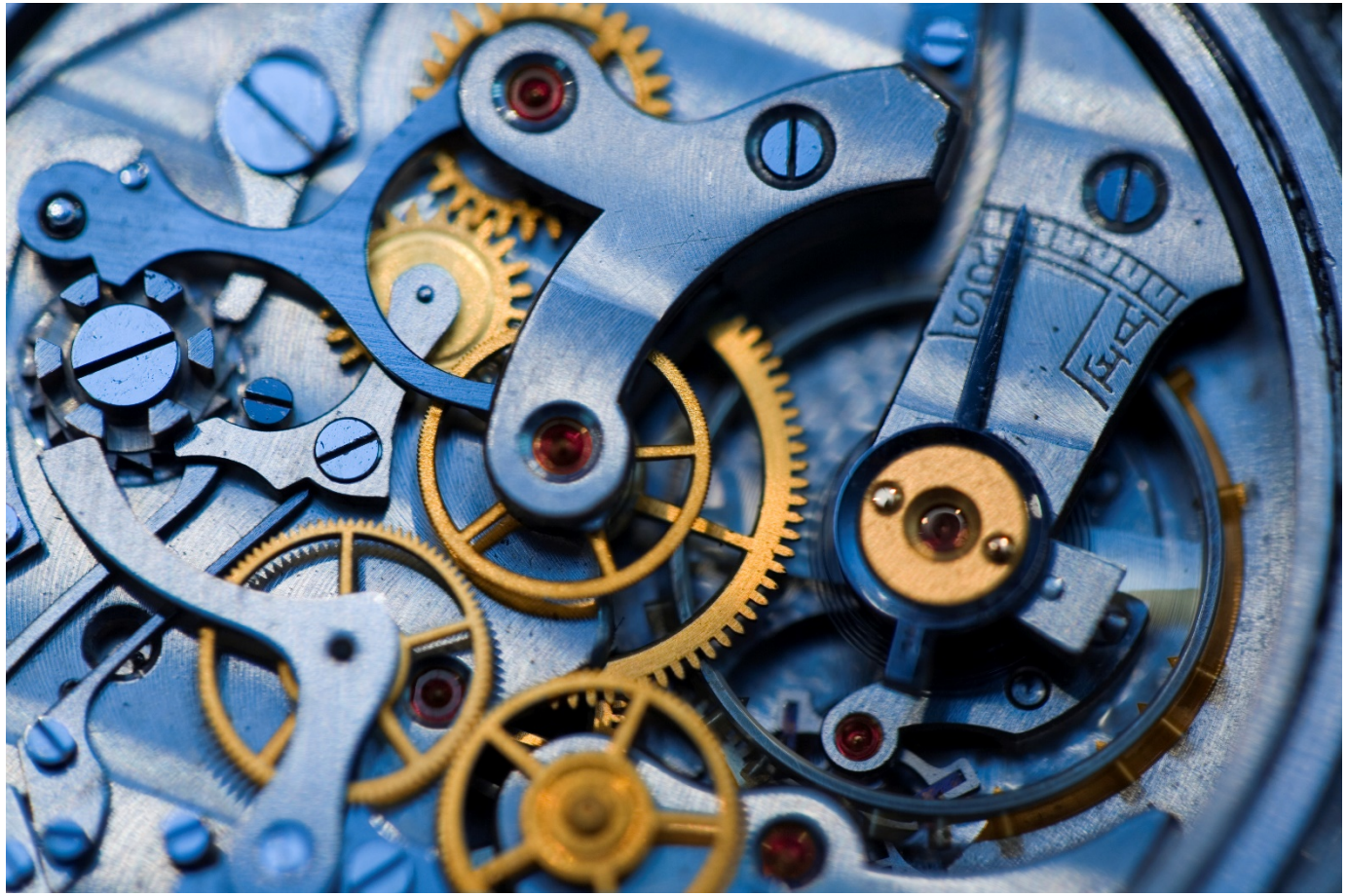
- **Differential Diagnosis:**
  - Previllous trophoblasts in early gestations
  - Persistent Trophoblastic Disease following Complete Mole
    - No villi due to sampling
    - Residual molar implantation site
    - Choice of terminology does not have clinical impact
  - Placental Site Trophoblast Tumor (PSTT) or Epithelioid Trophoblast Tumor (ETT)
    - “Syncytiotrophoblast-poor” choriocarcinoma

Mimic of Choriocarcinoma:

Early gestion with trophoblast shell in hematosalpinx/ectopic pregnancy

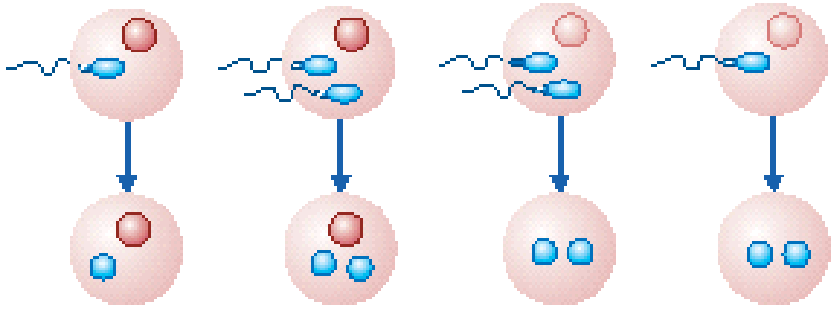


Complete Hydatidiform Moles (CHM)



Classic Complete Hydatidiform Mole – Genetics

- Diploid with diandry (2p)
  - p57 is absent because it is expressed only from the maternal genome…in cytotrophoblasts and stromal cells



Ploidy	2n	3n	2n	1n>2n (duplication)
Parents	Biparental	Biparental	Paternal	Paternal
Chorio Ca risk	Low	Low	Elevated	Elevated

20%
46,XX or XY
Genome-wide hetero-zygosity

80%
46,XX
Genome-wide LOH

Biparental Complete Hydatidiform Mole

- CHM variant that are ***diploid but biparental (1M:1P)***
- Recurrent
- Autosomal Recessive
- Maternal effect -- failure to establish maternal imprint
- Specific trans-acting genes*:*
  - *NALP7/NLRP7* (MIM 609661)
    - 19q13.42
    - Negative regulator of interleukin-1-β, which may in turn regulate inflammatory proteases needed for blastocyst implantation
  - *C6orf221* (MIM 611687)
    - 6q13
    - aka Embryonic Stem Cell-associated Transcript 1; ECAT1
    - Member of eutherian oocyte- and embryo-expressed KHDC1/DPPA5/ECAT1/OOEP gene family at 6q13
    - Oocyte specific expression

Complete Hydatidiform Mole

- As the gestational age increases, the molar villi uniformly grow to macroscopic size, forming grape-like cysts. This entity is so named because of the “water drop” cysts (Greek - “hydatisia”) cluster together forming a false conception (Latin “mole”).

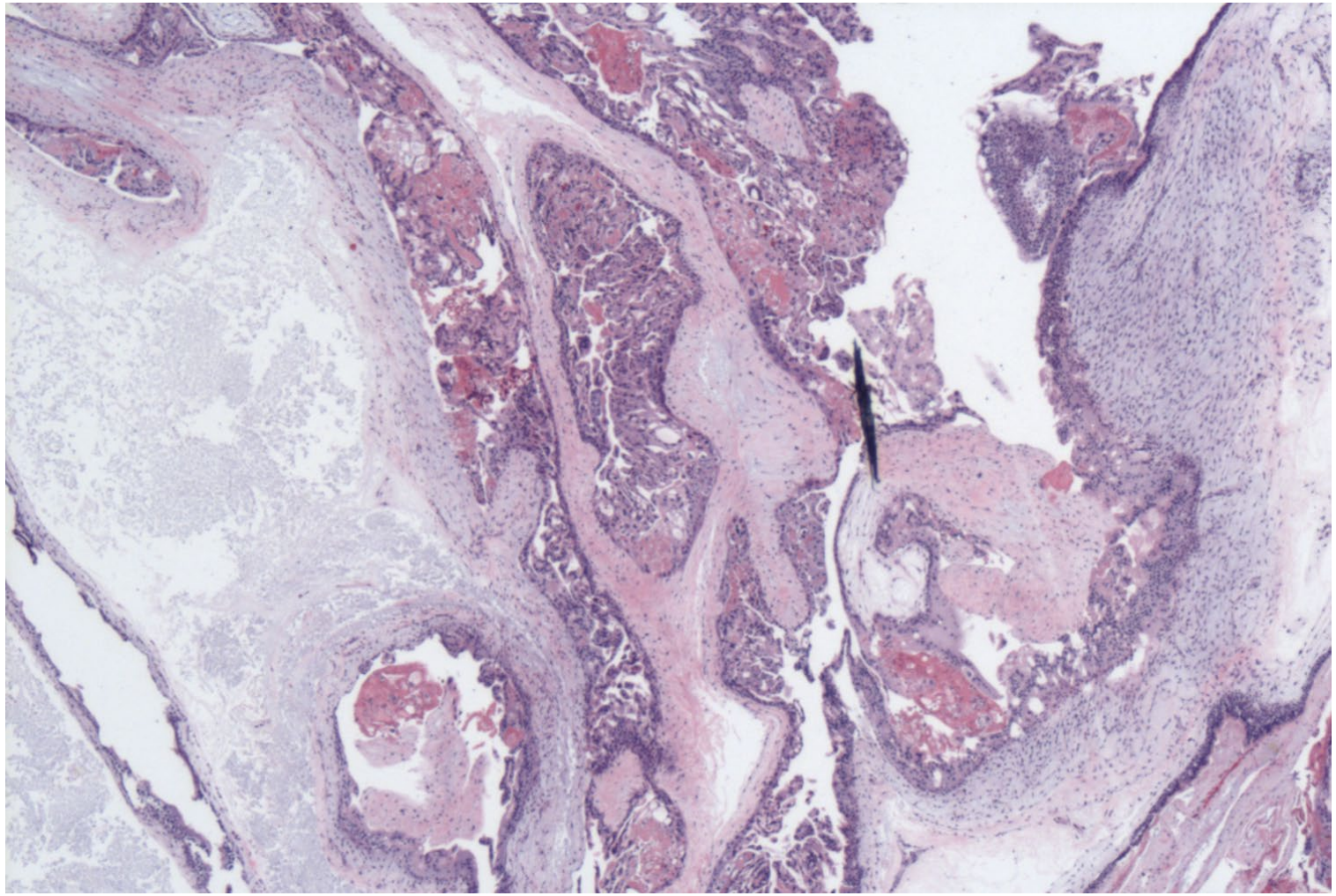
- Embryonic development does not occur.

Photos courtesy of Dr. E. Mason

Complete Hydatidiform Mole

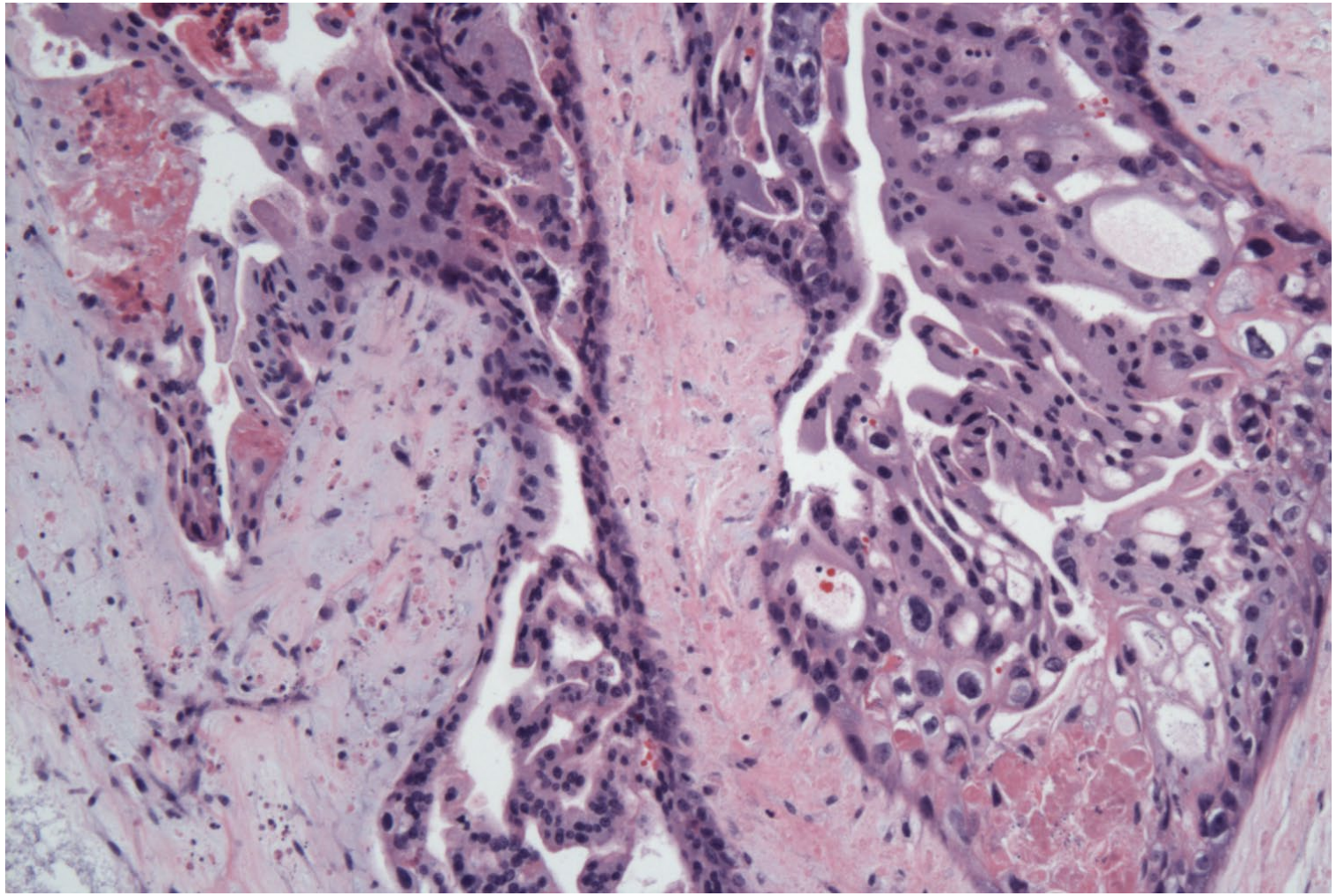
Histological Features

- Complete mole ≈ Choriocarcinoma plus villi
- Trophoblast atypia (usually)…yes, even more than usual
- Circumferential trophoblast hyperplasia
- Molar (atypical) implantation site
- Histological features evolve with time
  - Blue myxoid stroma, similar to early normal gestatations
  - Villi have narrow cleft-like invaginations to the stroma
  - Progressive stromal cell death degeneration
  - Vessels without blood may be present very early
  - Then cavitation of villous stroma



Complete Hydatidiform Mole

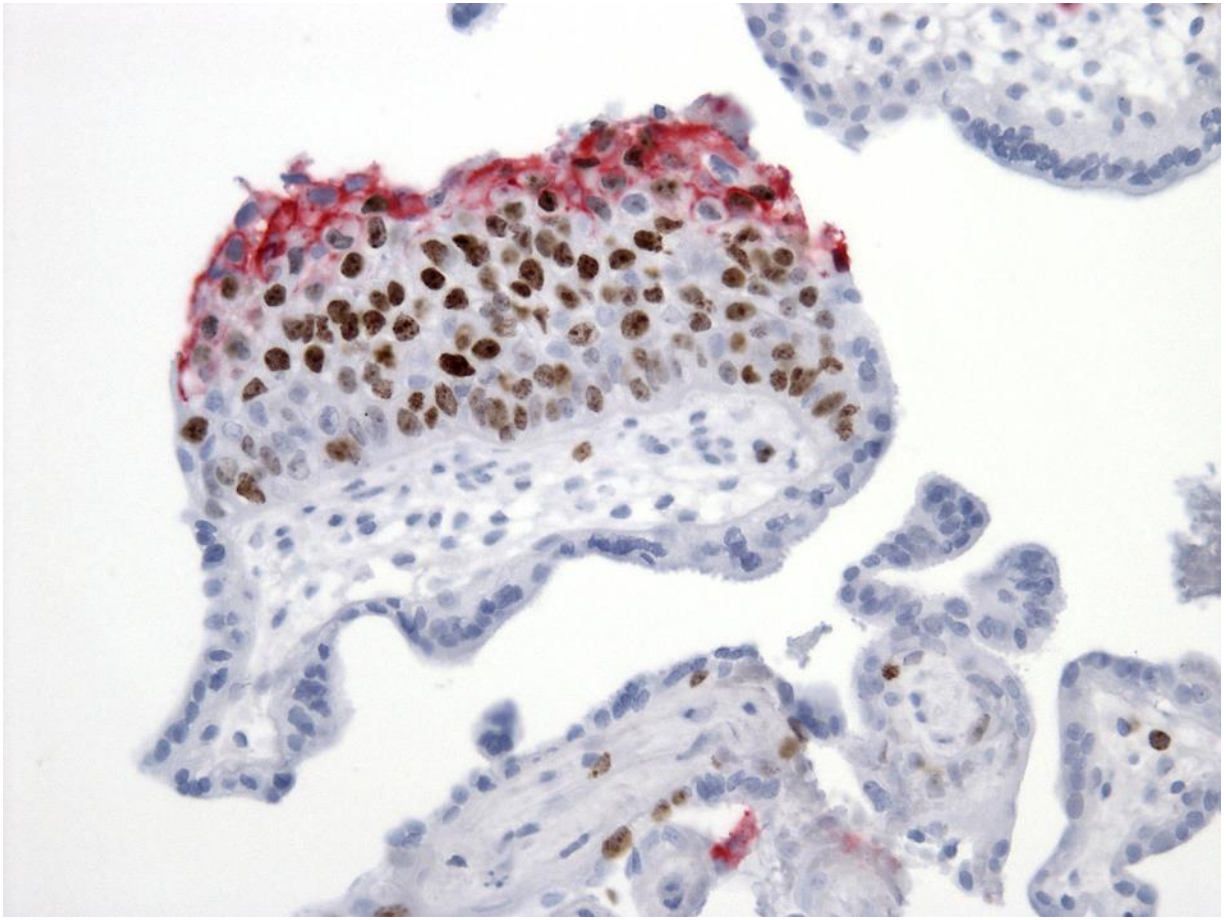
- **Cavitation**
- **Absence of fetal vessels**



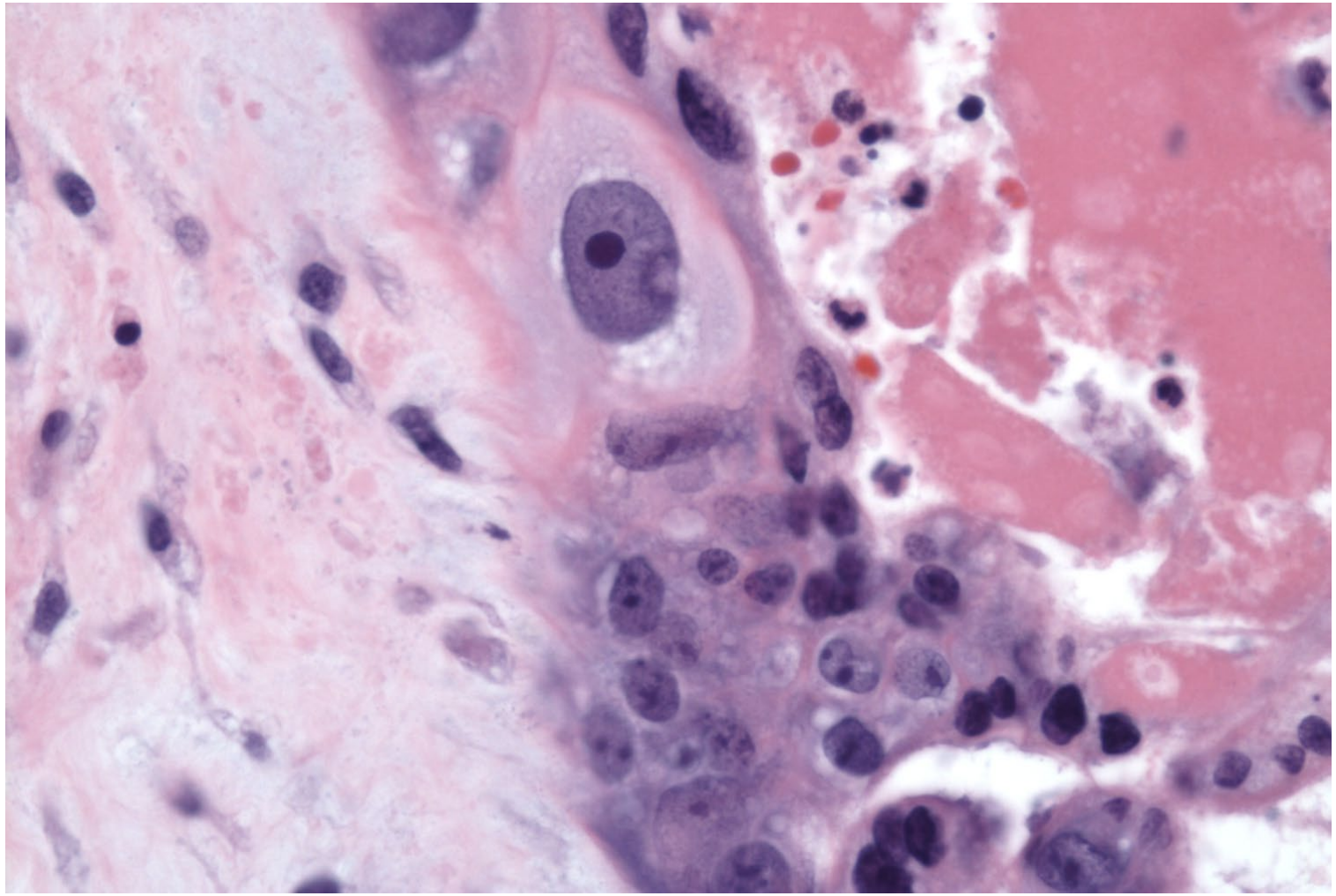
Complete Hydatidiform Mole

- **Trophoblast hyperplasia**
  - **Circumferential**
  - **Exuberant**

CHM are distinct from the normal progression from proliferation to differentiation

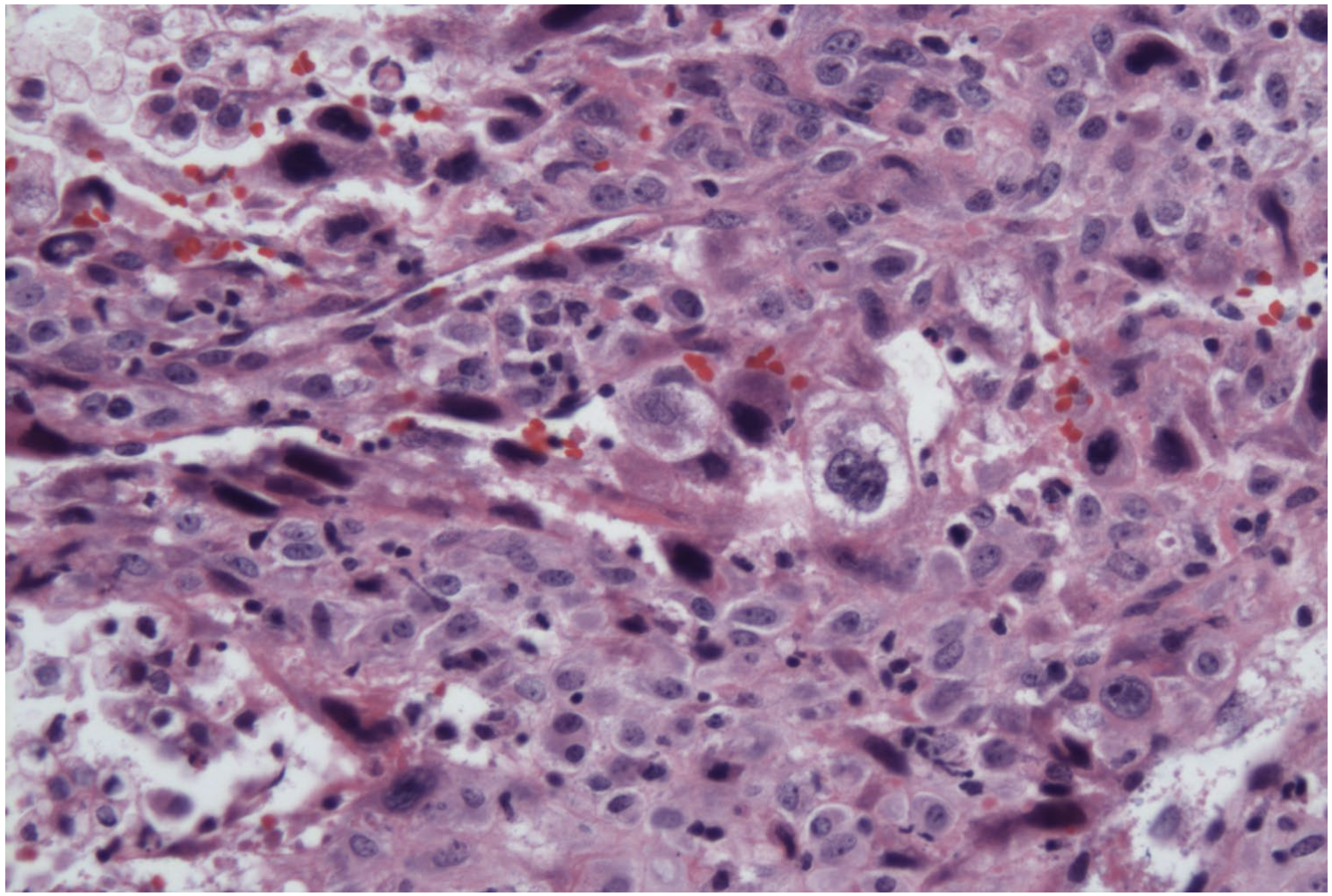


MelCAM | CD146
Ki-67 | MIB1



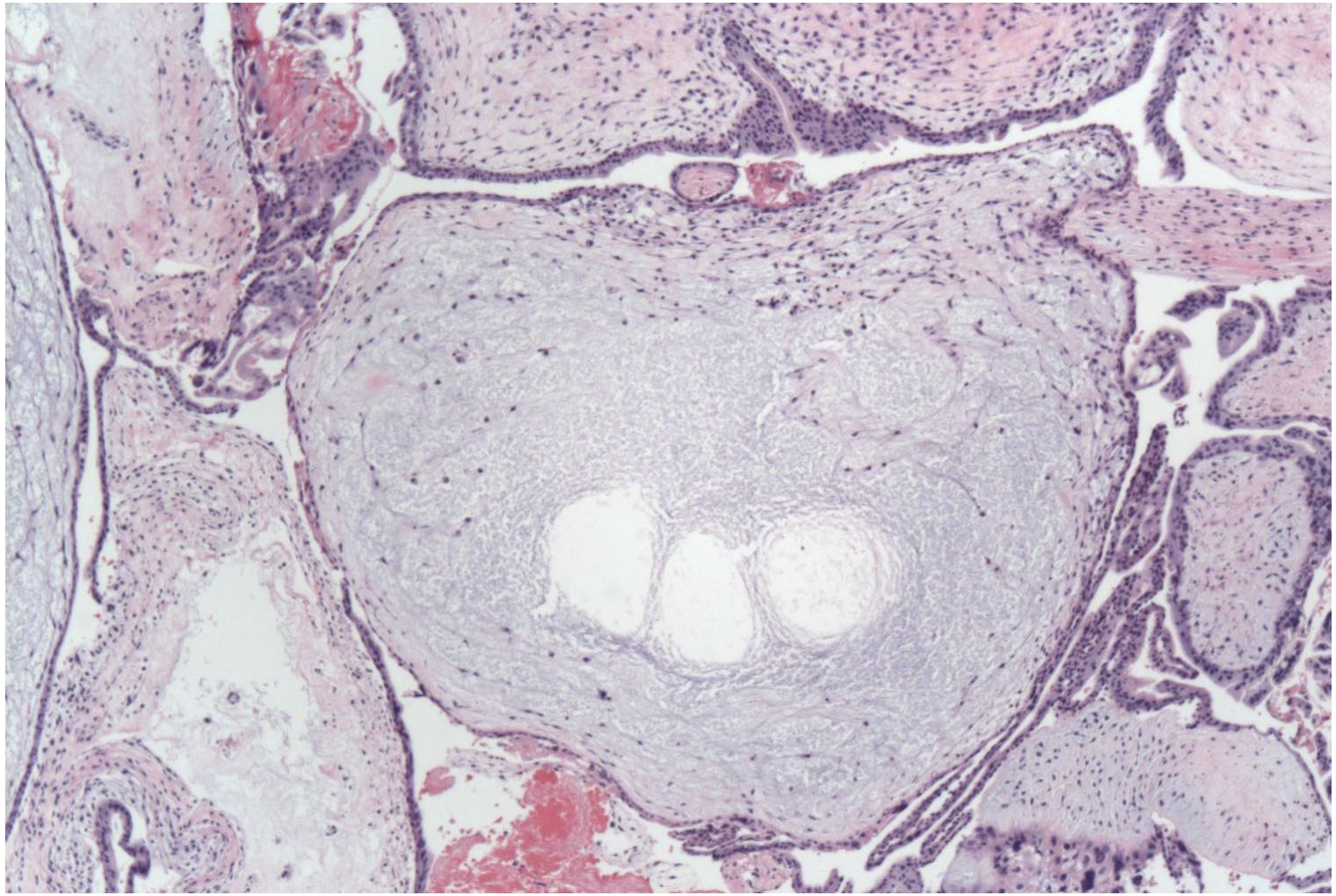
Complete Hydatidiform Mole

- **Trophoblast atypia**
  - **May range from modest to severe**



Molar Implantation Site

- **Distinctive – easy to see; more atypical than usual**
- **May be your first clue**
- **Pitfall: mimics ChorioCa or PSTT**



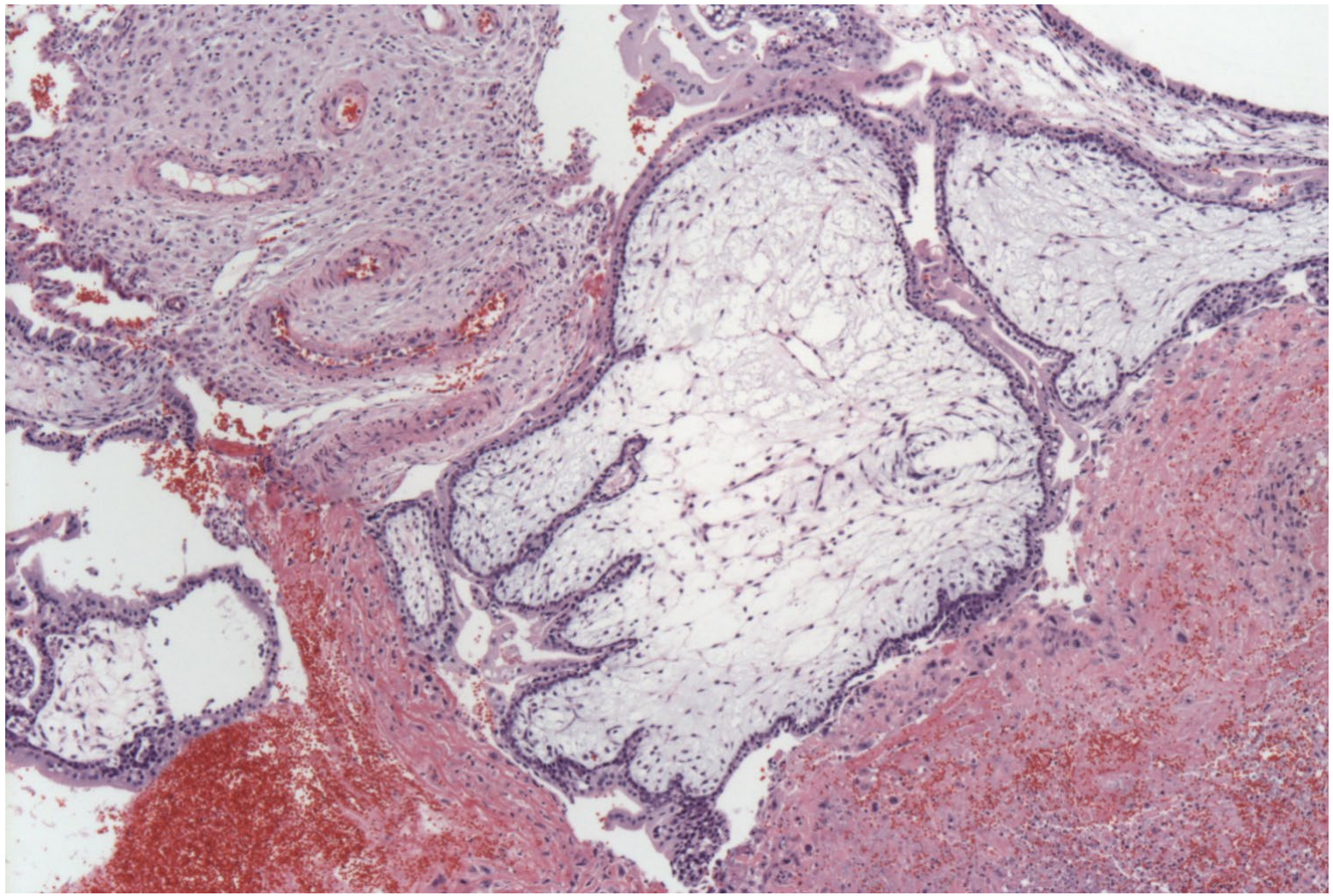
Complete Hydatidiform Mole

“Degenerating” CHM have less atypia and hyperplasia, may be confused with non-molar hydropic villi.



Early Complete Hydatidiform Mole

Keep et al. *Hum Pathol*, 1996

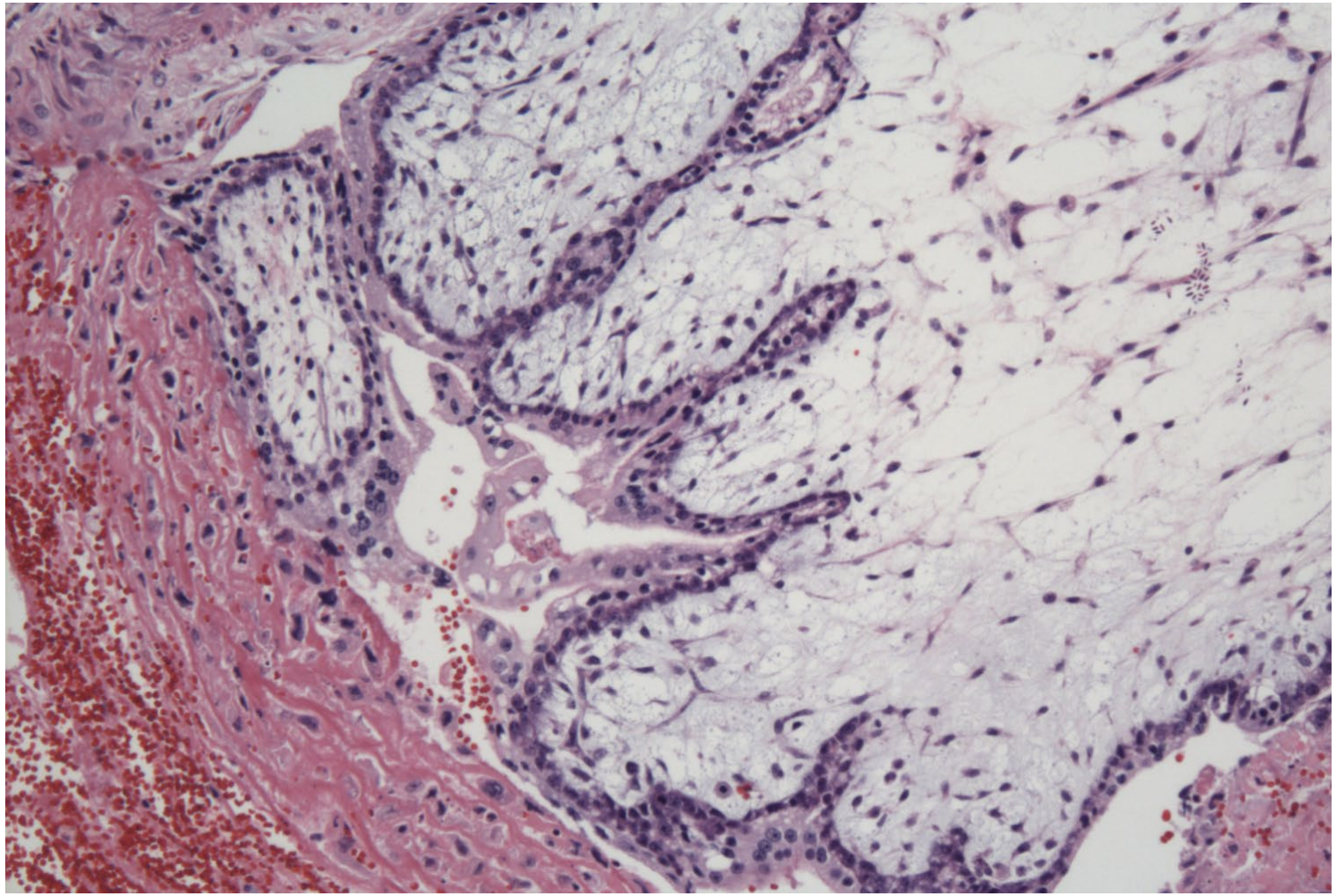


Early Complete Mole

Note:

Blue myxoid stroma

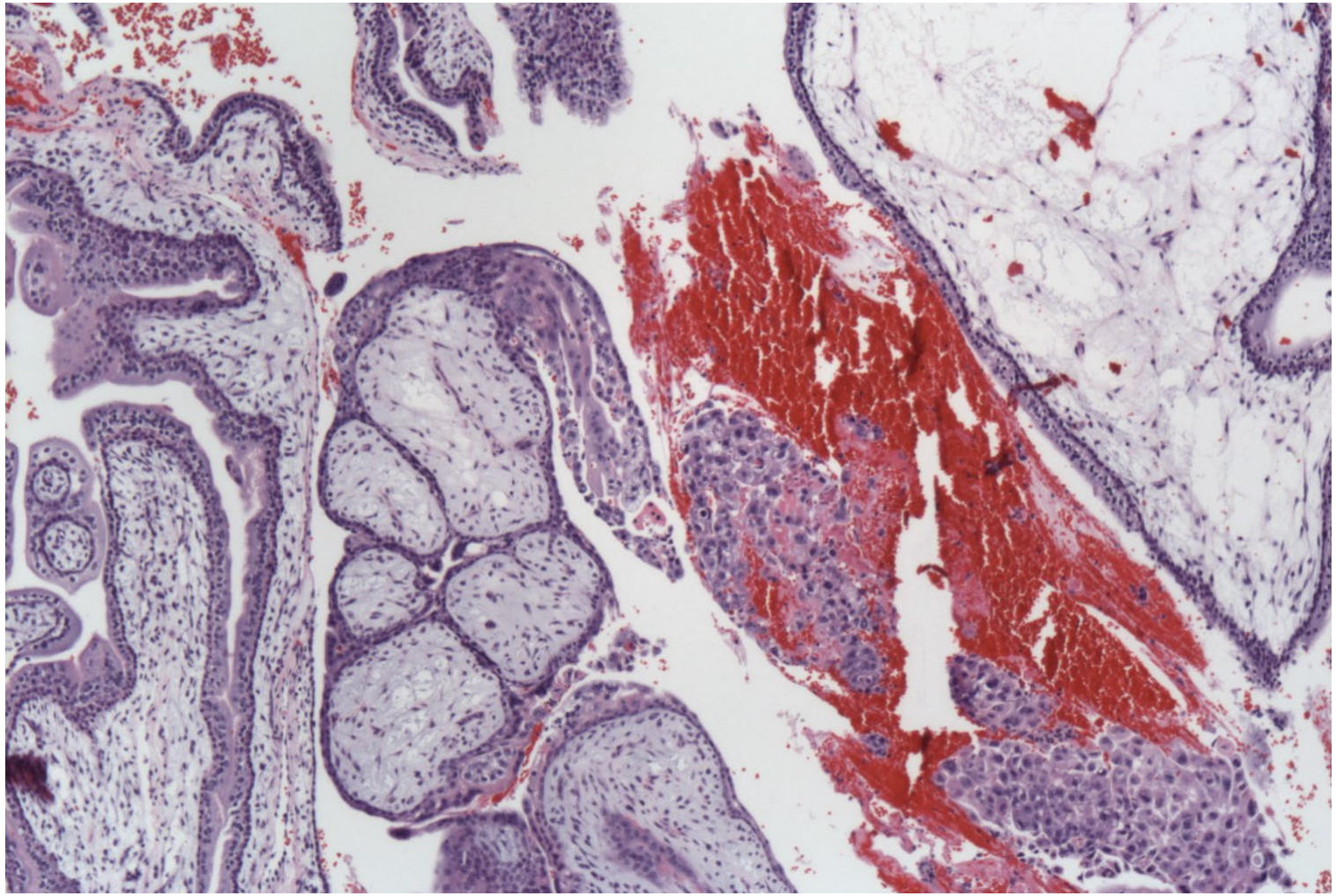
Pitfall: also found in very early gestations



Early Complete Mole

Note:

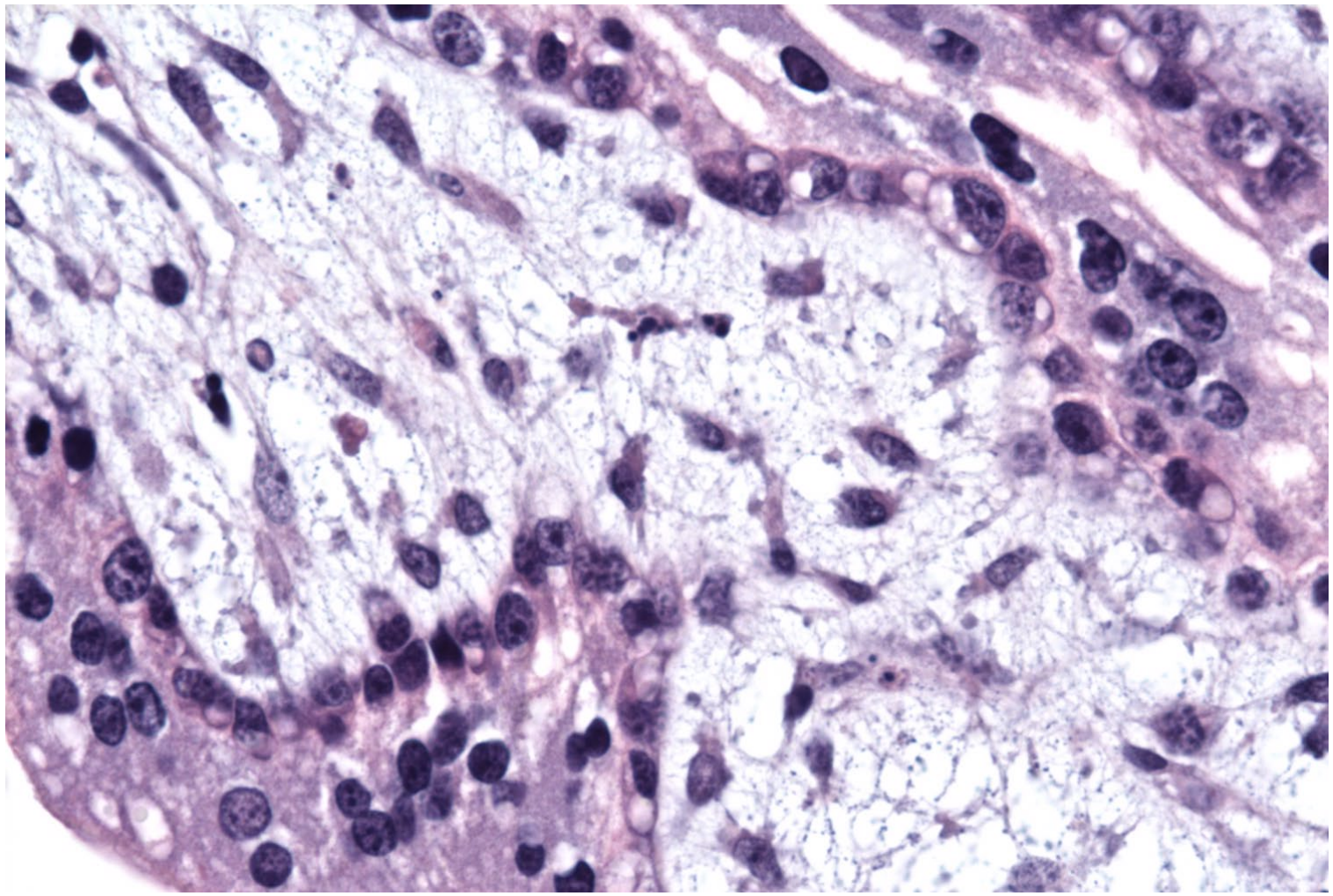
Deep cleft-like infolding of trophoblast layer



Early Complete Mole

Note:

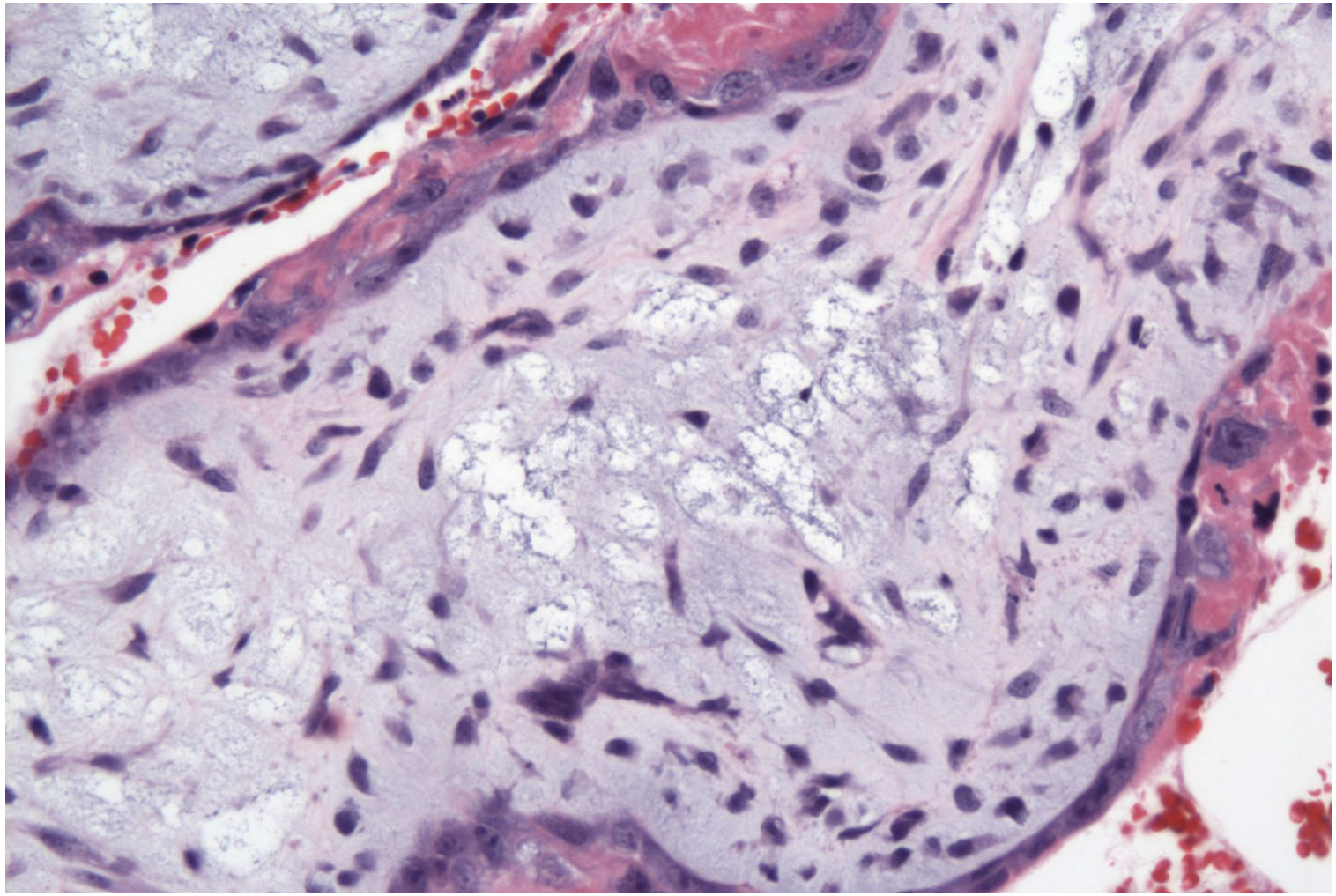
Features of both Early and Clasical CHM



Early Complete Mole

Note:

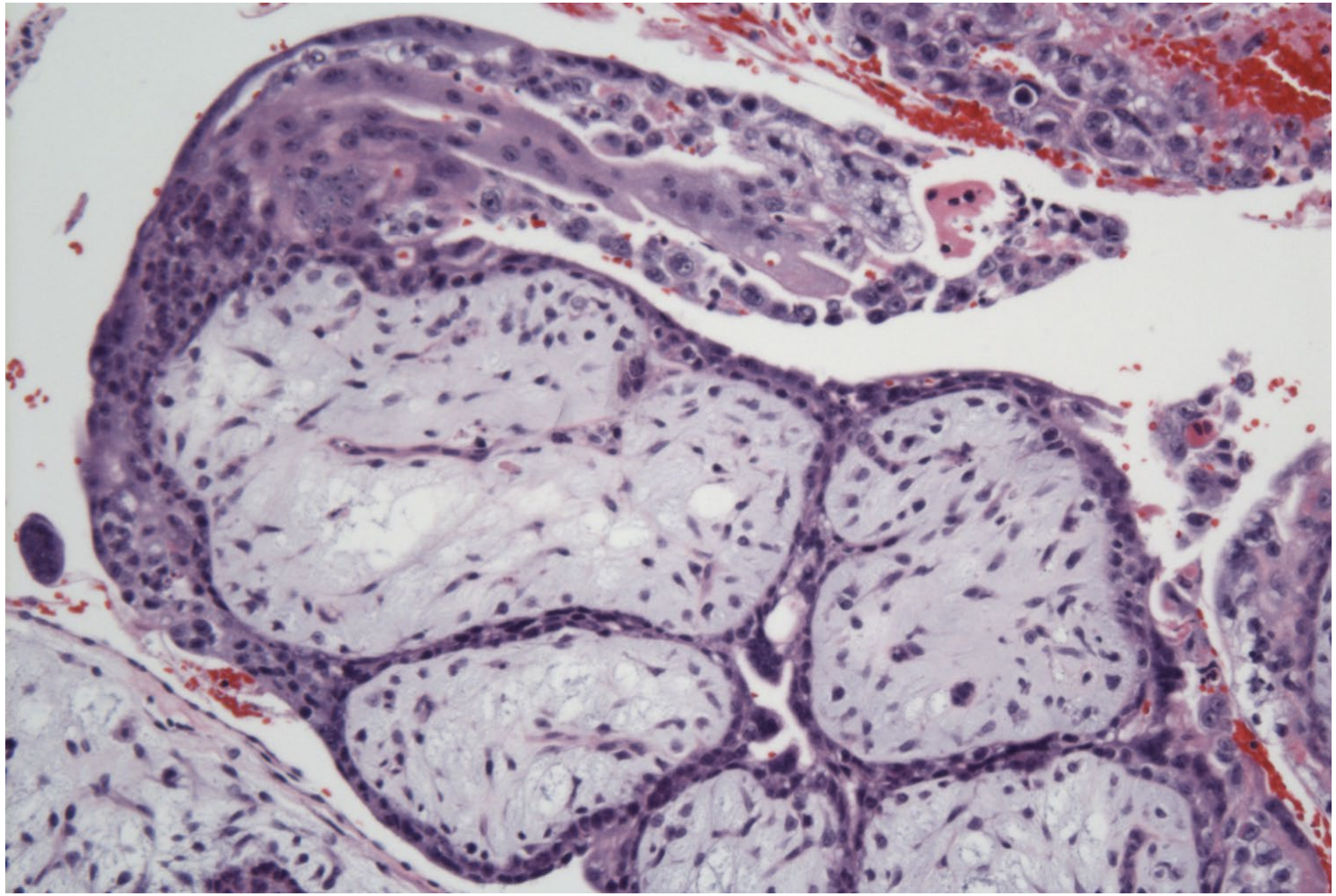
Stromal (and vascular) cell degeneration



Early Complete Mole

Note:

Early cavitation



Early Complete Mole

Note:

Early presentation more common intensively US screened populations

Complete Hydatidiform Mole

Differential Diagnosis

- Very Early Gestational Sac
- Early Abortus
- Hydropic Abortus
- Partial Mole
- Twin Gestation with Complete Mole as Co-Twin

Early Gestational Sac

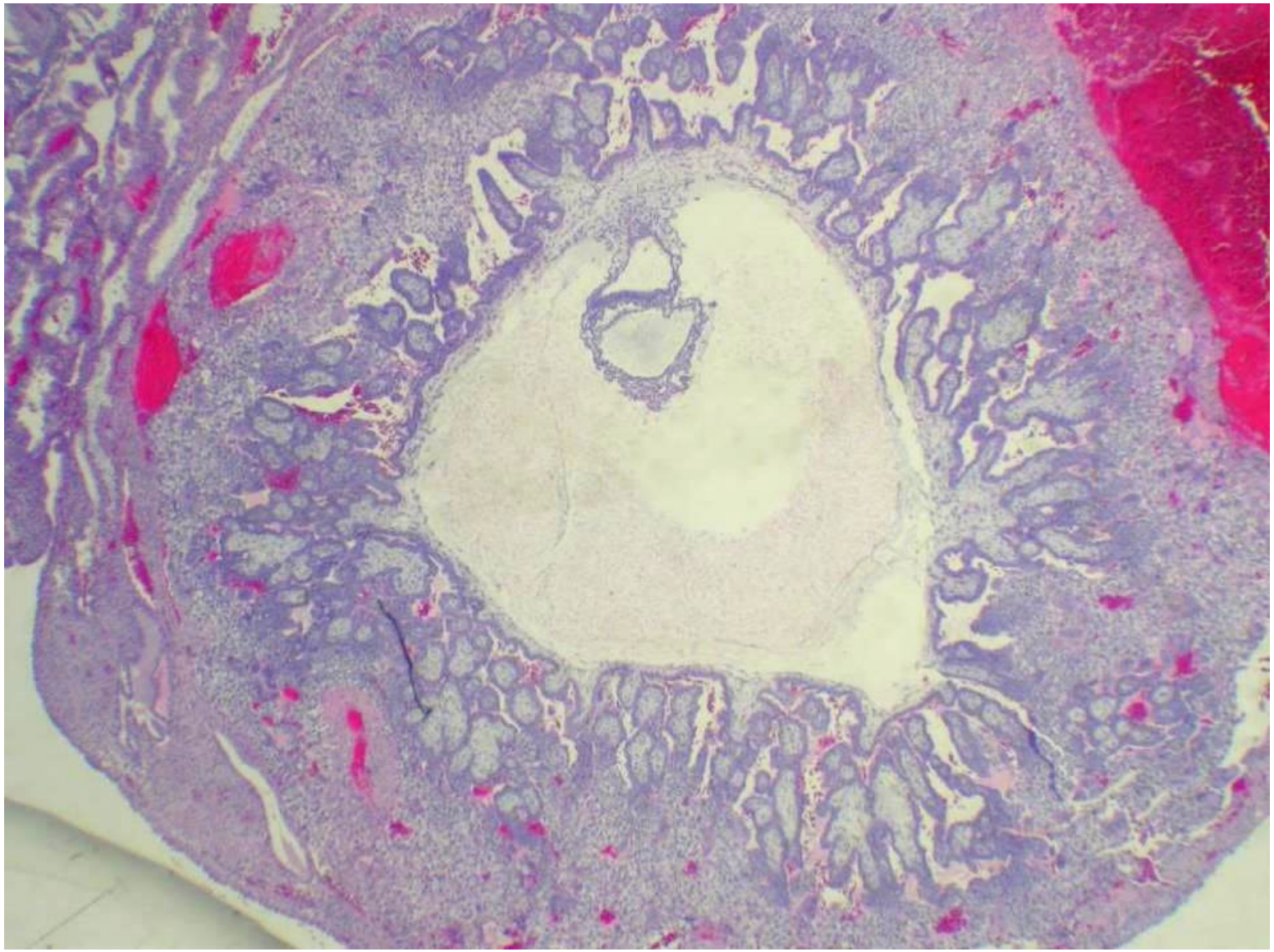
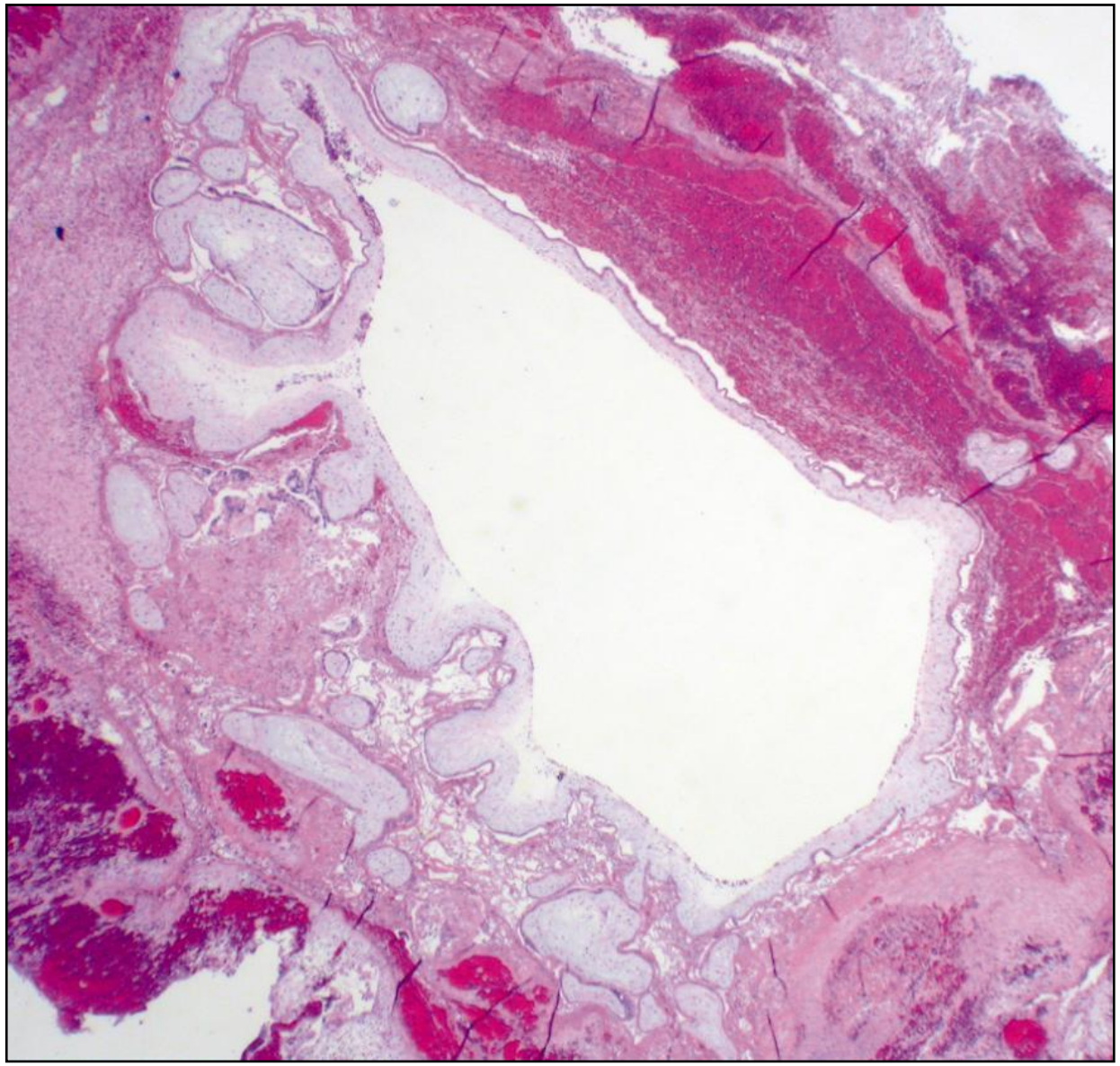


Image courtesy of Dr. T. Boyd

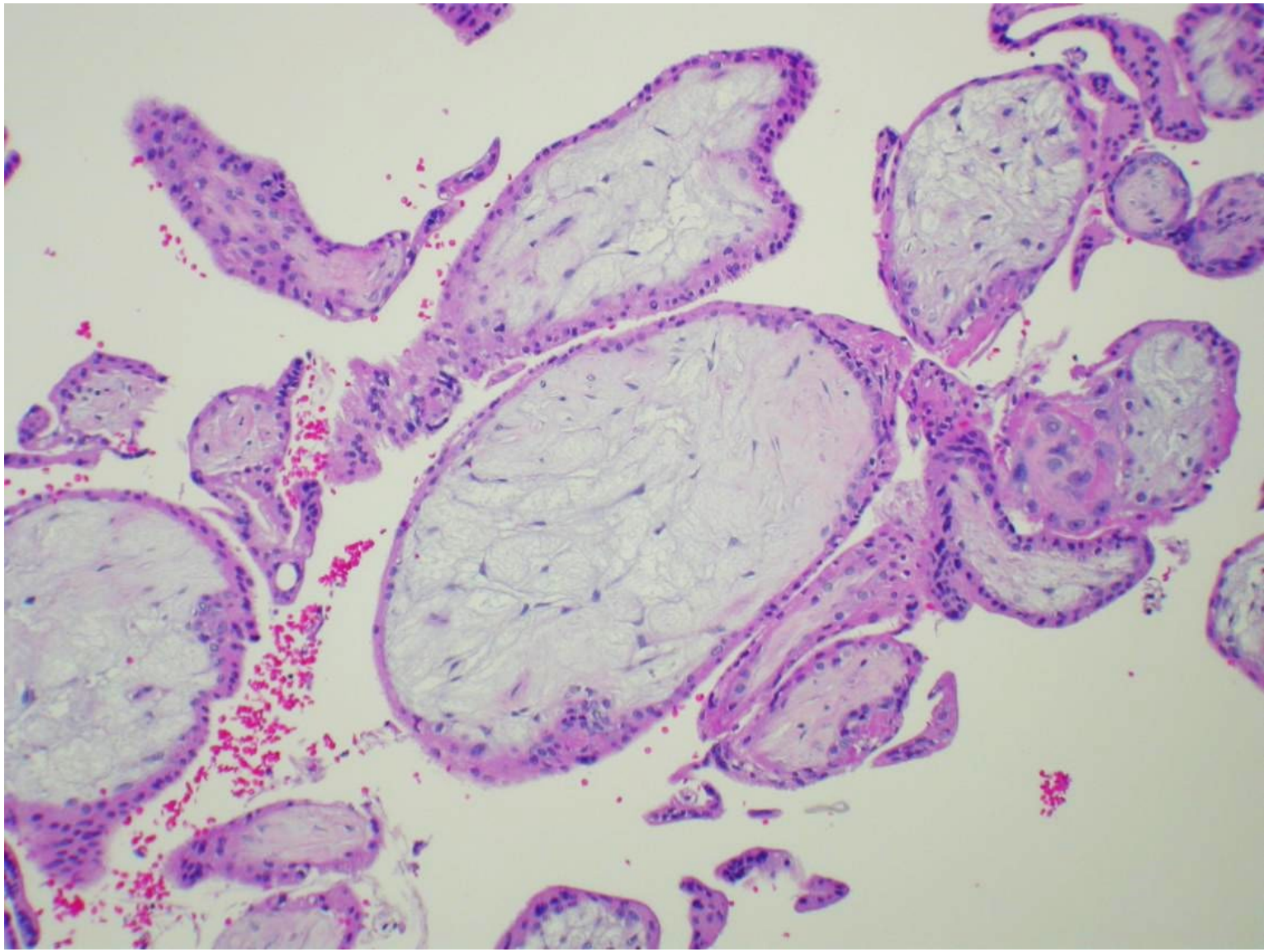
Early Gestational Sac



Clue – Never more than a single cavitated villi

Image courtesy of Dr. T. Boyd

Early Gestational Sac



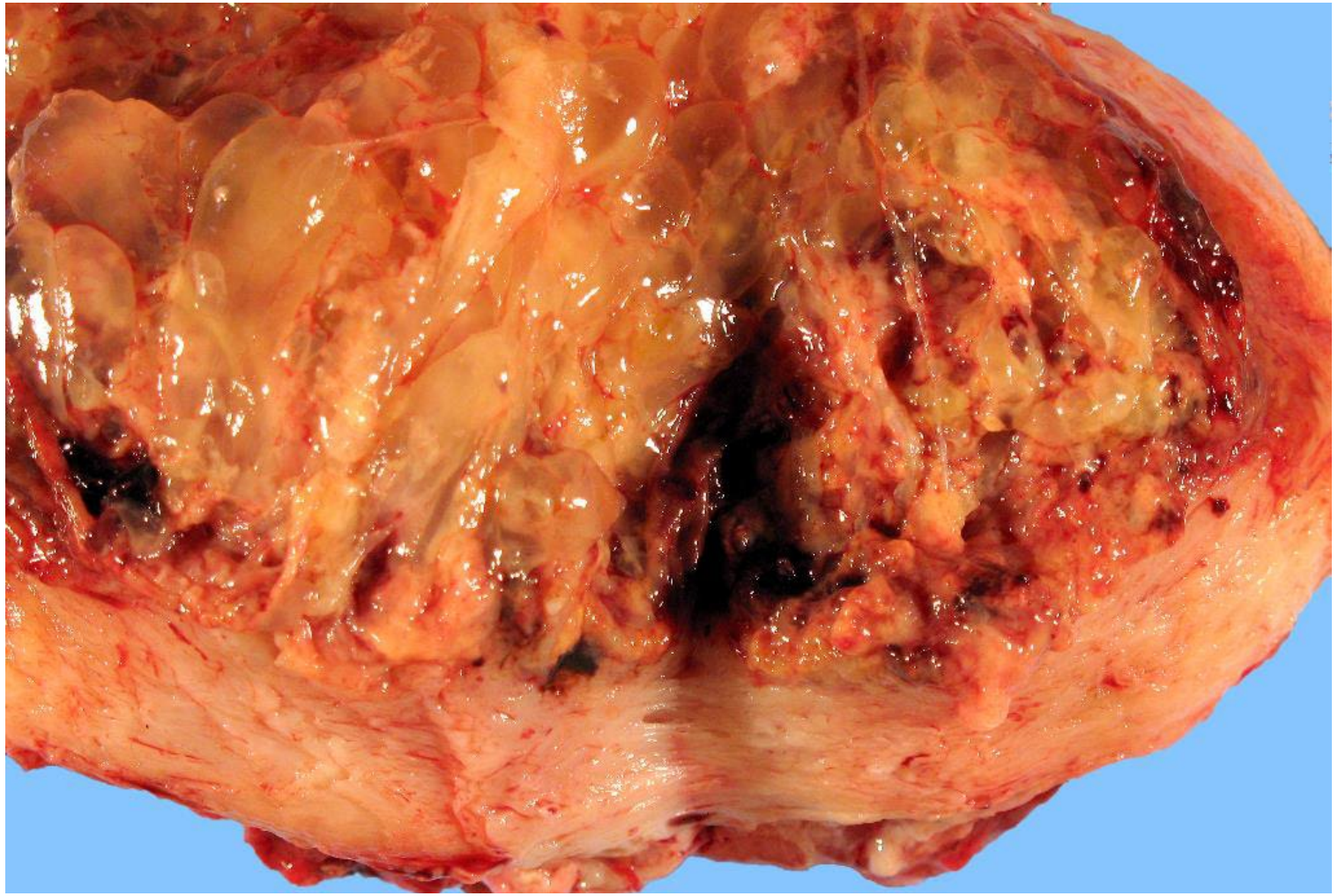
Clue – Symmetric swelling with attenuation (no hyperplasia), without cavitation

Image courtesy of Dr. T. Boyd

Invasive Complete Mole

“Chorioadenoma Destruens”

CHM
x
Placenta Increta

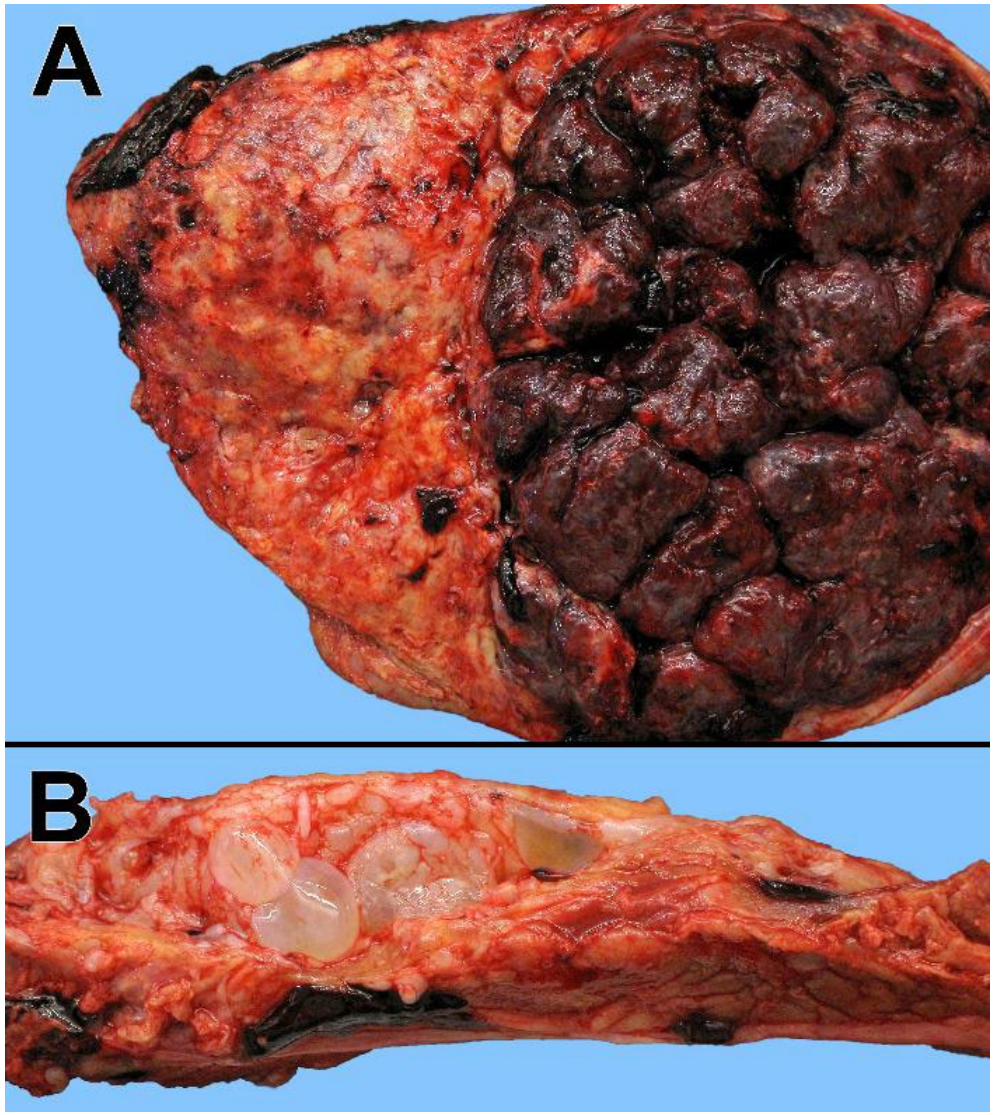


Things to keep in mind about Invasive Mole

- Not readily detectible by curettage
- More frequent in age > 40 yr and underdeveloped countries
- Hemorrhage may obscure villi grossly
- Vascular space invasion common
- Frequency of persistent or metastatic gestational trophoblastic disease (GTD):
  - CHM >> *Invasive Mole* > ChorioCA
- Villi may be scarce
- Pathobiologic mechanism unknown

Complete Hydatidiform Mole

in a Twin Gestation



Things to keep in mind about Molar Twins

- Rare
- CHM of interest, but PHM also possible as co-twin
- Pitfall – iatrogenic admixture of CHM co-twin by curettage mimics PHM
- Presence of normal co-twin often delays diagnosis
- Higher pre-evacuation β-hCG; clinical symptoms more likely
- Poses obstetrical management issues, but successful deliver possible

Ancillary tools for complete mole

- Genetics
  - Flow cytometry for DNA index (2n or 4n ploidy)
  - Karyotype (46,XX or 46,XY)
  - Microarray
    - SNP analysis may detect genome-wide LOH (uniparental) if derived from single sperm
  - Microsatellite polymorphisms
    - Diandry if parental DNAs collected
- Immunohistochemistry
  - Leverage underlying pathobiology of aberrant imprinting

cyclin-dependent kinase inhibitor 1C (p57, Kip2) (CDKN1C)

- Imprinted, with preferential expression of the maternal allele
- Strong inhibitor of several G1 cyclin/Cdk complexes and a negative regulator of cell proliferation
- Tumor suppressor candidate and plays a role in Beckwith-Wiedemann syndrome
- Part of an imprinted gene region on 11p15.5 with IGF2 and H19

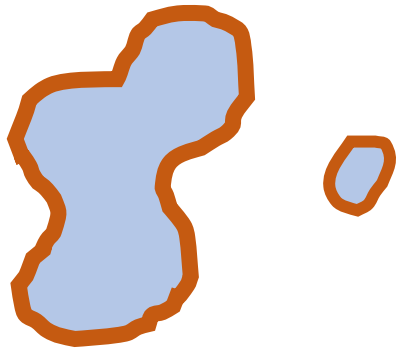
Castrillion et al. *Am J Surg Pathol*, 2001

p57 IHC

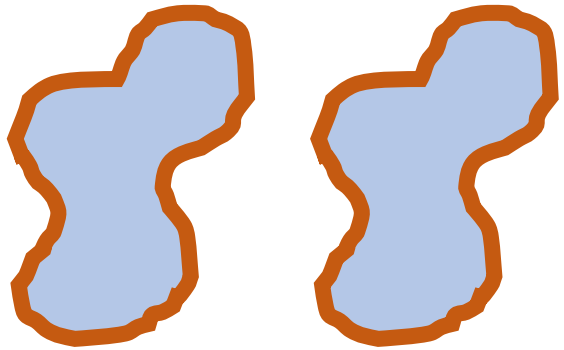
Relaxation Of Imprinting
In
Extra-Villous Trophoblasts

No nuclear staining in villous cytotrophoblasts and villous stromal cells

Murphy's Law for Reproduction – Watch out for unusual p57 staining patterns!!



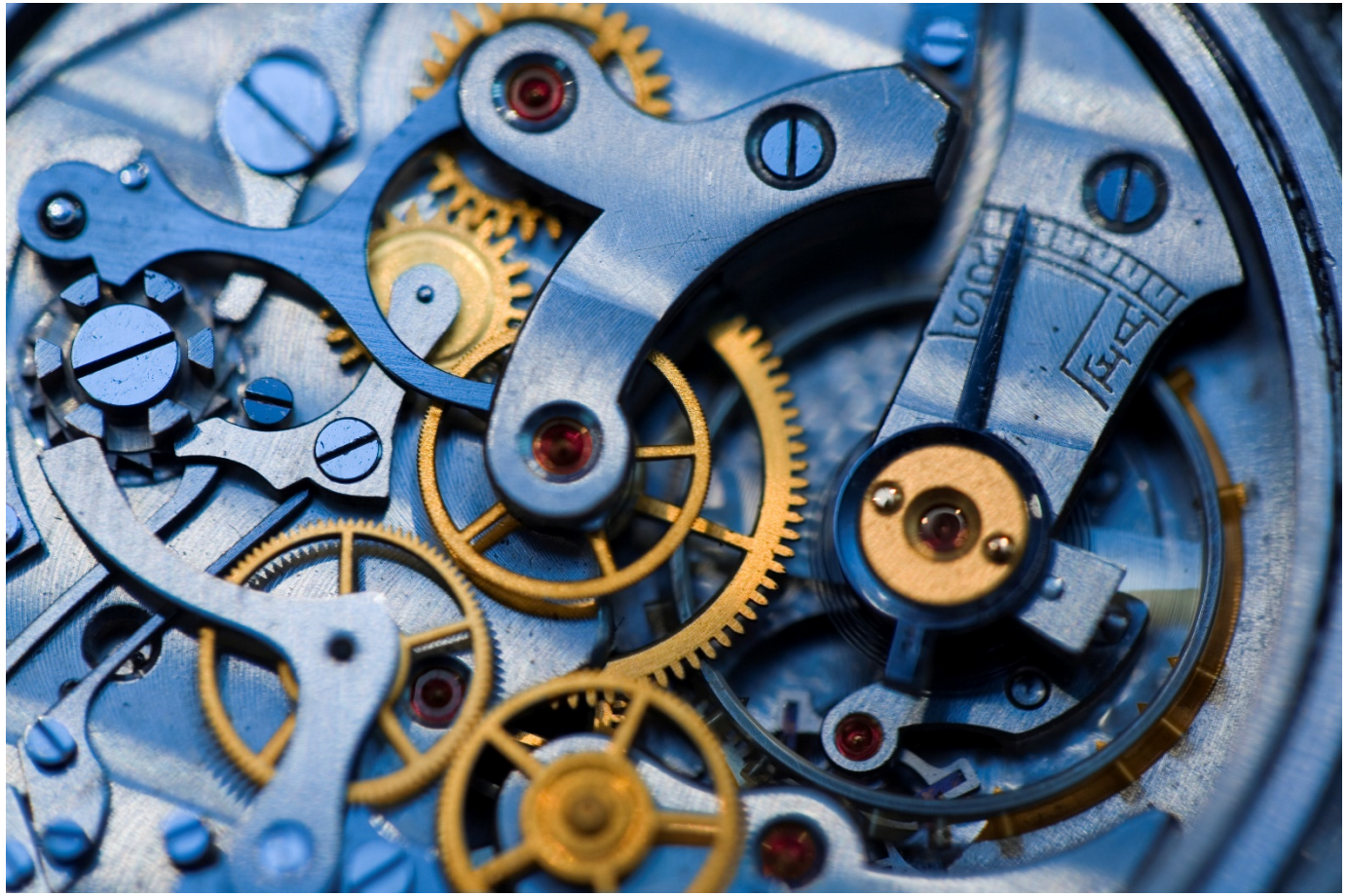
Twin with CHM Co-Twin

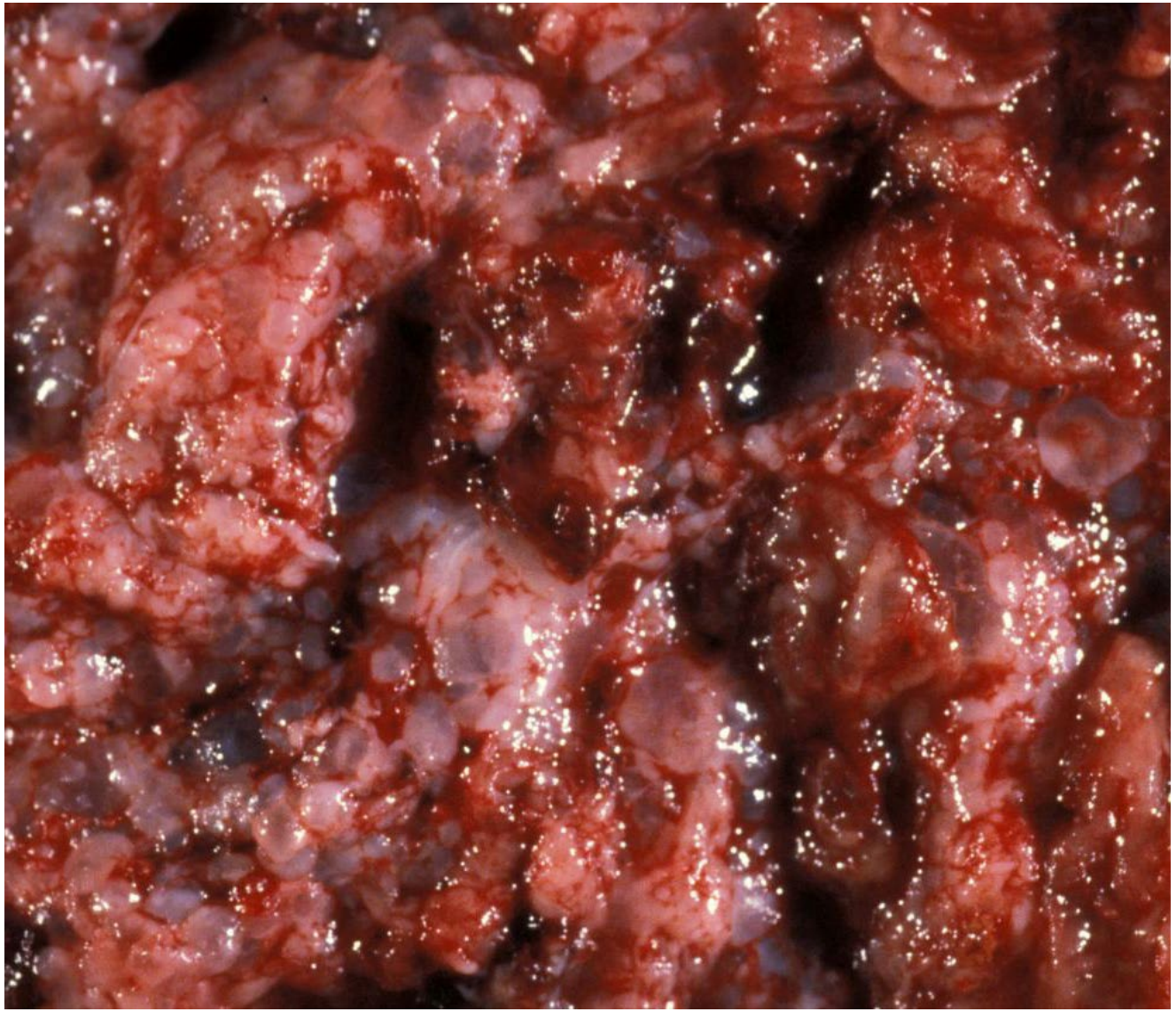


Chimeric/Mosaic Gestation

- Some behave like CHM
- Also seen in PHM mimics
  - Placental Mesenchymal Dysplasia
  - Beckwith–Wiedemann syndrome

Partial Hydatidiform Moles

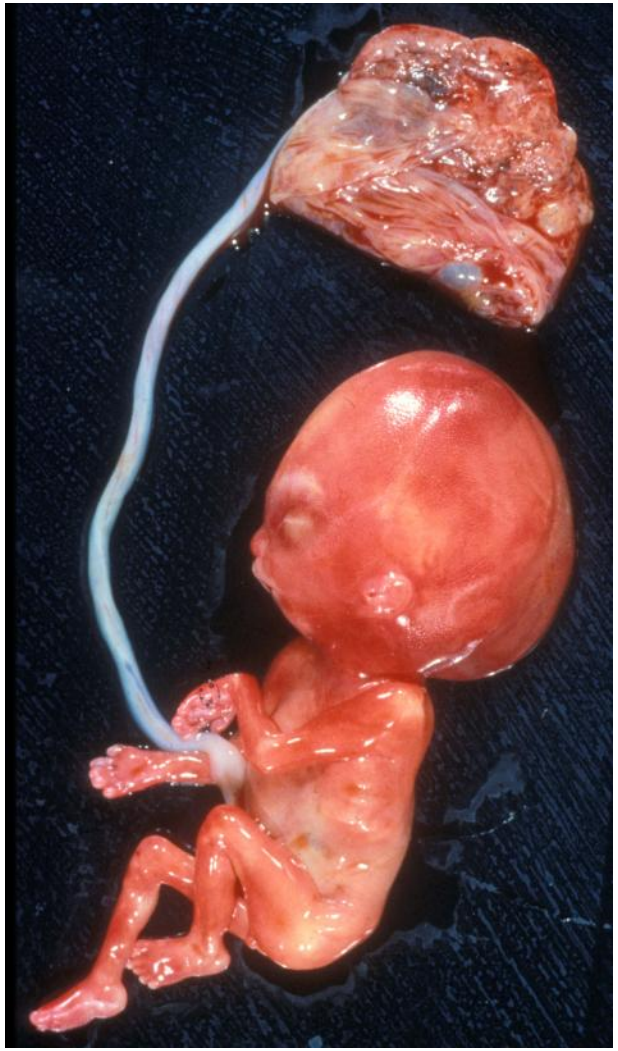


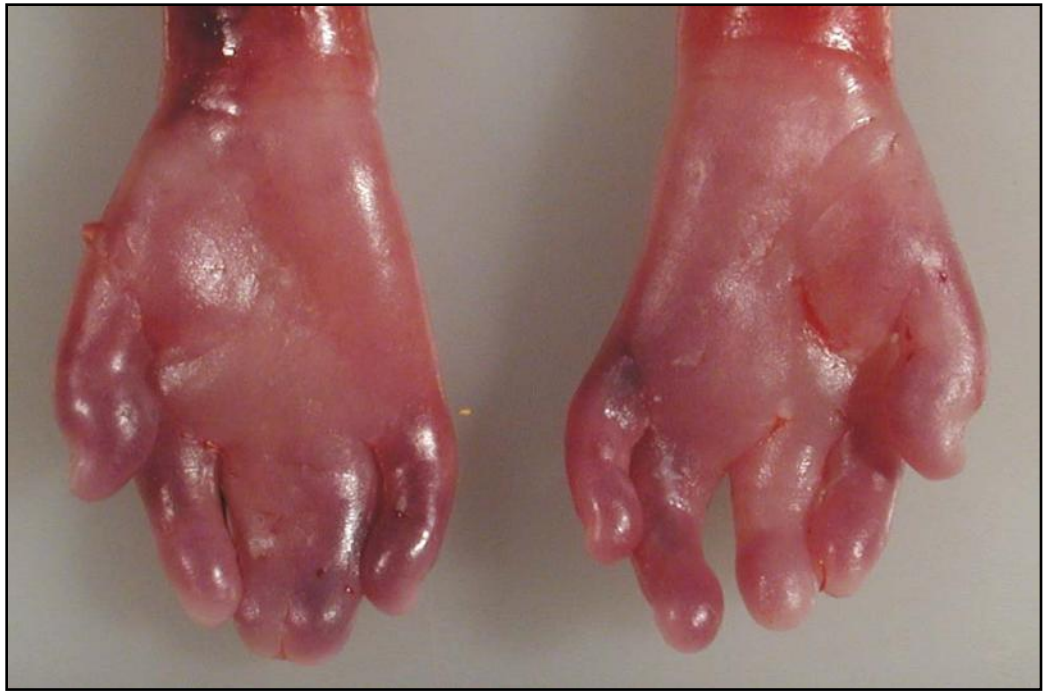


Partial Hydatidiform Mole

- Image courtesy of Dr. T. Boyd

Partial Hydatidiform Mole – Maldeveloped fetuses with 3-4 syndactyly



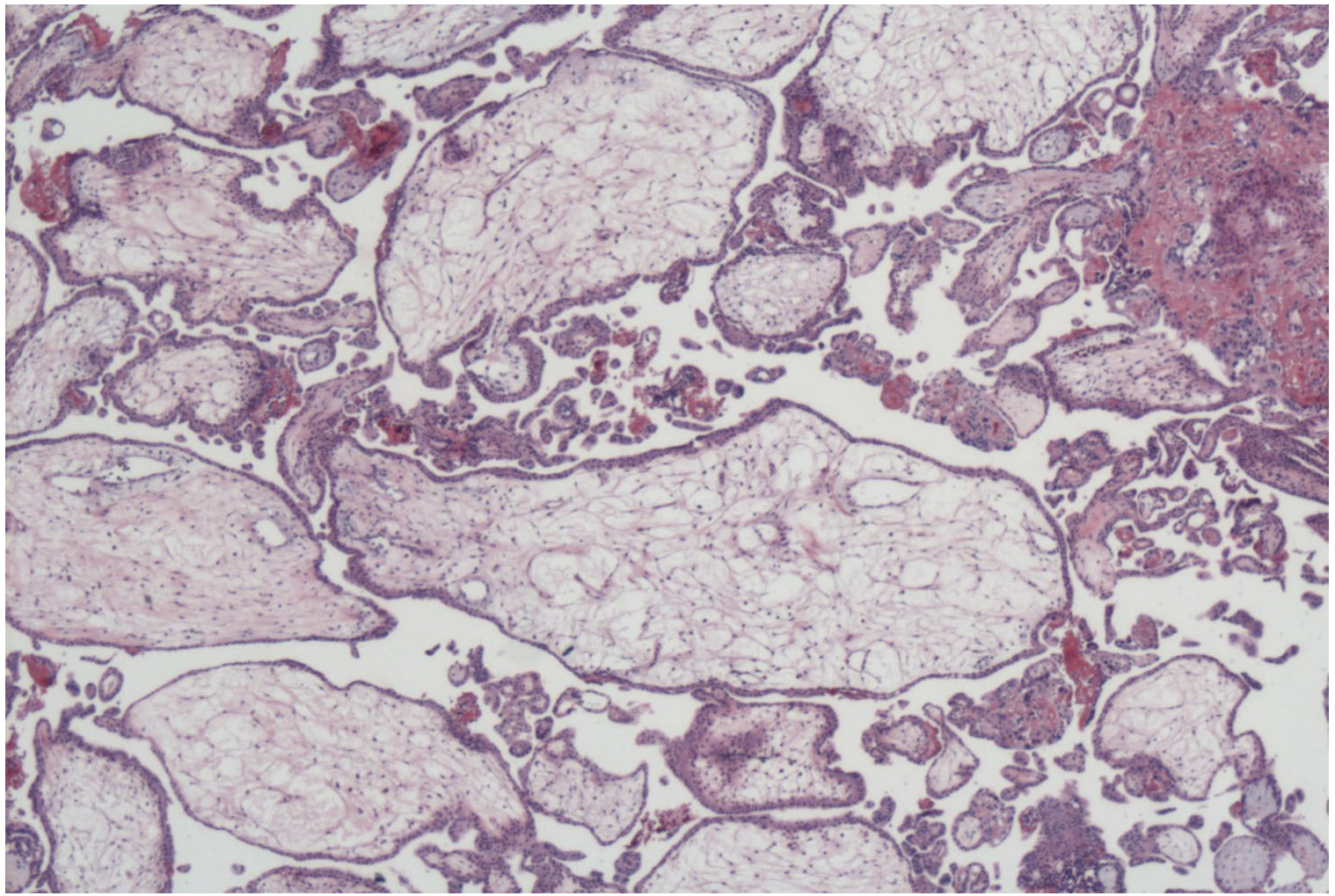


Images courtesy of Dr. T. Boyd

Partial Hydatidiform Mole

Intermixed Biphasic Population of Villi by Size

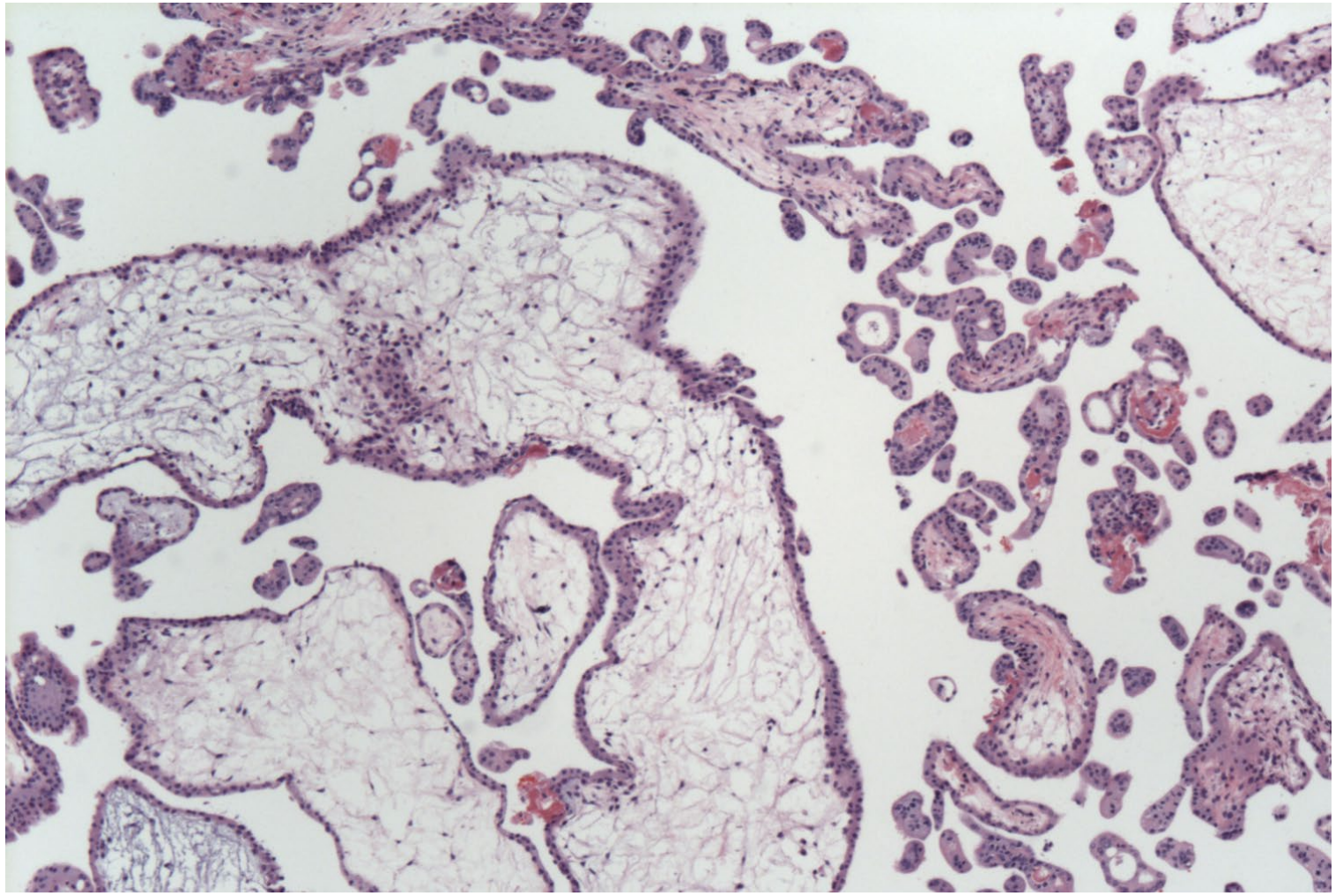
proposed stringent threshold for villous enlargement:
≥2.5 mm

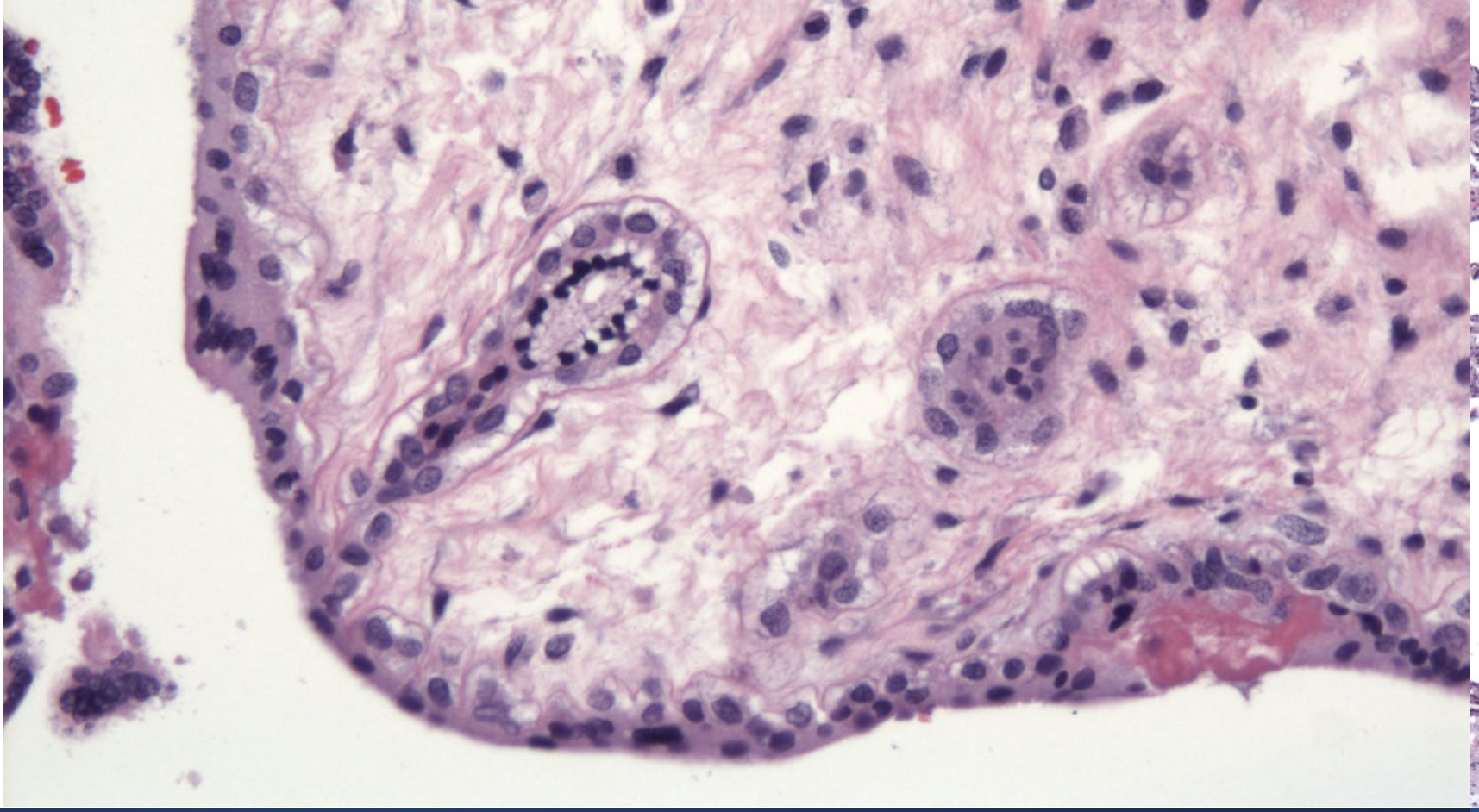


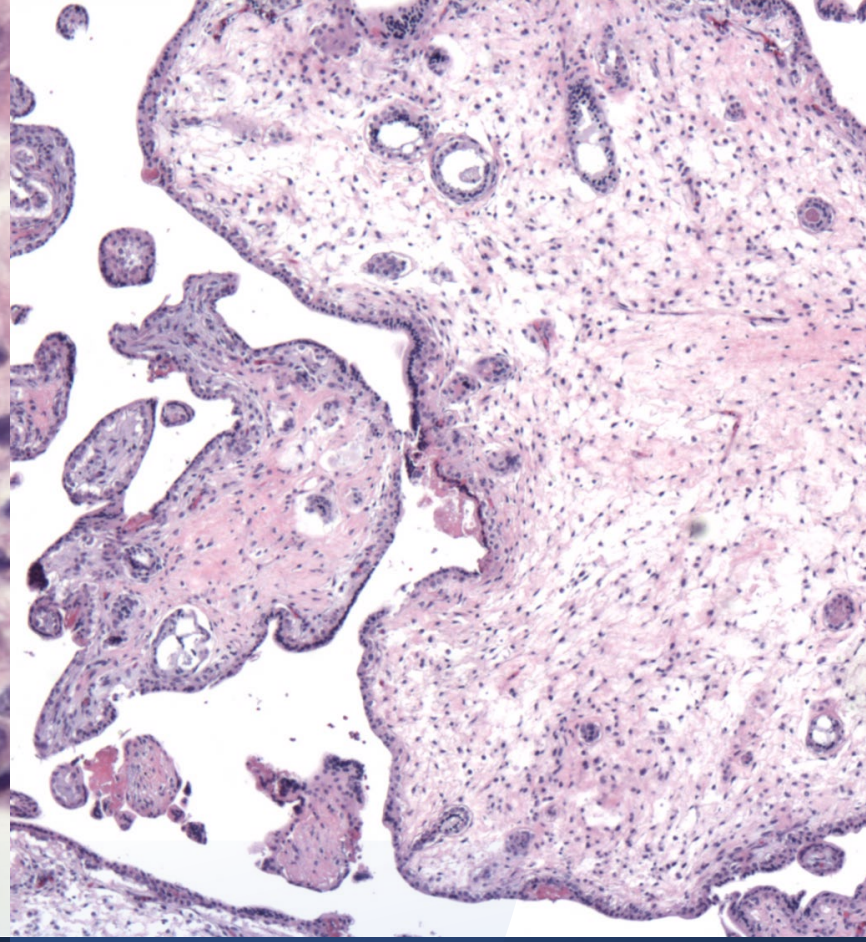
Partial Hydatidiform Mole Have Irregularly Shaped Enlarged Villi

Partial Hydatidiform Mole

Irregular Shapes in Larger Villi





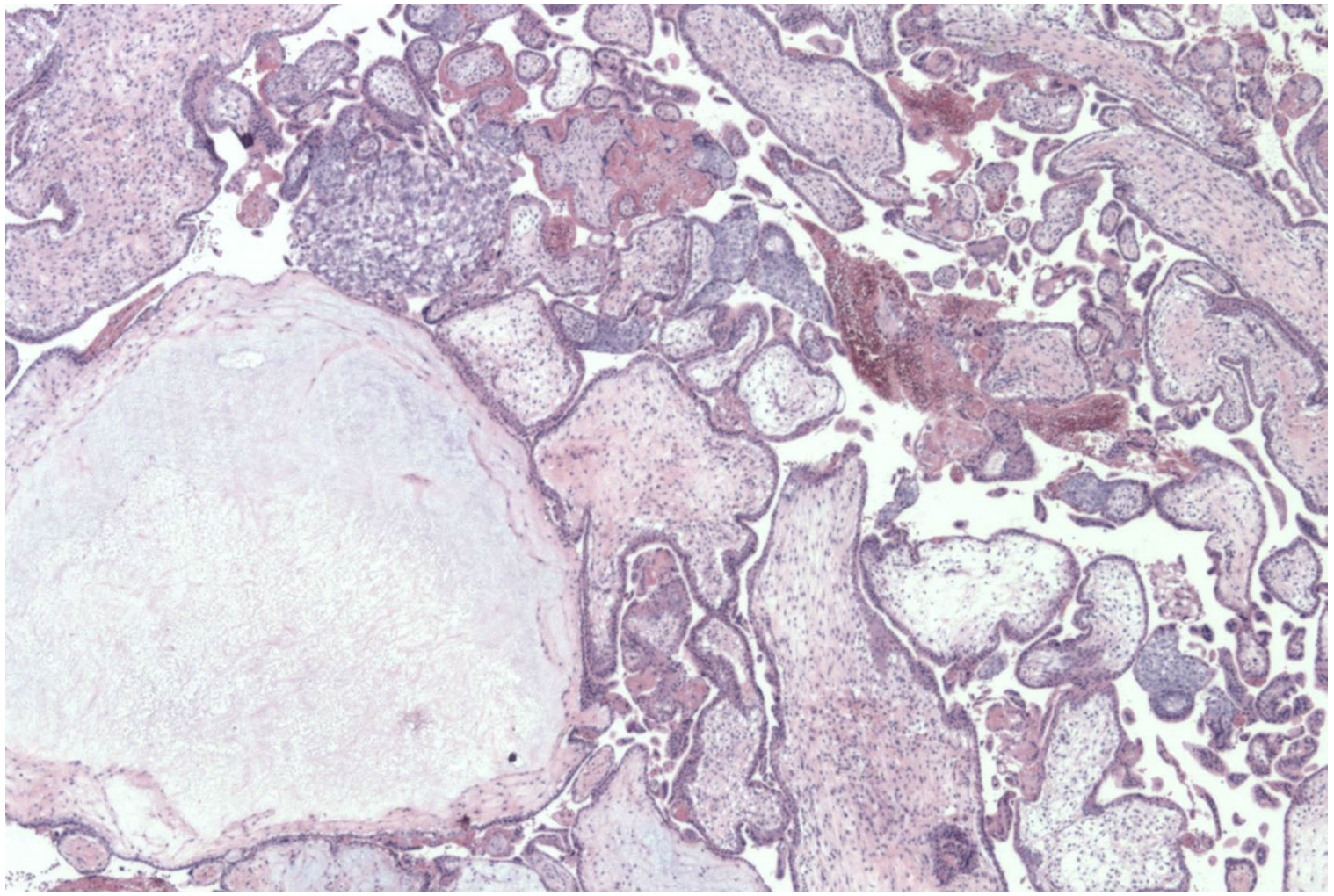


Partial Hydatidiform Mole – Inclusions Reflect Shape Complexity

Partial Hydatidiform Mole

Scattered Cavitation of Larger Villi

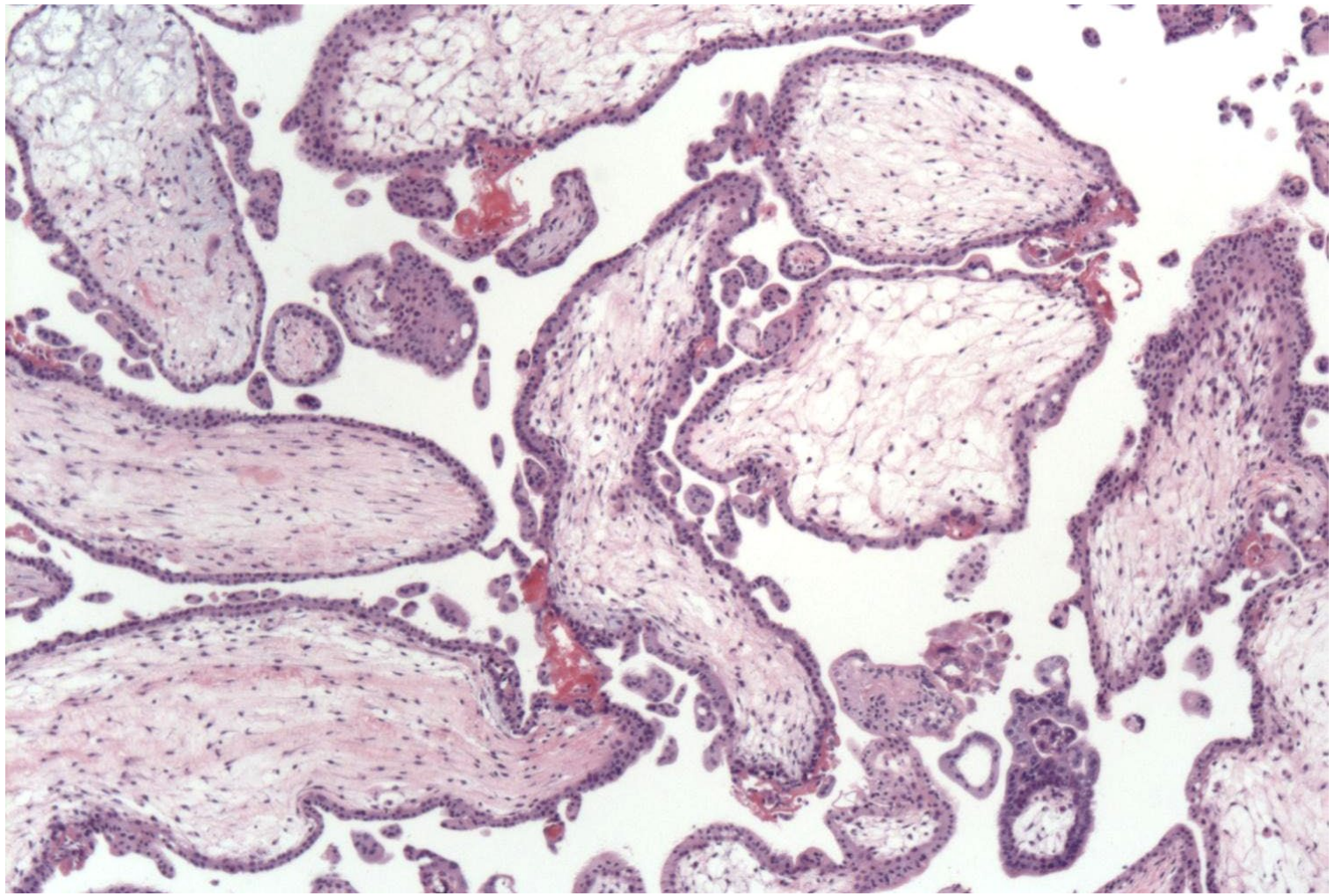
my favorite criteria



Partial Hydatidiform Mole

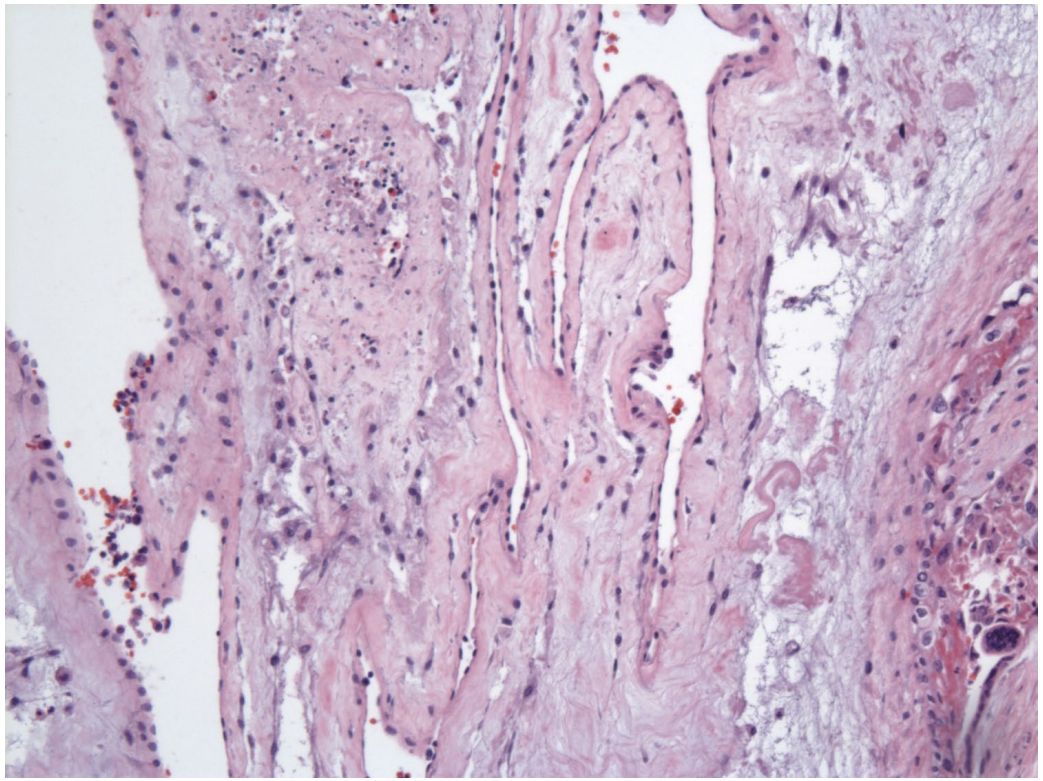
Trophoblastic Hyperplasia

Proliferation commensurate to size & “tagging”

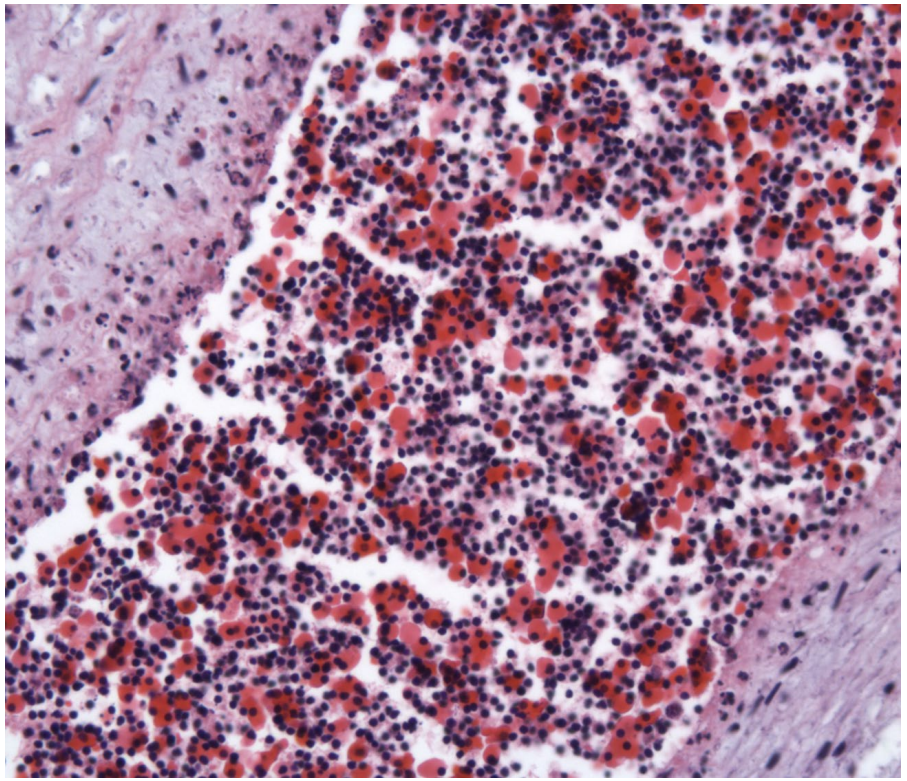


Fetal Development in Partial Mole

Amnion and Chorion



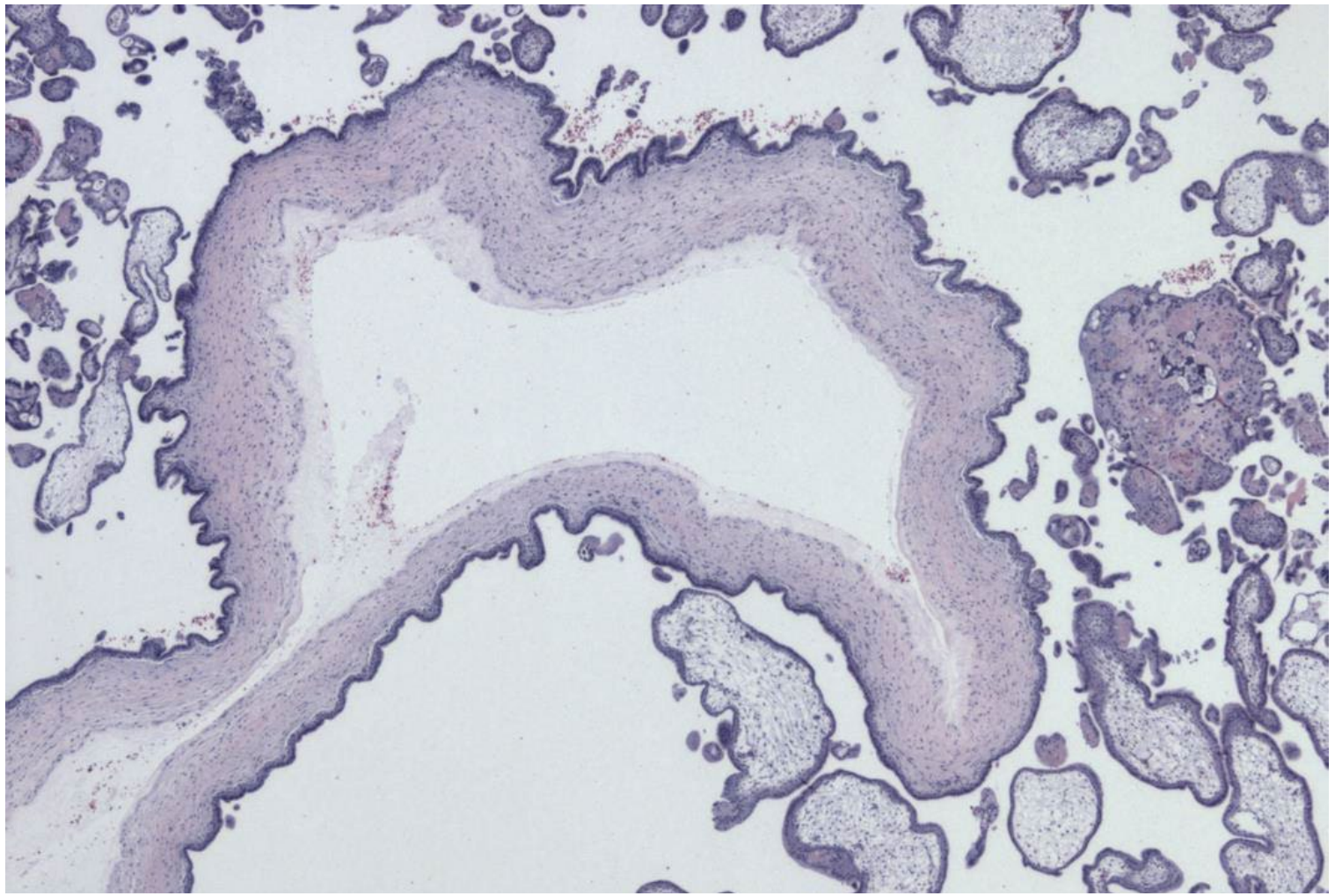
Fetal blood (common) and Embryo (uncommon)



Numerous Nucleated Fetal Red Blood Cells
Not Typically Found In CHM

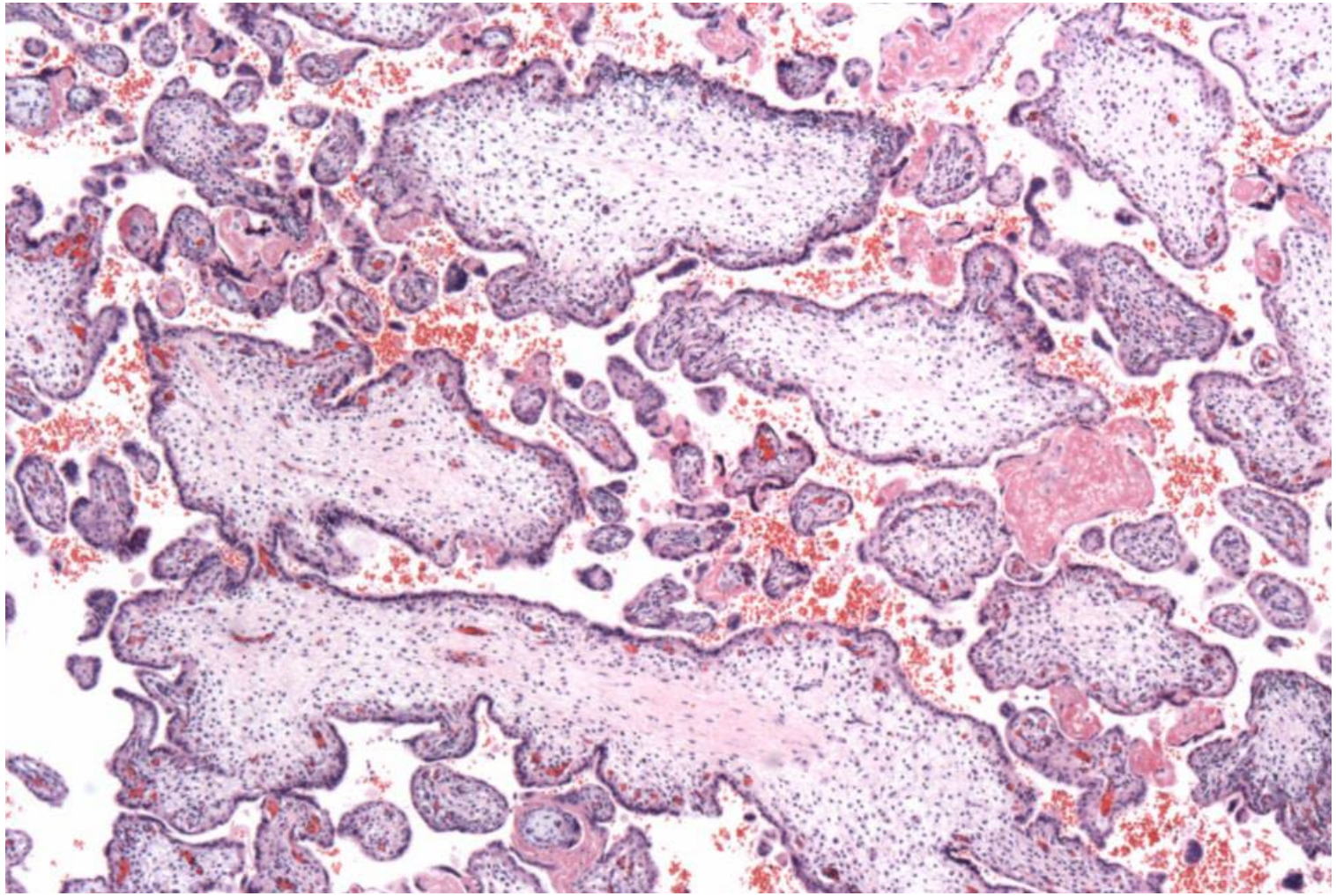
Diploid partial mole mimic (ish CEP17x2, nl p57 IHC)

Chorionic plate mimicking a cavitated villus



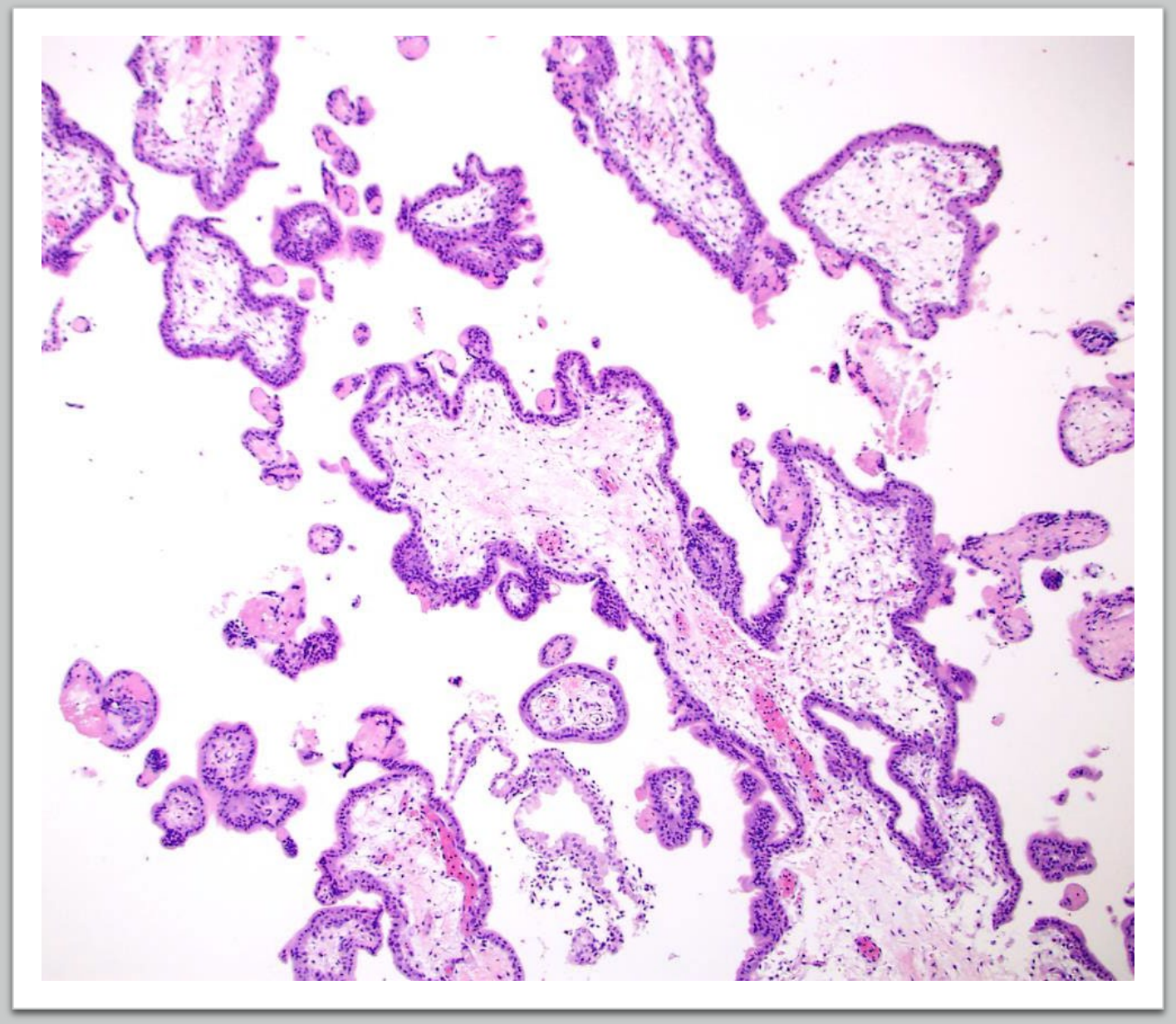
Trisomy 21 mimicking partial mole

Dysmorphic villi with dimorphism but without cavitation



Trisomy 13 is a very frequent PHM mimic

Best aneusomy mimic that I've seen was trimsomy 11 (because it has 3 copies of p57 locus, presumable 2 from the father)

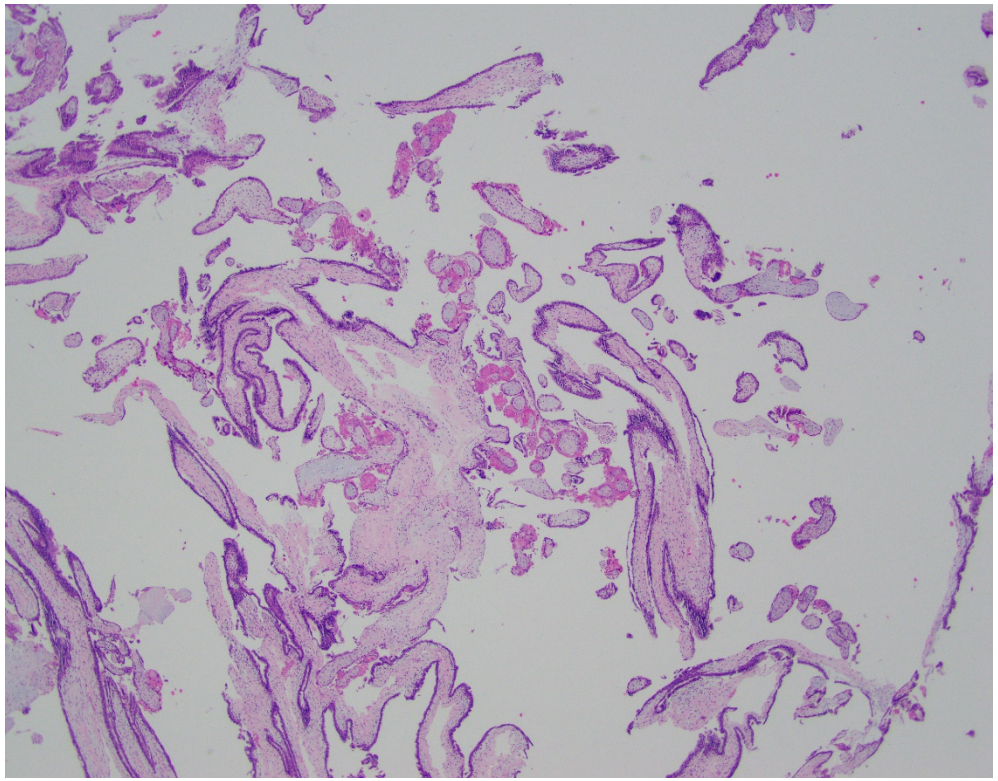


Partial Hydatidiform Mole
Are Diandric Triploid Gestations Favoring Placental Growth

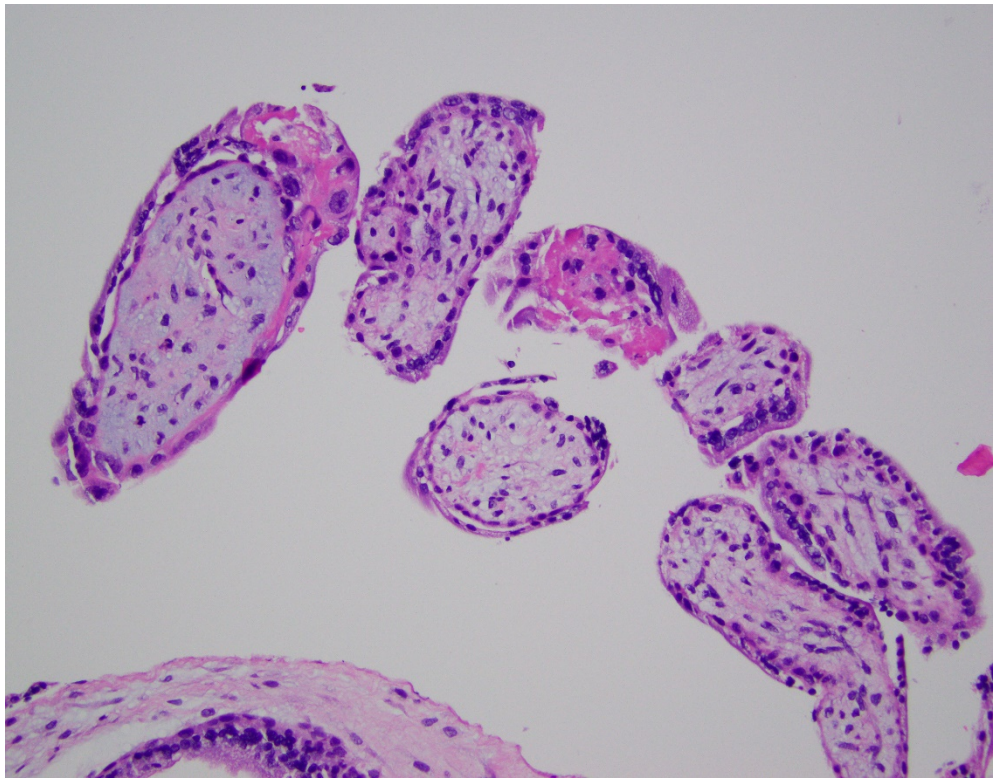
	Redline et al. *Hum Pathol,* 1998	Han et al. *Am J Surg Pathol,* 2020	Various Case Reports
Starting population	Spontaneous abortion (832)	Prenatal screening for aneuploidy	
Refined population	Triploid (65)	Triploid (20)	
Methodology	Karyotype & Microsatellite PCR	Genotype Testing	
Digynic (1P:2M)	Non-molar (31%) Fetal tissue more frequently found	Non-molar (35%)	
Diandric (2P:1M)	Partial mole (61%) phenotypic spectrum including “early”, “ancient”, “suggestive”	Partial mole (65%) Only ¼ diagnostic by (+) cistern and >2.5 mm ¾ had focal or incomplete phenotype	
Tetraploid Triandric (3P:1M)			Rare cases with features resembling partial mole

Non-molar Triploidy (digynic - 2M1P)

Not dimorphic



Villous sclerosis, without cavitation



Determination of Ploidy for PHM – The Solution, A Helping Hand or Unnecessary?

Methods

- Karyotype
- Flow cytometry – DNA analysis
- In situ hybridization
- Microsatellite “fingerprinting”
- Microarray
- Whole genome/exome sequencing

Issues

- Requires living fetal cells
- Needs whole nuclei
- Inconclusive with 1 chromosome
- Complicated without parental DNA
- Bioinformatics
- Bioinformatics

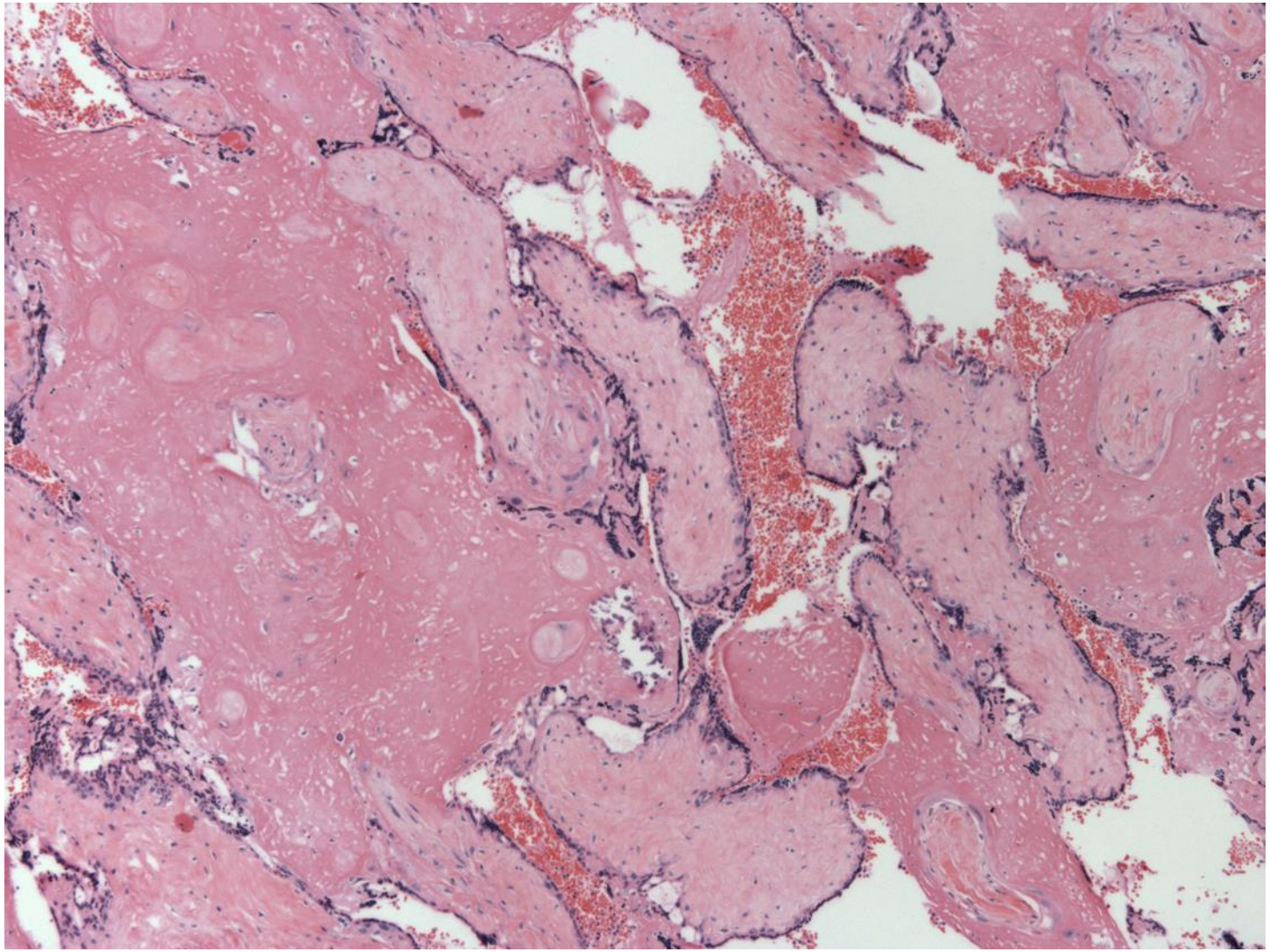
- All:
  - Instrumentation, Cost, & Time
  - Parent Of Origin
  - Data you didn’t seek or on your radar

Do you really need copy number analysis?

- **RESULTS:**
- 260 cases of PHMs
- Blinded pathologic review showed sensitivity of 88% and specificity of 95% in diagnosing PHMs with histology alone vs. histology with ancillary testing.
- 100% of PHMs (n=56) expressed p57 staining and 100% of CHMs (n=57) had absent staining
- 145 subjects had clinical follow-up data
  - 16 diagnosed with GTD (by serum hCG).
  - 13 cases of cases of clinical GTN histologically resembling ***"retained placenta"***
  - Only 2 had adverse outcomes (ETT and ChorioCA)

Soong et al. *Unpublished*

“Persistent” PHM looks like “funny” retained POC



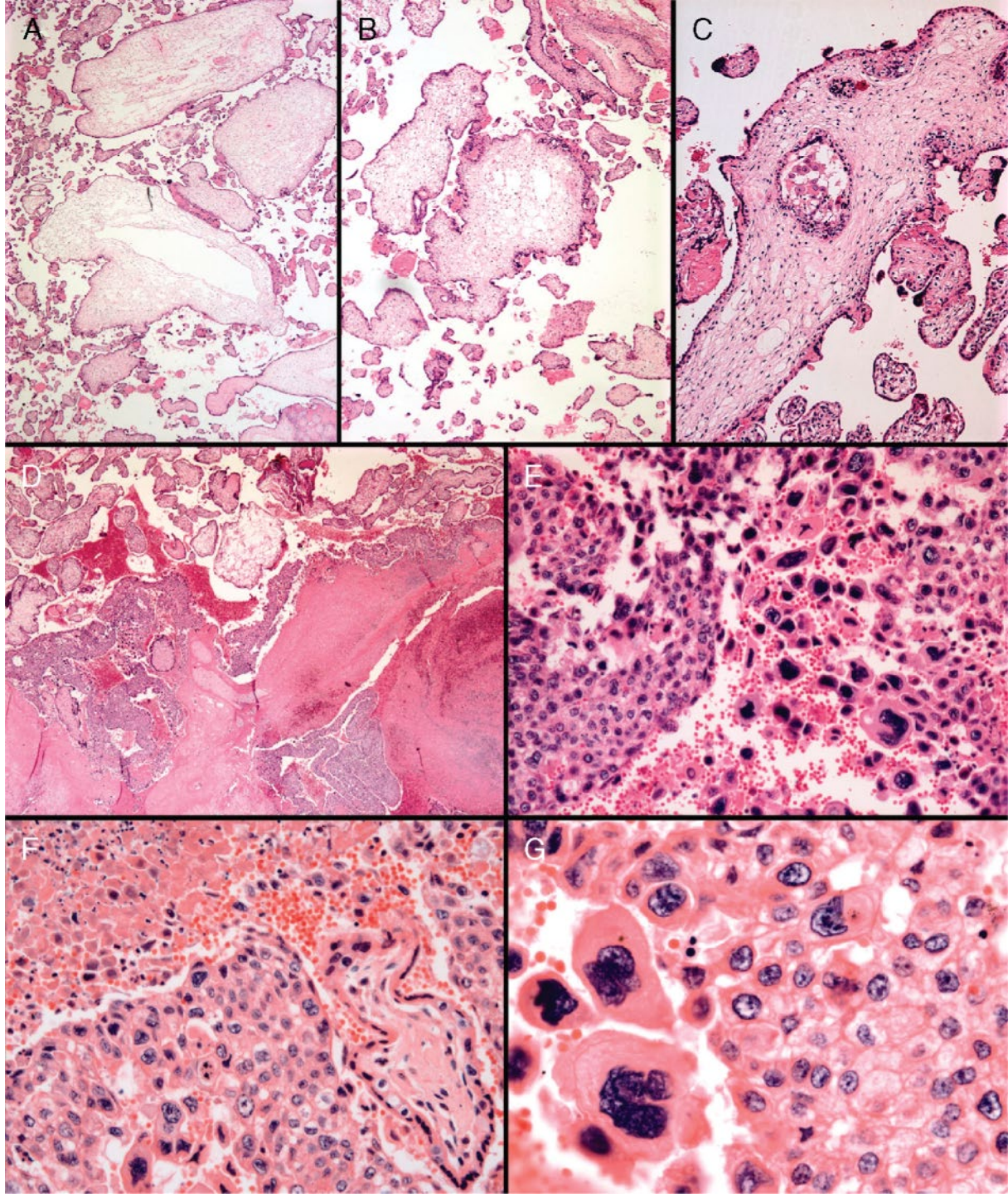
The exception to the rule

International Journal of Gynecological Pathology
27:247–251, Lippincott Williams & Wilkins, Baltimore

Case Report

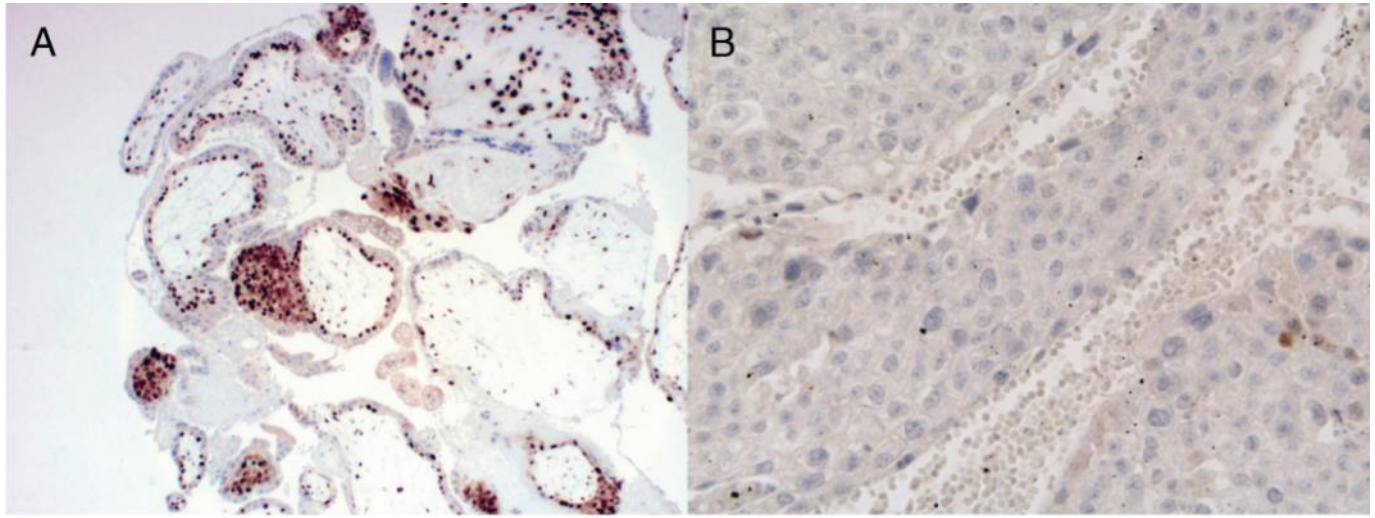
Intraplacental Choriocarcinoma Arising in a Second Trimester Placenta With Partial Hydatidiform Mole

Fabiola Medeiros, M.D., Michael J. Callahan, M.D., Julia A. Elvin, M.D., Ph.D.,
David M. Dorfman, M.D., Ph.D., Ross S. Berkowitz, M.D., and Bradley J. Quade, M.D., Ph.D.



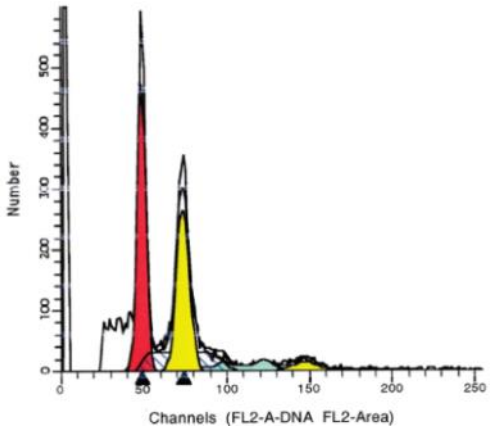
Partial Hydatidiform Mole

P57 expression retained in PHM (A) and lost in ChorioCA (B)

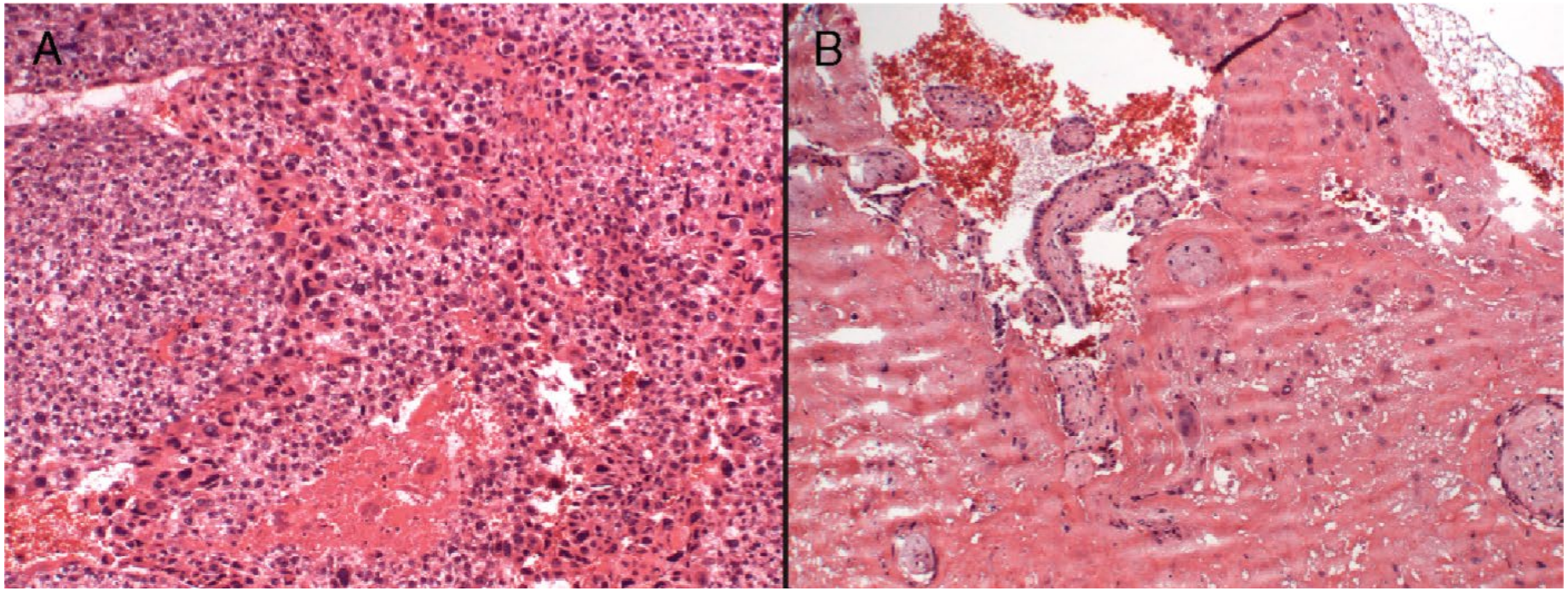


Triploid gestation (yellow peak) in placental

C



Metastasis From Intraplacental Choriocarcinoma Arising In Partial Mole



Diagnosing Possible Molar Gestations in General Surgical Pathology Practice

The Scream by Edvard Munch - NPR

A Practical Approach to Molar Pregnancies

- **Absence of villi does not exclude molar gestation… but it moves it down the list**

- **Risk of Persistent GTD (including recurrence or metastasis)**
  - CHD >> PHM (~20% v. ~2%, but metastatic risk closer to normal gestations for PHM)

- **Strategy should focus on finding every CHM**
  - Use p57 liberally…it works well, is cheap, and adds little delay
  - Ask for help if the p57 doesn't make sense (you may have found a chimeric or mosaic gestion with the potential to behave like a CHD biologically)
  - Use genetic information when you have it, after excluding a CHM
    - Some aneusomies (e.g., +13, +11, +21) are excellent mimics of PHM
    - Triploidy ≠ PHM… but 3n plus dysmorphic villi (suggestive histology) is sufficient, in my opinion
    - I don't wait for karyotype or microarray in most cases (volume too high), but I add my name to cytogenetic report distribution and check it later
    - Non-canonical p57 might be twin or chimera/mosaic

Timely Topic –

Maternal & Placental SARS-CoV-2

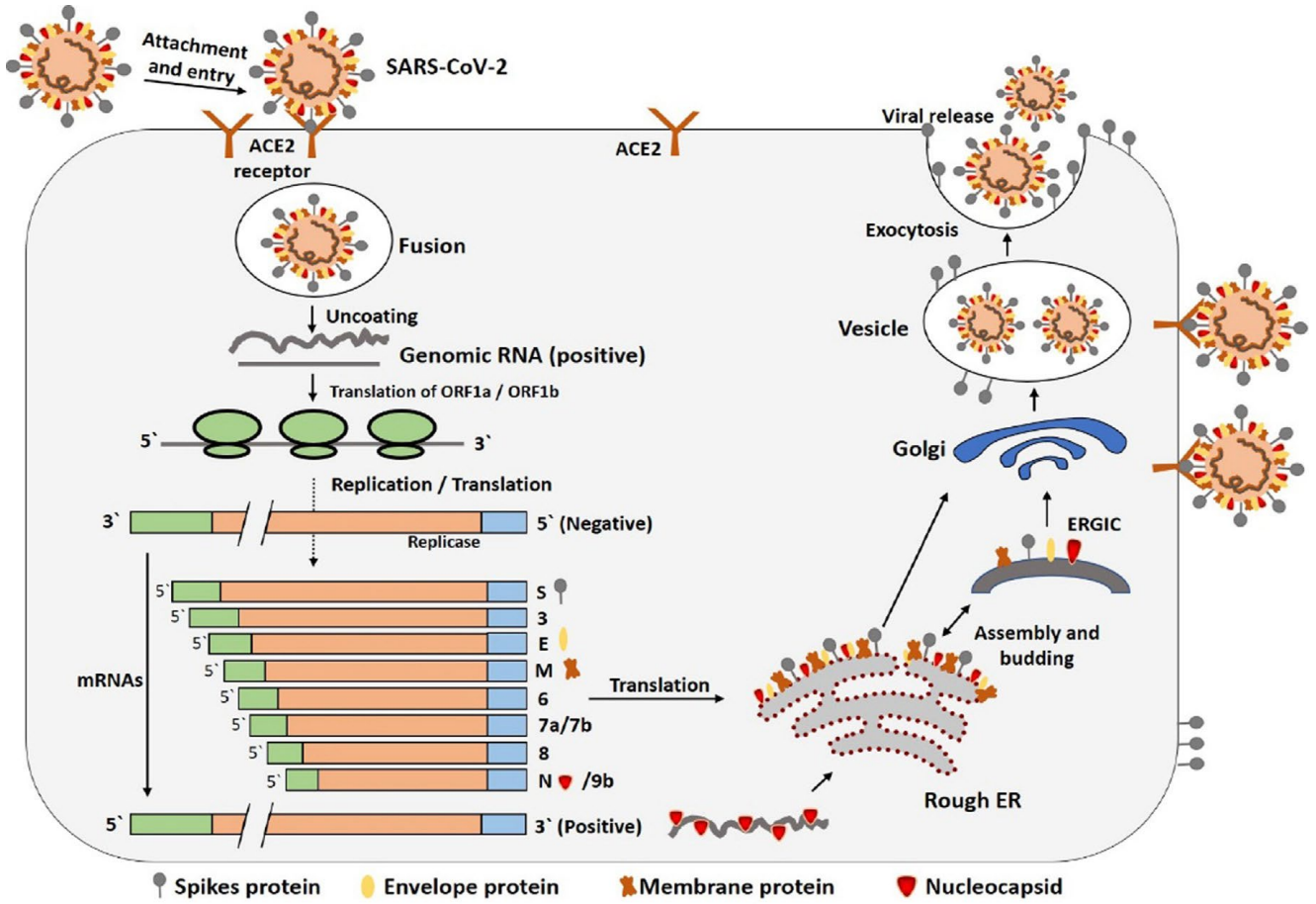
Fast Breaking Story

- From non-traditional outlets
  - Public (news) media
  - Social media
  - Professional list serves/bulletin boards, word-of-mouth
- Pre-publication release (not peer reviewed)…
  - the early standard practice for pandemic

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

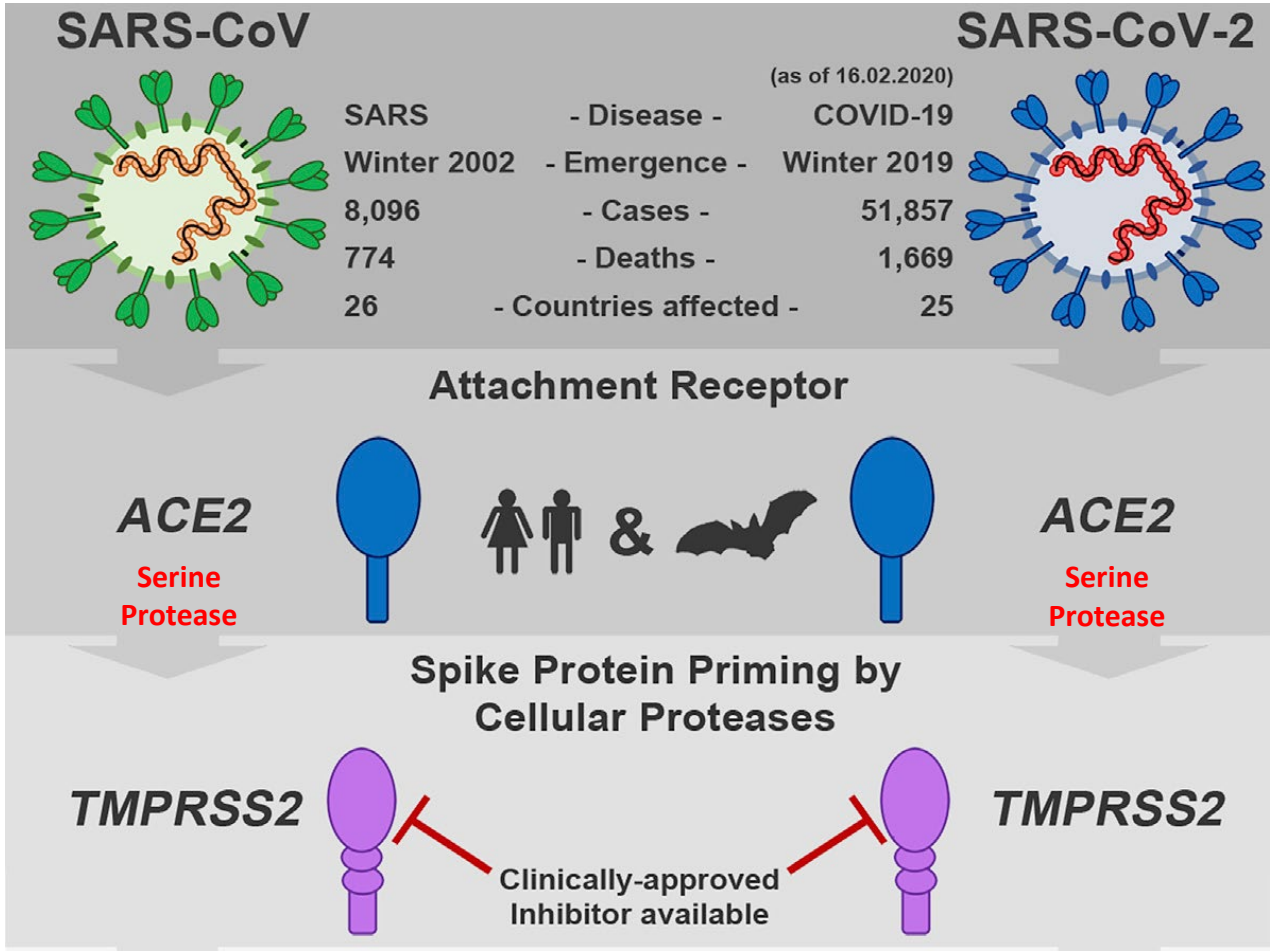
Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Fig. 3. The life cycle of SARS-CoV-2 in host cells; begins its life cycle when S protein binds to the cellular receptor ACE2. After receptor binding, the conformation change in the S protein facilitates viral envelope fusion with the cell membrane through the endosomal pathway. Then SARS-CoV-2 releases RNA into the host cell. Genome RNA is translated into viral replicase polyproteins pp1a and 1ab, which are then cleaved into small products by viral proteinases. The polymerase produces a series of subgenomic mRNAs by discontinuous transcription and finally translated into relevant viral proteins. Viral proteins and genome RNA are subsequently assembled into virions in the ER and Golgi and then transported via vesicles and released out of the cell. ACE2, angiotensin-converting enzyme 2; ER, endoplasmic reticulum; ERGIC, ER–Golgi intermediate compartment.



M.A. Shereen et al. J Adv Res 24 (2020) 91–98

SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor



Hoffmann et al., 2020, Cell 181, 271–280
April 16, 2020 ª 2020 Elsevier Inc.
https://doi.org/10.1016/j.cell.2020.02.052

Transmission to the fetus and neonate:

How often and by what mechanism(s)?

- In utero – transplacental
- Intra-partem – vaginal contact
- Post-partem – breast milk

Journal Information

Online ISSN: 1543-2165
Print ISSN: 0003-9985
Frequency: Monthly

Article Citation:
David A. Schwartz (2020) An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes. Archives of Pathology & Laboratory Medicine In-Press.

https://doi.org/10.5858/arpa.2020-0901-SA

Early Online Release

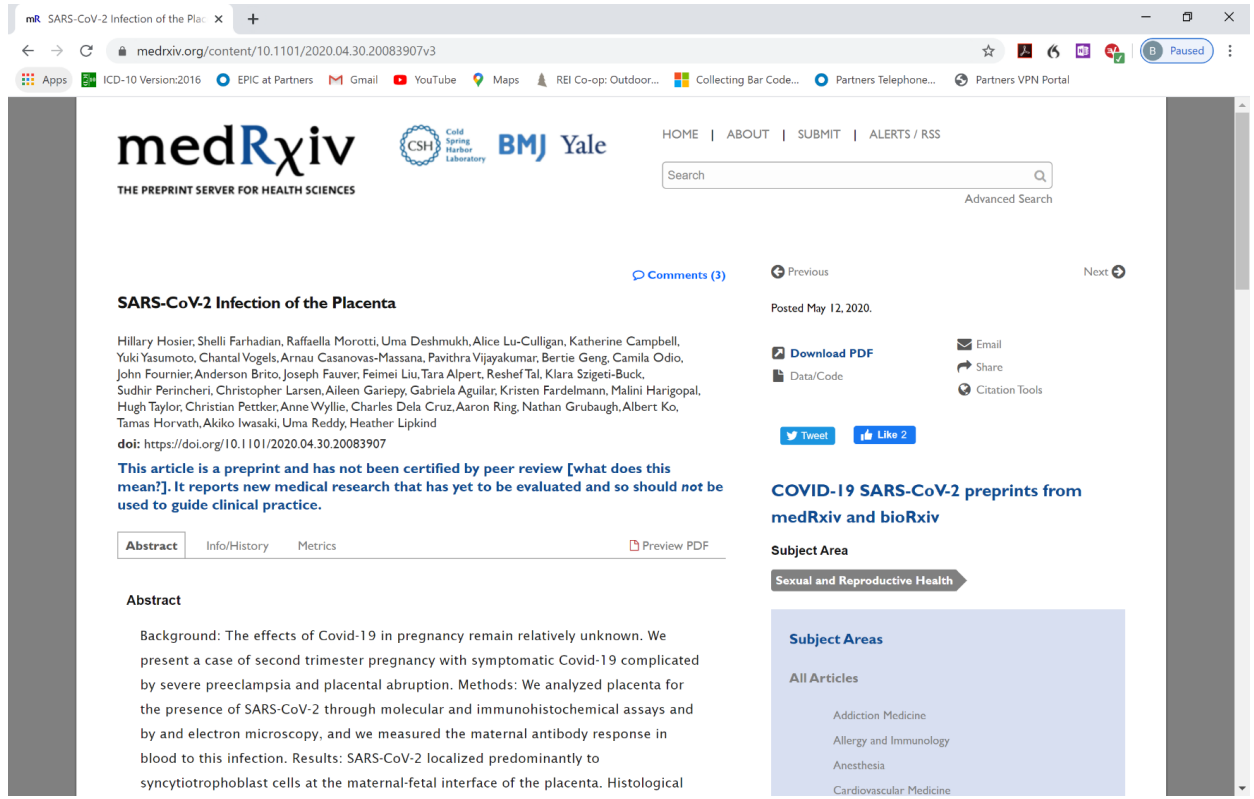
An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes

David A. Schwartz, MD, MS Hyg

The author has no relevant financial interest in the products or companies described in this article.

Corresponding author: David A. Schwartz, MD, MS Hyg, Department of Pathology, Medical College of Georgia, Augusta University, 1950 Grace Arbor Court, Atlanta, GA 30329 (email: davidalanschwartz@gmail.com).

The emergence of a novel coronavirus, termed SARS-CoV-2, and the potentially life-threating respiratory disease that it can produce, COVID-19, has rapidly spread across the globe creating a massive public health problem. Previous epidemics of many emerging viral infections have typically resulted in poor obstetrical outcomes including maternal morbidity and mortality, maternal-fetal transmission of the virus, and perinatal infections and death. This communication reviews the effects of two previous coronavirus infections - severe acute respiratory syndrome (SARS) caused by SARS-CoV and Middle East respiratory syndrome (MERS) caused by MERS-CoV - on pregnancy outcomes. In addition, it analyzes literature describing 38 pregnant women with COVID-19 and their newborns in China to assess the effects of SARS-CoV-2 on the mothers and infants including clinical, laboratory and virologic data, and the transmissibility of the virus from mother to fetus. This analysis reveals that unlike coronavirus infections of pregnant women caused by SARS and MERS, in these 38 pregnant women COVID-19 did not lead to maternal deaths. Importantly, and similar to pregnancies with SARS and MERS, there were no confirmed cases of intrauterine transmission of SARS-CoV-2 from mothers with COVID-19 to their fetuses. All neonatal specimens tested, including in some cases placentas, were negative by rt-PCR for SARS-CoV-2. At this point in the global pandemic of COVID-19 infection there is no evidence that SARS-CoV-2 undergoes intrauterine or transplacental transmission from infected pregnant women to their fetuses. Analysis of additional cases is necessary to determine if this remains true.



New England Study

Modern Pathology (2020) 33:2092–2103
https://doi.org/10.1038/s41379-020-0639-4

USCAP

ARTICLE

Check for updates

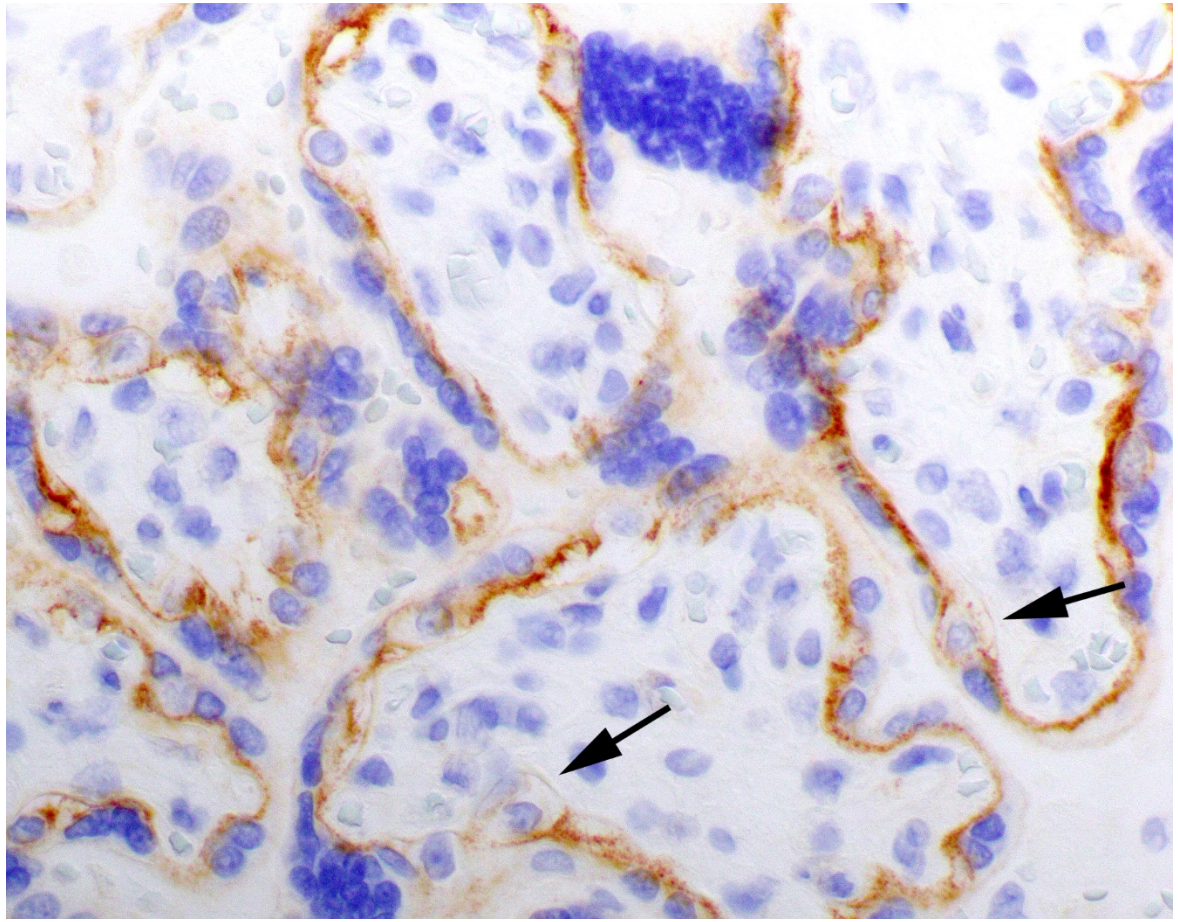
SARS-CoV-2 can infect the placenta and is not associated with specific placental histopathology: a series of 19 placentas from COVID-19-positive mothers

Jonathon L. Hecht[1] · Bradley Quade[2] · Vikram Deshpande[3] · Mari Mino-Kenudson[3] · David T. Ting[4,5] · Niyati Desai[4] · Beata Dygulska[6] · Taryn Heyman[7] · Carolyn Salafia[8] · Dejun Shen[9] · Sara V. Bates[10] · Drucilla J. Roberts[3]

Received: 19 June 2020 / Revised: 24 July 2020 / Accepted: 24 July 2020 / Published online: 2 August 2020

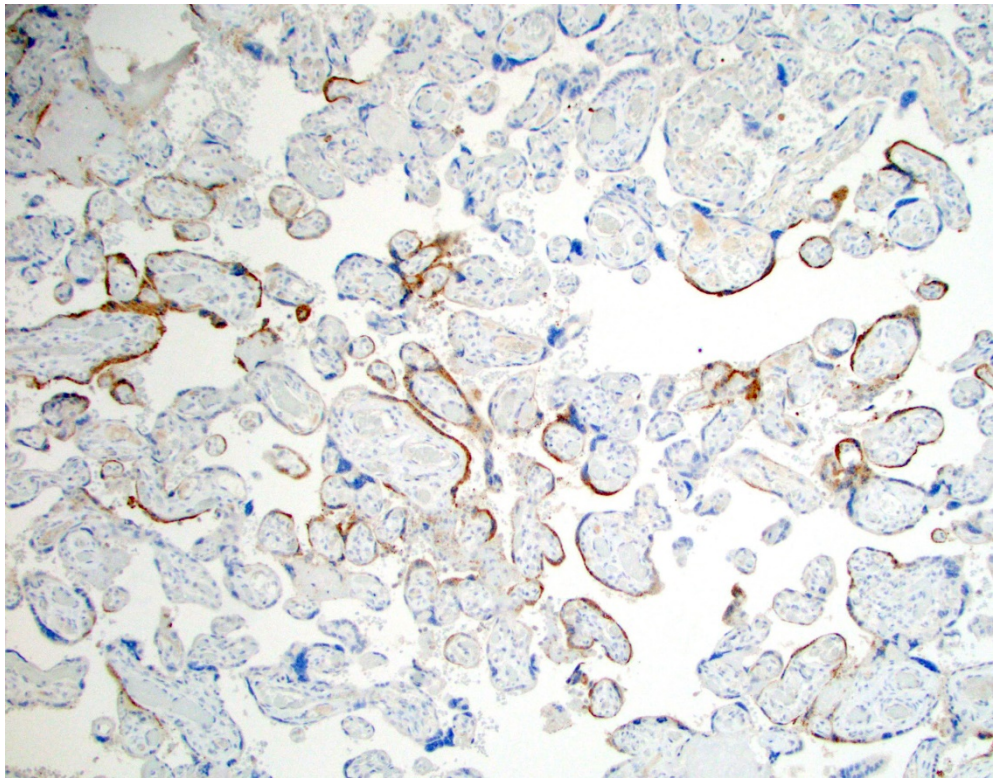
- 19 COVID-19 exposed placentas
- ACE2 in syncytiotrophoblasts (ST) with polarized distribution skewed to ***basal*** side
- TMPRSS2 only present weakly in the villous endothelium and rarely in the ST
- Combined expression pattern may limit infection
- 2/19 infected placenta (“cherry picked”), no specific pathogy

ACE2

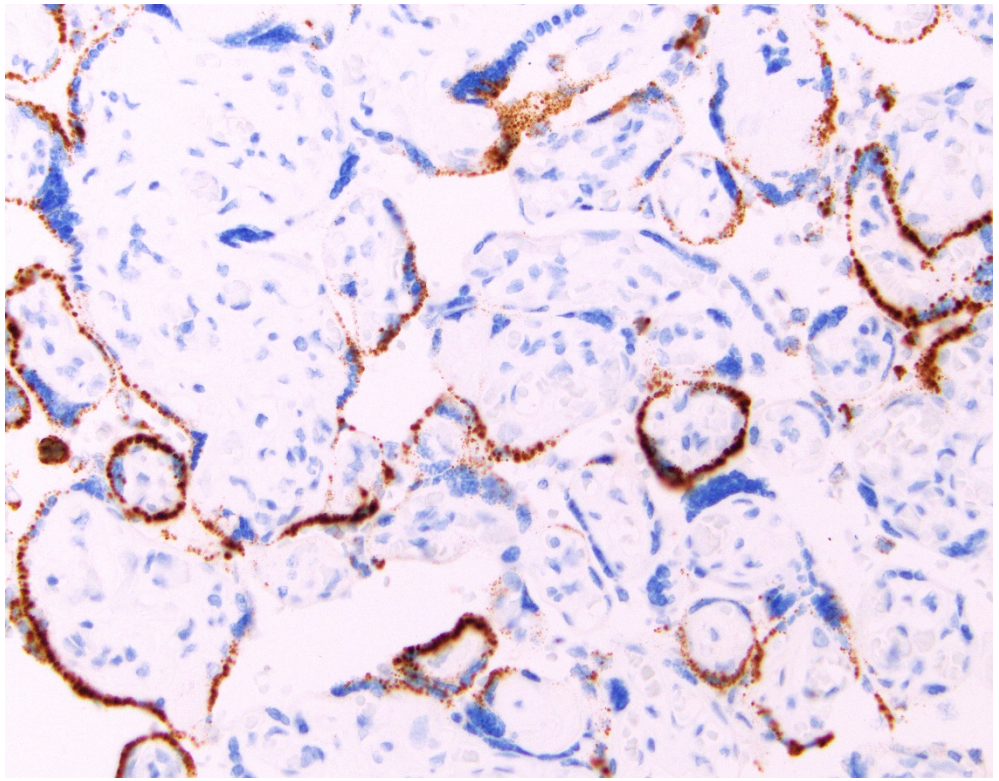


Accumulation of More Case: Mother and Baby both COVID-19+

Spike protein IHC

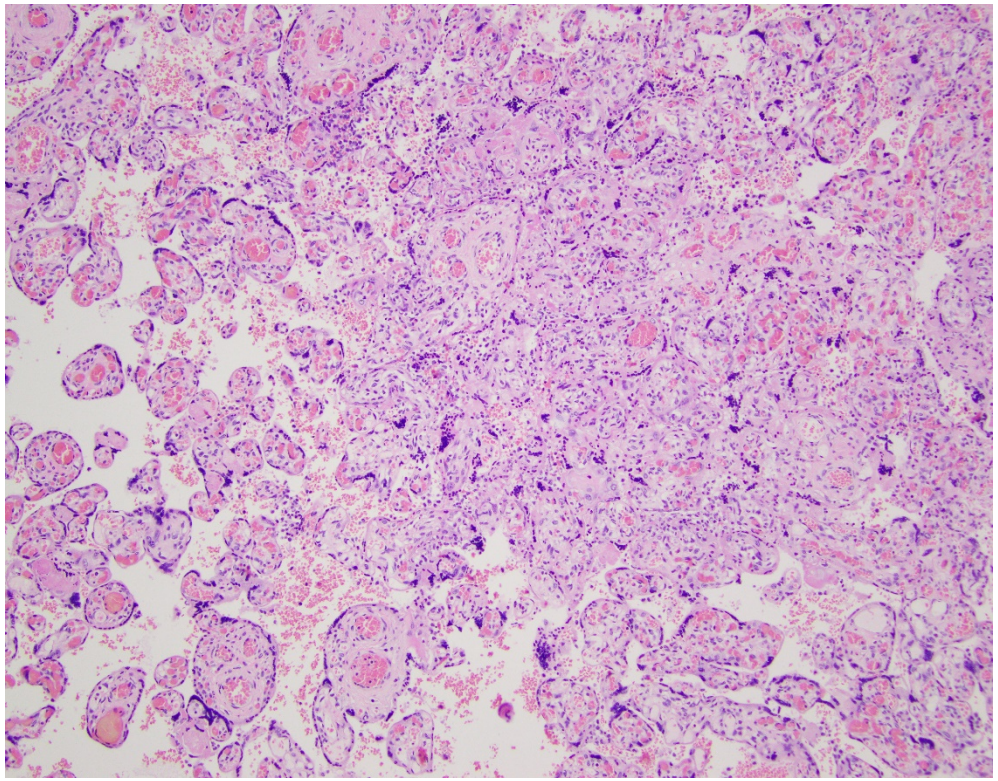


Spike protein mRNA ISH

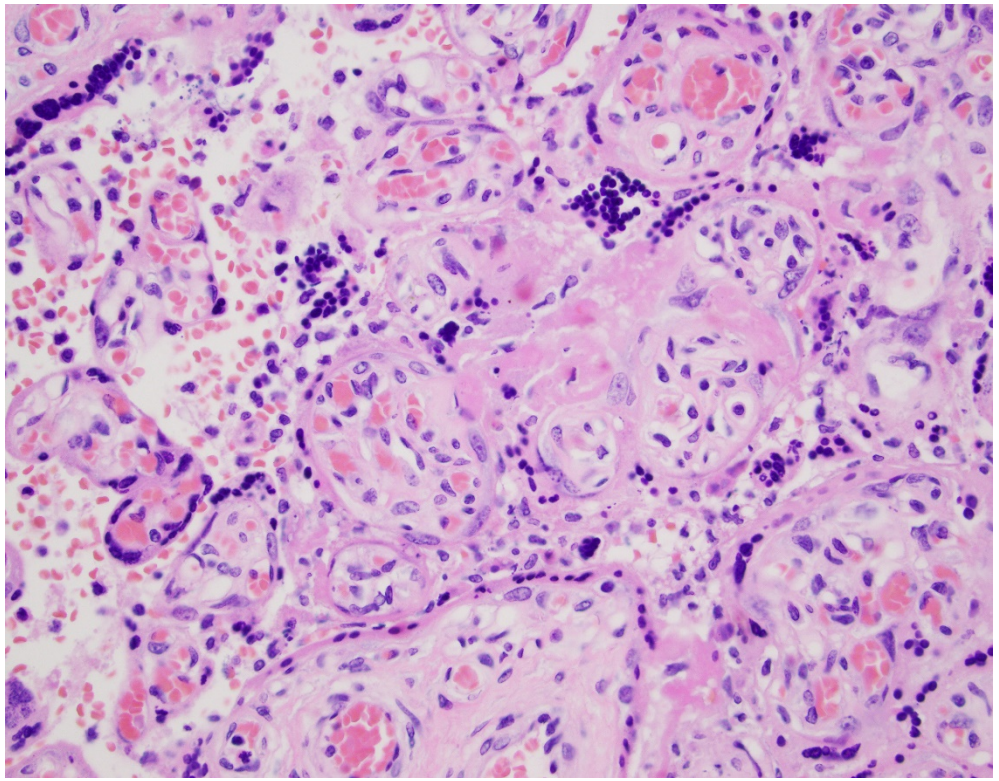


COVID-19 Placentitis

Various Sized Clusters Of Aggregated Villi

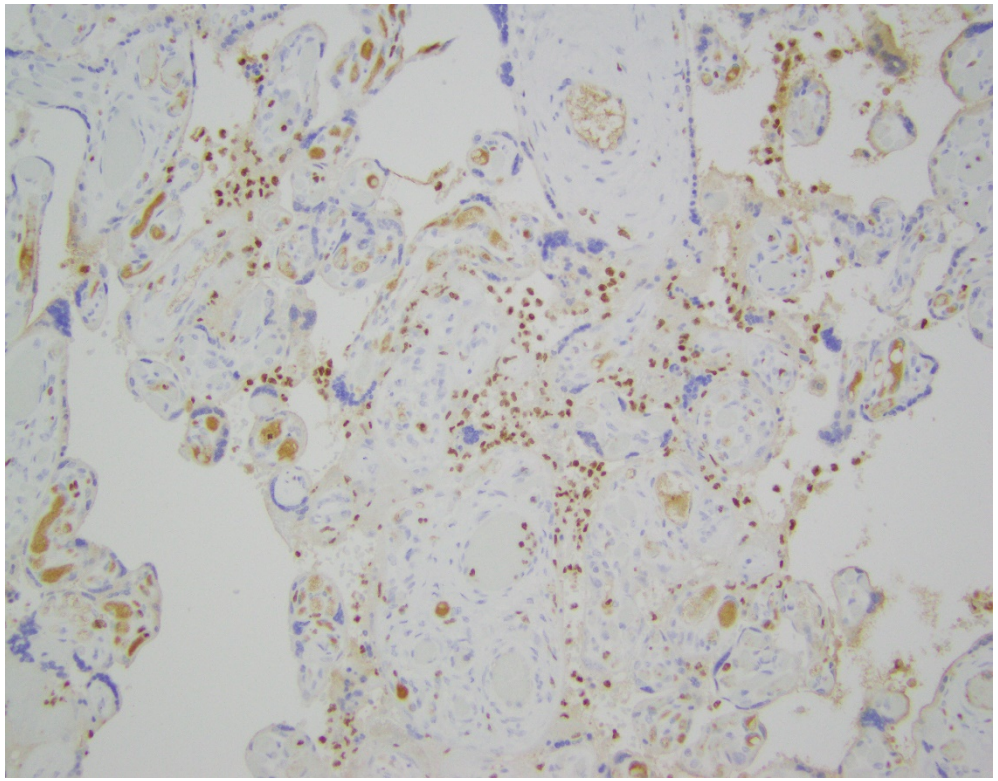


Chronic Histiocytic Intervillositis & Early Placental Infarction/Intervillous Fibrin

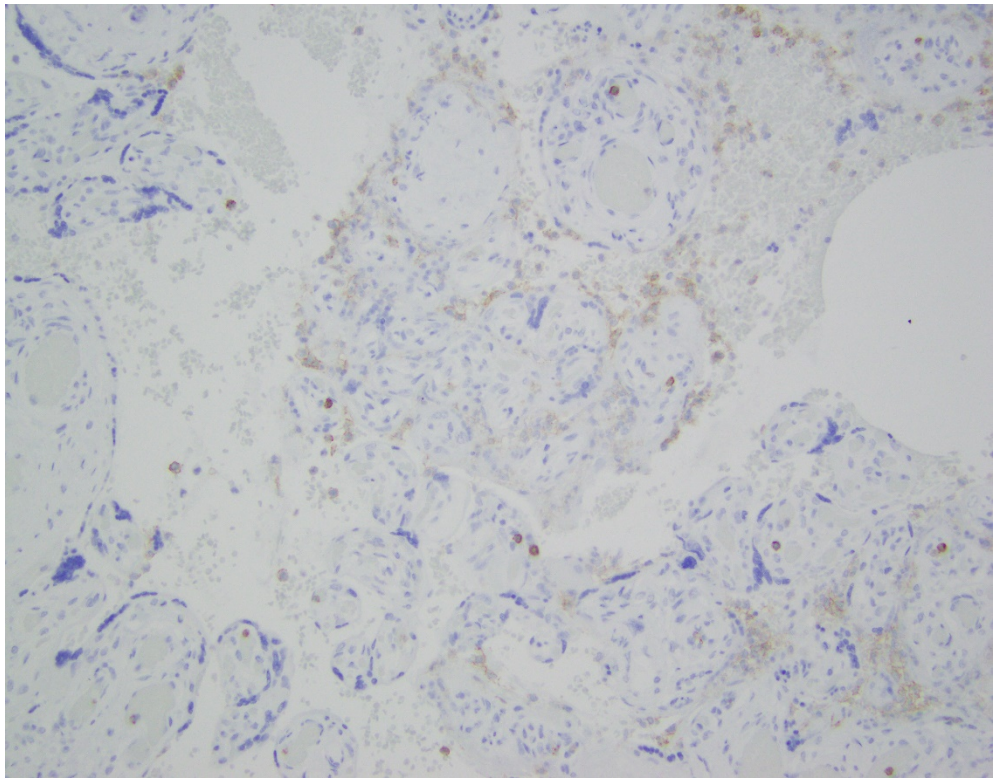


COVID-19 Placentitis As Variant of Chronic Histiocytic Intervillositis

Macrophages (PU.1)



Lymphocytes (LCA/CD45)



Take Away Messages

- **Placental infection uncommon** in most CoVID-19(+) mothers

- Mechanism (and clinical implications) of placental infection partially understood
  - **Maternal viremia low**

  - **ACE2** present in syncytiotrophoblasts…mostly on stromal side…and very low **TMPRSS2**, potentially limiting placental infection

- Role of ancillary testing for placenta not established…but **Anti-Spike IHC** likely to be helpful

- BOLO for **emerging pattern of histopathology** when SARS-CoV-2 infection present
  - **Atypical chronic histiocytic intervillositis** with
    - Mixed inflammatory infiltrate with PMN and macrophages
    - Necrosis / infarction
    - Perivillous fibrin deposition


KEEP
CALM
AND
WASH
YOUR
HANDS
www.cdc.gov/handwashing
CDC
U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

Acknowledgements

- BWH / New England Trophoblast Disease Center
  - Ross Berkowitz
  - Neil Horowitz
  - Kevin Elias
  - Fabiola Medeiros
  - Rinda Soong
- Harvard
  - Dru Roberts
  - Johnathan Hecht

Thank You and Best Wishes for the New Year