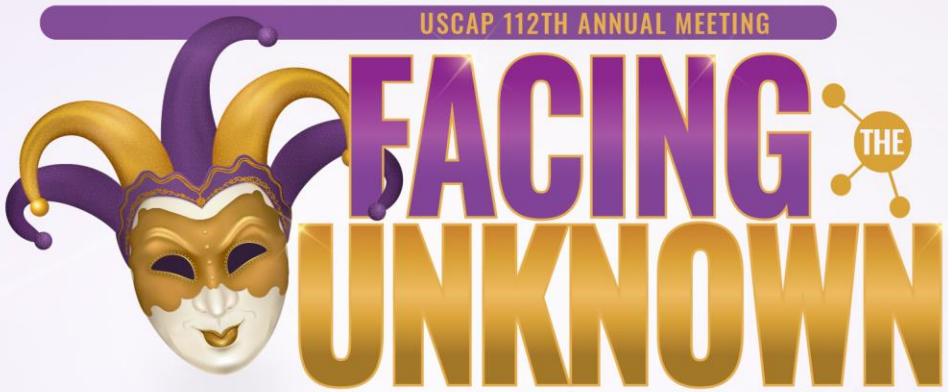
Mimics of Molar Pregnancy in Products of Conception Specimens

Ricardo R. Lastra, MD

Associate Professor

University of Chicago



USCAP
UNITED STATES AND CANADIAN ACADEMY OF PATHOLOGY
Creating a Better Pathologist

Important Information Regarding CME

The **CME/evaluation** process will only be available on the USCAP website until **September 30, 2023**.

No claims can be processed after that date!

After **September 30, 2023** you will NOT be able to obtain any CME credits for attending this meeting.

Disclosure of Relevant Financial Relationships

The faculty, committee members, and staff who are in position to control the content of this activity are required to disclose to USCAP and to learners any financial relationships that have occurred within the last 24 months with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients. USCAP has reviewed the disclosures and mitigated all relevant financial relationships.

The following faculty reported relevant financial relationships:

Ricardo R. Lastra, Consultant for ArsenalBio, Inc

USCAP staff associated with the development of content for this activity reported no relevant financial relationships.

Introduction

Hydatidiform moles

- Abnormal placental development
  - Hydropic villi
  - Excessive trophoblastic hyperplasia
- Excess paternal genome
- Divided into:
  - Complete hydatidiform mole
  - Partial hydatidiform mole
  - Invasive hydatidiform mole

Introduction

WHO 2019 Classification of Gestational Trophoblastic Diseases

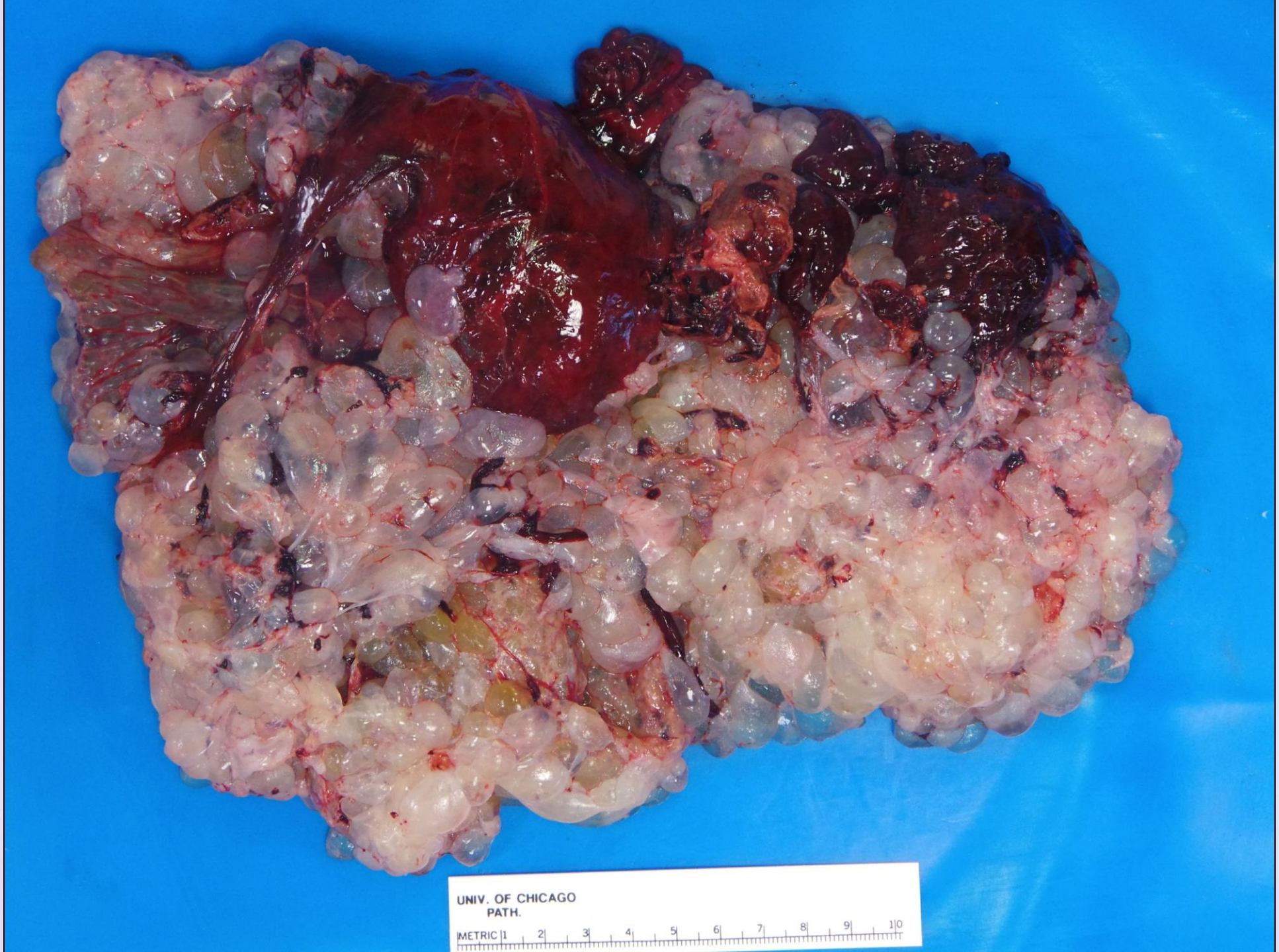
Putative Trophoblastic Cell of Origin		Gestational Trophoblastic Disease Classification		Genetic Features
Chorionic villous trophoblast		Hydatidiform mole	Complete hydatidiform mole	Androgenetic paternal or inherited mutations (*NLRP7* or *KHDC3L*)
			Partial hydatidiform mole	Diandric monogynic triploidy
			Invasive hydatidiform mole	Dependent on prior mole
		→ Atypical villous lesions		Unknown in most cases
Intermediate trophoblast	Villous IT	Gestational choriocarcinoma		Androgenetic XX following CHM
	Implantation site IT	Placental site trophoblastic tumor		Preferential requirement of paternal X chromosome
		Exaggerated implantation site		Unknown
	Chorionic-type IT	Epithelioid trophoblastic tumor		Preferential requirement of paternal X chromosome
		Placental site nodule/Atypical placental site nodule		Unknown
	Mixed IT	Mixed trophoblastic tumors		Unknown

Complete Hydatidiform Mole

- Hydatidiform mole without embryonic development
- Genetic etiology
  - Androgenetic diploidy
    - Dilpoid
    - Only paternal genetic material
  - Familial/inherited cases (uncommon)
    - Biparental diploid
    - Mutations in *NLRP7* or *KHDC3L* (abnormal expression of maternal germline)

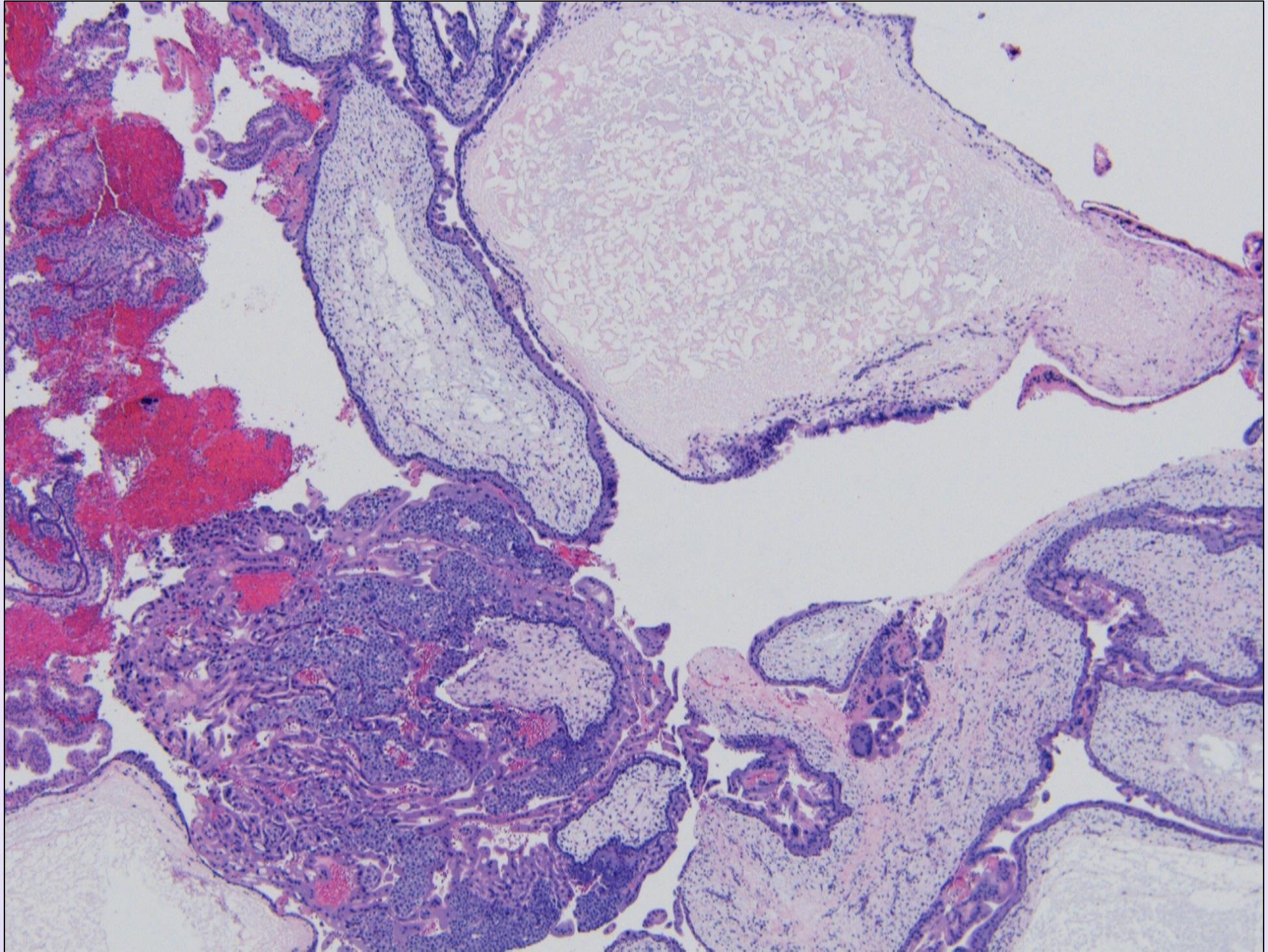
Complete Hydatidiform Mole
Gross

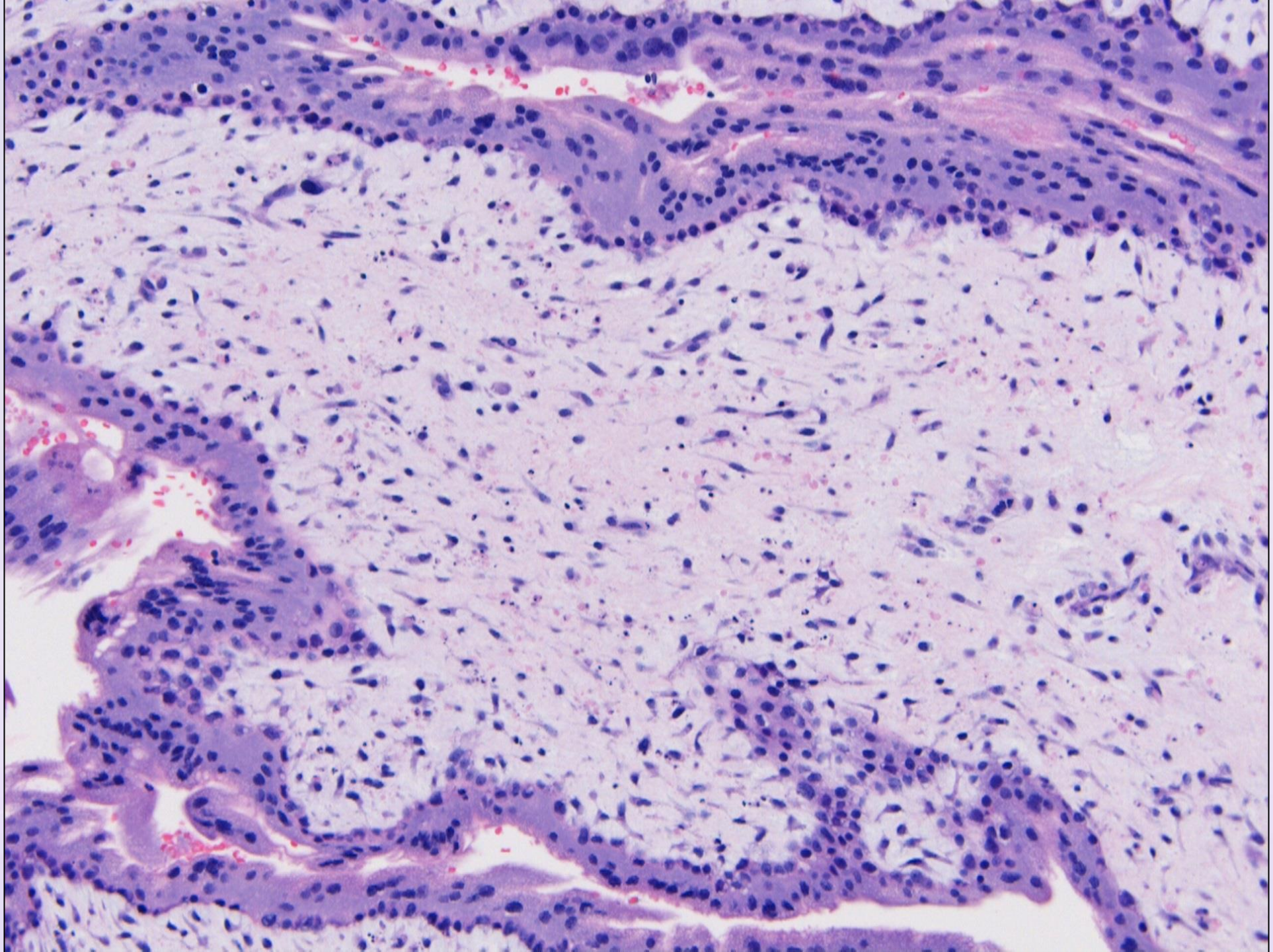
- Bulky bloody tissue
- Vesicle formation
- Absent fetal parts
- If early - non-recognizable by gross evaluation

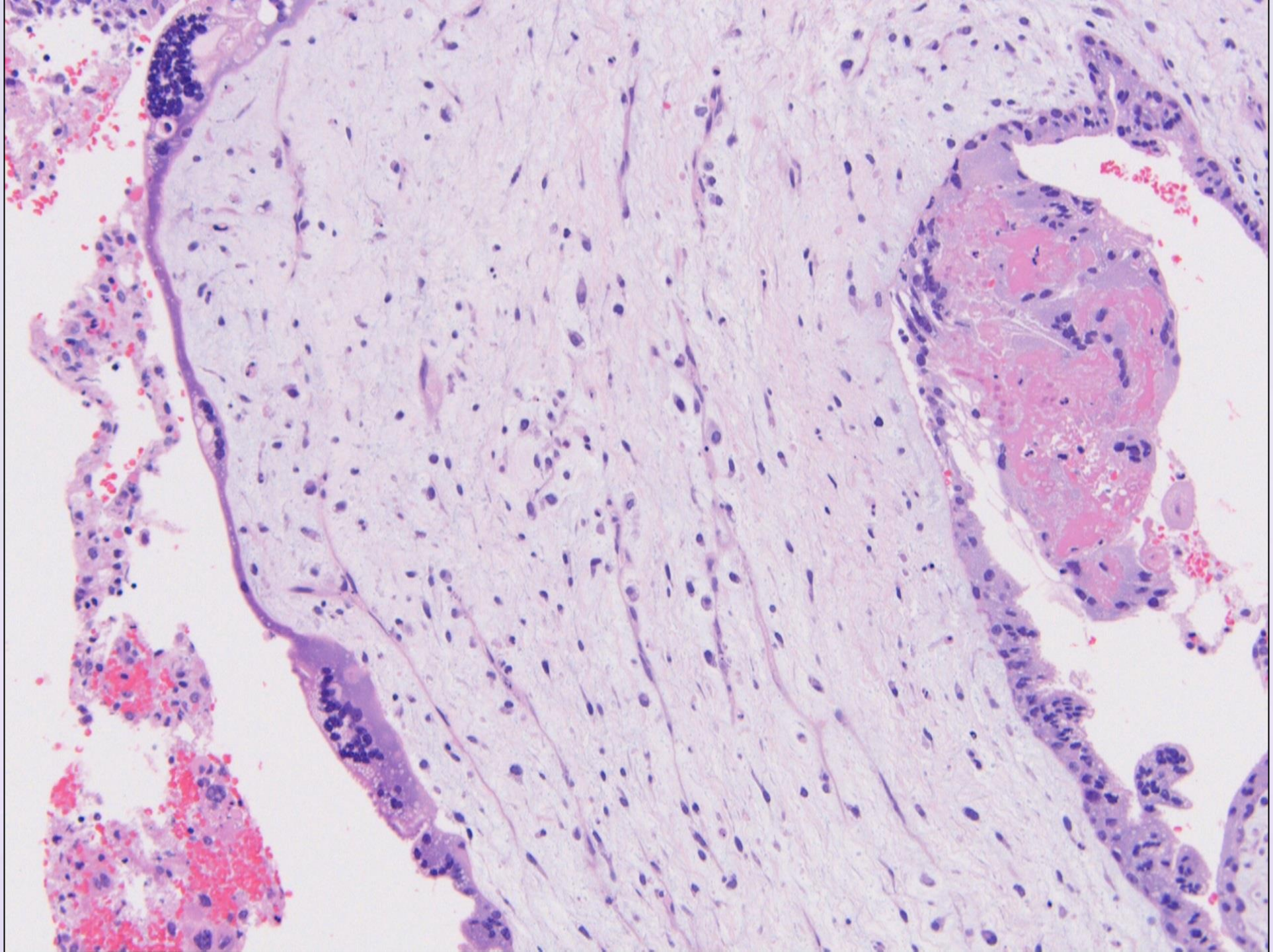

UNIV. OF CHICAGO
PATH.
METRIC 1 2 3 4 5 6 7 8 9 10

Complete Hydatidiform Mole
Histology

- Diffuse enlargement of villi
- Marked hydropic change/cisternae formation
- Prominent circumferential trophoblastic proliferation (often atypical)
- Hypercellular and myxoid villous stroma with karyorrhexis and abortive vessels
- No fetal parts
- Often associated exaggerated placental site







Partial Hydatidiform Mole

- Hydatidiform mole with a spectrum of villous morphology
- Villi range from normal to hydropic with mild trophoblastic hyperplasia
- Genetic etiology
  - Diandric triploid
    - Two set of chromosomes from father
    - One set of chromosomes from mother

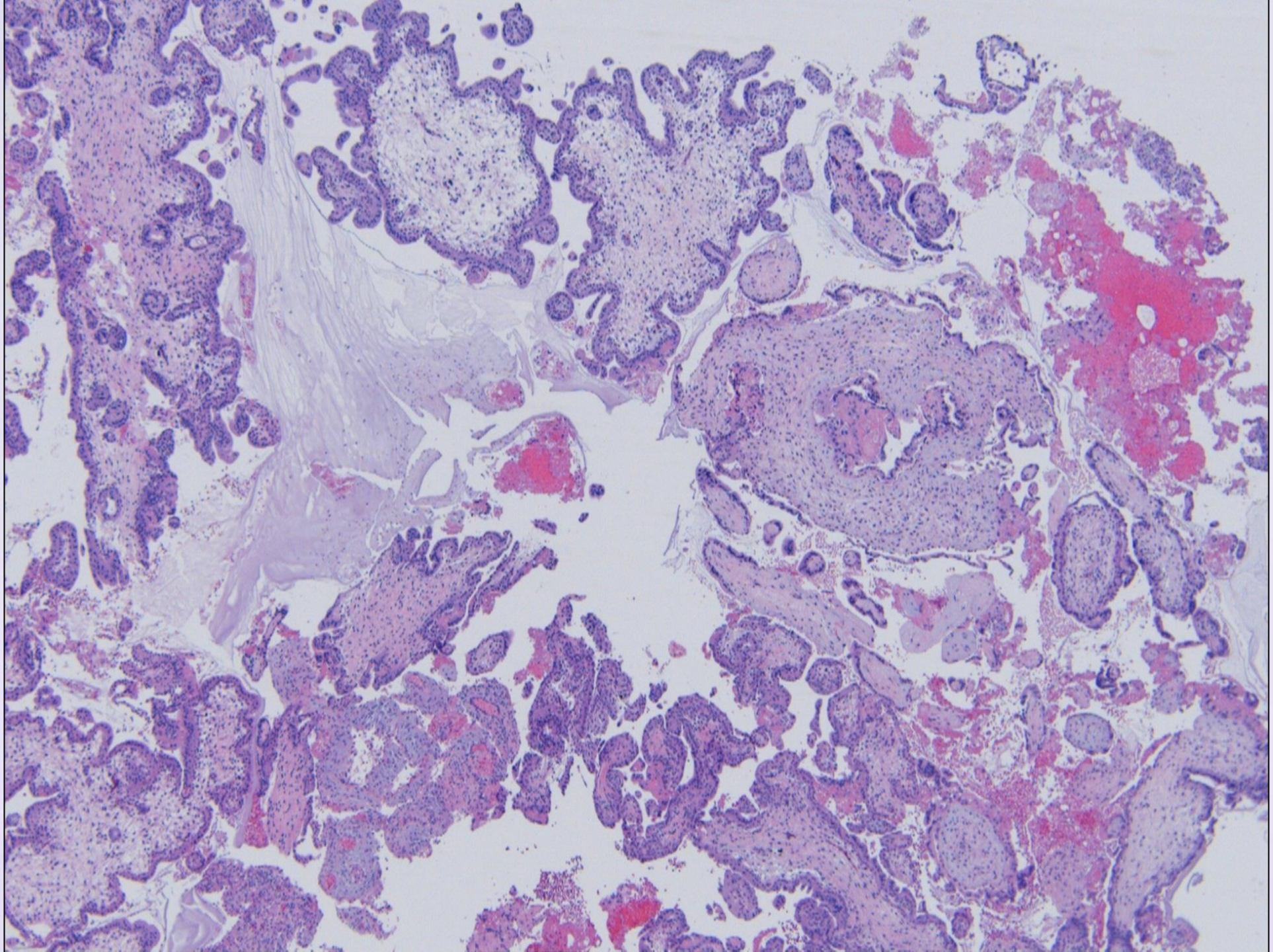
Partial Hydatidiform Mole
Gross

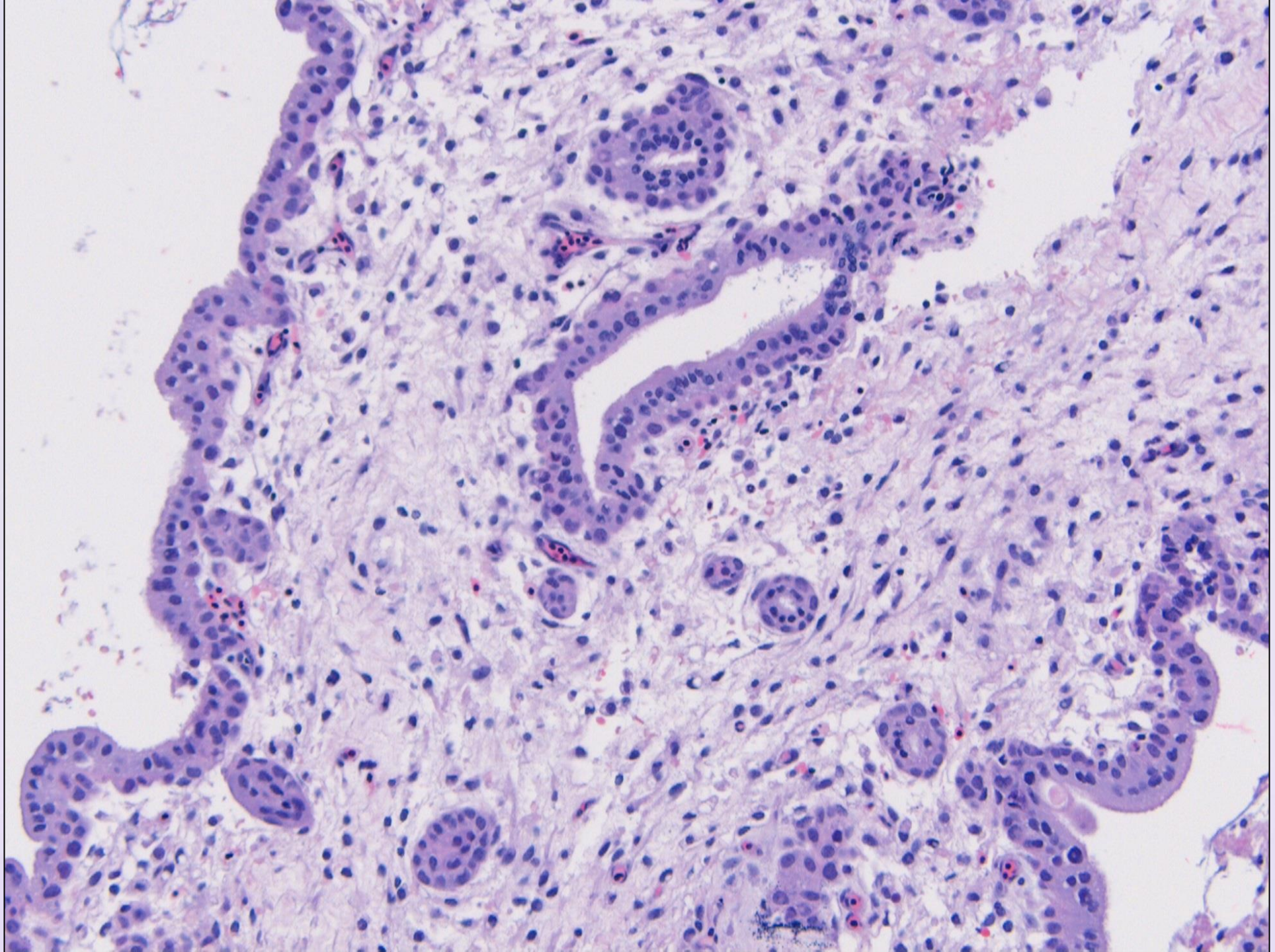
- Gross evaluation
  - Difficult to recognize
  - Normal to mild hydropic change
  - Fetal parts or intact fetus present

Partial Hydatidiform Mole
Histology

Two separate villous populations

- Normal sized but fibrotic villi
- Enlarged villi with mild hydropic change
  - Mild trophoblastic hyperplasia
  - Peripheral scalloping
  - Trophoblastic pseudoinclusions
  - Fetal parts present (fetal structures or nucleated RBCs)





Hydatidiform Moles
Clinical Consequences

Complete hydatidiform mole

- Persistent GTD – 15-20%
- Choriocarcinoma – 2-3%
- Increased risk of subsequent CHM
- Follow β-hCG
- **Avoid pregnancy for 12 months**

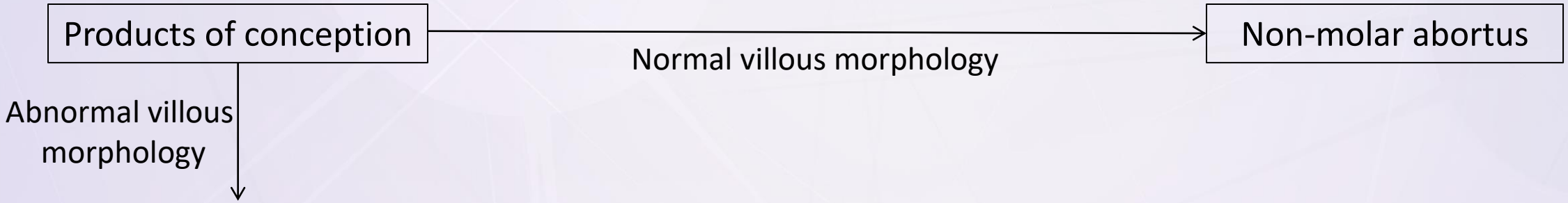
Partial hydatidiform mole

- Persistent GTD – 0.5-5%
- Choriocarcinoma – <0.5%
- Follow β-hCG
- **Avoid pregnancy for 6 months**

Problematic for women undergoing infertility treatment or women with advanced maternal age

Hydatidiform Moles

Diagnosis

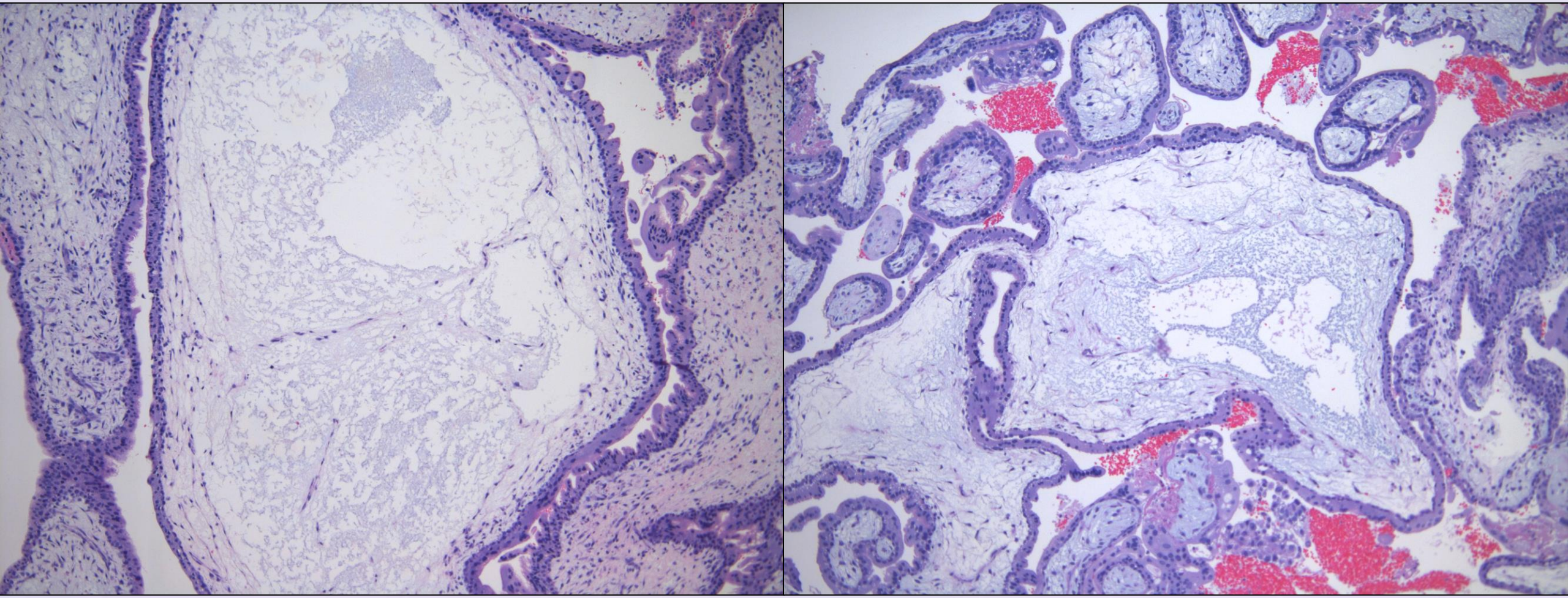


Abnormal Villous Morphology

- Hydropic change

Abnormal Villous Morphology

Hydropic change

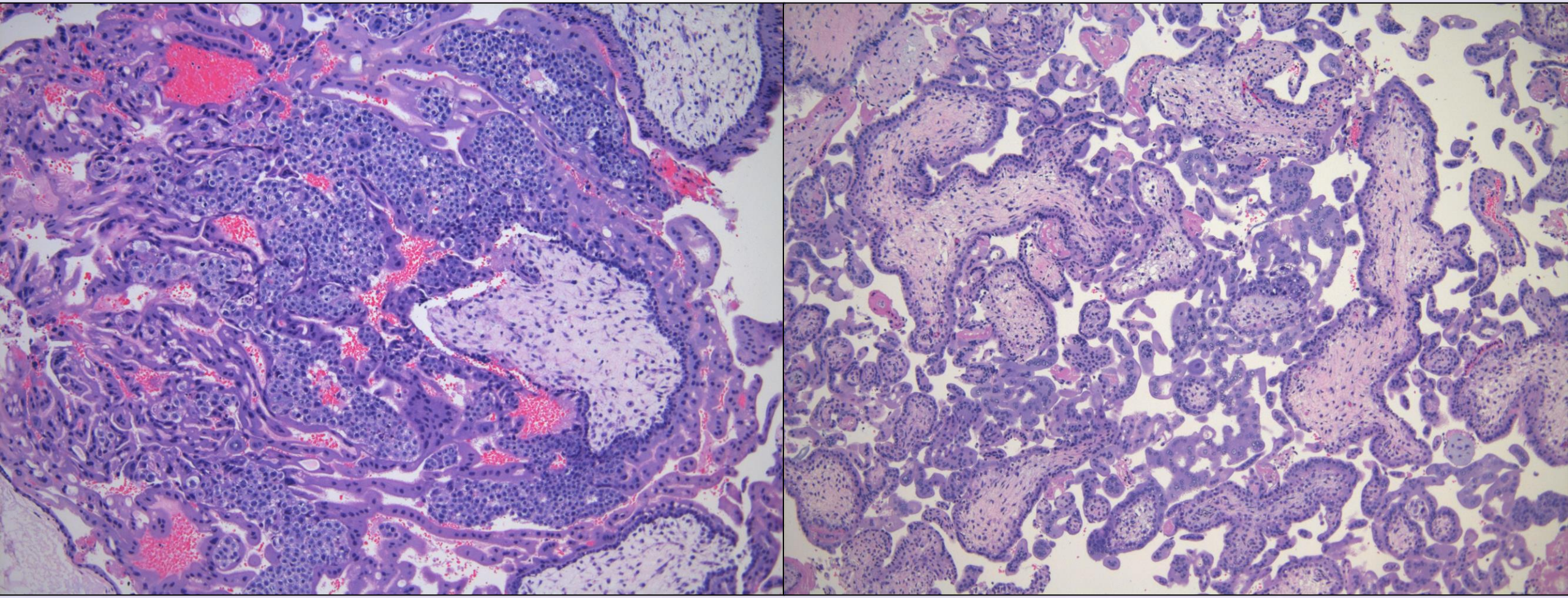


Abnormal Villous Morphology

- Hydropic change
- Unusual/peripheral trophoblastic hyperplasia

Abnormal Villous Morphology

Trophoblastic hyperplasia

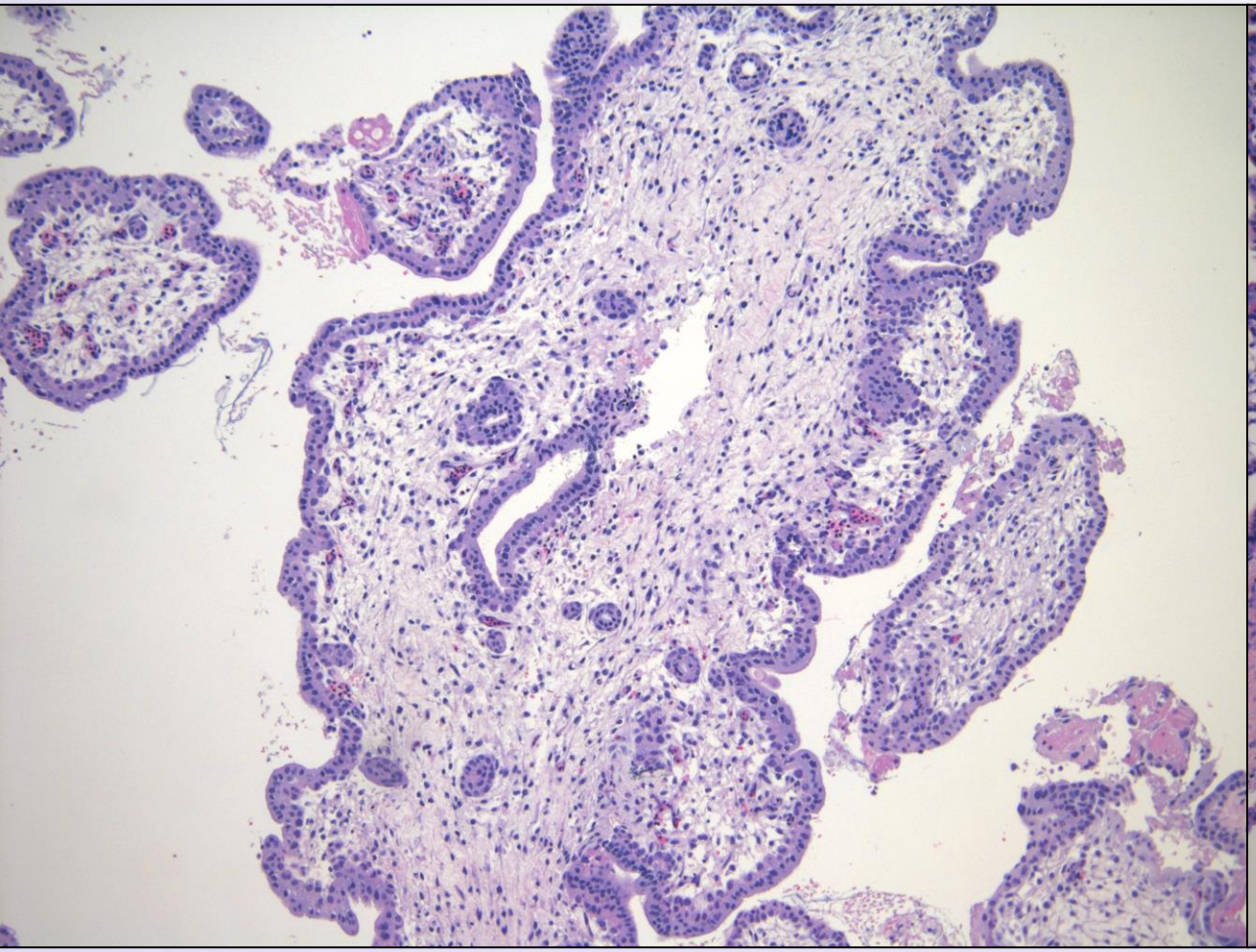


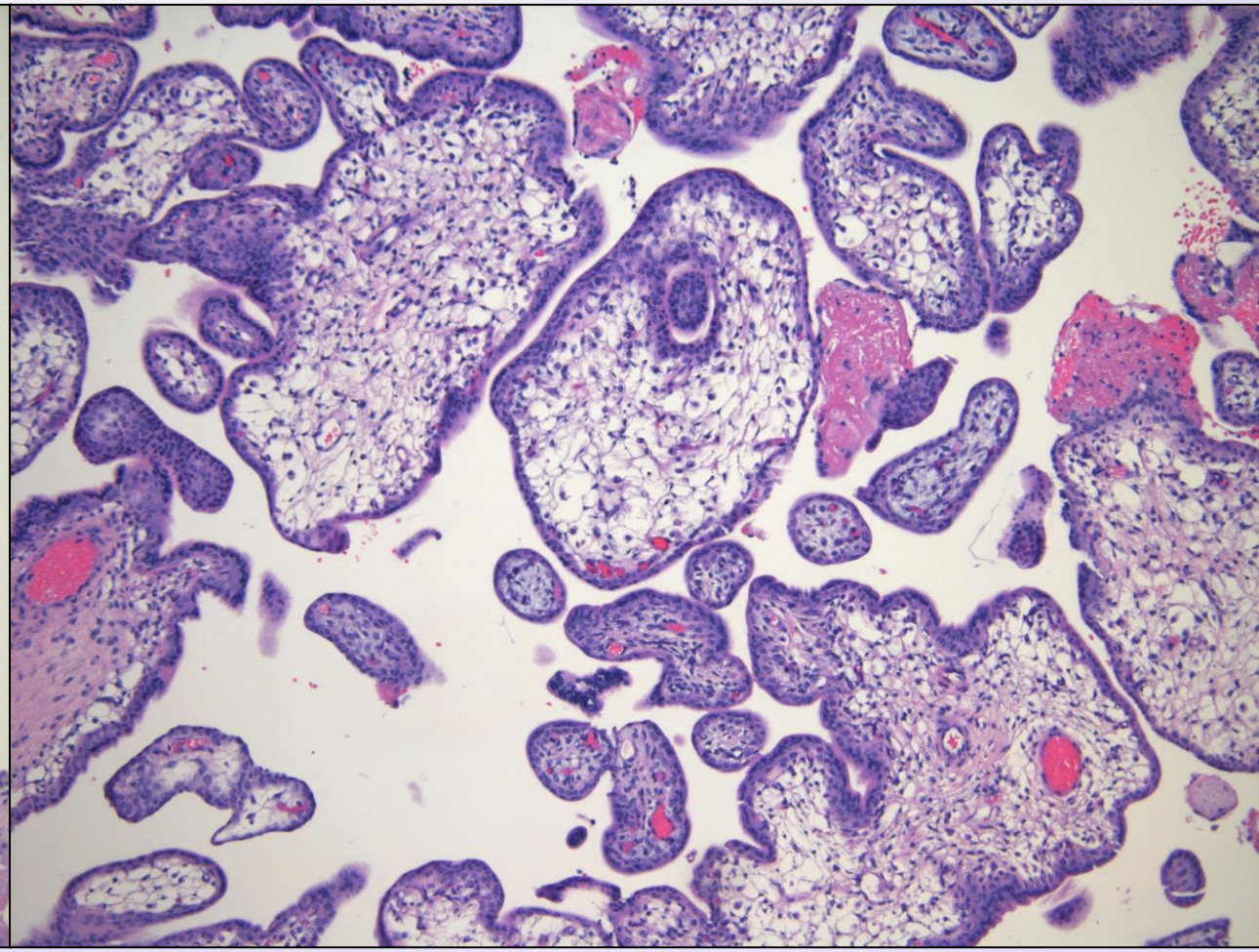
Abnormal Villous Morphology

- Hydropic change
- Unusual/peripheral trophoblastic hyperplasia
- Peripheral scalloping and trophoblastic pseudoinclusions

Abnormal Villous Morphology

Scalloping and Pseudoinclusions



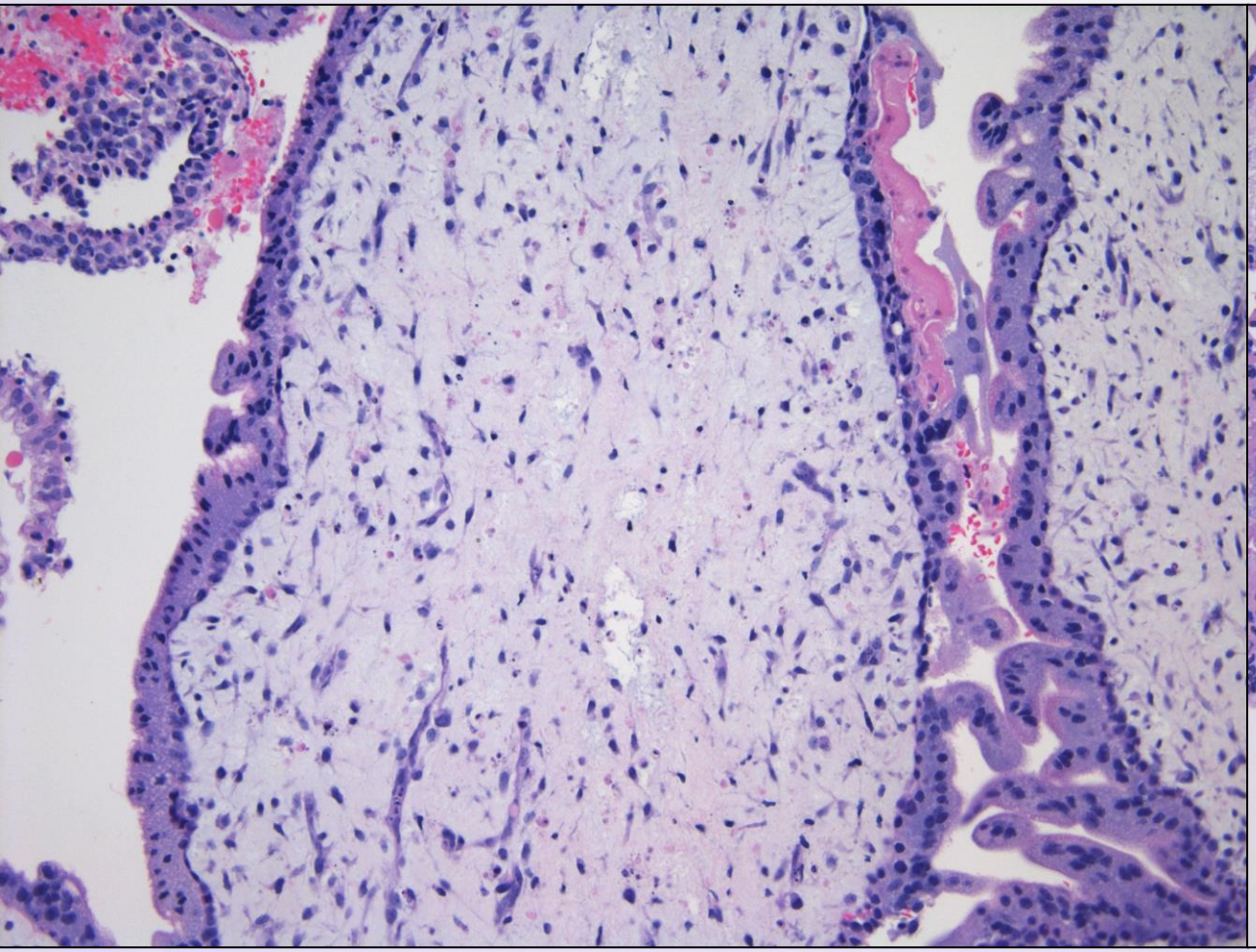


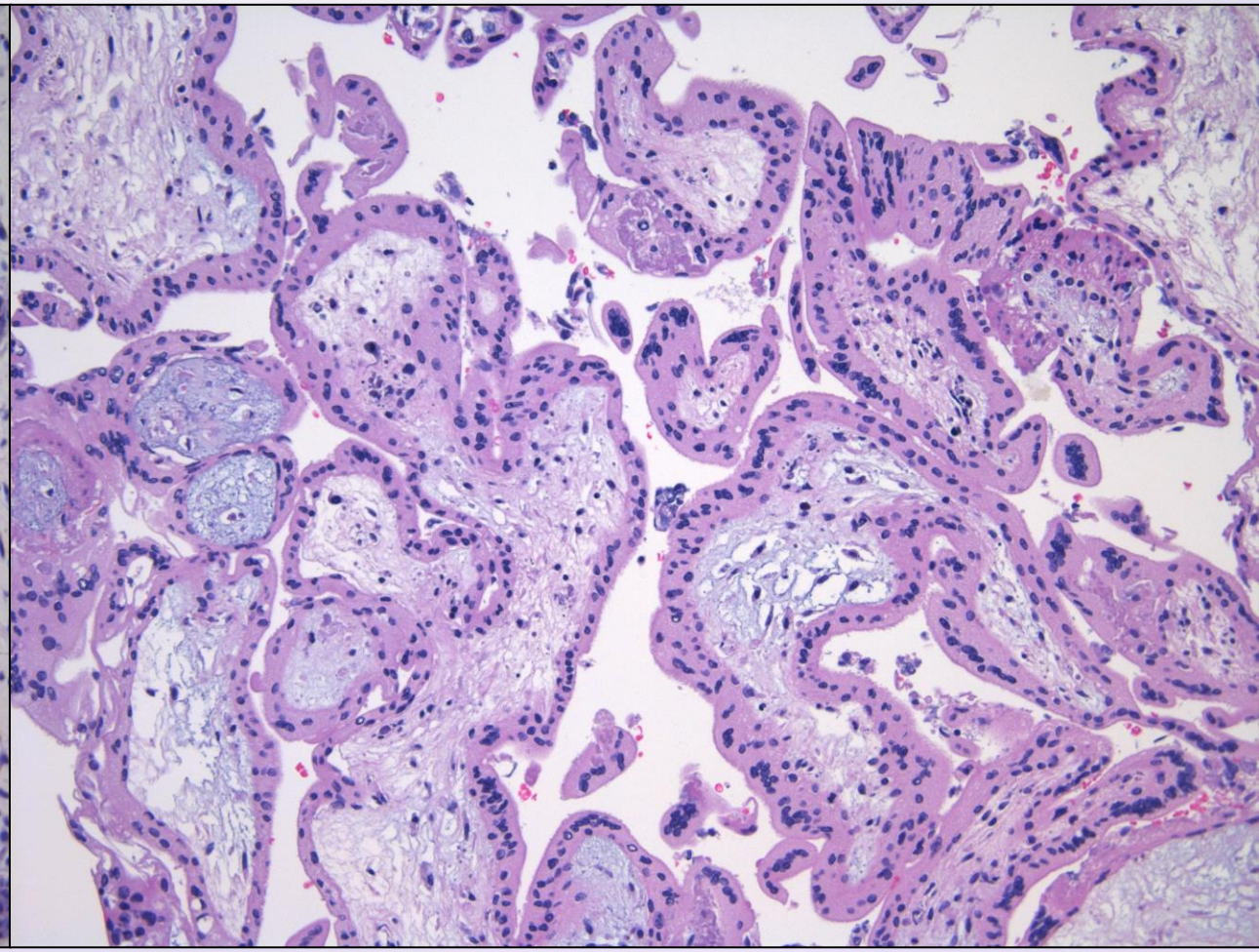
Abnormal Villous Morphology

- Hydropic change
- Unusual/peripheral trophoblastic hyperplasia
- Peripheral scalloping and trophoblastic pseudoinclusions
- Unusual stromal change (myxoid stroma, karyorrhectic debris, abortive vessels formation)

Abnormal Villous Morphology

Stromal Change



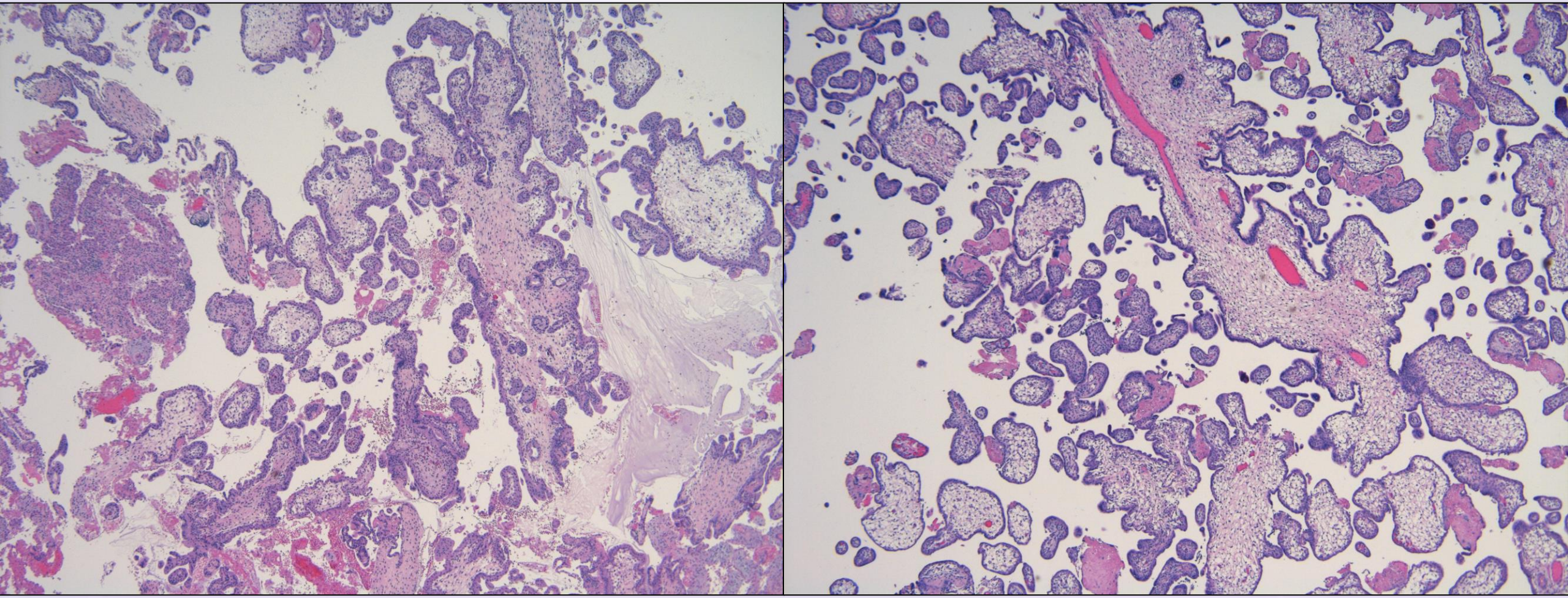


Abnormal Villous Morphology

- Hydropic change
- Unusual/peripheral trophoblastic hyperplasia
- Peripheral scalloping and trophoblastic pseudoinclusions
- Unusual stromal change (myxoid stroma, karyorrhectic debris, abortive vessels formation)
- Two distinct villous populations

Abnormal Villous Morphology

Dual villous population

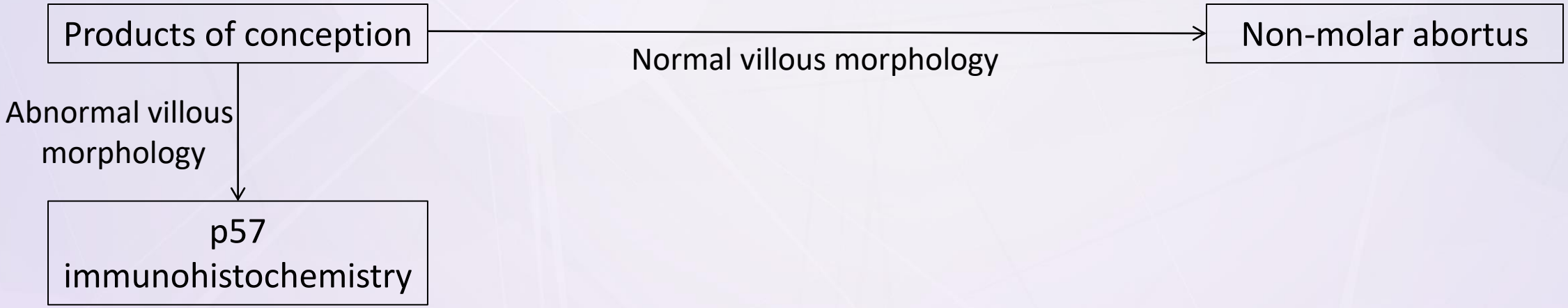


Abnormal Villous Morphology

Abnormal villous features in early hydatidiform moles can be very subtle

Early CHM and PHM can have very similar morphologic appearance

Hydatidiform Moles
Diagnosis

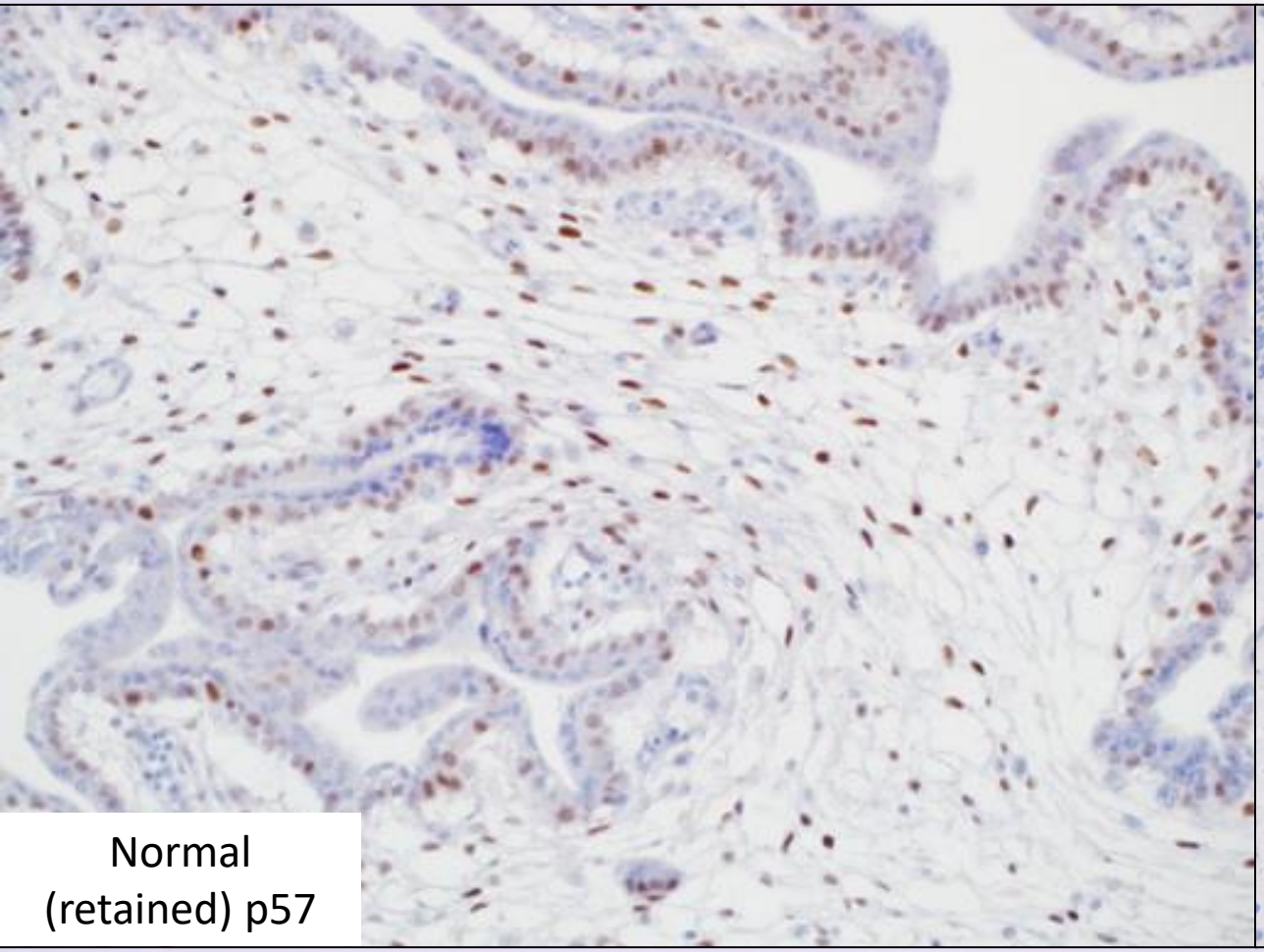


p57 Immunohistochemistry

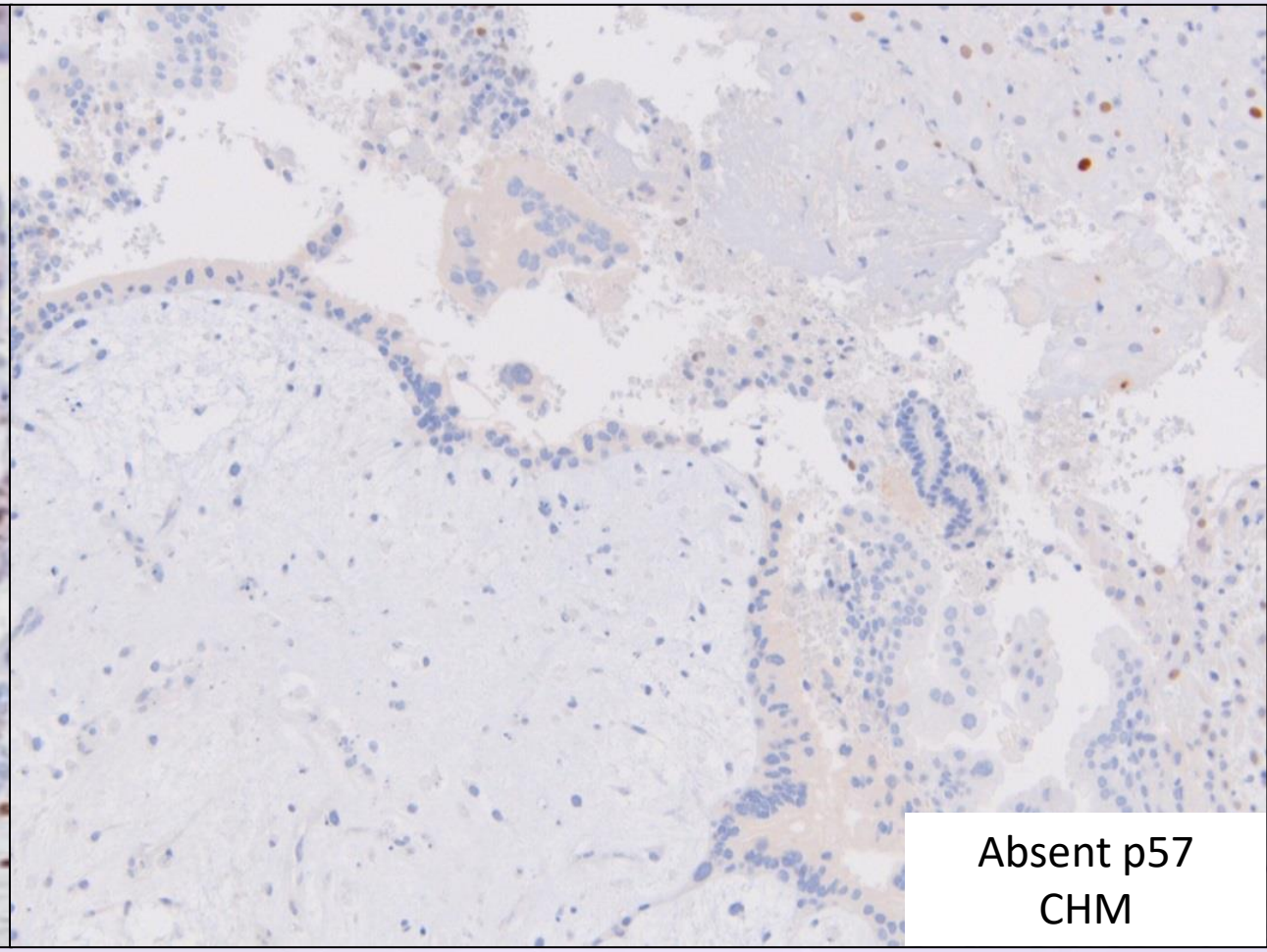
- p57 (*CDKN1C*) is located on chromosome 11p15.5
- Paternally imprinted, maternally expressed
- Normally expressed in villous stromal cells and cytotrophoblast
- Loss of p57 staining – lack of maternal DNA

Diagnosis of CHM

p57 Immunohistochemistry

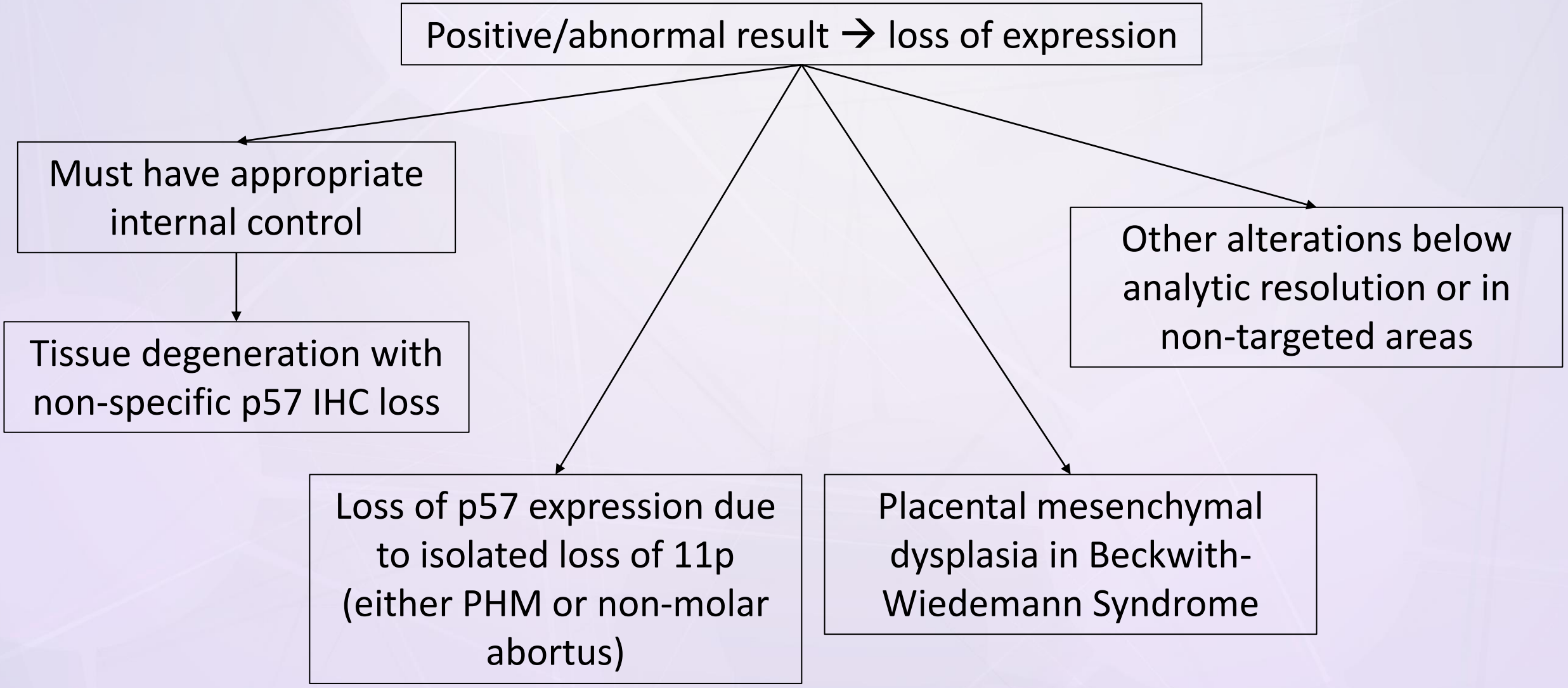


Normal (retained) p57

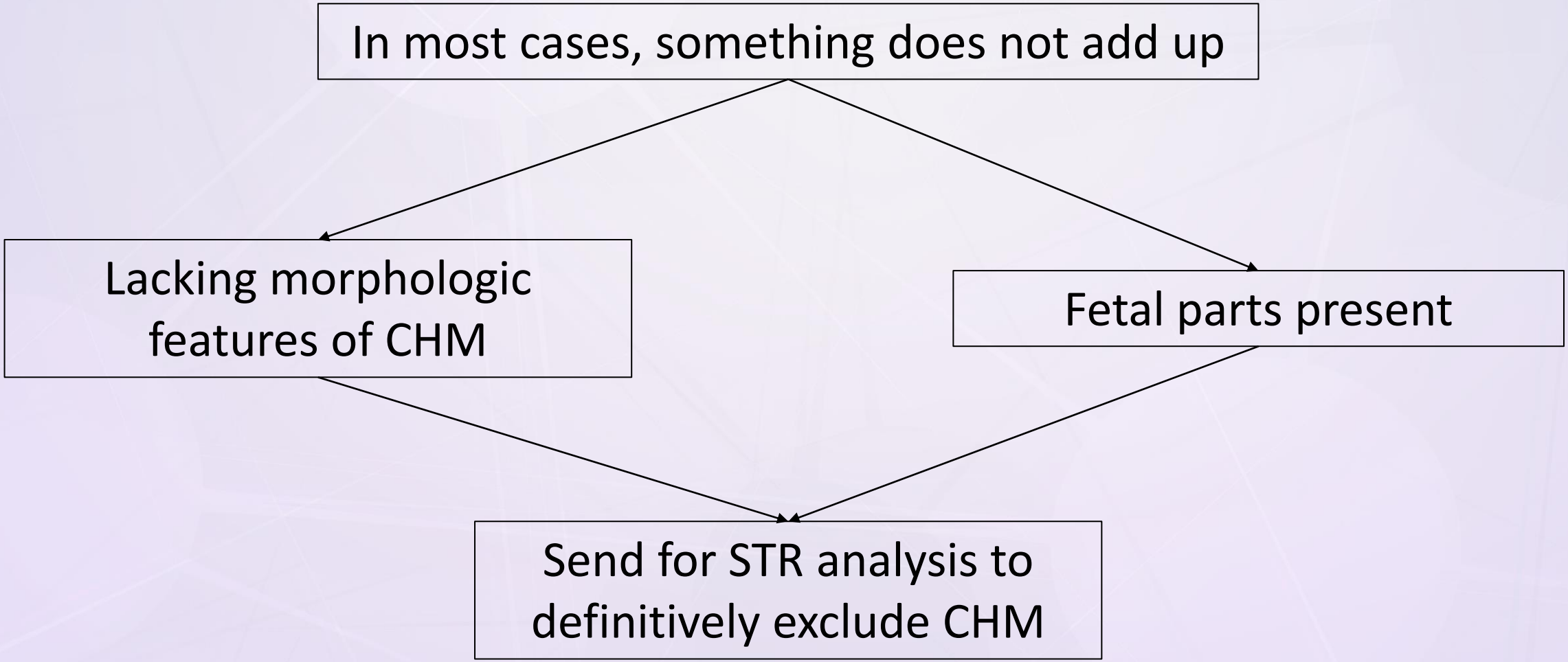


Absent p57 CHM

p57 Loss in non-CHM



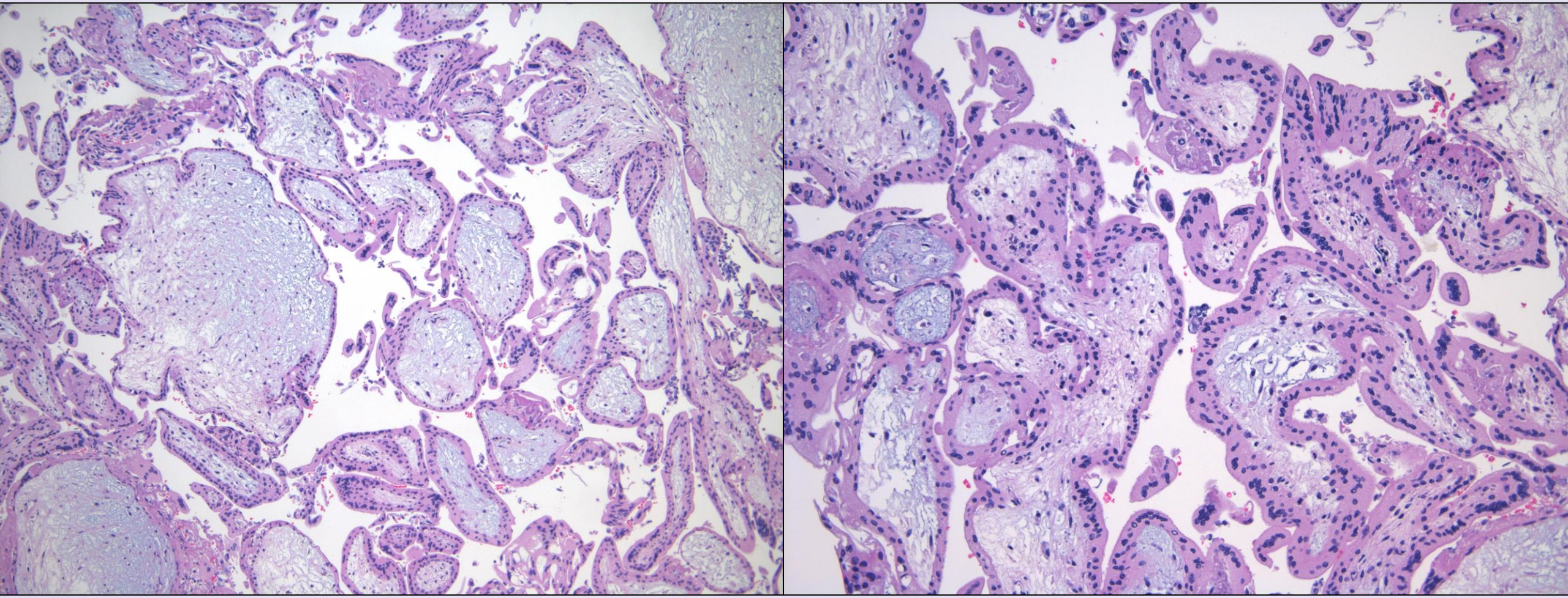
p57 Loss in non-CHM



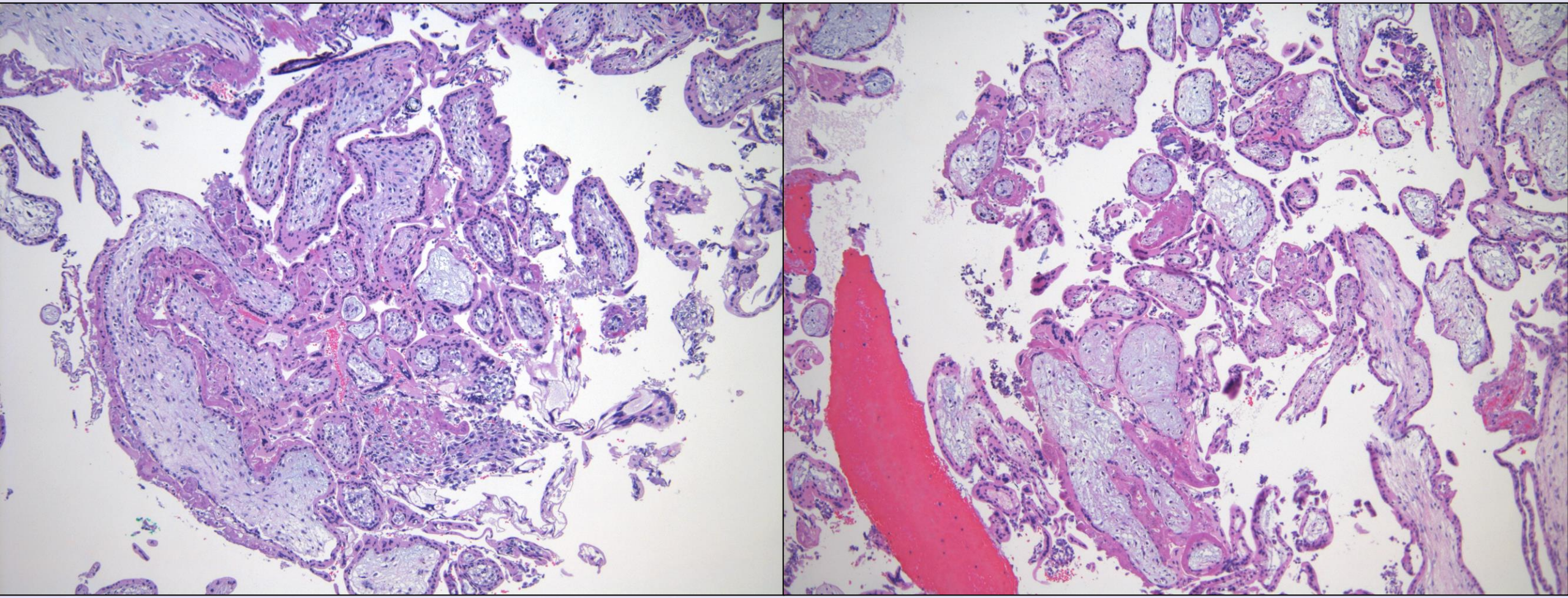
Case 1

38-year-old patient with missed abortion at 10 weeks, undergoing dilation and curettage

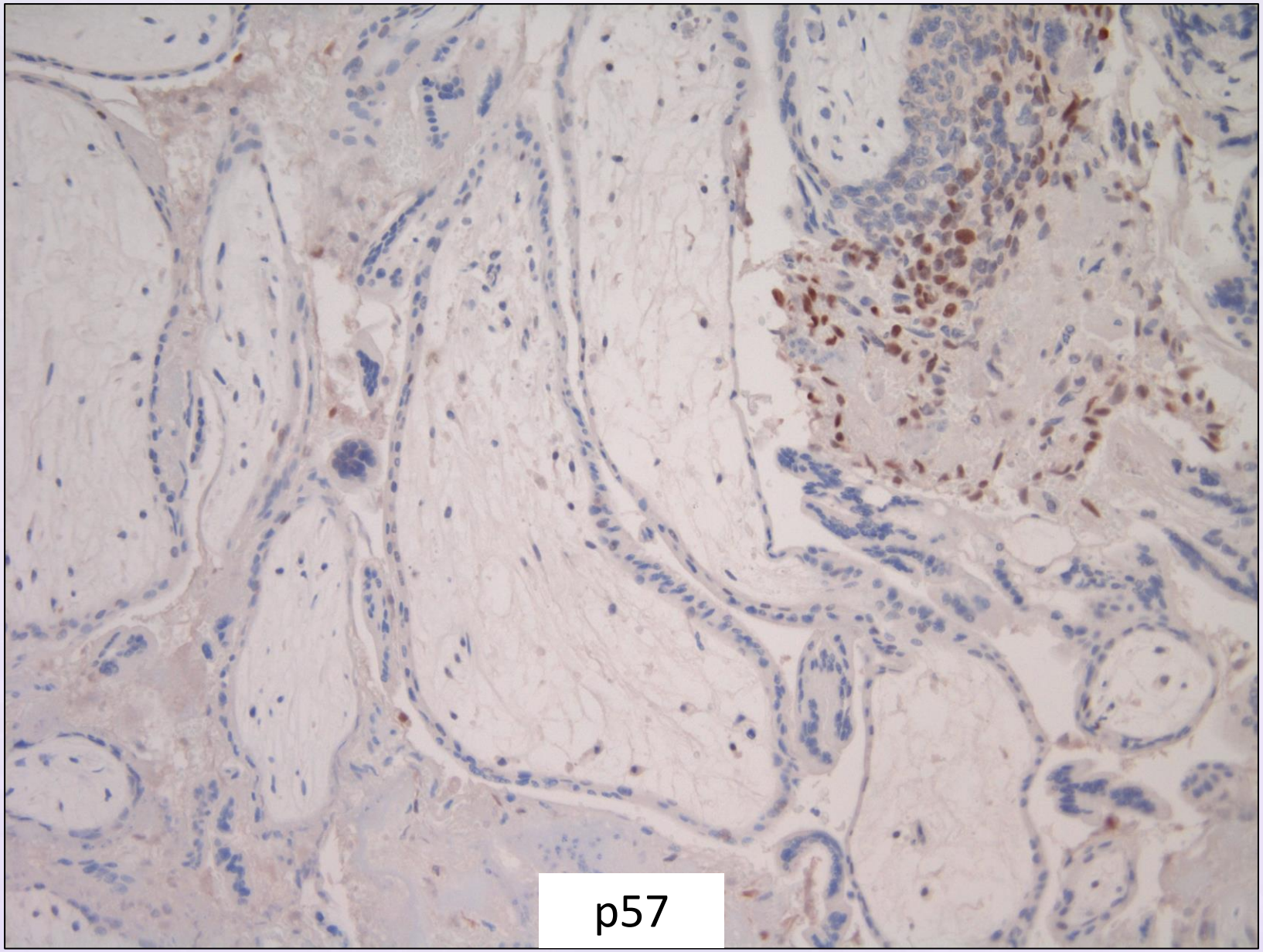
Case 1



Case 1



Case 1



p57

Case 1

Some abnormal villous morphology but not convincing for CHM

↓

p57 essentially lost in cytotrophoblast and villous stromal cells

Decent internal control

↓

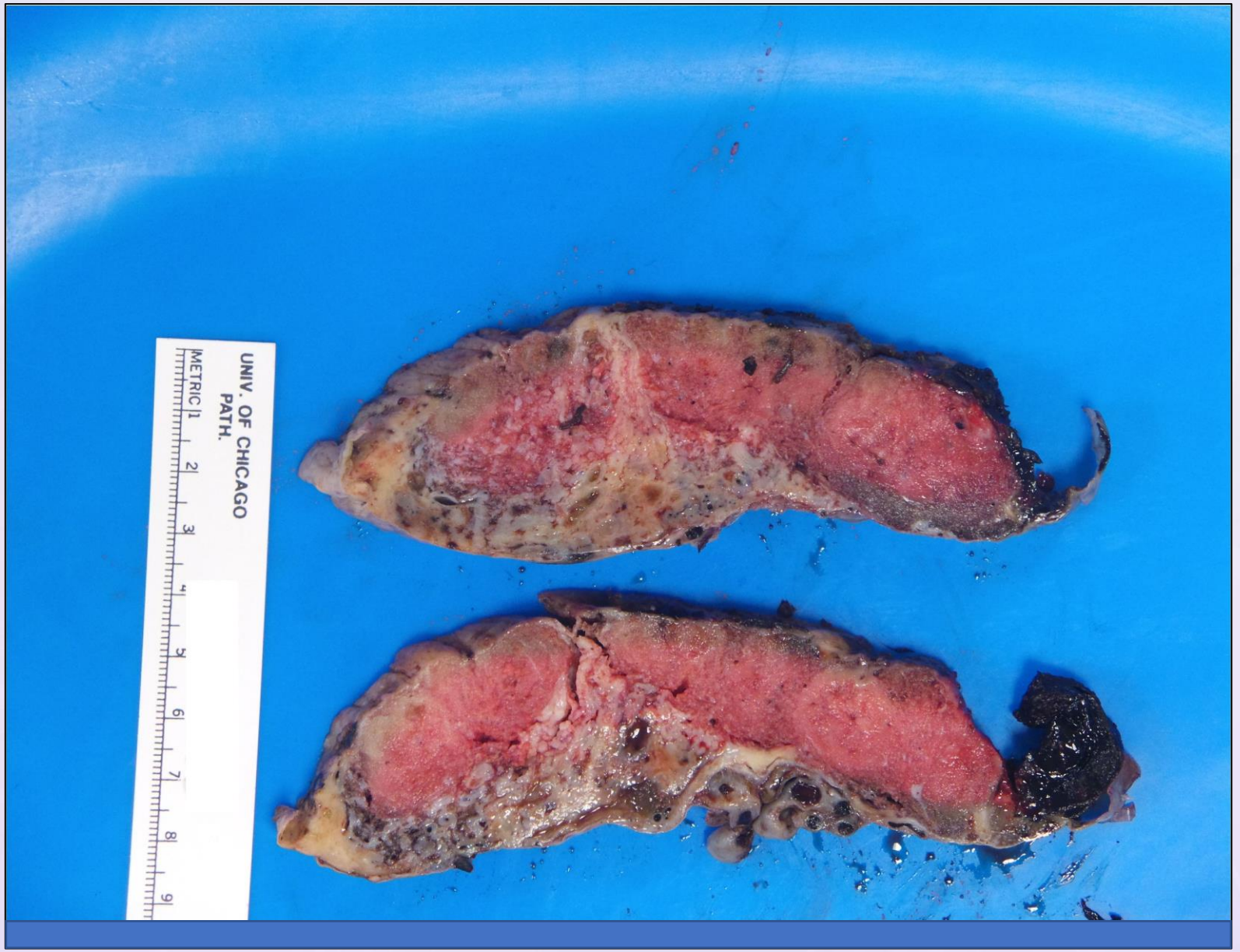
STR analysis – balanced biparental diploid

NOT Complete hydatidiform mole

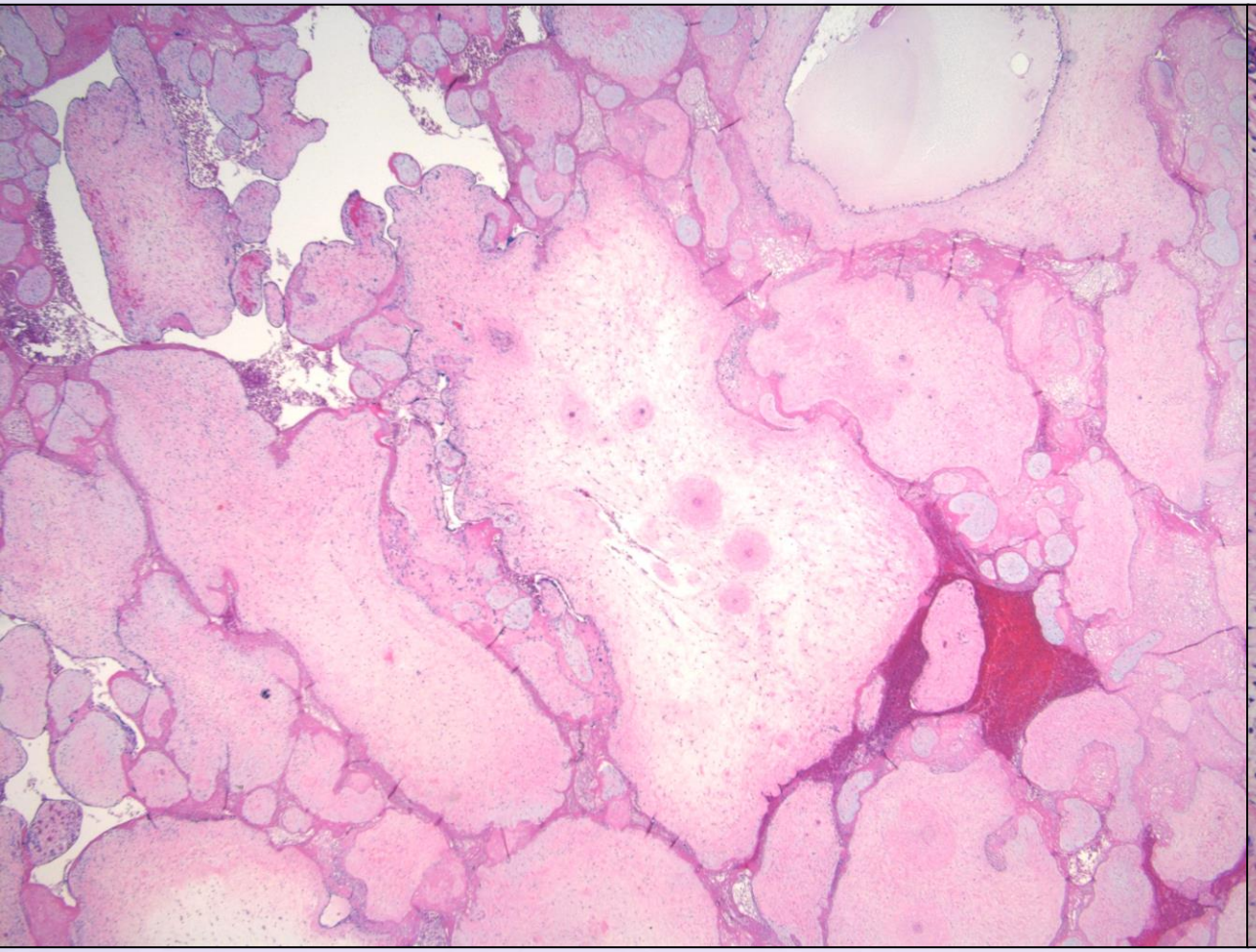
Case 2

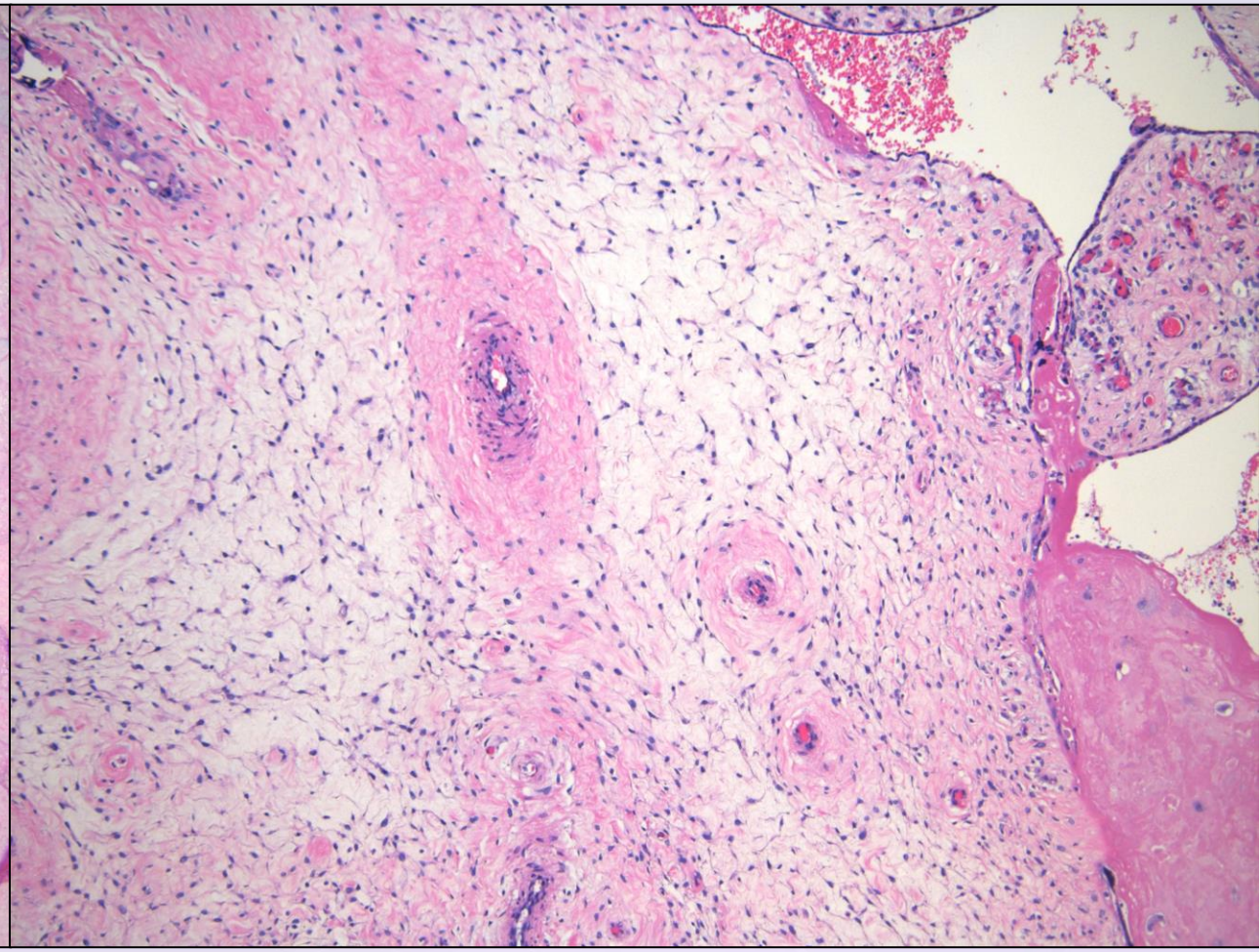
22-year-old patient at 27 weeks gestation, undergoing vaginal delivery for IUFD. Pregnancy complicated by IUGR and ultrasonographic imaging concerning for partial hydatidiform mole versus large chorangioma. Cell-free DNA demonstrated normal karyotype.

Case 2

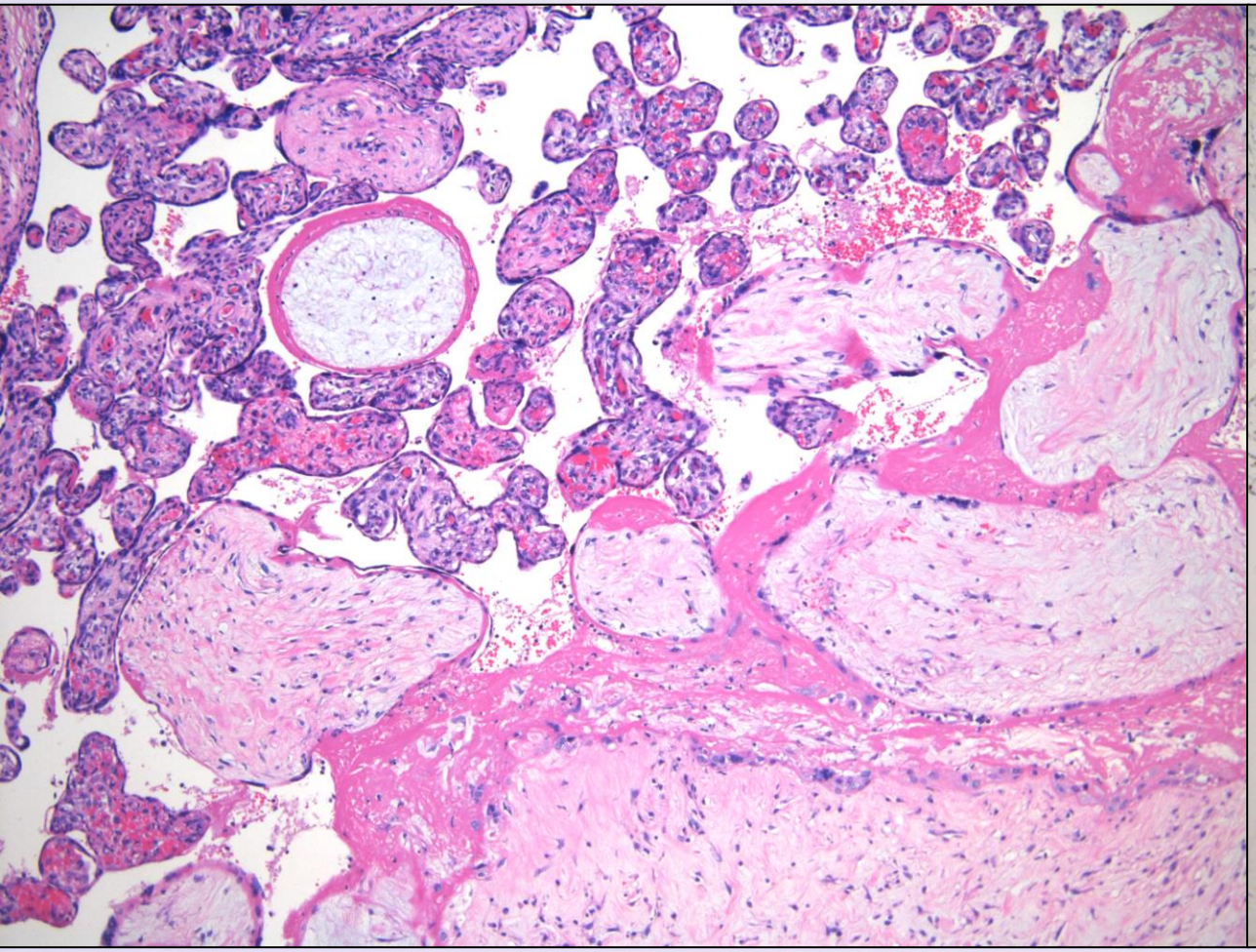


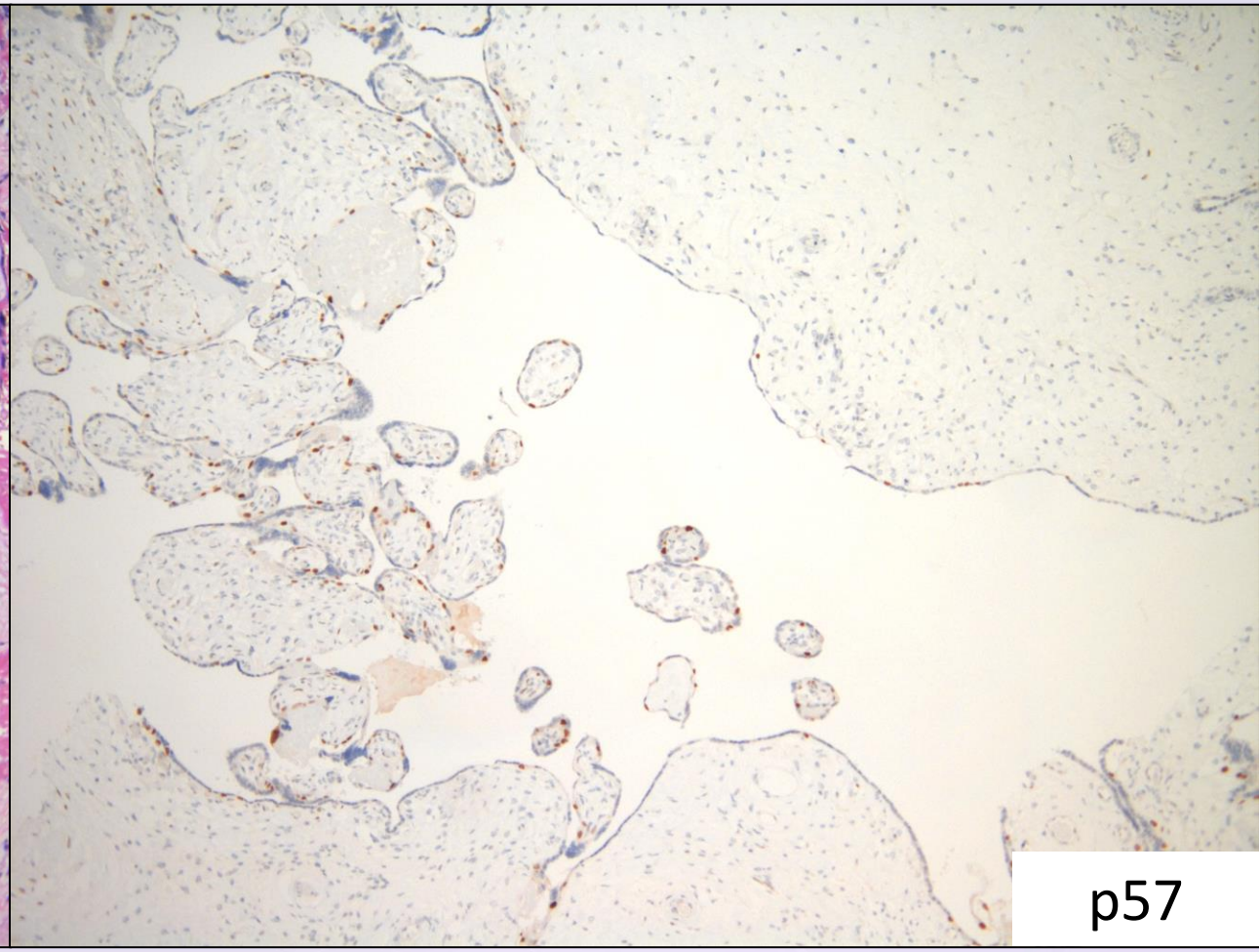
Case 2





Case 2





p57

Case 2

Abnormal villous architecture

Enlarged villi, prominent thick-walled vessels, dual villous population

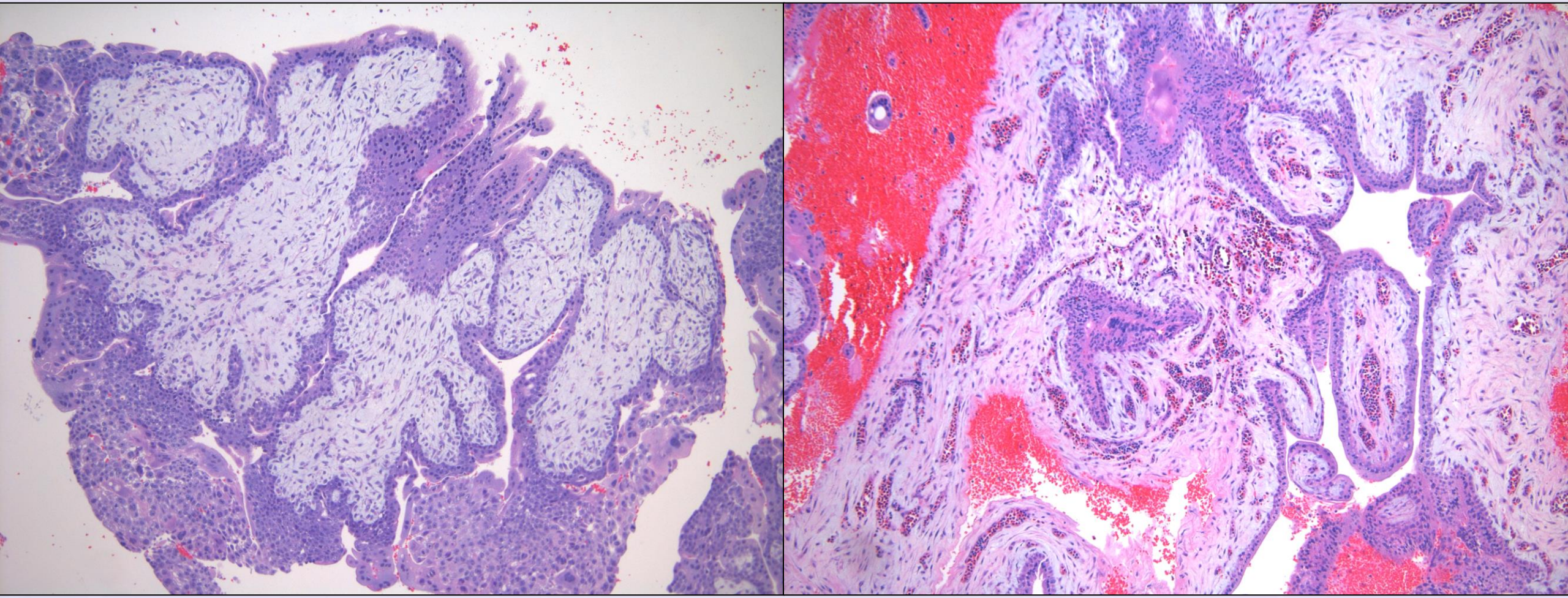
- Abnormal pattern of p57 expression (similar in both villous populations)
- Fetus present with development until week 27 and normal cfDNA karyotype
- Absence of classic CHM features (trophoblastic hyperplasia, stromal change)

Placental mesenchymal dysplasia

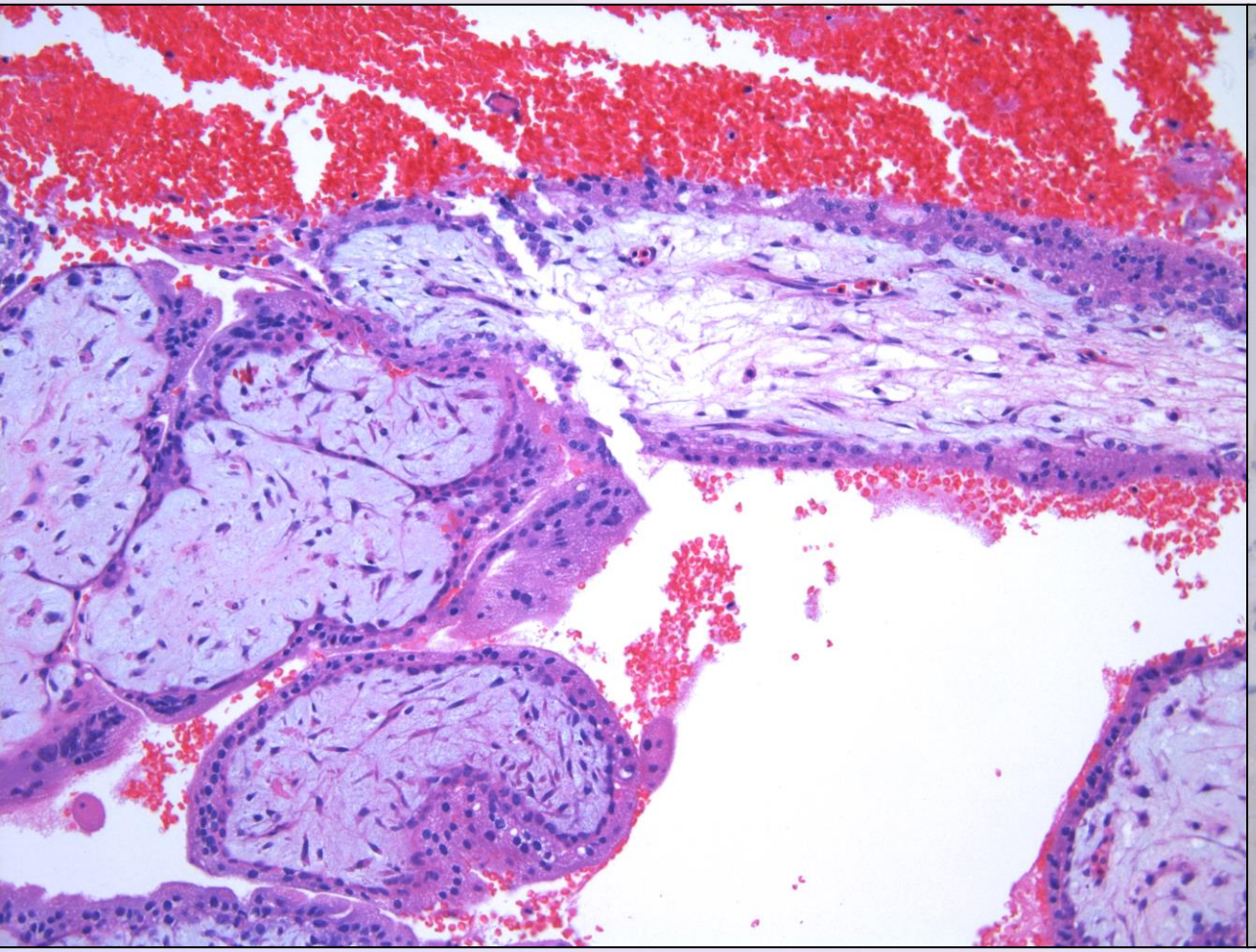
Case 3

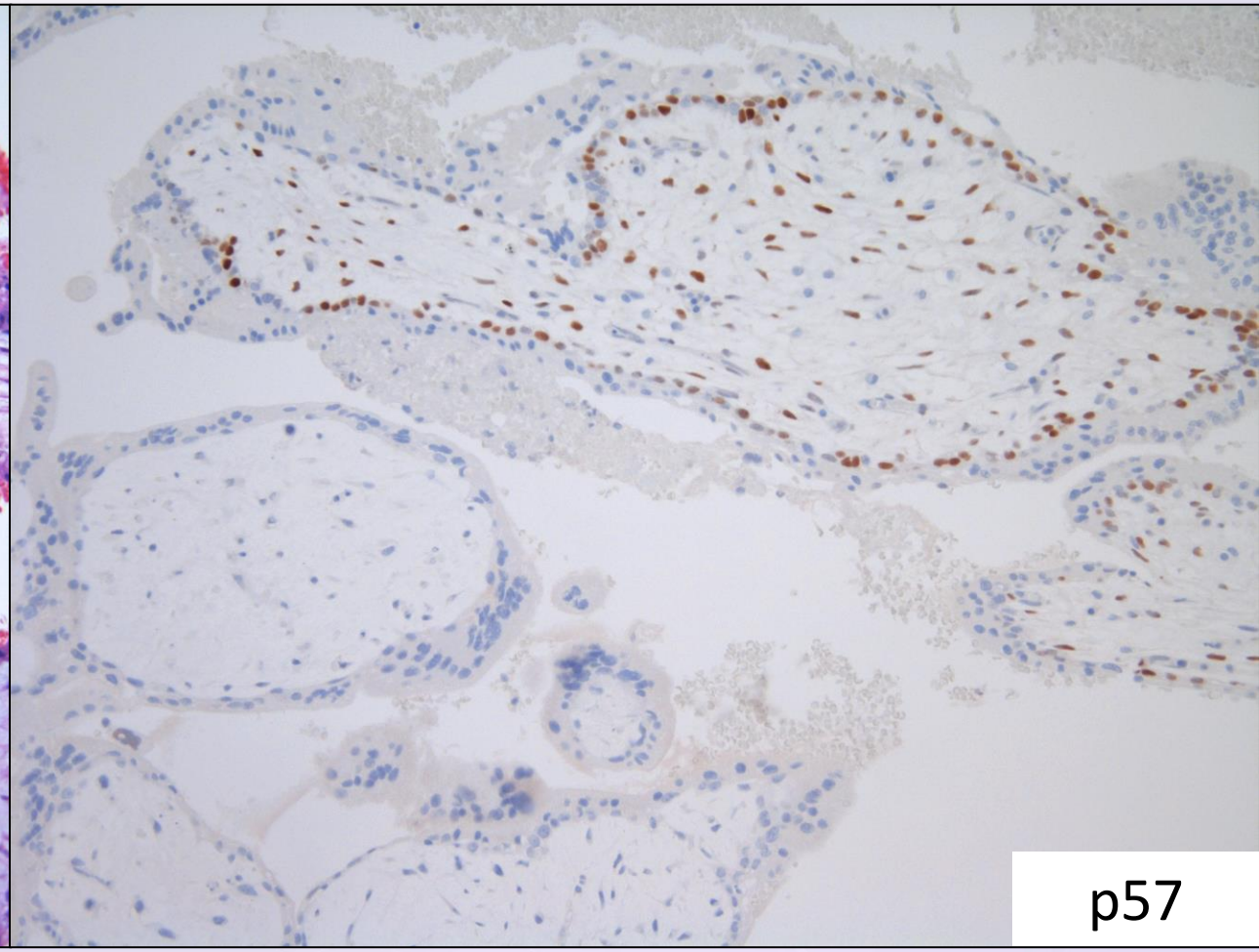
25-year-old patient with missed abortion at 8 weeks, undergoing dilation and curettage

Case 3



Case 3





p57

Case 3

Two morphologically distinct villous populations

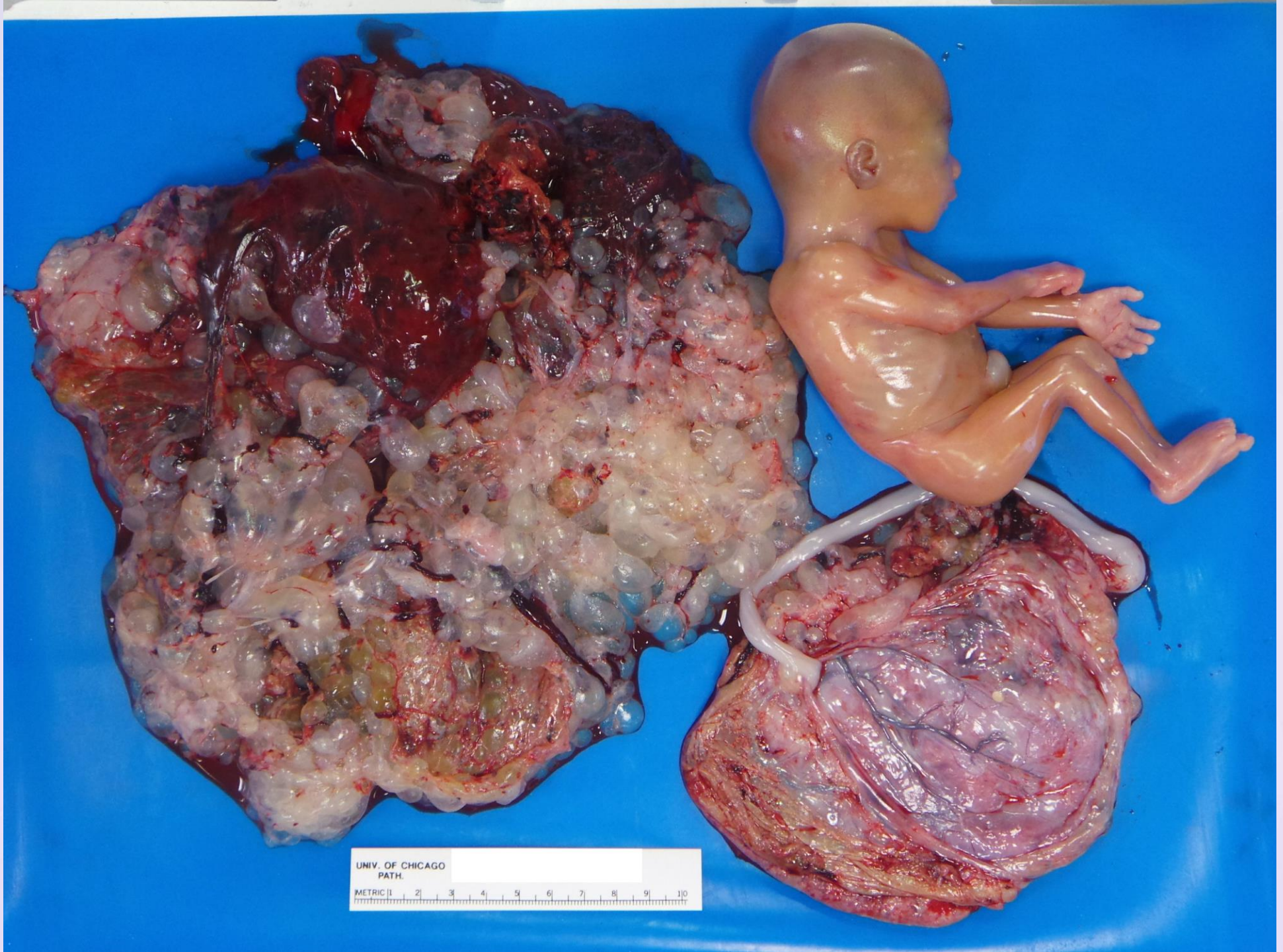
↓

One of them with classic CHM morphologic features

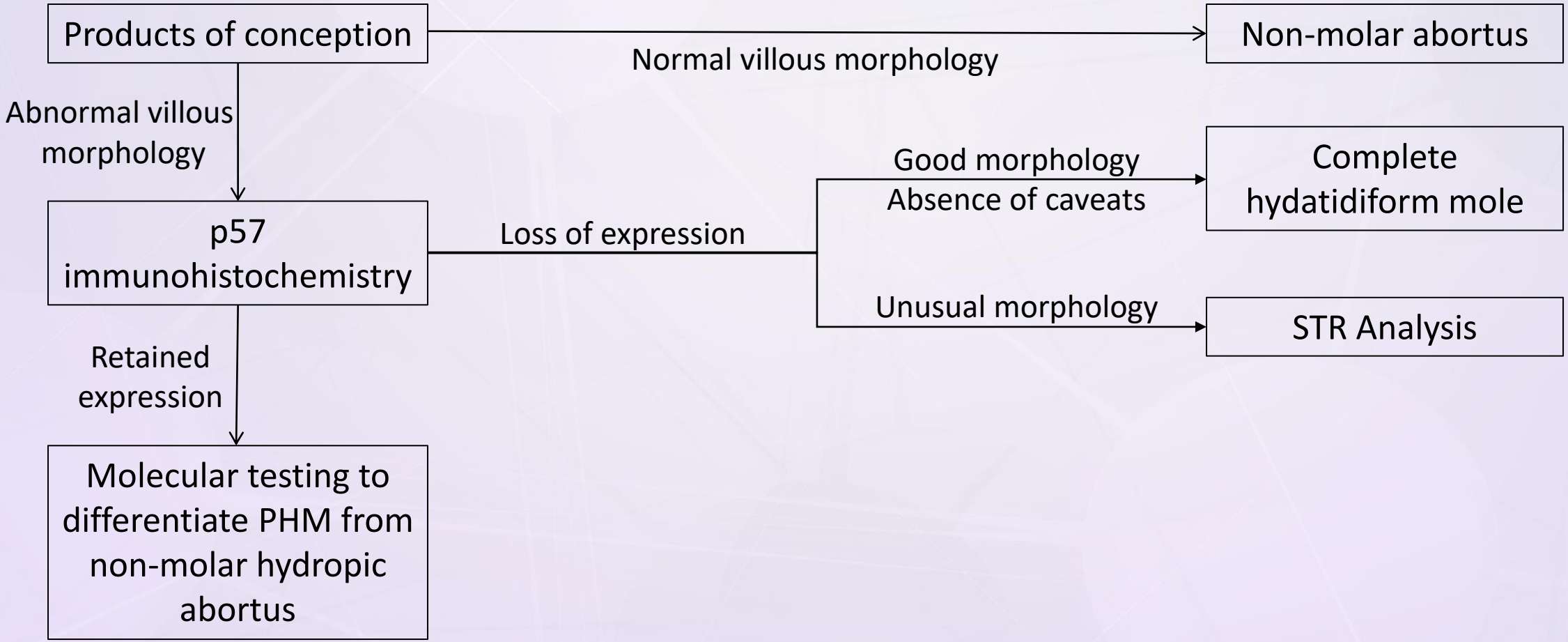
↓

p57 loss in the villi with CHM-like morphology, and retained in the second villous population (with nRBCs)

Twin pregnancy with complete hydatidiform mole component


UNIV. OF CHICAGO
PATH.
METRIC 1 2 3 4 5 6 7 8 9 10

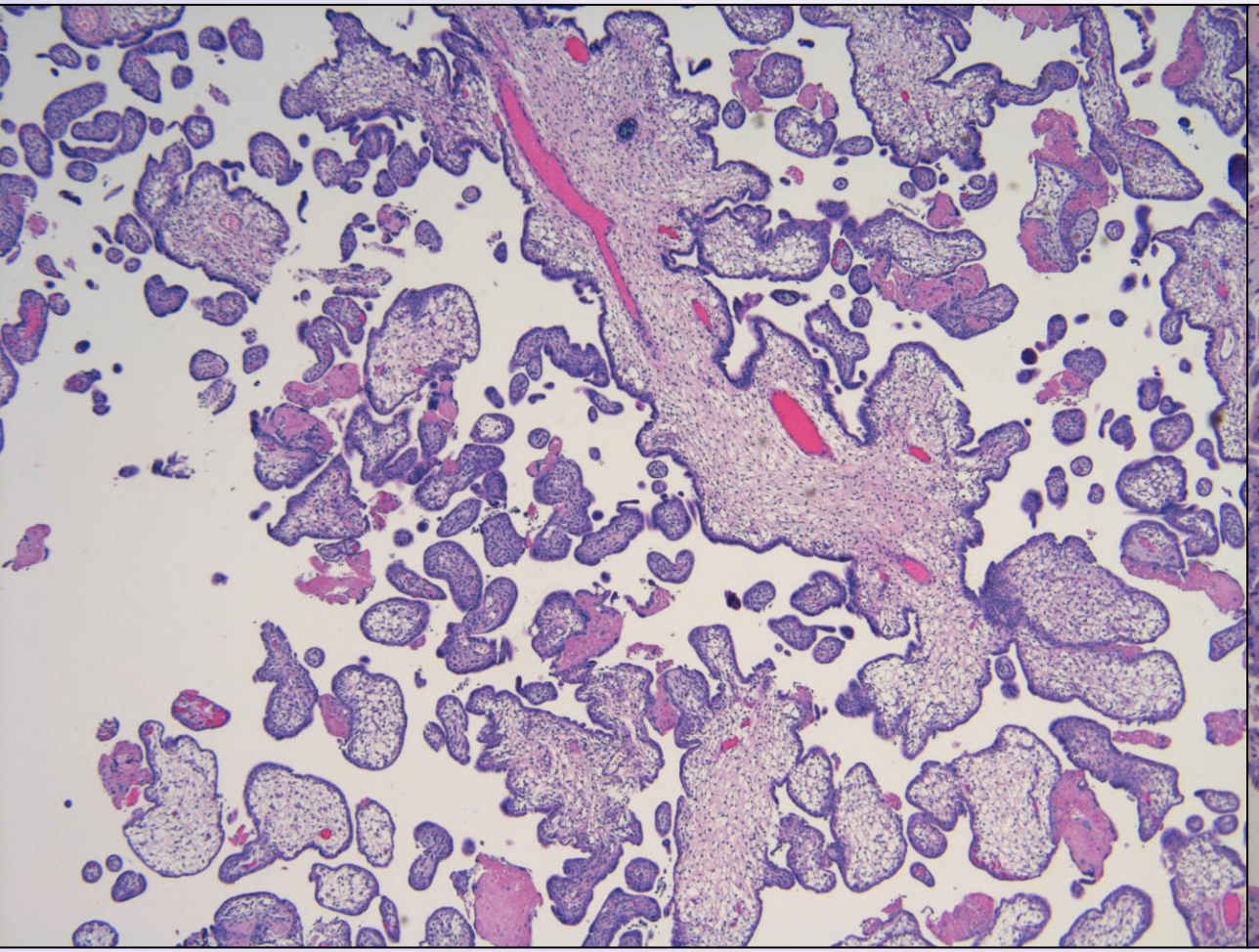
Hydatidiform Moles
Diagnosis

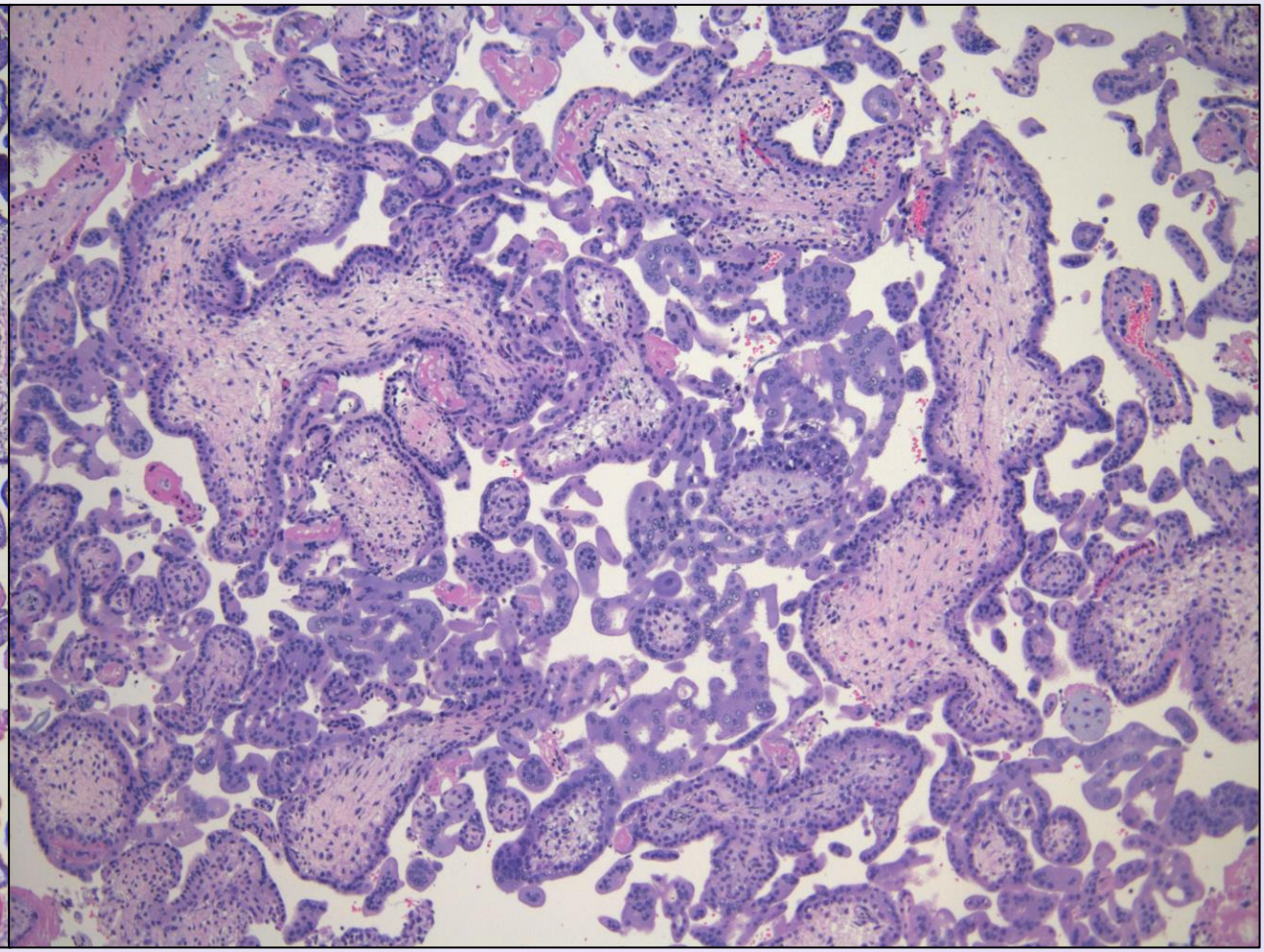


Case 4

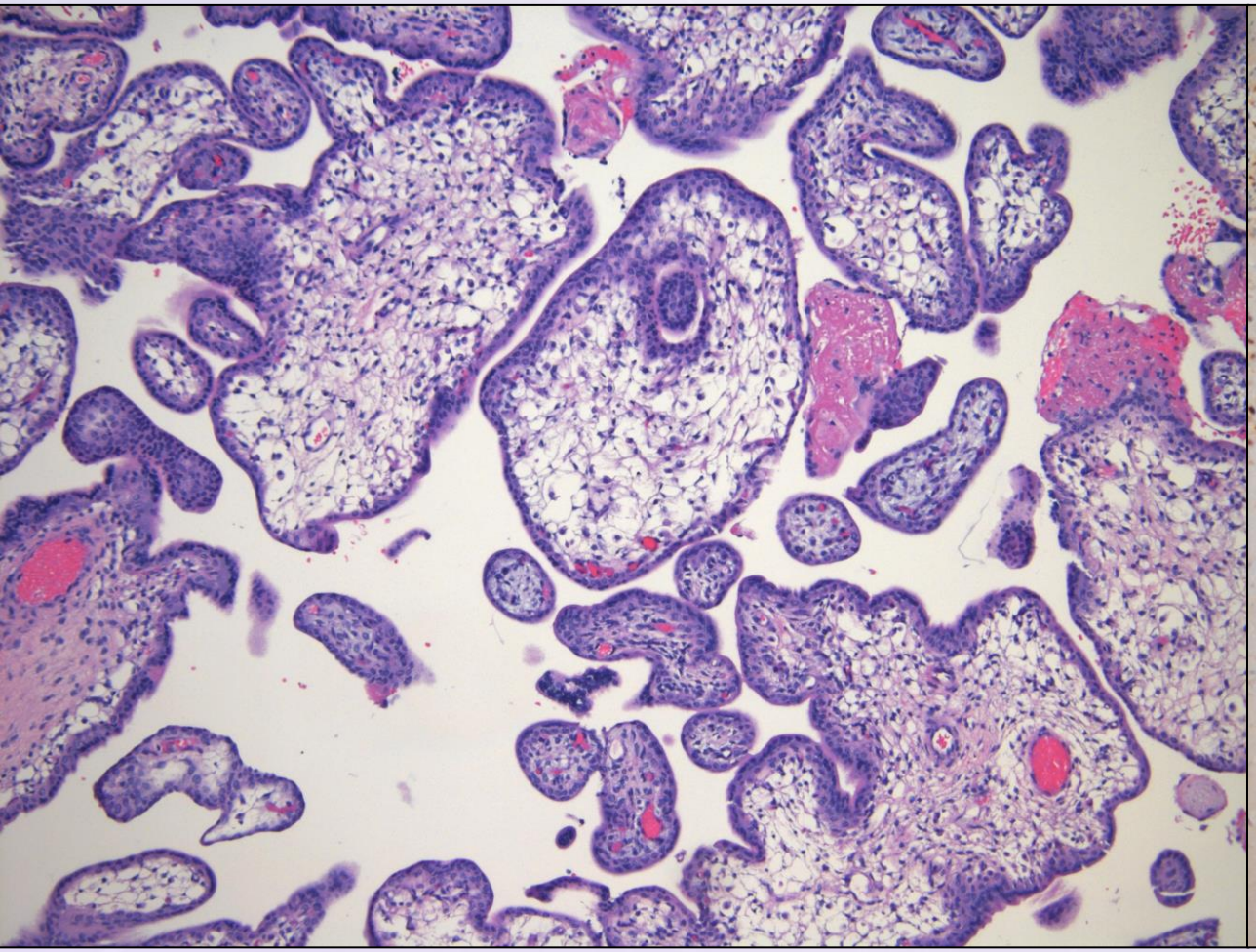
38-year-old patient with missed abortion at 10 weeks, undergoing dilation and curettage

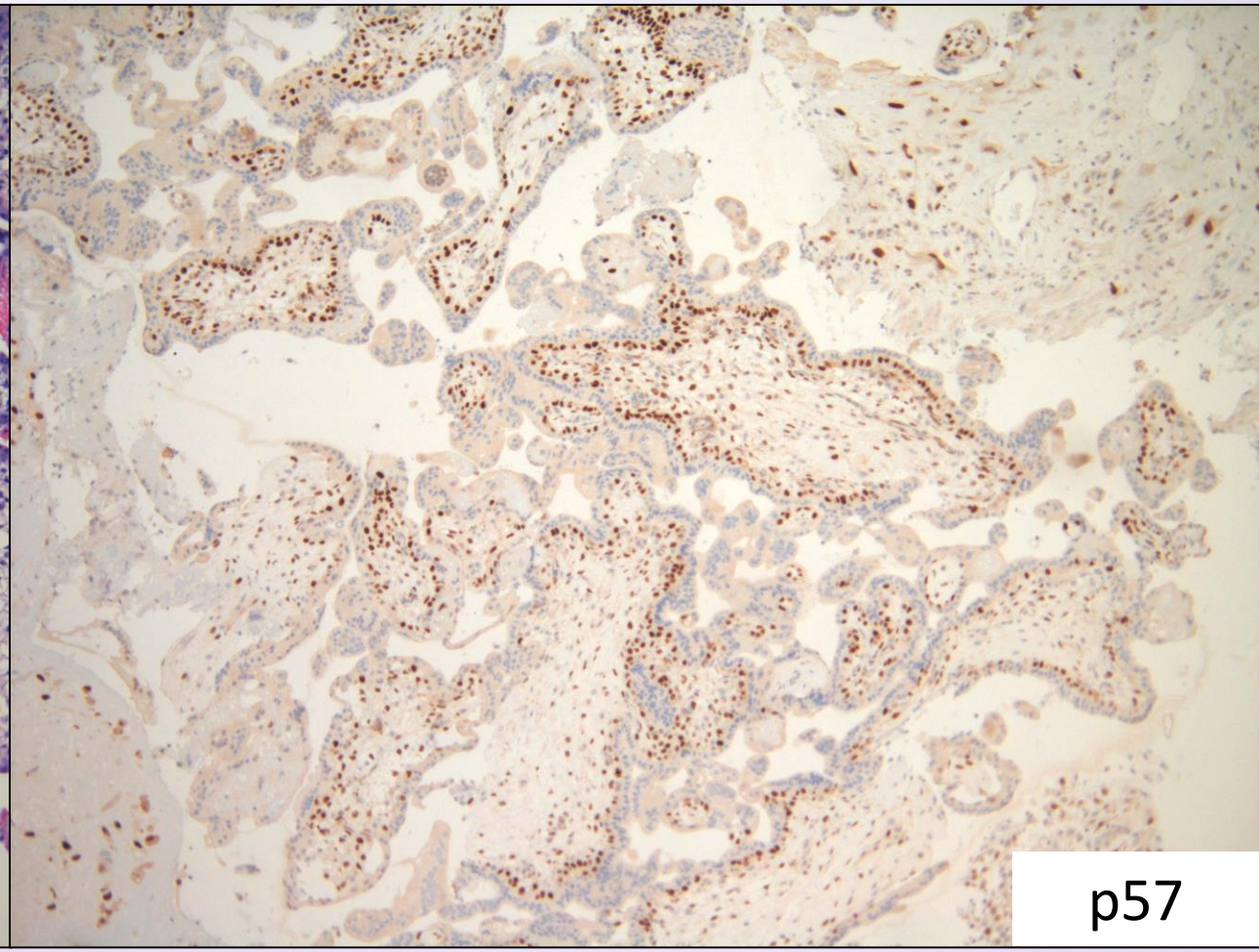
Case 4





Case 4



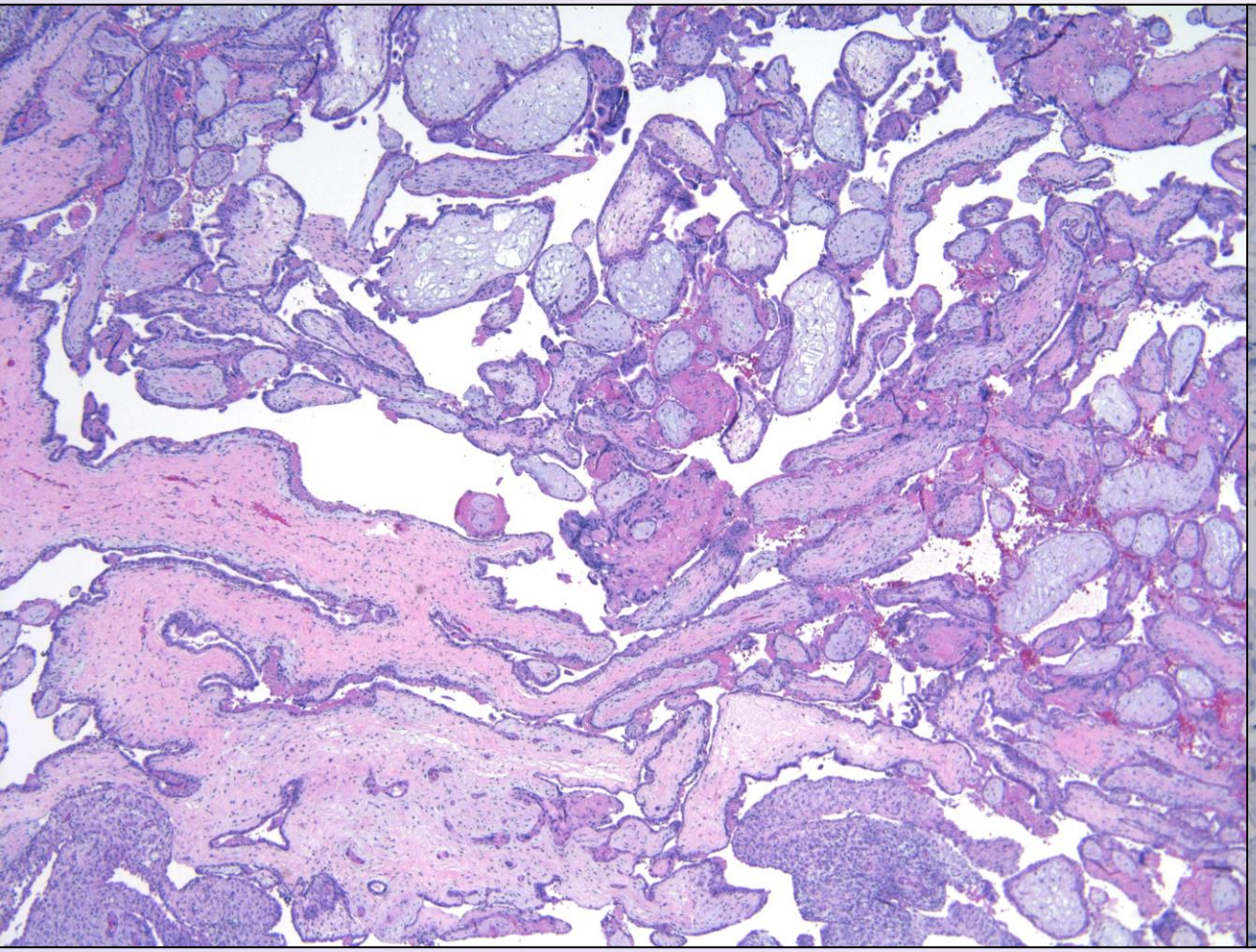


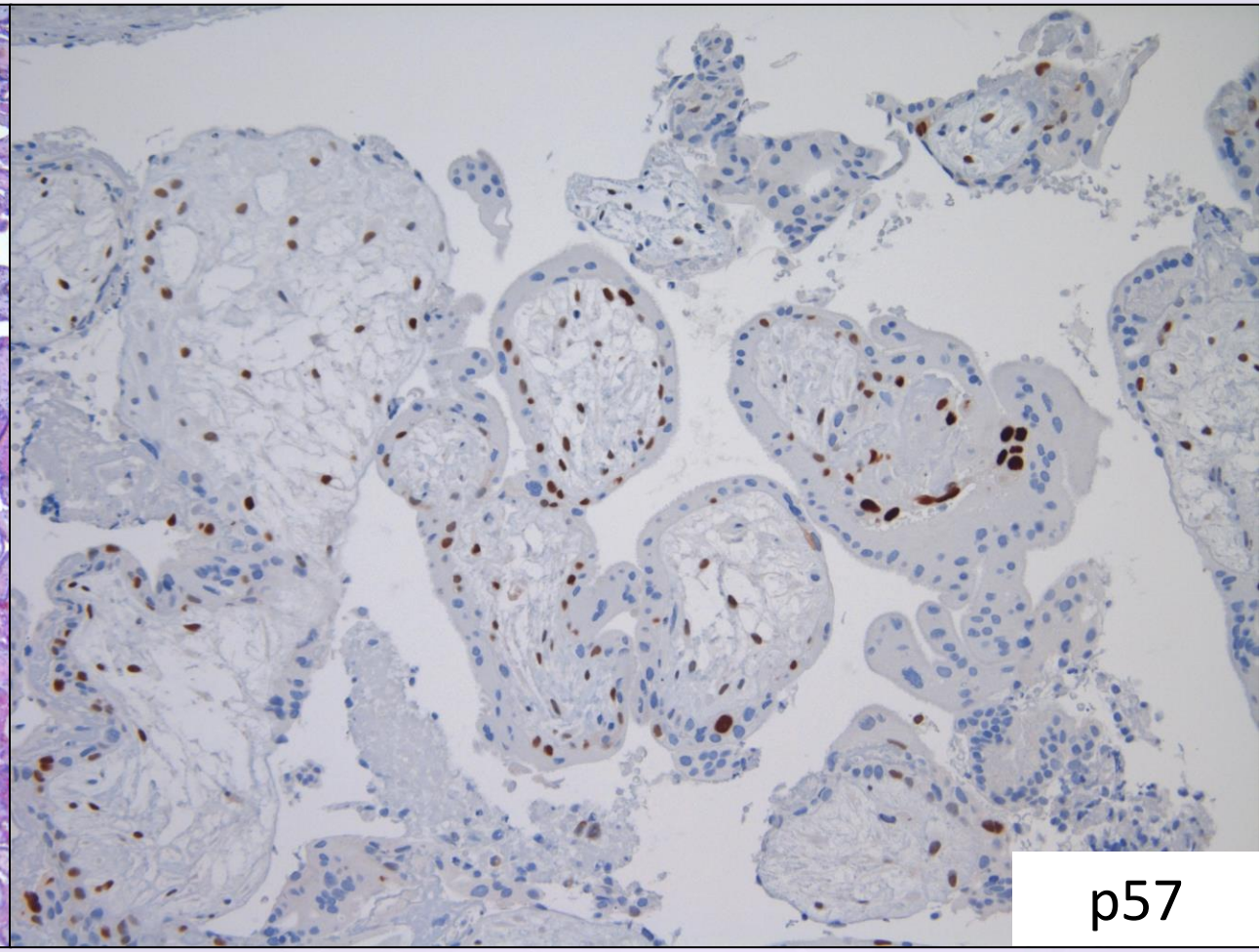
p57

Case 5

29-year-old patient with missed abortion at 9 weeks, undergoing dilation and curettage

Case 5

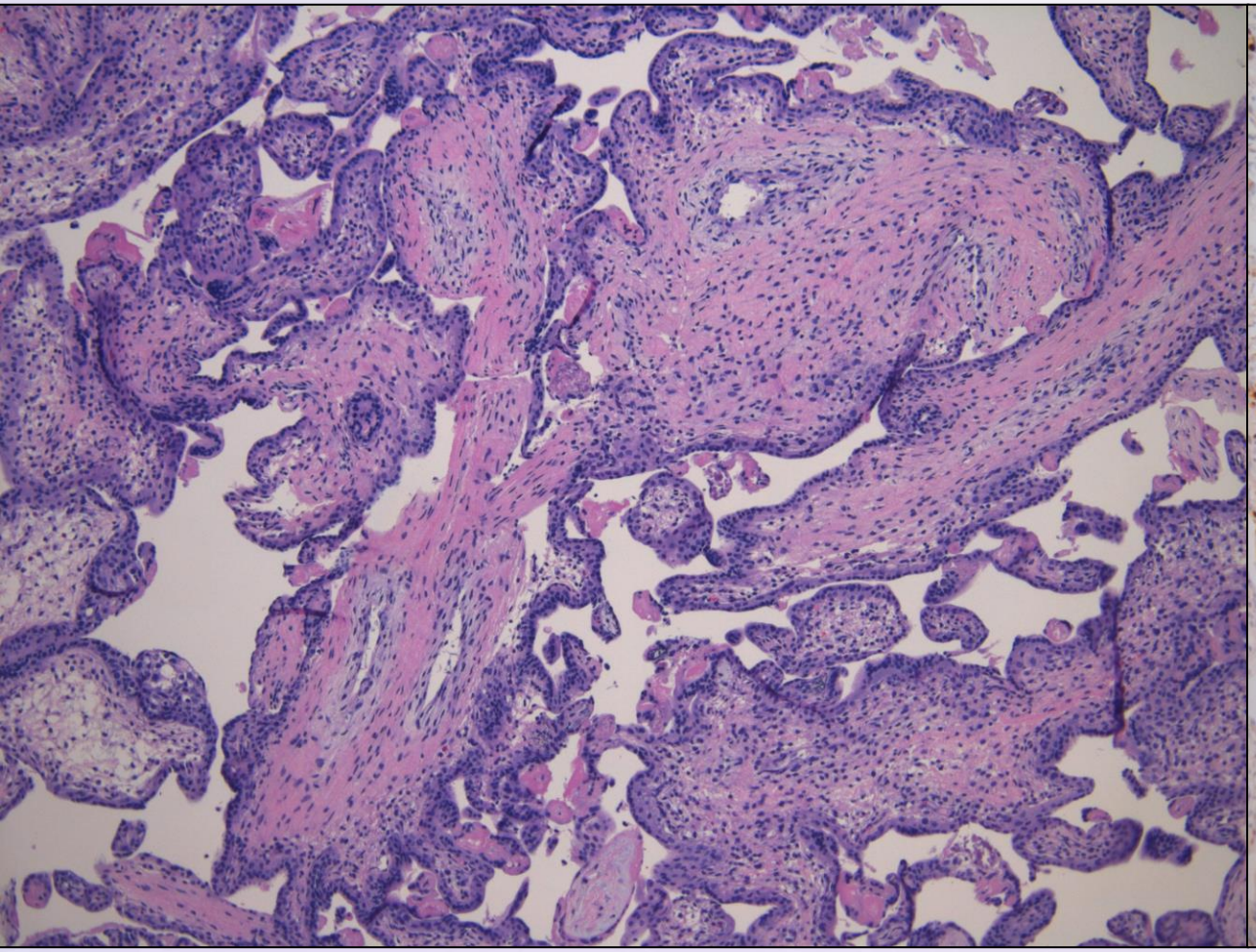


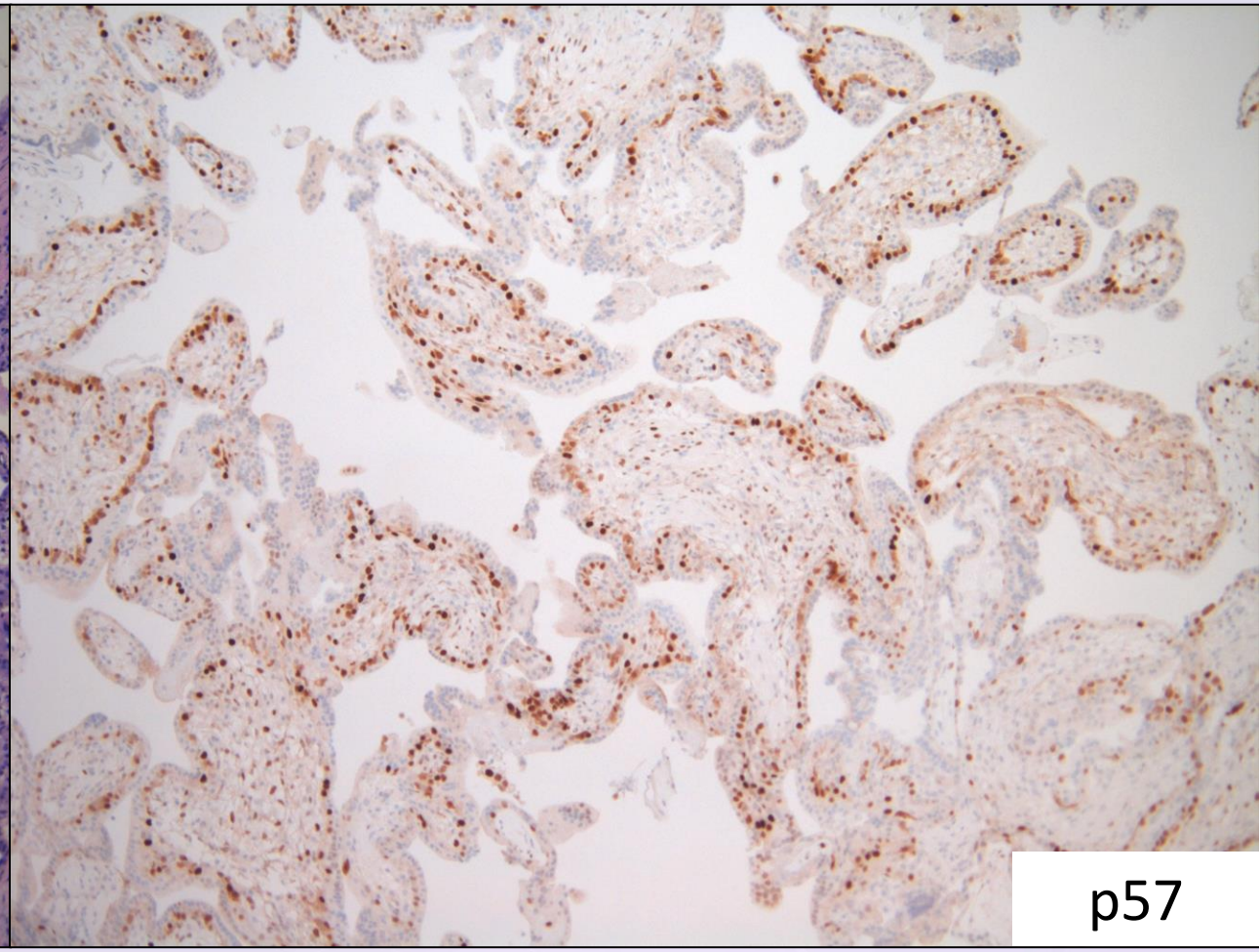


Case 6

27-year-old patient with missed abortion at 10 weeks, undergoing dilation and curettage

Case 6





p57

Hydatidiform Moles
Diagnosis – Chromosomal Analysis

Karyotyping
- Requires fresh tissue
- Labor intensive

FISH
- Probe against specific chromosome
- Diploid vs triploid
- False negatives
  - Nuclear truncation

Do not tell us where the additional genetic material is coming from

↓

Cannot definitively diagnose PHM

Hydatidiform Moles
Diagnosis – Molecular Testing (STR Analysis)

STR by PCR – compares:

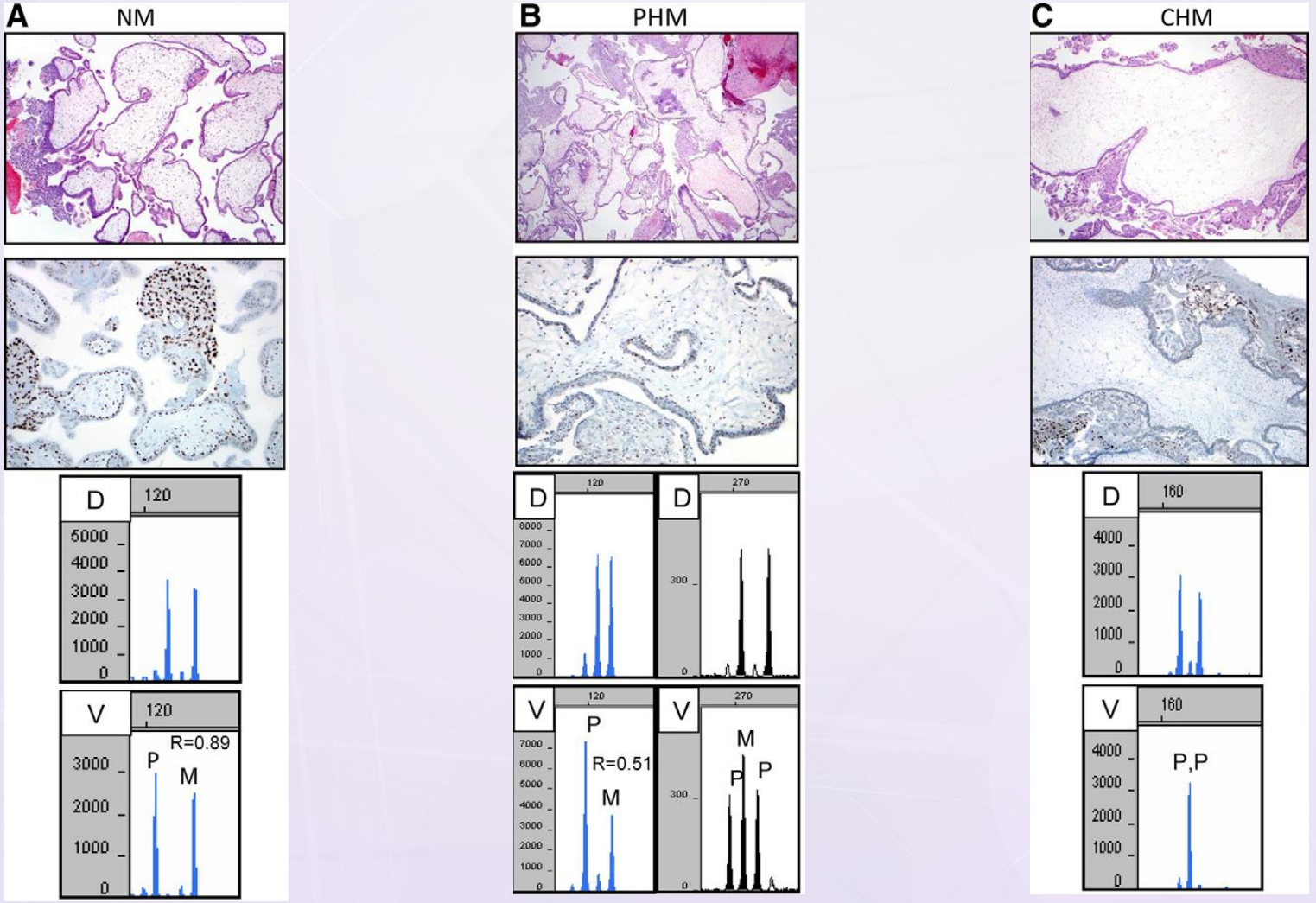
- Mother DNA (from decidua)
- Fetal DNA (from chorionic villi)

- Comparison of STRs at various loci
  - Similar to identity testing

GOLD STANRARD FOR DIAGNOSING PHM

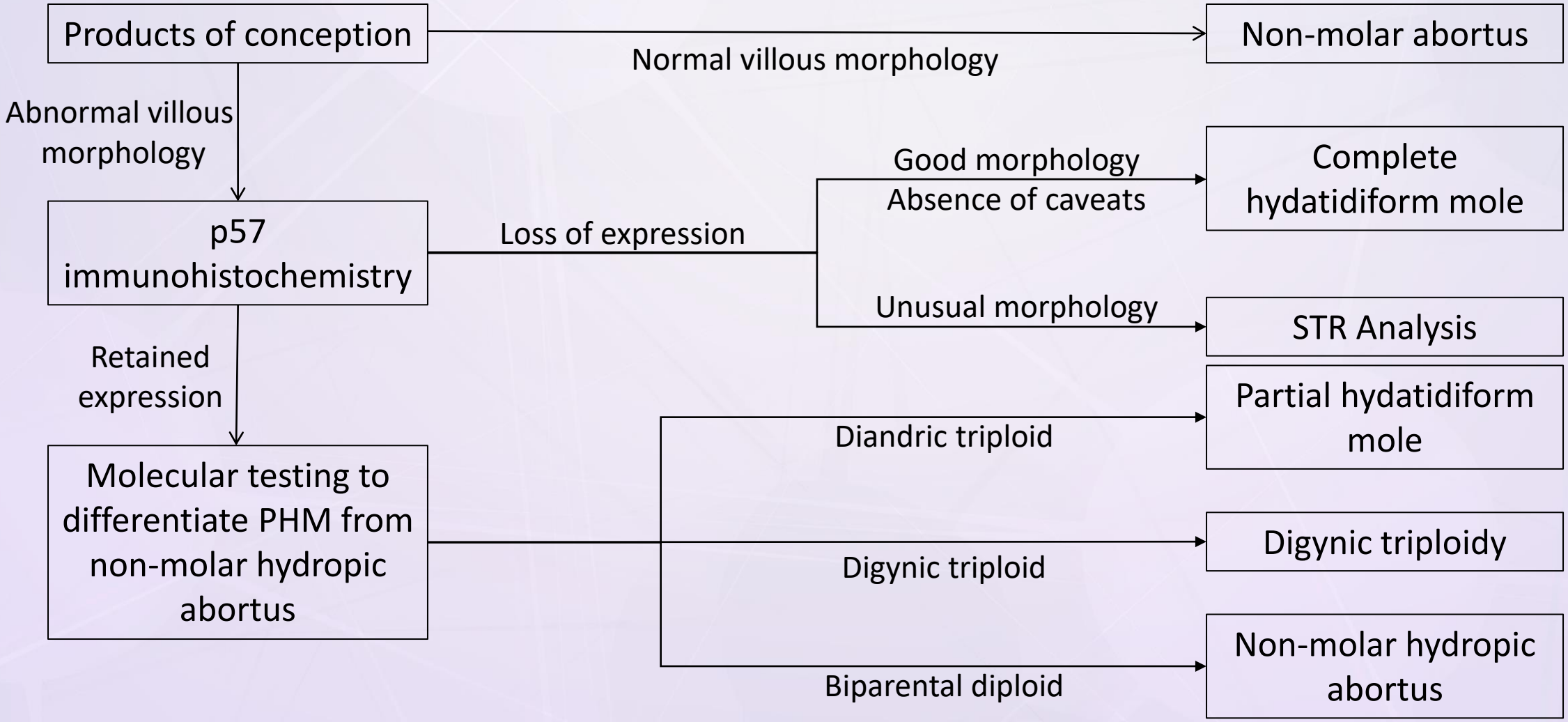
Hydatidiform Moles

Diagnosis – Molecular Testing (STR Analysis)

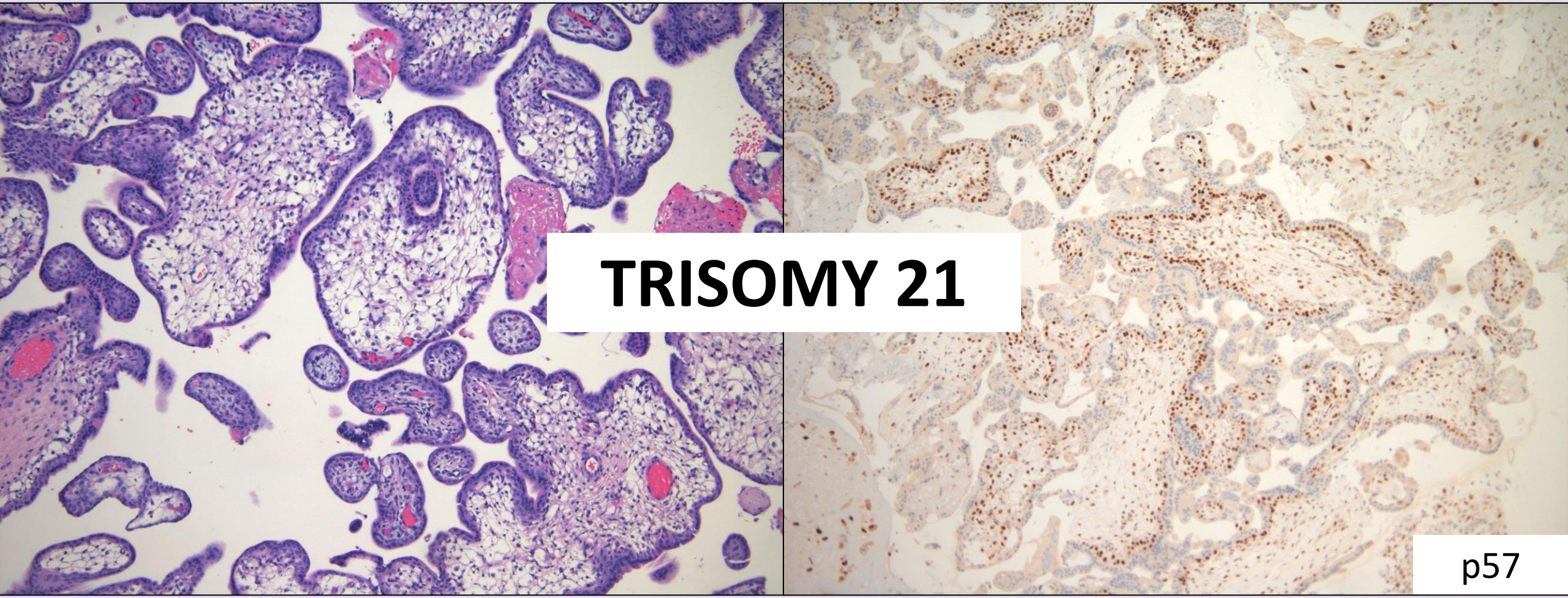


Murphy, K. et al. Molecular Genotyping of Hydatidiform Moles. Analytic Validation of a Multiplex Short Tandem Repeat Assay. *J Mol Diagn.* 2009 Nov;11(6):598-605

Hydatidiform Moles
Diagnosis



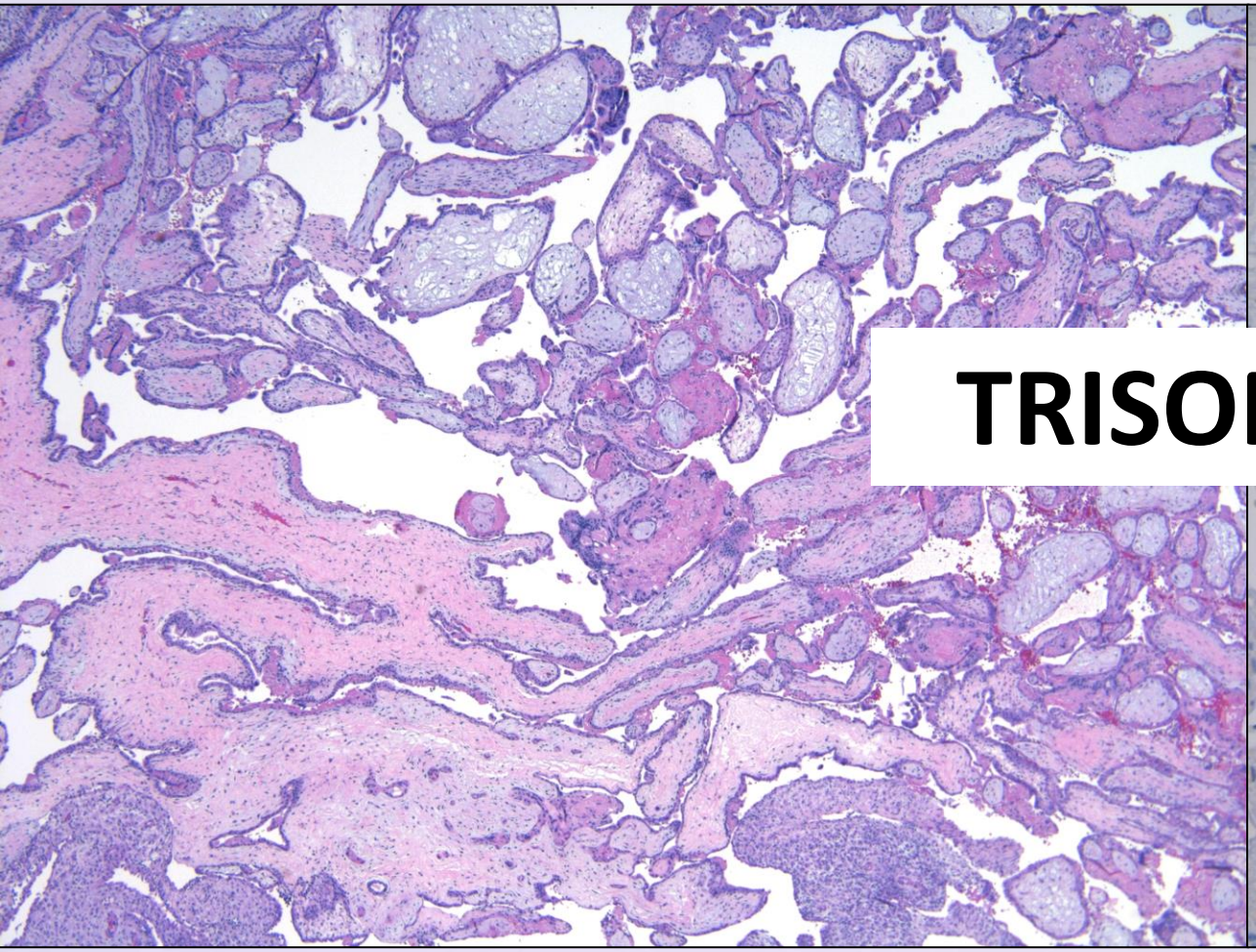
Case 4



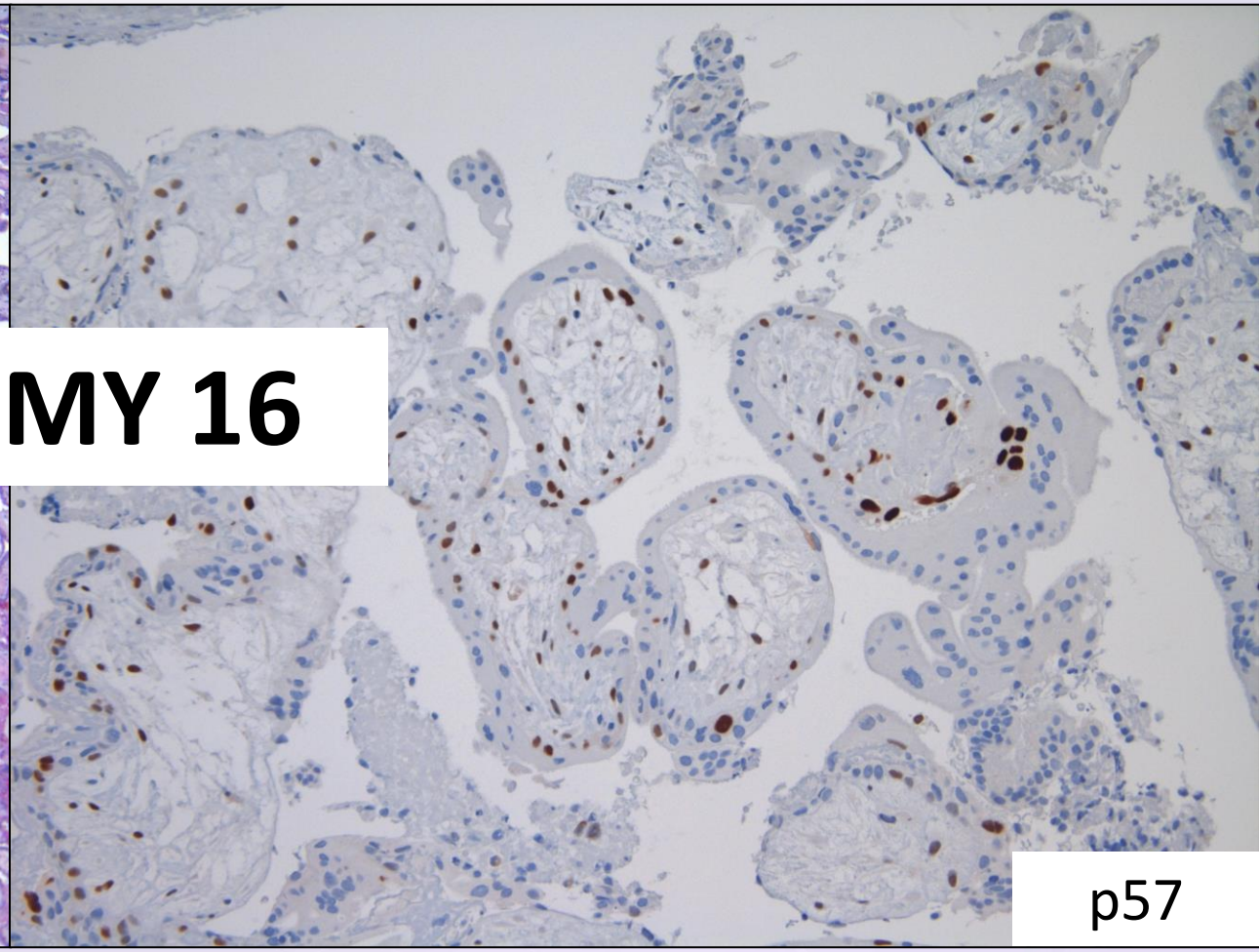
TRISOMY 21

p57

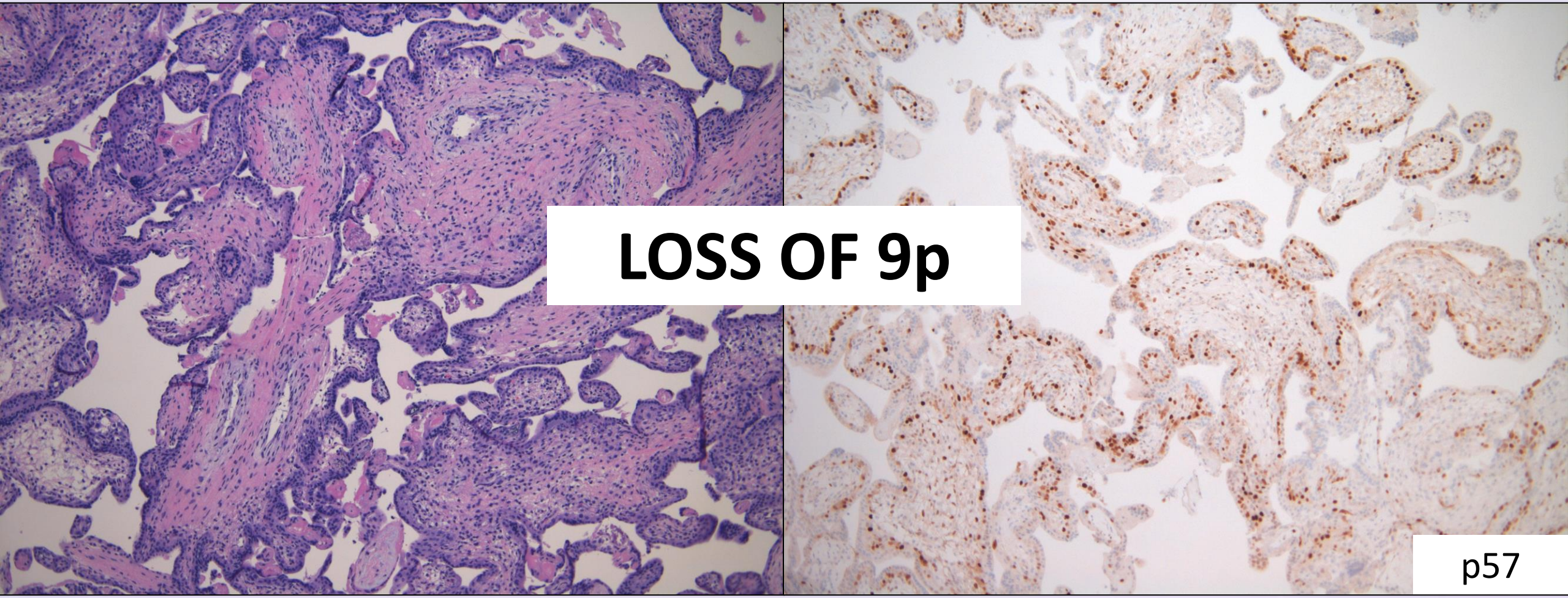
Case 5



TRISOMY 16



Case 6



Conclusion

- Diagnosis of hydatidiform moles carries both clinical and emotional consequences
- In the right setting, loss of p57 by immunohistochemistry is usually sufficient to diagnose CHM
- Diagnosis of PHM required molecular testing for proper patient management

THANK YOU!