Maternal vascular remodeling

Arteries

- Larger uterine arteries dilate to accommodate increased flow, vessels also increase # of vascular smooth muscle cells (proliferation phase followed by stretching)
- Endometrial arterioles thin out vascular smooth muscle
- Implantation site-
  - Intermediate trophoblast surround vessels
  - Invasive intermediate trophoblast occlude lumens in 1st trimester
  - Muscular wall is replaced by thick layer of fibrin/fibrinoid
  - Changes extend proximally into inner 1/3 of myometrium during 2nd and 3rd trimesters

Veins

- Larger uterine veins dilate
- Endometrial veins thin out vascular smooth muscle
- Implantation site-
  - Intermediate trophoblast surround vessels with no muscle
  - Large cisterns parallel to basal plate are formed

Trophoblast mediated remodeling affects vessels under 1st TM implantation site

Maternal vascular remodeling

Diameter of placenta:

~5cm at 11 weeks

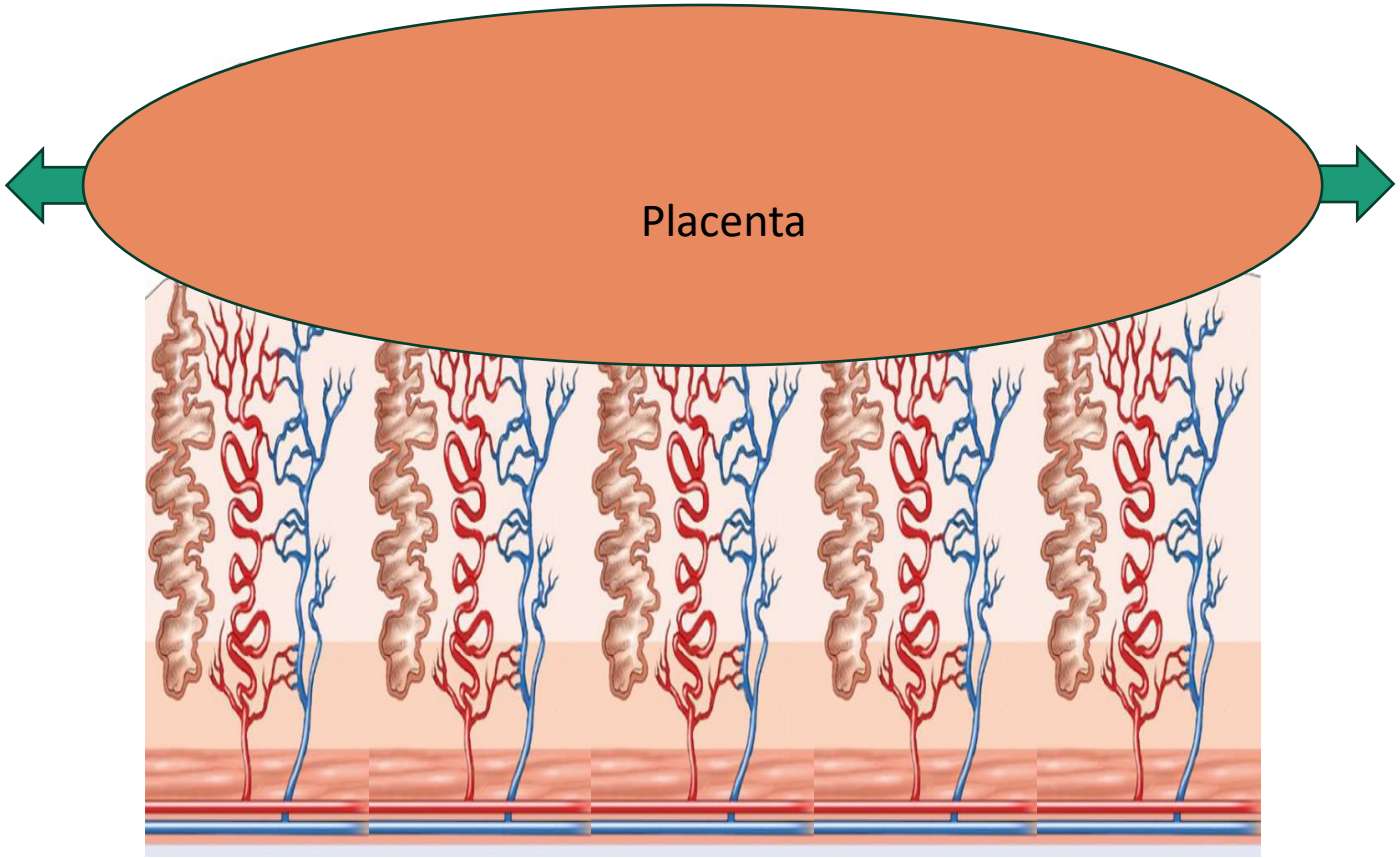
~22 cm at 38 weeks

Distance between arterioles at implantation site:

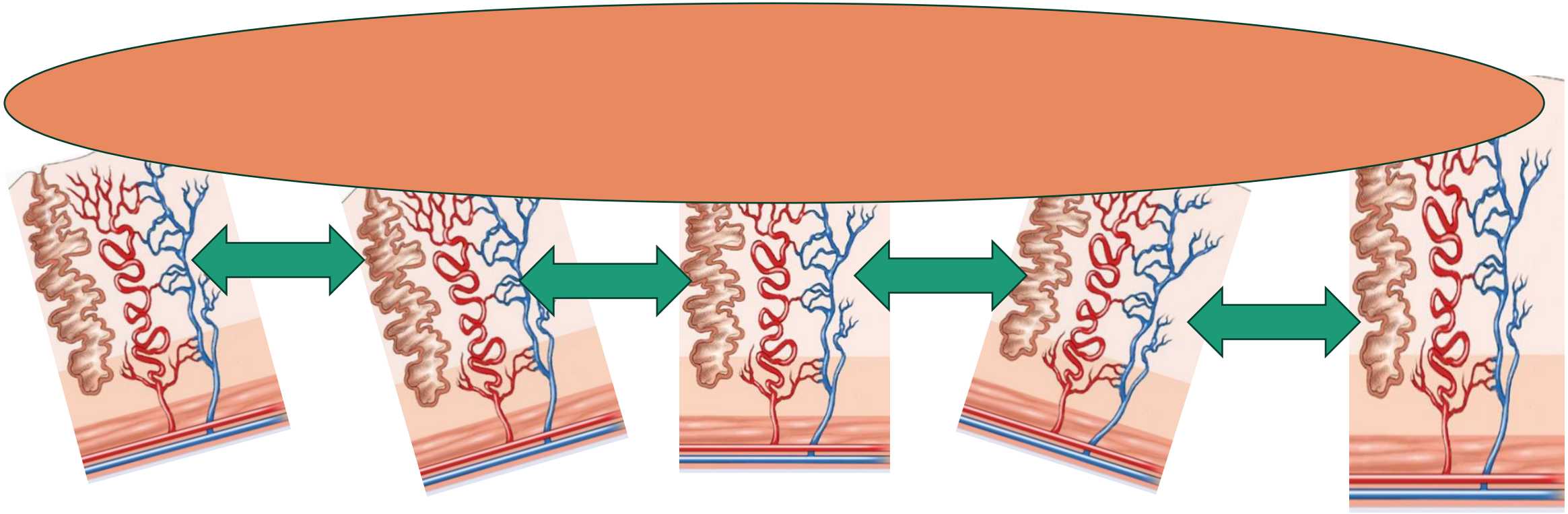
~1.4mm in progravid endometrium

Distance between arterial openings on mature placenta:

~118-211mm apart on basal plate of mature placenta



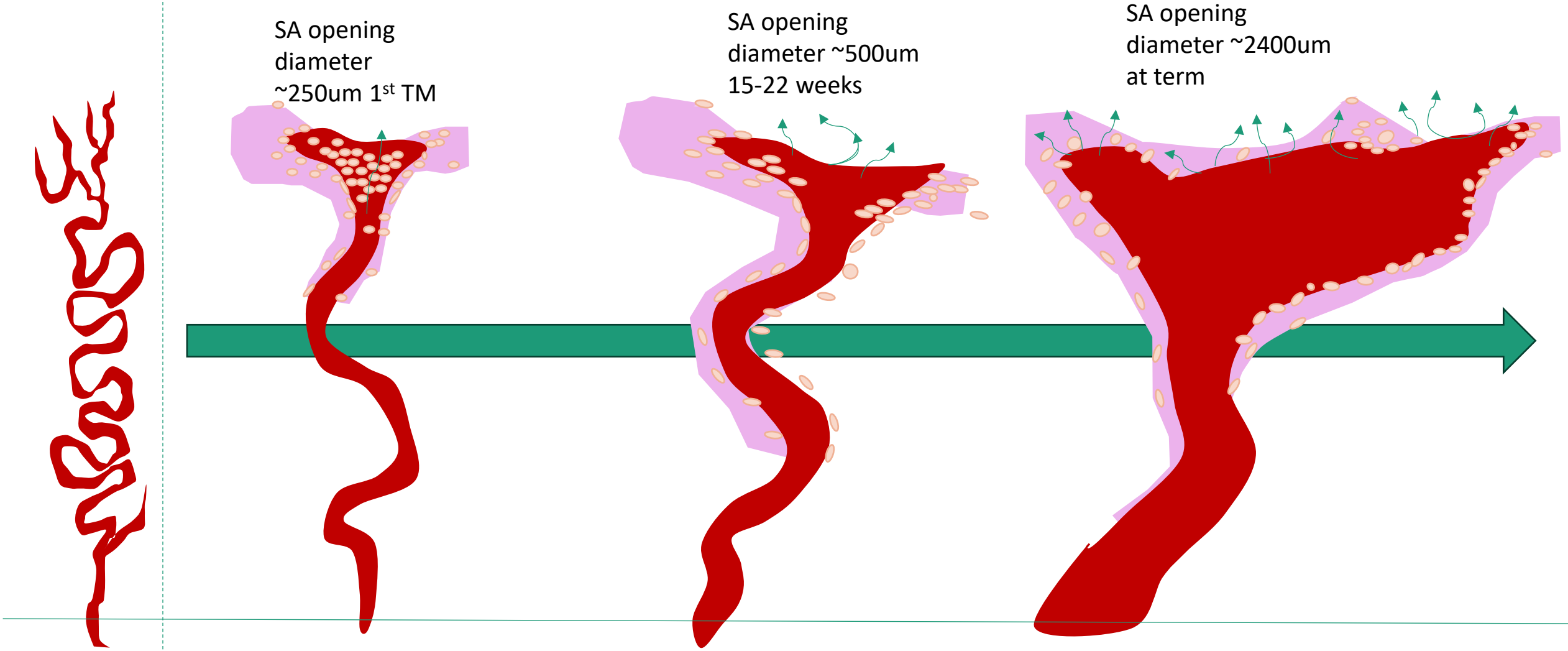
RAMSEY EM. Vascular adaptations of the uterus to pregnancy. Ann N Y Acad Sci. 1959 Jan 9;75:726-45. PMID: 14436112.



As uterus stretches, distance between remodeled vessels grows, placenta grows interstitially

RAMSEY EM. Vascular adaptations of the uterus to pregnancy. Ann N Y Acad Sci. 1959 Jan 9;75:726-45. PMID: 14436112.

Arterial remodeling



Approximate measurements from Harris J.W.S., Ramsey E.M. The morphology of human uteroplacental vasculature. Contrib Embryol.1966;38:43–58

Venous remodeling

Table 1

Number of Spiral Arteries With and Without Physiological Changes in the Placental Bed From Single Placentae

	Normal Pregnancy	Severe Preeclampsia and Intrauterine Growth Retardation
Area examined	32 cm^2	7 cm^2
Number of spiral arteries	45	10
With physiological changes	43 (96%)	1 (10%)
Without physiological changes	2 (4%)	8 (90%)

Brosens, Ivo A. "The utero-placental vessels at term—the distribution and extent of physiological changes." *Placental Vascularization and Blood Flow: Basic Research and Clinical Applications*. Boston, MA: Springer US, 1988. 61-67.

Cardiovascular adaptations

- Cardiac output increases 25% at 6 weeks gestation
  - peripheral vascular resistance drops
  - HR rises
  - plasma volume expands
- CO continues to rise, cresting at 35-40% above pre-pregnant values at 20-24 weeks gestation
  - Time of maximal uterine tissue and vessel growth
- The fraction of CO to the uterus doubles from 6 -> 12%
  - Increased distal iliac artery impedance
  - Reduced uterine artery impedance

All this blood is to perfuse the placenta, how does it circulate in the placenta?

J. Obstet. Gynaec. Brit. Cwlth.
Nov. 1969. Vol. **76.** pp. 979–989.

VASCULAR ANATOMY OF THE HUMAN PLACENTA AND ITS SIGNIFICANCE FOR PLACENTAL PATHOLOGY

BY

J. S. WIGGLESWORTH, *Senior Lecturer in Paediatric Pathology,*
Institute of Child Health, Hammersmith Hospital, London, W.12

FIG. 4
Tensol cast of part of placenta showing spiral arteries entering centres of fetal lobules. Fetal arteries white, spiral arteries red.

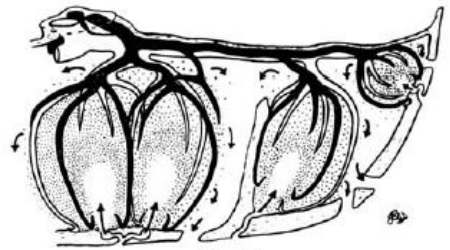


FIG. 11
Diagram of circulation through intervillous space in relation to fetal lobular pattern. Density of stippling indicates density of fetal villi.

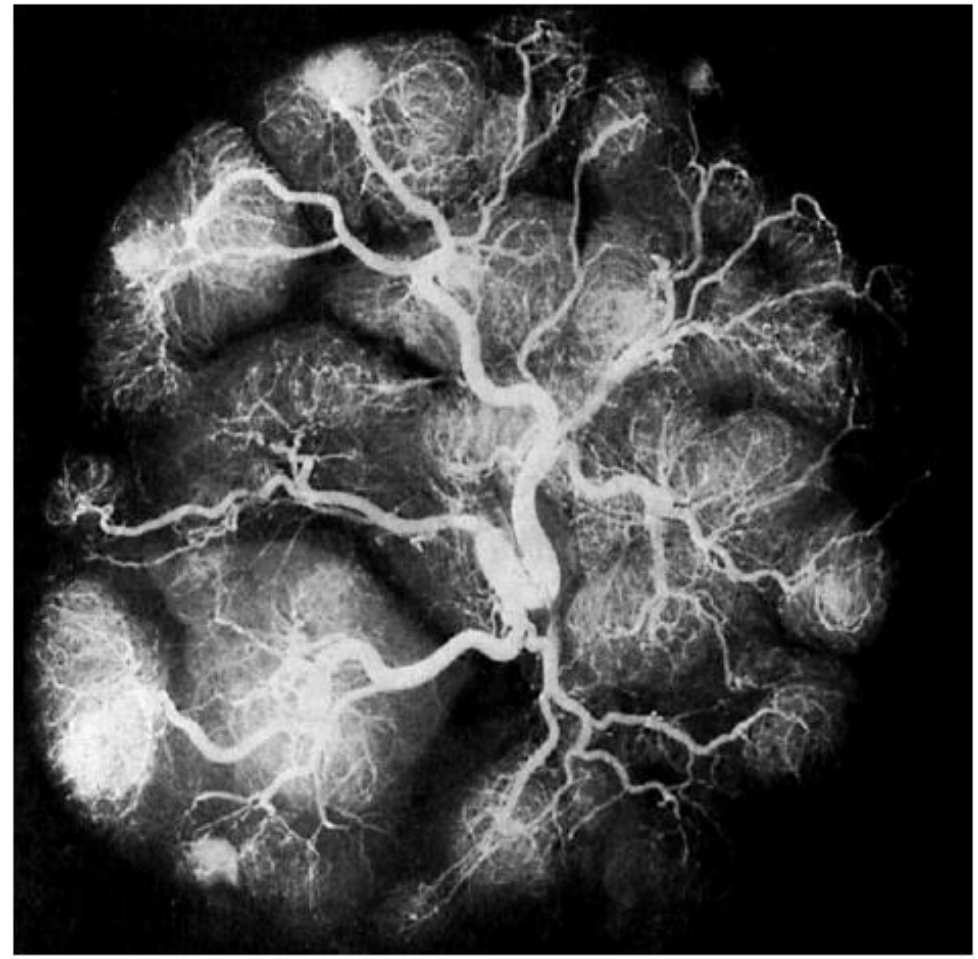


FIG. 2
X-ray of placenta showing umbilical arterial system injected with Ba. gelatine. Note lobular pattern.

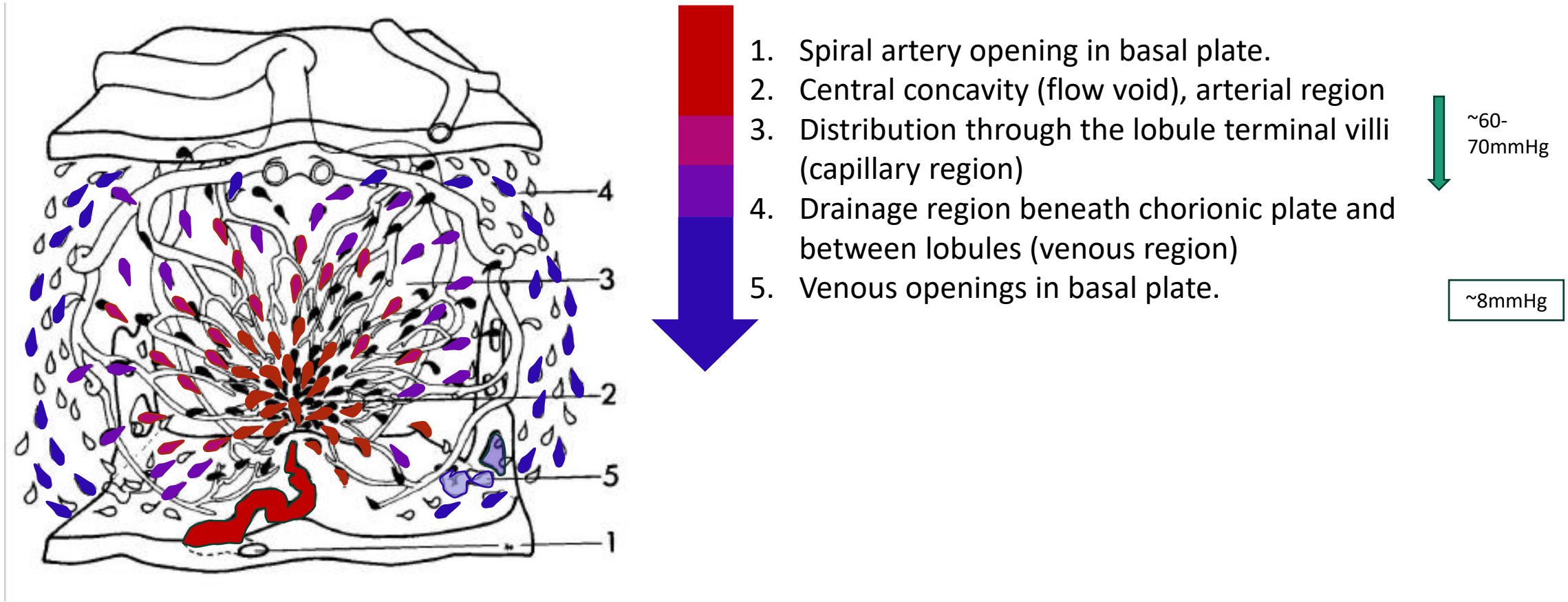
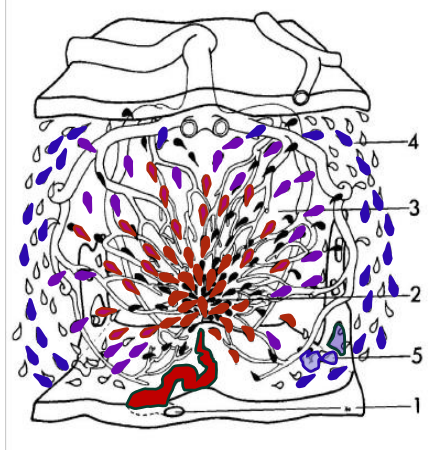
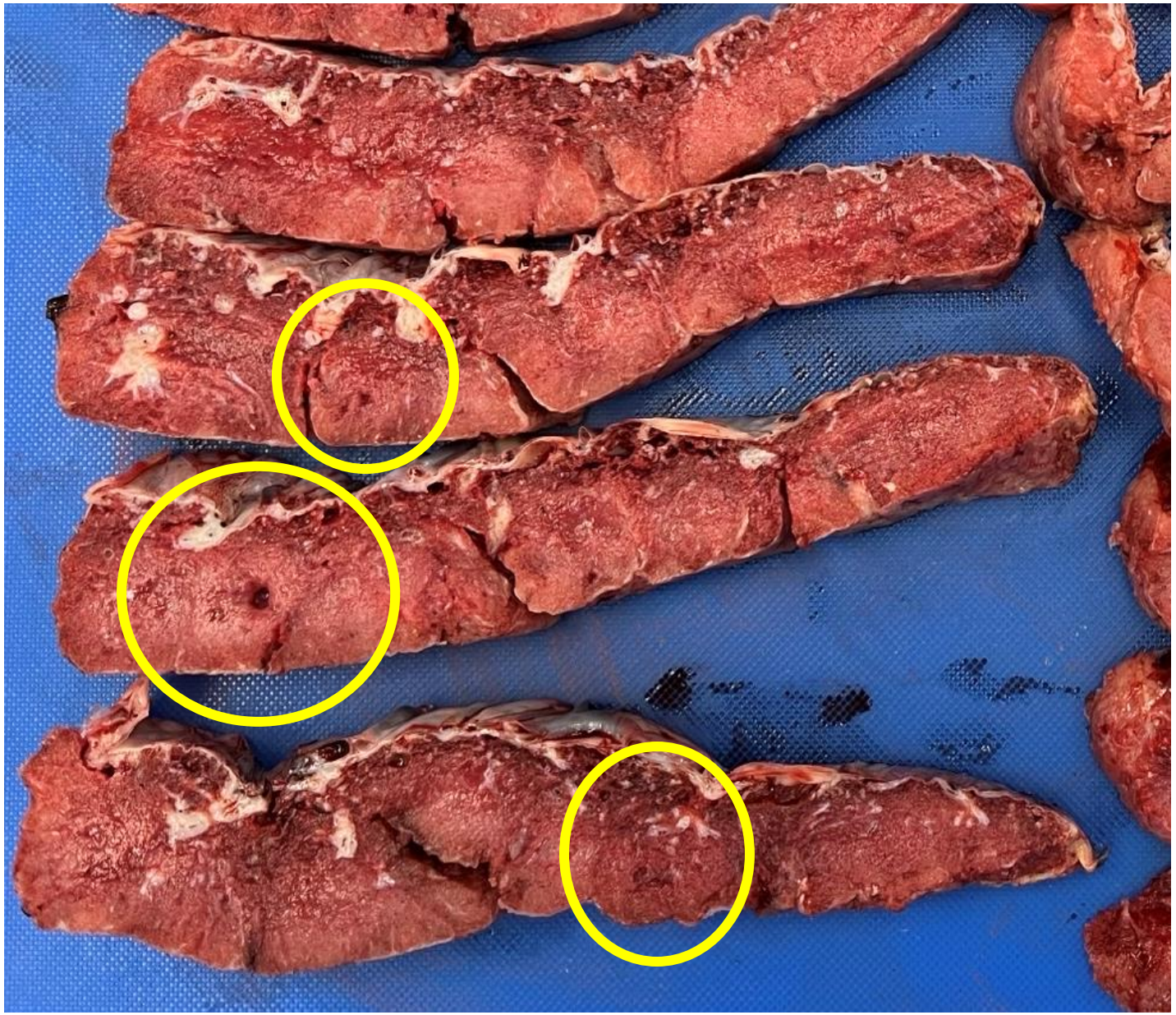


Figure 4. Beck T. Der materne Blutfluss durch die menschliche Plazenta [Maternal blood flow in the human placenta (author's transl)]. Z Geburtshilfe Perinatol. 1982 Apr-May;186(2):65-71. German. PMID: 7202298.



Mature placenta is comprised of ~200 lobules

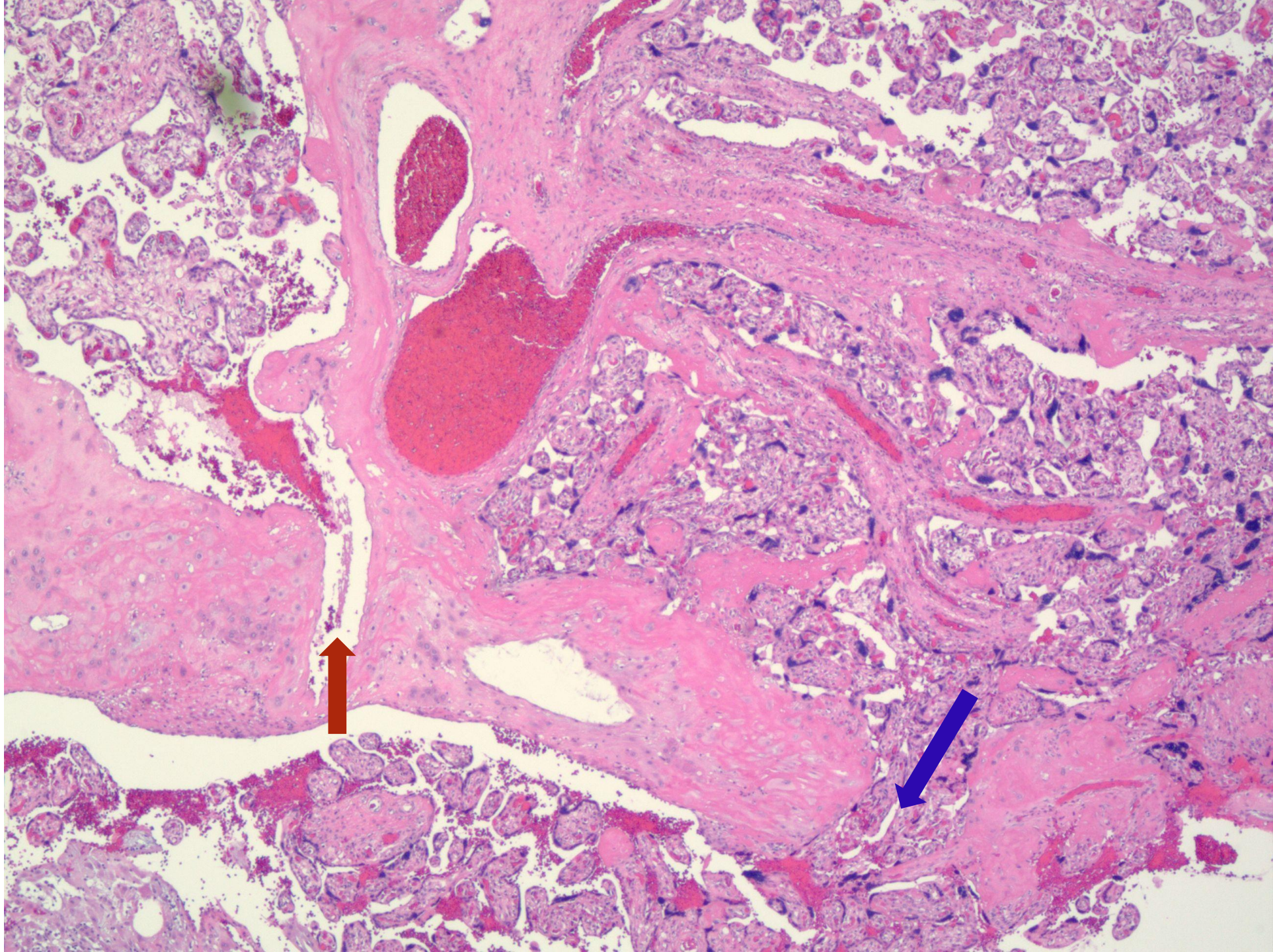


Lobules with central flow voids

The physical openings of arteries and veins look very similar in the basal plate

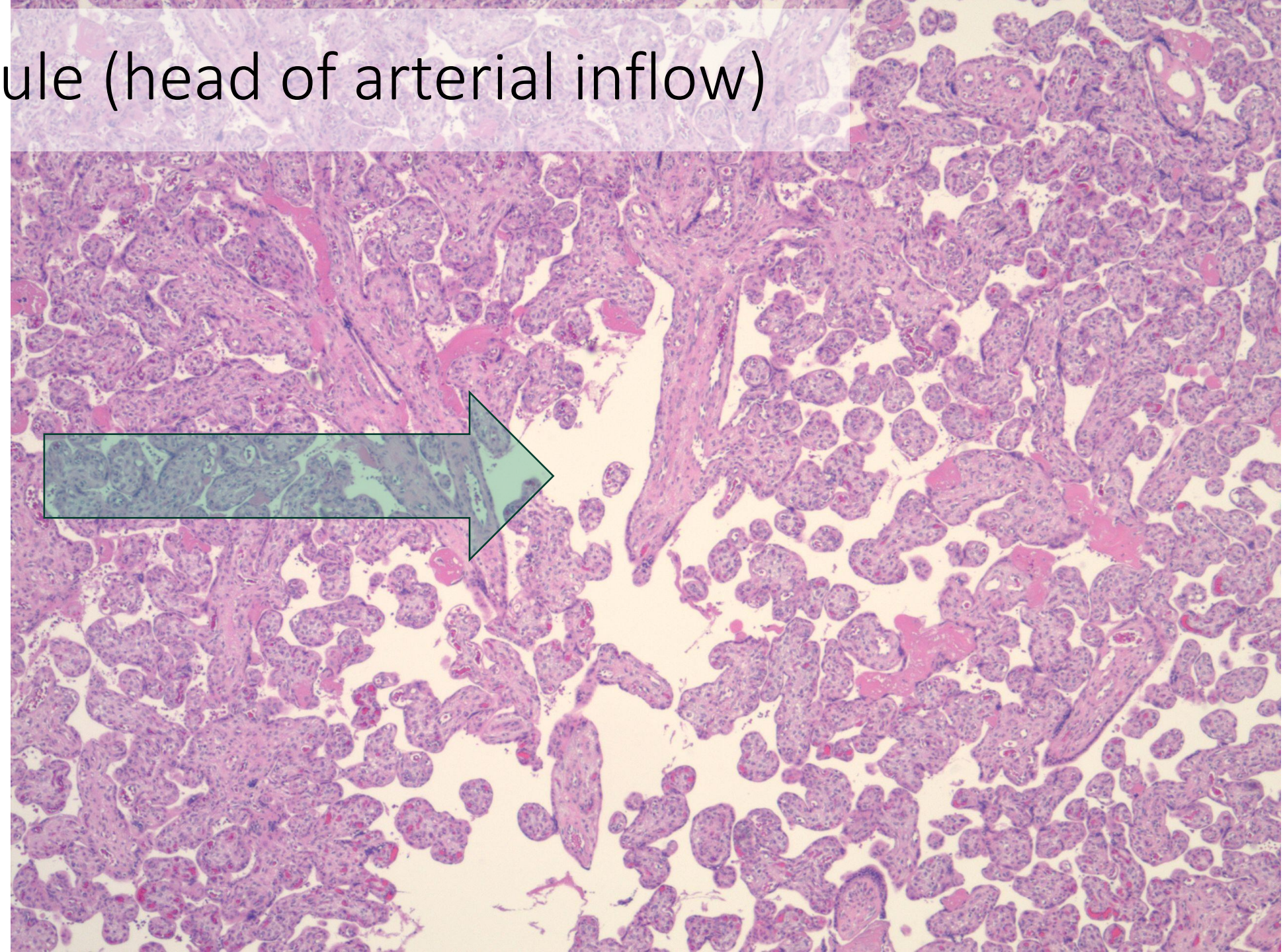
Arteries push villi aside.

Veins draw them in.



Center of Lobule (head of arterial inflow)

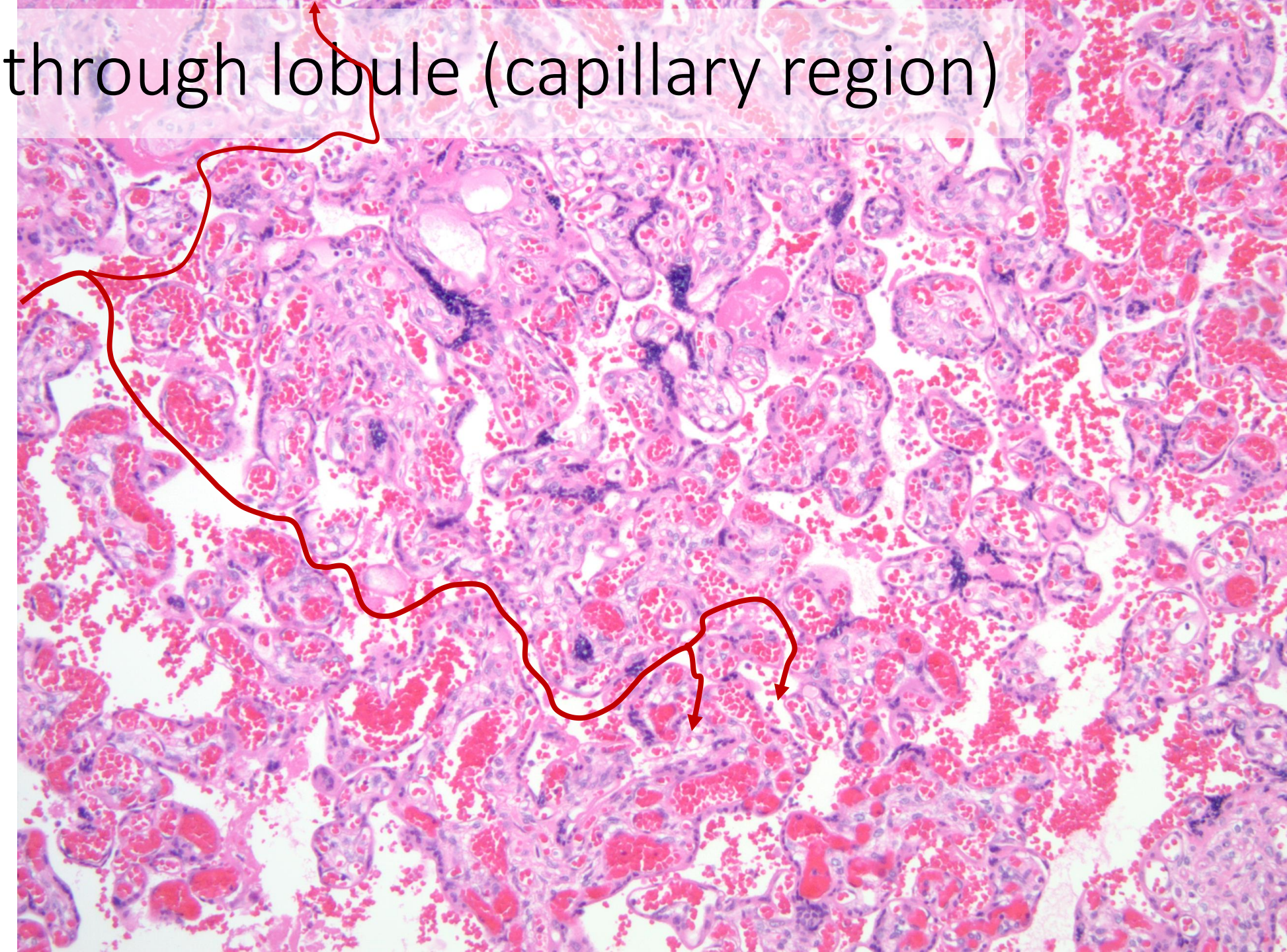
- Villi are pushed apart by inflow of maternal blood in flow void, resulting in “empty space”
- Villi show fewer vasculosyncytial membranes, appear relatively “immature”
- Highest point of pressure in the intervillous space, most rich in O2



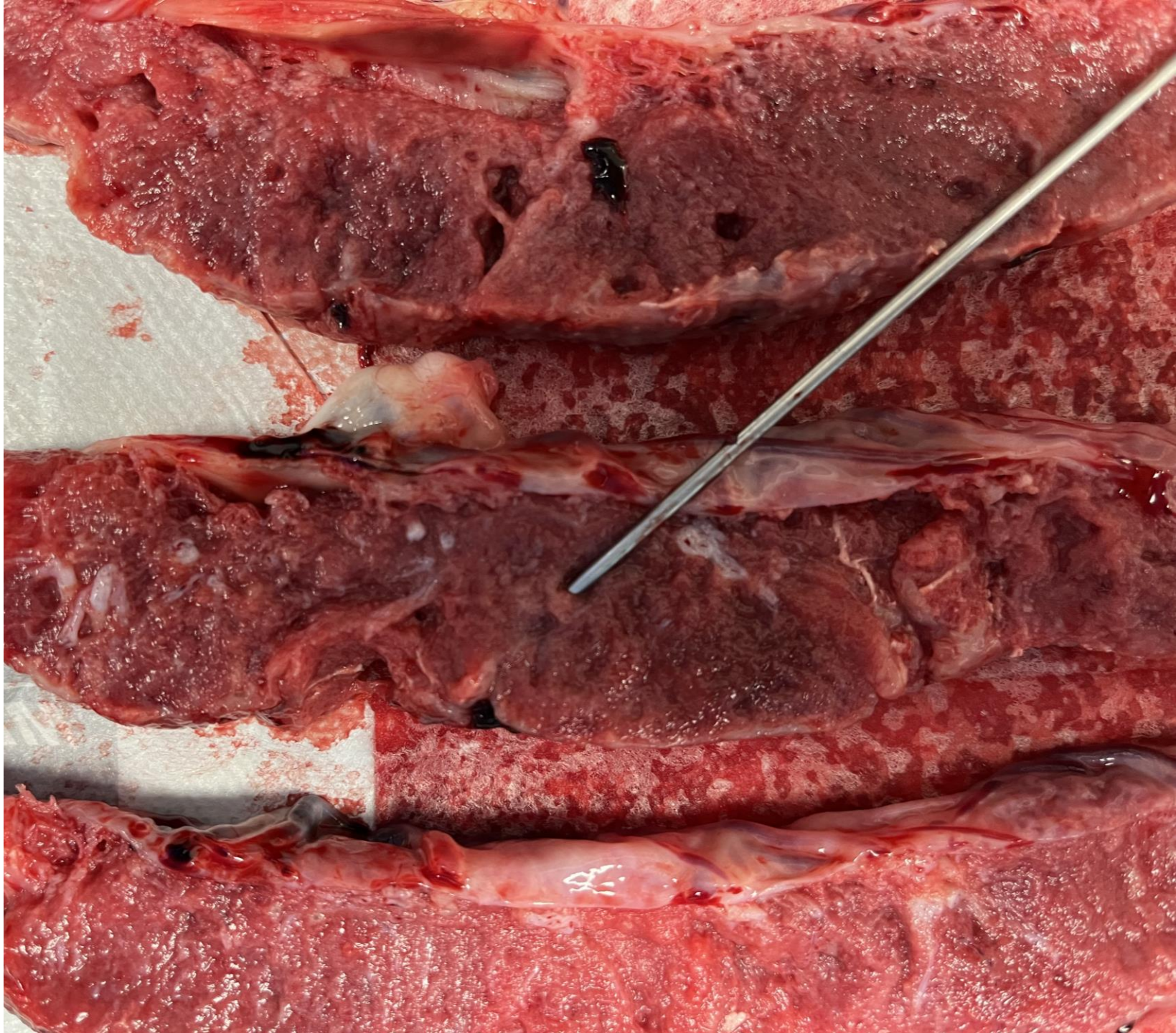
Distribution through lobule (capillary region)

Adjacent mature villi are connected by nuclear bridges of syncytiotrophoblast (bridging knots)

Creates channels for blood to course through

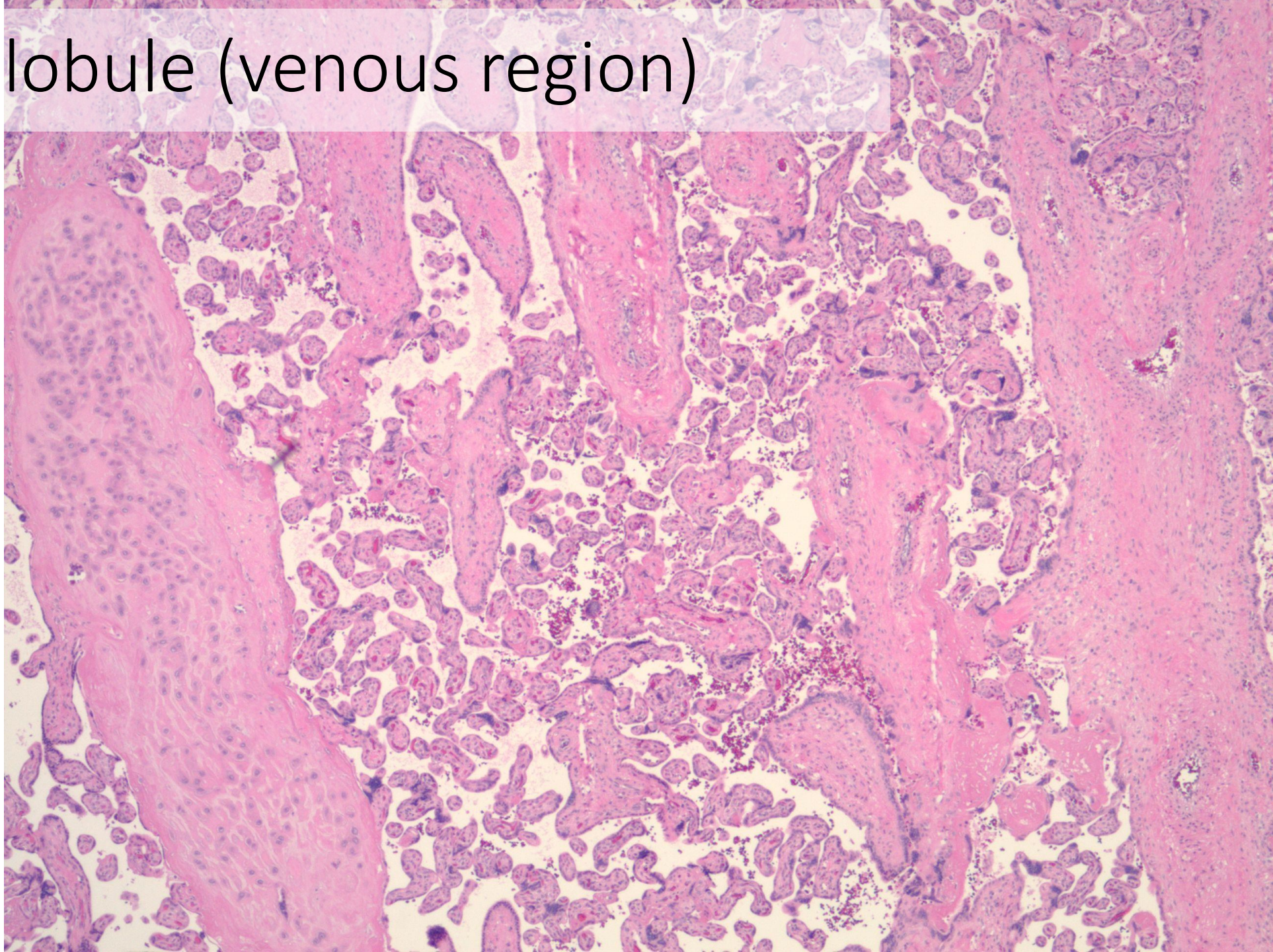


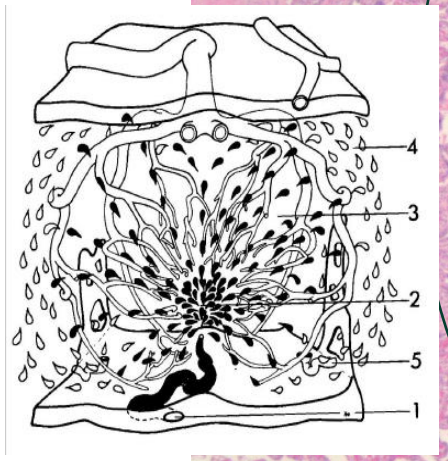
- A probe inserted into the flow void (lobule center) of the mature placenta will pass through the inflow tract to the basal plate/septa, but not through adjacent parenchyma



Periphery of lobule (venous region)

- Villi are more separated
- Villi are often elongated in the direction of flow
- Stem villi, vellus septa often at periphery
- Villi are very small and loose under chorionic plate




4
3
2
5
1

Why spend so much time on the lobular architecture?

- Understanding the arterial/capillary/venous zones of the placenta helps to make sense of vascular lesions such as infarcts, thrombi, fibrin deposition and hematomas
- The concept of variable intervillous space pressure helps to make sense of fetal vascular lesions as well- the two circulations are not independent
- Inflammatory conditions such as chronic villitis, and chronic histiocytic intervillositis also relate to the lobular architecture
  - VUE involves the venous zones first
  - CHI often associated with fibrin deposition in the venous zones

Components of MVM-Amsterdam Criteria

- Placenta weight less than 10% and/or thin cord
- Infarcts (any preterm, >5% nonmarginal at term)
- Retroplacental hemorrhage

- Accelerated villous maturation
- Distal villous hypoplasia
- *Decidual arteriopathy should be noted*
- EVT proliferation in cell islands- needs more study
- EVT microcysts- needs more study
- Laminar decidual necrosis- needs more study

Khong TY, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Arch Pathol Lab Med. 2016 Jul;140(7):698-713. PMID: 27223167.

Is the problem the trophoblast?

Are the trophoblast doing a faulty job not fully remodeling the spiral arteries?

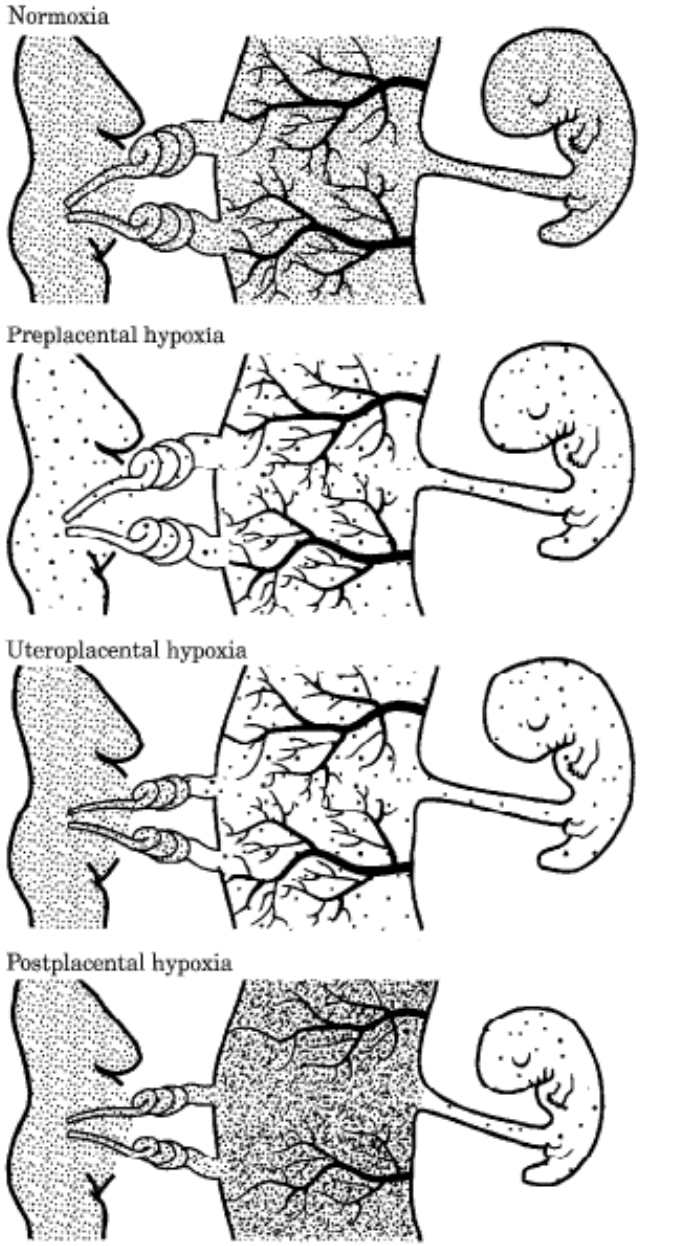
or

Are they making compromises to have a successful pregnancy?

“Successful pregnancy outcome is dependent upon transformation of the decidual spiral arterioles by invading extravillous cytotrophoblast, **such that** uteroplacental blood flow increases more than 10-fold during normal pregnancy. Failure of this process may result in the development of intrauterine growth restriction (IUGR) and/or pre-eclampsia.”

Kingdom J. Adriana and Luisa Castellucci Award Lecture 1997. Placental pathology in obstetrics: adaptation or failure of the villous tree? Placenta. 1998 Jul-Aug;19(5-6):347-51.

Kingdom JC, Kaufmann P. Oxygen and placental villous development: origins of fetal hypoxia. Placenta. 1997 Nov;18(8):613-21; discussion 623-6. doi: 10.1016/s0143-4004(97)90000-x. PMID: 9364596.



igure 2. The origins of fetal hypoxia. The degree of point shading mbolizes the degree of oxygenation.

Cause of Preeclampsia

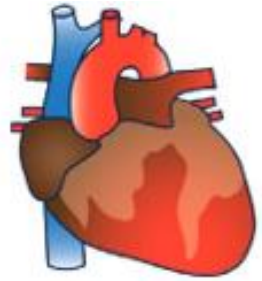
- For the past 50+ years, the placenta has been considered the problem
- FGR and preeclampsia have been considered the result of the poor placental development
- Placental insufficiency has been attributed to poor spiral artery conversion

  Poor vascular supply -> poor organ growth

  But sometimes the placenta is normal or even large for age?

  Preterm preeclampsia (small placenta) and term preeclampsia (not always small) must be different?

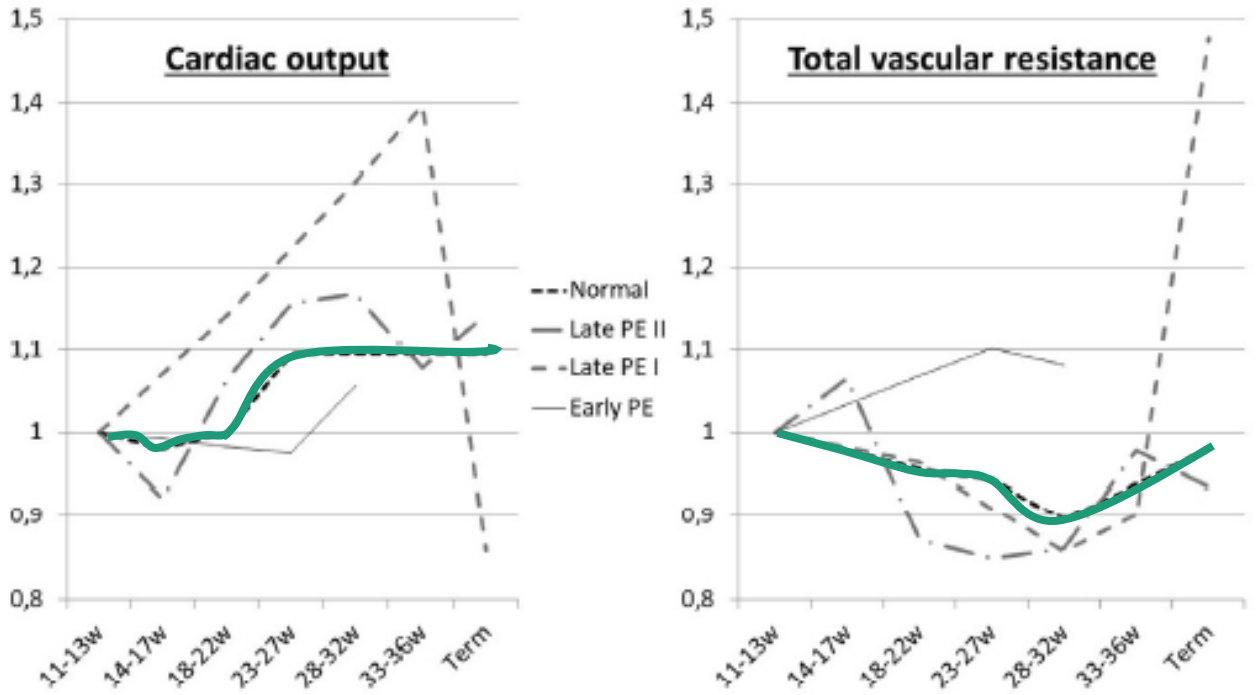
Cardiovascular adaptations



- Cardiac output increases 25% at 6 weeks gestation
  - peripheral vascular resistance drops
  - HR rises
  - plasma volume expands
- CO continues to rise, cresting at 35-40% above pre-pregnant values at 20-24 weeks gestation
  - Time of maximal uterine tissue and vessel growth
- The fraction of CO to the uterus doubles from 6 -> 12%
  - Increased distal iliac artery impedance
  - Reduced uterine artery impedance
- These changes are affected by factors from placenta, but are not directly caused by trophoblast mediated remodeling of spiral arteries

Normal pregnancy involves massive plasma volume expansion and decreased peripheral vascular resistance

FIGURE 2
The longitudinal changes in cardiac output and peripheral resistance



Longitudinal changes in cardiac output and peripheral resistance expressed as a product of 12-week measurements, reported in normal pregnancies,[18] early-onset preeclampsia,[21] late-onset preeclampsia type I (crossover),[24] and late-onset preeclampsia type II (high-output).[28] Adapted from Gyselaers.[29]

PE, preeclampsia.

Masini. The two phenotypes of preeclampsia and differential treatments. Am J Obstet Gynecol 2022.

Preeclampsia has two phenotypes which require different treatment strategies

Giulia Masini, MD; Lin F. Foo, BM, BSc (Hons), PhD, MRCOG; Jasmine Tay, BMedSci, BMBS, PhD, MRCOG; Ian B. Wilkinson, MA, DM, FRCP, FAHA; Herbert Valensise, MD, PhD; Wilfried Gyselaers, MD, PhD; Christoph C. Lees, MD, FRCOG

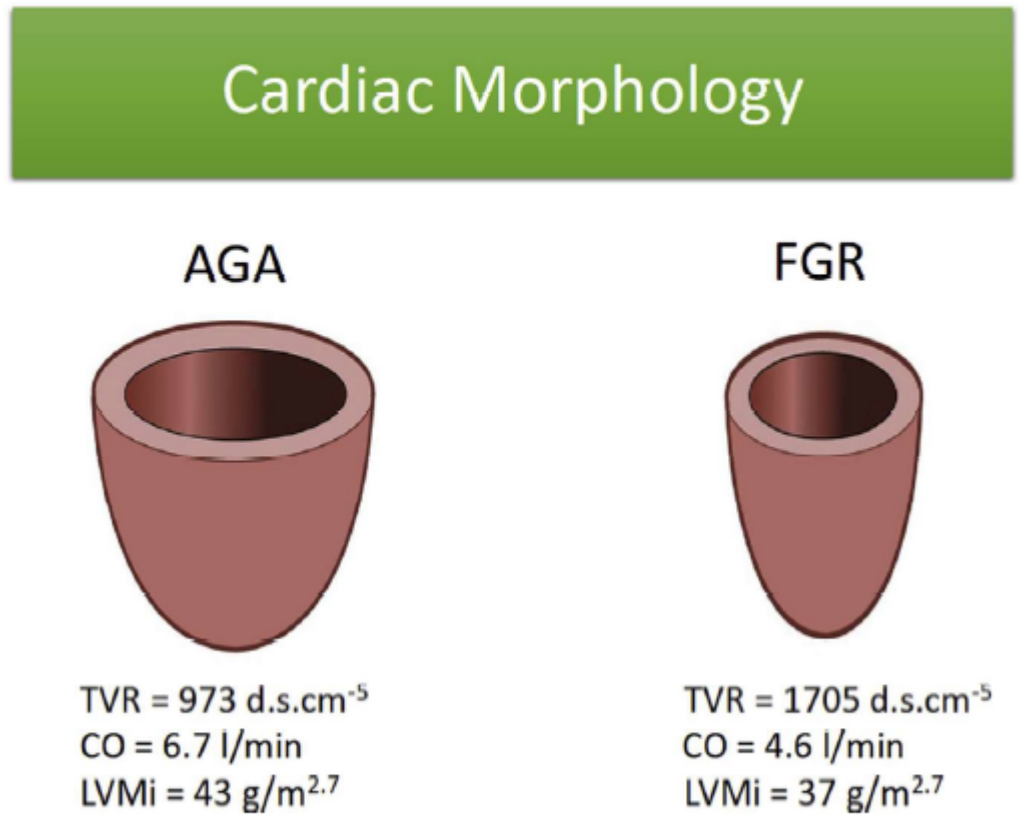
FIGURE 1
Schematic representation of changes in the cardiac parameters and arterial function in PE, FGR, or the combination of both complications[5]

	FGR	PE	PE + FGR
Cardiac Output	↓	↑ ↑	↓ ↓
Total Peripheral Resistance	↑	↓ ↓	↑ ↑
Maternal Pulse	→	→	→
Augmentation Index	↑	↑	↑
Pulse Wave Velocity	↑	↑	↑

FGR, fetal growth restriction; *PE*, preeclampsia.

Masini. The two phenotypes of preeclampsia and differential treatments. Am J Obstet Gynecol 2022.

FIGURE 6
Representation of the cardiac morphologic adaptation in pregnancies with normal fetal growth and in those with FGR



Adapted from Vasapollo et at.[86]

AGA, appropriate for gestational age; *CO*, cardiac output; *FGR*, fetal growth restriction; *LVMi*, left ventricular mass index; *TVR*, total vascular resistance.

Masini. The two phenotypes of preeclampsia and differential treatments. Am J Obstet Gynecol 2022.

How do these “2 types of preeclampsia” relate to the pathologic diagnosis of MVM?

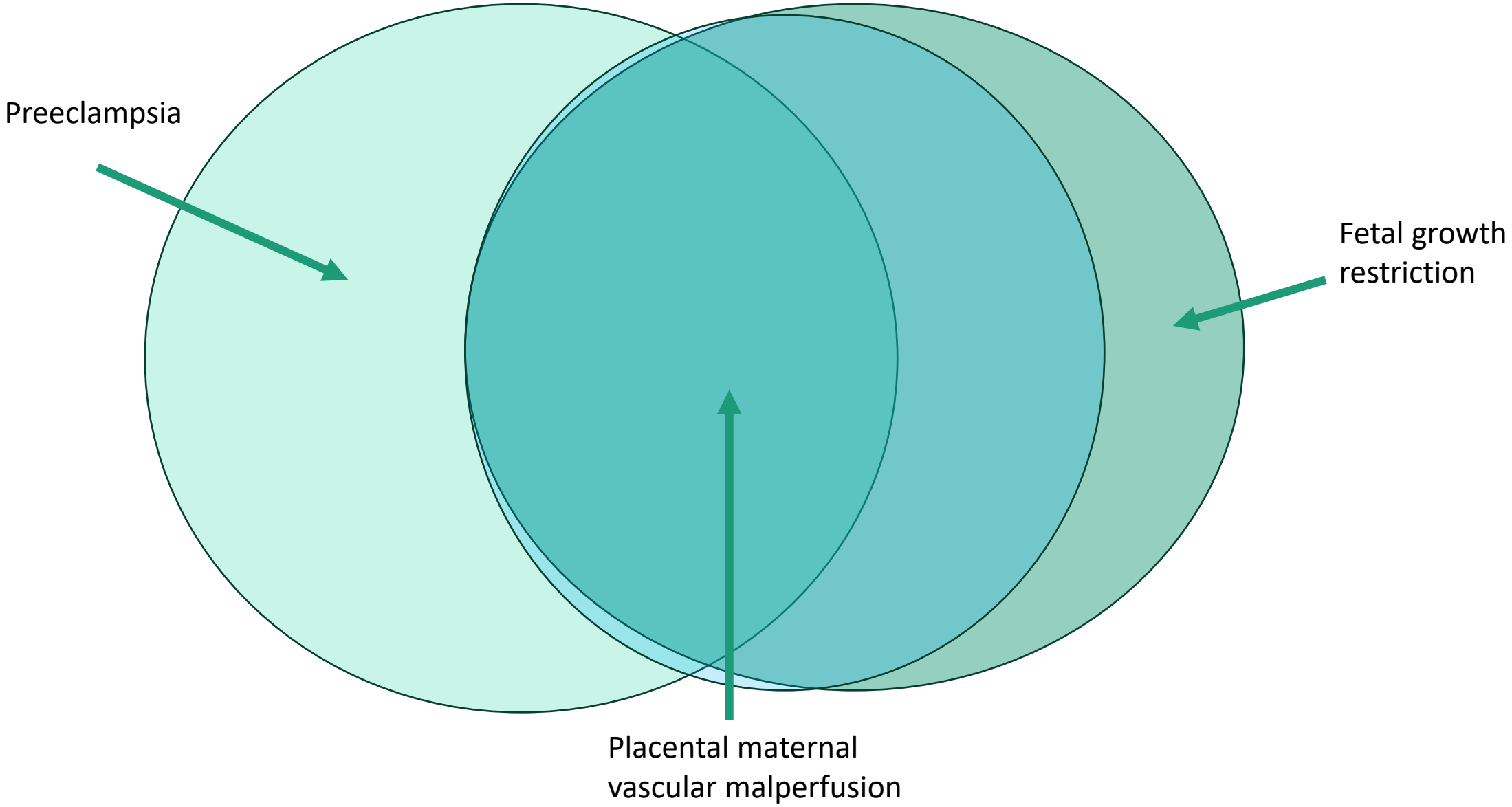
<u>Early onset PE, PE with FGR, FGR alone</u>

- Placenta weight <10th percentile
- Decidual arteriopathy (hypertrophic, fibrinoid necrosis, acute atheromatous change, incomplete adaptation in basal plate)
- Accelerated villous maturation/DVH

<u>Late onset PE</u>

- Small, normal or increased placenta weight
- Appropriate, variable or delayed villous maturation
- Increased numbers of extravillous trophoblast
- Hypertrophic decidual arteriopathy

The constellation of features we define as “MVM” are in some but not all cases of preeclampsia, and most cases of FGR with or without preeclampsia.



The “placenta fault” paradigm: Maternal vascular malperfusion

MVM can cause hypoplasia of the placenta

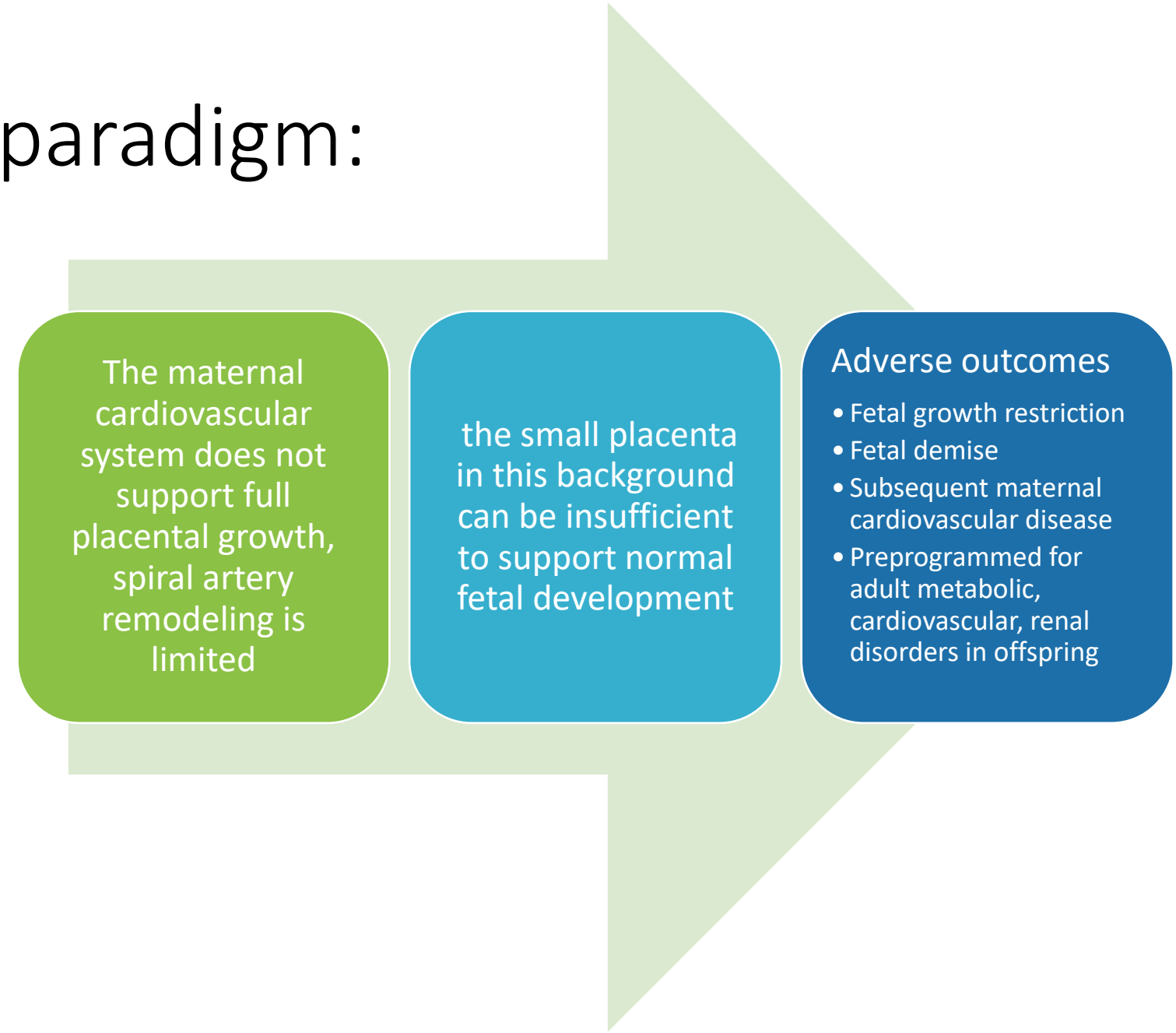
the small placenta can be insufficient to support normal fetal development

Adverse outcomes

- Fetal growth restriction
- Fetal demise
- Severe preterm preeclampsia

The updated paradigm:

Maternal vascular malperfusion



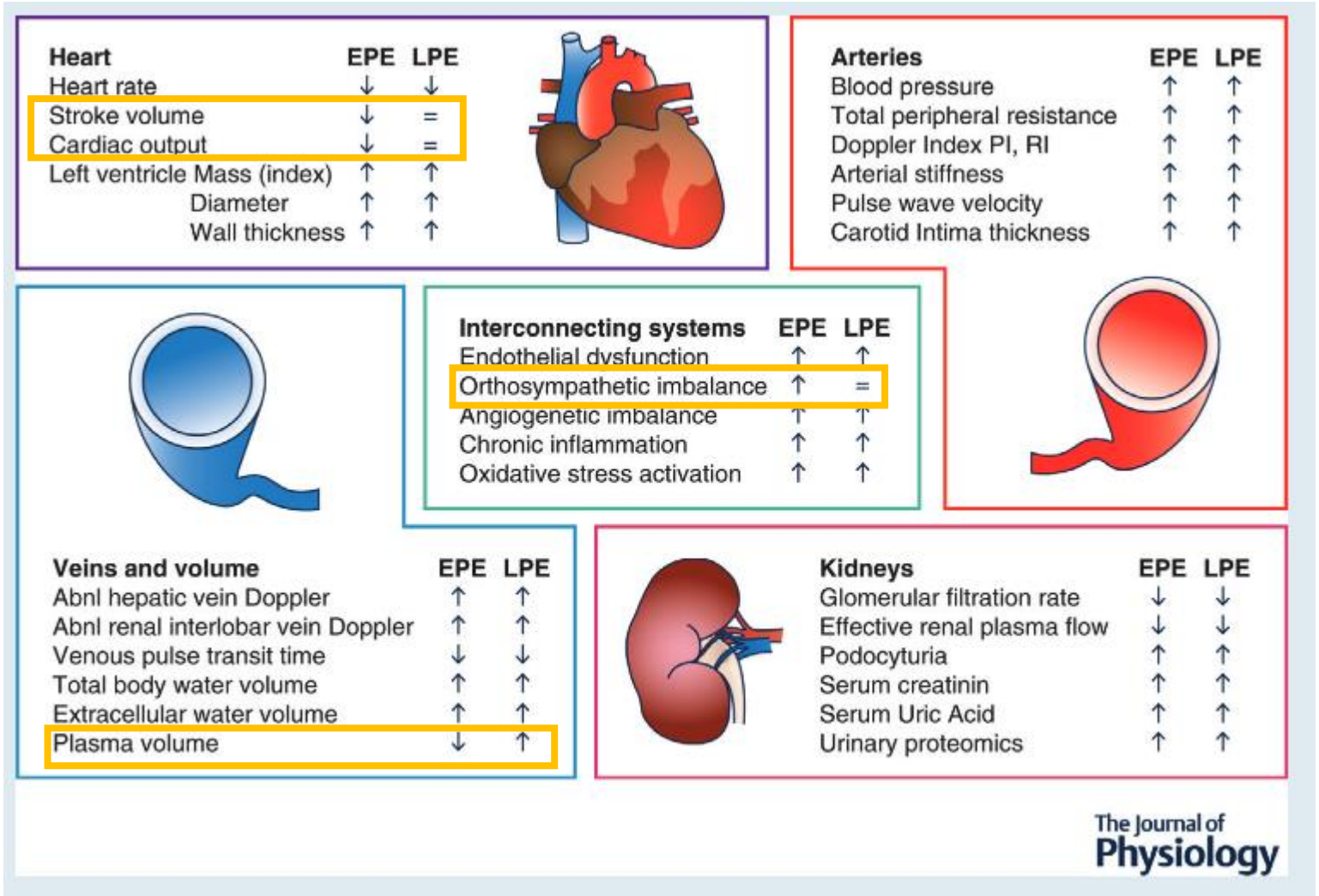
J Physiol 597.18 (2019) pp 4695–4714

TOPICAL REVIEW

Preeclampsia: a gestational cardiorenal syndrome

Wilfried Gyselaers[1,2] and Basky Thilaganathan[3,4]

[1] *Department of Obstetrics & Gynaecology, Ziekenhuis Oost-Limburg, Schiepse Bos 6, 3600 Genk, Belgium*
[2] *Department Physiology, Hasselt University, Agoralaan, 3590 Diepenbeek, Belgium,*
[3] *Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust, UK*
[4] *Molecular and Clinical Sciences Research Institute, St George's University of London, UK*



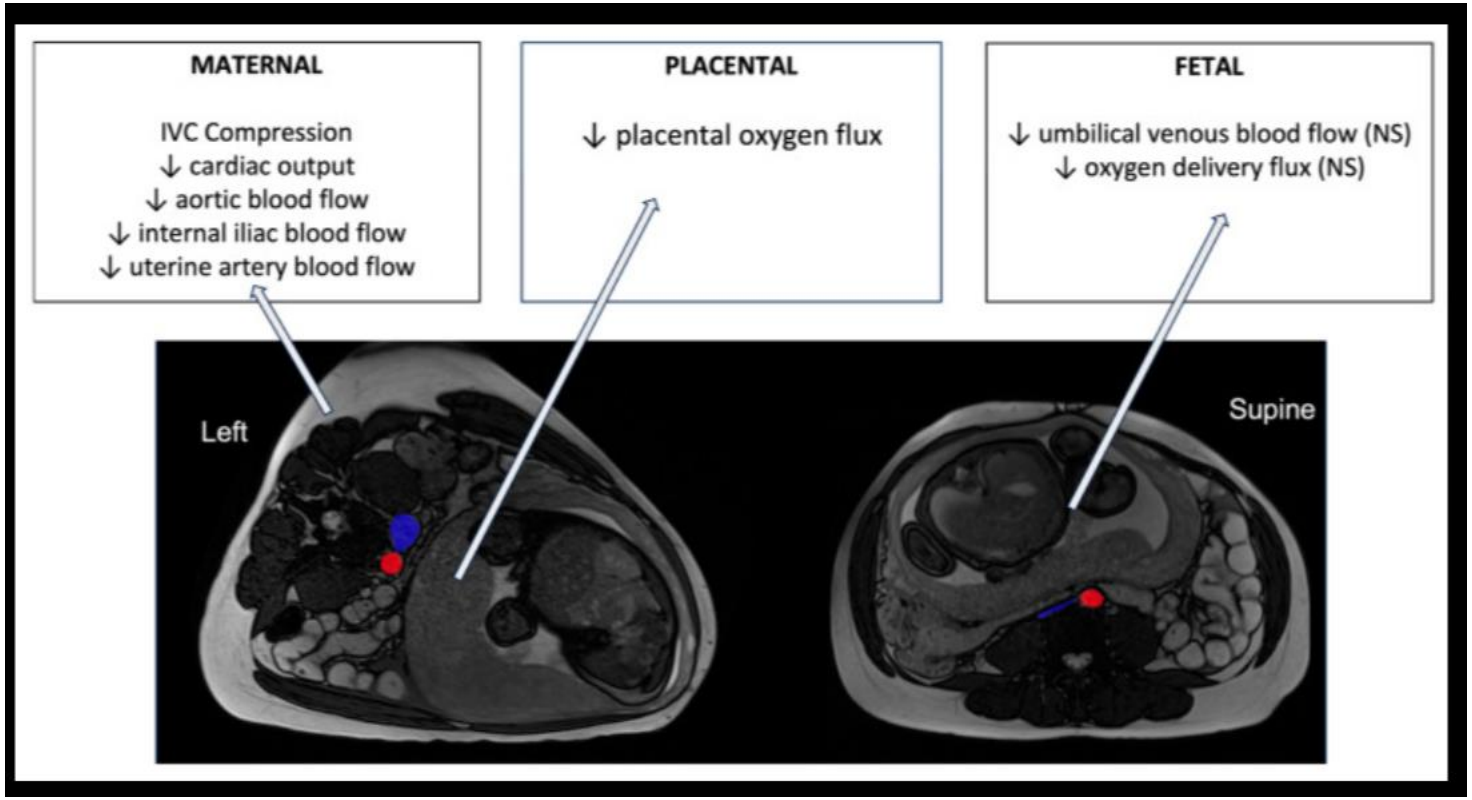
Early PE: venous hypertension with increased venous tone

Late PE-I: Venous overfill in a system at max capacitance

Late PE-II (obesity): increased external pressure with increased intrabdominal pressure

Venous compression and stillbirth

- McCowan LME, Thompson JMD, Cronin RS, Li M, Stacey T, Stone PR, Lawton BA, Ekeroma AJ, Mitchell EA. Going to sleep in the supine position is a modifiable risk factor for late pregnancy stillbirth; Findings from the New Zealand multicentre stillbirth case-control study. PLoS One. 2017 Jun 13;12(6):e0179396
- Wilson DL, Fung AM, Skrzypek H, Pell G, Barnes M, Howard ME, Walker SP. Maternal sleep behaviours preceding fetal heart rate events on cardiotocography. J Physiol. 2022 Apr;600(7):1791-1806.
- Clark AR, Fontinha H, Thompson J, Couper S, Jani D, Mirjalili A, Bennet L, Stone P. Maternal Cardiovascular Responses to Position Change in Pregnancy. Biology (Basel). 2023 Sep 21;12(9):1268.



Pathologic changes indicative of MVM (from Amsterdam consensus)

- Small placenta for gestational age
- Thin umbilical cord for age
- Accelerated villous maturation
- Distal villous hypoplasia
- Infarcts
- Decidual arteriopathy

Khong TY, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Arch Pathol Lab Med. 2016 Jul;140(7):698-713. PMID: 27223167.

Other pathologic changes of MVM before Amsterdam

- Immature intermediate trophoblast of basal plate
- Increased placental site multinucleated trophoblast
- Increased intervillous fibrin

Pediatric and Developmental Pathology 7, 237–249, 2004
DOI: 10.1007/s10024-003-8083-2

Maternal Vascular Underperfusion: Nosology and Reproducibility of Placental Reaction Patterns

Raymond W. Redline,[1*] Theonia Boyd,[2] Valarie Campbell,[3] Scott Hyde,[4] Cynthia Kaplan,[5] T. Yee Khong,[6] Heather R. Prashner,[7] Brenda L. Waters,[8] for the Society for Pediatric Pathology, Perinatal Section, Maternal Vascular Underperfusion Nosology Committee

How many features do you need to diagnose MVM?

- Amsterdam criteria do not state.
- Many in practice recommend at least 2 for diagnosis of MVM
  - PW <10th, AVM, DVH, decidual arteriopathy
  - Thin cord alone, retroplacental hemorrhage alone less commonly cited as criteria

Small placenta

By definition, a trimmed disc weight below the 10th percentile for gestational age

- Formalin fixation may add ~4% to the tissue weight
- Values below the 3rd percentile most clinically significant

Associations

- Maternal vascular malperfusion
  - Especially hypertension with renal impairment
- Constitutionally small placenta
  - Especially if using 10th percentile cut off
- Chronic villitis, viral infection
- Malnutrition, short interpregnancy interval
- Chromosomal abnormality
- Uterine constraint

Accelerated villous maturation

- Villi appear more mature than expected histology for gestational age
  - Difficult to diagnose after 36 weeks
  - Increased numbers of smaller terminal villi with vasculosyncytial membranes
  - Fewer larger intermediate villi than expected for age
  - Increased syncytial knotting for age
  - Usually accompanied by perivillous fibrinoid along stem villi and beneath chorionic plate
  - Often with fibrinoid necrosis of individual villi

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

By virtue of the use of this phrase, accelerated villous maturation may be difficult to recognize in a term placenta, but it is a reproducible pattern to diagnose prior to term. It is diagnosed by identifying a diffuse pattern of term-appearing villi with increased syncytial knots and intervillous fibrin, usually alternating with areas of villous paucity (figure 12)"

Khong TY, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Arch Pathol Lab Med. 2016 Jul;140(7):698-713. PMID: 27223167.

Sampling and Definitions of Placental Lesions

Amsterdam Placental Workshop Group Consensus Statement

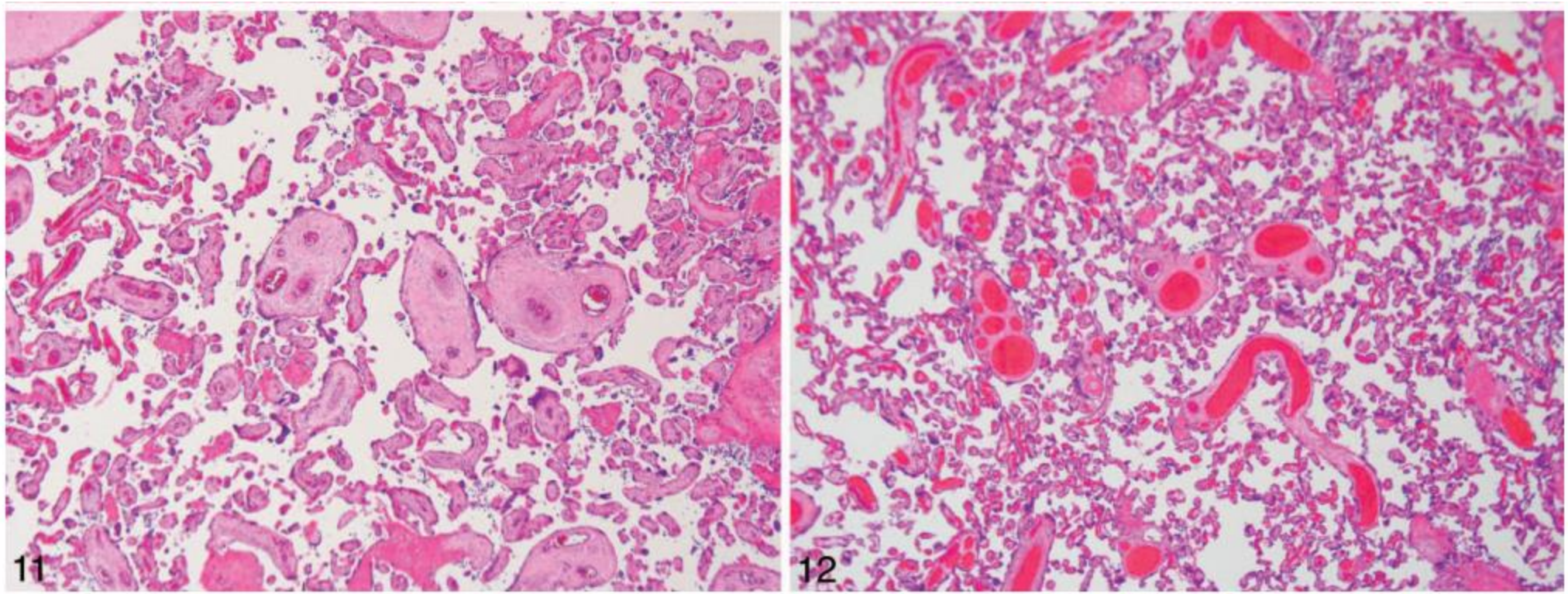


Figure 11. *Distal villous hypoplasia: there is a paucity of villi, many of which are thin and elongated (hematoxylin-eosin, original magnification ×4).*

Figure 12. *Accelerated villous maturation: there is a combination of areas with increased syncytial knots and intervillous fibrin deposition (hematoxylin-eosin, original magnification ×4).*

Diagnosing accelerated villous maturation from Amsterdam criteria is hard. We don't agree very well.

Table 2. Overall Agreement for Entire Group of 6 Examiners and for the Subset of 4 Examiners[a]

Finding	Mean Prevalence, %	Positive Agreement, Estimate (95% CI)	Negative Agreement, Estimate (95% CI)	Fleiss κ, Estimate (95% CI)
All 6 examiners				
ACA, any	11.2	0.62 (0.55–0.69)	0.94 (0.89–0.97)	0.56 (0.43–0.68)
Fetal stage 2	2.0	0.73 (0.66–0.79)	0.99 (0.98–1.00)	0.73 (0.39–1.00)
VUE, any	11.2	0.65 (0.58–0.72)	0.94 (0.90–0.97)	0.59 (0.46–0.73)
VUE, AV	8.3	0.55 (0.48–0.62)	0.96 (0.92–0.98)	0.51 (0.28–0.74)
FVM, any	18.5	0.39 (0.32–0.46)	0.82 (0.75–0.87)	0.21 (0.12–0.29)
AV, small	9.2	0.28 (0.22–0.35)	0.91 (0.86–0.94)	0.19 (0.07–0.31)
AV, large	3.0	0.22 (0.17–0.29)	0.97 (0.93–0.99)	0.19 (0.01–0.37)
VSK, any	2.0	0.23 (0.18–0.30)	0.95 (0.91–0.97)	0.19 (0.06–0.31)
MVM/AVM	3.7	0.19 (0.14–0.25)	0.97 (0.94–0.99)	0.16 (−0.03 to 0.34)
Subgroup of 4 examiners				
ACA, any	13.5	0.77 (0.69–0.83)	0.94 (0.90–0.98)	0.72 (0.58–0.86)
Fetal stage 2	2.3	0.88 (0.83–0.93)	0.997 (0.97–1.00)	0.89 (0.64–1.00)
VUE, any	13.8	0.79 (0.71–0.85)	0.96 (0.91–0.98)	0.74 (0.59–0.90)
VUE, AV	7.5	0.64 (0.53–0.74)	0.96 (0.91–0.98)	0.61 (0.37–0.85)
FVM, any	17.3	0.50 (0.42–0.58)	0.86 (0.80–0.91)	0.37 (0.23–0.50)
AV, small	11.0	0.38 (0.30–0.46)	0.90 (0.84–0.94)	0.28 (0.13–0.43)
AV, large	3.3	0.51 (0.43–0.60)	0.99 (0.94–0.99)	0.49 (0.16–0.83)
VSK, any	4.5	0.44 (0.36–0.53)	0.97 (0.92–0.99)	0.41 (0.10–0.72)
MVM/AVM	3.7	0.20 (0.15–0.28)	0.97 (0.93–0.99)	0.18 (−0.21 to 0.56)

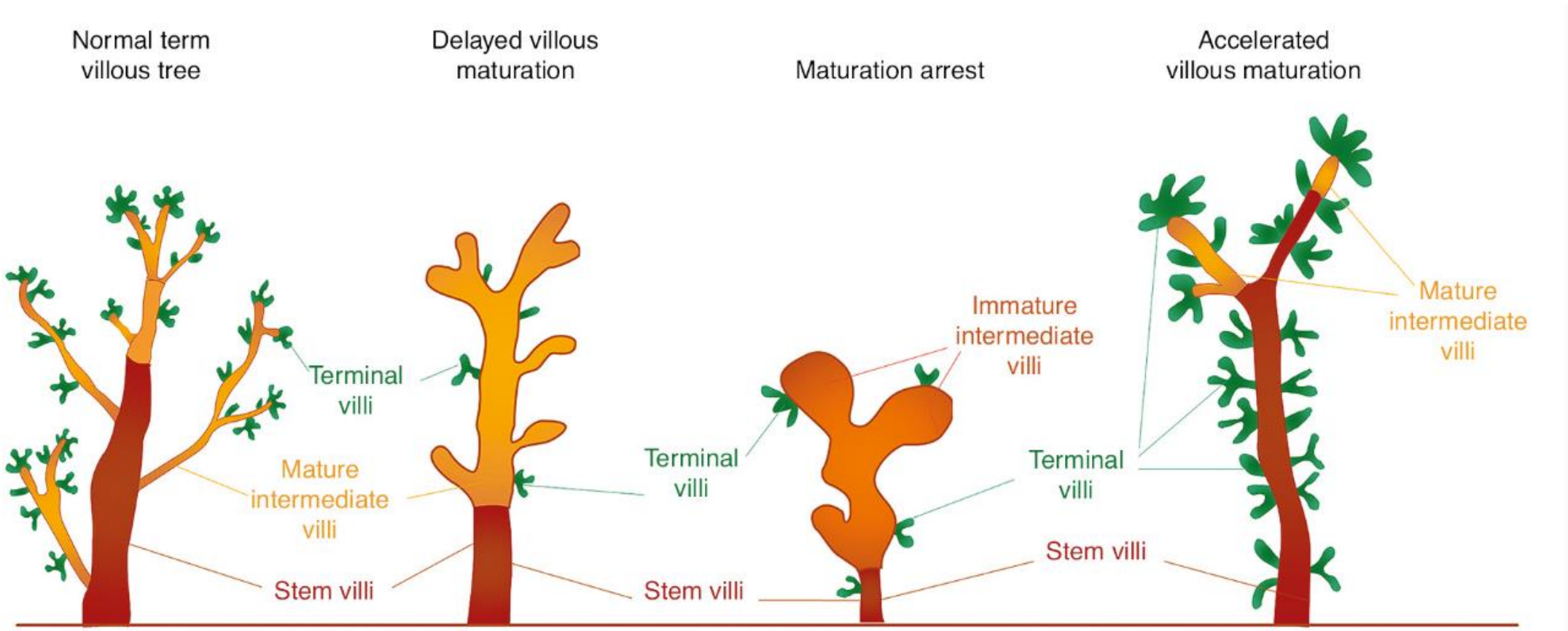
Abbreviations: ACA, acute chorioamnionitis; AV, large, at least 1 large focus of avascular villi; AV, small, exclusively small foci of avascular villi; fetal stage 2, fetal inflammatory response in umbilical artery; FVM, fetal vascular malperfusion; MVM/AVM, maternal vascular malperfusion/accelerated villous maturation; VSK, any, villous stromal vascular karyorrhexis; VUE, villitis of unknown etiology; VUE, AV, VUE with associated avascular villi.

[a] Observers A, B, C, and D (see text and Table 4).

Why should there be poor agreement?

- Focus on microsocpic appearance of slide without context of expected morphology for arterial, capillary, venous zones of lobule
- Wigglesworth described the lobule, with variable villous density and suggested there were different morphologies (immature appearing centers)
- Fox ignores lobular architecture when describing percentages of small villi in horizontal divisions (subchorionic third, mid-third, basal third)

- The Amsterdam document alludes to physiologic differences in villous morphology throughout cotyledon, but does not describe diagnosis in this context



~60% terminal villi

Larger percentage of mature terminal villi than expected for age

Jaiman, Sunil, et al. "Disorders of placental villous maturation in fetal death" *Journal of Perinatal Medicine*, vol. 48, no. 4, 2020, pp. 345-368. https://doi.org/10.1515/jpm-2020-0030

J. Obstet. Gynaec. Brit. Cwlth.
Nov. 1969. Vol. **76**. pp. 979–989.

VASCULAR ANATOMY OF THE HUMAN PLACENTA AND ITS SIGNIFICANCE FOR PLACENTAL PATHOLOGY

BY

J. S. WIGGLESWORTH, *Senior Lecturer in Paediatric Pathology,*
Institute of Child Health, Hammersmith Hospital, London, W.12

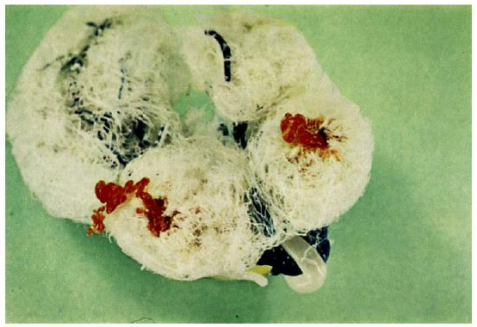


FIG. 4
Tensol cast of part of placenta showing spiral arteries entering centres of fetal lobules. Fetal arteries white, spiral arteries red.

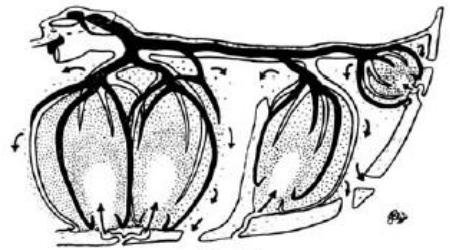


FIG. 11
Diagram of circulation through intervillous space in relation to fetal lobular pattern. Density of stippling indicates density of fetal villi.

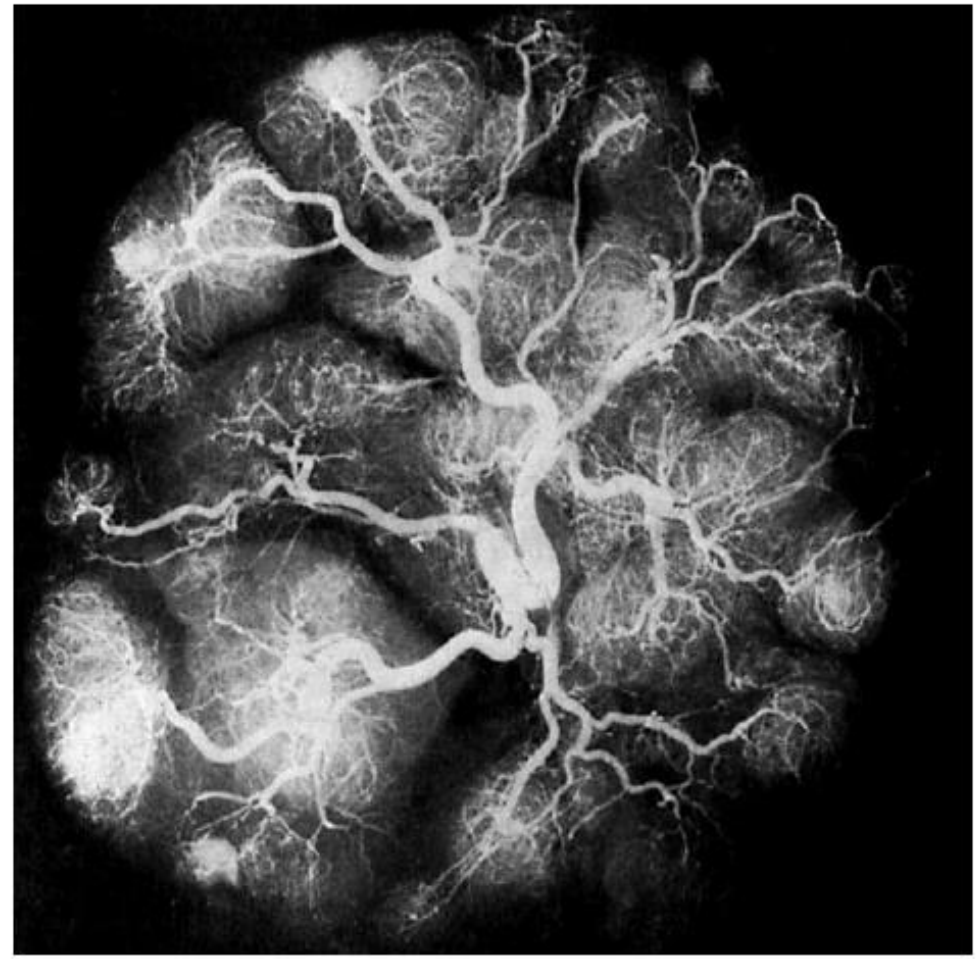
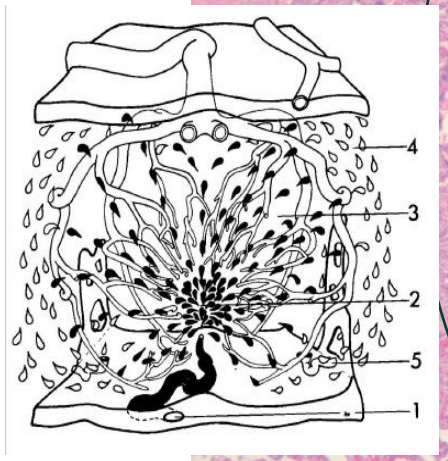
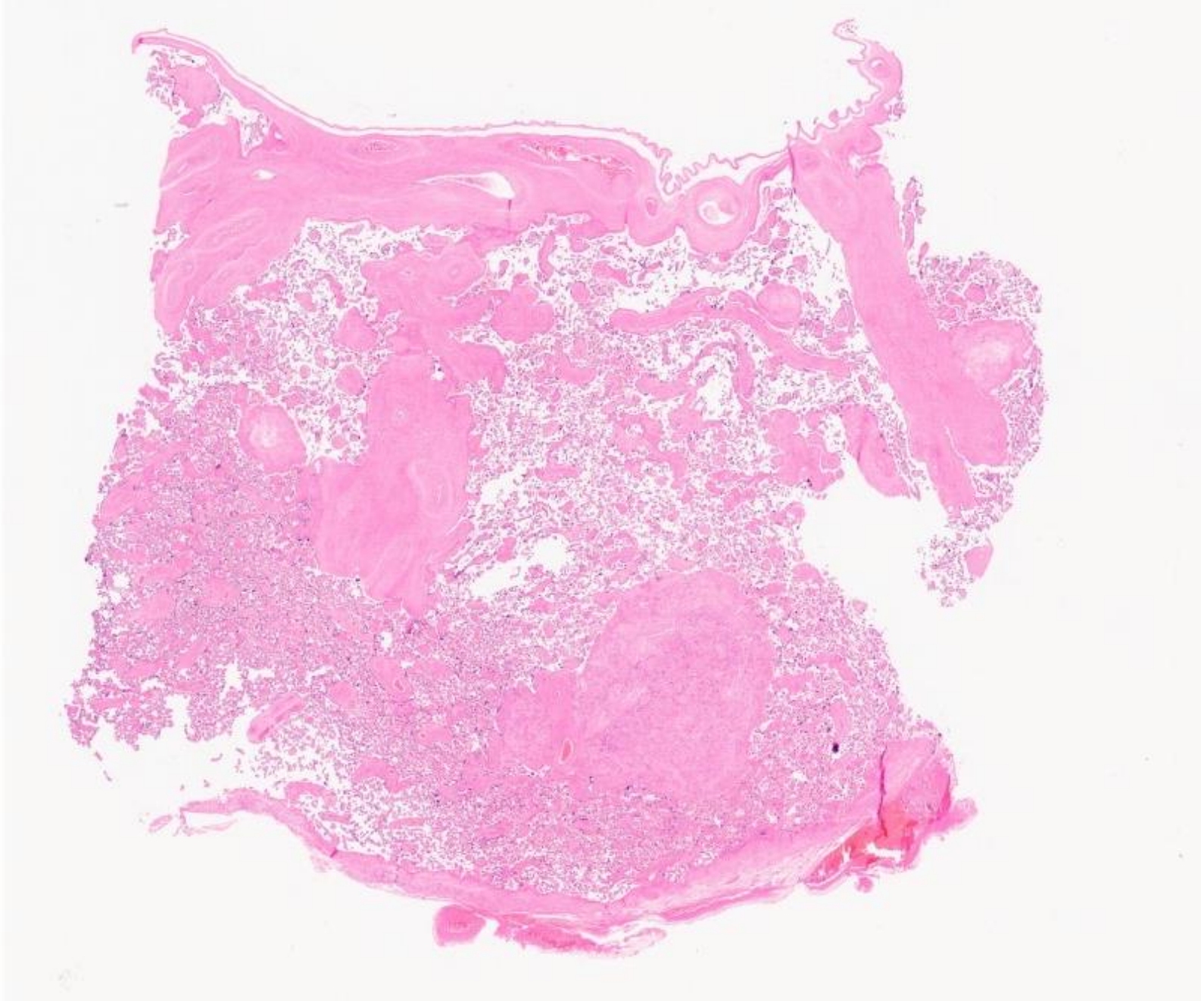


FIG. 2
X-ray of placenta showing umbilical arterial system injected with Ba. gelatine. Note lobular pattern.

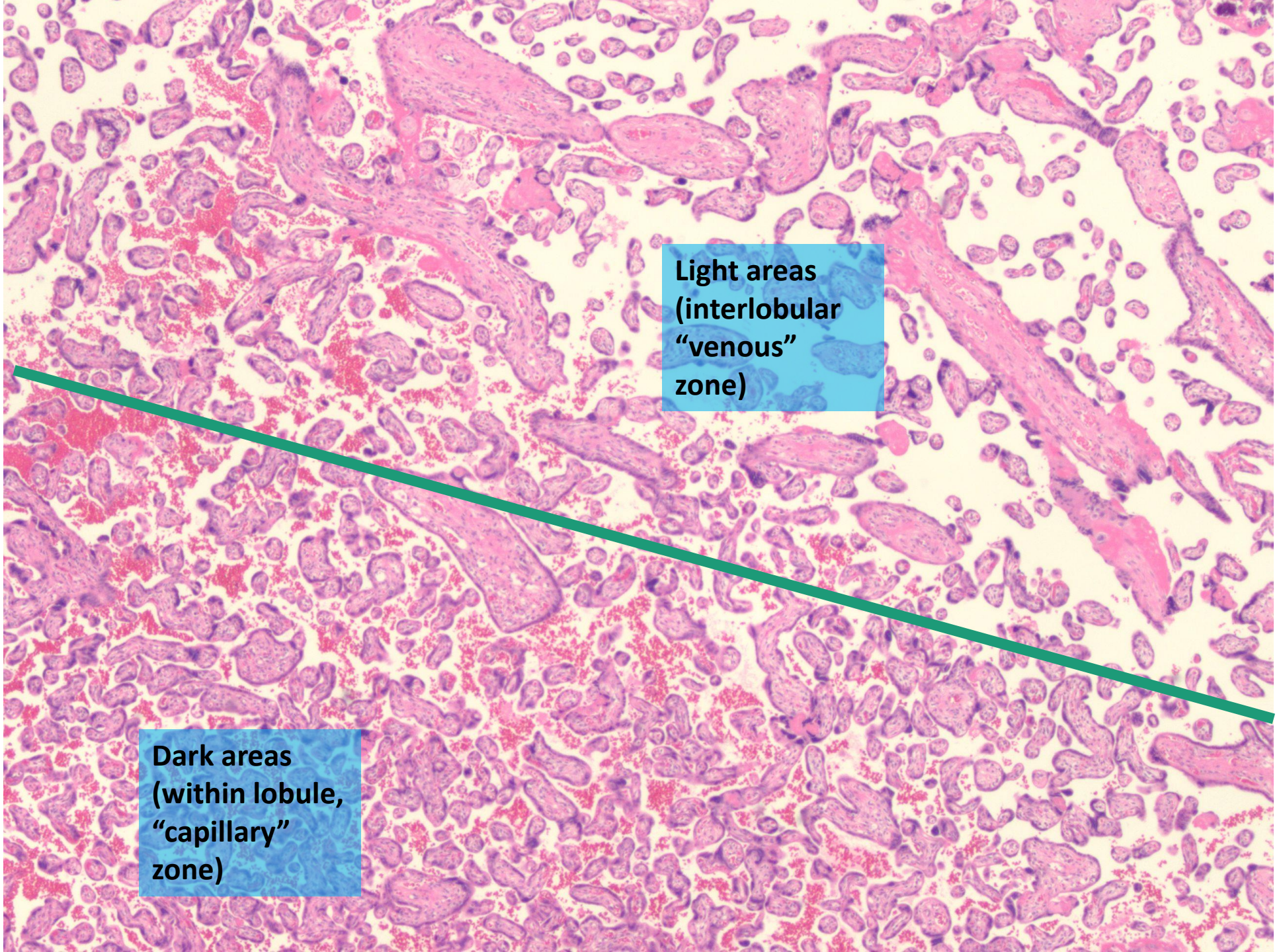

4
3
2
5
1

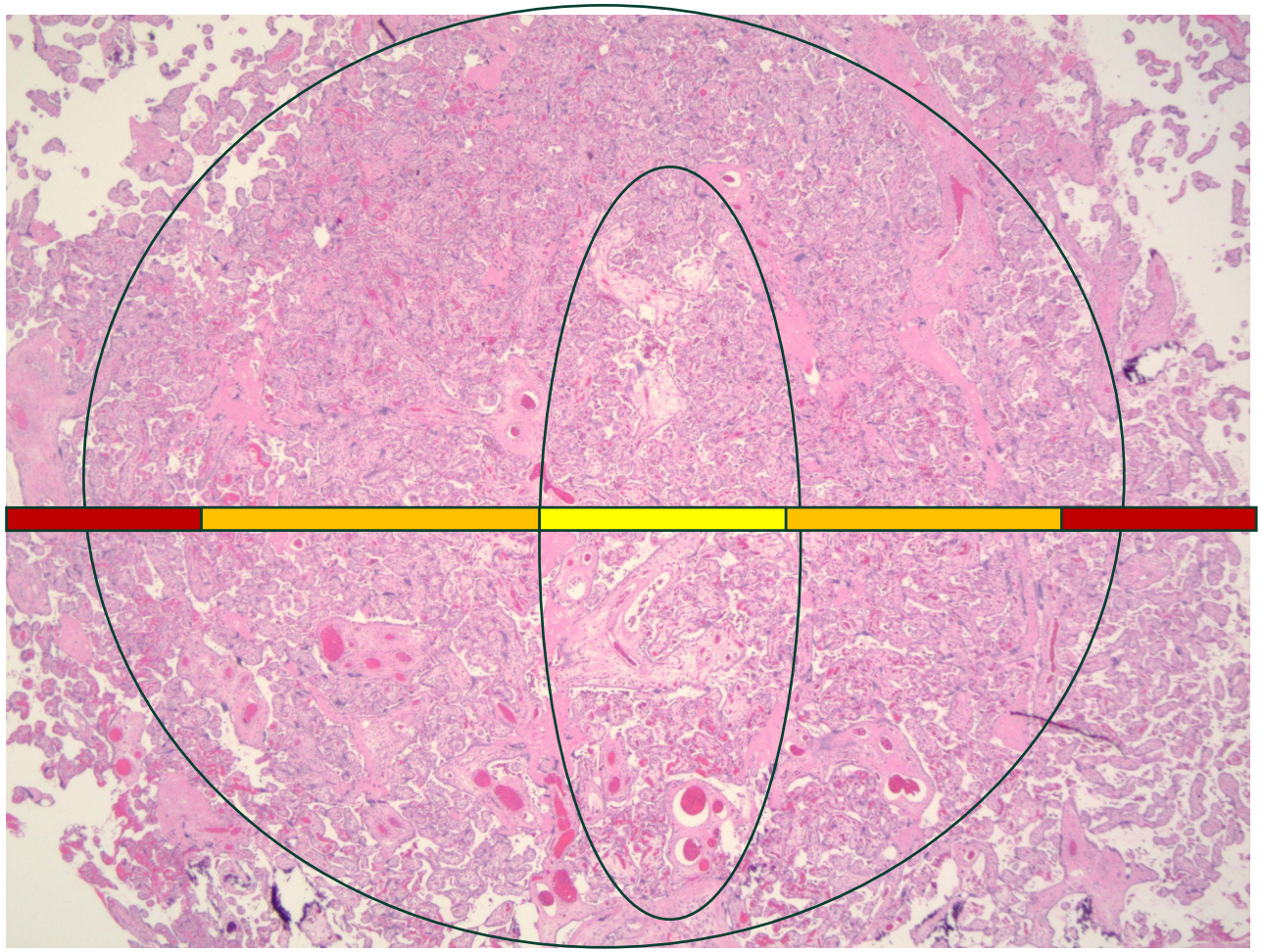
Some pathologists make the diagnosis of accelerated villous maturation after 36 weeks by recognizing “light” and “dark” areas, visible at 1x looking at the slide

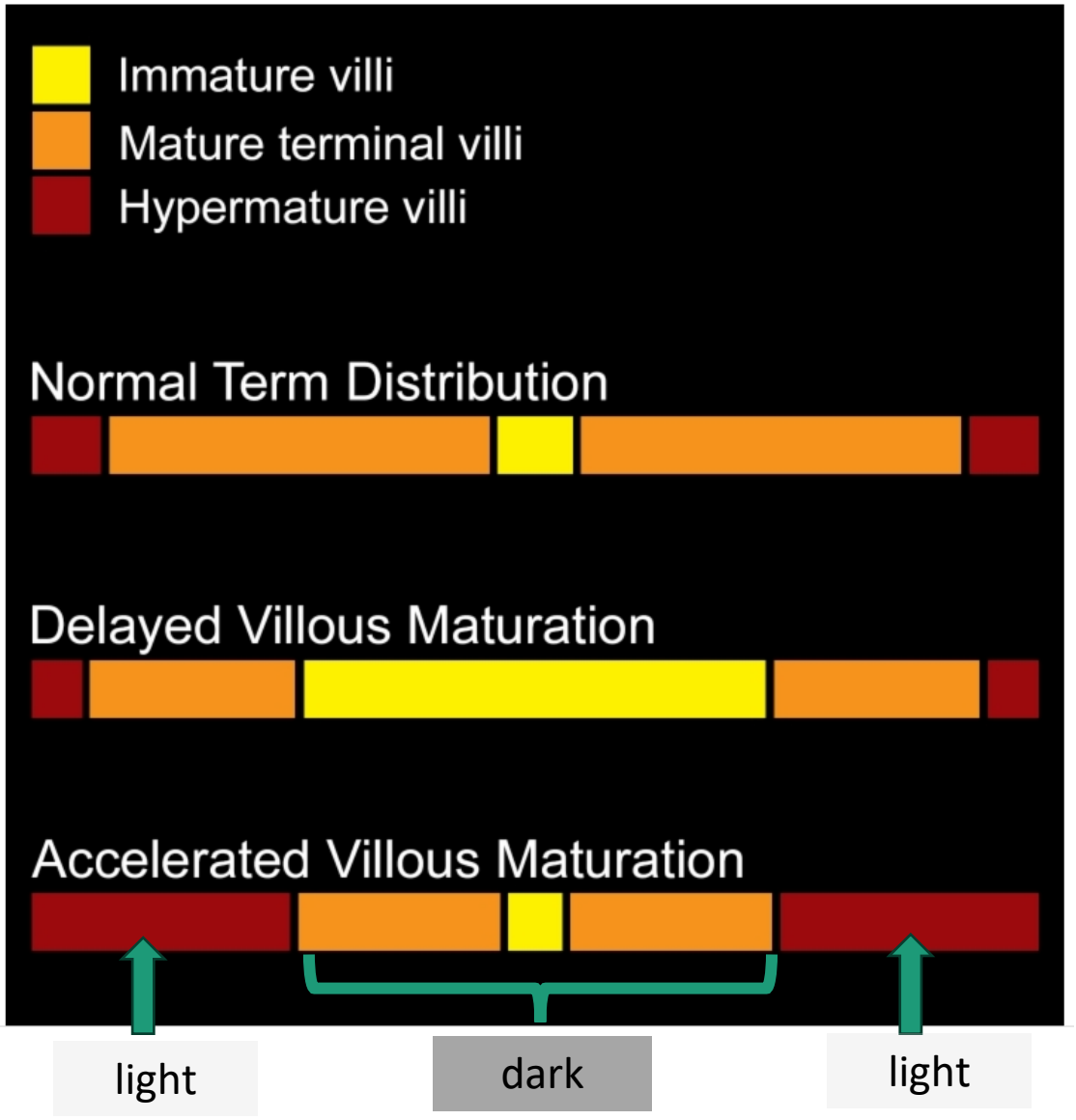


Light: areas of sparse, small caliber villous growth

Dark: areas of dense villi, frequent bridging knots, agglutination, aggregations with fibrin






Immature villi
Mature terminal villi
Hypermature villi
Normal Term Distribution
Delayed Villous Maturation
Accelerated Villous Maturation
light
dark
light

Accelerated villous maturation

- Villi appear more mature than expected histology for gestational age
  - Difficult to diagnose after 36 weeks
  - Increased numbers of smaller terminal villi with vasculosyncytial membranes
  - Fewer larger intermediate villi than expected for age
  - Increased syncytial knotting for age
  - Usually accompanied by perivillous fibrinoid along stem villi and beneath chorionic plate
  - Often with fibrinoid necrosis of individual villi

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

By virtue of the use of this phrase, accelerated villous maturation may be difficult to recognize in a term placenta, but it is a reproducible pattern to diagnose prior to term. It is diagnosed by identifying a diffuse pattern of term-appearing villi with increased syncytial knots and intervillous fibrin, usually alternating with areas of villous paucity (figure 12)"

Khong TY, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. Arch Pathol Lab Med. 2016 Jul;140(7):698-713. PMID: 27223167.

Distal Villous Hypoplasia

- Sparse, small, elongated distal villi
  - Some appear to contain only a single capillary loop with a syncytiotrophoblast knot
  - Few distal villi between stem villi
  - Very few intermediate villi
- Diagnostic criteria
  - Involves >30% of parenchyma on slide
    - Focal- on one slide
    - Diffuse – on more than one slide
  - Parenchyma beneath chorionic plate, at borders of lobule (venous zones) may show this histology, need to hold out for more extensive (>30%) changes, involving central areas of lobule

Khong TY et al: Sampling and definitions of placental lesions: Amsterdam placental workshop group consensus statement. Arch Pathol Labb Med 140 (7): 698-713;2016.

Sampling and Definitions of Placental Lesions

Amsterdam Placental Workshop Group Consensus Statement

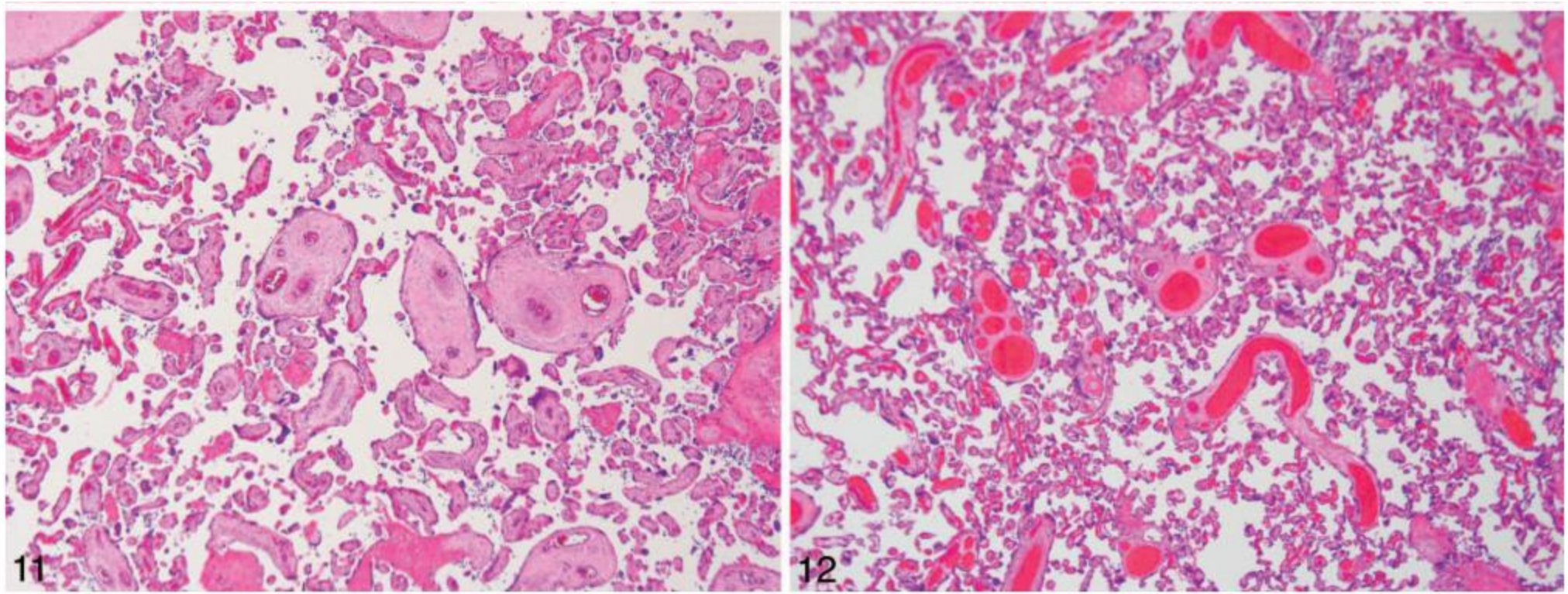
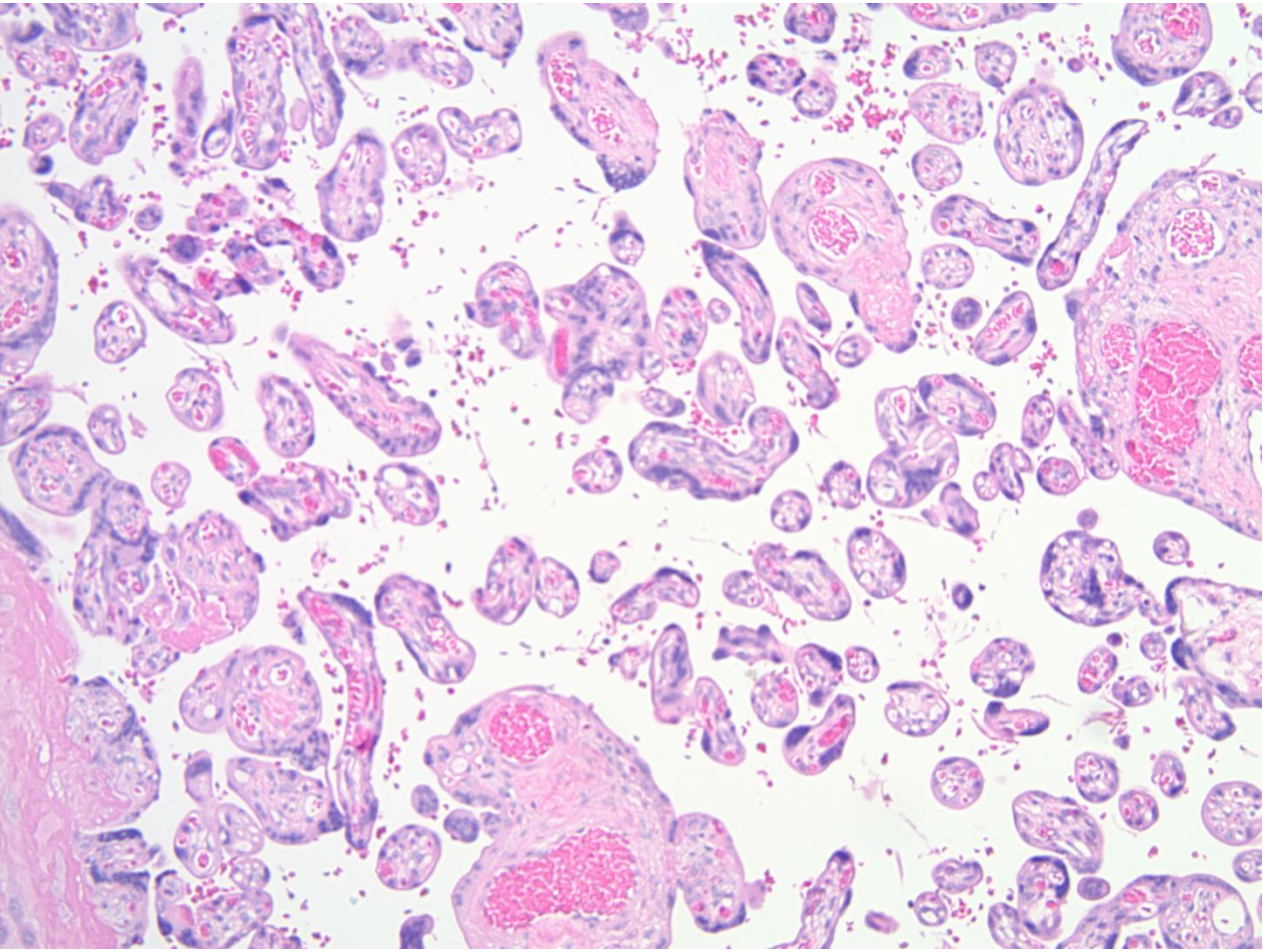
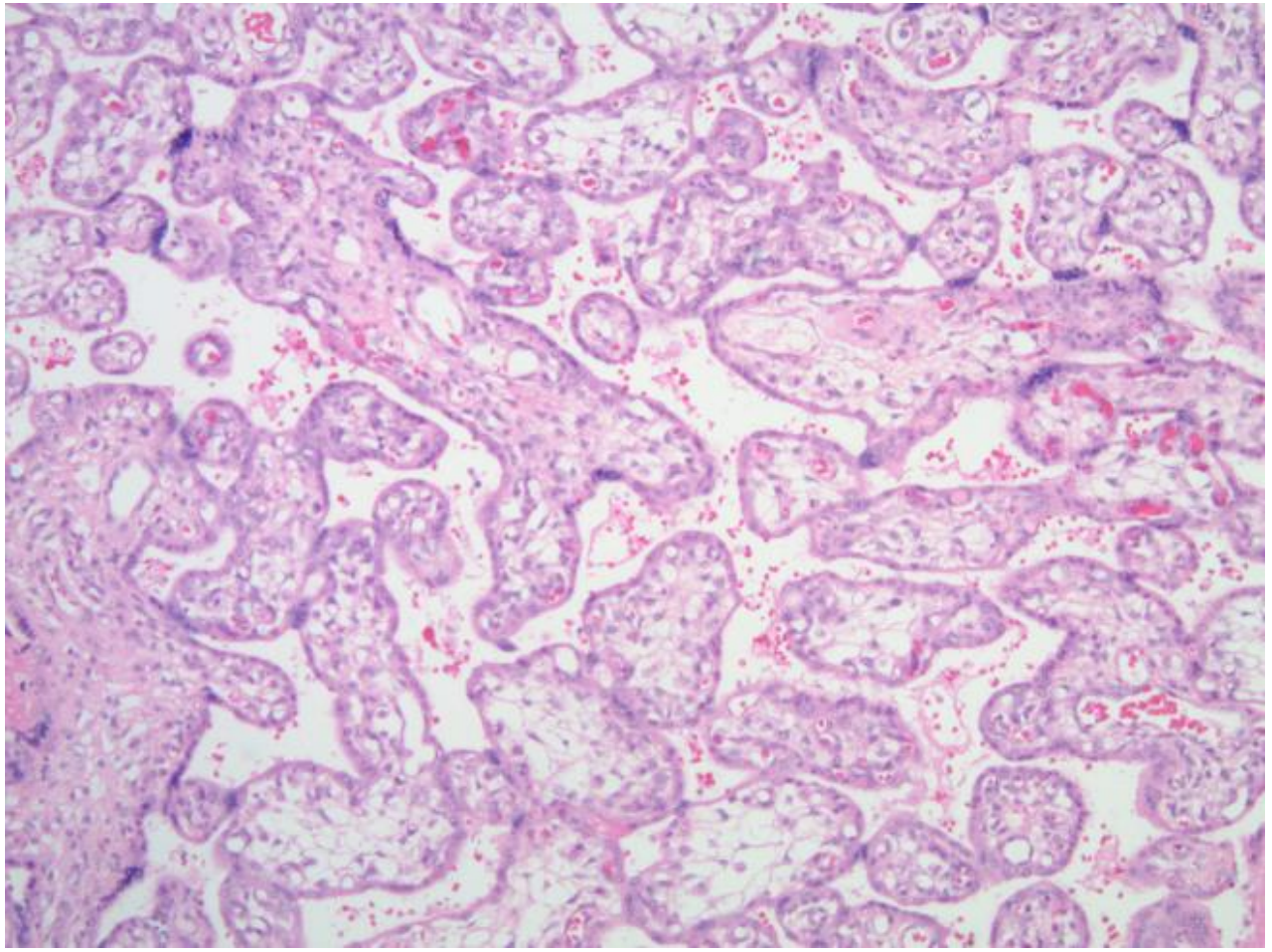


Figure 11. *Distal villous hypoplasia: there is a paucity of villi, many of which are thin and elongated (hematoxylin-eosin, original magnification ×4).*

Figure 12. *Accelerated villous maturation: there is a combination of areas with increased syncytial knots and intervillous fibrin deposition (hematoxylin-eosin, original magnification ×4).*

Distal villous hypoplasia

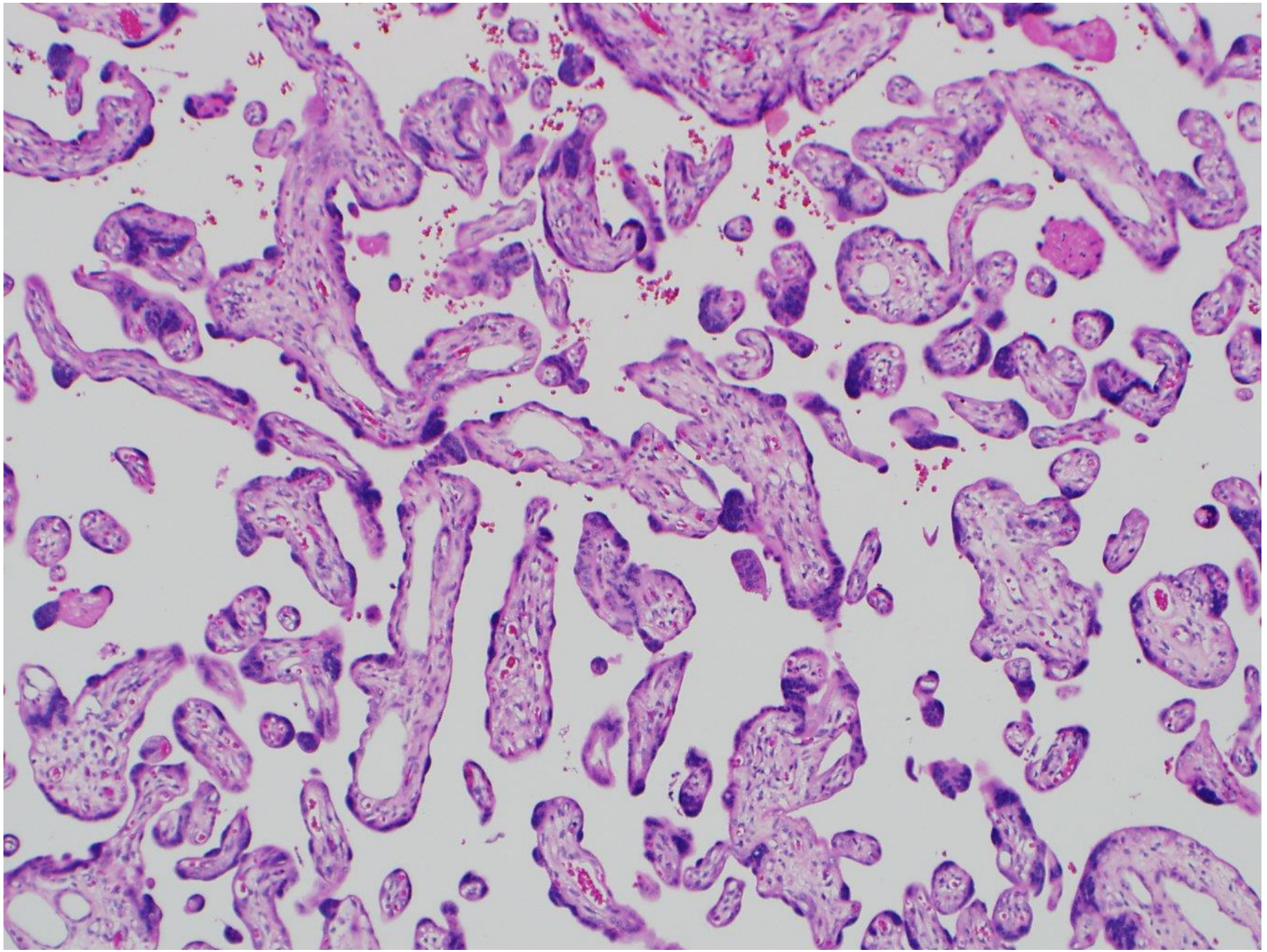




In DVH (left) the villi are widely spaced, and of very small caliber for age.
Compare with normally developed early 3rd trimester villi (right).

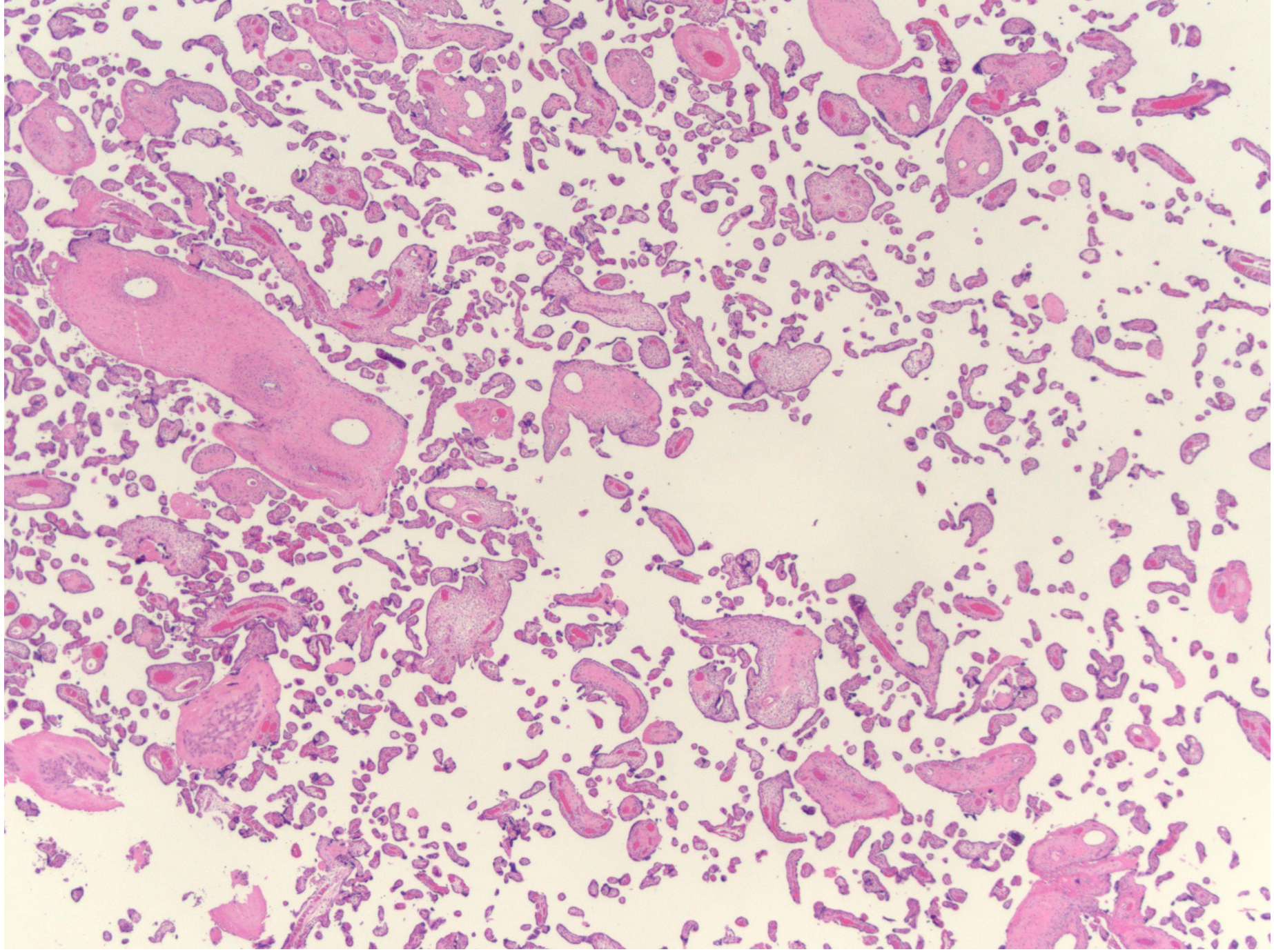
Distal villous hypoplasia

Hypermature, small, sparse villi



Distal villous hypoplasia

Hypermature, small, sparse villi



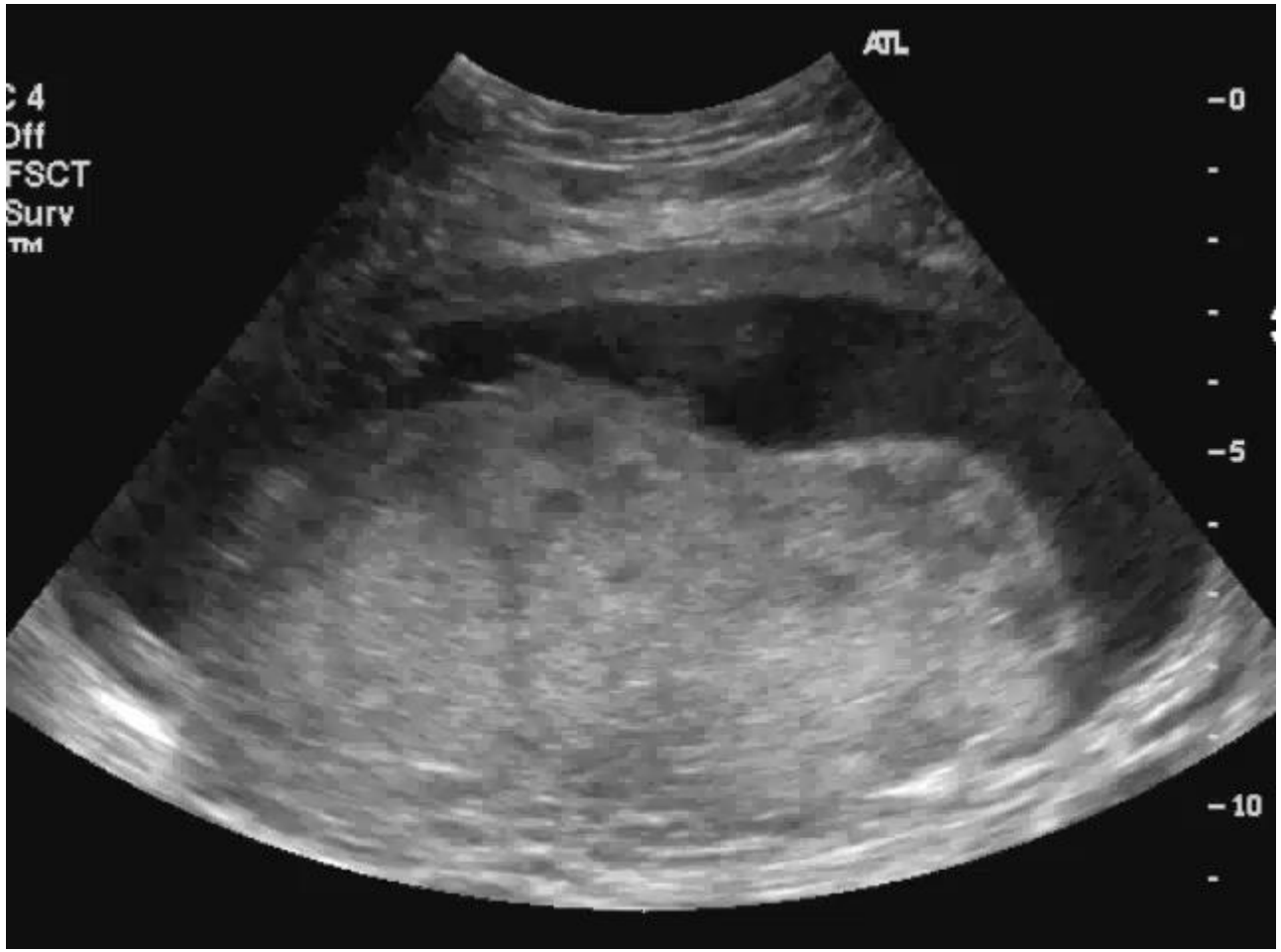
A placenta clinic approach to the diagnosis and management of fetal growth restriction

John C. Kingdom, MD, FRCSC; Melanie C. Audette, MD, PhD; Sebastian R. Hobson, MBBS, MPH, FRANZCOG; Rory C. Windrim, MD, MSc, FRCSC; Eric Morgen, MD, MPH, FRCPC

FEBRUARY 2018 American Journal of Obstetrics & Gynecology S803

Distal villous hypoplasia has a characteristic gross morphology seen on ultrasound:

- “cupcake” placenta, small diameter and unusually thick
- “wobbly” appearing in vivo
- Placenta “deflates” after delivery, losing enlarged appearance
- Weight in pathology is small for gestational age.



Decidual arteriopathy

- Previous terminology: maternal decidual vasculopathy
- Occurs in <1% of uncomplicated pregnancies
- Pathologic subtypes
  - Mural hypertrophy – arterial/arteriolar wall thickness >1/3 of vessel diameter
    - Often with perivascular lymphoid cells
    - On a continuum with fibrinoid necrosis decidual arteriopathy
  - Fibrinoid necrosis – muscular wall is replaced by fibrin +/- foam cells
  - Acute atherosis- fibrinoid necrosis of vessel wall with numerous intimal and intramural foamy macrophages
  - Thrombosis
  - Absence of spiral artery remodeling in basal plate (central 2/3)- persistence of vascular smooth muscle
  - Persistence of luminal trophoblast in 3rd trimester (basal plate)

Infarcts

- Grossly visible lesions
- General rule of thumb- 1 infarct, 1cm or less in size within 1cm of margin at term not pathologic
- Most show collapse of intervillous space
  - Subset of infarcts at disc margin show associated pervillous fibrin separating villi
- Progressive loss of villous nuclear basophilia with degeneration
  - First change is often collapse of intervillous space and smudging of syncytiotrophoblast nuclei
  - Early infarcts show small amount of fibrin surrounding injured villi with acute inflammation

Infarction hematoma/Rounded Intraplacental Hematoma

- Rounded area of central hemorrhage surrounded by a cuff of infarcted villi
- Often with decidual arteriopathy or thrombus in underlying basal plate decidua
- Clinical associations similar to placental abruption

Neville G, Russell N, O'Donoghue K, Fitzgerald B. Rounded intraplacental hematoma - A high risk placental lesion as illustrated by a prospective study of 26 consecutive cases. Placenta. 2019 Jun;81:18-24. PMID: 31138427.

Bendon RW. Nosology: infarction hematoma, a placental infarction encasing a hematoma. Hum Pathol. 2012 May;43(5):761-3. PMID: 22079357.

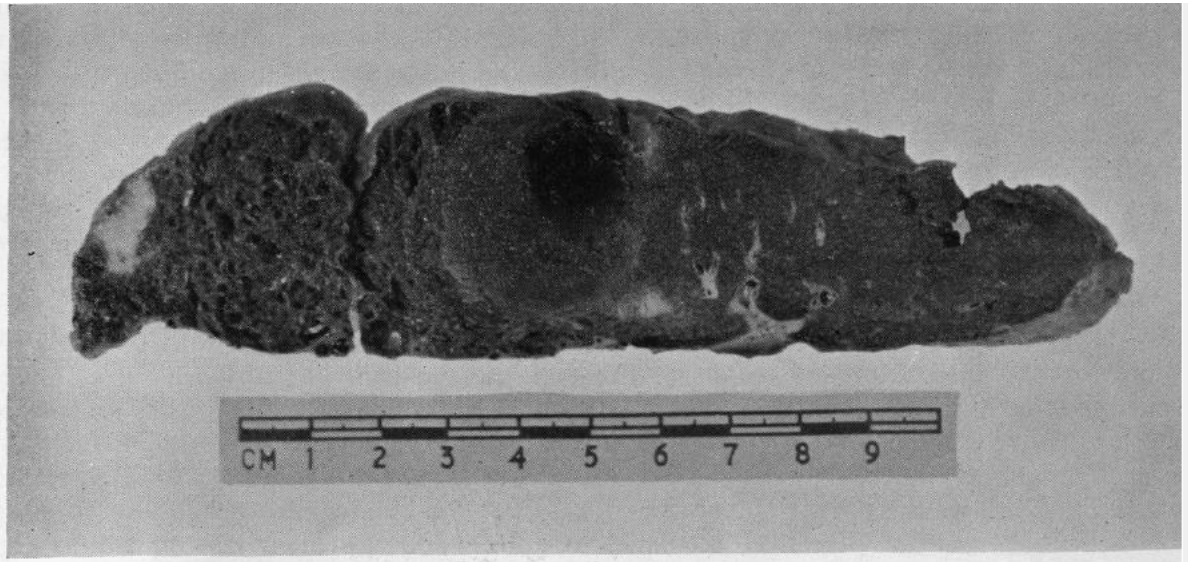


FIG. 2

Section through a fixed placenta from a case of fulminating pre-eclampsia showing a well-circumscri recent infarct with a central area of blood clot.

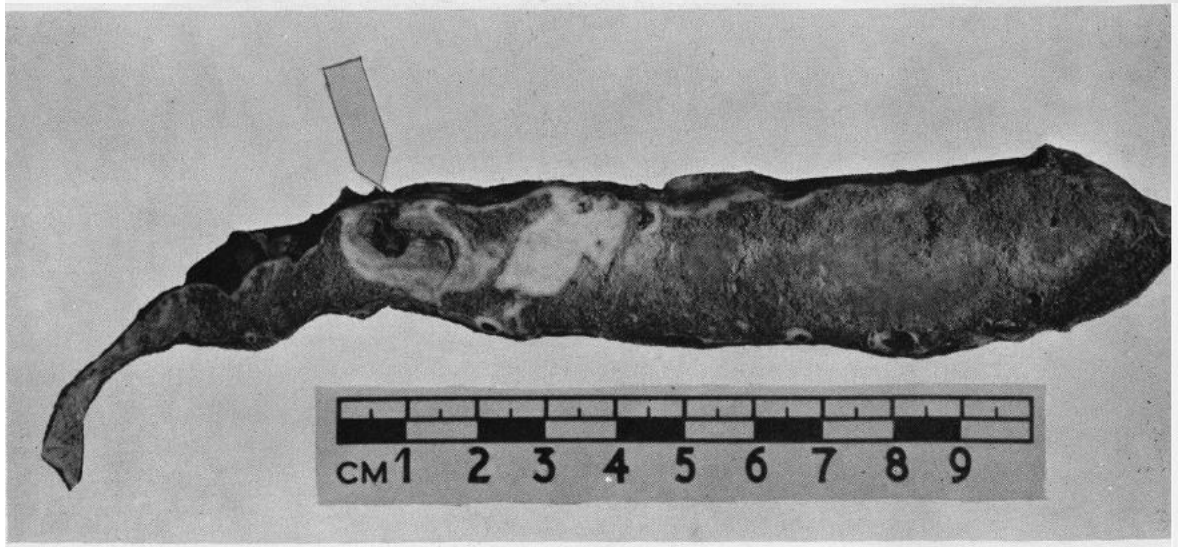


FIG. 3

Section through a fixed placenta from a case of pre-eclampsia with an old cavitated infarct. The ma indicates the central punctum.

MORPHOLOGICAL VARIATIONS IN THE INSUFFICIENT PLACENTA

BY

J. S. WIGGLESWORTH*, M.D., M.B., B.Chir.(Cantab.), *Beit Memorial Fellow*
Department of Morbid Anatomy, University College Hospital Medical School, London

Journal of Obstetrics and Gyneacology of the British Commonwealth, 1964.

J. Obstet. Gynaec. Brit. Cwlth.
Nov. 1969. **Vol. 76.** pp. 979–989.

VASCULAR ANATOMY OF THE HUMAN PLACENTA AND ITS SIGNIFICANCE FOR PLACENTAL PATHOLOGY

BY

J. S. WIGGLESWORTH, *Senior Lecturer in Paediatric Pathology,*
Institute of Child Health, Hammersmith Hospital, London, W.12

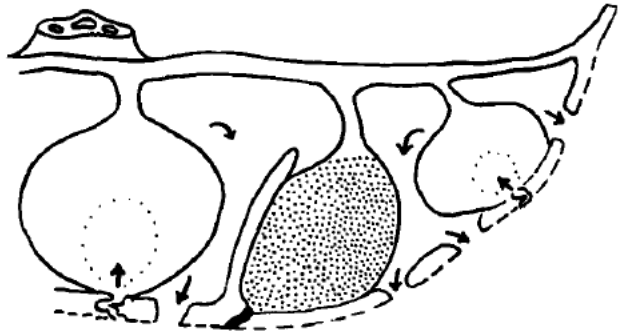


FIG. 12
Site of infarct formation in relation to lobules and intervillous circulation.

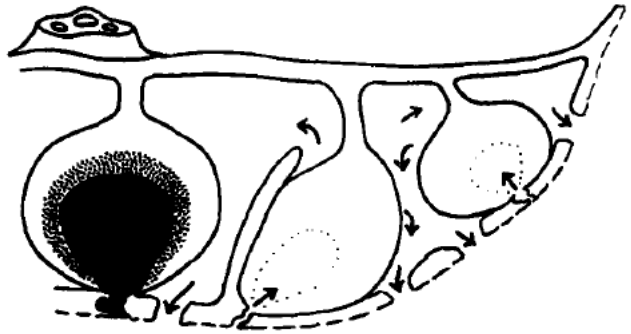


FIG. 13
Site of haematoma formation—in relation to lobules and intervillous circulation.

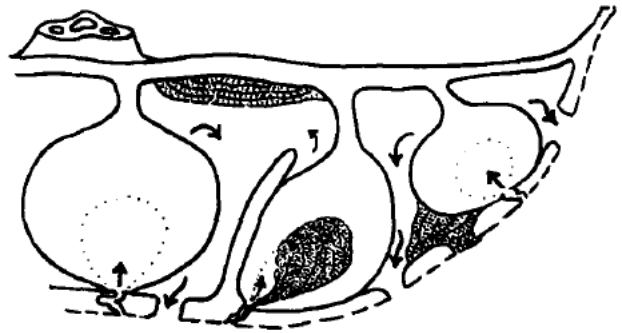


FIG. 14
Sites of intervillous thrombosis in relation to lobules and intervillous circulation.

Closely associated with infarction is the placental haematoma (basal decidual haematoma of Wilkin). This lesion consists of a mass of blood clot in the centre of a fetal cotyledon which is usually infarcted (Fig. 13). It represents rupture of a damaged spiral artery; the rupture often occurs proximal to its thrombosed entry to the intervillous space by a process of gradual aneurysmal dilatation (Wigglesworth, 1964). The lesion is most often found in association with maternal hypertension (Wilkin, 1965) and is significantly associated with perinatal mortality and morbidity.

Grading MVM

- Amsterdam criteria do not provide a grading system
- Grading systems generally refer to a severity of clinical disease
- What disease aspect for MVM?
  - Strength of association for severe preeclampsia?
  - Strength of association for FGR?
  - Strength of association for maternal vascular disease in the decade after pregnancy?

Grading MVM for clinical severity

High grade MVM- has one or more of the following:

- Distal villous hypoplasia
- Placenta weight less than 3rd percentile
- Multiple infarcts

HG MVM associated with the following in decreasing order of prevalence: abnormal pulsed flow Doppler, FGR, abnormal BPP, severe PE, oligohydramnios

Table 3. Indications for Placental Submission Significantly Associated With High-Grade Histopathology and ≥ 2 × Increase Over Population Prevalence.

	MVM High Grade	FVM High Grade	ACA High Grade	VUE High Grade	FSV High Grade	MAVC Any	Increased NRBC
	% positive[a]	% positive	% positive	% positive	% positive	% positive	% positive
All placentas	4.9	1.0	7.8	3.2	2.8	0.7	3.3
Antenatal conditions	Abn PFD 28.6	Clin FGR 2.1	Clin CA 27.1	IVF/ART 16.7	PGDM 12.4	>42 weeks 7.9	>42 weeks 10.5
	Clin FGR 18.2		Mat Temp 20.5	Drug abuse 9.5			UC entang 7.0
	Abn BPP 16.1		Prol ROM 19.6				
	Sev PE 12.7						
	Oligo 10.6						
Gross placental abnormalities	PW Z <−1.5 41.7	FPR Z <−1.5 5.3		PW Z <−1.5 8.3	PW Z >+1.5 8.2	PW Z <1.5 2.8	UC >70 cm 8.0
	FPR Z >+1.5 12.0	UCI <3 2.1		FPR Z >+1.5 6.8			
Adverse outcomes	SGA Z <−2.0 32.8	IUFD 14.8	Apg5 <6 22.1	SGA Z <−2.0 10.3	LGA Z >+2.0 15.3	SGA Z <−2.0 6.9	IUFD 48.1
	SGA Z −1.5/2 22.0	SGA Z <−2.0 5.2			IUFD 11.1		Apg5 <6 11.0
	SGA Z −1/1.5 15.5	SGA Z −1.5/2 3.5					

Abbreviations: Abn BPP, abnormal biophysical profile; Abn PFD, abnormal umbilical pulsed flow Doppler testing; ACA, acute chorioamnionitis; FGR, fetal growth restriction; FPR, fetoplacental ratio; FSV, fetal stromal vascular maldevelopment; FVM, fetal vascular malperfusion; IUFD, intrauterine fetal death; MAVC, meconium associated fetal vascular changes; MVM, maternal vascular malperfusion; NRBC, nucleated red blood cells; PGDM, pregestational diabetes mellitus; PW, placenta weight; SGA, small-for-gestational age; UCI, umbilical cord insertion; VUE, idiopathic chronic villitis (so-called villitis of unknown etiology).

[a]Percentage of placentas with each indication showing column-specific high-grade histopathology.

Zhou YY, Ravishankar S, Luo G, Redline RW. Predictors of High Grade and Other Clinically Significant Placental Findings by Indication for Submission in Singleton Placentas From Term Births. Pediatr Dev Pathol. 2020 Aug;23(4):274-284.

Grading MVM for SGA

Maternal vascular malperfusion	1 point: fibrinoid necrosis/acute atherosis, muscularization of basal plate arterioles, mural hypertrophy of membrane arterioles, basal decidual vascular thrombus, single infarct, increased syncytial knots, villous agglutination, increased perivillous fibrin deposition, distal villous hypoplasia, retroplacental blood/hematoma	High-grade	Score of ≥4
		Low-grade	Score of 2–3
	2 points: multiple infarcts, retroplacental hematoma with hemosiderin or infarct, placental hypoplasia[b]	None	Score of 0–1

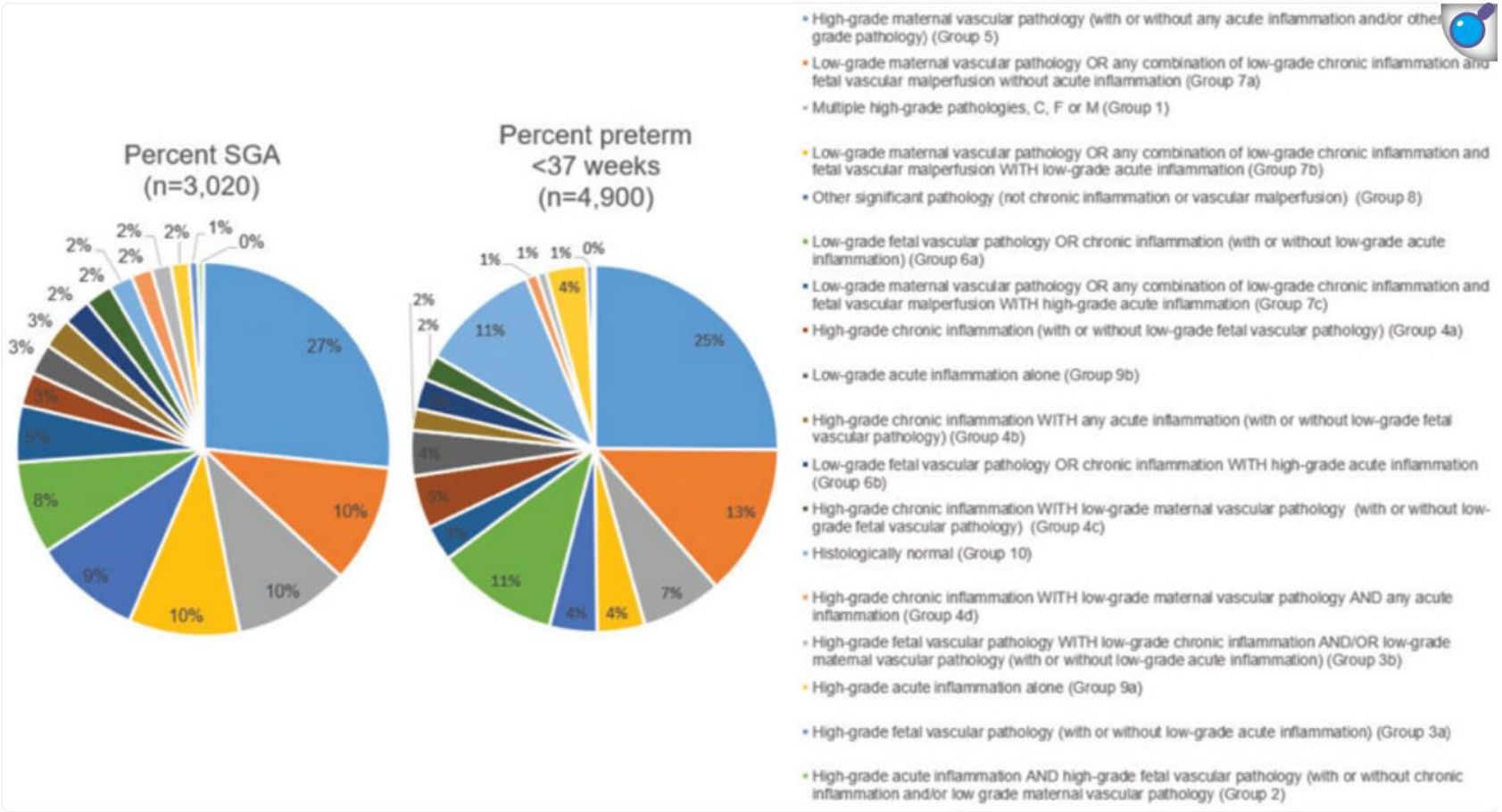
Freedman AA, Keenan-Devlin LS, Borders A, Miller GE, Ernst LM. Formulating a Meaningful and Comprehensive Placental Phenotypic Classification. Pediatr Dev Pathol. 2021 Jul-Aug;24(4):337-350

High grade MVM and FVM associated with SGA

					Percent SGA	OR	95% CI
Multiple high-grade pathologies (C, F, M)	1		771	4.1%	39.0%	14.08	10.49, 18.90
All three high-grade pathologies (triple threat)	1a	CFM, aCFM, ACFM	34		38.2%		
High-grade fetal AND maternal vascular pathology	1b	FM, cFM, aFM, acFM, AFM, AcFM	113		48.7%		
High-grade maternal vascular pathology AND high-grade chronic inflammation	1c	CM, CfM, aCM, aCfM, ACM, ACfM	536		38.2%		
High-grade fetal vascular pathology AND high-grade chronic inflammation	1d	CF, CFm, aCF, aCFm	88		31.8%		

Freedman AA, Keenan-Devlin LS, Borders A, Miller GE, Ernst LM. Formulating a Meaningful and Comprehensive Placental Phenotypic Classification. Pediatr Dev Pathol. 2021 Jul-Aug;24(4):337-350

Grade of MVM associated with more SGA and preterm births



Freedman AA, Keenan-Devlin LS, Borders A, Miller GE, Ernst LM. Formulating a Meaningful and Comprehensive Placental Phenotypic Classification. Pediatr Dev Pathol. 2021 Jul-Aug;24(4):337-350

MVM grade in index pregnancy did not predict recurrent preterm birth

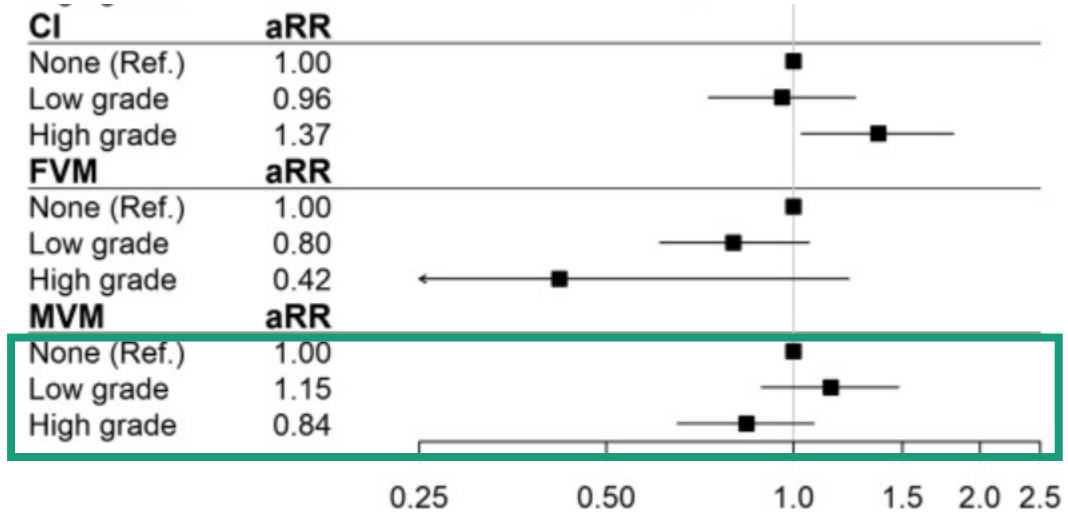


Figure 2. Placental histology and risk of recurrent preterm birth
Risk ratio adjusted for presence of remaining placental lesions, race, gestational age at index pregnancy, and maternal age.

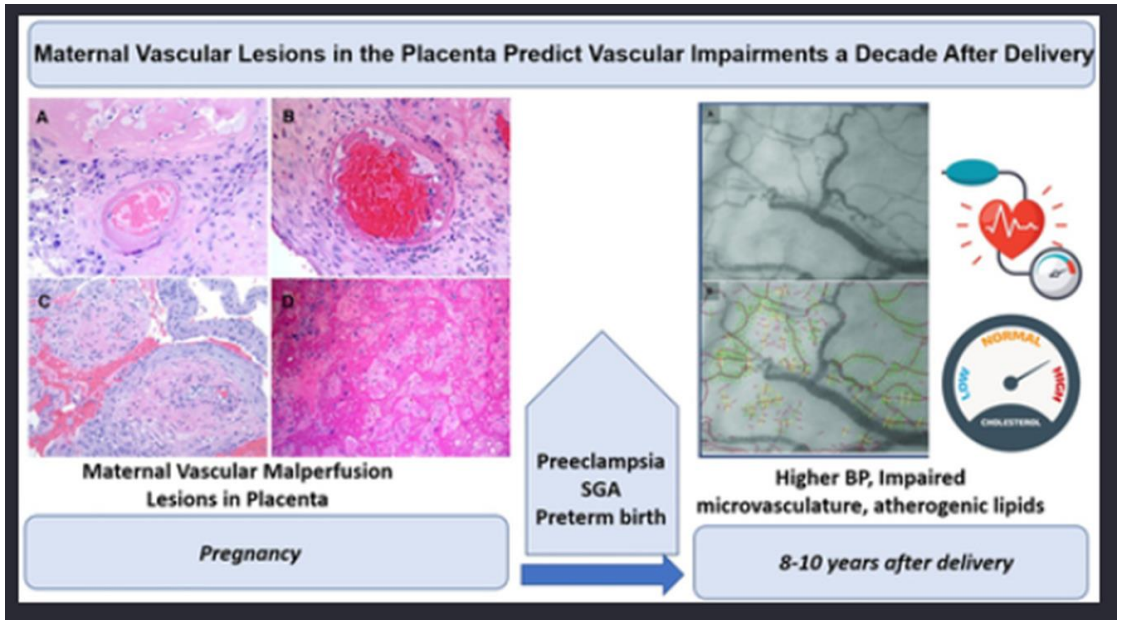
Suresh SC, Freedman AA, Hirsch E, Ernst LM. A comprehensive analysis of the association between placental pathology and recurrent preterm birth. Am J Obstet Gynecol. 2022 Dec;227(6):887.e1-887.

Hypertension
Volume 79, Issue 2, February 2022; Pages 424-434
https://doi.org/10.1161/HYPERTENSIONAHA.121.18394

ORIGINAL ARTICLE

Maternal Vascular Lesions in the Placenta Predict Vascular Impairments a Decade After Delivery

Janet M. Catov, Matthew F. Muldoon, Robin E. Gandley, Judith Brands, Alisse Hauspurg, Carl A. Hubel, Marie Tuft, Mandy Schmella, Gong Tang, and W. Tony Parks



Maternal Vascular Lesions in the Placenta Predict Vascular Impairments a Decade After Delivery: Supplemental Material

Catov JM[1, 2], Muldoon MF[3], Gandley RE[1], Brands J[1], Hauspurg A[4], Hubel CA[1], Tuft M[5], Schmella M[6], Tang G[5], Parks WT[7]

MVM feature	Description	Points
Decidual vasculopathy	Persistent vascular smooth muscle in basal vessel, mural hypertrophy, fibrinoid necrosis or atheromatous	4
Infarct	(Did not define size)	3
Accelerated maturation	increased syncytial knots, a decrease in the percentage of intermediate villi and/or distal villous hypoplasia (zones of abnormally long, thin, unbranched terminal villi)	2
Perivillous fibrinoid	>3% villi with small foci of fibrinoid material within or adjacent to villi	1
Intervillous fibrin	Irregular zones of fibrinoid material tightly encasing the entrapped villi	1

“Since the launch of our study the Amsterdam consensus statement has added low placental weight to this diagnosis, but our analysis revealed this feature alone is unrelated to maternal cardiometabolic health after delivery so we did not include it.”

Parks system predicts maternal vascular impairments

Table 3. Blood Pressure, Microvascular Features, and Cholesterol According to Severity of MVM (Range 0–9)

	Per 1 unit increase in MVM severity			
	Unadjusted	*P* value	Adjusted*	*P* value
Systolic blood pressure, mm Hg	1.23	0.001	1.05	0.010
Diastolic blood pressure, mm Hg	1.08	0.0001	0.89	0.003
Vessel density, μm/mm^2*	−30	0.423	−60	0.211
Vessel diameter, μm*	−0.10	0.003	−0.08	0.039
Red blood cell filling, %*	0.50%	0.001	0.30%	0.085
Perfused boundary region, μm*	−0.013	0.071	−0.010	0.267
Total cholesterol, mg/dL	2.26	0.014	1.57	0.148
LDL-cholesterol, mg/dL	2.04	0.065	1.66	0.194

LDL indicates low-density lipoprotein; and MVM, maternal vascular malperfusion.
* Adjusted for race, age, follow-up time, prepregnancy obesity, sodium, preeclampsia, small for gestational age birth, preterm delivery, antihypertensive medication use.

MVM severity was correlated with more adverse microvascular features (r=−0.14 for estimated mean vessel diameter and r=0.14 for RBC filling percent), LDL-cholesterol (r=0.11), diastolic BP (r=0.17), and systolic BP (r=0.15; P<0.05 for all measures). Similarly, after accounting for confounders, systolic and diastolic BP, microvessel diameter and RBC filling were more adverse as MVM severity increased (Table 3).

Catov JM, Muldoon MF, Gandley RE, Brands J, Hauspurg A, Hubel CA, Tuft M, Schmella M, Tang G, Parks WT. Maternal Vascular Lesions in the Placenta Predict Vascular Impairments a Decade After Delivery. Hypertension. 2022 Feb;79(2):424-434.

Gross patterns of umbilical cord coiling: Correlations with placental histology and stillbirth

L.M. Ernst [a,*], L. Minturn [a], M.H. Huang [a], E. Curry [a], E.J. Su [b]

[a] Northwestern University Feinberg School of Medicine, Department of Pathology, Chicago, IL, USA
[b] Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Chicago, IL, USA

Placenta 34 (2013) 583–588

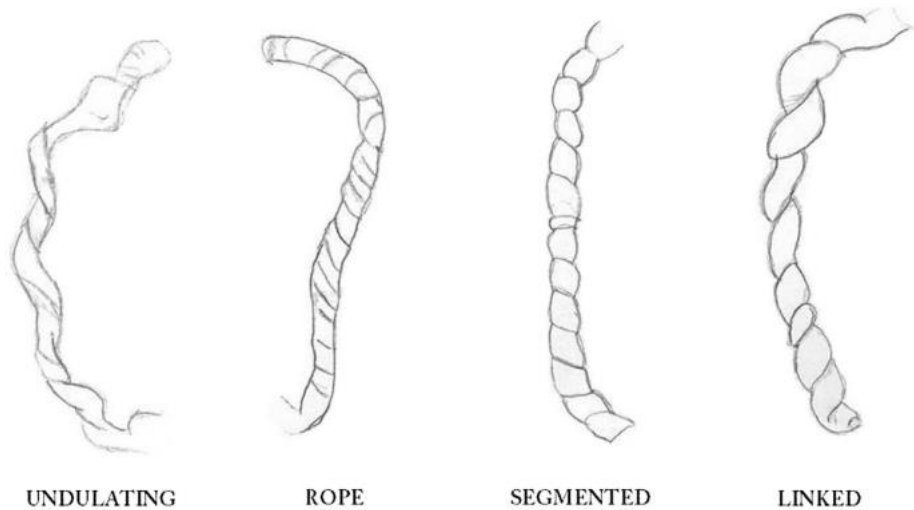


Fig. 1. Schematic representation of the four gross umbilical cord coiling patterns.

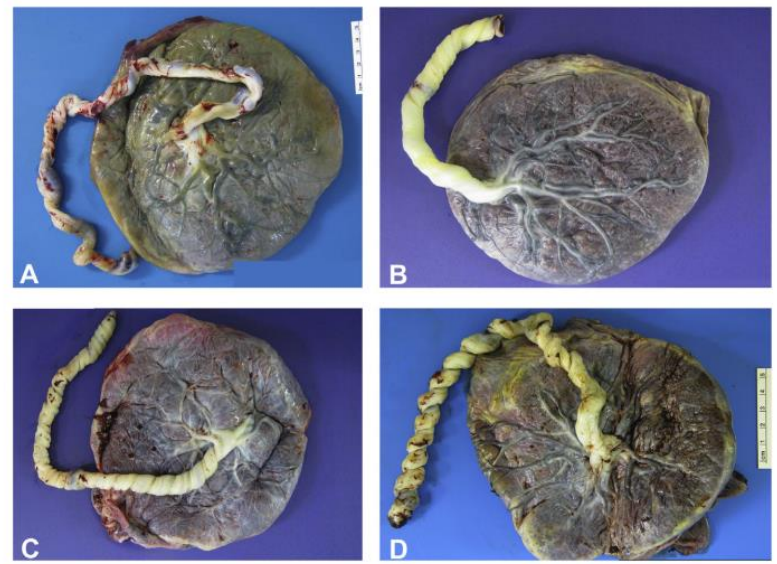
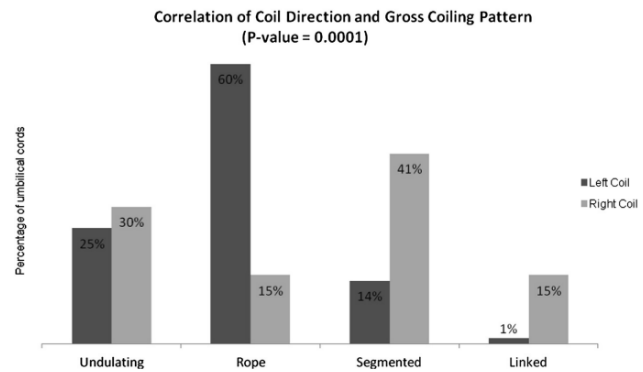


Fig. 2. Placental images representing the four gross umbilical cord coiling patterns. A. Undulating pattern, B. Rope pattern, C. Segmented pattern, D. Linked pattern.

Table 3
Correlations of dichotomized coiling patterns.

Coiling pattern	Frequency *N* (%)	Abnormal cord insertion *N* (%)	Fetal thrombi *N* (%)	Avascular villi *N* (%)	Villous stromal-vascular karyorrhexis *N* (%)	Fetal thrombotic vasculopathy *N* (%)	Stillbirth *N* (%)
Undulating + Rope	246 (77)	42 (17)	48 (20)	39 (16)	7 (3)	14 (6)	8 (3)
Segmented + Linked	72 (23)	11 (16)	25 (35)	24 (33)	7 (10)	11 (15)	10 (14)
P-value		NS	0.007	0.001	0.012	0.008	0.001



Fetal vascular malperfusion-thrombi

- Muscular vessels
  - Cord thrombi
    - Occlusive or non-occlusive
    - See loss of vascular smooth muscle basophilia with established occlusive thrombi
  - Chorionic plate vessel thrombi
    - Occlusive or non-occlusive thrombi in lumen
    - Organizing mural thrombi with calcification
    - Intramural fibrin deposition
  - Stem villous vessel thrombi
    - Occlusive or non-occlusive thrombi in lumen
    - Organizing mural thrombi with calcification
    - Intramural fibrin deposition

Fetal vascular malperfusion- large vessel lesions

- Progressive changes of chorionic plate and stem villous vessel obliteration
  - Early – loss of endothelial integrity with extravasation of RBC into vessel wall
  - Evolving- ingrowth of fibroblasts into lumen with eventual septation
  - Late- complete loss of lumen, obliteration
- Results from cessation of perfusion from proximal vessels
  - Due to obstruction
  - Due to fetal demise
- Changes called “hemorrhagic endovasculosis/ HEV” in older literature

Fetal vascular malperfusion- distal villous lesions

- Avascular villi
  - groups of villi with sclerotic appearing stroma, loss of all vessels
  - syncytiotrophoblast is usually maintained
- Villous stromal/vascular karyorrhexis
  - groups of villi with karyorrhexis of villous vessels and stromal cells
  - Usually affects all vessels in villi, not focal
- Definitions
  - “Small”- foci of 2-4 villi
  - “Intermediate”- 5-10 villi
  - “Large” - >10 villi

High grade FVM

- Distal villous criteria
  - 2 or more foci, totaling >45 villi over 3 sections or average of >15 AV or VSVK per slide +/- thrombus
- Thrombi criteria
  - 2 or more occlusive or nonocclusive thrombi in chorionic or stem villous vessels
  - Any umbilical cord thrombus

TABLE 2. Infant Long-term and Neurological Outcomes Comparing Controls With All FTV Cases, Nonsevere FTV Cases, Severe DV-FTV Cases, and Severe LV-FTV Cases

Infant Long-term and Neurological Outcomes	All Controls (%)	All FTV Cases (%)	Nonsevere FTV Cases (%)	Severe DV-FTV Cases† (%)	Severe LV-FTV Cases‡ (%)
Subjects with ≥12 mo follow-up (N)§	54	73	27	28	34
Average length of follow-up ≥12 mo	36.15 mo	33.49 mo	36.22 mo	33.94 mo	27.65 mo *
Hypertonia	1.3	5.5	0.0	7.1	8.8
Hypotonia	0.0	8.2*	3.7	17.9*	5.9
Hyperreflexia	0.0	6.8[t]	0.0	10.7*	5.9
Weakness	0.0	8.2*	7.4	14.3*	5.9
Spasticity	0.0	2.7	0.0	7.1	2.9
Cerebral palsy	0.0	2.7	0.0	10.7*	2.9
Speech/language delay	11.1	21.9	11.1	32.1*	23.5
Motor delay	5.6	13.7	7.4	17.9	14.7
Cognitive delay	0.0	6.8[t]	0.0	7.1	11.8*
Global developmental delay	0.0	4.1	0.0	10.7*	2.9
Encephalopathy	0.0	4.1	0.0	7.1	2.9
Ventriculomegaly	0.0	1.4	0.0	0.0	2.9
Hydrocephalus	0.0	1.4	0.0	3.6	2.9
Cerebral infarct	0.0	2.7	0.0	7.1	0.0
Thrombosis/vasculopathy	0.0	6.8[t]	0.0	14.3*	8.8[t]
Seizures	1.9	8.2	7.4	10.7	8.8
Organ failure	1.9	2.7	0.0	3.6	2.9
Growth retardation	3.7	9.6	7.4	17.9*	8.8
Any developmental problem	16.7	35.6*	25.9	42.9*	41.2*

*Significant *P*-value compared with all controls <0.05.
[t]*P*-value compared with all controls between 0.05 and 0.10.
†Severe DV-FTV cases defined as ≥2 foci average ≥15 avascular villi and/or stromal-vascular karyorrhexis.
‡Severe LV-FTV cases defined as umbilical artery or vein thrombus, or ≥2 chorionic plate and/or stem villous vessel thrombi.
§*P*-value calculated from percent subjects with ≥12 months follow-up out of total subjects in the category.

“At this stage of our understanding of the pathophysiology of fetal blood flow, findings consistent with FVM are thrombosis, segmental avascular villi, and villous stromal-vascular karyorrhexis. Other possible markers, such as vascular intramural fibrin deposition, stem vessel obliteration/fibromuscular sclerosis, and vascular ectasia, should also be sought.”

Recurrence of FVM?

Yes, especially for 2nd trimester demise cases with hypercoiled cords

- Slack JC, Boyd TK. Fetal Vascular Malperfusion Due To Long and Hypercoiled Umbilical Cords Resulting in Recurrent Second Trimester Pregnancy Loss: A Case Series and Literature Review. Pediatr Dev Pathol. 2021 Jan-Feb;24(1):12-18. PMID: 32986509.
- Less clear for cases of FVM at term, understudied.

Are the maternal and fetal circulations really independent?

- MVM and FVM, as well as chronic villitis frequently go together, suggesting the variables are linked
- Could it be a sort of V/Q matching, guiding fetal blood to richer oxygenation sources like in the lung?
- Could increased pressure in the intervillous space from MVM create a limit to fetal perfusion?

Umbilical Doppler Studies

- In the second half of pregnancy, fetal circulation is normally continued forward flow in the umbilical arteries during systole and diastole
  - The fetal heart beats rapidly at 160-200bpm with low resistance in the placental vascular bed-> constant forward flow during diastole
- When resistance to forward flow is high in the placental vascular bed, umbilical doppler studies show absent or reversed end diastolic flow (AREVD)
- Umbilical artery doppler studies are used when there is IUGR, to better monitor fetal well being
- When AREDV is present, placental insufficiency is likely cause of IUGR and early delivery may be warranted

Placental pathology associated with absent or reversed end diastolic volume on fetal umbilical doppler sutdies

- Small for gestational age placenta with distal villous hypoplasia, fibrinoid necrosis of individual villi, infarcts
- Extensive avascular villi (fetal vascular malperfusion)
- Massive perivillous fibrin deposition

Grading MVM for clinical severity

High grade MVM- has one or more of the following:

- Distal villous hypoplasia
- Placenta weight less than 3rd percentile
- Multiple infarcts

HG MVM associated with the following in decreasing order of prevalence: abnormal pulsed flow Doppler, FGR, abnormal BPP, severe PE, oligohydramnios

Table 3. Indications for Placental Submission Significantly Associated With High-Grade Histopathology and ≥ 2 × Increase Over Population Prevalence.

	MVM High Grade	FVM High Grade	ACA High Grade	VUE High Grade	FSV High Grade	MAVC Any	Increased NRBC
	% positive[a]	% positive	% positive	% positive	% positive	% positive	% positive
All placentas	4.9	1.0	7.8	3.2	2.8	0.7	3.3
Antenatal conditions	Abn PFD 28.6	Clin FGR 2.1	Clin CA 27.1	IVF/ART 16.7	PGDM 12.4	>42 weeks 7.9	>42 weeks 10.5
	Clin FGR 18.2		Mat Temp 20.5	Drug abuse 9.5			UC entang 7.0
	Abn BPP 16.1		Prol ROM 19.6				
	Sev PE 12.7						
	Oligo 10.6						
Gross placental abnormalities	PW Z <−1.5 41.7	FPR Z <−1.5 5.3		PW Z <−1.5 8.3	PW Z >+1.5 8.2	PW Z <1.5 2.8	UC >70 cm 8.0
	FPR Z >+1.5 12.0	UCI <3 2.1		FPR Z >+1.5 6.8			
Adverse outcomes	SGA Z <−2.0 32.8	IUFD 14.8	Apg5 <6 22.1	SGA Z <−2.0 10.3	LGA Z >+2.0 15.3	SGA Z <−2.0 6.9	IUFD 48.1
	SGA Z −1.5/2 22.0	SGA Z <−2.0 5.2			IUFD 11.1		Apg5 <6 11.0
	SGA Z −1/1.5 15.5	SGA Z −1.5/2 3.5					

Abbreviations: Abn BPP, abnormal biophysical profile; Abn PFD, abnormal umbilical pulsed flow Doppler testing; ACA, acute chorioamnionitis; FGR, fetal growth restriction; FPR, fetoplacental ratio; FSV, fetal stromal vascular maldevelopment; FVM, fetal vascular malperfusion; IUFD, intrauterine fetal death; MAVC, meconium associated fetal vascular changes; MVM, maternal vascular malperfusion; NRBC, nucleated red blood cells; PGDM, pregestational diabetes mellitus; PW, placenta weight; SGA, small-for-gestational age; UCI, umbilical cord insertion; VUE, idiopathic chronic villitis (so-called villitis of unknown etiology).

[a]Percentage of placentas with each indication showing column-specific high-grade histopathology.

Zhou YY, Ravishankar S, Luo G, Redline RW. Predictors of High Grade and Other Clinically Significant Placental Findings by Indication for Submission in Singleton Placentas From Term Births. Pediatr Dev Pathol. 2020 Aug;23(4):274-284.

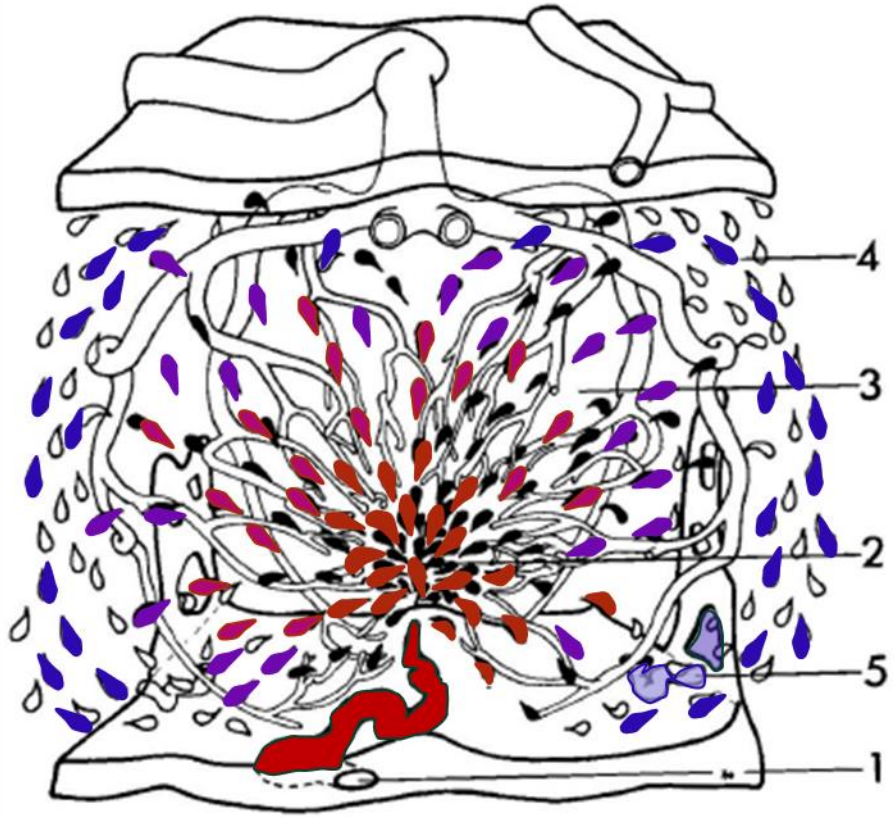
Intervillous space pressure and FVM?

British Journal of Obstetrics and Gynaecology
January 1994, Vol. 101, pp. 57–63

REPRODUCTIVE SCIENCE

The effects of maternal vascular pressure on the dimensions of the placental capillaries

A. L. KARIMU *Graduate Research Student*, G. J. BURTON *University Lecturer*
Department of Anatomy, University of Cambridge



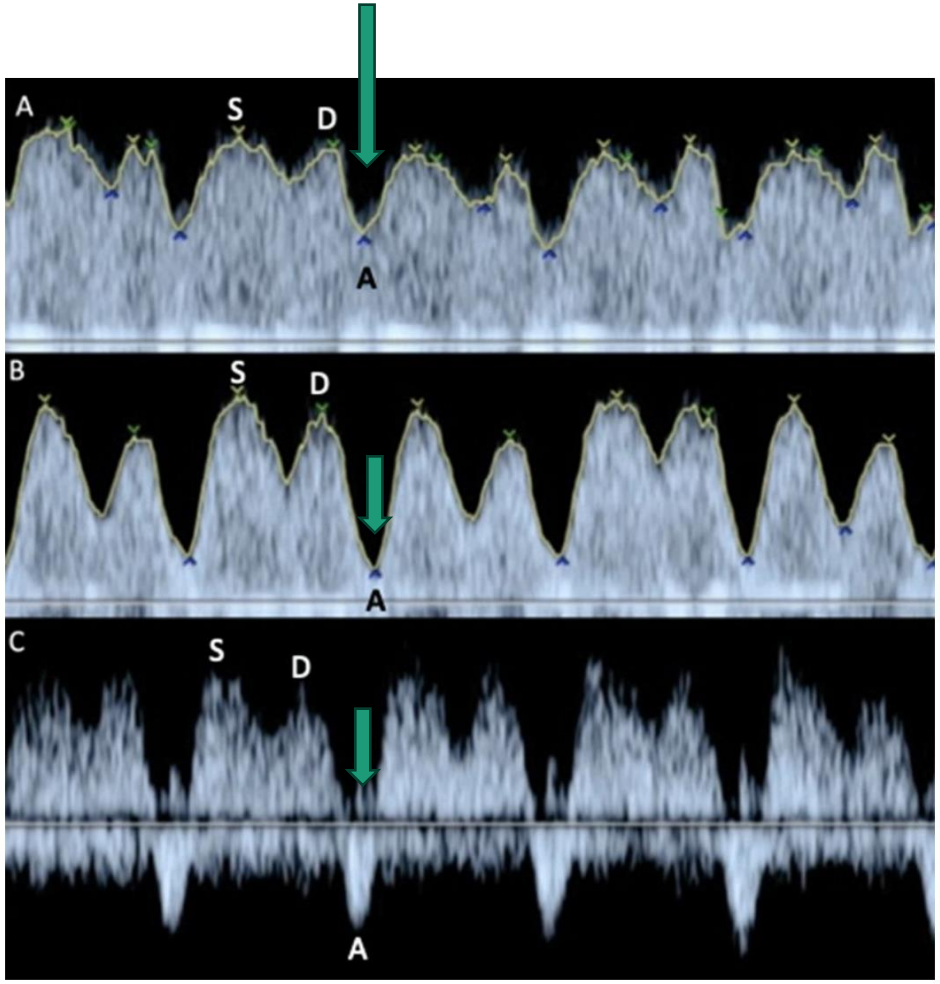
Increased IVS pressure could create increased afterload for the fetal circulation, leading to AREDV.

As hypoxia exacerbates the condition, right heart failure could ensue with diastolic dysfunction and abnormal venous dopplers in the ductus venosus.

Severe placental dysfunction leads to redistribution of fetal blood to brain and myocardium

Get increased afterload on the right ventricle (attributed to increased resistance to flow in peripheral vasculature, with brain sparing), likely also from increased resistance to flow in the placenta!

Ominous sign, absent/reversed ductus venosus a-wave identifies fetus at highest risk of in utero demise



DV progression from normal to abnormal flow, producing the characteristic reversal in the A-wave. a Normal ductus venosus Doppler flow waveform. b Resistive A-wave, and c reversed A-wave

Image from:
Melber, Dora & Ballas, Jerasimos. (2021). Clinical Applications for Doppler Ultrasonography in Obstetrics. Current Radiology Reports. 9. 10.1007/s40134-020-00377-9.

Journal of
Clinical Medicine

MDPI

Review

Maternal Venous Hemodynamic Dysfunction in Proteinuric Gestational Hypertension: Evidence and Implications

Wilfried Gyselaers [1,2]

1 Department of Obstetrics & Gynaecology, Ziekenhuis Oost-Limburg, Schiepse Bos 6, 3600 Genk, Belgium; wilfried.gyselaers@zol.be; Tel.: +32-89327524

2 Department Physiology, Hasselt University, Agoralaan, 3590 Diepenbeek, Belgium

"In accordance with the pathophysiologic interpretation of abnormal maternal venous Doppler flow patterns explained above, a triphasic ductus venosus Doppler waveform suggests for the IUGR fetus a state of activated venous hemodynamics, possibly intravenous hypertension predisposing to congestion related organ dysfunction. As fetal urine production is an important contributor to the amniotic fluid volume [185] and composition [186], the question arises whether renal venous congestion is an underrecognized mechanism underlying the well-known condition of oligo-amnion in IUGR. In parallel, fetal renal venous congestion may also contribute to the link between the reduced number of nephrons in IUGR neonates as compared to those with normal birthweight [187], and the related predisposition for early onset end stage renal disease [187,188,189], cardiovascular disease [190] and dysfunctions of other organ systems [191] in adults who used to be dysmature newborns."

Gyselaers W. Maternal Venous Hemodynamic Dysfunction in Proteinuric Gestational Hypertension: Evidence and Implications. J Clin Med. 2019 Mar 11;8(3):335.