



Most pregnancies are normal

but when they are "abnormal"

some mom's may blame themselves

and/or their doctors:

MOM



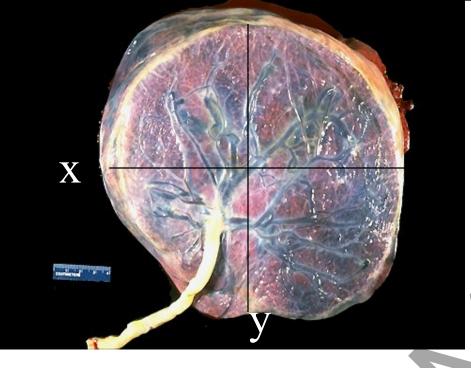
Placenta

Nutrient "buffer" to "regulate" supply

Nutrient Sink taking away from Fetus (50% rule)



Baby



Autopsy of the Pregnancy

Placenta Goes to Pathology:

- 1. Sick Mom
- 2. Sick Baby
- 3. Abnormal Placenta



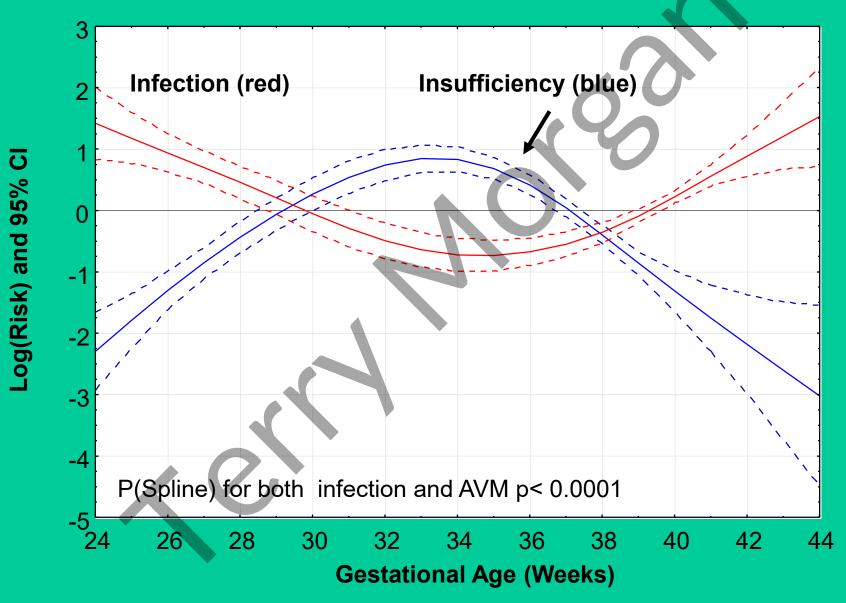
Placentas from Complicated Pregnancies

1252 placentas from University of Oklahoma

- 10% of all deliveries submitted to pathology
- Features of <u>uteroplacental insufficiency</u> (40%)
- Meconium (27%)
- Chorioamnionitis (21%)
- Abruption (9%)
- Villitis (4%)

(Beebe L. et al, Obstet & Gynecol. 1996; 87 (5): 771-8)

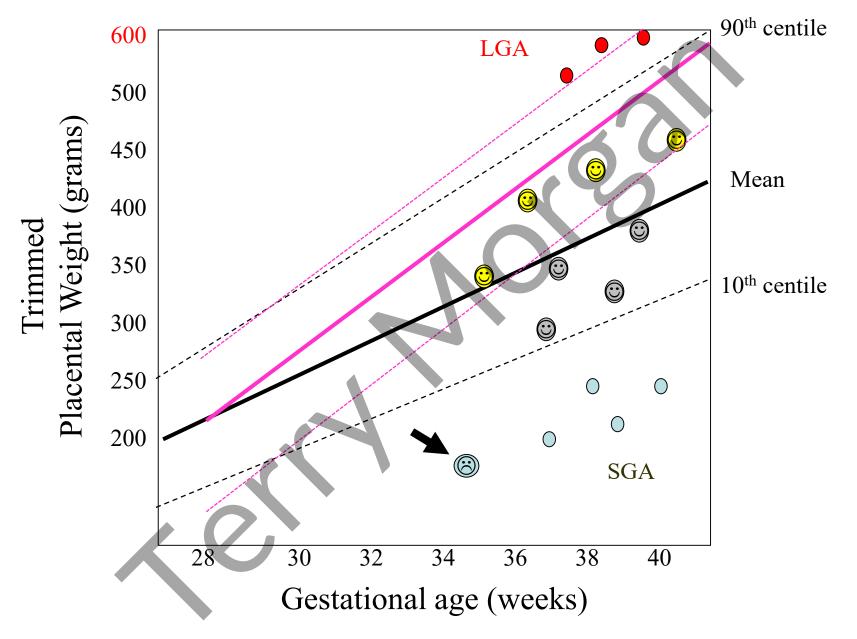
Placental Pathology in OHSU Singletons:



"Uteroplacental Insufficiency" Maternal Vascular Malperfusion

- Small for gestational age: (age x 10) 50 g
- Infarctions
- Accelerated villous maturation

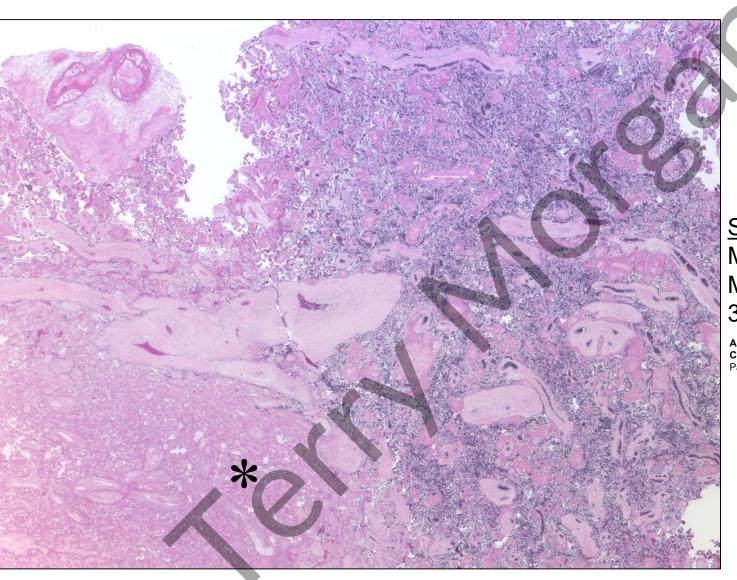
Chorangiosis (fetal angiogenesis in villi)







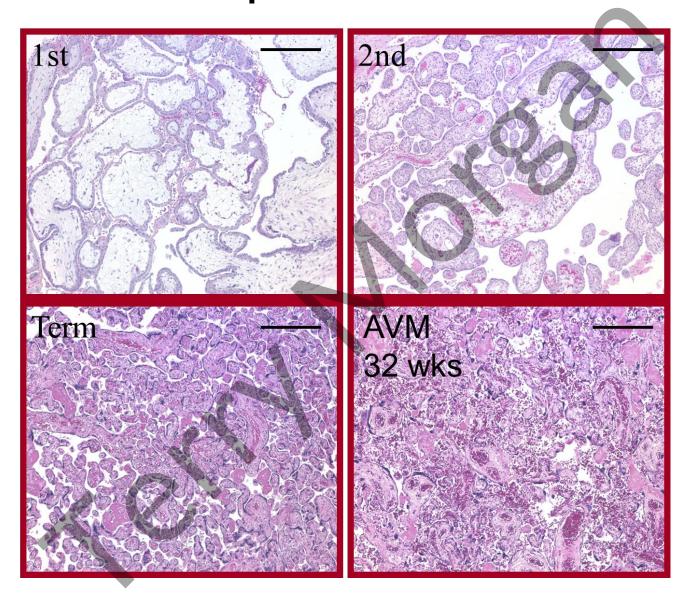


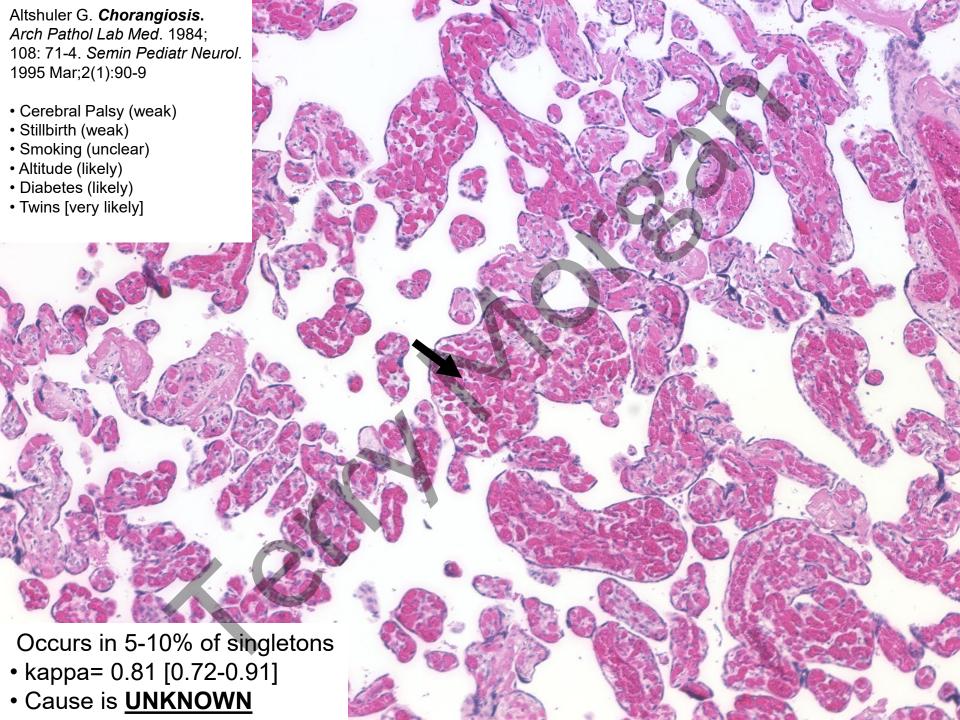


Snapshot of Maternal Vascular Malperfusion (MVM) 34 weeks' PET/IUGR

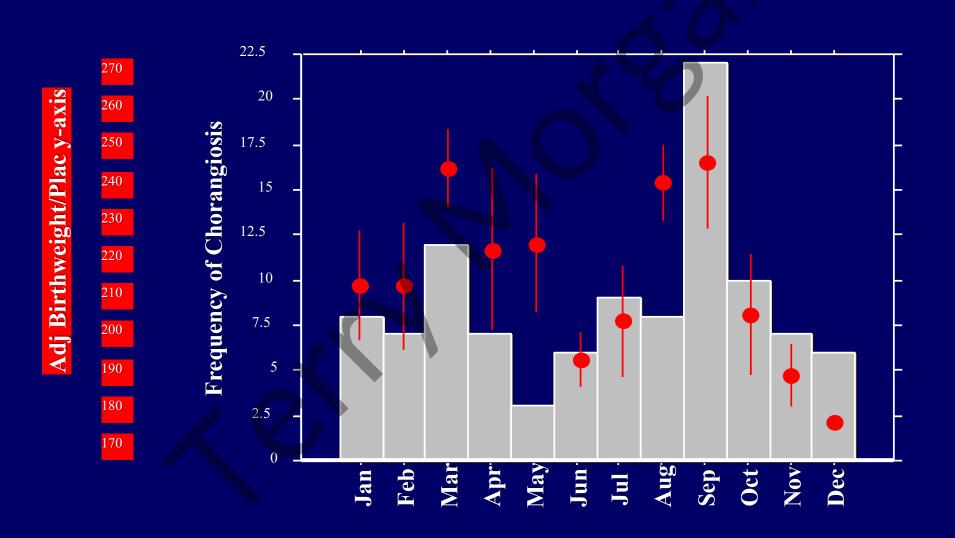
Amsterdam Placental Workshop Consensus Statement: Khong T, et al. Arch Pathol & Lab Med. 140:698-713

AVM is Reproducible < 38 weeks'

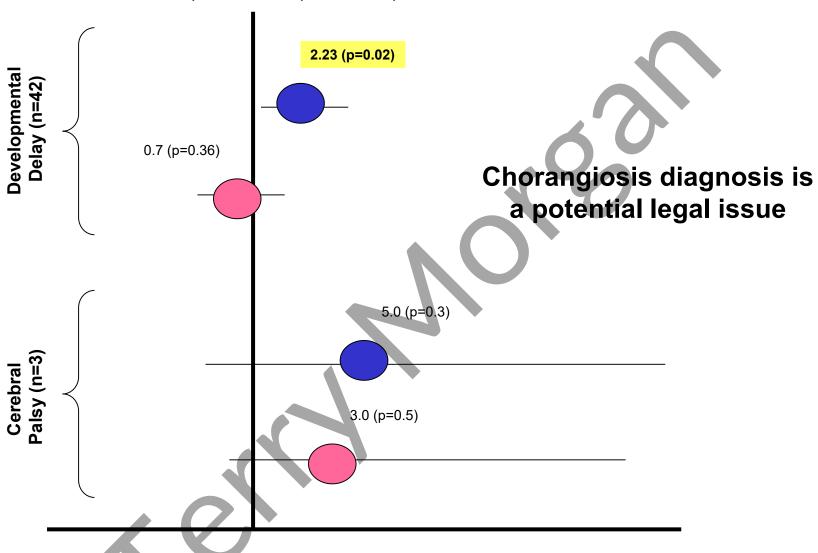




Potential Relationship Between *Chorangiosis Frequency* and Birthweight Relative to Placental y-axis length (*Reserve Capacity*)



Null OR=1.0 Compared with Expected Frequencies



- Male Cases (n=103 babies with >10 year followup)
- Female Cases (n=77 babies with >10 year followup)

Gaps in Knowledge

Is MVM a multifactorial disease with

- Severity problem?
- Timing problem?

What is the underlying pathophysiology?

What are the long-term impacts on baby's health?

Multifactorial Hypothesis

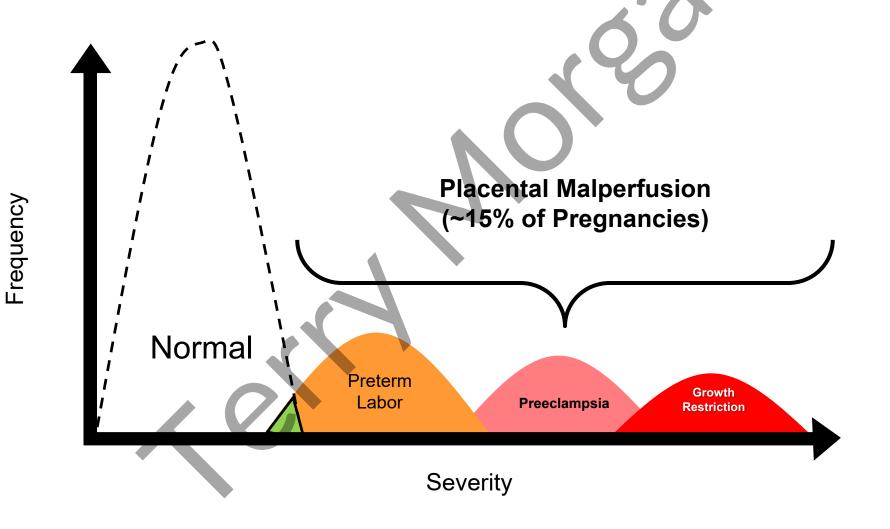


Table 2. Gross and Histologic Findings in Preterm Birth: Oregon Health & Science University Experience^a

	No. (%) of Cases				
Variable	PTL with IAI $(n = 68)$	PTL without IAI $(n = 179)$	Preeclampsia ($n = 121$)	FGR (n = 29)	
SGA placenta	0 [Reference]	0	12 (10) ^b	28 (97) ^c	
Gross infarction	4 (6) [Reference]	21 (12) ^d	30 (25)°	10 (35) ^c	
AVM	13 (19) [Reference]	106 (59) ^c	70 (58) ^c	16 (55) ^b	

AVM=accelerated villous maturation; FGR=fetal growth restriction; IAI=intra-amniotic infection; PTL=preterm labor; SGA=small for gestational age.
^aGross and histologic data from the Department of Pathology, Oregon Health & Science University (OHSU), diagnosed by a single placental pathologist (T.K.M.) scoring for small placentas (SGA), which were defined as less than the 10th percentile when using trimmed weight and adjusting for gestational age, gross infarctions (usually 1–2 cm in diameter), and AVM, which was defined as term villous morphologic findings with conspicuous syncytial knotting and perivillous fibrin deposition before 38 weeks' gestation. (9) PTL with or without IAI was defined by the presence or absence of histologic chorioamnionitis (Figure 1). Severe precelampsia and late-onset FGR were defined clinically by the maternal fetal medicine faculty at the OHSU. Findings were compared by \$\frac{\chi^2}{\chi^2}\$ analysis with the Fisher exact probability test when appropriate.

 $^{^{6}}P < .01.$

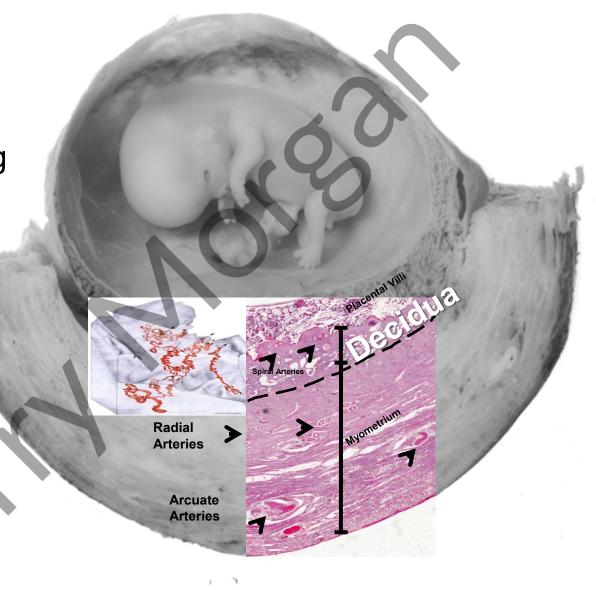
 $^{^{}c}P < .001$.

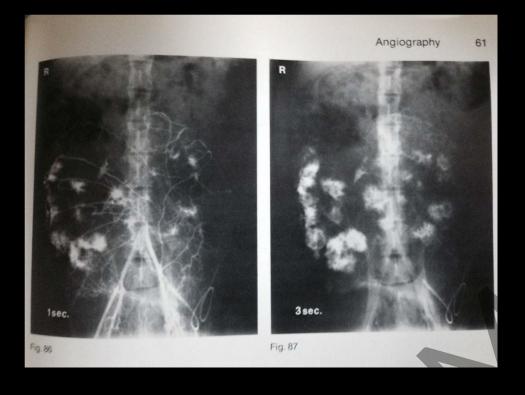
 $^{^{\}rm d}P < .05$.

Spiral Artery Angiogenesis Is the "Soil"

Upstream Remodeling

Variance Across Placental Bed

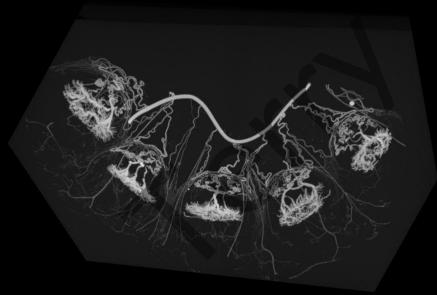




Dr. Elizabeth Ramsey's Day 115 Rhesus Pregnancy Angiography:

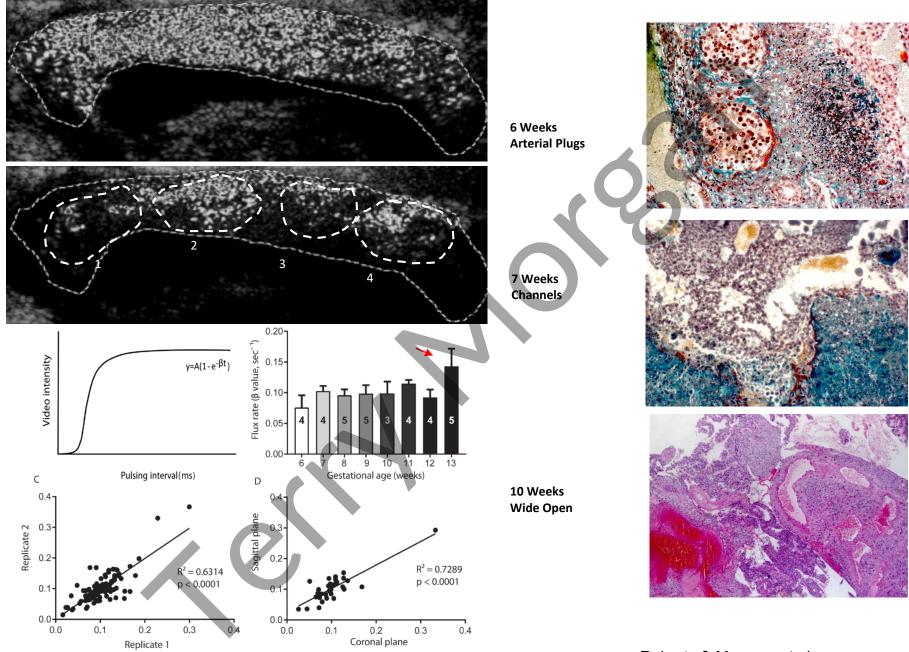
Variable "Spurts"—
Blood Flow Heterogeneity
Between Cotyledons—

(Placental Vasculature and Circulation. Ramsey E, Donner M. 1980. WB Saunders Co.)



Variable Spiral Artery Growth and Branching in Mouse Uterus

Courtesy Dr. Monique Rennie



Roberts & Morgan, *et al*. Hum Reprod. 2017. 32(12): 2382-93

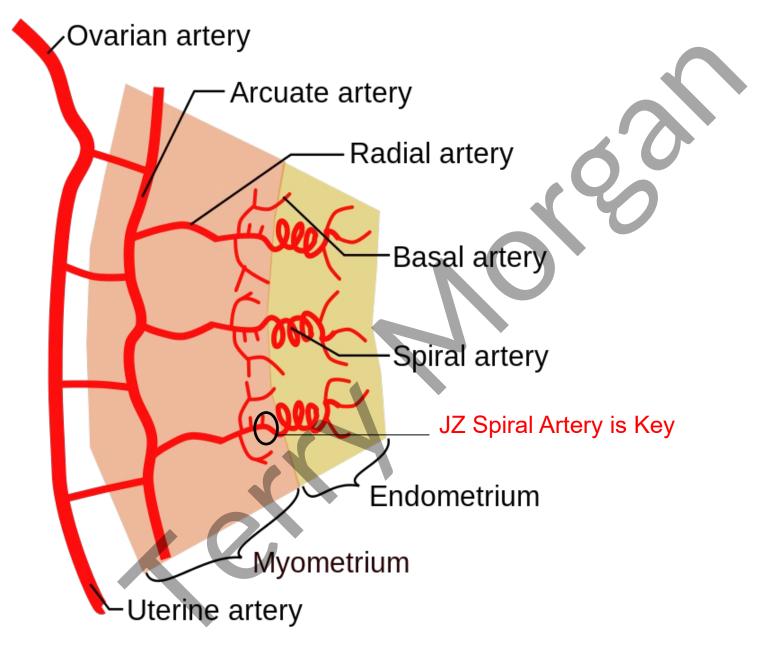
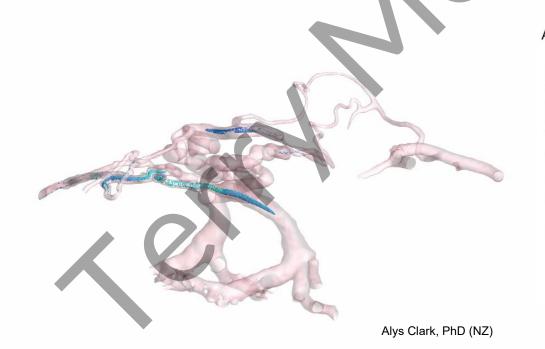
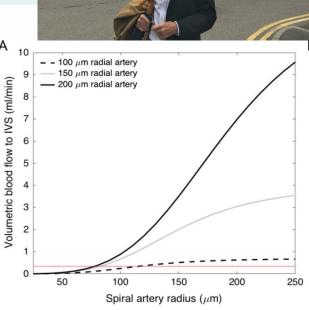


Table III Size of junctional zone spiral arteries (JZSAs) acquired from serial sections of Boyd Collection samples.

Sample ID	Gestational week	No. of JZSAs	Mean luminal diameter \pm SD (μ m)
H710	6.1	3	50.0 ± 3.6
H750	7.0	5	74.6 ± 6.5
H937	7.6	4	62.0 ± 10.4
H916	8.4	4	100.0 ± 12.4 ◀
H630	9.6	5	99.6 ± 8.4
H653	11.3	3	125.0 ± 15.0
H691	12.3	4	501.3 ± 54.7
H1094	13.3	4	250.0 ± 124.6
H671	18.5	3	>600 (outside range)
Secretory endometrium	_	4	50.0±3
Menstrual endometrium	_	3	45.0 ± 5.0

'No.' indicates how many different blood vessels were examined in each sample. Allerkamp H, et al. Hum Reprod. 2021; 36(3): 571-86





James J. Hum Reprod 2018; 33(8):1430-41

Placental "Insufficiency" and Developmental Programming

