

Maternal-Placental Syndromes

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Chief of Obstetrics and Maternal Fetal Medicine

Adverse Pregnancy Outcomes

Placental Cause

- Definite
 - Placenta previa/accreta (0.5%/0.2%)
 - Abnormal placental or cord morphology (velamentous, vasa previa)
 - Tumors (e.g. trophoblastic neoplasia, choriangioma)
- Likely
 - Twin to twin transfusion syndrome (0.1%)
 - Miscarriage (up to 20%)
 - Fetal death (0.1%)
 - Preeclampsia/gestational hypertension (6-8%/15%)
 - Fetal growth restriction (3-10%)
 - Abruption (1%)
- Suspected
 - Preterm birth (10-12%)
 - Oligohydramnios (up to 5%)

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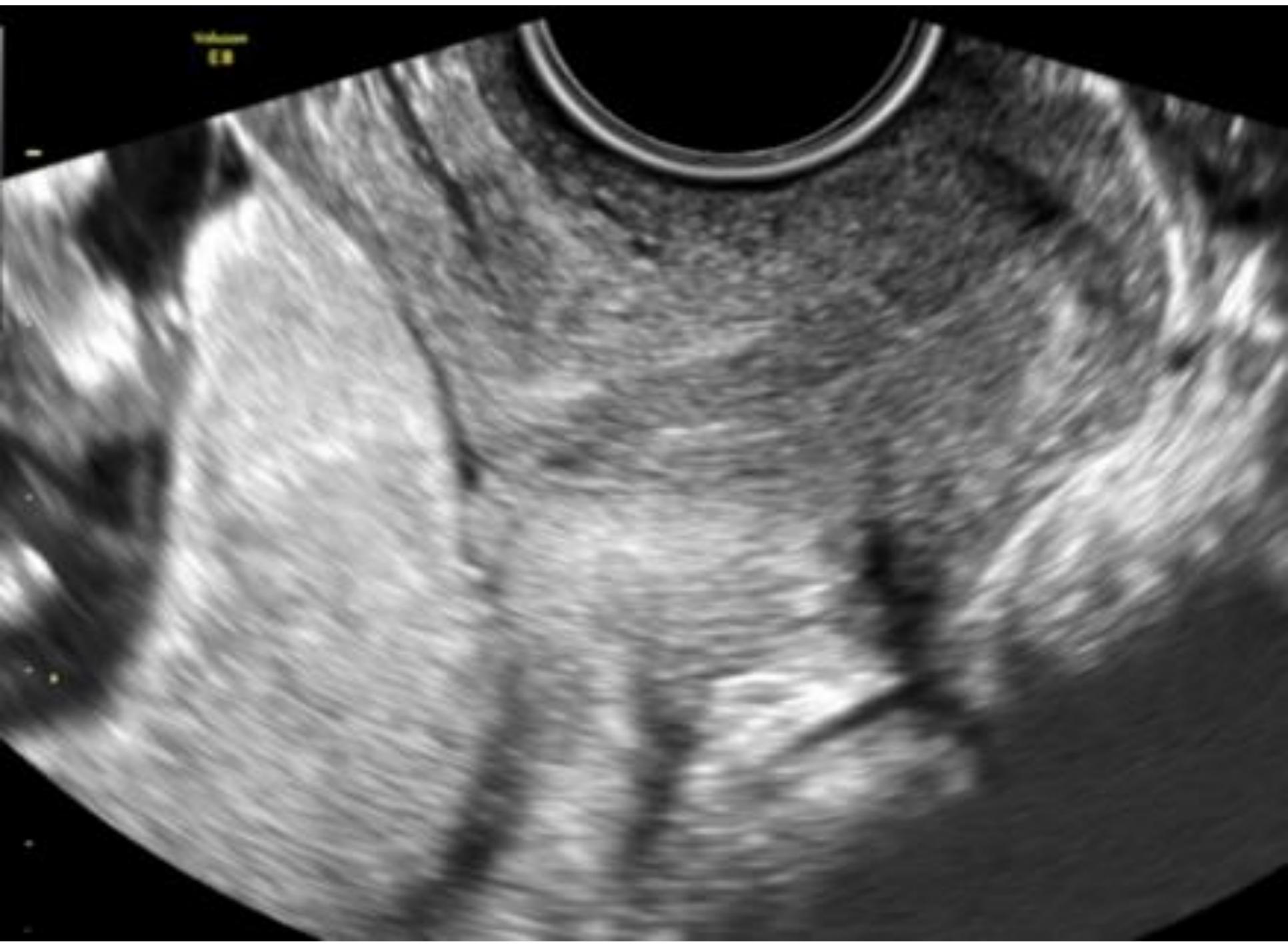
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Other Placental Conditions

- Gestational Diabetes
- Hyperemesis gravidarum
- Fatty liver of pregnancy
- Cholestasis of pregnancy
- Pruritic urticarial papules and plaques of pregnancy (PUPPP)

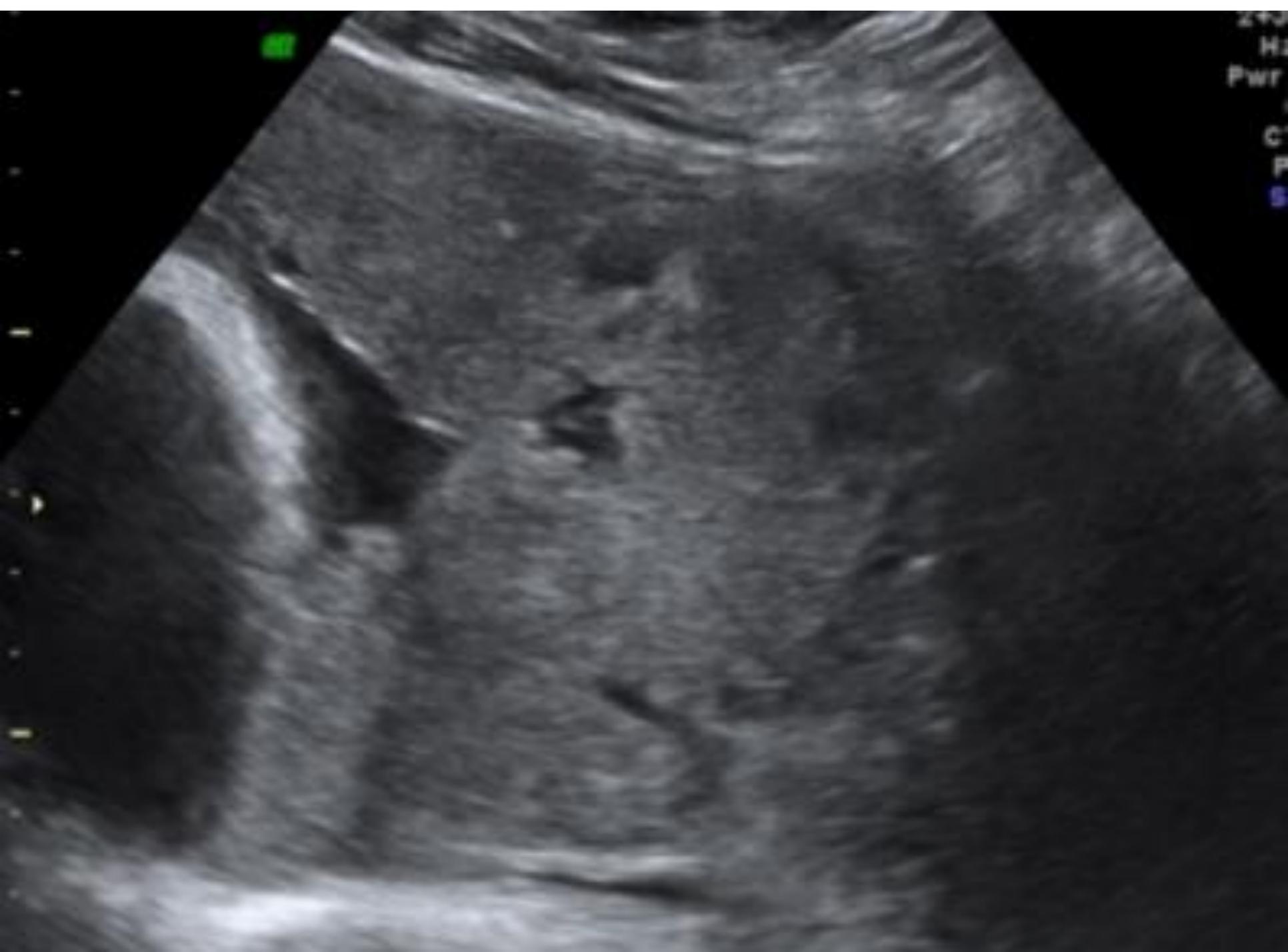
Placenta Previa

- Covers the internal os
- Risk factors
 - Advanced maternal age
 - Multiparity
 - Multiple gestation
 - Prior uterine surgery (CD, myomectomy, curettage)
 - Substance abuse (smoking, cocaine)
 - Abnormal placental development
- Delivery by cesarean
- Risks:
 - Bleeding (antepartum, intraoperative)
 - Fetal growth abnormalities
 - Preterm birth
 - Accreta



Placenta Accreta

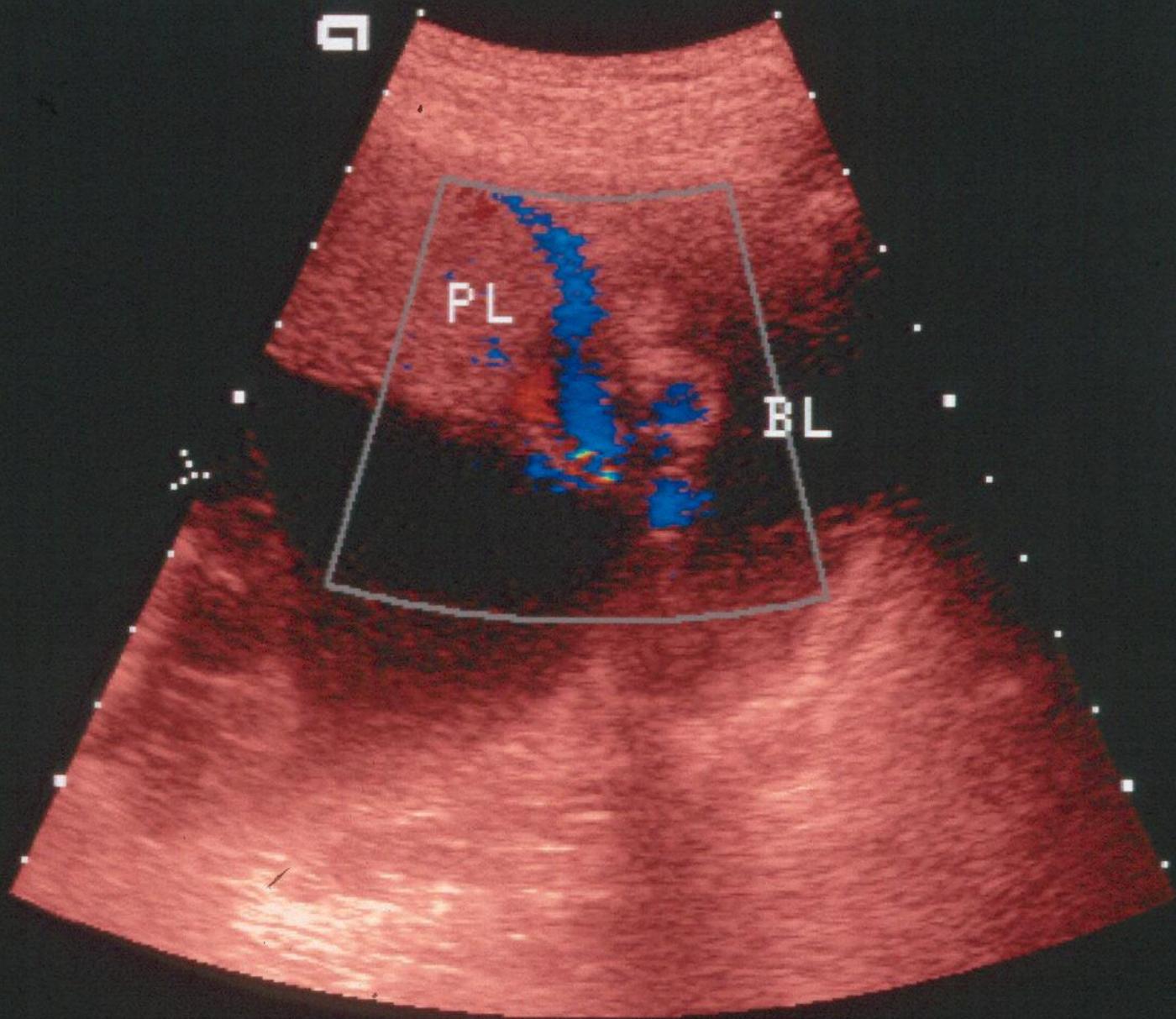
- Morbidly adherent placenta (accreta, increta, percreta)
- Risk factors
 - Prior uterine surgery
 - Placenta previa
- Preterm delivery
- Morbidity and mortality



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Abnormal Morphology

- Abnormalities
 - Succenturiate lobe
 - Circumvallate placenta
 - Velamentous cord insertion
 - Vasa previa
- Risks
 - Stillbirth
 - Fetal bleeding
 - Growth restriction
 - Cesarean delivery

Twin to Twin Transfusion Syndrome (TTTS)

- Monozygotic pregnancies
- Disequilibrium in fetal blood circulation
- Fluid overload in recipient
- Intravascular volume contraction in donor
- Risk of stillbirth, PTB, neurologic damage

Pregnancy Loss

Early pregnancy loss	Loss before 10 wk
Fetal death	10 0/7–19 6/7 wk
Stillbirth	At least 20 wk

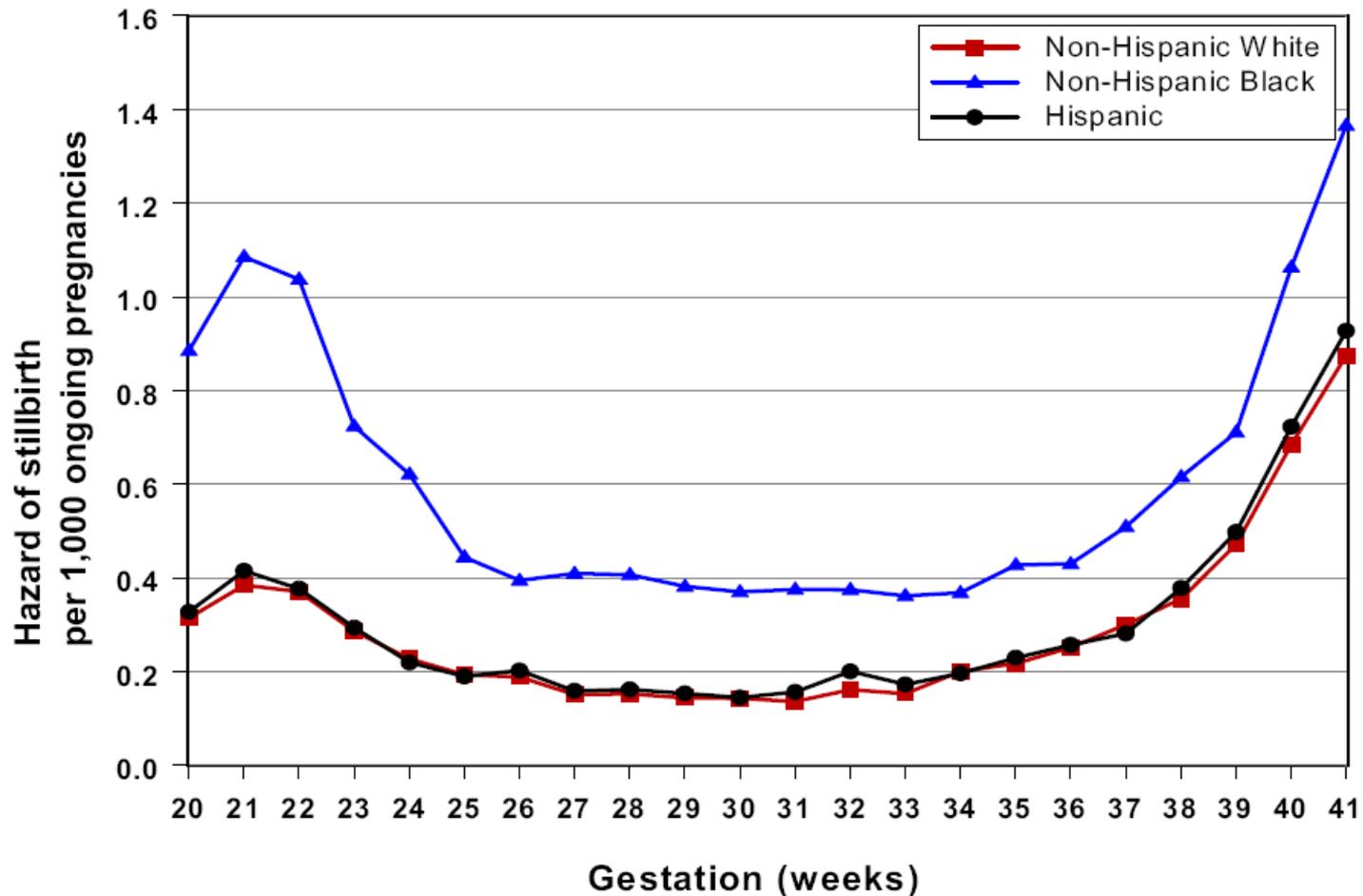
Stillbirth

- About 1 in 160 pregnancies in the US
- About 26,000 per year
- Equal to number of deaths due to preterm birth
PLUS the number of deaths due to SIDS
- Equal to the number of infant deaths
- Antepartum vs intrapartum

Stillbirth Hazard Among Singletons, 2001 - 2002

Willinger et al., Am J Obstet Gynecol 2009;201:469.e1-8

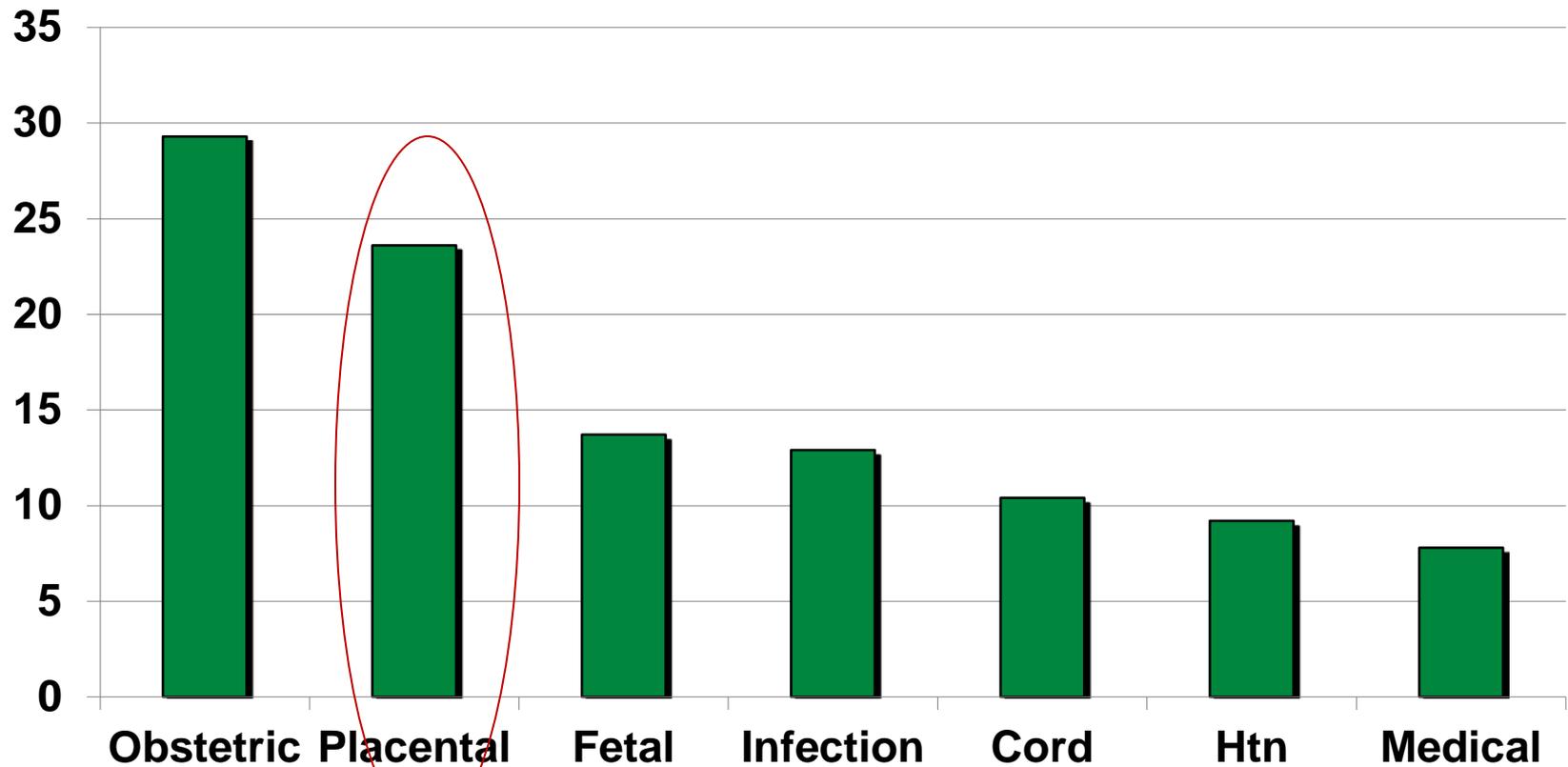
FIGURE
Stillbirth hazard among singletons, 2001–2002



Hazard of stillbirth for singleton pregnancies by gestational age and race/ethnicity, 2001–2002

Probable / Possible Cause of Death Broad Categories

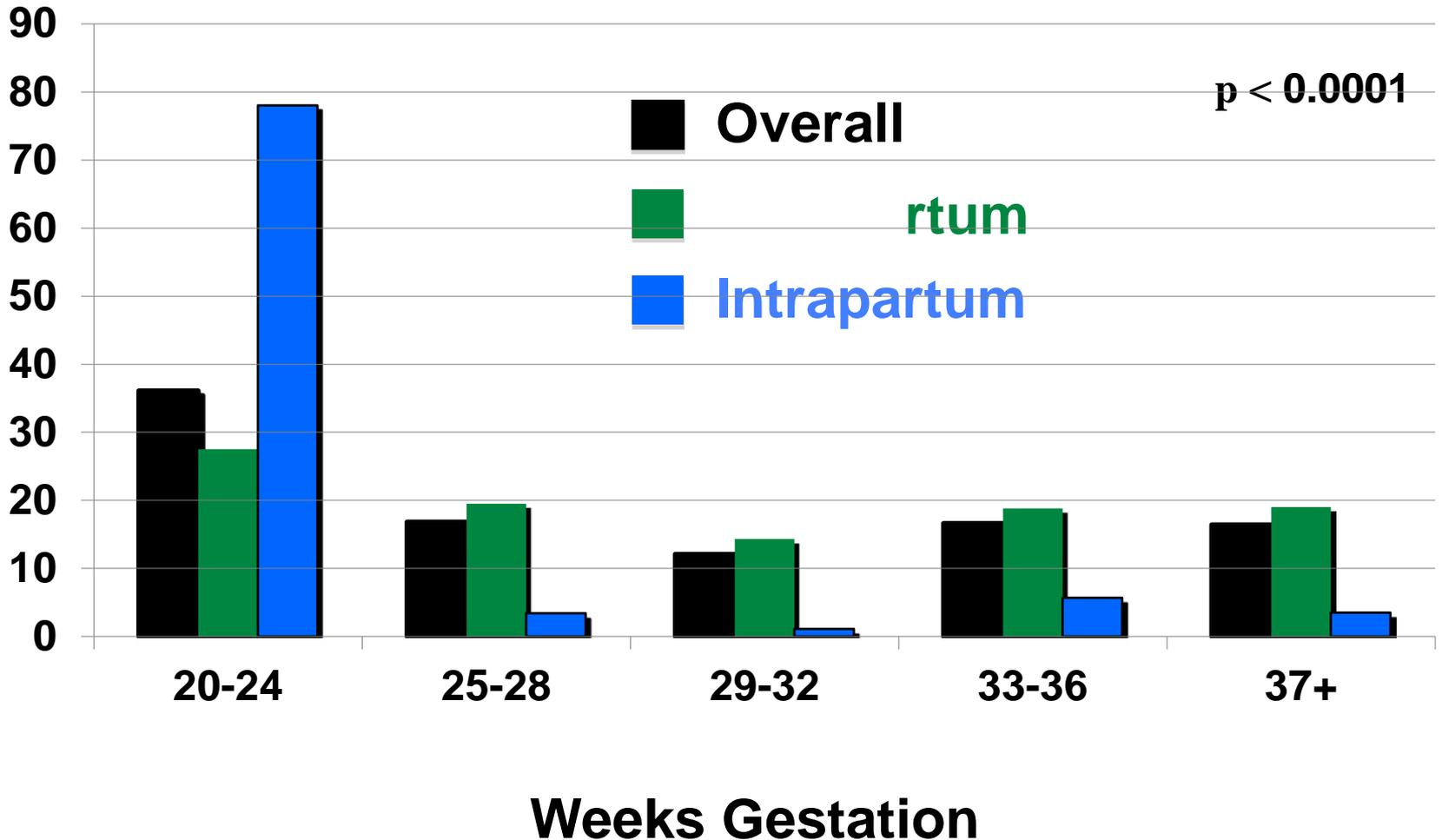
Percent



Timing in Gestation of Stillbirths

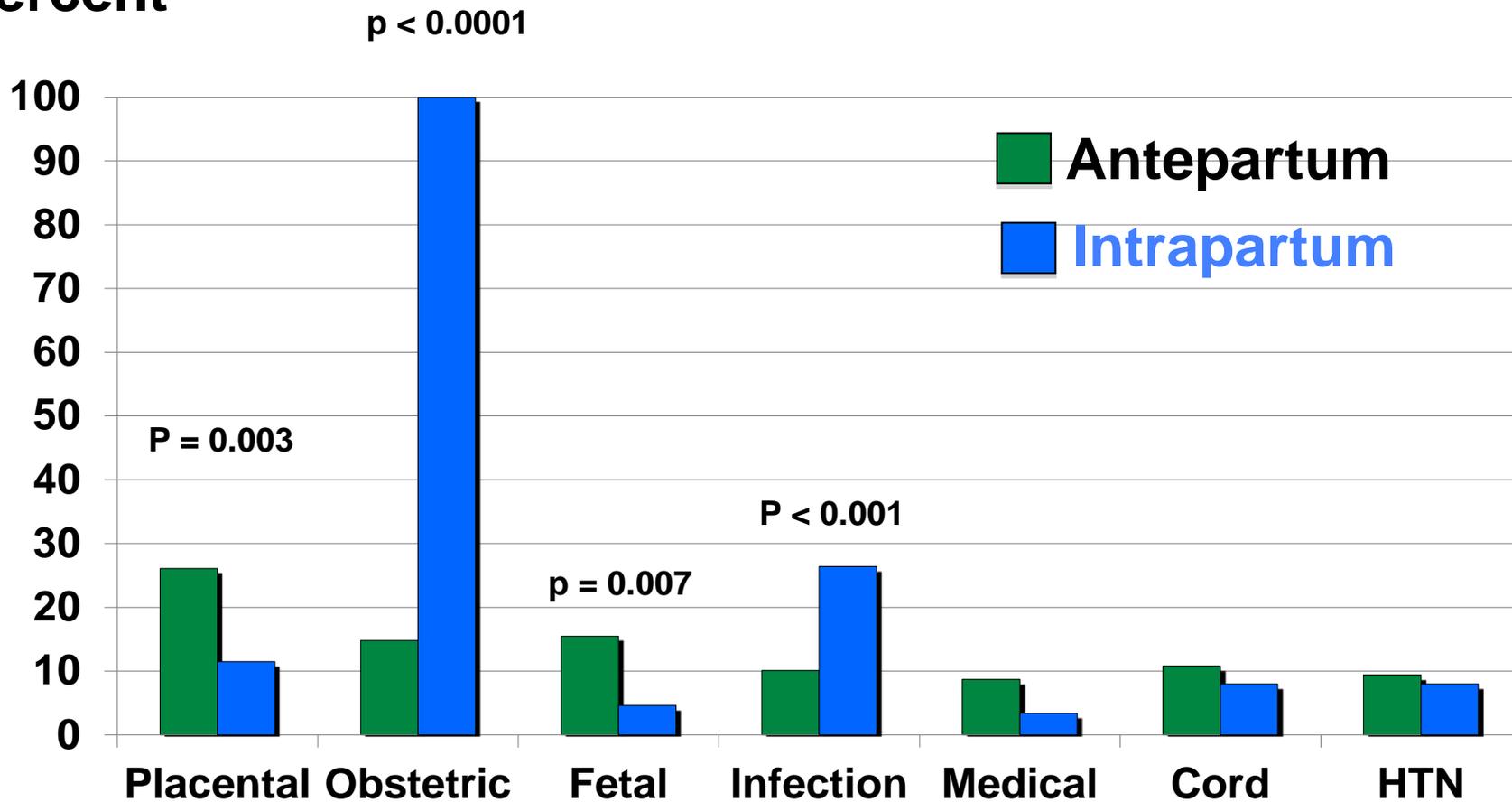
SCRN; JAMA 2011;306:2459-68

Percent



Probable / Possible Cause of Death by Timing of Death

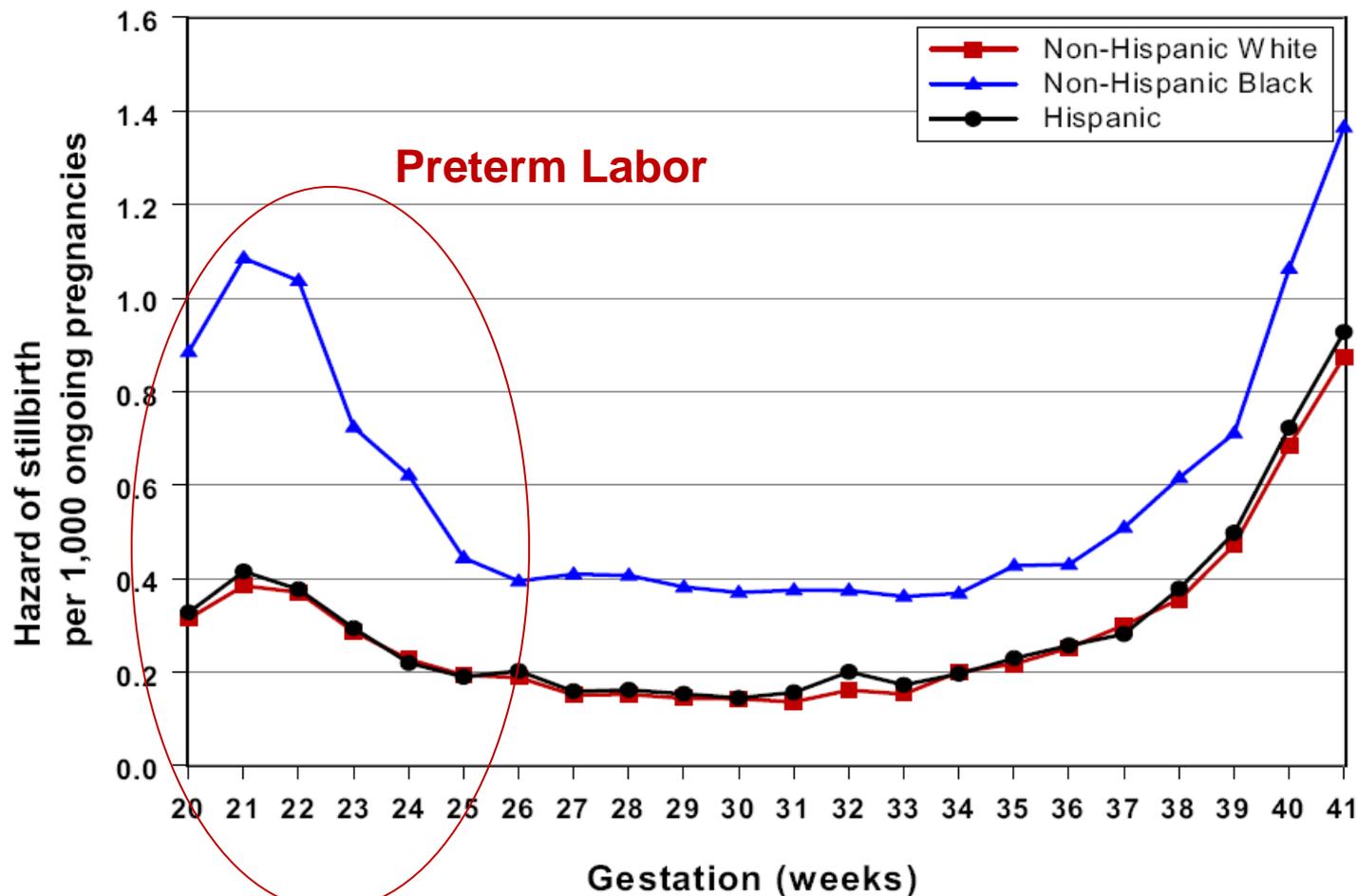
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Stillbirth Hazard Among Singletons, 2001 - 2002

Willinger et al., Am J Obstet Gynecol 2009;201:469.e1-8

FIGURE
Stillbirth hazard among singletons, 2001–2002



Hazard of stillbirth for singleton pregnancies by gestational age and race/ethnicity, 2001–2002

Preeclampsia

- Specific to human pregnancy
- Multi-organ disease
- Major cause of maternal and perinatal mortality



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Hypertension in Pregnancy

*Report of the American College of Obstetricians and Gynecologists'
Task Force on Hypertension in Pregnancy*

Hypertension in Pregnancy was developed by the Task Force on Hypertension in Pregnancy: James M. Roberts, MD, Chair; Phyllis A. August, MD, MPH; George Bakris, MD; John R. Barton, MD; Ira M. Bernstein, MD; Maurice Druzin, MD; Robert R. Gaiser, MD; Joey P. Granger, PhD; Arun Jeyabalan, MD, MS; Donna D. Johnson, MD; S. Ananth Karumanchi, MD; Marshall Lindheimer, MD; Michelle Y. Owens, MD, MS; George R. Saade, MD; Baha M. Sibai, MD; Catherine Y. Spong, MD; Eleni Tsigas; and the American College of Obstetricians and Gynecologists' staff: Gerald F. Joseph, MD; Nancy O'Reilly, MHS; Alyssa Politzer; Sarah Son, MPH; and Karina Ngaiza.

Obstet Gynecol 2013;122:1122-31

Pregnancy Related Hypertension

- Gestational hypertension
- Preeclampsia
 - Without severe features
 - With severe features
- Superimposed preeclampsia
- Eclampsia

TABLE E-1. Diagnostic Criteria for Preeclampsia

Blood pressure	<ul style="list-style-type: none">• Greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure• Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy
and	
Proteinuria	<ul style="list-style-type: none">• Greater than or equal to 300 mg per 24-hour urine collection (or this amount extrapolated from a timed collection) or <ul style="list-style-type: none">• Protein/creatinine ratio greater than or equal to 0.3*• Dipstick reading of 1 + (used only if other quantitative methods not available)
Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:	
Thrombocytopenia	<ul style="list-style-type: none">• Platelet count less than 100,000/microliter
Renal insufficiency	<ul style="list-style-type: none">• Serum creatinine concentrations greater than 1.1 mg/dl or a doubling of the serum creatinine concentration in the absence of other renal disease
Impaired liver function	<ul style="list-style-type: none">• Elevated blood concentrations of liver transaminases to twice normal concentration
Pulmonary edema	
Cerebral or visual symptoms	

*Each measured as mg/dl.

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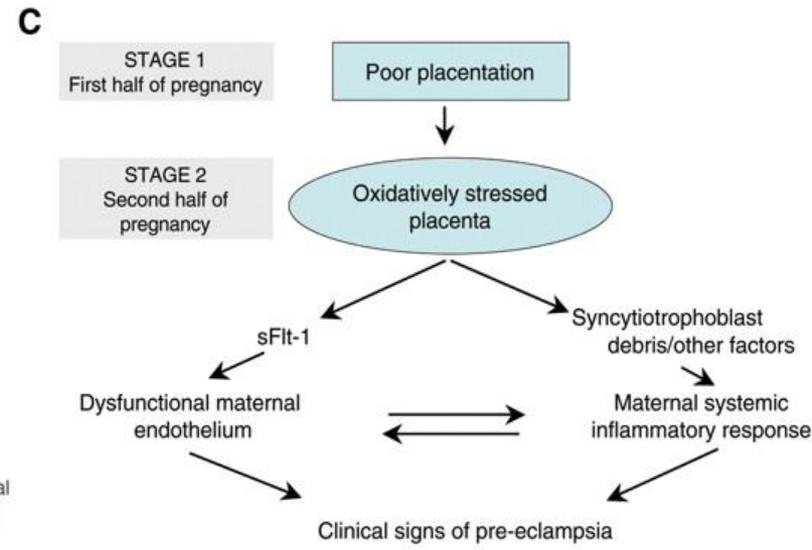
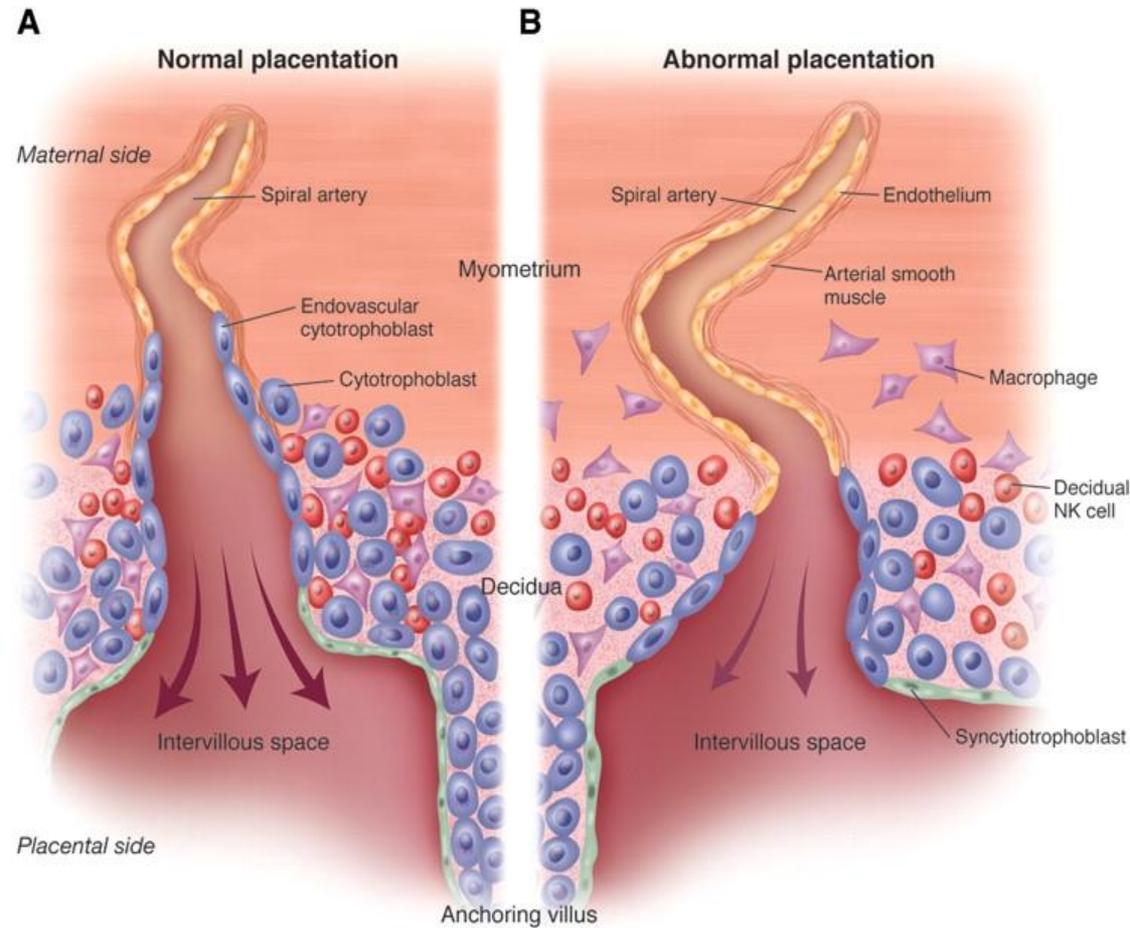
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Placentation & Preeclampsia



Pathogenesis of Preeclampsia

Abnl trophoblast invasion

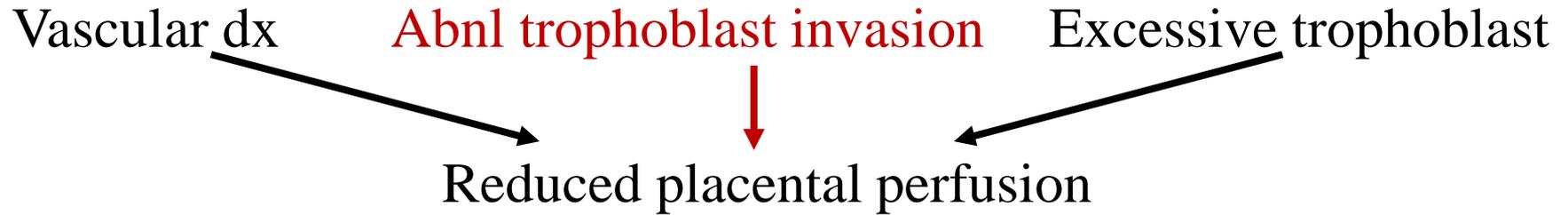


Reduced placental perfusion

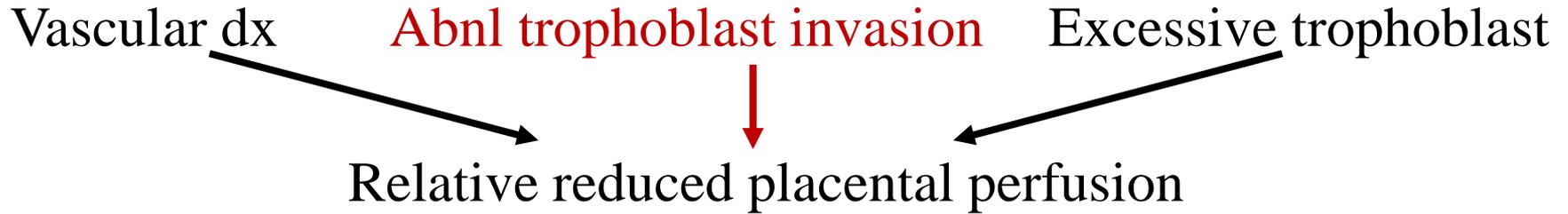
Pathogenesis of Preeclampsia



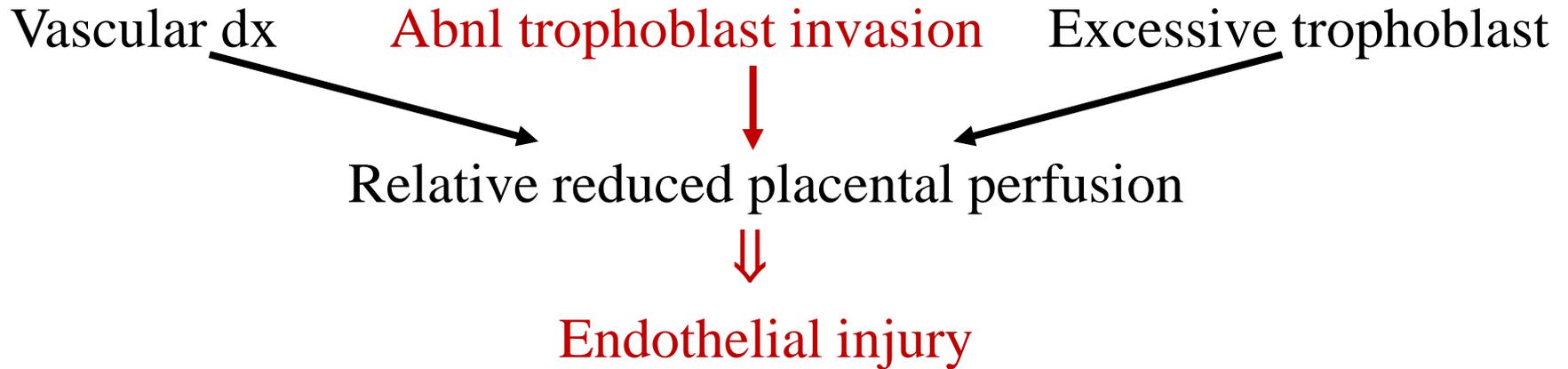
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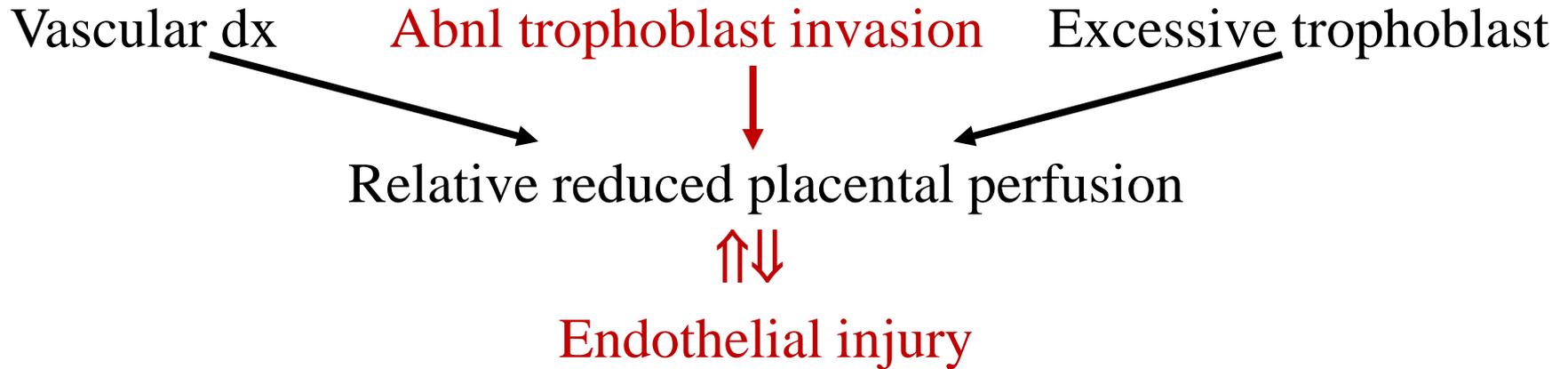
Pathogenesis of Preeclampsia



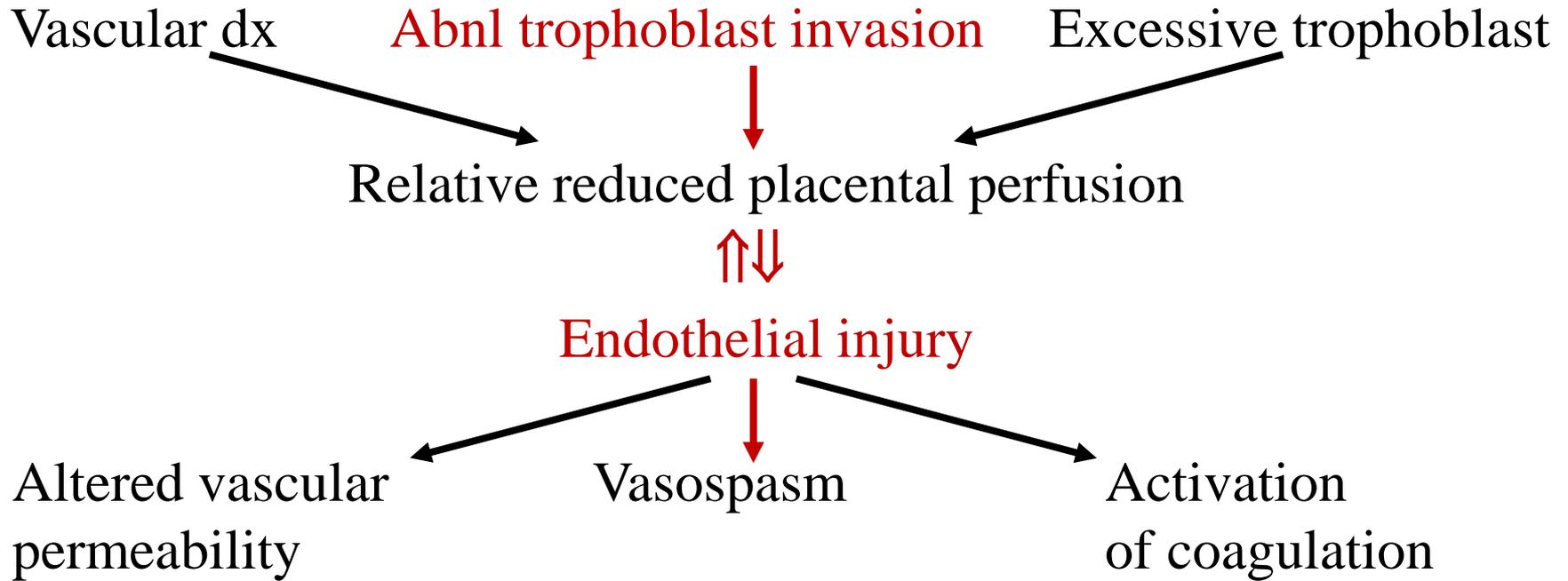
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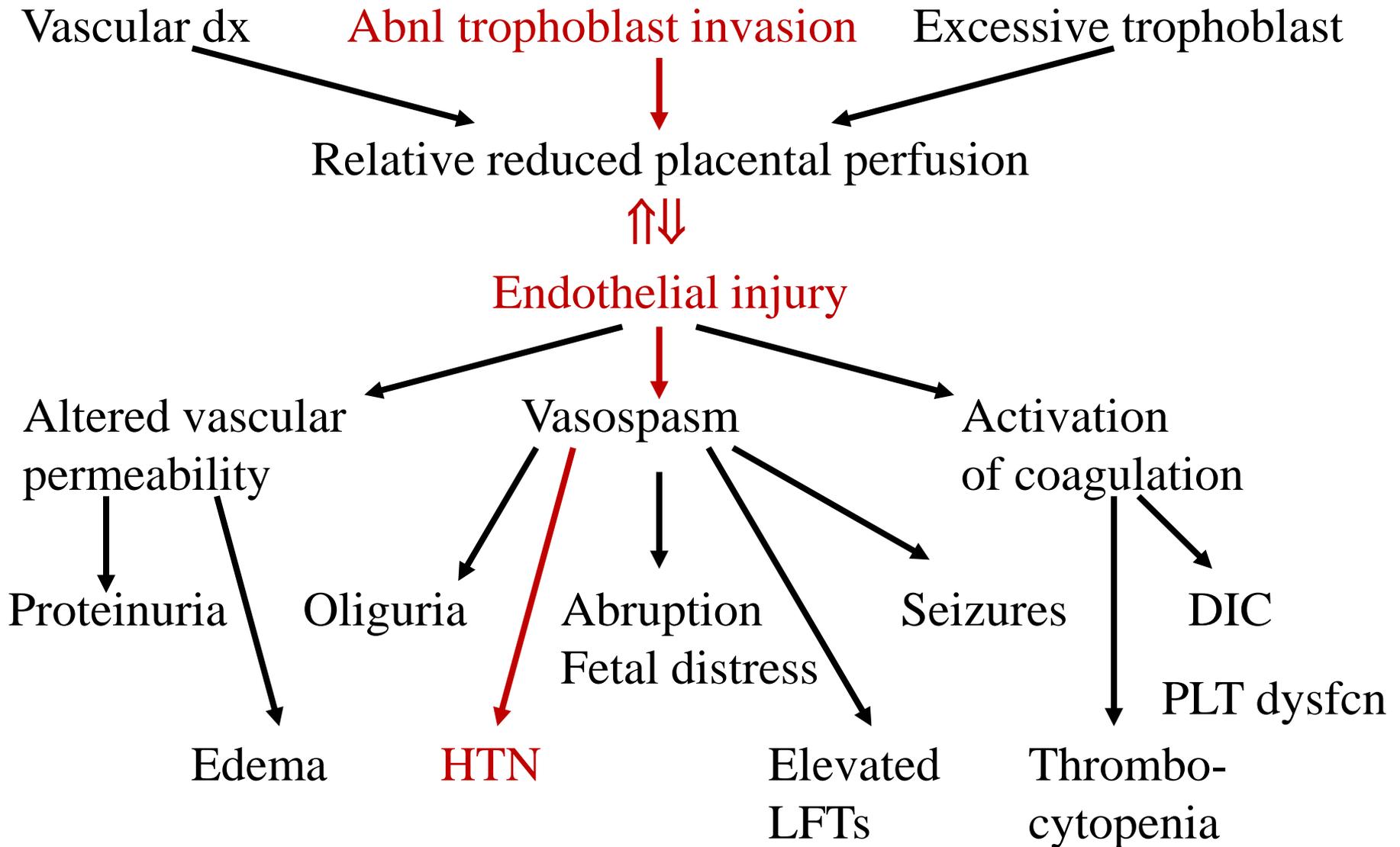
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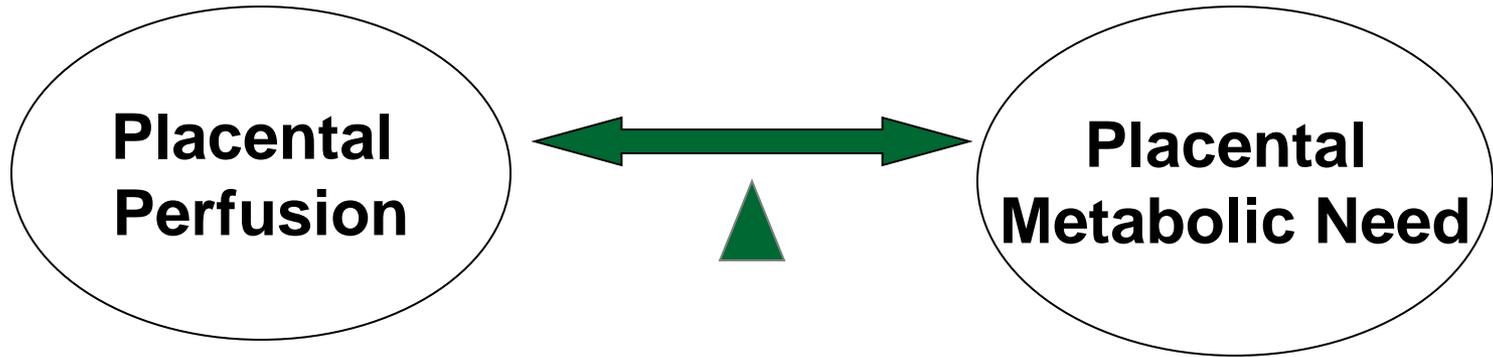
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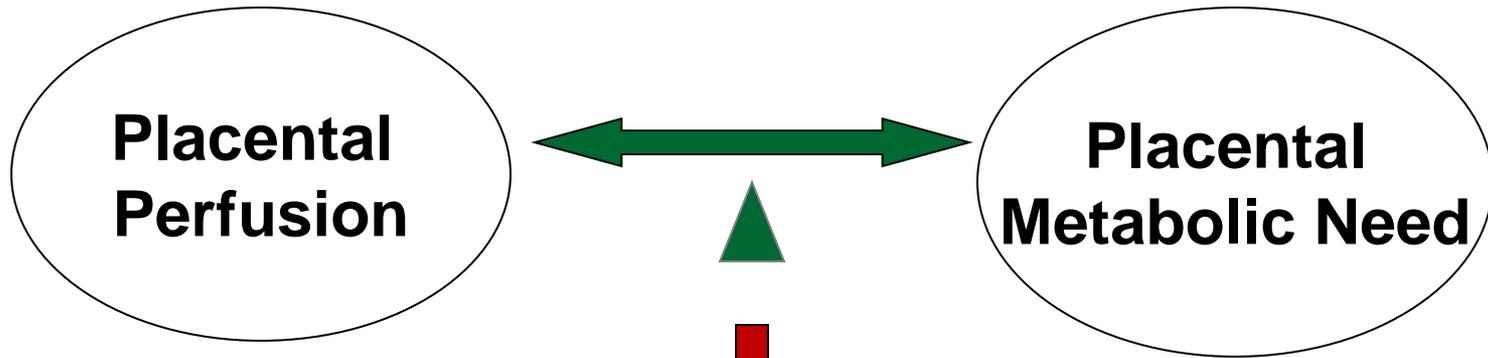
Pathogenesis of Preeclampsia



Normal Pregnancy



Preeclampsia



**Release Factors into Maternal
Circulation**



Endothelial Dysfunction



**Blood Pressure Increase
and Organ Damage**

Placental Abruption

- Premature separation of the placenta
- Overlaps with other adverse pregnancy outcomes
- Major cause of maternal mortality and morbidity
- Diagnosis is clinical and imprecise

Fetal Growth Restriction Definitions

EFW < 10th percentile
(10% of population) ← Favored by
ACOG

EFW > 2 SD below mean
(~ 3rd percentile)

EFW or AC < 5th percentile
(most clinically applicable)

Fetal Growth Restriction

- Associated with perinatal mortality and morbidity
- Common reason for indicated preterm delivery
- Differentiate between small for gestational age (80%) and true growth restriction (20%)
- Intrinsic (20%) versus extrinsic (80%)

Preterm Birth

- Delivery between 16 and 36 6/7 weeks
- Classification
 - Spontaneous
 - With intact membranes
 - Following premature rupture of membranes
 - Non-spontaneous

Causes of Preterm Birth

Spontaneous preterm labor	31 – 50%
pPROM	6 – 40%
Multiples and complications	12 – 28%
Hypertensive disorders	12%
Fetal growth restriction	2 – 4%
Antepartum hemorrhage	6 – 9%
Cervical/uterine abnormality	8 – 9%

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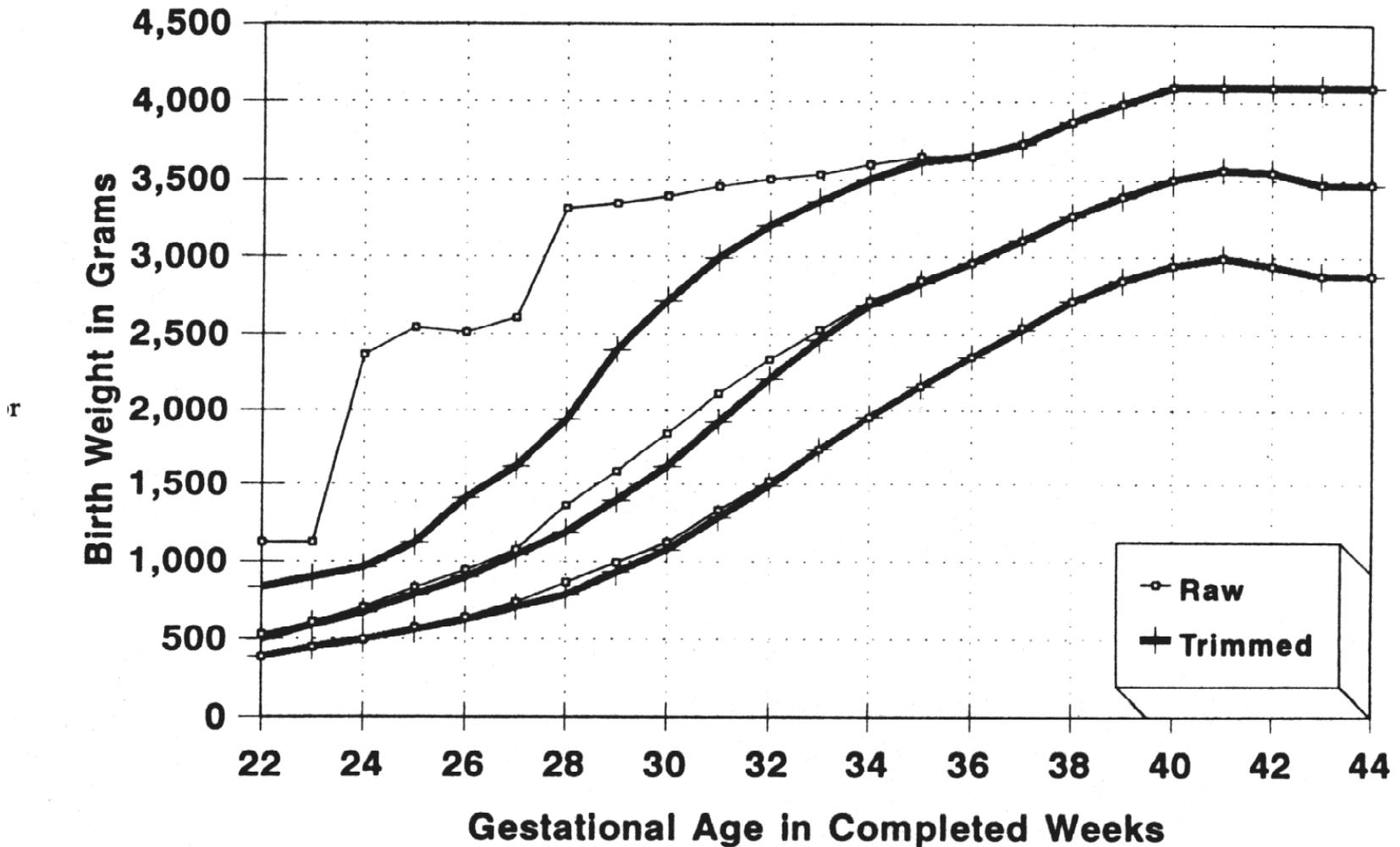
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OBSTETRICS & GYNECOLOGY



A United States National Reference for Fetal Growth

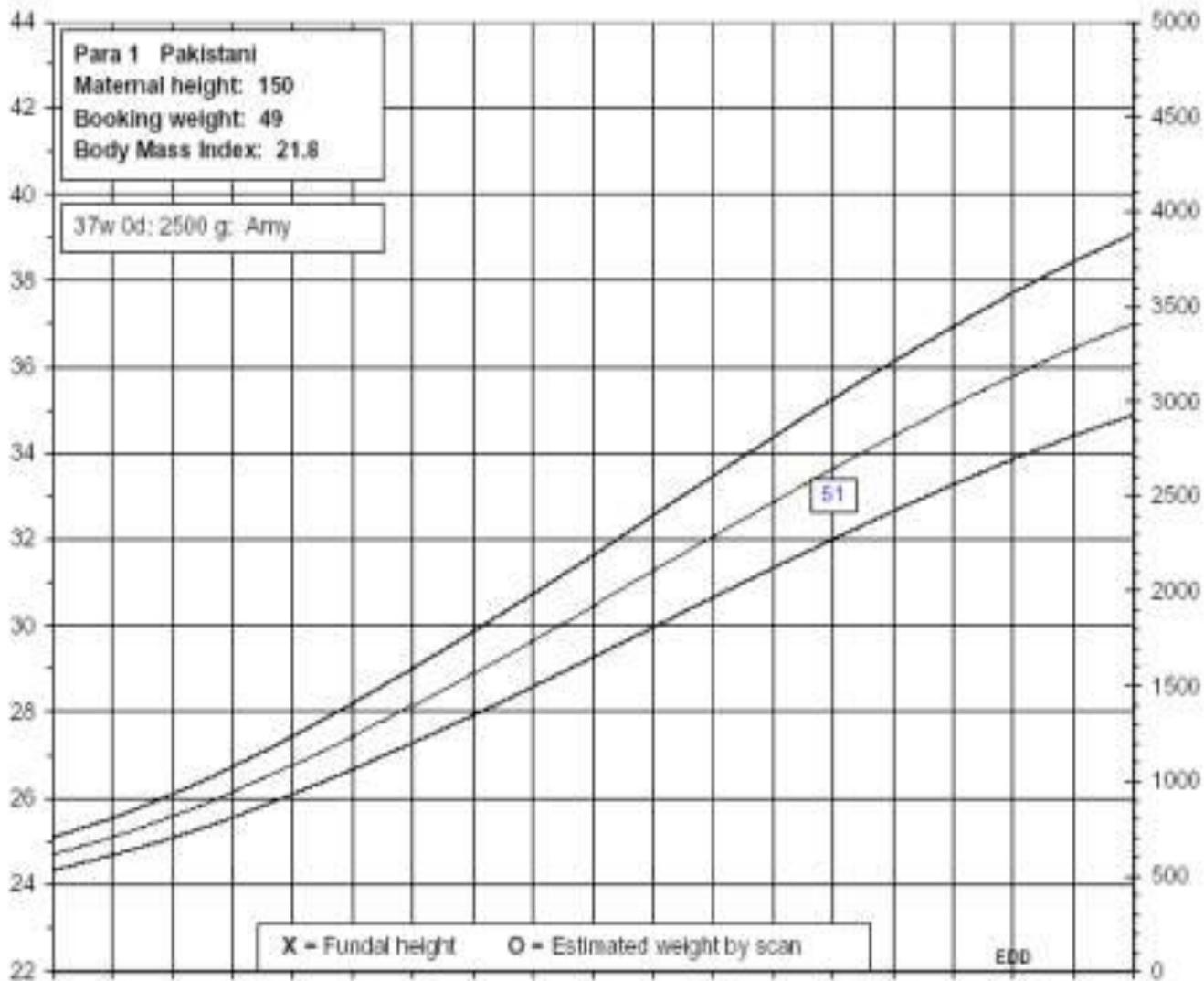


CUSTOMISED ANTENATAL GROWTH CHART

Mrs Small (1 DOB: 01/01/75)

Fundal height (cm)

Weight (g)



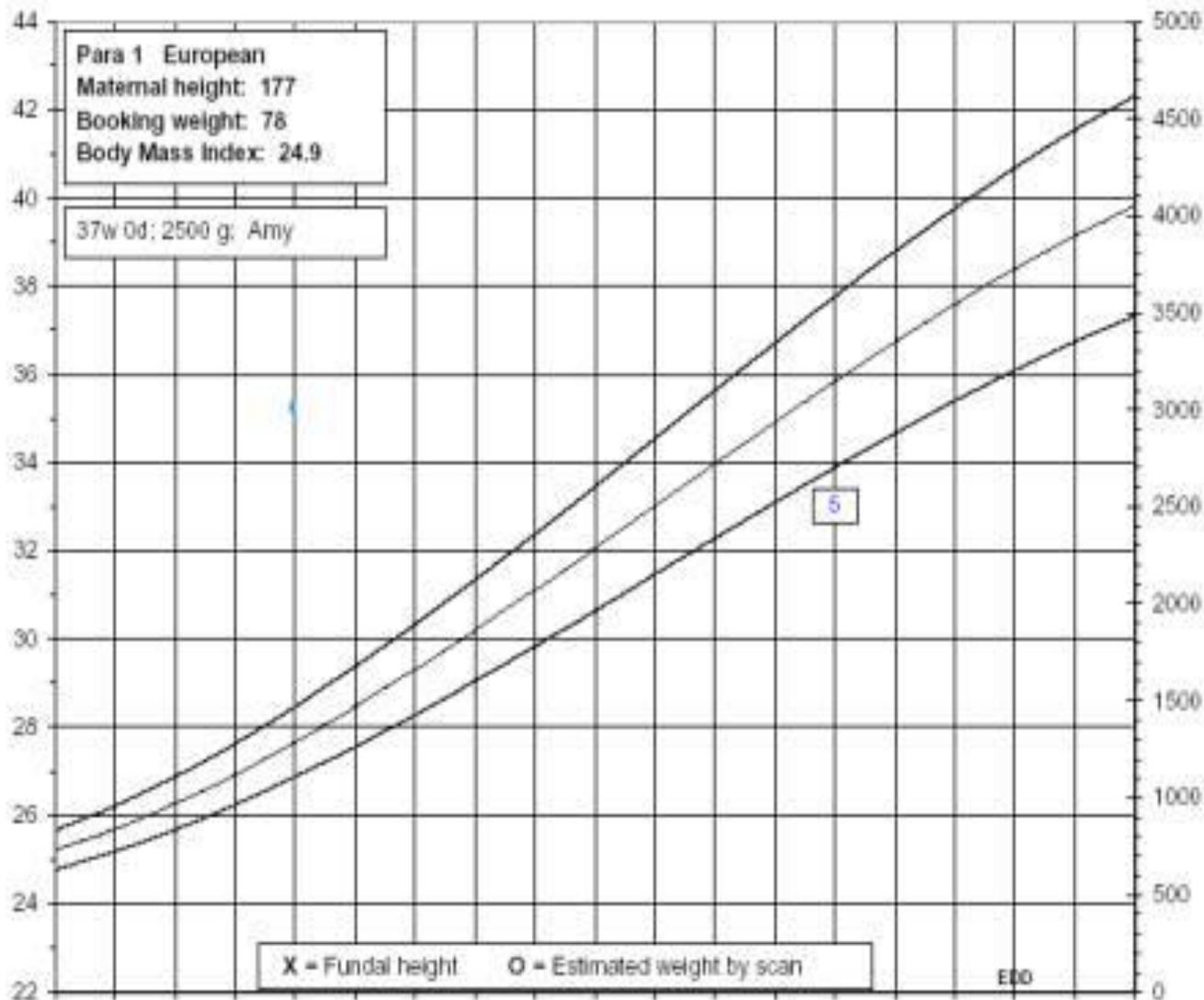
Gestation week 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42
 Sunday 11 18 25 1 8 15 22 29 6 13 20 27 3 10 17 24 1 8 15
 Aug Aug Aug Sep Sep Sep Sep Oct Oct Oct Oct Nov Nov Nov Nov Dec Dec Dec

CUSTOMISED ANTENATAL GROWTH CHART

Mrs Large (1 DOB: 01/01/75)

Fundal height (cm)

Weight (g)



Gestation week	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
Sunday	11 Aug	18 Aug	25 Aug	1 Sep	8 Sep	15 Sep	22 Sep	29 Sep	6 Oct	13 Oct	20 Oct	27 Oct	3 Nov	10 Nov	17 Nov	24 Nov	1 Dec	8 Dec	15 Dec

FGR and Prematurity

Standard Population Norms

Bukowski et al. Am J Obstet Gynecol 2001;185:463-7

PERCENTILE STANDARD NORMS	PRETERM N = 44	TERM N = 44	P
<5 th	3 (6.8)	1 (2.3)	0.366
<10 th	5 (11.4)	2 (4.5)	0.272

FGR and Prematurity

Individualized Growth Potential

Bukowski et al. Am J Obstet Gynecol 2001;185:463-7

PERCENTILE G.R.O.W.	PRETERM N = 44	TERM N = 44	P
<5 th	10 (22.7)	2 (4.5)	0.008
<10 th	13 (29.5)	2 (4.5)	<0.001

Fetal growth and onset of delivery: A nationwide population-based study of preterm infants

Nils-Halvdan Morken, MD,^{a,c} Karin Källen, PhD,^b Bo Jacobsson, MD, PhD^{c,d}

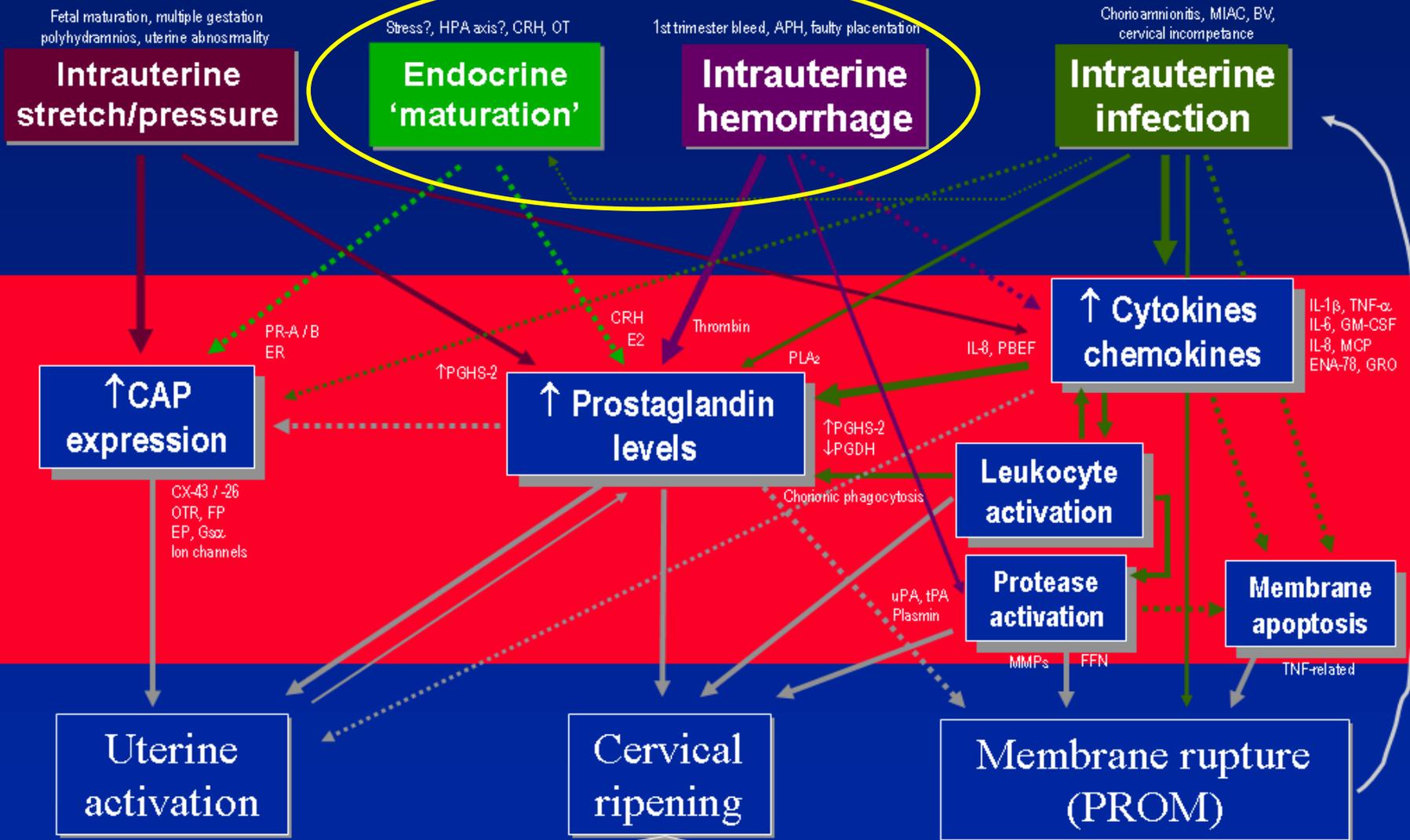
Table III Odds ratio, with 95% CI, for SD classes (<-3, -3 to -2.1, -2 to -1.1, 1to1.9, and 2 to 2.9) versus appropriate for gestational age (-1 SD to 0.99 SD) among infants born after spontaneous preterm labor, compared with term infants (born spontaneously after at least 37 completed weeks of pregnancy)*

SD classes	< 28 wks (95% CI)	28-31 wks (95% CI)	32-33 wks (95 % CI)	34-36 wks (95% CI)
<-3	9.3 (6.2-13.8)	13.3 (10.3-17.2)	5.9 (4.4-7.9)	3.1 (2.6-3.6)
-3 to -2.1	2.6 (2.0-3.3)	3.2 (2.7-3.8)	1.9 {1.6-2.2}	1.2 {1.1-1.3}
-2 to -1.1	1.8 (1.6-2.1)	2.0 (1.8-2.2)	1.3 {1.2-1.5}	1.0 {1.0-1.0}
1 to 1.9	0.6 (0.5-0.7)	0.5 (0.5-0.6)	0.7 (0.7-0.8)	1.1 (1.1-1.2)
2 to 2.9	0.4 (0.2-0.7)	0.4 (0.2-0.6)	0.8 (0.6-1.0)	1.6 (1.5-1.7)

Trigger events

Points of convergence

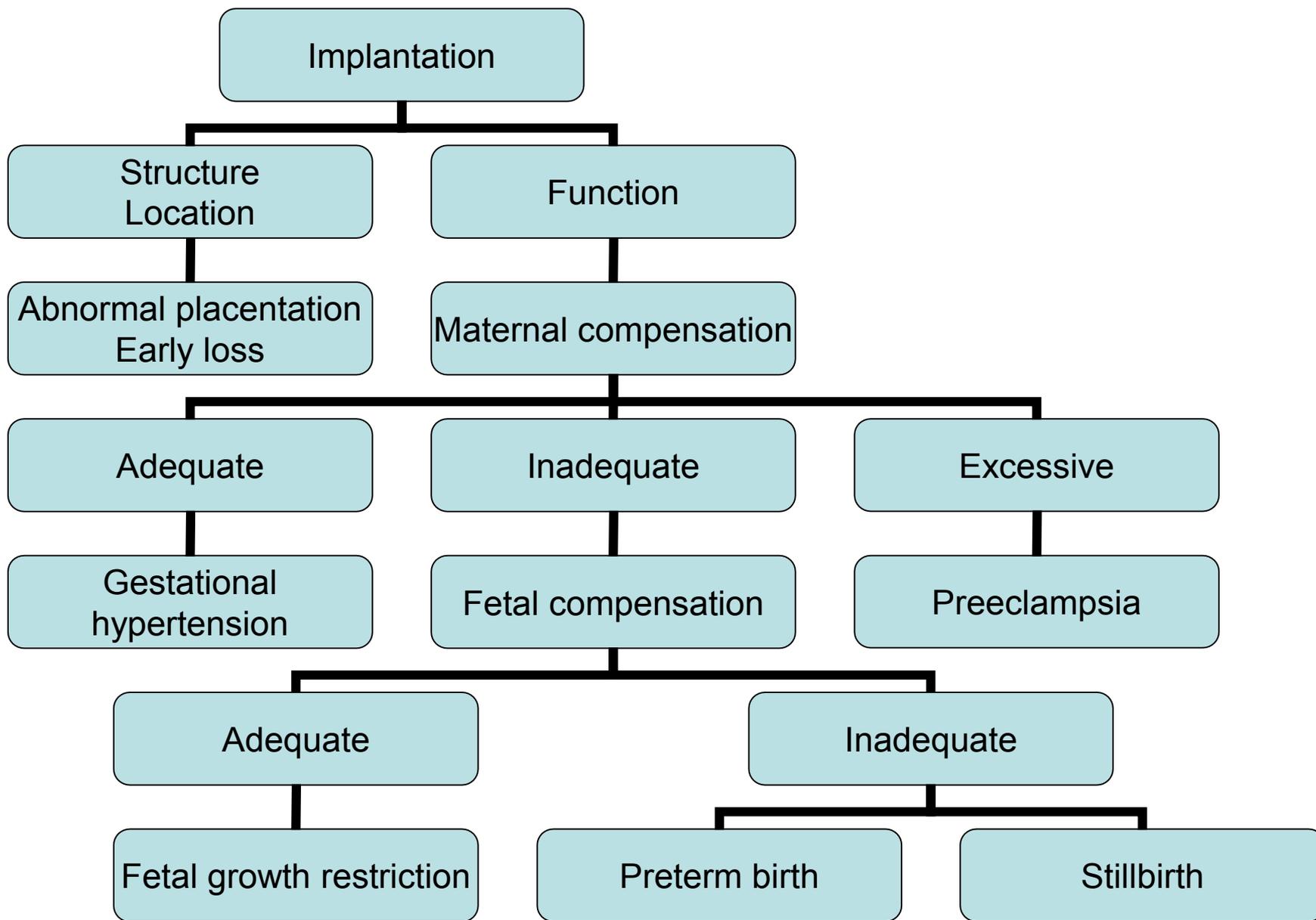
Clinical end points



Unifying Theory of Placental Conditions

- Co-occurrence of the various conditions
- Overlap in risk factors
- Occurrence of one condition increases risk for all conditions in future pregnancies

Unifying Theory of Placental Conditions



Tip of the Iceberg

Adverse Pregnancy Outcomes



Tip of the Iceberg

Adverse Pregnancy Outcomes

Long Term Outcomes



Tip of the Iceberg

Adverse Pregnancy Outcomes

Offspring

Mother



Tip of the Iceberg

Adverse Pregnancy Outcomes

Offspring

Directly Related

**Neuromotor dysfunction
Broncho-pulmonary dysplasia
Retinopathy of prematurity**



Tip of the Iceberg

Adverse Pregnancy Outcomes

Offspring

Directly Related

Neuromotor dysfunction
Broncho-pulmonary dysplasia
Retinopathy of prematurity

Developmental Programming

Cardiovascular disease
Metabolic dysfunction
Neurobehavioral

Tip of the Iceberg

Adverse Pregnancy Outcomes

Mother

Directly Related

Stroke

Renal failure

Operative morbidity



Tip of the Iceberg

Adverse Pregnancy Outcomes

Mother

Directly Related

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Operative morbidity

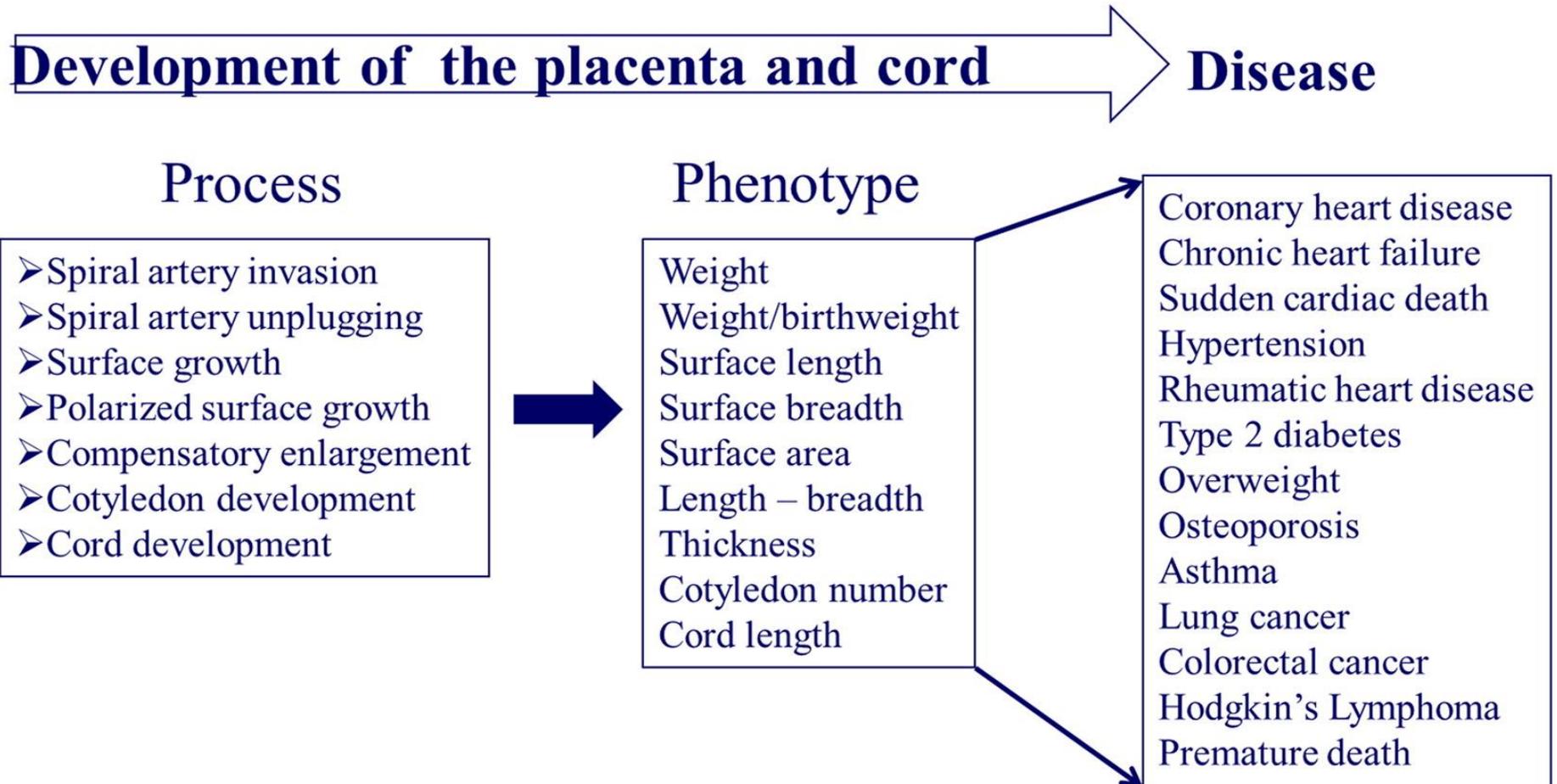
Maternal Programming

Cardiovascular disease

Metabolic dysfunction

Placental Programming

Barker & Thornburg Placenta 2013;34:841-845



Tip of the Iceberg

Adverse Pregnancy Outcomes

Mother

Directly Related

Stroke

Renal failure

Operative morbidity

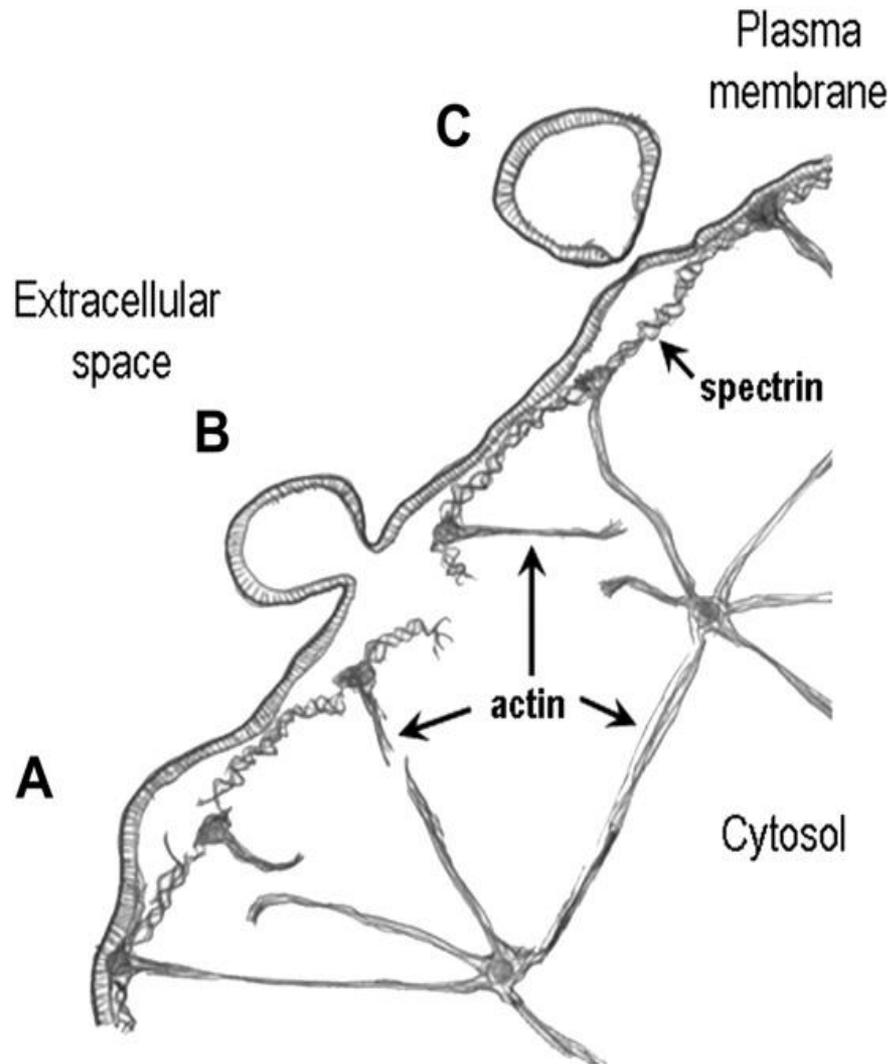
Maternal Programming

Cardiovascular disease

Metabolic dysfunction

Microparticles/Microchimerism

Microparticles



Microparticles

Medical conditions associated with increased circulating MPs [14,17,18]^a

Ischaemic heart disease

Cerebrovascular events

Metabolic syndrome

Diabetes

Heparin induced thrombocytopenia

Antiphospholipid antibody syndrome

Thrombotic thrombocytopenic purpura

Sickle cell disease

Sepsis

Challenges

- Evidence of placental involvement indirect

Multiple markers of abnormal placentation

- Biochemical
 - PAPP-A, AFP, Inhibin A, sFlt-1, PlGF etc
- Ultrasonic
 - Utero-placental Doppler flow velocimetry (uterine and umbilical)
 - Placental appearance (echolucencies and calcification)
 - Placental size (depth and volume [3D])
- Other modalities
 - MRI (structure, flow and metabolism [MRI spectroscopy])
- Indirect assessment
 - Through assessment of fetal growth

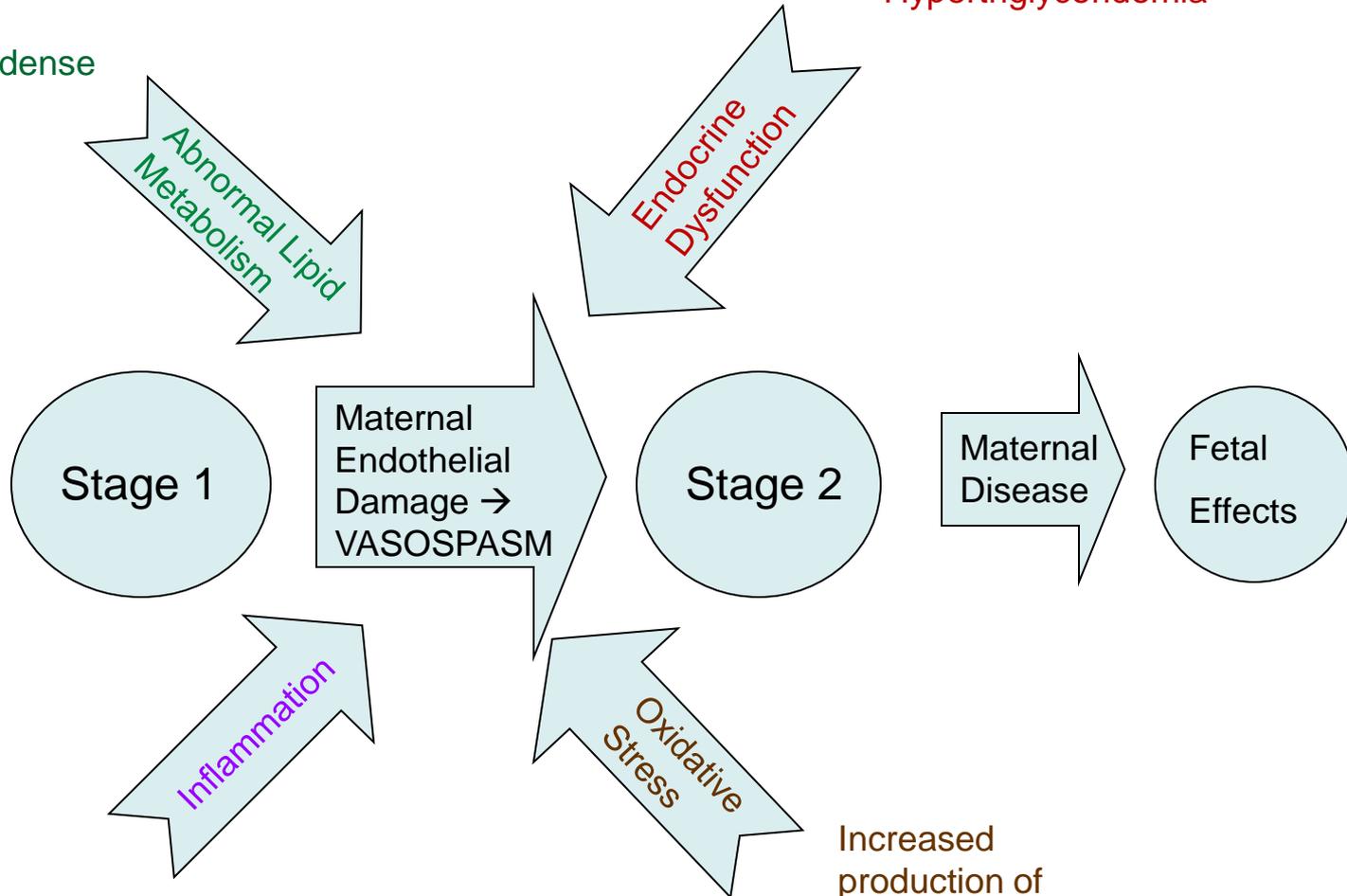
Challenges

- Evidence of placental involvement indirect
- Likely abnormality starts early
- Research in OB is heuristic (similarity, familiarity, availability)
- Too much hubris in the field
- Likely wrong in many assumptions
- We may have strayed too far
- Many interaction and compensations

Hypertriglyceridemia
Reduced HDL
Predominance of small, dense
LDL cholesterol

Insulin resistance
Hyperinsulinemia
Hypertriglyceridemia

Reduced Placental
Perfusion
Abnormal vascular
remodeling of spiral
arteries
Release of toxic
factors



Inflammatory cytokines → +
endothelial damage

Increased
production of
free radicals and
lipid peroxides →
+endothelial cell
damage