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PREVENTION OF PERINATAL NEUROLOGICAL MORBIDITY IN THE VERY PRETERM

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Neurological morbidity and pregnancy

Prematurity and low birth weight, particularly fom IUGR, is considered to be the leading identifiable risk factor for the development of severe NM.

The precise etiological factor for the development of the majority of cases of NM has not been identified.

Causes of neurological morbidity in the perinate

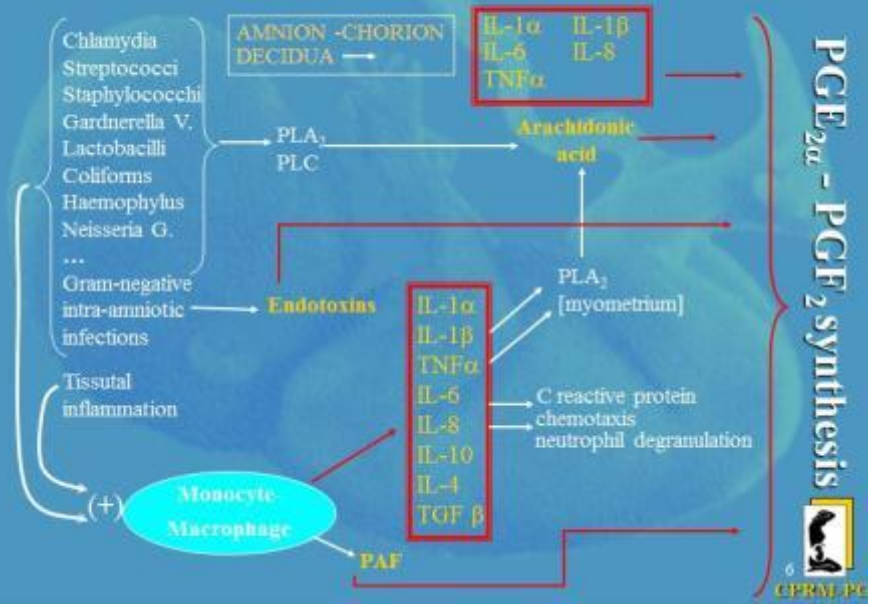
- Malformations
- Toxins
- Metabolic derangements
- Trauma
- Infection- inflammation
- **Hypoxia-ischaemia**
- Coagulation disorders
- Maternal thyroid dysfunction
- Prematurity - IUGR
- RDS
- Multiples

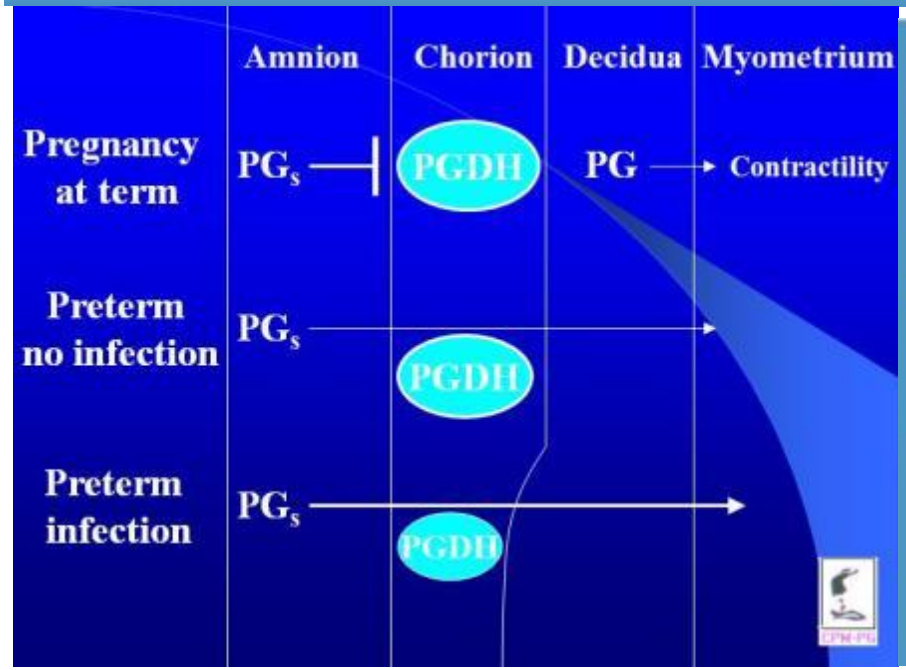
The infection paradigm in premature births

Several large epidemiological studies have documented that women with an altered vaginal ecosystem are at increased risk of pregnancy complications

(preterm birth – chorio-amnionitis – post partum infections)

Citokines, PGs and preterm delivery





1830 pregnant women (8-14 and 30-34 wks)

30% of microbiological positivity

⇓

GARDNERELLA V. MYCOPLASMA H. UREAPLASMA U.

CHLAMYDIA T. TRICHOMONAS V. STREPTOCOCCUS B

⇓

52%

THREATENING PRETERM LABOR

Di Renzo et al 1998

Bacterial enzymes

- Mucinase
- Sialidase
- Protease
- Collagenase

} Mucolytic enzymes

Sialidases activity in cervico-vaginal fluid (cut-off 10000 unit/mg mucus) was associated to presence of:

- Ureaplasma urealyticum
- Streptococcus agalactiae B
- Gardnerella vaginalis
- Chlamydia trachomatis

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Correlation between preterm labor and sialidase activity (180 cases)

	%
Sensivity	100
Specificity	67
Positive predictive value	71,4
Negative predictive value	100
Diagnostic accuracy	80

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Correlation between microbiological positive (M+) or negative (M-) vaginal/cervical smears and sialidase activity presence (S+) or absence (S-) in vaginal and cervical fluids

Vaginal fluid	M+/S+	M-/S+	M-/S-
Term labor	23%	48%	28%
Preterm labor	37%	62%	—
Cervical fluid			
Term labor	18%	38%	43%
Preterm labor	50%	50%	—

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Vaginal homeostasis

⇓

Lactobacilli

⇓

pH 3.7 – 4.2

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Vaginal pH values were obtained by colorimetric reading of paper strips carried by special gloves

Cut–off point of pH ⟶ 4,5

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750 pregnant women ⟶ 35% pH greater than 4,6

Only 27%

signs and symptoms of vaginitis

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Vaginal pH was positive (>4.6) in:

Bacterial vaginosis	75%
Chlamydia trachomatis	45%
Streptococco group "B"	53%
Fungal vaginitis	16%
Escherichia coli	60%

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Multiple pregnancy

The incidence of cerebral palsy is higher among twins and triplets than among singletons.

Studies have found that twins make up about 10% of total cases and one study found that 4.5% were among infants of normal birth weight.

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- We are now aware, for example, that the risk of at least one child being affected by cerebral palsy is 1.5 % in twin, 8% in triplet, and 43% in quadruplet gestation.

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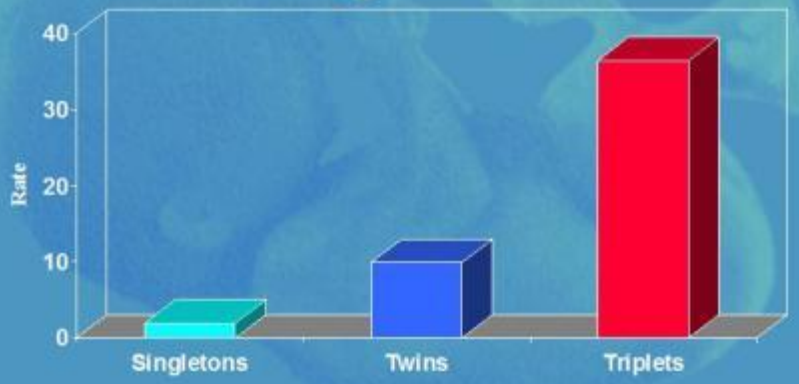
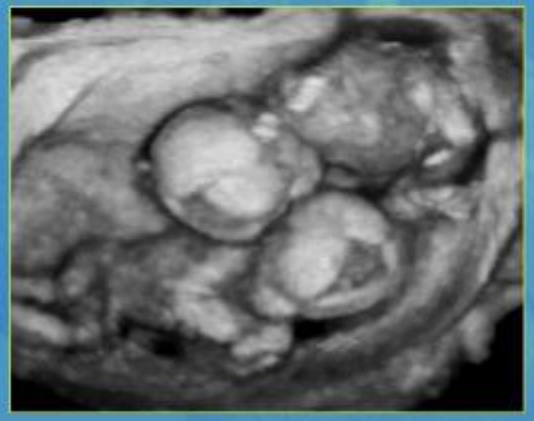
- The incidence of white matter damage after the death of one twin is in 25 % in monochorionic survivors but only 3 % in dichorionic survivors.

Relative frequencies of cerebral palsy in multiple pregnancies as compared to singletons



From Blickstein, NEJM 1999

MONOAMNIOTIC MONOCHORIONIC TWINS



DETERMINATION OF THE CHORIONICITY IN SECOND TRIMESTER

Sonographic counting of separated placentas is an accurate method of determining the chorionicity in the second trimester

PLACENTA 1

TWO SEPARATED PLACENTAS

PLACENTA 2

MONOCHORIONIC
BIAMNIOTIC TWINS

BICHORIONIC
BIAMNIOTIC TWINS

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BIAMNIOTIC
BICHORIONIC
TWINS

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TWIN TO TWIN TRANSFUSION SYNDROME

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Mechanisms Involved in Fetal Hypoxemia due to Placental Insufficiency

Feto-maternal immunologic tolerance alterations
Failure of the endothelial vasodilator tone control and alteration of the NO systems
Reduction of maternal plasmatic expansion
Increased maternal blood viscosity at low shear rate

↓

Inappropriate trophoblastic invasions
Placental hemodynamic alterations with reduction of placental perfusion

↓

- Persistence (or increase) of high impedance to flow (with notch) in the FVW of uterine arteries
- Persistence (or increase) of high impedance to flow in the umbilical arteries

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Mechanisms Involved in Fetal Hypoxemia due to Placental Insufficiency

- Decrease of placental gas exchange → Fetal hypoxemia → Fetal hemodynamic alterations
- Decrease of the substrates supplied to the fetus → Decrease of fetal growth rate; Fetal biophysical alterations

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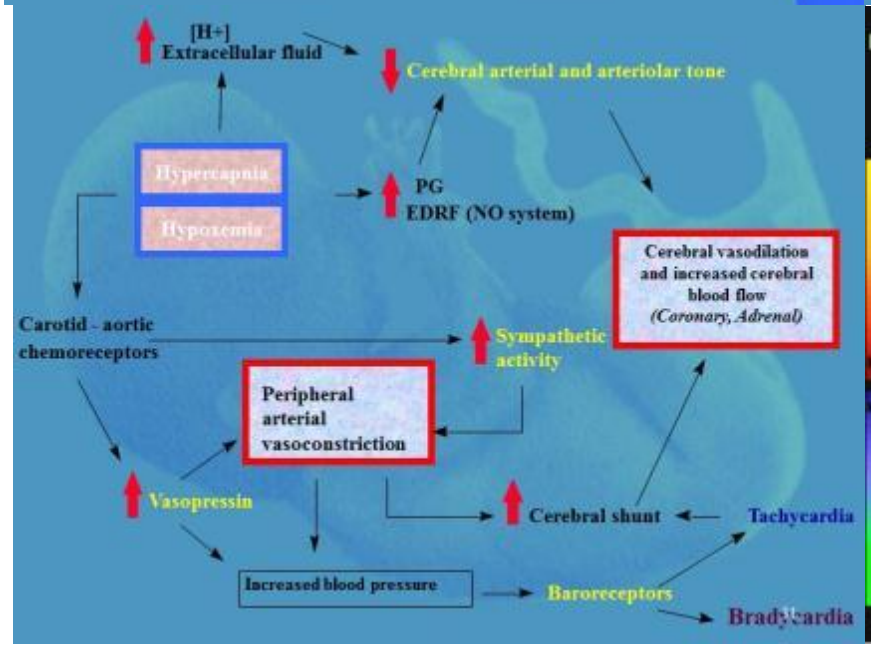
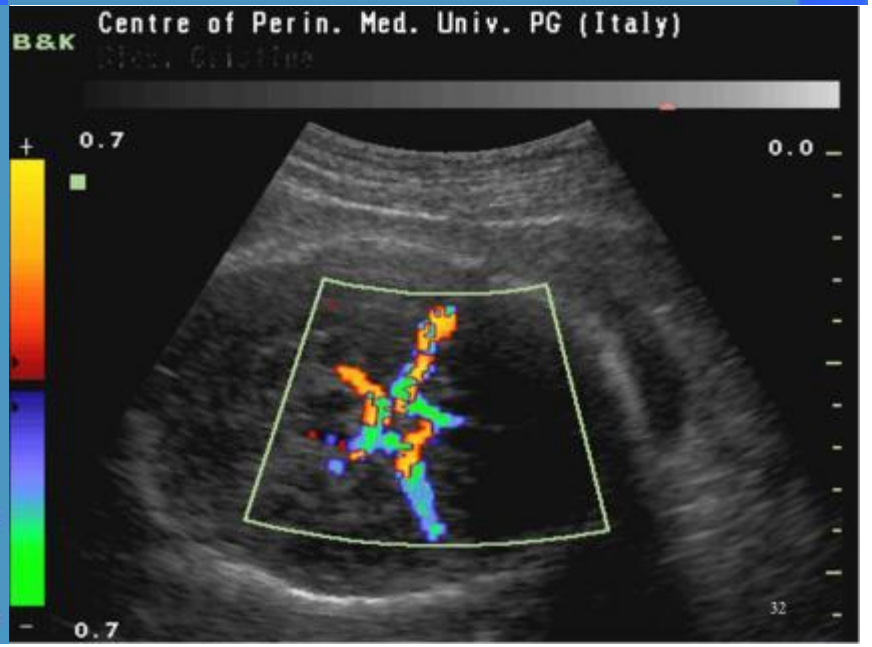
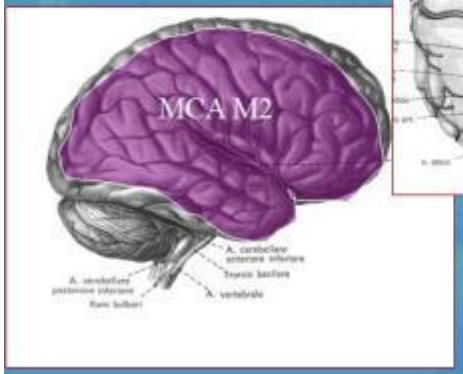
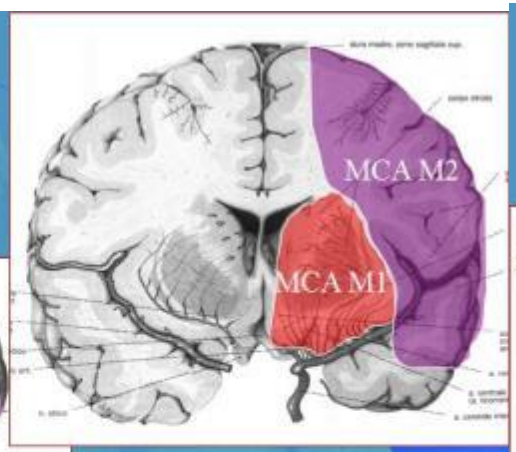




Fetal brain areas supplied by different portions of the MCA





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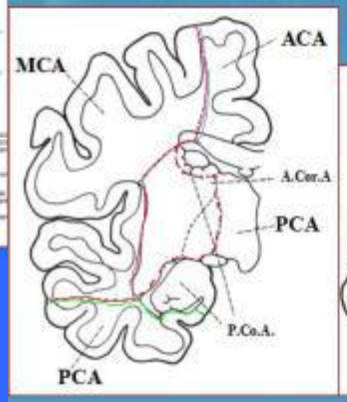
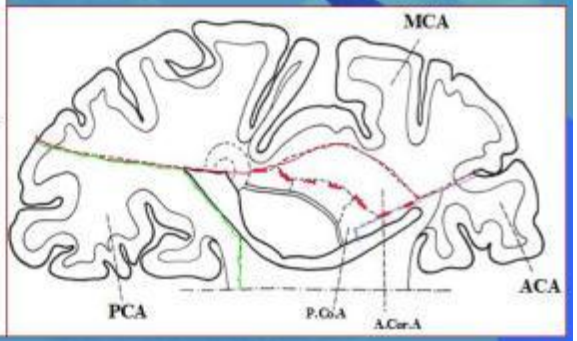
Fetal brain areas supplied by different cerebral vessels





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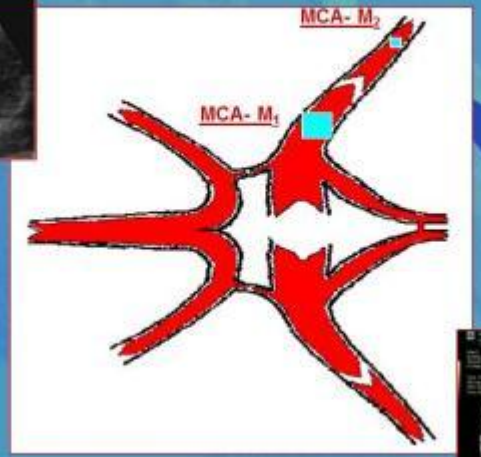
Circle of Willis



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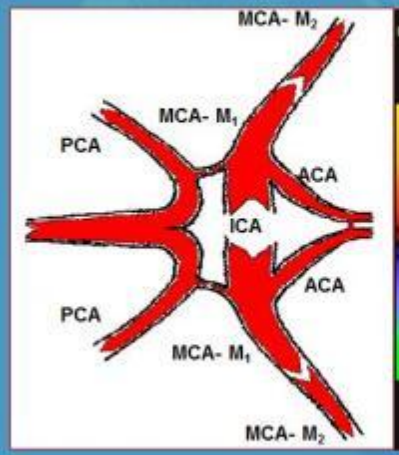
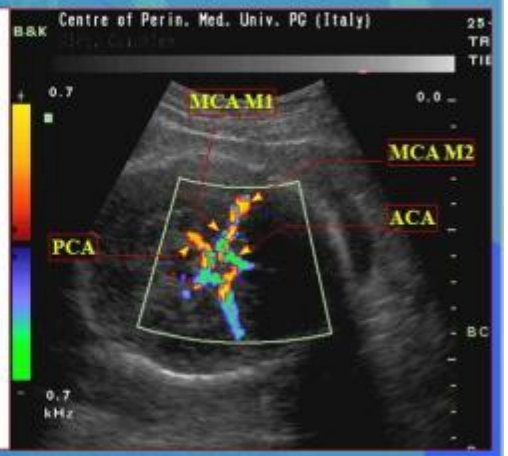
Circle of Willis





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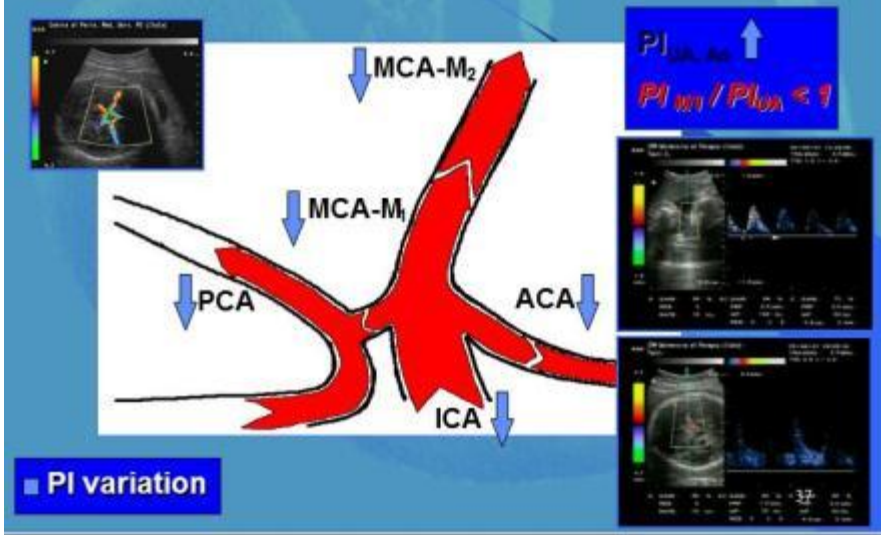
"Early Stage of Hemodynamic Redistribution" - Fetal Cerebral Circulation During Hypoxemia due to Placental Insufficiency - "Brain Sparing"



- PI variation

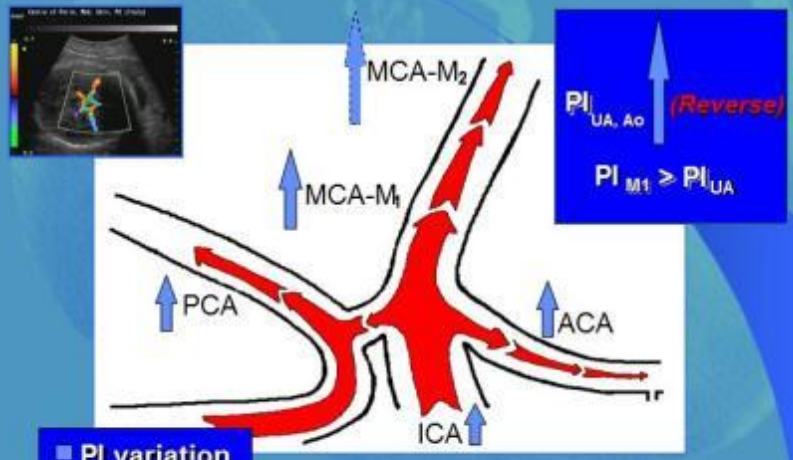
Fetal Hemodynamics
-"Early Stage of Hemodynamic Redistribution" –
-"Brain Sparing"-

Fetal vessels		Impedance to flow
Middle cerebral artery-M2	(MCA-M2)	↓
Middle cerebral artery-M1	(MCA-M1)	↓
Anterior cerebral artery	(ACA)	↓
Posterior cerebral artery	(PCA)	↓
Internal carotid artery	(ICA)	↓
Common carotid artery	(CCA)	↓
Aorta	(Ao)	↑
Umbilical artery	(UA)	↑
Renal artery	(RA)	↑
External iliac artery	(EIA)	↑
Femoral artery	(FA)	↑
Pulmonary valve	(PV)	↑
Aortic valve	(Ao V)	↓
Mitral valve	(MV)	=
Tricuspid valve	(TV)	=
Inferior vena cava	(IVC)	=
Ductus venosus	(DV)	=
Umbilical vein	(UV)	=

Fetal Hemodynamics and "Placental Insufficiency"

"Decompensation Stage"

"Decompensation Stage" - Fetal Cerebral Hemodynamics



- PI variation

Conclusions

- Fetal cerebral adaptation to hypoxia: initial → "Cerebral sparing" M2/M1>1
- Fetal cerebral adaptation to hypoxia: subsequent → Decrease PI in all cerebral areteries with preferential flow in MCA. "Brain sparing" effect (C/P<1)
- Fetal decompensation to hypoxia → Disappearing brain sparing signs in ACA
- Fetal terminal signs → Disappearing brain sparing signs in MCA