Cardiovascular fetal programming and remodelling
Long term effects of adverse fetal environment on the heart

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Fetal growth restriction
(and other conditions leading to adverse fetal environment)

Adaptation = Epigenetics = Permanent “programming”
1986 Barker (MRC Unit, Southampton, UK):
Coronary heart disease mortality rates
IUGR

*target organ in hypoxic centralization*

Adaptive response
Progressive failure

Permanent Epigenetic changes

CLINICAL MONITORING

CARDIAC PROGRAMMING
CLASSIC HYPOTHESIS

Fetal growth restriction
Epigenetic changes in metabolic regulation
Normalization of diet (or overnutrition)
Insulin resistance
Obesity/Diabetes/
Hypertension
Cardiovascular disease

ALTERNATIVE/COMPLEMENTARY HYPOTHESIS

Fetal growth restriction
Epigenetic changes in cardiac regulation
Persistence of abnormal cardiac function
Lack of ability to further adaptation
Cardiovascular disease
Postnatal persistence of cardiovascular remodeling

Fetal cardiac dysfunction

Intrauterine growth restriction

Hypertension, coronary disease, stroke, obesity, diabetes

Cardiovascular disease in adulthood

Fetal cardiovascular programming

Cardiovascular remodeling

globular heart
↓ longitudinal motion
↓ stroke volume
↑ heart rate
= cardiac output

hypertension
pre-arteriosclerosis

TA 90/65
clMT = 0.386 mm

TA 115/80
clMT = 0.434 mm

IMPACT OF LATE IUGR/SGA

near term SGA fetuses without signs of poor prognosis also presented CV remodeling

decreased systolic motion

right S’

impaired relaxation

TAPSE

E dec

IRT

Data are median±SEM. *P<0.05 adjusted by GA, birthweight centile and preeclampsia.
cardiovascular remodelling in IUGR

NORMAL

Crispi 2010, Cruz-Lemini 2013, Stergiotou 2014
cardiovascular remodelling in IUGR

NORMAL

IUGR
more globular heart
systolic & diastolic dysfunction

increased aIMT

Crispi 2010, Cruz-Lemini 2013, Stergiotou 2014
NORMAL

ART

Thicker ventricular walls
Dilated atria
Systolic & diastolic dysfunction

ART

Systemic & pulmonary hypertension
in infancy & childhood

aIMT

pressure overload
Fetal cardiovascular remodeling & programming of adult disease

- hyperglycemia
- embryo manipulation
- toxics
- hypoxia
- undernutrition
- infection

- Twin-to-twin transfusion syndrome
  - limited utility in staging or predicting prognosis

- Maternal diabetes
  - potential utility in predicting outcome?

- Assisted reproductive technologies

- Intrauterine growth restriction
  - prediction of postnatal hypertension

BIOLOGIC PROGRAMMING AND AGE
Fetus

Problem evident

Brain organization

Child

4P medicine
- Predictive
- Preventive
- Personalized
- Participatory

IDENTIFICATION OF RISK

INDIVIDUAL BIOMARKERS

INTERVENTION

WINDOW OF OPPORTUNITY

BIRTH
fetal composite CV score for the prediction of postnatal hypertension
sensitivity 90%, specificity 77%

IDENTIFICATION OF RISK

INDIVIDUAL BIOMARKERS

INTERVENTION

WINDOW OF OPPORTUNITY

Fetus

Functional / structural organ remodeling

Problem evident

Cruz-Lemini FMF 2013, Skilton Pediatric 2012, Rodriguez 2013
Fetal cardiovascular remodeling & programming of adult disease

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Intrauterine growth restriction
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BC NATAL