FUTURE OF PEDIATRICS TALKS!
A VIRTUAL SUMMER SERIES

Pediatric Health Network
Children's National
Meet Our Speaker

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• No financial or business interest, arrangement or affiliation that could be perceived as a real or apparent conflict of interest in the subject (content) of their presentation.

• No unapproved or investigational use of any drugs, commercial products or devices

Adre du Plessis, MBChB
Prenatal Pediatrics
Building a Bridge for Children from High-Risk Pregnancies

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Chief, Division of Prenatal and Transitional Pediatrics
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Objectives

This presentation will provide the pediatrician with an enhanced understanding of:

1. developmental plasticity and its role in the long-term outcome of the high-risk fetus;
2. the expanding role of the pediatrician in the prenatal and postnatal care of the high-risk fetus; and
3. the unmet challenges for detection, surveillance and long-term monitoring of the offspring of high-risk pregnancies.
What is the role of the pediatrician in fetal care?

Pediatricians are increasingly involved in fetal care for several major reasons

• **During pregnancy**
  • Pediatric subspecialists increasingly involved
  • Counseling families
  • Planning to manage hazardous transition
• 50 years experience with ‘the ex-utero fetus’ – prematurity and NICU care
• Advancing fetal diagnostics

• **After birth**
  • Care of fetal anomalies and their complications
  • Prenatal origins of later chronic disorders
Consequences of Fetal Adversity: Timing of Manifestations

- Fetal Adversity
- Fetal
- Neonatal
- Childhood
- Adulthood
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Environmental Influences on the Genome

Environmental influences → Epigenetic modification → Range of Phenotypes

Single Genotype
Identifying Fetal-Onset Conditions in Utero

Currently we identify only the tip of the iceberg!
Congenital anomalies may have important developmental effects
The fetus is not a lesion!

Fetus Brain Growth with Congenital Heart Disease
Developmental Plasticity

• Characteristics of developmental plasticity (DP)
  • Nature of the response depends on the nature of the environmental cue
  • There are critical windows of plasticity in different organ systems
  • Duration of developmental plasticity is time-limited: operates longer for processes associated with growth and metabolism (e.g., the brain)

• Some environmental influences are clearly pathological and result in developmental disruption and teratogenesis – with no adaptive advantage – rather than channeling development
Fetal Origins of Lifespan Health Risk (Barker Hypothesis)

Dutch Famine (“Winterhonger) 1944-1945

- The fetus adopts anticipator physiology
- Plasticity – two-edged sword
The growth-restricted fetus
Fetal Growth Restriction

• Fetus not meeting its genetically destined growth potential
• Placental insufficiency is the leading cause
• BW <10\(^{th}\) percentile for gestational age (Kingdom & Smith, 2000)

PLUS

• Evidence of placental insufficiency (decreased umbilical artery Doppler flow) (Figueras & Gratacos, 2014)
• Between 3 – 15% pregnancies in the developed world
• Up to 6-old greater in low-income countries
• Global incidence of ~30 million/year (de Onis et al. 1998; Bernstein et al. 2000; Lackman et al. 2001; Fang, 2005; Chauhan & Magann, 2006; Figueras & Gratacos, 2014)
Brain Development in Fetal Growth Restriction

**Structural Deficits**
- Reduced head circumference
- Reduced total and grey matter volume
- Reduced hippocampal and cerebellar volume
- Reduced total cell number
- Reduced myelin content/ delayed myelination
- Thin cortex with altered gyrification
- Reduced connectivity
Brain Development in Fetal Growth Restriction

**Functional Deficits**

- Motor
  - Impaired gross, fine, and visuomotor skills
  - Cerebral palsy
- Cognition and learning
  - Decreased IQ/impaired executive function
  - Memory (esp. verbal) impairment
- Behavior
  - Social interaction deficits/Autistic spectrum disorders
  - Attentional deficits/Hyperactivity
  - Anxiety, irritability, and depression
Fetal Growth Restriction: Consequences and Timing of Manifestation

- Fetal demise
- Prematurity related brain injury
- Perinatal asphyxia

Infancy, Childhood, Adulthood
- Obesity
- Diabetes
- Hypertension
- Dyslipidemias
- Heart disease
- Stroke
- Attentional disorders
- Developmental delay
- Behavioral dysfunction
- Autism
- Mood disorders
- Schizophrenia
Mental health disorders are now recognized as the most common complication of pregnancy.

Maternal stress and depression may have profound effects on fetal development.
Prenatal Stress Questionnaires

Healthy Pregnant Volunteers (n=90)

• Prenatal Stress/Anxiety
  • 27% tested positive for stress/anxiety

• Edinburgh Postnatal Depression Scale
  • 8% tested positive for depression

Limperopoulos et al. 2019
## Fetal Brain Growth and Maternal Psychological Distress

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Limperopoulos et al. 2019
Brain Plasticity

Fetal Environment
Aberrant Development

Birth
Brain Plasticity

Fetal Environment Aberrant Development

Postnatal Window of Opportunity for Developmental Intervention

~ 3 years
The Prenatal Pediatrics Institute at Children’s National
Prenatal Pediatrics – Subspecialty Program Directors

- Prenatal Cardiology: Mary Donofrio
- Prenatal Neurology: Adre du Plessis
- Prenatal Neurosurgery: Carlos Sanchez
- Prenatal Orthopedics: Matthew Oetgen
- Prenatal Urology: Hans Pohl
- Prenatal Nephrology: Marva Moxey-Mims
- Prenatal Surgery: Tim Kane
- Prenatal Genetic Counseling: Anne Lawrence
- Prenatal Genetics: Jamie Fraser
- Prenatal ENT: Brian Reilly
- Prenatal Imaging: Dorothy Bulas
- Prenatal Blood Disorders: Alexis Leonard
- Prenatal Endocrinology: Andrew Dauber
- Prenatal Reconstructive Surgery: Albert Oh
- Prenatal Genetics: Jamie Fraser
Multidisciplinary Programs supporting Prenatal Pediatrics

- Critical Care Delivery Program
- Perinatal Palliative Care Program
- Positive Re-evaluation of Urogenital Differences (PROUD) Program
- Skeletal Dysplasia Program
- Cardiac Neurodevelopmental Outcome (CANDO) Program
- Perinatal Mental Health Program
- Perinatal Mental Health Support Program
- Prenatal-Neonatal Transition Program
- Spina Bifida Program
- Colorectal-Pelvic Anomaly Program
- Heterotaxy Program
Summary

The current and future state of Prenatal Pediatrics

• The focus should expand beyond anatomic malformations

• Major obstetric complications (placental failure; pre-eclampsia; infection; diabetes, maternal stress/depression, substance abuse; many others) pose significant risk to the infant, child, and adult, potentially across the lifespan

• The focus on the whole fetus not only ‘abnormalities in pictures’

• There is an urgent need for improved communication, referral, and monitoring of the high-risk fetus before and after birth