What is the role of developmental biology in relation to intervention in the future?

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Conflict of Interest Statement:
I do not have an affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.
General Conceptual considerations

• Prenatal Alcohol Exposure in not easily preventable
  • A majority of pregnancies are unplanned (among 18-29 year-olds, N Engl J Med 2016; 374:843-852)
  • Alcohol consumption is a self-medication response
  • Alcohol consumption can escalate into addiction
  • Prevention programs ignore the contribution of the father to FASD

• However, the effects of prenatal alcohol exposure can be minimized
  • Prenatal alcohol exposure ≠ FASD
Conceptual Scheme for Prenatal Intervention

- **Body Plan**
  - **Organogenesis** → **Organ Growth**

- **Placental Growth**

- **Developmental Stage-specific Intervention Opportunity**

- **Trimester**
  - 1: Neurogenesis & Migration
  - 2: **Organogenesis** → → → **Organ Growth**
  - 3: Gliogenesis, Brain Maturation

- **Pregnancy Awareness**
  - Planned
  - Unplanned
Conceptual Scheme for Prenatal Intervention

- **Unplanned Pregnancy**
  - Neurogenesis & Migration
  - Gliogenesis, Brain Maturation

- **Planned Pregnancy**
  - Safety Zone: 95%
  - Danger Zone: 10%

- **Growth Rate**:
  - 10%

- **Trimester**:
  - Trimester 1
  - Trimester 2
  - Trimester 3

- **Body Plan**
  - Planned
  - Unplanned
Considerations for Prenatal Interventions

• Better, quicker, cheaper diagnosis

• **Developmental Stage-specific Interventions**
  • Harm reduction strategies (development is resilient)
  • Biomedical interventions
Predicting birth outcomes

- HEa = Heavily exposed/infant affected
- HEua = Heavily exposed/infant apparently unaffected
- UE = Apparently unexposed controls
Predicting HEa and UE pregnancies

Harm Reduction 1: Reducing toxicity burden

Harm Reduction 2: Reducing ‘Allostatic Load’
Better nutrition
Better prenatal care

hsa-miR-15b-3p
hsa-miR-337-3p
hsa-miR-342-5p
hsa-miR-423-3p
hsa-miR-503-5p
Considerations for Prenatal Interventions

• Better, quicker, cheaper diagnosis

• **Developmental Stage-specific Interventions**
  • Harm reduction strategies
  • Biomedical interventions
INTERIM UPDATE

A correction was published in November 2017 for this title. Click here to view the correction

ACOG COMMITTEE OPINION

Number 713 • August 2017
(Reaffirmed 2018)

Committee on Obstetric Practice

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists’ Committee on Obstetric Practice in collaboration with committee members Yasser Y. El-Sayed, MD, Ann E.B. Borders, MD, MSc, MPH, and the Society for Maternal-Fetal Medicine’s liaison member Cynthia Gyamfi-Boamah, MD, MSc.

INTERIM UPDATE: This Committee Opinion is updated as highlighted to reflect a limited focused change to clarify that, among specific populations, antenatal corticosteroids should be administered when a woman is at risk of preterm delivery within 7 days.

Antenatal Corticosteroid Therapy for Fetal Maturation

ABSTRACT: Corticosteroid administration before anticipated preterm birth is one of the most important antenatal therapies available to improve newborn outcomes. A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks and 33 6/7 weeks of gestation who are at risk of preterm delivery within 7 days, including for those with ruptured membranes and multiple gestations. It also may be considered for pregnant women starting at 23 0/7 weeks of gestation who are at risk of preterm delivery within 7 days, based on a family’s decision regarding resuscitation, irrespective of membrane rupture status and regardless of gestational number. Administration of betamethasone may be considered in pregnant women between 34 0/7 weeks and 36 6/7 weeks of gestation who are at risk of preterm birth within 7 days, and who have not received a previous course of antenatal corticosteroids. A single repeat course of antenatal corticosteroids should be considered in women who are less than 34 0/7 weeks of gestation who are at risk of preterm delivery within 7 days, and whose prior course of antenatal corticosteroids was administered more than 14 days previously. Rescue course corticosteroids could be provided as early as 7 days from the prior dose, if indicated by the clinical scenario. Continued surveillance of long-term outcomes after in utero corticosteroid exposure should be supported. Quality improvement strategies to optimize appropriate and timely antenatal corticosteroid administration are encouraged.
Conceptual Scheme for Prenatal Intervention

Pregnancy Awareness

Body Plan

Organs

Neurogenesis & Migration → Organogenesis → Organ Growth

Gliogenesis, Brain Maturation

Trimester

Developmental Stage-specific Intervention Opportunity

Placental Growth
In utero binge ethanol exposure during the height of cortical interneuron migration increases MGE-derived interneurons in the embryonic mPFC.
Conceptual Scheme for Prenatal Intervention

Organogenesis → Organ Growth

Neurogenesis & Migration

Gliogenesis, Brain Maturation

Body Plan

Developmental Stage-specific Intervention Opportunity

Placental Growth

Trimester

1

2

3

Pregnancy Awareness

Planned

Unplanned
Predicting birth outcomes

Plasma miRNA Profiles in Pregnant Women Predict Infant Outcomes following Prenatal Alcohol Exposure

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Abstract

Fetal alcohol spectrum disorders (FASD) are difficult to diagnose since many heavily exposed infants, at risk for intellectual disability, do not exhibit craniofacial dysmorphology or growth deficits. Consequently, there is a need for biomarkers that predict disability. In both animal models and human studies, alcohol exposure during pregnancy results in significant alterations in circulating microRNAs (miRNAs) in maternal blood. In the current study, we asked if changes in plasma miRNAs in alcohol-exposed pregnant mothers, either alone or in conjunction with other clinical variables, could predict craniofacial dysmorphology or growth deficits. Eighty-eight pregnant women at two perinatal care clinics in western Ukraine were recruited into the study. Detailed health and alcohol consumption histories, and 2nd and 3rd trimester blood samples were collected. Birth cohort infants were assessed by a psychologist and classified as unexposed (UN), heavily exposed but apparently unaffected (HEa) or heavily exposed but apparently unaffected (HEua). miRNAs were assessed in plasma samples using RT-QPCR. ANOVA identified 11 miRNAs that were all significantly different. The geometric mean fold change of six of these miRNAs was used to predict birth outcomes.

ANOVA Model: HEa>(HEua ≈ UE)
Maternal miRNAs, elevated in the HEa group result in decreased placental and fetal growth, and blood flow.
Conclusions

• Developmental stage-appropriate interventions are feasible
• We do not have to achieve perfection to make a difference
• We need better, quicker ways to identify ‘at risk’ pregnancies
• Harm reduction strategies are available
  • Managing poly-drug use, allostatic load, nutrition, access to prenatal care
  • Exploit Resiliency of fetal development
• Biomedical interventions to promote pregnancy health
  • Are associated with risk for doing harm
  • But are already a part of clinical practice to manage difficult pregnancies
  • May be used to facilitate growth of organs like the placenta, resulting in better fetal outcomes.