Translational Research in FASD

Amy Elliott, Ph.D.
February 27, 2014
Overview

- Describe research projects within the region on prenatal alcohol exposure
- Impact of research in prenatal alcohol exposure for this region
THE WAY IT SHOULD WORK

Laboratory Research

Patient-oriented Clinical Research

Population-based Clinical Research

Clinical Trials
Community-Based Research

Engaging community-based partners is not an option; it is a priority
Center for Health Outcomes & Prevention Research (CHOPR)
CHOPR Institutional Partners

Bubble size indicates number of partners
Safe Passage Study

A Prospective Study on the Relationship Between Prenatal Alcohol Exposure, Stillbirth & Sudden Infant Death Syndrome
Aberdeen Area Infant Mortality Study (1992-1996)

- 9 tribes and 1 urban area in the Northern Plains participated
- Sample Size
  - 72 deaths
  - 38 of 72 (53%) confirmed as SIDS
- Significant risk factors for SIDS
  - Maternal drinking during periconceptional period: ↑ 6x
  - Maternal binge drinking during the 1st trimester: ↑8x
  - Two or more layers of clothing at death: ↑6x

Iyasu et al., JAMA 2002
PASS Network – Phase II

Clinical Sites:
Northern Plains
South Africa

Physiology Asmt Center

Developmental Biology & Pathology Center
Children’s Hospital
Boston

Data Coordinating Center
DM-STAT
Boston

NICHD and NIAAA
• Study Offices
Infant Mortality Rate by County, 2005-2009

U.S. = 6.75

South Dakota = 7.09

Note: “Significantly” refers to statistical significance at the 0.05 level. Although a county’s rate is from 2007. See technical notes for more complete explanations. Source: South Dakota Department of Health.
Infrastructure

• Community Sites
  – Tribal Resolutions (renewed annually)
  – Partner prenatal clinics & hospitals
  – Pathologists
  – Services for women & children (e.g., WIC; Healthy Start)
Partners

Sioux Falls (SD)
- Sanford Health
- Sanford Women’s, Sioux Falls
- LCM Pathologists, Sioux Falls

Spirit Lake/Altru (ND)
- Mercy Hospital, Devil’s Lake, ND
- Spirit Lake MCH – IHS, Fort Totten, ND
- Altru Clinic, Devil’s Lake, ND
- University of North Dakota

Pine Ridge (SD)
- Pine Ridge IHS
- Oglala Lakota College, Dept. of Nursing
- WIC

Rapid City (SD)
- Rapid City Regional Hospital
- Native Women’s Health Center
- USD Sanford School of Medicine
- WIC
- Black Hills Ob-Gyn
- Black Hills Peds
- Rapid City Community Health
- Clinical Lab of the Black Hills
PASS Common Study Protocol

Recruitment
12,000 pregnant women

Exposure Hx
Fetal/Infant Physio
3D & Doppler U/S
Psychosocial
SES, Maternal Saliva
Nutrition
Autopsy, Neuropath, Classification

Prenatal week

Postnatal month

6 ~22 ~30 34+ birth 1 12

Fetal demise
Infant demise

Main Study
Embedded Study

Fetal demise
Infant demise

All subjects
Embedded only
Safe Passage Study
Step 1
- Life-threatening event
- Asphyxia and brain hypoperfusion
- Head lifting or turning

Step 2
- Failure of arousal
- Progressive asphyxia

Step 3
- Hypoxic coma

Step 4
- Bradycardia and gasping

Step 5
- Failure of autoresuscitation resulting in death
Brainstem Analysis in the DBPC

Consistent evidence for brainstem abnormalities involving the neurotransmitter serotonin (5-HT) in SIDS

Filiano and Kinney, 1994
The 5-HT System in the Medulla: Role in Respiratory and Autonomic Control

Upper Airway Control

CO₂ sensitivity

Parasympathetic

Sympathetic

Heart Rate; Heart Rate Variability

Blood Pressure

Temperature

Upper Airway Control

Gasping

Baroreceptor Reflex

Parasympathetic

Sympathetic

Heart Rate; Heart Rate Variability

Blood Pressure

Temperature
Cardio-respiratory Activity During Head-Up Tilting

Heart Rate

Breathing

Tilting

Flat

Head Up
Physiologic Assessments of the Neonate
Fetal and Maternal ECG
Monica Analyses

Fetal heart rate

Maternal heart rate

Uterine activity
Sample of Community Collaboration

American Indian Cultural Issues surrounding...

- Collection of tissue & bloods, particularly post-mortem
  - Individual choice, options on consent
- Genetics studies
  - Separate informational sheet on genetics studies
PASS Prospective Study
CONSORT Chart as of December 16, 2013

Enrolled
n=10,142 (75.3%)

Pregnancy Outcome*
n=9,327 (98.5%)

Outcome Known at 12 Months for SIDS determination*
n=7,041 (91.4%)

Approached
15889

3% re-enrollments***
95.9% at least 1 prenatal visit*
1.1% twins

88.4% overall visit compliance

1.5% withdrawn after enrollment**
3.4% demise

*of those eligible for contact
Maintaining commitment in longitudinal study

• Involvement since beginning of project helped create ownership

• Tribal community meetings

• Regular contact & updates with prenatal clinic & hospital partners

• Transparency in protocol changes & process
Effects of Prenatal Environment on Brain Development: A Longitudinal Study in Preterm Infants

Sanford Research: Amy J. Elliott, Ph.D.
Columbia University: Michael Myers, Ph.D.
Bill Fifer, Ph.D.
Philip Grieve, Ph.D.

Investigators conduct EEG recordings on prematurely born infants in the Rapid City neonatal intensive care unit to determine if prenatal alcohol exposure affects patterns of EEG activity which are known to be essential for forming normal connectivity within the developing cortex. The overall goal of the study is to identify early in life EEG profiles that will better predict which exposed infants are at greater risk for later cognitive deficits.

Rapid City Coordinators: Jessica Gromer RN, Carol Robinson RN, Amy Willman RN
DNA methylation as a biomarker in fetal alcohol spectrum disorders

Sanford Research: Susan Puumala, Ph.D. (Co-PI)
Amy Baete, BA (Study coordinator)

Mayo Clinic: Myra Wick, M.D., Ph.D. (Co-PI)

University of North Carolina: Philip May, PhD (Co-I)

• Ancillary project to the FASER study
• Enroll children with confirmed diagnosis of FAS or pFAS and matching controls
• Collect blood samples
• Assess genome-wide DNA methylation differences in cases and controls
• Goal is to evaluate DNA methylation as a possible diagnostic biomarker for FAS or pFAS
FASER Sioux Falls
Fetal Alcohol Spectrum Epidemiology Research

- Collaborative Effort with the University of New Mexico-CASAA
- Goal is to assess, for the first time in a general U.S. population, the minimal prevalence and estimate the true prevalence of Fetal Alcohol Spectrum Disorders for 1st-Graders in three areas. (Montana, South Dakota, North Carolina)

- A better understanding of the public health and clinical impact of FASD in the general population will guide the way to better diagnosis, intervention, and prevention.
- NIH/NIAAA Funding

Prevalence of FASD from In-School Studies
Source: May et al., DDRR, 2009.

![Graph showing prevalence of FASD with current estimate and means for different regions]
Oglala Sioux Tribe CHOICES Program

<table>
<thead>
<tr>
<th>Location</th>
<th>Team Members</th>
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</thead>
<tbody>
<tr>
<td>Sioux Falls</td>
<td>Jessica Hanson, PhD (PI)</td>
</tr>
<tr>
<td>Pine Ridge</td>
<td>Susan Pourier, BS (Project Coordinator)</td>
</tr>
<tr>
<td>Kyle</td>
<td>Katana Jackson, MSW (Interventionist)</td>
</tr>
<tr>
<td>Rapid City</td>
<td>Jessica Gromer, RN (Site Manager)</td>
</tr>
</tbody>
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- Prevention with non-pregnant American Indian women
  - Reduction/abstention in alcohol consumption
  - Increase utilization of effective contraception
- Evidence-based intervention that utilizes motivational interviewing and self-guided change
- Sites
  - Pine Ridge – 2-sessions, one-on-one or Group CHOICES
  - Kyle – 4-sessions, one-on-one
  - Rapid City – Group CHOICES
    **All sites include a contraceptive counseling session with a health care provider.**
- All sites also include a 3- and 6-month post-intervention follow-up to assess alcohol and contraception behaviors.

Either one of these behavior changes reduces risk for an alcohol-exposed pregnancy.

Key CHOICES citations at: [http://www.cdc.gov/ncbddd/fasd/research-preventing.html](http://www.cdc.gov/ncbddd/fasd/research-preventing.html)

Funding is from award # 1R24MD008087-01 from the National Center on Minority Health and Health Disparities (Hanson, PI)
What Community-Based Research has Created
Collaborative Research Center for American Indian Health

- CRCAIH brings together tribal communities and health researchers in SD, ND and MN. Our goal is to build tribal research infrastructure to improve American Indian health through examination of social and environmental influences using transdisciplinary teams.
Partners

- Phil May, Ph.D. – University of North Carolina
- Larry Burd, Ph.D., University of North Dakota
- Hannah Kinney, MD, Children’s Hospital – Boston
- Bill Fifer, Ph.D. & Michael Myers, Ph.D. – Columbia University
- Hein Odendaal, MD – University of Stellenbosch
- Kim Dukes, Ph.D. – DM-stat
- Lisa Sullivan, Ph.D. – Boston University
- Gary Hankins, MD – University of Texas Med Center
- Kim Noble, MD, Ph.D. – Columbia University
- Mary Ann Sens, MD – University of North Dakota
- Brad Randall, MD
- Don Haabe, MD – Rapid City Regional
- Laurie Nelsen – Emory University
- Ken Warren, MD (NIAAA)
- Bill Dunty, Ph.D. (NIAAA)
- Dale Hereld, MD, Ph.D. (NIAAA)
- Rosalind Breslow, Ph.D. (NIAAA)
- Marian Willinger, Ph.D. (NICHD)
- Rick Goldstein, MD – Dana Farber Cancer Center
- Peter Hammond – University of London
- Tatiana Foroud – University of Indiana
Acknowledgements

- Gene Hoyme, MD
- Jessica Hanson, Ph.D.
- Susan Puumala, Ph.D.
- Jyoti Angal, MPH
- Amy Baete, BA
- Jaymi Russo, MS
- Katie Burgess, MPH
- Tricia Crotwell, Ph.D.
- Jessica Gromer, RN
- Deb Tobacco, MS
- Bethany Norton, MS
- Luke Mack
- Catherine Stoops, MD
- Peter Van Eerden, MD
- DenYelle Kenyon, Ph.D.
- Victoria Grey Owl, Ph.D.
- Emily White Hat, JD
- Jennifer Prasek
- Ann Marie Hess
- Temana Aldalcio
- Roxi Miller
- Kaushal Chaudhary
- Whitney Adler
- Leah Bangston
- Lisa Bear Robe
- Mary Berdahl
- Chaleen Brewer
- Cathy Christopherson
- Alex Drasey
- Christa Friedrich
- Kathy Harris
- Jessica Holsworth
- Marge Jackson
- Amber Ogaard
- Debby Olson
- Carol Robinson
- Marcia Smith
- Mary Thum
- Amy Willman
- Amy Willson
- Marcia Smith
- Leah Bangston
- Cathy Roling
- Ashley Miller
Funding Acknowledgements

• CRCAIH: NIMHD U54-MD008164
• PASS: NICHD U01-HD045935 (Elliott)
  – ARRA supplement – NIAAA
  – ARRA supplement – NIDCD
  – ARRA supplement - NICHD
• FASER: NIAAA U01-AA019894 (May)
• NICU: R37 HD032774 (Fifer)
• Columbia Clinical & Translational Research Center (Noble)
• NIMHD: R24-MD-008087 (Hanson)
Thank you. Questions?

Our hospital, clinic and community partners make this work possible.