Epigenetic Impact of Unresolved Trauma and Poor Nutrition

3rd Annual Conference on Native American Nutrition
Prior Lake, MN
October 5, 2018

Donald Warne, MD, MPH
Oglala Lakota
Associate Dean of Diversity, Equity and Inclusion
Director, Indians Into Medicine (INMED) Program
University of North Dakota School of Medicine & Health Sciences
Pine Ridge Reservation
Kyle, S.D.
Traditional View of Public Health
Social Determinants of Health

Life-enhancing resources, such as food supply, housing, economic and social relationships, transportation, education and health care, whose distribution across populations effectively determines length and quality of life.

AI Health Disparities

Average age at death in ND (2010 – 2014):

77.4 Years in the White Population

56.6 Years in the AI Population

Diabetes Death Rates
(Rate/Per 100,000 Population)

- US All Races: 25.2
- IHS Total: 77.7
- Great Plains: 119.9
2.5 times as many AI/ANs as whites live below poverty level

Adults ≥18 years who live below federal poverty level

<table>
<thead>
<tr>
<th>Group</th>
<th>2005</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Black</td>
<td>21%</td>
<td>21%</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>AI/AN</td>
<td>23%</td>
<td>20%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>18%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Source: CDC Health Disparities and Inequalities Report 2011, MMWR, Vo. 60
Poverty in North Dakota
Poverty in South Dakota
American Indians and Alaska Natives as a Share of the Total Population, by State, 2009-2011

Total: 2.5 million = 1% of U.S. Population

American Indian and Alaska Native includes people of Hispanic origin.
SOURCE: KCMU analysis of 2009 - 2011 ACS.
Historical Context
You will do well to try to inoculate the Indians by means of Blankets, as well as to try every other method that can serve to interrupt this execrable Race. I should be very glad your scheme for hunting them down by stages could take effect.

Effect but presumed it at too great a distance to think of that at present.
You will do well to try to inoculate the Indians by means of Blanketts, as well as to try every other method that can serve to Extirpate this Execrable Race. I should be very glad your Scheme for hunting them Down by Dogs could take effect...
Historical Context
VALUE OF AN INDIAN SCALP

Minnesota Paid Its Pioneers a Bounty for Every Redskin Killed

It is not generally known in latter day Minnesota history that the state treasury once paid out cash as bounties for Sioux Indian scalps, just as this and many other states are now paying for wolf scalps. State Treasurer Koerner yesterday, in looking over the 1863 report of State Treasurer Charles Schaff, discovered the following item among the disbursements of that year:

J. C. Davis, Sioux scalp............$25

This item occurs in the list of disbursements, amounting in all to $7,370.06, under the head “Suppressing Indian War.” The $25 paid to J. C. Davis for
VALUE OF AN INDIAN SCALP

Minnesota Paid Its Pioneers a Bounty for Every Redskin Killed

It is not generally known in latter day Minnesota history that the state treasury once paid out cash as bounties for Sioux Indian scalps, just as this and many other states are now paying for wolf scalps. State Treasurer Koerner yesterday, in looking over the 1863 report of State Treasurer Charles Schaff, discovered the following item among the disbursements of that year:

J. C. Davis, Sioux scalp $25

This item occurs in the list of disbursements, amounting in all to $7,870.06, under the head "Suppressing Indian War." The $25 paid to J. C. Davis for...
AI/AN Population by County

Source: U.S. Census Bureau, 2010 Census Redistricting Data (Public Law 94-171) Summary File, Table P1.
AI/AN Population Decline and Recovery, 1492 – 2010
Inter-Generational Basis for Chronic Disease Disparities Among American Indians and Alaska Natives

Historical Trauma

Genocide

Chronic Disease Disparities
Historical trauma

• Collective emotional wounding across generations that results from massive cataclysmic events – Historically Traumatic Events (HTE)*

• Trauma is held personally and transmitted over generations. Family members who have not directly experienced the trauma can feel the effects generations later
Epigenetics

- The study of changes in the regulation of gene activity and expression that are not dependent on DNA sequence.

- Methylation
- Histones
- Telomeres
Epigenetics

Epigenetic mechanisms are affected by these factors and processes:
- Development (in utero, childhood)
- Environmental chemicals
- Drugs/Pharmaceuticals
- Aging
- Diet

Epigenetic factor

Health endpoints:
- Cancer
- Autoimmune disease
- Mental disorders
- Diabetes

Chromatin

DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.

Histones are proteins around which DNA can wind for compaction and gene regulation.

Gene

Histone tail

DNA accessible, gene active

DNA inaccessible, gene inactive

Histone modification
The binding of epigenetic factors to histone “tails” alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.
Inter-Generational Basis for Chronic Disease Disparities Among American Indians and Alaska Natives

Historical Trauma

- Abuse (physical, sexual)
- Neglect
- Abandonment
- Forced Removal
- Loss of culture & language
- Forced Christianity
- Lost traditional parenting & family structure

Genocide

Gestational Stressors

Birth

Chronic Disease Disparities

© Warne & Lajimodiere 2012
Inter-Generational Basis for Chronic Disease Disparities Among American Indians and Alaska Natives

Historical Trauma

Gestational Stressors

Birth

Childhood Stressors

Chronic Disease Disparities

Genocide

WIC

FDPIR

Boarding School Experiences

- Abuse (physical, sexual)
- Neglect
- Abandonment
- Forced Removal
- Loss of culture & language
- Forced Christianity
- Lost traditional parenting & family structure

© Warne & Lajimodiere 2012
Intergenerational Nutritional Effects

“Nutritional Epigenetics”
&
Developmental Origins of Health and Disease
Illinois Study

- N=15,287 Black and 117,708 white matched pairs of infants and mothers.
- Mothers were born between 1956-75, infants between 1989-1991

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean infant birthweight</td>
<td>3139 g</td>
<td>3434</td>
</tr>
<tr>
<td>Mean parental birthweight</td>
<td>3133</td>
<td>3377</td>
</tr>
<tr>
<td>% low birthweight infants</td>
<td>12%</td>
<td>5%</td>
</tr>
<tr>
<td>% lbw born to women with lbw</td>
<td>18%</td>
<td>9%</td>
</tr>
<tr>
<td>% lbw born to women not lbw</td>
<td>11%</td>
<td>5%</td>
</tr>
</tbody>
</table>
Results

- Father’s birthweight had effect on infant birthweight but not as strong as mothers.

- Each 100 g increase in maternal birthweight was associated with 24-27 g increase in infant birthweight.
Dutch Famine Studies
Susser and Stein, Nutrition Reviews, 1994

- Dutch famine winter lasted 6 months, from November 1944-when nazis imposed transport embargo on west Holland until-
- May 7, 1945 when Holland was liberated from the occupation
- Strong evidence for critical stages of development in several physiological systems
Affects of Famine

- Fertility decreased
- Maternal weight fell during pregnancy with famine exposure
- Third trimester famine exposure had strong effect on birthweight
- Third trimester famine exposure was associated with infant mortality
Obesity in Young Men after Famine Exposure in Utero and early Infancy
(Ravelli et al NEJM, 1976)

- N=300,000 Dutch military inductees at age 19

- Famine exposure in first 2 trimesters lead to 80% higher prevalence of overweight (p<0.0005)

- Famine exposure in last trimester or famine exposure in first 5 months of life associated with 40% lower prevalence of overweight (p<0.005)
<table>
<thead>
<tr>
<th>Mother's exposure to famine prior to conception was associated with lower self-reported measures of mental health and quality of life in her adult offspring.</th>
<th>Stein et al. Epidemiology. 2009 Nov;20(6):909-15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children born to women who were exposed to famine while they were in utero have increased neonatal adiposity and poor health 1.8 times more frequently in later life</td>
<td>Painter et al. BJOG, 2008 Sep;115(10):1243-1249.</td>
</tr>
</tbody>
</table>
Developmental programming of type 2 DM and CVD

**ENVIRONMENTAL FACTORS**
- Maternal protein restriction
- Maternal anaemia
- Placental insufficiency
- Maternal calorie restriction

**FETAL ADAPTATIONS TO INTRAUTERINE ENVIRONMENT**
- Altered hormone production and tissue sensitivity to hormones
- Redistribution of blood flow
- Changes in organ and tissue growth and development

**LOW BIRTH WEIGHT**

**PERMANENT CHANGES IN ORGAN AND TISSUE STRUCTURE AND FUNCTION**
- Liver: glucoseogenesis, glucose uptake
- Pancreas: β-cell mass, insulin secretion
- Skeletal muscle: muscle mass, insulin sensitivity, lipid oxidation
- Adipose tissue: insulin stimulated glucose uptake
- CV System: no. of cardiomyocytes, vasculogenesis, angiogenesis

**AGING**

**CHRONIC DISEASE**
- TYPE 2 DIABETES
- CERTAIN TYPES OF CANCER
- CV DISEASE

**POSTNATAL EXCESS/ADEQUATE NUTRITION**

©2010 by American Society for Nutrition

Inter-Generational Basis for Chronic Disease Disparities Among American Indians and Alaska Natives

Historical Trauma

Gestational Stressors

Childhood Stressors

Birth

Chronic Disease Disparities

Genocide

WIC

FDPIR

Boarding School Experiences

• Abuse (physical, sexual)
• Neglect
• Abandonment
• Forced Removal
• Loss of culture & language
• Forced Christianity
• Lost traditional parenting & family structure

Adverse Childhood Experiences

• Abuse (physical, sexual)
• Neglect
• Substance Abuse in home
• Mental Health Dx in home
• Witnessing violence
• Divorce
• Food insecurity
• Family member in prison

© Warne & Lajimodiere 2012
ACE Study Pyramid

- Adverse Childhood Experiences
- Social, Emotional, & Cognitive Impairment
- Adoption of Health-risk Behaviors
- Disease, Disability, and Social Problems
- Early Death
- Death

Scientific Gaps
ACES can have lasting effects on....

Health (obesity, diabetes, depression, suicide attempts, STDs, heart disease, cancer, stroke, COPD, broken bones)

Behaviors (smoking, alcoholism, drug use)

Life Potential (graduation rates, academic achievement, lost time from work)

ACES have been found to have a graded dose-response relationship with 40+ outcomes to date.

Risk for Negative Health and Well-being Outcomes

*This pattern holds for the 40+ outcomes, but the exact risk values vary depending on the outcome.*
Inter-Generational Basis for Chronic Disease Disparities Among American Indians and Alaska Natives

Historical Trauma

Gestational Stressors

Childhood Stressors

Adulthood Stressors

Birth

Chronic Disease Disparities

Boarding School Experiences
- Abuse (physical, sexual)
- Neglect
- Abandonment
- Forced Removal
- Loss of culture & language
- Forced Christianity
- Lost traditional parenting & family structure

Adverse Childhood Experiences
- Abuse (physical, sexual)
- Neglect
- Substance Abuse in home
- Mental Health Dx in home
- Witnessing violence
- Divorce
- Food insecurity
- Family member in prison

Adverse Adulthood Experiences
- Alcoholism & SA
- Suicide rates / death rates
- Poverty / Poor nutrition
- Racism / Toxic Stress
- Role models
  - Few positive
  - Many negative
  - Parenting

© Warne & Lajimodiere 2012
Inter-Generational Basis for Chronic Disease Disparities Among American Indians and Alaska Natives

Historical Trauma

Gestational Stressors

Childhood Stressors

Birth

Adulthood Stressors

Chronic Disease Disparities

Boarding School Experiences
- Abuse (physical, sexual)
- Neglect
- Abandonment
- Forced Removal
- Loss of culture & language
- Forced Christianity
- Lost traditional parenting & family structure

Adverse Childhood Experiences
- Abuse (physical, sexual)
- Neglect
- Substance Abuse in home
- Mental Health Dx in home
- Witnessing violence
- Divorce
- Food insecurity
- Family member in prison

Adverse Adulthood Experiences
- Alcoholism & SA
- Suicide rates / death rates
- Poverty / Poor nutrition
- Racism / Toxic Stress
- Role models
  - Few positive
  - Many negative
  - Parenting

© Warne & Lajimodiere 2012
South Dakota Health Survey

The survey included questions on:

• Basic information, including age, sex, race;
• Self-reported health status, including chronic diseases, depression, and other health issues;
• Mental Health Screening;
• Access to services, including cost, distance, and other access issues; and
• Adverse Childhood Experiences.
<table>
<thead>
<tr>
<th></th>
<th>AI</th>
<th>Non-AI</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td>.0001</td>
</tr>
<tr>
<td>Not employed</td>
<td>31.60%</td>
<td>7.58%</td>
<td>9.64%</td>
<td></td>
</tr>
<tr>
<td>Employed part time</td>
<td>11.91%</td>
<td>19.63%</td>
<td>18.97%</td>
<td></td>
</tr>
<tr>
<td>Employed full time</td>
<td>49.59%</td>
<td>54.47%</td>
<td>54.05%</td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>6.89%</td>
<td>18.31%</td>
<td>17.34%</td>
<td></td>
</tr>
<tr>
<td>Income (%FPL)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>&lt;50% FPL</td>
<td>38.90%</td>
<td>12.73%</td>
<td>15.17%</td>
<td></td>
</tr>
<tr>
<td>50–138% FPL</td>
<td>22.48%</td>
<td>10.18%</td>
<td>11.33%</td>
<td></td>
</tr>
<tr>
<td>138–250% FPL</td>
<td>17.29%</td>
<td>22.46%</td>
<td>21.98%</td>
<td></td>
</tr>
<tr>
<td>250–400% FPL</td>
<td>11.13%</td>
<td>28.75%</td>
<td>27.11%</td>
<td></td>
</tr>
<tr>
<td>&gt;400% FPL</td>
<td>10.20%</td>
<td>25.88%</td>
<td>24.42%</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Less than high school</td>
<td>9.95%</td>
<td>3.23%</td>
<td>3.85%</td>
<td></td>
</tr>
<tr>
<td>High school diploma or GED</td>
<td>39.29%</td>
<td>32.40%</td>
<td>33.05%</td>
<td></td>
</tr>
<tr>
<td>Vocational or 2-yr. degree</td>
<td>24.86%</td>
<td>23.87%</td>
<td>23.96%</td>
<td></td>
</tr>
<tr>
<td>4-year college degree</td>
<td>22.47%</td>
<td>25.69%</td>
<td>25.39%</td>
<td></td>
</tr>
<tr>
<td>Advanced or graduate degree</td>
<td>3.44%</td>
<td>14.81%</td>
<td>13.75%</td>
<td></td>
</tr>
<tr>
<td>Adverse Childhood Experiences Domains</td>
<td>American Indian (n = 516)</td>
<td>Non-American Indian (n = 7078)</td>
<td>Significance</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>--------------</td>
<td></td>
</tr>
<tr>
<td><strong>Abuse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional Abuse</td>
<td>30.10%</td>
<td>17.41%</td>
<td>.0008*</td>
<td></td>
</tr>
<tr>
<td>Physical Abuse</td>
<td>24.51%</td>
<td>12.31%</td>
<td>.0002*</td>
<td></td>
</tr>
<tr>
<td>Sexual Abuse</td>
<td>15.53%</td>
<td>9.60%</td>
<td>.0263*</td>
<td></td>
</tr>
<tr>
<td><strong>Neglect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional Neglect</td>
<td>25.87%</td>
<td>14.00%</td>
<td>.0005*</td>
<td></td>
</tr>
<tr>
<td>Physical Neglect</td>
<td>15.89%</td>
<td>2.78%</td>
<td>&lt;.0001*</td>
<td></td>
</tr>
<tr>
<td><strong>Household Dysfunction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother Treated Violently</td>
<td>23.76%</td>
<td>5.31%</td>
<td>&lt;.0001*</td>
<td></td>
</tr>
<tr>
<td>Household Substance Abuse</td>
<td>50.04%</td>
<td>21.49%</td>
<td>&lt;.0001*</td>
<td></td>
</tr>
<tr>
<td>Household Mental Illness</td>
<td>24.36%</td>
<td>13.89%</td>
<td>.0032*</td>
<td></td>
</tr>
<tr>
<td>Parental Separation or Divorce</td>
<td>39.34%</td>
<td>20.17%</td>
<td>&lt;.0001*</td>
<td></td>
</tr>
<tr>
<td>Incarcerated Household Member</td>
<td>22.57%</td>
<td>3.73%</td>
<td>&lt;.0001*</td>
<td></td>
</tr>
</tbody>
</table>
## AI ACE Disparities in South Dakota

<table>
<thead>
<tr>
<th>Number of ACEs (Score)</th>
<th>AI</th>
<th>Non-AI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>16.84%</td>
<td>50.02%</td>
<td>&lt;.0001*</td>
</tr>
<tr>
<td>1</td>
<td>21.59%</td>
<td>23.02%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>16.20%</td>
<td>9.60%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>12.99%</td>
<td>6.09%</td>
<td></td>
</tr>
<tr>
<td>4–5</td>
<td>13.10%</td>
<td>7.38%</td>
<td></td>
</tr>
<tr>
<td>≥6</td>
<td>19.28%</td>
<td>3.89%</td>
<td></td>
</tr>
</tbody>
</table>

Note: *statistically significant
Prevalence: Mental Health Screens

Participants who screened positive for a condition using standardized mental health screening tools

Statewide
Urban
Rural
Isolated
Reservation

* Participants who screened positive for a condition using standardized mental health screening tools
Research and Programming Needs

- Improve understanding of Historical Trauma, Epigenetics, and Nutritional Epigenetics
- How do we prevent ACEs?
  - Home visiting, parenting skills, community engagement
  - *Is poor nutrition an ACE?*
- How do we mitigate the impact of HT and ACEs?
- Develop a Diverse Workforce
- UND INMEDI & MPH Program
- PhD in Indigenous Health
Blackfeet Saying

A child is sacred. And when that child comes into the home, the family must welcome it. And if the child is happy and feels the want, he will come into this world very, very strong. And not to know this is to know nothing.
Donald Warne

donald.warne@med.und.edu