Toxic Stress:

What Is It?
Why Should I Care?
What Can I Do About It?

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and Child Development (EBCD)
My 3 Objectives For Today

- Provide a very general overview of advances in developmental science
- Present an organizing, integrated, ecobiodevelopmental framework
- Discuss a public health approach towards the prevention of toxic stress and its lifelong consequences
Childhood Adversity has Lifelong Consequences.

Significant adversity in childhood is strongly associated with unhealthy lifestyles and poor health decades later.
## ACE Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Women (n=9,367)</th>
<th>Men (n=7,970)</th>
<th>Total (n=17,337)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abuse</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Emotional</td>
<td>13.1%</td>
<td>7.6%</td>
<td>10.6%</td>
</tr>
<tr>
<td>- Physical</td>
<td>27.0%</td>
<td><strong>29.9%</strong></td>
<td>28.3% <strong>1:4!</strong></td>
</tr>
<tr>
<td>- Sexual</td>
<td>24.7%</td>
<td>16.0%</td>
<td>20.7%</td>
</tr>
<tr>
<td><strong>Household Dysfunction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mother Treated Violently</td>
<td>13.7%</td>
<td>11.5%</td>
<td>12.7%</td>
</tr>
<tr>
<td>- Household Substance Abuse</td>
<td>29.5%</td>
<td>23.8%</td>
<td>26.9% <strong>1:4!</strong></td>
</tr>
<tr>
<td>- Household Mental Illness</td>
<td>23.3%</td>
<td>14.8%</td>
<td>19.4%</td>
</tr>
<tr>
<td>- Parental Separation or Divorce</td>
<td>24.5%</td>
<td>21.8%</td>
<td>23.3%</td>
</tr>
<tr>
<td>- Incarcerated Household Member</td>
<td>5.2%</td>
<td>4.1%</td>
<td>4.7%</td>
</tr>
<tr>
<td><strong>Neglect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Emotional</td>
<td><strong>16.7%</strong></td>
<td><strong>12.4%</strong></td>
<td><strong>14.8%</strong></td>
</tr>
<tr>
<td>- Physical</td>
<td>9.2%</td>
<td><strong>10.7%</strong></td>
<td><strong>9.9%</strong></td>
</tr>
</tbody>
</table>

* Wave 2 data only (n=8,667)  
Data from [www.cdc.gov/nccdphp/ace/demographics](http://www.cdc.gov/nccdphp/ace/demographics)
ACEs Impact Multiple Outcomes

Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Risk Factors for Common Diseases  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Prevalent Diseases  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

General Health and Social Functioning  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

ACEs  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Sexual Health  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Mental Health  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Multiple Somatic Symptoms  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Cancer  Liver Disease  Chronic Lung Disease  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Sexually Transmitted Diseases  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Ischemic Heart Disease  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Teen Paternity  Fetal Death  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Teen Pregnancy  Unintended Pregnancy  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Sexual Dissatisfaction  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Early Age of First Intercourse  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Depression  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Sleep Disturbances  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Memory Disturbances  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Panic Reactions  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Poor Anger Control  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Poor Self-Rated Health  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Hallucinations  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Difficulty in job performance  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

High perceived stress  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Married to an Alcoholic  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Difficulty in job performance  Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV

Smoking  Alcoholism  Promiscuity  High Perceived Risk of HIV
Developing a Model of Human Health and Disease

Early childhood ecology strongly associates with lifelong developmental outcomes

How do you begin to define or measure the ecology?

What are the mechanisms underlying these well-established associations?
Defining **Adversity** or **Stress**

- How do you define/measure adversity?

- Huge **individual variability**
  - **Perception** of adversity or stress (subjective)
  - **Reaction** to adversity or stress (objective)

- National Scientific Council on the Developing Child (Dr. Jack Shonkoff and colleagues)
  - **Positive** Stress
  - **Tolerable** Stress
  - **Toxic** Stress

Based on the **REACTION** (objective physiologic responses)
Defining Adversity or Stress

- **Positive Stress**
  - Brief, infrequent, mild to moderate intensity
  - Most normative childhood stress
    - Inability of the 15 month old to express their desires
    - The 2 year old who stumbles while running
    - Beginning school or daycare
    - The big project in middle school
  - **Social-emotional buffers** allow a return to *baseline*
    (responding to non-verbal clues, consolation, reassurance, assistance in planning)
  - **Builds motivation and resiliency**
  - Positive Stress is **NOT** the **ABSENCE** of stress
Defining Adversity or Stress

- **Toxic Stress**
  - Long lasting, frequent, or strong intensity
  - More extreme precipitants of childhood stress (ACEs)
    - Physical, sexual, emotional abuse
    - Physical, emotional neglect
    - Household dysfunction
  - **Insufficient social-emotional buffering**
    (Deficient levels of emotion coaching, re-processing, reassurance and support)
  - Potentially permanent changes and long-term effects
    - Epigenetics (there are life long / intergenerational changes in how the genetic program is turned **ON** or **OFF**)
    - Brain architecture (the mediators of stress impact upon the mechanisms of brain development / **connectivity**)
Critical Concept #2

Epigenetics:

- Which genes are turned on/off, when, and where
- Ecology (environment/experience) influences how the genetic blueprint is read and utilized
- Ecological effects at the molecular level
- Stress-induced changes in gene expression

“Genes may load the gun, but the environment pulls the trigger”

“Epigenetics: Not your parents’ genome!”
Through epigenetic mechanisms, the early childhood ecology becomes biologically embedded, influencing how the genome functions.
Critical Concept #3

Developmental Neuroscience:

• **Brain Architecture** is experience dependent (individual connections or "synapses" and complex circuits of connections or "pathways" are both dependent upon activity)

• **Ecology** (environment/experience) influences how brain architecture is formed and remodeled (plasticity)

• **Diminishing cellular plasticity** limits remediation

• Early childhood adversity -> **vicious cycle of stress**

• **Potentially permanent** alterations in brain architecture and functioning
Two Types of Plasticity

- **Synaptic Plasticity** –
  - Variation in the **STRENGTH** of individual connections
  - “from a whisper to a shout”
  - Lifelong (how old dogs learn new tricks)

- **Cellular Plasticity** –
  - Variations in the **NUMBER (or COUNT)** of connections
  - “from one person shouting to a stadium shouting”
  - Declines dramatically with age (**waning by age 5**)
Differential Brain Maturation

- The Brake – PFC (with some hippocampal help)
  Frontal lobes:
  Abstract thought, reasoning, judgment, planning, impulse and affect regulation, consequences

Parietal Lobe:
Integration of sensory data and movement

Occipital Lobe:
Visual processing

Cerebellum:
Smooth movements Coordination

Brain Stem & Cranial Nerves:
Vital functions Swallowing

Temporal lobe (outside):
Processing sound and language

Limbic System (inside):
Emotions and impulsivity

+ The Gas Pedal +
Amygdala

+ The Brake – PFC (with some hippocampal help)
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+ The Gas Pedal +
Amygdala
Out of Balance?

Prefrontal Cortex
- Cold Cognition
- Judgmental
- Reflective
- Calculating
- Think about it

Biological maturity by 24

Amygdala
- Hot Cognition
- Emotional
- Reactive
- Impulsive
- Just do it

Biological maturity by 18

Adapted from Ken Winters, Ph.D.
Impact of Early Stress

CHILDHOOD STRESS

Hyper-responsive stress response; calm/coping

Chronic “fight or flight;” cortisol/norepinephrine

Changes in Brain Architecture
Declining plasticity in the developing brain results in potentially permanent alterations in brain functioning and development.
Eco-Bio-Developmental Model of Human Health and Disease

Ecology Becomes Biology, and together they drive development across the lifespan.
The critical challenge now is to translate game-changing advances in developmental science into effective policies and practices for families with children to improve education, health, and lifelong productivity.
Advantages of an *EBD* Framework

- Though grounded in developmental science, the simplicity of the EBD framework may promote understanding as well as support for translation (early investments are the right thing to do biologically).

- Psychosocial stressors and other salient features of the ecology are every bit as biological as nutrition or lead (no distinction between mental and physical health, just healthy vs. unhealthy development).

- Emphasizes the dimension of time – to reflect the on-going, cumulative nature of benefits and threats to health and wellness.
Development results from an ongoing, re-iterative, and cumulative dance between nurture and nature.
Advantages of an EBD Framework

• Underscores the need to improve the early childhood ecology in order to:
  – Mitigate the biological underpinnings for educational, health and economic disparities
  – Improve developmental/life-course trajectories
• Changing the early childhood ecology demands a PUBLIC HEALTH approach and COLLABORATION!!!

• Highlights the pivotal role of toxic stress
  – Not just “step on the gas” or enrichment
  – But “take off the brake” by treating, mitigating or immunizing against toxic stress
Reinventing the Wheel - All over again?

Models

Maslow’s Hierarchy of Needs
(Theoretical - 1943)

Needs

Self-Actualization
Need to know, explore and understand

Unmet needs are potential sources of STRESS!!
Linking **Childhood Experiences** and **Adult Outcomes**

- **Childhood Adversity** → **Black Box** → **Poor Adult Outcomes**

**Advocacy to minimize childhood adversity (e.g. - efforts to address poverty, food scarcity, domestic violence, parental substance abuse)**

**Health and social services to deal with adverse outcomes (e.g. - efforts to address the behavioral, social, health and economic consequences)**
Linking **Childhood Experiences** and **Adult Outcomes**

**Toxic Stress**
- Epigenetic Modifications
- Disruptions in Brain Architecture

**Behavioral Allostasis**
- Maladaptive behaviors
- Non-communicable Diseases

Improve caregiver/community capacity to prevent or minimize toxic stress (e.g. efforts to promote the safe, stable and nurturing relationships that turn off the physiologic stress response)

Improve caregiver/community capacity to promote healthy, adaptive coping skills (e.g. efforts to encourage rudimentary but foundational SE, language, and cognitive skills)
Critical Concept #5

For young children, parent/caregiver support is critical:

- Turns off physiologic stress response by addressing physiologic and safety needs (PROTECT = Maslow levels 1+2)
- Turns off the physiologic stress response by promoting healthy relationships and attachment (RELATE = Maslow level 3)
- Notes and encourages foundational coping skills as they emerge (NURTURE = Maslow levels 4+5)

Pediatricians are ideally placed to:

- Promote this sort of “Purposeful” Parenting
- Advocate / participate public health approach to address TS
Social-Emotional Safety Nets
A Public Health Approach to “Toxic Stress”

Universal Primary Preventions
Anticipatory guidance
Consistent messaging (CTC)
No identification
No stigma
Ceiling effects = Limited evidence base

Targeted Interventions
(for those “at risk”)
Nursing home visits (NFP)
Parenting programs (PPP)
Early Intervention
Less ceiling=More evidence
Requires screening
Issues with stigma

Evidence-Based Treatments
(for the symptomatic)
PCIT; TB-CBT; Pharmacotx
Treatment works!
Screening / stigma / access
WHAT are we DOING?!

Universal Primary Preventions
Bright Futures
Connected Kids / HS - NCH
Circle of Security / VIP
Relationships as a “vital” sign
Decrease Stress/Build Skills

Targeted Interventions
Screening for risks
(assess the ecology - SEEK)
Refer to/advocate for EBI
Collaborating/Developing EBI
ID Risks/Provide EBI

Evidence-Based Treatments
Screening for diagnoses
Common factors approach
Refer for/advocate for EBT
Collaborating/Developing EBT
ID Symptoms/Provide EBT
Public Health Implications

• ACE data provide a working model for understanding and addressing the childhood antecedents of adult disease.

• Is there a gap between what we do and what we know?

• What we DO:
  – 95% of the trillions of dollars that we spend on health is on treatment and NOT prevention
Public Health Implications

• What we **KNOW**:
  
  – That **70% of early deaths are preventable**, with...

  – The **majority (40% overall)** due to **behavioral patterns** that lead to **chronic disease**.

  – **Behavioral Allostasis** due to toxic stress?

McGinnis, Williams-Russo and Knickman, 2002
Proximal Causes of Death: Chronic Disease

EXHIBIT 2
Total Deaths And Age-Adjusted Death Rates (Per 100,000 Population) For The Fifteen Leading Causes Of Death In The Total U.S. Population, 2003

<table>
<thead>
<tr>
<th>Cause</th>
<th>Rate (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases of heart</td>
<td>(232.3)</td>
</tr>
<tr>
<td>Malignant neoplasms (cancer)</td>
<td>(190.1)</td>
</tr>
<tr>
<td>Cerebrovascular diseases (stroke)</td>
<td>(53.5)</td>
</tr>
<tr>
<td>Chronic lower respiratory diseases</td>
<td>(43.3)</td>
</tr>
<tr>
<td>Accidents (unintentional injuries)</td>
<td>(37.3)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>(25.3)</td>
</tr>
<tr>
<td>Influenza and pneumonia</td>
<td>(22.0)</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>(21.4)</td>
</tr>
<tr>
<td>Nephritis, nephrotic syndrome, nephrosis</td>
<td>(14.4)</td>
</tr>
<tr>
<td>Septicemia</td>
<td>(11.6)</td>
</tr>
<tr>
<td>Intentional self harm (suicide)</td>
<td>(10.8)</td>
</tr>
<tr>
<td>Chronic liver disease and cirrhosis</td>
<td>(9.3)</td>
</tr>
<tr>
<td>Essential hypertension/hypertensive renal disease</td>
<td>(7.4)</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>(6.2)</td>
</tr>
<tr>
<td>Assault (homicide)</td>
<td>(6.0)</td>
</tr>
</tbody>
</table>

Acute causes of death are the exception, not the rule

NOTE: Numbers in parentheses are age-adjusted death rates per 100,000 population.
Distal Causes of Death: Unhealthy Lifestyles

Table 2. Actual Causes of Death in the United States in 1990 and 2000

<table>
<thead>
<tr>
<th>Actual Cause</th>
<th>No. (%) in 1990*</th>
<th>No. (%) in 2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>400 000 (19)</td>
<td>435 000 (18.1)</td>
</tr>
<tr>
<td>Poor diet and physical inactivity</td>
<td>300 000 (14)</td>
<td>400 000 (16.6)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>100 000 (5)</td>
<td>85 000 (3.5)</td>
</tr>
<tr>
<td>Microbial agents</td>
<td>90 000 (4)</td>
<td>75 000 (3.1)</td>
</tr>
<tr>
<td>Toxic agents</td>
<td>60 000 (3)</td>
<td>55 000 (2.3)</td>
</tr>
<tr>
<td>Motor vehicle</td>
<td>25 000 (1)</td>
<td>43 000 (1.8)</td>
</tr>
<tr>
<td>Firearms</td>
<td>35 000 (2)</td>
<td>29 000 (1.2)</td>
</tr>
<tr>
<td>Sexual behavior</td>
<td>30 000 (1)</td>
<td>20 000 (0.8)</td>
</tr>
<tr>
<td>Illicit drug use</td>
<td>20 000 (&lt;1)</td>
<td>17 000 (0.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1 060 000 (50)</strong></td>
<td><strong>1 159 000 (48.2)</strong></td>
</tr>
</tbody>
</table>

*Data are from McGinnis and Foege.¹ The percentages are for all deaths.

If these unhealthy lifestyles are manifestations of behavioral allostasis, a **FUNDAMENTAL** cause of death is **TOXIC STRESS**!
By 2030, **90%** of the morbidity in high income countries will be due to **NCDs (Non-Communicable Diseases)**.

Most NCDs are due to **unhealthy behaviors** (overeating / inactivity, smoking, alcohol, and illicit drugs).

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**Fig. 1.** The proportional distribution of disability-adjusted life years, contributable to infectious diseases and NCDs for (top) the world, (middle) high-income countries, and (bottom) low-income countries for 2002 and 2030 (3).
How do those automatic processes form in the first place!?
A **Public Health** Dilemma:

Do we continue to treat **disease**, the **unhealthy lifestyles** that lead to disease, or the **TOXIC STRESS** that leads to the adoption of unhealthy lifestyles??
What is Toxic Stress?

- A physiologic stress response that is excessive or prolonged (reflects an inability to “turn it off”)

- Results in potentially permanent changes in:
  - Gene expression (epigenetics)
  - Brain development (neuroscience)
  - Behavior (allostasis)
• Why should I care?

- **Toxic stress** is a **MEDIATOR** between early childhood adversity and less than optimal outcomes in learning, behavior and health (see Clancy Blair – poverty and executive function)

- Understanding the **BIOLOGY** underlying these well established associations opens up new opportunities for **primary prevention** and **early intervention**
SUMMARY

• What can I do?
  
  – Understand the ecobiodevelopmental framework (advocate for a public health approach to address toxic stress)
  
  – Help children figure out how to turn off their stress response (in a healthy way!)
  
  – Intervene early for those children who are at high risk or appear unable to turn off their stress response
CONCLUSION:

It is easier to build strong children than to repair broken men.

Frederick Douglass