

LEARNING OBJECTIVES

- Identify key factors of toxic stress in children
- Detect biological impacts toxic stress has on a child's developing body
- Develop a plan for treating toxic stress in children



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PROFESSIONAL PRACTICE GAP

Addressing the need for awareness and appropriate treatment strategies related to toxic stress beyond being aware of adverse childhood experiences.



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EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - 1995-1997 study
- Two Waves
 - 1st wave: looked at abuse & household dysfunction
 - 2nd wave: neglect items added



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EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Abuse
 - Psychological
 - Physical
 - Sexual
 - Neglect
 - Emotional
 - Physical



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EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Household dysfunction
 - Divorce or separation
 - Intimate partner violence
 - Substance use
 - Mental illness
 - Criminal behavior



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EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Around 63% of adults have at least 1 ACE
 - 12% have 4 or more ACEs
- Behavioral Risk Factor Surveillance
 - Found similar data to ACE study
- Study of children show similar data



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EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Health outcomes
 - Dose response theory
 - Increase risk of leading causes of death
- Additional research shows similar risk across populations
 - Including pediatric patients
- Risk of death increases



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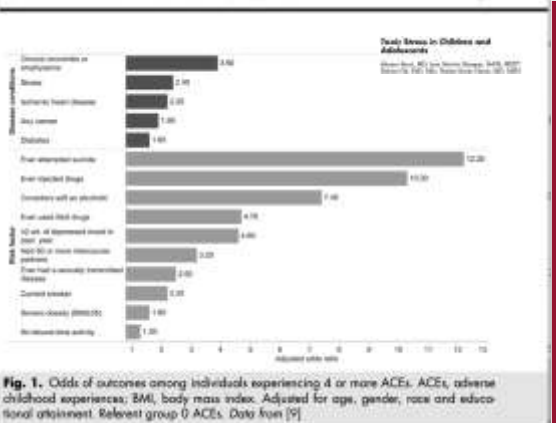


Fig. 1. Odds of outcomes among individuals experiencing 4 or more ACEs. ACEs, adverse childhood experiences; BMI, body mass index. Adjusted for age, gender, race and educational attainment. Relevant group: 0 ACEs. Data from [9].

EARLY LIFE ADVERSITY

- There are additional traumatic & stressful events
 - Community violence
 - Bullying
 - Experiencing houseless-ness
 - Parental stress
 - Economic hardship
 - Racism
 - Historical trauma
 - Discrimination



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TOXIC STRESS



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STRESS RESPONSE

POSITIVE

Physiological response to mild or moderate stressor

Brief activation of stress response elevates heart rate, blood pressure, and hormone levels

Hormonal stressors quickly through body's natural coping mechanisms

Height test at school, play of game

TOLERABLE

Adaptive response to low to high stressor

Prolonged activation of stress response results in short-term systemic changes

Hormonal stressors through buffering effect of coping skills or other interventions

Immigration, natural disaster

TOXIC

Maladaptive response to intense and sustained stressor

Prolonged activation of stress response is chronic through poor interventions and interventions of health disparities

Chronic stressors contribute to chronic stress response

Abuse, neglect, household dysfunction

Figure 1. Spectrum of the stress response: positive, tolerable, and toxic.



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MEET JOY



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TYPES OF STRESS

Positive



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TYPES OF STRESS

Tolerable



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TYPES OF STRESS

Toxic Stress



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STRESS RESPONSE: BIOLOGY

- The Stress Response
 - Central Nervous System
 - Amygdala
 - Hypothalamus
 - Hippocampus
 - Prefrontal cortex
 - Brainstem
 - Locus coeruleus
 - Medulla oblongata

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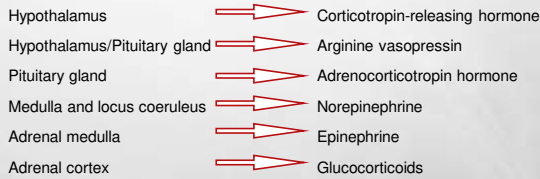
STRESS RESPONSE: BIOLOGY

- The Stress Response
 - Peripheral Nervous System
 - Sympatho-adrenomedullary (SAM)
 - Hypothalamic-pituitary-adrenal
 - Adrenal medulla
 - Adrenal cortex
 - Peripheral changes

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STRESS RESPONSE: BIOLOGY



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HPA axis

The HPA axis controls the body's response to stress and is a complex interplay of stress interactors. The HPA axis is composed of:

1. The **hypothalamus** which releases AVP and CRH to the pituitary gland
2. The **pituitary gland** which secretes ACTH when stimulated by AVP and CRH
3. The **adrenal cortex** which secretes glucocorticoids (cortisol) when stimulated by ACTH

SAM axis

The SAM axis mediates a rapid response to stress through interconnected neurons and regulates autonomic functions in multiple organ systems. The SAM axis is composed of:

1. The **sympathetic neurons** which release epinephrine and norepinephrine and activate the body's "fight or flight" response
2. The **parasympathetic neurons** which withdraw the activity of the sympathetic response and promote the body's "rest and digest" response
3. The **adrenal medulla** which when triggered by the sympathetic neurons secretes circulating epinephrine and activate the body's "fight or flight" response

Fig. 3. Stress response pathway. HPA axis, hypothalamic-pituitary-adrenal axis; SAM axis, sympathoadrenomedullary axis; AVP, arginine vasopressin; CRH, corticotropin-releasing hormone; ACTH, adrenocorticotropin hormone.



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STRESS RESPONSE: EFFECTS

- Classic Flight-or-Fight-or-Freeze
 - Blood circulation
 - Respiration
 - Metabolism



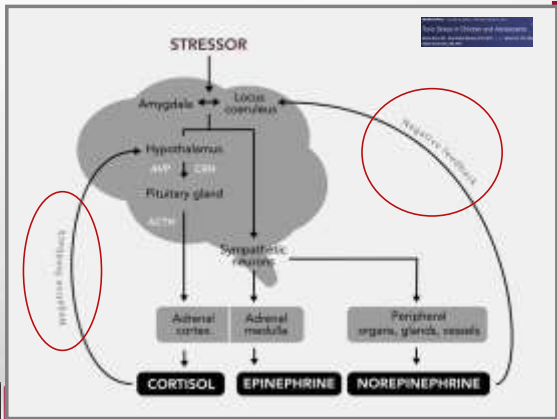
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STRESS RESPONSE: EFFECTS

- Behavioral Changes
 - Increased arousal
 - Improved cognition
 - Euphoria
 - Decreased pain perception
 - Rise in body temperature



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TOXIC STRESS: DYSREGULATION

- Loss of homeostasis of the system
 - Prolonged exposure disrupts these mechanism
 - Decrease ability to regulate SAM and HPA
 - Prolong activation leads to:
 - Alteration in stress hormones
 - Initially excessive
 - Eventually deficient



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TOXIC STRESS: DYSREGULATION

- Biological alterations
 - Nervous
 - Endocrine
 - Immune



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TOXIC STRESS: CLINICAL OUTCOMES

- Systemic alterations
 - Neurological
 - Psychiatric
 - Behavioral
 - Endocrine
 - Metabolic



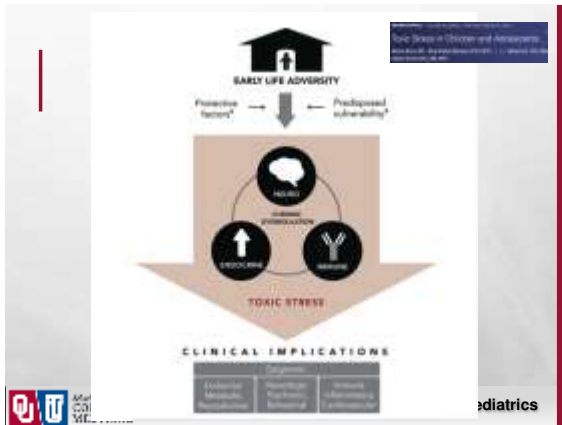
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TOXIC STRESS: CLINICAL OUTCOMES

- Systemic alterations
 - Cardiac
 - Reproductive
 - Immune
 - Inflammatory
 - Genetic



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“Approaches to minimizing toxic stress that only look at measures of adversity, such as ACE scores or biomarkers, will miss out on opportunities to support the relational health that promotes flourishing despite adversity.”

- AAP Preventing Childhood Toxic Stress: Partnering with Families and Communities to Promote Relational Health



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TOXIC STRESS VS RELATIONAL HEALTH

Toxic Stress: defines the problem.

“Toxic stress explains how many of our society’s most intractable problems (disparities in health, education, and economic stability) are rooted in our shared biology but divergent experiences and opportunities.”

Relational Health: defines the solution.

“Relational health explains how the individual, family, and community capacities that support the development and maintenance of SSNRs also buffer adversity and build resilience across the life course.”



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TOXIC STRESS VS RELATIONAL HEALTH

- Relational Health
 - Definition
 - Contribution
 - Clinical care
 - Prevention
 - Primary
 - Secondary
 - Tertiary



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Public Health Level	Types of Prevention	Approaches to their Stress	Examples	Approaches to Relational Health
3	Tertiary	Indicated treatments for toxic stress related diagnoses (e.g., anxiety, depression, PTSD)	ABC RDT CPT TF-CBT	Repair strained or compromised relationships
2	Secondary	Targeted interventions for those at higher risk for toxic stress responses	Parent/Child ACEs SDOH RHC	Identify and address potential barriers to SSNRs
1	Primary	Universal prevention for all	Positive parenting RCH Play Consistent messaging	Promote SSNRs by building 2-generational skills



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APPLICATIONS TO PRACTICE

- Applications to Practice
 - Promote Safe Stable Nurturing Relationships (SSNRs)
 - Core focus of Family Center Pediatric Medical Homes
 - Reduce Sources of Stress within Families
 - Core Life Skills



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FUTURE APPLICATIONS

- Population-Level Changes
 - Training program
 - System-wide changes in appointments
 - Coordination across systems
- Focus on Social Determinants of Health
 - Racism
 - Historical trauma
 - Poverty
 - Demographic risk factors



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REFERENCES

- Shonkoff, JP, Boyce WT, Levitt P, et al. Leveraging the Biology of Adversity and Resilience to Transform Pediatric Practice. *Pediatrics*. 2021;147(2):e20193845
- Shonkoff, JP, Garner, AS, & THE COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, COMMITTEE ON EARLY CHILDHOOD, ADOPTION, AND DEPENDENT CARE, AND SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS. *Pediatrics* 2012;129:e232–e246. www.pediatrics.org/cgi/doi/10.1542/peds.2011-2663 doi:10.1542/peds.2011-2663 PEDIATRICS
- Oral, R, et al. Adverse childhood experiences and trauma informed care: the future of health care. *Pediatric Research* Vol 79 No1 January 2016
- Garner A, Yagnian M. COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS, COUNCIL ON EARLY CHILDHOOD. Preventing Childhood Toxic Stress: Partnering With Families and Communities to Promote Relational Health. *Pediatrics*. 2021;148(2):e2021052582
- Franke, HA "Toxic Stress: Effects, Prevention, and Treatment" *Children* 2014, 1, 390-402
- Bucci, M. et al. "Toxic Stress in Children and Adolescents" *Advances in Pediatrics* 63 (2016) 403-428
- Boyce WT, Levitt P, Martinez FD, et al. Genes, Environments, and Time: The Biology of Adversity and Resilience. *Pediatrics*. 2021;147(2): e20201651



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OPPORTUNITIES TO IMPROVE: AAP POLICY STATEMENT

- "Expand Toolbox of Effective Strategies for Strengthening the Foundations of Healthy Development in the Face of Adversity"
 - AAP projects show how we can enact change
 - Immunizations
 - Back to Sleep
 - Car Seats
 - The "Next Great Projects"
 - Relationship between childhood experiences and adult disease
 - Biology, Physical, and Social Environments
 - Reducing Global Poverty

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OPPORTUNITIES TO IMPROVE: AAP POLICY STATEMENT

- "Compelling Need to Revisit the Criteria Used to Designate an Intervention as Evidence Base and to Strengthen Measurement Capacity in the Early Childhood Period"
 - Challenging Federal Guidelines on outcome measurements
 - Improving measurement capacity

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OPPORTUNITIES TO IMPROVE: AAP POLICY STATEMENT

- "The Potential Benefits of 2 Complementary Pathways Toward Greater Impact on the Health and Development of Young Children and Families Facing Adversity."
 - Pathway 1
 - Pathway 2



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GENE ENVIRONMENT TIME FRAMEWORK



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TOXIC STRESS: GENES

- Gene-environment correlation (rGE) \Rightarrow Genetic variation & environmental exposures are correlated, but not casually interactive
- Specific environmental conditions (GxE) \Rightarrow Variations happen only in specific environmental exposures
- Epigenetic gene-regulatory processes (eGEs) \Rightarrow Environmental exposures regulate or calibrate level of gene expression



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