



# Intergenerational Transmission of Toxic Stress: Exploring the Role of the Infant Gut Microbiome

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## INTRODUCTION

- Toxic stress = persistent elevation of the hypothalamic-pituitary-adrenal axis in response to chronic childhood stressors (e.g. maltreatment)<sup>1</sup>
- Toxic stress increases risk for chronic disease, but underlying biobehavioral mechanisms are not well understood
- The gut microbiome regulates communication between gastrointestinal & central nervous systems (e.g. “gut-brain axis”)<sup>2</sup>
- Animal studies indicate gut microbiota are sensitive to early life stress, but this is not well studied in humans<sup>3</sup>
- Improved understanding of the relationship between stress & infant gut microbiome may uncover novel intervention targets for toxic stress prevention

## OBJECTIVES

**Purpose:** To explore the relationship between maternal stress, infant stress, and the infant gut microbiome among mother-infant dyads.

### Specific Aims:

1. Characterize the composition and structure of the gut microbiome of infants (age 2-6 months)
2. Examine associations between infant gut microbiome composition and indicators of infant stress
3. Examine associations between infant gut microbiome composition and indicators of maternal stress

## METHODS

This study is an innovative collaboration between the Yale School of Nursing & the Yale Microbial Sciences Institute & is funded by a Yale “All Points West” Pilot Grant

**Sample:** 40 maternal-infant dyads (infant age 2-6 months)

**Exclusions:** Infants eating solid foods, with a history of preterm birth (<37 weeks), or with gastrointestinal disorder

**Procedures:** Data collected remotely due to COVID-19 pandemic. Mothers completed online questionnaires and self-collected saliva and stool samples.

### Variables & Measures:

#### Indicators of Maternal Stress:

- Adverse Childhood Experiences (ACE questionnaire)
- Mental health (e.g. PTSD checklist, depression scale)
- Sleep disturbance (Pittsburgh Sleep Quality Index)
- Parenting stress (Parenting Stress Index)
- Inflammation (salivary cytokines)
- COVID-19 pandemic (Covid Responses to Stress Scale)

#### Indicators of Infant Stress:

- Sleep (Brief Infant Sleep Questionnaire)
- Inflammation (salivary cytokines)

Infant Gut Microbiome: Community composition of stool based on 16S (V4) rRNA gene sequence analysis

#### Maternal & Infant Characteristics:

- Infant birth and health history
- Mother & infant diet history
- Demographic characteristics

**Planned analyses:** Multivariate regression, adjusting for maternal and infant characteristics (e.g. diet, medications)

## RESULTS

Data collection ongoing; 38 dyads currently enrolled

### Preliminary Descriptive Findings:

- Mean maternal age: 32.2 years
- Mothers’ self-reported race/ethnicity:
  - 69% Non-Hispanic White
  - 18% Hispanic/Latina
  - 5.2% Asian
  - 5.2% Native American/Pacific Islander
  - 2.6% Non-Hispanic Black/African American
- 32% receiving state/federal aid (e.g. WIC, SNAP)
- 92% married or living with partner
- Infant sex: 55% female, 45% male
- 58% infants breastfed, 21% formula fed, 21% both

### Next Steps & Study Timeline:

- Data collection completion: expected April 2021
- Lab & statistical analyses: Spring/Summer 2021
- Dissemination of findings: Fall 2021

## REFERENCES

1. Shonkoff JP, Garner AS, Siegel BS, et al. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*. 2012;129(1)
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3. Hantsoo, L. et al. Childhood adversity impact on gut microbiota and inflammatory response to stress during pregnancy. *Brain, Behavior, and Immunity* 75, 240-250 (2019).