Facilitator Guide: The Biomedical Influences of Poverty

Learning Goals and Objectives

1. **Recognize the physiologic consequences of poverty on child health, behavior and development.**
    a. Describe the pathophysiologic consequences of toxic stress (*Knowledge*)
    b. Explain how epigenetic forces contribute to health disparities and perpetuate intergenerational poverty (*Knowledge*)
    c. Discuss the physiologic consequences of exposure to environmental contaminants that are prevalent in impoverished communities (*Knowledge*)
2. **Describe the relationship between child poverty and lifelong health disparities using the Life Course Model.**
    a. Explain the role of critical periods, sensitive windows and allostatic load in creating health disparities (*Knowledge*)
    b. Analyze existing evidence of the link between adverse health events and adult health inequities (*Skill*)
    c. Investigate potential clinical interventions that might mitigate the effects of toxic stress during childhood (*Skill*)
    d. Reflect on how understanding the effects of biologic influences on intergenerational poverty affect one's personal assumptions, biases and approaches to caring for individual families (*Attitude*)

This module is designed to cover the core principles of the biomedical influences of childhood poverty. The materials for this module are divided into three sections: Pre-Work, Interactive in-classroom session and optional Dig Deeper activities and resources. The Pre-Work and Interactive session materials make up the core of the module, while the Dig Deeper activities are designed for further exploration for individuals with interest or for programs who have more time to allot to this material.

1. **Pre-Work:** This consists of a breakdown of each section of the presentation with the related materials (video clips, articles), designed to be completed by learners to prepare them for the in-class presentation and discussion. Facilitators should review the Pre-work document so as to be able to discuss the material with their learners at the onset of the presentation.

2. **Presentation:** The facilitator guide serves as a guide with background information for the presenter for the slides and the discussion. It aims to tie together the ideas and materials in the clips and articles.

3. **Dig Deeper**: This section includes possible activities and further resources for facilitators, learners or programs that would like to go further in depth into these topics.

In-Person Presentation/Discussion/Activities

		Time (min)	Format (e.g. small group, large group, etc.)
Section 1	Review Pre-work	5	Large Group
Section 2	How Poverty 'Gets Under Our Skin' – Toxic Stress, Epigenetics and Environmental Toxins	20	Group and pairs
Section 3	Timing is Everything – Critical Windows, Biologic Plasticity and the Importance of Acting Early	15	Large group
Section 4	Re-Framing the Problem: Intergenerational Poverty and Cognitive Bias	10	Large group
Section 5	Bias reflection	10	Large group

Section I – Introduction of Module and Review Pre-work

Facilitator's Role

Outline:

- Present slides 1-6
- Briefly (1 min) review Goals, Objectives and Roadmap
- Engage learners in 5 minute discussion of the prework: Had learners previously come across information regarding the pathophysiology of toxic stress?

Section 2 - How Poverty 'Gets Under Our Skin' – Toxic Stress, Epigenetics and Environmental Toxins

Objectives Covered:

- Describe the pathophysiologic consequences of toxic stress
- Explain how epigenetic forces contribute to health disparities and perpetuate intergenerational poverty
- Discuss the physiologic consequences of exposure to environmental contaminants that are prevalent in impoverished communities

Facilitator's Role

Outline:

- Present slides 7-19
- Connect the content of the pre-work to the cases.
- Help learners identify risk factors for the children in these cases.
- Help learners identify key components of the history that could relate to toxic stress.

Guidelines:

This section consists of two cases which can be found posted along with the prework, facilitators' guide and presentation, as well as below. Consider how you want to deliver the cases based on your setting. Paper copies of the cases for the learners could be used to allow learners to highlight or underline as they identify toxic stressors or epigenetic risk factors. Please review the videos below as the learners will have reviewed them prior to this classroom-based session in the prework. Guide the learners through the concept of toxic stress and help them connect to clinical experiences where this may have played a role.

Videos to review:

Center on the Developing Child – Harvard University

- Brain Development
  - http://developingchild.harvard.edu/resources/experiences-build-brain-architecture/ (2min)
  - http://developingchild.harvard.edu/resources/serve-return-interaction-shapes-brain-circuitry/ (1min 45sec)
- Toxic Stress
  - http://developingchild.harvard.edu/resources/toxic-stress-derails-healthy-development/ (2min)

Background for Cases – Toxic Stress

We provide here a very cursory overview of the complex science emerging around the biological pathways associated with living in poverty. We provide summaries and the associated references for stress physiology and its influence on brain development and the immune system, and then contextualize it through two cases.

Case #1: Cameron (Toxic Stress)

Slide #8: Read thru the case one time, we will revisit it.

This is your first time to meet Cameron, a 3 year old male, who comes to the clinic with his mother, 16 month old half-sister and maternal boyfriend for a well-child exam. Cameron has scattered clinic supplies (gloves, otoscope caps, etc) across the room prior to your arrival. His mom provides her cell phone to Cameron in order for him to sit still. Mom has concerns for Cameron's appetite and growth following IUGR and FTT that a previous doctor had diagnosed. Though his weight is less than 5%, Cameron's BMI is ~25%. Diet history notes significant snacks and sugar sweetened beverages. The family has SNAP and WIC benefits, and a food insecurity screen is negative.

Speech, both phonologic and expressive components, lag. When asked about language examples, maternal boyfriend describes Cameron's skill operating cell phones and video games. Overall, Cameron demonstrates 1-3 words phrases with ~50% clarity. He does not identify his age, his gender, or name any body parts, though mom explains that he is 'shy'. There is no family history of speech or hearing disorders. Cameron had been in private daycare briefly before the family moved.

Cameron warms during the encounter. However, as you raise your hands to his eye level to check his ears, you notice that he jerks away. The exam, beyond the presence of extensive dental caries, is normal. The visit concludes with a discussion of speech delay, the need for audiology and developmental evaluation, and a dental referral is made for treatment of extensive dental caries. Mom agrees to return in 2-3 months for speech follow up.

Cameron and his family return 16 days later. Mom and boyfriend had a physical altercation one week earlier, and are now reunited. Due to the mom and boyfriend being briefly incarcerated, Cameron and his sister were placed in temporary kinship care. The children did not witness IPV though awoke during the ensuing caregivers' arrest. Cameron and his sister were assessed by a child abuse pediatrician at Human Service intake and found to be without injury. Mom lost her job during incarceration. Maternal boyfriend, also, is unemployed. Cameron plays with his mom's cellphone, has intermittent eye contact and this time does not flinch during your exam.

(Transition by explaining we will return to discuss the case after we review the biomedical influences of poverty.)

Slide #9: Stress Physiology

Stress is the brain's response to stimuli. Stress is a normal and necessary for development, though, lack of appropriate stress response can harm health.
Current research proposes three distinct stress responses:

- **Positive:** brief stress response that allows skill acquisition (control/manage)
- **Tolerable:** serious event potential for negative impact brain architecture mitigated by adult that allows recovery (cope)
- **Toxic:** strong, frequent or prolonged stress response adversely effects brain architecture and lowers stress response threshold.

Stress physiology is best understood through the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic-adrenomedullary (SAM) system. Stress hormones - Corticoid-Releasing Hormone (CRH), cortisol, norepinephrine and adrenaline – interact with additional mediators, cytokines and the parasympathetic nervous system. Upon stressor recognition, the hypothalamic-pituitary-adrenal (HPA) axis activates. The hypothalamus releases Corticoid-Releasing Hormone (CRH) and arginine-vasopressin (AVP) to stimulate the pituitary gland. (CRH, also, serves as neurotransmitter reaching the amygdala, hippocampus and cerebral cortex with direct effect on synaptogenesis). In response to CRH, the anterior pituitary secretes adrenocorticotropin hormone (ACTH) which triggers glucocorticoids, including cortisol, and mineralocorticoids via adrenal cortex activation. Metabolic and cognitive adaptations follow. Catecholamines and glucocorticoids initiate lipolysis, glycogenolysis and protein catabolism to increase blood glucose. Neuronal pathways heighten attention. Feedback loops employ glucocorticoid and mineralocorticoid receptors for either propagation or discontinuation. If stress hormones remain elevated, muscular atrophy, insulin resistance, hypertension, amenorrhea, impotence and poor wound healing can result.

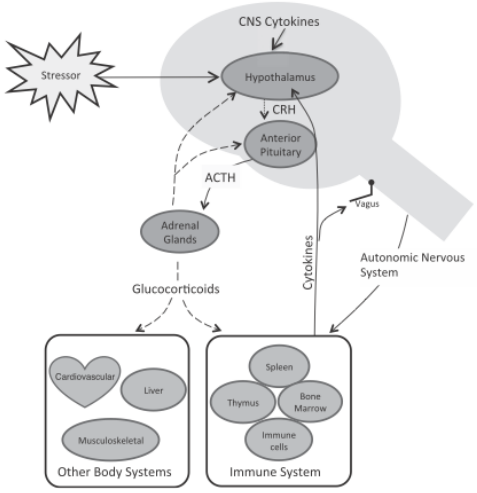


FIGURE 1
Relationship between the HPA axis, immune systems, and other body systems. Glucocorticoids are indicated by dashed lines, corticotropin-releasing hormone (CRH) by dotted lines, and cytokines by solid lines. ACTH, adrenocorticotropic hormone (ie, corticotropin); CNS, central nervous system.

Cortisol, a primary inflammatory and metabolic agent in the neuroendocrine-immune network, varies in response to prolonged stress. Cortisol release has a circadian rhythm, peaking shortly after waking (duration of time awake rather than time of day) and declining during the day. Altered pattern occurs chronic stress thereby changing both peak and nadir values. Acute and chronic socioeconomic stressors, also, modify cortisol. Past stress experience raised baseline cortisol and blunted peak level though current stress bolstered morning rise and zenith. Given the correlation SES and health outcomes, abnormal stress physiology is a proposed mechanism for poor health.

- Johnson SB, Riley AW, Granger DA, Riss, J The Science of Early Life Toxic Stress for Pediatric Practice and Advocacy. *Pediatrics* 2013;131:319–327
- Francis DD. Conceptualizing Child Health Disparities: A Role for Developmental Neurogenomics. *Pediatrics* 2009;124: S196–S202

Slide #10 – Toxic Stress

Toxic stress, the unremitting prolonged stress response that adversely effects brain architecture and lowers stress response threshold, has many factors associated with it. These include hunger, inadequate housing, witness to violence, neglect and abuse, carefiver mental health and/or substance abuse, or an otherwise unresponsive caregiver. Toxic stress can have direct physiologic impact by altering brain architecture, immune mediation and cellular viability.

Slide #11 – Toxic Stress Consequence

Early Brain Development relies on genetic and environmental interaction for sequential skill acquisition. The HPA axis influences brain development: CRH is a neurotransmitter reaching the amygdala, hippocampus and frontal cortex and the absence of glucocorticoids catalyze neuronal maturation. In animal models, prenatal stress reduces hippocampal concentration of receptors for glucocorticoids and mineralocorticiods.. The hippocampus

inhibits the HPA axis; therefore, reduced receptors may limit HPA regulation and enable increased basal or inducible glucocorticoid secretion. Similarly, children born to mothers with stress, depression and anxiety – behaviors that produce low parental care - have higher association with elevated basal HPA activation. In contrast, settings of extreme deprivation (originally studies in Romanian orphanages) note an absence of circadian pattern.

- S. J. Lupien, B. S. McEwen, M. R. Gunnar, C. Heim. Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat. Rev. Neurosci*. 2009,10,434-445 .
- Carlson M, Dragomir C, Earls F, Farrell M, Macovei O, Nystrom P, Sparling J. Effects of social deprivation on cortisol regulation in institutionalized Romanian infants. *Soc. Neurosci.* Abstr., 21 (1995), p. 524

The child's environment plays a powerful role in brain development. Poverty has hypothesized neurocognitive effects suggesting accumulative impact on adult executive function and working memory. A recent study sought to clarify familial poverty impact on infant brain growth. Specifically, 'infants from low-income families had lower volumes of gray matter, tissue critical for processing of information and execution of actions'. Additionally, brain growth varied with socioeconomic status (SES), 'with children from lower-income households having slower trajectories of growth during infancy and early childhood. Volumetric differences were associated with the emergence of disruptive behavioral problems'. However, it is VERY important to note that poverty is not deterministic – in other words we do not know which children exposed to poverty will have negative impacts on brain growth, as the science on resilience is emerging.

- Hanson JL, Hair N, Shen DG, et al. Family poverty affects the rate of human infant brain growth. PLoS One 2013;8:e80954.
- Hart B, Risley TR (1995) Meaningful Differences in the Everyday Experience of Young American Children. Baltimore: Paul Brookes. 268

Immune Capacity. Some theorize that poverty impacts health through differential activation of the immune system, resulting in pro-inflammatory physiology. Recognized by Azad, et al. inflammation is a key pathway in many diseases including rheumatoid arthritis, cardiovascular and neurodegenerative diseases, asthma, diabetes, and obesity among others. Extensive cross sectional studies link low SES to increased systemic immune activation, inflammation, poor health outcomes. Interluekin 6 (IL-6) is a surrogate biomarker for chronic inflammation. Though en vivo physiology utilizes IL-6 for both pro-inflammatory and anti-inflammatory process, measuring IL-6 response to environmental triggers serves as a global indicator of the intensity of innate immune capacity or activation. Analyzing IL-6 ex vivo stimulation through an SES gradient, research found IL-6 was twice as intense for low SES children compared to high SES.

- Azad MB, Lissitsyn Y, Miller GE, Becker AB, HayGlass KT, et al. (2012) Influence of Socioeconomic Status Trajectories on Innate Immune Responsiveness in Children. PLoS ONE 7(6): e38669. doi:10.1371/journal.pone.0038669

Heightened immune activation may explain why early life adversity is associated with childhood asthma. Intimate partner violence (IPV) and household disarray (deterioration, disarray, hardship) were associated with greater odds for childhood asthma. Specifically, 'an increased odds of asthma was observed in children of mothers experiencing IPV chronically (OR 1.8, 95% CI 1.0 to 3.5) and in children experiencing housing disarray (OR 1.5, 95% CI 1.1 to

2.0) compared with those not exposed to these risks. In stratified analyses, a greater effect of IPV on asthma was noted among children living in disarrayed or deteriorated housing or among children whose mothers were experiencing housing hardship'

- Suglia, S. J Epidemiol Community Health 2010;64:636e642

Slide #12: Reflection

Have participants pair in twos for the reflection exercise, then share their conversation with the larger group. Each pair can either reflect on Cameron's case, or if they have their own clinical case that can also be used, time permitting.

What particular risk factors can you identify as present in the patient's life?

a. How did toxic stress contribute to disease for that patient?
b. How might toxic stress contribute to disease for that patient?
c. How might toxic stress influence diseases such as obesity, ADHD, substance abuse and developmental delay?

Case #2: John (Epigenetics)

Slide #14: Read thru the case one time, we will revisit it.

John is a 5 year old male who you've cared for since birth. He has persistent asthma, allergic rhinitis, recurrent AOM with left tympanic rupture and conductive hearing loss, speech delay, obesity, and environmental smoke exposure. John comes in today complaining of left otorrhea, and during the visit the parents reveal that he was recently hospitalized for asthma exacerbation. On further questioning you learn he stopped taking his controller medication one month ago. Today on exam his O2 sat is 97% with wheezing throughout. On reviewing the medical record you note that he has missed multiple Pulmonary and PCP appointments in the past year.

Additional information:

- Birth history: Full-term, LGA, IDM born to 32yo G7P6 mother with DM, obesity, asthma, and tobacco use.
- Ten ED visits by 1st birthday and NAT evaluation at 9 months for facial bruising consistent with hand imprint.
- Poorly-controlled persistent asthma: Fifteen ED visits, five hospitalizations (PICU once). Several documents question medication compliance.

(Transition by explaining we will return to discuss the case after we review epigenetic influences of poverty.)

Slide #15: Epigenetics

Inside the nucleus of each cell in our bodies, we have chromosomes, which contain the code for characteristics that pass to the next generation. Within these chromosomes, specific segments of genetic code, known as genes, make up long, double-helix strands of DNA. Children inherit approximately 23,000 genes from their parents, but not every gene does what it was designed to do. Experiences and environment leave a chemical "signature" on genes that determine whether and how the genes are expressed. Collectively, those signatures are called the epigenome.

Epigenetics examines how environmental or developmental processes can alter the effects of a person's genes without actually changing the sequence of the gene's DNA itself. Three mechanisms have been identified: DNA methylation, histone modification and non-coding RNA (ncRNA) interaction. DNA methylation, for example, 'silences' a gene. Early gestation is a critical period for DNA methylation and prenatal nutrition has significant influence for the provision of necessary dietary factors, such as folate, riboflavin, and B12.

Other pediatric disease examples which propose epigenetic modification include: 1) Fetal Alcohol Syndrome Disorder: alcohol inferferes with folate metabolism therby altering DNA methylation patterns in mouse models.; 2) Asthma: maternal smoke exposure produces global DNA methylation change during fetal development; 3) Gestational Diabetes: distinct DNA methylation pattern is noted for infants of diabetic mothers compared to controls.

Puumala SE, Hoyme HE. **Epigenetics in Pediatrics.** *Pediatrics in Review* 2015;36;14

Slide #16: Epigenetic Case - Reflection

(FROM AAP "The Potential Role of Epigenetics in Asthma Sample Scenario What Role Does Epigenetics Play in this Case?") Have participants pair in twos for the reflection exercise, then share their conversation with the larger group.

1) What are potential epigenetic factors contributing to John's disease?
The possible reasons for the asthma/wheezing are considered to be a combination of:

- **a.** Maternal obesity
- **b.** Exposure to environmental smoke
- **c.** Exposure to stress
- **d.** Fetal growth enlargement

2) How might epigenetic factors impact John's future health and economic well-being?
These factors are associated with a variety of health issues later in adolescence and adulthood, as they alter the short-term and long-term of expression of genes, having a dramatic effect on the expression of various disease states. Candidate genes include growth factors (impacting lung growth), immunomodulatory factors, stress impacting cortisol metabolism, previous RSV infection perhaps producing inflammatory airway damage, and second hand smoke exposure in

pregnancy. Virtually all of these risk factors have been associated with various changes in epigenetic marks. Remember, the genes have not been altered. The expression of the genes is potentially altered and that may be as important as inheriting a genetic predisposition for a certain problem.

Diagnosis

The proper documentation of the information in this case scenario, such as second hand smoke exposure, can assist the pediatrician in the diagnosis of disorders later on. While these risk factors might not appear to be relevant in early-life when the child appears healthy, the epigenetic marks have been set to program asthma, and thus their importance will be clear later.

Treatment

No specific therapeutic intervention currently exists for the information documented in this scenario, yet it is reasonable to surmise that in the future various modalities will be available to alter epigenetic risks (expressed as epigenetic marks). The goal at present is to recognize that we can prevent not just childhood disease but also adult diseases, perhaps even neurodegenerative disease, by the counseling and interventions we provide to patients when they are children.

Epigenetic and Prevention Messages

Epigenetic susceptibility should not be thought of as deterministic, instead it should be considered a trajectory. Changes that can have positive influences (cleaner air, less stressful home environment, less secondhand smoke exposure, etc.) can influence epigenetic marks such as DNA methylation toward more favorable gene expression profiles.

As noted above, knowledge of epigenetic risk factors going forward will assist the pediatrician in their anticipatory guidance and prevention of various problems for their patients. This means that recognizing and preventing even teenage and adult disease is part of our role as pediatricians, and that this role begins even before birth. These risk factors are just as important as the standard risk factors (past medical history and social history) currently used in office visits. In fact, many of the standard risk factors we think about work through epigenetics, we just didn't realize it. Prenatal and perinatal risk factor information can have a significant impact for the rest of a patient's life.

3) How might initial knowledge of epigenetic impact your approach to anticipatory guidance and asthma prevention with John's family? Divide learners into pairs or two small groups in order to read these two potential and differing responses to John's presentation.

Response #1:

A quick review of his records demonstrates poor disease comprehension and management, medication non-compliance and potential medical neglect. He is not only at risk

for significant illness from lack of controller access, but also, environmental smoke exposure is an ongoing trigger for deterioration. When you speak about the importance of daily inhaled controller and smoking cessation, mom states her discomfort with steroid use for her young child. Moreover, she seems pre-contemplative regarding quitting smoking. Mom feels asthma is better requiring fewer ED visits (2-3 this year). He uses his controller and Albuterol only when he is 'sick' but the medications cannot be found since home remodeling began last month - mold is present in bathroom. After prescribing new controller and albuterol, mom requests a note for school – absent two weeks – and more 'of the little pill'. Feeling frustrated by familial reluctance to initiate appropriate care, you exit the room saying, "he won't get better without your help". Clearly, John's parents are not prioritizing his health.

Response #2

John's health is impaired. However, the root cause may be more complicated than poor disease comprehension and non-compliance. Starting by asking parents what triggers they identify for John's asthma, parents note several factors, including smoke exposure. Mom seems pre-contemplative regarding quitting smoking, but on further questions she reveals she stopped smoking cold turkey after his last admission, but restarted after one week. This time she accepts nicotine replacement and smoking cessation support. Mom discloses financial stress with unemployment, car accident and recent move to shared house with maternal grandmother. Staff in both the Asthma Clinic of the nearby tertiary hospital as well as within your clinic mobilize to assist family.

Optional Handout

Below we have included figures that can be of assistance for learners in conceptualizing the interactions of experience, epigenetic changes, behavior and brain development, as well as the role of stress and resilience.

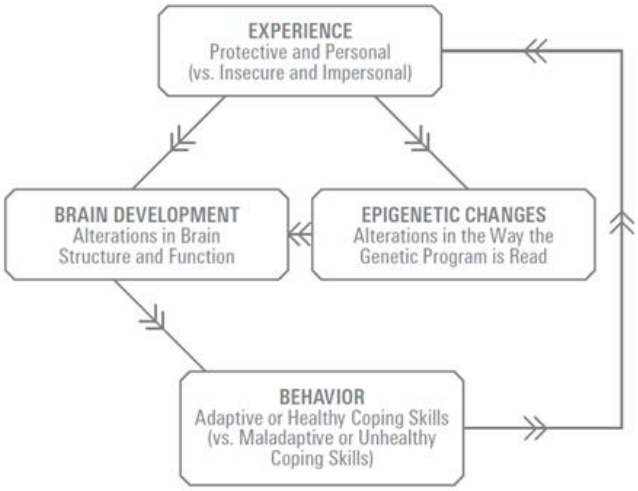


Figure 1
Development results from on-going and cumulative interactions between experience, biology, and behavior. If early childhood experiences are protective and personal, adaptive or healthy coping skills are more likely. If early experiences are insecure or impersonal, maladaptive or unhealthy coping skills are more likely.

https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/EBCD/Pages/The-Science.aspx

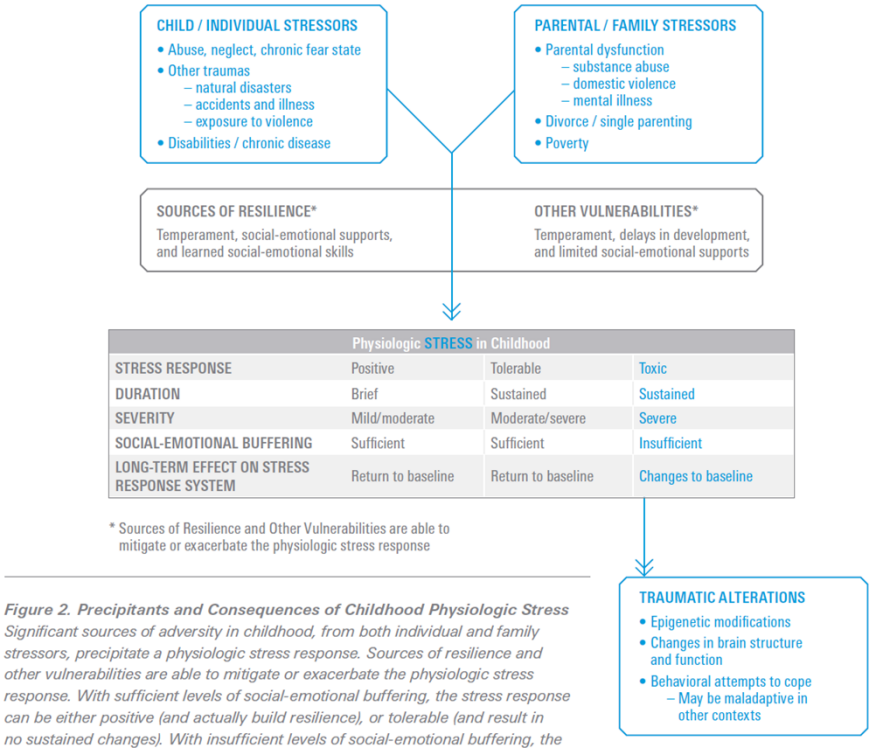


Figure 2. Precipitants and Consequences of Childhood Physiologic Stress
Significant sources of adversity in childhood, from both individual and family stressors, precipitate a physiologic stress response. Sources of resilience and other vulnerabilities are able to mitigate or exacerbate the physiologic stress response. With sufficient levels of social-emotional buffering, the stress response can be either positive (and actually build resilience), or tolerable (and result in no sustained changes). With insufficient levels of social-emotional buffering, the physiologic stress response is sustained or severe and becomes toxic, resulting in potentially permanent alterations to the epigenome, brain structure, and behavior. These traumatic alterations may actually be adaptive in threatening or hostile environments, but they are often maladaptive in other, less threatening contexts.

Environmental Disparities:

Slide #17: Environmental Toxins

Review the article below on Environmental Disparities (reference and link below). Explore with learners the Flint, Michigan example and the interplay between racial segregation, residential location, and environmental exposure to lead.

Flint, Michigan has approximately 102,000 residents, more than 40% of which live in poverty (41.3%). - Available at http://www.census.gov/quickfact (accessed 3/7/16)

Prior to April 2014, Flint bought Lake Huron water from Detroit. To cut costs, Flint officials joined the Karegnondi Water Authority to build their own Lake Huron intake system. Until it could be completed in 2016, Flint would pull water from the Flint River.

In mid-September, a Virginia Tech researcher and lead expert, Marc Edwards, concluded that Flint water was 19 times more corrosive than Detroit water. The city had allowed the water to flow through an old system without corrosion control, leaching lead from the pipes as it traveled to Flint spigots. Despite Edwards' findings and complaints from residents, state and local officials insisted testing showed lead in homes to be at acceptable levels.

Dr. Mona Hanna-Attisha's research demonstrated otherwise. She compared routine blood lead test results for 1,746 kids in Flint before and after April 2014. The percentage of kids in Flint with elevated blood lead levels of 5 micrograms per deciliter or more had doubled since the switch. In certain ZIP codes, it had tripled. While no level of lead in the body is safe, the Centers for Disease Control and Prevention (CDC) uses a level of 5 micrograms per deciliter to identify children living in environments that expose them to lead hazards. Toxicity builds slowly and silently, and the effects are permanent.

- Sturgeon M. True grit: Pediatrician proves Michigan community's water was poisoning children. AAP News November 11, 2015

Slide #18: What are the Health Effects of Lead?

Lead can affect almost every organ and system in your body. Children six years old and younger are most susceptible to the effects of lead.

Children: Even low levels of lead in the blood of children can result in: 1) Behavior and learning problems, 2) Lower IQ and Hyperactivity, 3) Slowed growth, 4) Hearing Problems, and 5) Anemia. In rare cases, ingestion of lead can cause seizures, coma and even death.

Pregnant Women Lead can accumulate in our bodies over time, where it is stored in bones along with calcium. During pregnancy, lead is released from bones as maternal calcium and is used to help form the bones of the fetus. This is particularly true if a woman does not have enough dietary calcium. Lead can also cross the placental barrier exposing the fetus the lead.

This can result in serious effects to the mother and her developing fetus, including: 1) Reduced growth of the fetus, and 2) Premature birth.

- Learn about Lead. Available at http://www.epa.gov/lead/learn-about-lead#effects (accessed 3/7/2016)

The Flint water crisis is a chronic toxic exposure of an entire population in a sharply demarcated geographic area. Several key aspects point to the long-term health and social consequences:

The manifestations of this toxic exposure depend on where along the life course a person may be. At different ages, critical structures and functions are injured or altered to different degrees. These changes may not manifest in functional derangements for months or years after exposure. The science of epigenetics addresses the interaction between genes and the environment, suggesting that some of these changes can be passed on from one generation to the next.

Blood lead levels do not indicate peak lead exposures beyond a 30- to 35-day window. The damage from lead toxicity may be done months before the first blood lead level is taken or after the last is drawn, especially for newborns and children younger than 6 years of age. This suggests that the findings related to elevated lead levels measured in Flint children are merely the tip of the iceberg of actual exposure across children living in Flint.

Documented risks of learning, behavioral, and cognitive problems are present for all potentially exposed children in Flint. Aggressive and impulsive behaviors - that can emerge in adolescence related to lead exposure put children in the crosshairs of the criminal justice system, unemployment and underachievement.

The risk of kidney problems, hypertension, gout and stillbirths may affect exposed adults in Flint over the coming years and decades.

- **Flint Water Advisory Task Force Final Report, p. 54**
  https://www.michigan.gov/documents/snyder/FWATF_FINAL_REPORT_21March2016_517805_7.pdf

Slide #19: Environmental Disparities

The burden of disease attributable to environmental factors is not distributed equally across the population. On the contrary, diseases with high environmental contributions such as asthma and lead poisoning disproportionately affect poor and minority communities (Rauh et al, 2008). The residential environment, particularly in urban settings, plays a large role in creating and perpetuating these disparities.

Factors that lead to these disparities include:

- Poor or unequal enforcement of city building codes

- Housing stock age and maintenance
- Location of pollution sources (e.g. industrial plants, transportation depots)
- Overcrowding
- Inadequate garbage removal
- Community empowerment
- Access to legal counsel

Disparities in Indoor Exposures: Homes in urban centers often contain elevated levels of pollutants that can precipitate or worsen asthma, allergies, and other diseases. Overcrowding, older housing stock, and lack of building code enforcement are major contributors in this area.

Common pollutants that are prevalent in poor, urban homes include:

- Indoor allergens, such as cockroaches, mice, molds, and dust mites
- Environmental tobacco smoke
- Nitrogen dioxide (from space heaters and inadequately maintained gas burners)
- Lead paint/dust

Disparities in Outdoor Exposures: Low-income, urban areas bear a disproportionate burden of outdoor air pollution as well. This is particularly true in minority communities. Disproportionate numbers of pollution sources such as industrial plants, diesel bus depots, and networks of highways are located in poor, minority communities. Longitudinal studies out of southern California demonstrated that the disparities there were typically the result of unequal siting of these facilities *into existing minority communities* rather than a phenomenon in which poorer people move into areas with existing toxic facilities due to lower cost of living (Morello-Frosch, 2002).

Examples of outdoor air pollutants that are prevalent in poor, urban environments include:

- Diesel particulate matter (DPM)
- Particulate matter (PM)
- Polycyclic aromatic hydrocarbons (PAH)

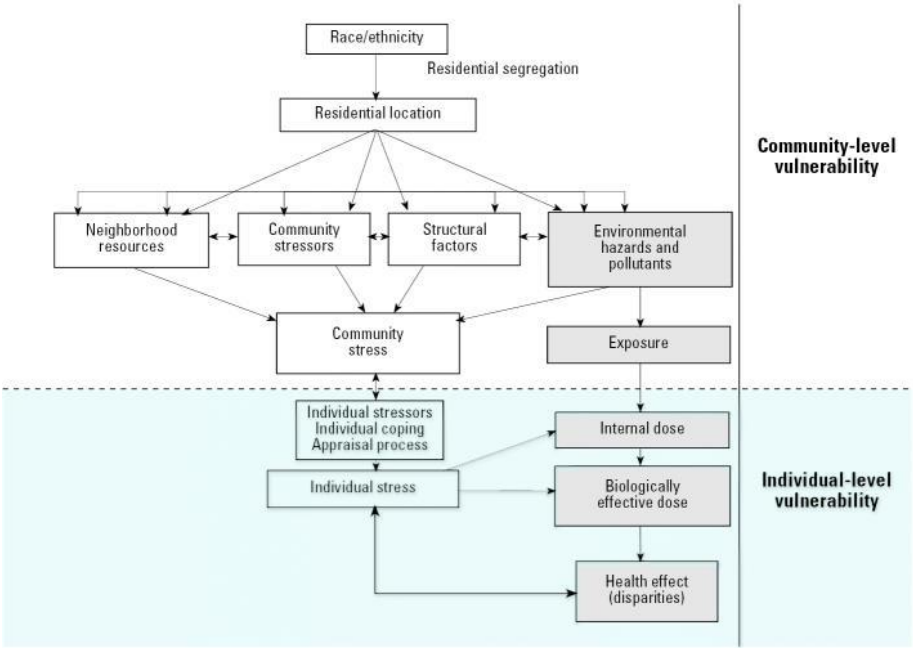
These air pollutants are important triggers for asthma and allergies. In, many of the hazardous air pollutants (HAP's) that are prevalent in poor, urban communities are also carcinogens. Figure 2 from the 2002 Morello-Frosch article cited above demonstrates the impact of both income and race on the lifetime risk of cancer associated with HAP exposure. As you can see, minority race and lower household income both contributed to increased cancer risk.

Rauh V. Landrigan P. Claudio L. Housing and health: intersection of poverty and environmental exposures. *Ann NY Acad Sci*, 2008; 1136: 276-288.

Morello-Frosch R. Pastor M. Porras C. Sadd J. Environmental justice and regional inequality in southern California: implications for future research. *Environmental Justice*, 2002; 110: 149-154.

Optional Handout

Below we have included a figure that can be of assistance for learners in conceptualizing the complex interplay between community and individual-level exposure to environmental toxins.



http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1253653/

Section 3: Timing is Everything – Critical Windows, Biologic Plasticity and the Importance of Acting Early

Objectives covered:

- Explain the role of critical periods, sensitive windows and allostatic load in creating health disparities
- Analyze existing evidence of the link between adverse health events and adult health inequities
- Investigate potential clinical interventions that might mitigate the effects of toxic stress during childhood

Facilitator's Role
Outline:

- Present slides 20-24
- Have the learners consider the relevance of the stages of development to the timing of early adversity.
- Help learners understand the relevance of SCEs in their clinical practice.
- Help learners commit to a change in their practice with the new knowledge acquired around toxic stress.

Guidelines:

The assigned pre-work and this CDC site link (CDC ACEs site: http://www.cdc.gov/violenceprevention/acestudy/index.html) will help you in guiding the learners through this section. This topic can feel overwhleming to learners as they may feel there is a lack of resources to support a child who is experiencing or who has experienced early adversity. Through the information in this section you can encourage them to assess and address early adversity in their clinical practice. You can equip them with strategies that will foster safe, stable, and nurturing relationships and environments.

Slide #21 – Timing is Everything

Early experiences or exposures can affect adult health in two ways - the chronic wear and tear of repeated damage over time or the biological embedding of specific physiological disruptions during sensitive developmental periods. If a physiological maladaptation occurs in response to cumulative exposure to adverse social and/or physical conditions, then an ensuing chronic disease can be seen as the consequence of repeated encounters with psychologically or physically toxic environments. When damaging exposures occur during sensitive periods in the early development of specific biological processes, the resulting disruptions can become biologically embedded and subsequent adult diseases appear as the latent (or delayed) outcomes of early environmental assaults. These are some key terms for this conversation:

- **Critical Period**: a fixed developmental opportunity for skill acquisition (ie Neural tube formation)
- **Sensitive Period**: a developmental phase when influencing factors have elevated influence on skill acquisition
- **Biologic Plasticity**: the continual process by which an experience impacts physiologic form and function so that there are new experiences
- **Allostatic Load**: the cumulative physiologic toll placed on the body by sequential adaption to life experience

- Center on the Developing Child at Harvard University (2010). *The Foundations of Lifelong Health Are Built in Early Childhood*. http://www.developingchild.harvard.edu

To explain the relationship between early adverse experience and later outcomes, distinct models are proposed. The **Diathesis Stress Model** proposes that some children are genetically more vulnerable to adversity. An alternate model, the **Differential Susceptibility to Context (DSC),** asserts select children are more genetically impressionable to the environment. These children, referred to as 'orchids', differ some other children who are less affected by environment (so-called 'dandelions')

- Garner AS, Forkey H, Szilagyi M. Translating Developmental Science to Address Childhood Adversity.Acad Pediatr. 2015 Sep-Oct;15(5):493-502

Slide #22: Adverse Childhood Experiences:

Reviewing this TEDTalk on Adverse Childhood Experiences by pediatrician Nadine Burke-Harris was a part of the prework for this module. (http://www.tedmed.com/talks/show?id=293066)

Slide #23: The ACE Study

The ACE Study developed as a retrospective review during HMO enrollment (n = 17,737; average age 57y, predominantly white, college-educated). By asking enrollees to indicate childhood exposure to seven domains (psychological, physical, or sexual abuse; violence against mother; or living with household members who were substance abusers, mentally ill or suicidal, or ever imprisoned), social and health behaviors and combined this data with physical exam. The ACE study and subsequent studies note strong graded relations between exposure to household dysfunction and abuse during childhood and the leading causes of adult morbidity and mortality, including coronary artery disease, asthma, and mental illness. Examples include alcoholism, depression, smoking, STD, severe obesity, drug abuse, suicide attempt, sexual promiscuity, physical inactivity, and poor self-health rating.

Persons who had ≥4 affected categories, compared to those with no experiences had:

- 4- to 12-fold increased health risks for alcoholism, drug abuse, depression, and suicide attempt;
- 2- to 4-fold increase in smoking, poor self-rated health, >50 sexual intercourse partners, and sexually transmitted disease;
- 1.4- to 1.6-fold increase in physical inactivity and severe obesity.

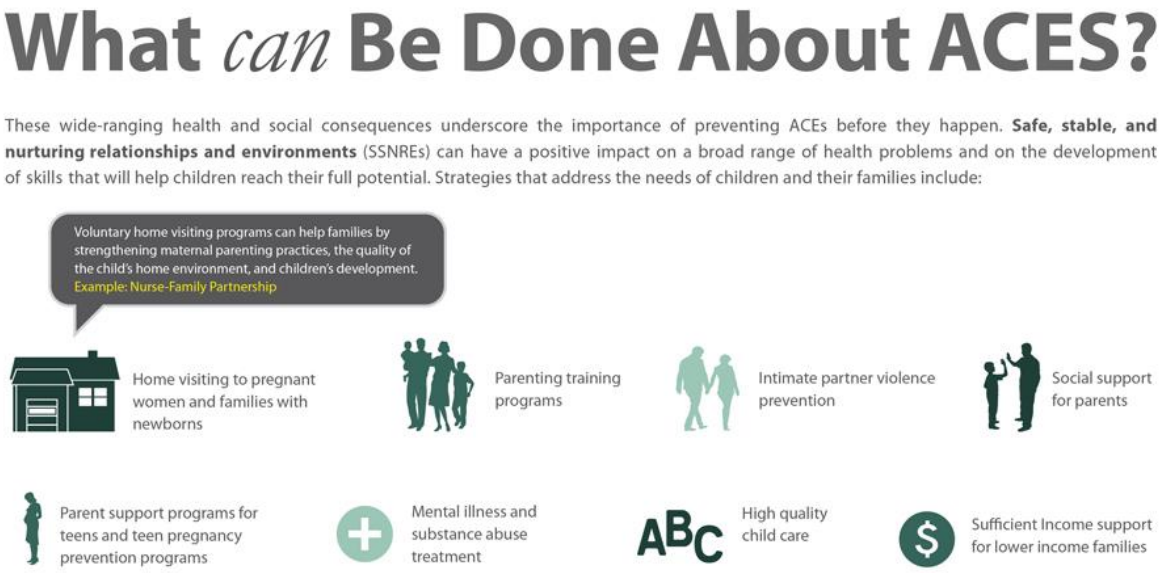
Adverse childhood experiences (ACE) contribute to risk for chronic physical and mental health. Poor children experience adverse childhood experiences more often than higher income peers.

- Gradient for ACE by multiples of FPL (http://childhealthdata.org/browse/survey/results?q=2257&r=1&g=458)

Therefore, interventions that buffer toxic stress and reduce ACE exposure offer significant benefit, both for childhood and adult health outcomes.

Slide #24: Childhood Interventions

What evidence based interventions do we have to address toxic stress and ACEs? There is an optional handout below that outlines some of the interventions that promote safe, stable and nurturing relationships and environments for our patients.



- http://www.cdc.gov/violenceprevention/acestudy/index.html

Discussion Options for this Section:

1) For children at risk for toxic stress, do family and child programs, compared to no interventions, modify health and development?
Yes, the evidence is strong in high quality child care and preschools, home visiting programs and some parent programs. Examples of sentinel programs include:

- The **Perry Preschool Project**, operating from 1962-1967 in Ypsilanti, MI, examined the impact of a rigorous participatory learning curriculum. Perry targeted 123 impoverished 3-4 year old African American preschoolers. Subsequent analyses demonstrate educational, economic and health benefits amongst participants, including greater overall educational attainment, higher monthly income, lower likelihood of incarceration and fewer teen pregnancies. Benefits persist more than 40 years after Perry concluded. Often, proponents for universal Early Childhood Education cite economic data from the Perry Project for preschool return on investment (ROI). ROI calculations note annual return of 7-10% for funds invested to high-quality early education.

- **The Abcedarian Project** enrolled children 0-5 years from a high risk socioeconomic population in North Carolina for either early educational child care, high-quality preschool and free health care (Intervention) or free diapers, formula and could attend other childcare or preschool (control). Research identified not only that invention children 'have significantly lower prevalence of risk factors for cardiovascular and metabolic disease in their mid-30s" but also "those who are obese or severely obese in their mid-thirties are already on a trajectory of above-normal BMI in the first 5 years of their lives".
    - - Frances Campbell et al Science 343, 1478 (2014)

- **Nurse Family Partnership (NFP)**
  The NFP is a home visitation program primarily serving low-income, single, teen, first-time mothers. Public health nurses receive program-specific training and the program runs from third-trimester to 2 years of age. Program aims are improve pregnancy outcomes through positive health related behaviors, help parents provide competent care for children, and, enhance maternal personal development (ie. family planning, educational achievement and workforce participation). Three randomized control trials, varied in setting and population, examined effect with positive benefit for reduced measures of child abuse & neglect; fewer subsequent births for mothers in late teens and early 20s; decreased prenatal smoking for mothers who smoked at study onset; and, improved cognitive/academic outcomes for children born to mothers with low psychologic resources. Morever, the Home Visiting Evidence of Effectiveness Summary (2011) noted the NFP had favorable impacts in seven domains: Child health, Child development and school readiness, Family economic self-sufficiency, Maternal health, Positive parenting practices, Reductions in child maltreatment, Reductions in juvenile delinquency, family violence, and crime. Importantly, effect was replicated in another sample; sustained at least one year; and, persisted at least one year after completion.

- **The Harlem Children's Zone (See the SDH module for introductory information)**
  Six years after the random admissions lottery, youth offered admission to the Promise Academy middle school score 0.283 standard deviations higher on a nationally-normed math achievement test and are 14.1 percentage points more likely to enroll in college. Admitted females are 12.1 percentage points less likely to be pregnant in their teens, and males are 4.3 percentage points less likely to be incarcerated.

2) How might you incorporate toxic stress knowledge into practice and what local resources can support these efforts?

Much of this ties into the Social Determinants of Health module. Screening and referral for evidence-based interventions that reduce toxic stress should be a priority for practices: food insecurity, housing insecurity, preschool/Head Start enrollment, among others.

A full discussion of this can be found in this article "Redesigning Health Care Practices to Address Childhood Poverty" *Acad Pediatr*. 2016 Apr;16(3 Suppl):S136-46 by Fierman A et al.

3) Given association with adult morbidity and mortality, does ACE screening reduce toxic stress compared to no screen?

The evidence is emerging about the link between ACE screening/interventions and adult morbidity/mortality. Learners here can share their perspectives.

- CDC ACEs site: http://www.cdc.gov/violenceprevention/acestudy/index.html
- - The Medium-Term Impacts of High-Achieving Charter Schools on Non-Test Score Outcomes, Will Dobbie, Roland G. Fryer, Jr, **NBER Working Paper No. 19581**, **Issued in October 2013 (http://www.nber.org/papers/w19581)**
- From Neurons to Neighborhoods Executive Summary (2000) – The National Academies Press: http://www.nap.edu/read/9824/chapter/2

Section 4:

Re-Framing the Problem - Intergenerational Poverty and Cognitive Bias

Objective covered:

- Reflect on how understanding the effects of biologic influences on intergenerational poverty affect one's personal assumptions, biases and approaches to caring for individual families

Facilitator's Role
Outline:

- Present slides 25-29
- Have the learners make a commitment to an open and honest discussion.
- Help the learners make the classroom a safe space, allowing them to speak from an honest perspective.

Guidelines:

This section allows for self-reflection while integrating newly-learned concepts about poverty and reflect on their personal beliefs about their patients. Guide the learners in reflecting on their assumptions of the children and their families in these videos. They should then incorporate the new concepts into a new framework for approaching their patients and families.

Slide #26: Intergenerational Poverty

Watch the following excerpt from PBS Frontline documentary 'Poor Kids' (http://www.pbs.org/wgbh/frontline/film/poor-kids/) then discuss using the questions on the following two slides. The video can be watched in 5 or 8 minute excerpts.

Option 1: Brittney excerpt – total 4min 37sec

Clips threaded in following order

1. 1:56-2:11 – Brittney's introduction "It's tough 'cause my mom and dad are poor"
2. 19:48-20:12 - Scene opens with families in line for Food Bank. Brittney describes her family's food insecurity and her hunger.
3. 21:02-22:11 – Brittney introduces Nutrition Club, a school-based program program to supplement weekend hunger. Her brother, Roger, describes his frustration with family's transition – food, housing and utility insecurity
4. 23:35-25:23 – Brittney and her mother eat pizza but her mother visualizes steak. Later, Brittney's mom describes her reaction to stress. Brittney worries about her mom's health.

5. 37:07-38:08 – Brittney will have a new baby brother or sister soon, though, Brittney voices her concern that family resources will not be enough. Still, Brittney sees her mother's happiness. She says, They don't really care if I'm happy…I just care that my family's happy".

Option 2: Kaylie – 7min 52sec

1. 6:04-7:52 – Kaylie's introduction describes her family as 'a poor family' then she and her brother – Tyler – share hunger experiences.
2. 28:13-28:36 – After losing their home, Kaylie's family moves into a hotel. The room has a single bed and lacks several items, including a refrigerator.
3. 33:16-34:04 then 35:03-36:06 – A portrait into Kaylie's life demonstrates limited social and material options.
4. 39:52-41:17 – As the family moves away form the hotel, stress is apparent. Kaylie, after a long day with her mother, says 'she really needs to work on the yelling".
5. 42:05-42:56 – After moving into a new house, Kaylie ponders what to do with her time as well as what contributed to the family's hardship.
6. 49:07-51:42 – Housing insecurity causes a return to a hotel as well as school absenteeism. Without school, Kaylie does not have positive thoughts about her future.

Slide # 27: Discussion Prompts: Intergenerational Poverty

1) What surprised you while watching Brittney or Kaylie?
2) Did you have any assumptions about the children and their families?
3) What do you see in the video that could influence Kaylie's or Brittney's health?
   a. What is your response to that as a provider?

Slide # 28: Discussion Prompts: Bias Reflection

1. Does the biomedical influence of poverty have significance in your practice?
2. What key factors must one know in order to understand poverty's influence on health?
3. Describe your personal reaction to the contrasting responses offered to John's case.
   a. Do you identify with or feel challenged by elements of either?

Slide #29: Dig Deeper

Options to recommend for further exploration for learners who express interest in these themes.