Leveraging the biology of adversity to address the roots of disparities in health and development

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Extensive evidence that personal experiences and environmental exposures are embedded biologically (for better or for worse) and the cumulative knowledge of more than four decades of intervention research provide a promising opportunity to mobilize evolving scientific insights to catalyze a new era of more effective early childhood policy and practice. Drawing on emerging hypotheses about causal mechanisms that link early adversity with lifelong impairments in learning, behavior, and health, this paper proposes an enhanced theory of change to promote better outcomes for vulnerable, young children by strengthening caregiver and community capacities to reduce or mitigate the impacts of toxic stress, rather than simply providing developmental enrichment for the children and parenting education for their mothers.

Decades of scientific advances and practical experience tell us that early childhood is a time of both great promise and considerable risk. Converging evidence from neuroscience, molecular biology, genomics, and epigenetics further indicates that the influence of the early years can extend over a lifetime, as it affects the foundations of learning, behavior, and both physical and mental health (1–3). Almost half a century of program evaluation data add extensive evidence to support the additional conclusion that a variety of intervention strategies can improve the life prospects of children who face the burdens of low family income, limited parent education, and social disadvantage—but the magnitude of their measured effects has been variable and the quality of program implementation has been uneven (4–7).

Science tells us that early experiences are embedded biologically (i.e., "built into our bodies") for better or for worse—and ongoing advances in the biology of adversity, the science of learning, and the disciplines of intervention research invite us to rethink the traditional modes of interaction among research, policy, and practice in the early childhood arena. To that end, the rapidly moving frontiers of the developmental sciences offer an unprecedented opportunity to leverage knowledge in the service of launching a new era in early childhood policy and practice that is committed to achieve substantially greater impacts than current efforts.

The convergence of increasing knowledge about child development and effective interventions provides multiple targets for fresh thinking, hypothesis-driven experimentation, and rigorous evaluation. These opportunities can be found across a complex landscape of early childhood policies and programs in education, health, and human services, ranging from approaches focused primarily on children and their parents to larger-scale initiatives that address more distal influences, such as community characteristics or broader social and economic forces. In wealthy nations, policymakers focus largely on preparing young children for success in school as an investment in the development of human capital to compete more effectively in a global economy (8). Although discussions in the poorest countries typically focus primarily on reducing preventable deaths and treating infectious disease, when funds earmarked for child survival compete with potential investments in early childhood development, science suggests that the reduction of significant adversity could advance progress toward both objectives (9–11).

Drawing on Advances in Science to Stimulate Fresh Thinking About Promoting Learning

Extensive research has identified multiple developmental impediments that limit the ability of children with normal cognitive potential to benefit from available learning opportunities. These include emotional problems associated with fear and anxiety, maladaptive social adjustment, disruptive behaviors, impairments in executive functioning, and a range of other difficulties that are often categorized rather loosely as socio-emotional problems or mental health disorders. Viewed separately, each of these impairments can play an important role in undermining a young child's ability to learn. Together, any combination of difficulties is likely to seriously disrupt the capacity to engage in productive, goal-directed activity. A common underlying problem that links all of these domains—diminished capacity for self-regulation in the areas of attention, emotion, and behavior—offers an example of one promising framework (among others) for the design and implementation of new strategies to reduce barriers to early learning (7).

At the time of school entry, children differ in how well they are able to focus and shift their attention, manage their feelings, control their impulses, follow rules and directions, and adapt to a variety of other demands. Many teachers contend that beginning school with a solid base of these foundational skills in executive function and self-regulation is more important than whether children know letters and numbers (12, 13). Understanding these individual differences is essential to determine the nature and intensity of assistance that all youngsters need to learn effectively.

The acquisition of executive function and self-regulatory skills corresponds closely to the extended development of the prefrontal cortex, which begins in early infancy and continues into the early adult years (14–16). Because these neural circuits have extensive interconnections with deeper brain structures that control responses to threat and stress (17–19), maturing executive functioning both influences, and is affected by, a young child's management of strong emotions (20, 21). Thus, repeated exposure to threatening situations can disrupt the development of the prefrontal cortex and lead to emotional problems as well as compromised working memory, attention, and inhibitory control (22–24). In contrast, well-developed capabilities in these important aspects of self-organization can help children (and adults) manage adversity more effectively (25).

As research on the development and underlying neurobiology of executive function and self-regulation skills continues to advance, its relatively untapped potential for informing early

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childhood education policy and practice is becoming increasingly compelling. To this end, there is an expanding evidence base on effective interventions in each of these domains, and recent data have linked self-regulation to the development of literacy and numeracy skills (26). The need for greater attention to this area, above and beyond the current focus on early language stimulation, is underscored by growing evidence of the exacerbation of early social class differences in development by emerging disparities in executive function skills and in the developing circuitry of the prefrontal cortex as early as the infant–toddler period (27–32).

Drawing on Advances in Science to Stimulate Fresh Thinking About Preventing Disease

The potential consequences of significant adversity and chronic stress in early childhood extend beyond the domains of socioemotional and cognitive development. They also have significant implications for the pathogenesis of adult disease. In this context, it is important to underscore the distinctions among normative stress that is an essential part of healthy development, tolerable stress (i.e., significant adversity that is managed through effective coping skills that are facilitated by supportive adults), and toxic stress (i.e., excessive and/or prolonged activation of stress response systems in the absence of the buffering protection of supportive and responsive adult caregiving) (3).

At the behavioral level, there is extensive evidence of a strong link between early adversity and a variety of health-threatening lifestyles in the adolescent and adult years (33–35). At the biological level, there is growing documentation of the extent to which the cumulative burden of excessive stress activation over time (which can result from chronic neglect as much as from overt abuse), as well as the timing of specific environmental insults during sensitive developmental periods (e.g., from prenatal alcohol exposure or significant thyroid hormone deficiency in infancy), can produce structural and/or functional disruptions that lead to a wide range of physical and mental impairments later in life (36–40).

The association between adverse childhood experiences and unhealthy adult behaviors (e.g., tobacco use, alcohol and illicit drug abuse, and unprotected sexual activity), compounded by the ongoing burdens of socioeconomic disadvantage, are potent risk factors for poor health. Beyond the consequences of these pathogenic behaviors, however, it is critically important to underscore the extent to which prolonged or excessive stress in early childhood has also been shown to cause physiological disruptions that persist into adulthood and lead to disease, even in the absence of later health-threatening lifestyles. These lasting biological manifestations of early adversity include alterations in immune function (41) and measurable increases in inflammatory markers (42, 43) that are known to be associated with poor health outcomes as diverse as cardiovascular disease (44–46), viral hepatitis (47), liver cancer (48), asthma (49), chronic obstructive pulmonary disease (50), autoimmune diseases (51), poor dental health (52), and depression (53–55), as well as increasing evidence of comorbidities related to overlapping pathophysiological mechanisms. Thus, significant adversity in early childhood can be a direct source of biological injury or disruption that may have lifelong consequences independent of whatever circumstances might follow later in life. In such cases, toxic stress can be viewed as the precipitant of a physiological memory that confers lifelong risk well beyond its time of origin.

The approach to childhood adversity discussed in this paper has two compelling implications for a full, lifespan perspective on health promotion and disease prevention. First, it postulates that excessive activation of stress response systems in early childhood can play an important causal role in the intergenerational transmission of poor health. Second, it underscores the need for the entire medical community to focus more attention on the roots of adult diseases that originate during the prenatal and early childhood periods and to rethink the concept of preventive health care within a system that currently perpetuates a scientifically untenable wall between pediatrics and internal medicine (40, 56). Both implications underscore the need for a transformative approach to the organization and financing of the current health-care system to promote greater horizontal (i.e., across medical, educational, and social services) and longitudinal (i.e., lifelong) integration (57). Beyond the need for enhanced coordination of services, however, breakthrough outcomes in reducing health disparities will require a new generation of intervention strategies whose individual impacts exceed those of existing efforts.

Creating a New Paradigm for Early Childhood Policy and Practice

Most current policies and services for young children living in disadvantaged circumstances are viewed by policymakers and the general public as investments in "school readiness" (as a short-term objective) in the service of promoting later academic achievement and future economic productivity (as a long-term goal). To this end, state-of-the-art early care and education programs provide enriched learning opportunities and sound nutrition for children and a combination of parenting education and social support for their families (usually focused exclusively on mothers), both in community-based centers and in the home (6). This approach is embedded in a policy environment that typically favors cognitive stimulation over the promotion of social and emotional well-being and an educational landscape that understands the foundational role of early language development for later literacy (58).

When children grow up in adverse circumstances associated with any combination of the three most frequently documented risk factors associated with poor education outcomes—significant economic hardship, limited parent education, and minority group status based on race or ethnicity—the burdens that are imposed on the caregiving environment can be substantial. When these threats to healthy development are magnified by chronic neglect or recurrent abuse, developing brain circuits may be disrupted; other maturing organs can also be affected adversely; metabolic regulatory systems may be impaired; and a foundation is laid for lifelong problems in learning, behavior, and both physical and mental health. Under such circumstances, significant adversity can overwhelm the capacity of most providers of early care and education, and the impacts of the programs are often limited.

Building on the demonstrated benefits of current interventions for many young children, the biology of adversity suggests that the magnitude and sustainability of program impacts on those who are the most vulnerable could be increased by greater investment in protection from the biological consequences of toxic stress. The challenge facing policymakers and practitioners is not the elimination of all stress, as low levels of manageable adversity have been shown to serve as a form of "stress inoculation" that can enhance later resilience (59). Rather, there is a clear need for enhanced interventions that strengthen the capacity of parents and other adult caregivers to help build the adaptive capacities and coping skills of children whose life circumstances impose extensive threats to their well-being. This need for protection is particularly critical for children who exhibit increased biological sensitivity to context—making them both most vulnerable in the face of adversity and most able to benefit from positive experiences (60, 61). Although many questions about precise causal mechanisms remain to be answered, advances in the biological sciences support the following two fundamental shifts in the dominant paradigm that drives current early childhood policy and practice.

Early Experiences and Environmental Influences Affect Lifelong Health, Not Just Educational Achievement. The extent to which early childhood policy is viewed primarily as falling within the jurisdiction of departments or ministries of education reflects a highly myopic view of its investment potential. Indeed, growing evidence of the early life origins of adult illness suggests that a promising strategy for reducing the prevalence of many of the most common (and costly) chronic diseases is to develop early, science-based interventions that reduce or mitigate the biological disruptions associated with toxic stress. By preventing the emergence of maladaptive physiological and behavioral responses to adversity, such interventions may prove to be effective in reducing rates of hypertension, cardiovascular disease, diabetes, and depression, among many other chronic conditions that are disproportionately associated with socioeconomic disadvantage. Thus, the current revolution in biology offers compelling investment opportunities in the prenatal and early childhood period for policymakers whose responsibilities lie in the realms of population health, not just for those whose accomplishments are measured exclusively in education outcomes (9, 40).

There Is a Clear Need for More Effective Strategies to Protect Children from the Biological Consequences of Significant Adversity, Not Just to Provide Enriched Learning Opportunities. Although curricular enhancements are certainly worthy of continuing attention, the biology of adversity suggests that children who experience toxic stress may be less able to benefit from good-quality early childhood programs because of impairments in their developing brain circuitry. This proposition is supported by extensive evidence (from both animal and human studies) of the vulnerability of the amygdala, hippocampus, and prefrontal cortex (PFC) to the disruptive effects of excessively activated stress response systems, beginning in the prenatal period and early infancy and, in the case of the PFC, extending well into the adult years (62, 63). As this knowledge base grows, it will be increasingly difficult to defend the absence of an explicit "brain protection" strategy that focuses on both primary prevention and "physiological healing" for young children whose life circumstances increase the risk of debilitating sequelae from toxic stress (6, 40). Moreover, although evidence of adult plasticity (particularly for PFC-mediated skills) provides reassurance that later remediation can produce positive benefits, the foundational importance of early sensitive periods suggests that better outcomes are likely to result when neural circuitry is "wired properly" from the beginning (1, 2).

Generating Hypotheses to Guide New Intervention Strategies

Healthy organizations (whether they are service programs, private businesses, or government agencies) recognize that continuing success depends on both high-quality performance in the present and proactive thinking about the future. In that spirit, multiple opportunities for innovation exist across a broad spectrum of early childhood policies and programs, ranging from capacity-building services focused on children and their caregivers to place-based initiatives designed to support families and reduce neighborhood sources of toxic stress. The logic model depicted in Fig. 1 offers a framework for augmenting the impacts of existing efforts through innovative intervention strategies informed by insights from the biological and behavioral sciences.

Human health and development are the product of a complex mixture of biological adaptations and disruptions that result from the dynamic interaction of genetic predispositions and environmental influences. These mediators are shaped by three foundations of healthy development—child–adult relationships, aspects of the physical environment, and nutrition—that provide important targets of intervention to improve life outcomes. Caregiver and community capacities have a major influence on the evolving quality of these foundations, and the extent to which policies and programs generate high returns on investment is tied to their effectiveness in strengthening those capacities. Guided by this logic model, there is an urgent need for creative, new strategies about how to produce substantially greater impacts on the skills of adult caregivers and the health-promoting characteristics of the communities in which vulnerable children are living. The following three hypotheses are presented as examples of innovative approaches to enhanced capacity building that are worthy of systematic testing and evaluation.

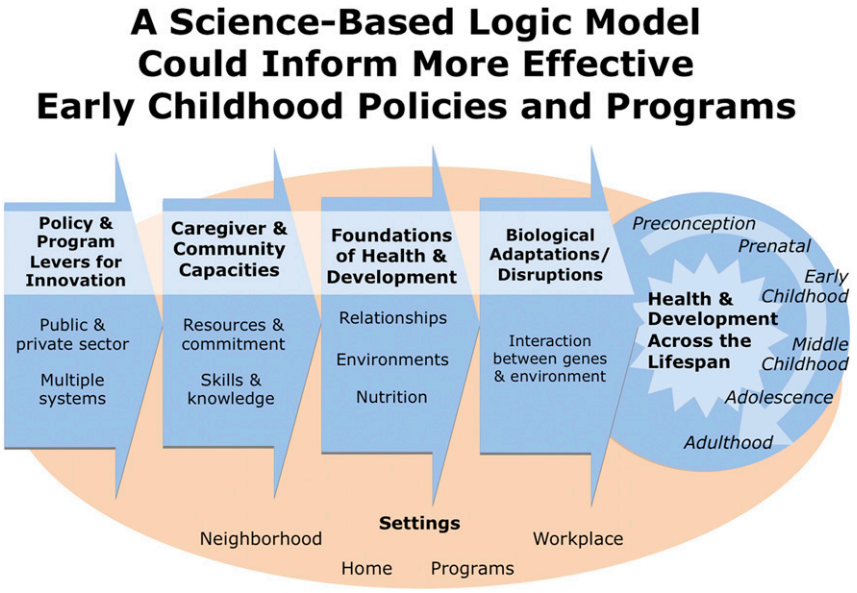

Fig. 1. A science-based logic model could inform more effective early childhood policies and programs (adapted from ref. 79).

Hypothesis A: Protecting Children from the Impacts of Toxic Stress Requires Selective Skill Building—Not Simply the Provision of Information and Support—for the Adults Who Care for Them. The time has come to address both the benefits and the limitations of parenting education and social support as cornerstones of early childhood policy and practice. On the positive side, the value of providing practical information and concrete assistance has tremendous intuitive appeal and a research base to support its positive effects, particularly for mothers with limited education. There is also reason for concern, however, that the magnitude of impact achieved by such interventions is typically modest (4, 5) and the absence of significant effects on parents and children who are facing substantial disadvantage is a reality that must be confronted. With this challenge in mind, the biology of adversity suggests that the promotion of resilience in the face of excessive stress early in life depends upon the availability of adults who can help young children develop effective coping skills that restore physiological homeostasis by bringing their stress response systems back to baseline. Central to this hypothesis is the required capacity of adult caregivers to provide that buffering protection through their own well-developed skills in problem solving, planning, monitoring, and self-regulation. That said, these critical skill areas are typically underdeveloped in both parents and early childhood service providers who have limited education, low socioeconomic status, and poor prior exposure to models of effective parenting. The likelihood is, therefore, relatively low that these skills will be sufficiently strengthened by the simple provision of information about child development. In contrast, training or coaching strategies focused explicitly on adult capacity building in these domains offer a promising new direction that is worthy of investigation, especially for parents and early childhood program staff whose needs are not sufficiently addressed by existing supports (64, 65).

Hypothesis B: Interventions That Improve the Caregiving Environment by Strengthening the Executive Function and Self-Regulation Skills of Vulnerable Parents Will Also Enhance Their Employability, Thereby Providing an Opportunity to Augment Child Outcomes by Strengthening the Economic and Social Stability of the Family. The long-standing disconnection between programs focused on remedial education, workforce preparation, and asset building for adults living in poverty vs. services focused on the developmental needs of poor children has been noted critically for decades. Much of that criticism has centered on problems related to fragmentation of effort and inefficient resource utilization. Science now offers a new argument for a conceptually unified, two-generation framework for reducing the cycle of poverty by focusing on a core set of adult capacities that are essential prerequisites for success in both the home and the workplace. The extended plasticity of the prefrontal cortex into the early adult years provides a strong rationale for such efforts (62). Young children learn these skills through creative, structured play with their peers and from the scaffolding provided by adults who have well-developed planning, monitoring, and self-regulating capacities of their own. Capitalizing on their extended window of plasticity, these skills can be enhanced through training and practice during any stage of development, from infancy through the young adult years (64, 66–70).

Hypothesis C: Community-Based Initiatives and Broad-Based, Systems Approaches Are Likely to be More Effective in Promoting Healthy Development and Reducing Intergenerational Disparities If They Focus Explicitly on Strengthening Neighborhood-Level Resources That Buffer Young Children from the Adverse Impacts of Toxic Stress. Motivated by extensive evidence that poverty and racial or ethnic minority status are risk factors for poor life outcomes, decades of place-based initiatives have been fueled by broad concepts such as collective efficacy, social empowerment, elimination of structural inequities, combating institutionalized discrimination, building social capital, and advancing social justice (71–74). Concurrently, the emergence of ecological models that emphasize the impact of socioeconomic and cultural influences on human development has added substantial scientific justification for policies and programs that focus on the broader context in which families raise children (75, 76). That said, the persistence of significant, socioeconomic disparities in health and development underscores the need for more effective intervention strategies at all levels, including place-based interventions. To that end, advances in the science of early childhood development and its underlying biology offer the opportunity to launch a new era in community-based action that is driven by theories of change that target causal mechanisms linking specific neighborhood-level interventions to explicit child outcomes (77). The biology of adversity provides one of many potential starting points by providing a compelling rationale for developing more effective approaches to reduce community-level precipitants of toxic stress in young children, such as endemic neighborhood violence and the absence of safe places for parents to congregate.

Confronting the Complexity of Measurement

Among the many challenges that confound early childhood policy and practice, the assessment of developmental skills and the measurement of change over time are among the most complex.

In 2006, the US Congress commissioned the National Research Council (NRC) to review the status of early childhood assessment and recommend appropriate measures to evaluate the impacts of public investments in young children. The final committee report underscored the complexity of the assessment challenge and provided an extensive overview of the benefits and limitations of existing measures but avoided endorsement of a preferred battery of instruments (78).

In view of the limited inclusion of health outcomes in most long-term follow-up studies, the full economic returns on investments that reduce toxic stress in early childhood are likely to be even higher when medical costs are included in the analyses. Healthcare expenditures that are paying for the consequences of unhealthy lifestyles (e.g., obesity and tobacco, alcohol, and substance abuse) are enormous, and the costs of chronic diseases whose roots germinate early in life include many conditions that consume a substantial percentage of current state and federal budgets (79, 80). Measurements of incremental improvements in health outcomes—including the development of intermediate biomarkers of relative risk for later disease—should therefore be incorporated into all longitudinal evaluations to calculate the full return on investments in young children.

Without minimizing the NRC's call for caution in the evaluation of developing skills in young children, the emerging capacity to measure biomarkers of adversity that may indicate increased risk for later disease presents a far more complicated challenge. Although an extensive discussion of the range of biological assays that have been associated with adverse experiences is beyond the scope of this paper, there is a clear need to operationalize the concept of toxic stress and to identify valid and reliable measures of its parameters. Candidates that appear to be worthy of study include measures of inflammation, stress hormone levels, cardiovascular reactivity, telomere length, oxidative stress, neuroimaging techniques, and epigenetic modifications that reflect early prenatal or postnatal experiences and environmental exposures.

Recognizing the critical importance of informed consent, confidentiality, and protection from inappropriate labeling of young children, the incorporation of biological measurement into early childhood policy and practice must be approached with considerable caution and sensitivity. The need for shared decision making and joint ownership among scientists, practitioners,

local communities, and parents is essential. This is particularly important for research conducted in communities of color, where the history of efforts to incorporate biology into public policy is stained with multiple examples of stigmatization, exploitation, and worse (81–83). If pursued in a thoughtful and responsible manner, however, the judicious use of biomarkers offers the potential for enhanced capacity to document physiological "healing" in highly vulnerable children following the delivery of effective services, thereby providing near-term evidence of effective reductions in the risk for diseases that may not emerge until several decades later.

Moving Forward

The ability to catalyze the design, implementation, and scaling of significantly more effective intervention strategies for vulnerable, young children will require a fundamental cultural shift in the relations among science, policy, and practice. Two recent documents from the American Academy of Pediatrics (AAP) provide a striking example of how this shift might evolve. After reviewing extensive evidence of the link between early adversity and lifelong health impairments, a technical report concluded that many adult diseases should be viewed as developmental disorders and that the focus and boundaries of pediatric practice deserve new thinking (40). In an official policy statement, the AAP endorsed a developing leadership role for the entire pediatric community to "catalyze fundamental change" in early childhood policy and services focused on the need for creative new strategies to reduce the precipitants of toxic stress and to mitigate their negative effects on health and development (56).

Notwithstanding both the spirit and the substance of this bold message, the task of translating science and commitment into breakthrough impacts in health promotion, disease prevention, and early childhood development is a formidable one. To that end, the availability of a single, integrated knowledge base and shared theories of change that can be applied across multiple policy and service sectors offers greater promise for productive collaboration than the simple call to improve communication among agencies that are guided by diverse practices and disconnected historical precedents. Forward movement along this pathway will require an innovation-friendly environment that welcomes new ideas, a strong belief in the value of learning from failure, and a broad definition of evidence that includes well-established, scientific concepts and rigorously analyzed evaluation findings (both qualitative and quantitative), as well as benefit–cost data and the results of properly conducted, randomized controlled studies.

Finally, without understating the potential lifelong influences of early experience, it is essential that policymakers understand the concept of adult neuroplasticity. This is especially true for brain circuits that are specialized for selected aspects of learning, which can continue to make adaptations in response to new experiences after their sensitive developmental periods have passed (84–86). It is also important to note that changes in mature brain circuits require highly tailored inputs and focused efforts to secure maximal attention. Stated simply, building brain circuitry correctly from the beginning is easier and generally leads to better outcomes, but it is never too late to invest in remediation. The proposed emphasis on explicit capacity building in parents with limited education, described earlier in this paper, draws on these concepts, particularly as they apply to skills that are mediated by the prefrontal cortex.

The biology of human development is a rapidly moving scientific frontier, the medical case for preventive intervention to combat toxic stress is increasingly persuasive, and the moral imperative for action on behalf of children experiencing significant adversity is compelling. The time has come to build on the best of what current efforts are achieving and to incorporate the biological sciences into a new era of increasingly effective early childhood policy and practice.

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