

Toxic stress caused by adverse childhood experiences: the hidden epidemic

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ABSTRACT

Adverse childhood experiences (ACEs) are associated with negative consequences for physical and mental health. ACEs are defined as harmful experiences from conception to age 18. They generate chronic toxic stress when exposed to emotional or sexual abuse or a dysfunctional home.

ACEs produce “programming” on brain plasticity with immunoneuroendocrinological, cerebral, and epigenetic changes. The result is suboptimal development of physical, mental, and emotional abilities. This “programming” can be mitigated by resilience, family and social support. When faced with new stressors, psychological and physiological dysregulation will occur, exposing the individual to disease.

Between the ages of 0 and 17, 55.9% have had 1 ACE, and 30.6% have had ≥ 2 ACEs. The consequences are aggression, drug addiction, obesity, asthma, depression/anxiety, decreased resilience, juvenile recidivism, and suicide.

Pediatricians are the ones who can detect, prevent, and mitigate ACEs.

Keywords: *adverse childhood experiences; child maltreatment; child sexual abuse.*

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Adverse childhood experiences (ACEs) cause toxic stress. ACEs have scientific and social impacts; they increase the risk of health problems and mortality throughout life, but they can be prevented.¹ ACEs are defined as chronic or recurring harmful experiences throughout childhood up to age 18.

WHAT ARE ACEs?

There are 10 conventional ACEs, grouped into three domains: abuse (physical, psychological, and sexual), neglect (physical, psychological), and dysfunctional home (witnessing domestic violence, witnessing drug addiction and/or alcoholism, mental health problems, family member in prison, and parental separation or divorce). Conventional ACEs do not include other adversities to which children are exposed, which is why expanded ACEs were created, adding a fourth domain, social determinants: family relationships (lack of affection and family support), community stressors (crime, violence, and death in the neighborhood); economic problems (insufficient money, scarce resources—non-monetary); victimization (bullying, violent and non-violent crime, police harassment); peer relationships (peer pressure, death of friends, problems with friends and peers, violence with friends); discrimination (racism, religious); schooling (poor quality, insecurity at school, academic problems); health (teenage pregnancy, inadequate access to healthcare, personal illness); well-being and juvenile justice (experiences in temporary or foster homes and in the judicial system); and media/technology/mass media.²

HOW DO WE DETECT ACEs?

For adults, questionnaires are available to detect conventional ACEs, which are scored from 0 to 10, depending on the type of ACE. For children aged 0 to 17, expanded ACE questionnaires are used, which include conventional ACEs and add 7 to 9 social domains; the score ranges from 0 to 17 or 19.³ These questionnaires do not record which ACEs were experienced, but rather the total number of ACEs. The higher the score, the greater the risk of developing physical and mental health problems throughout life. The importance of the expanded ACE questionnaire lies in the fact that 72.9% of children had at least one conventional ACE, and 63.4% had at least one expanded ACE. Additionally, 49.3% had both types of ACEs, while 13.9% had only one expanded ACE, which the conventional ACE would not have

recognized. This indicates the use of expanded ACE questionnaires in pediatric patients.⁴

HOW DO ACEs WORK?

Through stress, which has three categories of response:

1. Appropriate response, which is normal and essential for development: there is an increase in heart rate, blood pressure, and hormone levels—for example, a child facing a fight with peers. When they are cared for, and have the affection of their family, the physiological response disappears if the child is no longer exposed to stress.
2. Tolerable response to stress. The physiological response is greater but limited by the loving care of the family. The brain and organs recover.
3. Response to toxic stress. Severe, frequent, and prolonged stress can be harmful to children and adolescents and leave long-term consequences.

In toxic stress, a three-level “programming” occurs in the brain plasticity and immaturity of children and adolescents in various physiological systems.

Immunoneuroendocrinological changes

Children with ACE have increased inflammatory activity (increased fibrinogen, CRP, C-selectin)⁵ and increased activity of the κ B nuclear factor that regulates the expression of proinflammatory cytokine genes.⁶ Chronic stress programs a proinflammatory phenotype with activation of Th1 lymphocytes and monocytes/macrophages. Patients with depression who have experienced ACEs in childhood exhibit elevated proinflammatory cytokines, including IL-6, IFN- γ , IL-1 β , and IL-8, and decreased anti-inflammatory cytokines, such as IL-4 and IL-10.⁷ Stressful situations caused by ACEs activate the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system.⁸ Cytokines activate the HPA axis through the hypothalamus, causing the adrenal gland to release cortisol, epinephrine, and norepinephrine. These hormones stimulate the inflammatory response of monocytes by releasing proinflammatory cytokines.⁹ Oxytocin, a neuropeptide involved in feelings of love, truth, justice, and security, is decreased in ACE.¹⁰

Brain changes

ACE produces anatomical changes in children under 16 years of age, which are observable on

nuclear magnetic resonance imaging: a decrease in the size of the amygdala, hippocampus, prefrontal cortex, and corpus callosum, as these areas are more vulnerable than other areas of the brain due to their high density of glucocorticoid receptors. Hyperactivity of the HPA axis has been linked to a decrease in these brain areas.¹¹ Elevated cortisol levels in response to toxic stress, as well as in non-stressful situations, in children with ACEs stimulate microglia, cells that perform neurological “pruning” and destroy cortico-limbic and cortico-striated connections during childhood and adolescence. The result is suboptimal development of physical, emotional, and cognitive abilities, with a greater response to situations that threaten children. These abilities are fundamental to ethical and healthy decision-making; their deficiencies jeopardize people’s quality of life and longevity.

Epigenetic changes

Frequent epigenetic modifications include DNA methylation and telomere shortening. These alterations result in stable changes in gene activity without altering the DNA sequence. ACE causes DNA methylation of genes related to immunity and those involved in the glucocorticoid receptor pathway, resulting in lower gene expression and a state of HPA axis hyperactivity.¹² These epigenetic changes can be transmitted to up to three generations if people who suffered ACE did not have the opportunity to heal and transcend.

We can imagine primitive *Homo sapiens*: from the moment they woke up, they were surrounded by stressful experiences and in a permanent state of “alert” fearing attack by other humans or animals. They had to think about feeding themselves that day; they could not think about the next day or their future. Their immune system was activated to heal their wounds, and their HPA system was activated to keep them alert. They did not live long. Over time, humans evolved personally and socially. The “programming” to which they were exposed was cushioned by resilience, family, and social support. However, humans who have suffered one or more ACEs will have a strong sensitivity to future stressful situations: chronic illness, death of a loved one, family disaster, serious socioeconomic situation, which produce psychological (depression/anxiety) and physiological (neuroimmunoendocrinological) dysregulation that will predispose them to disease (Figure 1).^{13,14}

WHAT IS THE PREVALENCE OF ACEs?

The greater the number of ACEs, the greater the risk of developing physical and mental health problems throughout life. Thus, a child with multiple ACEs will be at greater risk of facing developmental difficulties.

Among 17 337 adults, 64.4% had at least 1 ACE; 26% had 1 ACE; 15.9% had 2 ACEs; 9.5% had 3 ACEs, and 12.5% had ≥4 ACEs;¹⁵ 6.9% of men and 10.5% of women had ≥5 ACEs; 14.9% of adults with low levels of education had ≥5 ACEs vs. 8.7% of adults with high levels of education.¹⁶

In pediatrics, the Kaiser Permanente group (California) studied 7056 children and observed that ACEs increase between the ages of 3 and 13: 15% of 3-year-olds, 17.5% of 5-year-olds, 30.5% of 10-year-olds, and 33.8% of 13-year-olds had ≥1 ACE.¹⁷ In the US, 38.1% to 55.9% of children aged 0-17 have had ≥1 ACE; 15% to 30.6%, ≥2 ACEs; and 10.3%, ≥3 ACEs.¹⁸

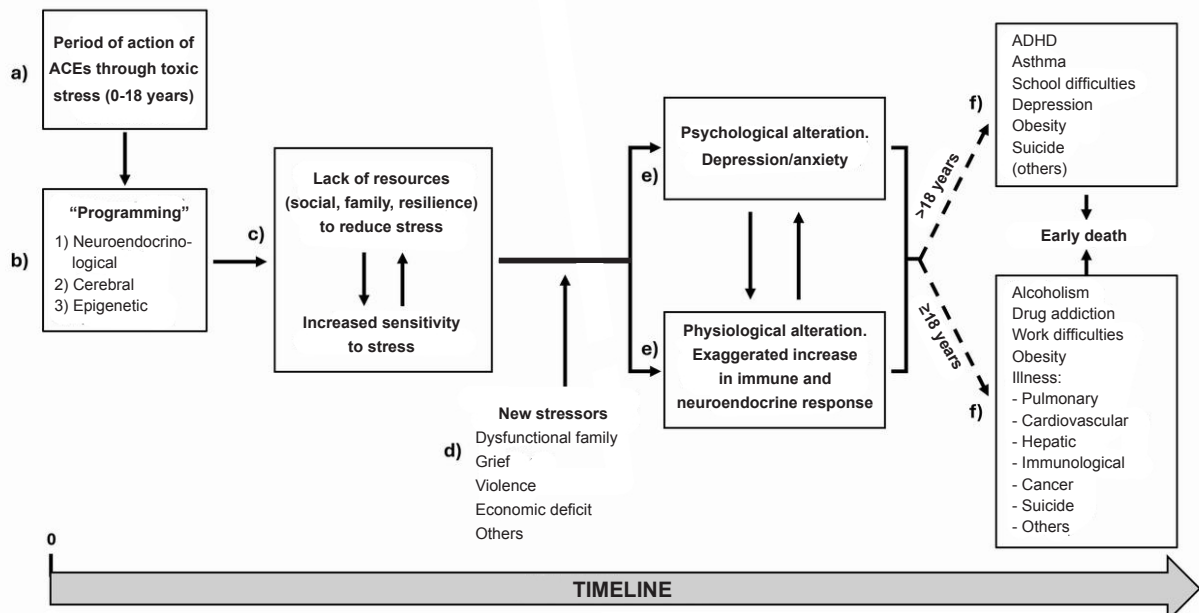
In Argentina, the Domestic Violence Office of the Supreme Court of Justice reports that, out of 13176 complaints filed in 2024, violence against children aged 0 to 17 accounted for 33%. Of 128 children aged 0 to 19, 50% suffered physical abuse; 30% were victims of sexual abuse; 10% were victims of neglect; and 3% suffered emotional abuse.¹⁹ In the Autonomous City of Buenos Aires, child abuse increased by 36% in 10 years.²⁰

ACE in pediatrics is as prevalent as other pathologies: anemia, hypertension, hypercholesterolemia, and developmental, emotional, and behavioral disorders. Pediatricians must be aware of them, take them into account, and be able to detect them.

WHAT ARE THE HEALTH IMPLICATIONS OF ACEs?

ACEs influence self-esteem and feelings of self-worth; they increase depression, anxiety, eating disorders, and rejection of health promotion programs,²¹ and cause developmental difficulties in children and adults. ACEs contribute to the perpetuation of cycles of poverty, violence, and family dysfunction, affecting entire generations.

Children who suffer ≥1 ACE develop maladaptive coping strategies without adequate family or social support, increasing the risk of social withdrawal, aggression, drug addiction, unhealthy relationships, difficulty regulating emotions and behaviors, learning disorders, asthma, obesity, psychiatric problems, decreased resilience, juvenile recidivism (crime), and

FIGURE 1. Effects of adverse childhood experiences over time

ACE: adverse childhood experiences; ADHD: attention-deficit hyperactivity disorder.

a) Action of ACE. b) Programming by toxic stress. c) Lack of resources to "buffer" stress. d) New stressors throughout life. e) Psychological and physiological reactivation. f) Lack of resources to reduce stress increases susceptibility and risk of disease in children, adolescents, and adults. Modified from references 15 and Res Pediatr Neonatol 6(3) RPN.0006382022. doi: 10.31031/RPN.2022.06.000638.

suicide.²²

Felitti showed that ACE has a dose-response relationship: the higher the number of ACEs, the greater the increase in pathologies. Patients with ≥ 1 ACE compared to 0 ACE have a 4 to 12 times higher risk of alcoholism, drug addiction, depression, and suicide attempts (2/3 of suicides are attributed to ACE); a 2 to 4 times higher chance of being smokers (the percentage of smokers with 0 ACE is 6%, but with ≥ 4 ACE it is 12%); a higher risk of sexually transmitted diseases; and a 1.4 to 1.6% higher chance of physical inactivity, obesity, and poor work capacity. It also increases the likelihood of developing cardiovascular disease, chronic lung disease, liver disease, autoimmune diseases, senility, early death, and suicide in adulthood.²³ ACEs are common and destructive.

WHAT SHOULD PEDIATRICIANS DO?

ACEs are underlying determinants of major public health problems. Understanding them enables us to identify and act. Healthy, safe, enriching relationships and sensitive childcare can counteract toxic stress. As ACEs are a fundamental cause of neurodevelopmental problems, in 2012, the American Academy

of Pediatrics recognized the critical role of pediatricians in preventing, detecting, and treating toxic stress.²⁴ Detecting ACEs accumulated during childhood makes it possible to identify children at risk of health problems in the medium and long term, as well as prevent the further spread of ACEs. Primary health care is ideally positioned to objectively assess ACEs by interacting with children and adolescents, as well as their families. These should play a "buffering" role for ACEs. Families would act as a "protective shield" against ACEs, thereby reducing toxic stress.

Since ACEs are predictors of antisocial behavior (physical abuse, antisocial behavior, loss of altruistic behavior), detecting ACEs during childhood can help reduce maladaptive behavior patterns, strengthening normal development in adolescence and adulthood.

SUGGESTIONS

- 1. Preventive actions.** Education and awareness about the consequences of ACEs for parents, teachers, and health professionals.
- 2. Incorporate them into primary care for detection.** Detection should be part of clinical practice and pediatric residents' training. However, only 4% of pediatricians in the US

ask about ACEs.²⁵ It is crucial to remember that ACEs-related behavior in childhood is difficult to notice and easy to misinterpret.

3. **Early interventions with a multidisciplinary approach.** Psychologists, educational psychologists, lawyers, social workers, and pediatricians can collaborate to mitigate the short- and long-term adverse effects.
4. **Strengthening support networks.** Psychosocial support programs, family therapy, and support groups.
5. **Incorporate ACEs into public health policies.** To prevent them and to promote the development of resilience.

In conclusion, the health of children, adolescents, and adults depends on having had a safe and healthy childhood. ■

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