

Stress and asthma during childhood and adolescence

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Practice Points

- Asthma has a serious impact on public health worldwide, with greater impact in developing countries.
- Allergen exposure does not explain the global prevalence of asthma, leading to alternative paradigms for understanding the disease, such as stress.
- With advances in the field, the homeostasis concept to explain stress responses is being replaced by allostasis and allostatic load.
- As the brain determines what is stressful or not, psychosocial factors such as parental models, low socioeconomic status and daily experiences, play an important role in allostatic load.
- The hypocortisolism hypotheses should explain the paradox between asthma and stress.
- Negative events increase the risk of asthma exacerbation not only immediately but also 5–7 weeks later.
- Stress in asthmatic children and adolescents may impact their school performance.
- Asthma can be viewed as a stressor – not only the children but the whole family need to adapt.
- Limitations imposed by the disease, such as isolation, negative experiences and stress, may increase the psychological vulnerability of asthmatic patients and their families.

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SUMMARY This article reviews interrelations between stress and asthma in children and adolescents, and the impact of the disease in the family system. A nonsystematic review was conducted searching PubMed, Medline and Scielo databases. Specific models have been developed to understand how hormones like cortisol may affect asthma in chronic stress. Various articles point to an association between asthma and stress during childhood and adolescence. Restrictions are not exclusively related to asthma patients but also exist in a social and family context, with parents having an important role in the management of the disease. There is strong evidence linking stress to asthma. Incorrect parental management of the disease may also be a source of stress for children and adolescents with asthma. Mothers, in particular, deserve careful attention, since they are usually the main caregivers. Emotional factors not only for the patient but for the entire family must be viewed closely with specific health programs designed to reduce the impact of the disease.

Asthma is the most common chronic disease in children and a serious public health problem worldwide. In developing countries, the impact of asthma is even larger, evidenced by the greater number of asthma-related deaths [101].

Allergen exposure, which was commonly considered to be the etiology of asthma, does not seem to be the main factor or explain the global patterns of the disease. The inter- and even intra-individual phenotypic variability of its clinical expression, coupled with an absence of exclusive biological or physiological markers make asthma a complex disease from the viewpoints of both its pathogenesis and etiological factors [1].

The speed of growth of the global asthma prevalence seen in the last decades cannot be explained by genetic factors. It may be related to other factors, such as changes in the mother's diet, smaller number of infections in breastfed infants, higher use of medications and smaller family size. Urban environment, pollution and lifestyle may also be associated with asthma, especially in early life when the lungs and immune system are developing [2]. Research in the field also describes interactions between stress, emotions, family factors, socioeconomic status and daily life triggers [3]. These factors lead to the questioning of the traditional risk factors and promote the construction of alternative paradigms for understanding the disease, including stress [4].

Different epidemiological studies have shown associations between asthma in children and adolescents and stress-related variables, such as indices of anxiety, depression and behavioral problems [5]. Nevertheless, the interactions between psychological and environmental factors are not

yet fully known, and more studies are needed to clarify their role in childhood asthma [6].

Stress, emotions, family factors, life events, early-life environment, socioeconomic status and psychosocial factors are receiving increasing attention in asthma research [3]. Depressive symptoms, loneliness, low school performance and anxiety have been associated with children and adolescents with asthma. Although it is an illness of low lethality, asthma impacts include not only the patient but their whole family, promoting rearrangements of relationships inside and outside the family system, with direct and indirect costs [1].

Stress: from a biological to psychosocial perspective

Claude Bernard published the first studies on stress in the second half of the 19th century. Walter Cannon had already used the term vaguely in 1935, but in 1936, the endocrinologist Hans Selye suggested using the word 'stress' to mean the syndrome caused by many adverse agents, and so the term was incorporated in the medical literature [7].

Initial studies with animals showed Selye that their bodies responded similarly to stressful stimuli, regardless of the nature of the damage, representing an effort to return to the body's internal homeostasis, to adapt to changes. He named this response 'general adaptation syndrome', and later, 'stress' [8]. Although, at first, Selye did not consider the psychological factors of stress important, they were later included in his work, and other authors, such as Lazarus and Folkman, made important contributions

to the concept, such as the inclusion of cognitive and coping variables to explain the different individual responses to stress [7].

Currently, stress is considered a complex response of the body involving physical and psychological reactions, and occurs when the body needs to adapt to situations and events that threaten its physical and mental stability. When intense or prolonged, stress-induced physiological changes may promote the manifestation of many symptoms and diseases. These changes are not only immediate, but also gradual, and may be exacerbated by external factors (e.g., adverse events or environmental changes) and/or internal factors (e.g., temperament, worldview and beliefs [9]).

With the advance of science and research in the field, the homeostasis concept to explain stress response has been replaced. Instead of understanding body parameters as fixed points, as in homeostasis, McEwen and Seeman argued that regulatory levels are variable and that their medium points reflect the changes in response to environmental challenges, proposing the term allostasis to understand how to achieve stability through change [102]. In the allostasis concept, the brain is the central mediator determining what is stressful or not, parameters vary and variation anticipates demands. When the need to cope with events is prolonged or excessive, with inefficient turning on and shutting off of body responses, the result is wear and tear on the body, a process called allostatic load. The allostasis concept helps to understand the effects of stress on health [10].

Psychosocial factors play an important role in allostatic load. Experiences, social economic status and parental models, among others, interact with temperament and genetics to influence the way we see the world. Mood and anxiety disorders are particularly influenced by these factors. Adverse early childhood experiences can especially modify the responsiveness of allostatic systems with long-term effects on health, as nervous, endocrine and immune systems are not matured enough at this time [102].

Stress in children & adolescents

Child and adolescent stress is similar to adult stress, possibly having physical and psychological consequences when excessive. Some of its most common symptoms are anxiety, anguish, depression, abdominal pain and muscular tension [11].

During development, children and adolescents face many tense situations and life changes that they are not yet mature enough to cope with [12]. Some examples include traumas, accidents, changing schools, peer rejection, parental separation, body and hormonal changes, poor family relations, poverty, excessively demanding parents and teachers, and personality-related factors, such as shyness, self-consciousness and anxiety [13].

Many children and adolescents with physical, psychological and behavioral problems are in fact experiencing stress. The stressing agent is rarely approached, and medical care is only provided after the manifestation of one or more symptoms. Diagnosis is also difficult, since stress-related symptoms may be caused by many other diseases, and younger children in particular are rarely capable of describing what is causing them stress [11,13].

Interrelation between stress & asthma

The interrelation between emotions, stress and asthma has been proposed since Hippocrates [14]. Although there is considerable interindividual variability, systematic studies confirmed this association, with 15–25% of asthma patients listing stress as a trigger for asthma attacks [15].

Approximately half of asthma cases are diagnosed before the third year of age and two-thirds are diagnosed before the fifth year of age [16]. Therefore, in addition to genetic susceptibility, the fact that asthma occurs in early childhood suggests the existence of adverse events in the first stages of life, including intrauterine life, an important period for the development of the child's immune and neuroendocrine systems [17].

The perinatal programming concept has been proposed to explain how uterine characteristics and early life stages can organize or influence the physiological responses of a child, regardless of genetic susceptibility [17].

Maternal stress promotes placental secretion of corticotropin-releasing hormone, making the fetal hypothalamic–pituitary–adrenal (HPA) axis secrete glucocorticoids, which may increase the child's future susceptibility to disease by influencing the immune system and CNS. The quality of parental postnatal care also affects regulation of the HPA axis. High cortisol levels in response to stress have been found in children at high risk of atopic diseases. Conversely, other studies describe hyperresponsiveness of the HPA axis and low levels of cortisol in response to stress, leading the

authors to conclude that children predisposed to asthma or allergies have an initially hyper-responsive HPA axis that becomes chronically hyperresponsive as the child develops [17].

Chen and Miller developed a model based on the hypocortisolism hypothesis to explain the paradox between asthma and stress [18]. Chronic stress not only reduces the number of cortisol receptors, but also their sensitivity, making the body more resistant to the anti-inflammatory properties of glucocorticoids. This same counterregulatory process occurs after prolonged exposure to high levels of epinephrine and norepinephrine, which reduces the sensitivity of adrenergic receptors in the lungs and lymphatic tissues, and increases expression of Th2 lymphocytes, which produce cytokines related to the beginning and maintenance of the inflammatory process.

Buske-Kirschbaum *et al.* found a significant association between cortisol levels and asthma status in children submitted to different stressing tasks, such as public speaking or solving math problems before an audience, suggesting that the adrenocortical system of asthmatic children is less responsive [19].

General practitioners are aware of the relationship between negative life experiences and asthma exacerbation. Serious negative events in the lives of asthmatic children, especially when combined with chronic stressors, such as poverty and mental illness or alcoholism in the family, among others, increase the likelihood of new asthma exacerbations. The monitoring of peak expiratory flow measurements and asthma symptoms has suggested that negative events increase the risk of asthma exacerbation not only immediately (1–2 days later), but also 5–7 weeks later [20].

Associations between asthma and many symptoms indicative of stress, such as irritability, restlessness, sadness, isolation and somatic complaints, have been described in the literature [21,22]. Depressive emotional states in particular impact on the autonomic nervous system, with a preponderance of vagal over sympathetic response (vagal bias) altering airway function in asthmatic patients [23]. Emotional arousal such as laughter or crying has also been associated with airway constriction in asthma attacks [24].

Recently, Mendes *et al.* used the Childhood Stress Scale to assess stress frequency in 54 children and adolescents aged 7–14 years seen at a pediatric pneumology outpatient clinic

in the city of Rio de Janeiro, Brazil [25]. Stress frequency was 38%, which is higher than that found by studies with Brazilian schoolchildren. Some of the study findings that stand out are the significant associations between stress in asthmatic patients and school difficulties, low socioeconomic level and duration of symptoms. Regarding school difficulties, absences resulting from constant medical visits and treatment complications may prevent the child from keeping up with the class and cause anxiety, excessive concern, sleeping difficulties, difficulties to develop abstract-thinking, difficulties to organize school material and, consequently, learning difficulties.

Restrictions imposed by the disease, such as avoiding running, jumping and physical activities, or even the social exposure brought about by some symptoms, such as tiredness and coughing, may lead to socializing difficulties and isolation. Children and adolescents may feel excluded and different, which may induce feelings of shame, excessive shyness and irritability, and affect their performance [25]. Depression symptoms may be elicited by the daily routines imposed by the disease and by the feeling of awkwardness experienced in social and family relations. A chronic disease with visible symptoms, such as breathlessness, and possibly fatal consequences may cause anxiety [25]. The literature also describes important relationships between severe asthma attacks and post-traumatic stress disorder in children [26].

The knowledge children and adolescents acquire from their experience dealing with asthma may facilitate symptom management and lead to better attack predictability and control, reducing the impact of the disease on emotional and physical health [27]. The existence of adaptation mechanisms suggests that children and adolescents who have had asthma for a shorter period experience more stress than those who have had the disease for a longer period [25,28].

Studies have reported that female children and adolescents with asthma are more likely to experience stress and emotional and behavioral disorders than their male counterparts. It is possible that this is related to their assumed greater ease of expressing their feelings [25,28].

Asthma is an important source of anxiety for the child and parents since it commonly begins during childhood and is chronic and potentially fatal during an attack. Negative events experienced by children with asthma,

such as hospitalizations and emergency room visits, and the impossibility of experiencing some important events for the development of their social skills may have a negative impact on their quality of life and the development of their social competence. This skill is essential for appropriate functioning in adult life [29].

Asthma impact on the families of children & adolescents

Parents project dreams and expectations on their children that may be temporarily incompatible with the disease, so children may experience an emotional setback [103]. The emergence of a chronic disease in the family forces all family members to change many of their habits and affects not only their bodies, but also their minds [30].

When a child is diagnosed with asthma, the parents become responsible for the long-term management of a chronic condition characterized by unpredictable and irregular attacks. Asthma affects not only the child but compromises the entire social context of the child. Therefore, the parents have an important role in the management of childhood asthma [31].

The limitations imposed by the disease in children mainly affect the parents, since they need to adapt and meet the needs of the affected child. The degree of disability caused by the disease and the way the parents deal with it will determine its impact on the family. Flexibility to adapt to the new situation is needed since it will change the daily routine [1].

Chronic disease is a stressful situation with a significant impact on the family. Parents must achieve at least three goals:

- Manage the disease or help the child to manage the disease;
- Help the child to deal with the reality of the disease and, at the same time, encourage the child to develop as normally as possible;
- Meet the two previous objectives without causing too much disruption to the family functioning [32].

Since asthma is a chronic disease, it may be seen as a stressor that affects the normal development of the child and also the relationships between the family members [2]. Mothers are more involved in the treatment process and are more often the ones who take the child to the hospital and interact with the healthcare team

that treats the child [33]. On average, mothers are present in eight out of every ten hospital visits. Given their greater involvement, mothers are more vulnerable to the different stressors associated with this situation, and of all the family members, they are the ones who have to make the most drastic changes to their lives [1].

Parents experience stress and tension when they reflect on their asthmatic child's special needs. Some of the stress factors include:

- Regular use of medications, since some medications may have important side effects, such as tachycardia, trembling and vomiting;
- Regular visits to physicians, other healthcare professionals and healthcare facilities;
- Inability to practice many sports;
- Daily pain and/or discomfort;
- Poor school attendance;
- Limitations imposed by extensive and complex therapeutic programs;
- Continuous need of care;
- Changes in the family routine [29].

Other adjustments are also needed, such as home adaptations and removal of carpets, plants, curtains and pets, since home hygiene is a preventive measure. Asthma may also affect healthy siblings, making them feel neglected, and asthmatic children, often making them feel disabled and awkward, and excluded from activities incompatible with the disease (e.g., certain games) [103].

Financial problems caused by therapeutic needs, such as frequent emergency room visits, and parental absences from work and risk of termination are also frequent. After some time, caregivers may also experience an emotional overload, in addition to the financial burden [34].

The isolation imposed by the disease on the child and family is also a source of stress for interpersonal relationships. The child's freedom and indoor and outdoor activities are limited to prevent asthma attacks triggered by physical effort or sudden weather changes, since repeated hospitalizations partly distance the child from the social and school environments. Attitudes of relatives or friends may further isolate the affected family either because they do not want to be disturbed, or do not know how to help or act around an asthmatic child [35].

The negative experiences and the stress associated with the disease and its treatment may make the patients and their families more vulnerable to psychological problems [29].

Conclusion

The child and adolescent with asthma should not only be viewed from the biological and environmental viewpoints, but also from the psychological and social viewpoints. Today, healthcare professionals are much more likely to recognize that stress may trigger or stem from asthma, but there is still a lot to do.

Understanding asthma and treating asthmatic children requires psychological interventions to promote identification of stressors and verification of their intensity. In this context, the family is essential. Since the home is the first mediator of experiences, it is capable of mitigating or exacerbating the impact of different stressors, influencing the disruption caused by asthma. The existence of family conflicts, weak family bonds and low levels of social support may hinder the ability of asthmatic children to adapt.

Children's and adolescents' knowledge of asthma acquired from their experience with the disease may facilitate symptom management, improve attack predictability and control, and reduce the impact asthma has on their emotional and physical health. Furthermore, identification of the child's and parents' concerns may lead to new treatment plans to address them.

Incorrect parental management of the disease may also be a source of stress for children and adolescents with asthma. Mothers in particular deserve careful attention, since they are usually the main caregivers.

Poor school performance of asthmatic children with stress indicates the need of a multidisciplinary intervention that includes professional education [25].

Misinformation and ignorance about the disease require the creation and implementation of health education strategies that help to prevent attacks and promote treatment adherence. The impact of stress on the daily lives of children and adolescents with asthma demands interventions and public policies that address these factors with the inclusion of a psychologist in healthcare teams and programs to help clinicians identify stress in these patients.

Future perspective

Although health programs that integrate asthma education with drug therapy increased from the 1980s onwards, few studies have been developed to understand the impact of psychotherapy on asthma patients' lives [36]. Cognitive-behavioral therapy has proven its efficacy in helping asthmatic adult patients with solving problems, adaptive behaviors, identifying and restructuring negative automatic thoughts and asthma-specific panic fear [36,37]. Specific cognitive-behavioral therapy interventions with children and adolescents should be constructed.

Human behavior and living is complex. Nowadays, asthma research is not only looking for specific genes or agents in the etiology of the disease. 'Interactions', 'multidiscipline' and 'complexity' are the keywords, with epigenetics enhancing interest in recent years. The study of stress is an important part of this intricate subject.

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