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Beyond endocrine features in non-classical congenital adrenal hyperplasia: a narrative review of psychoneuro-social perspectives in pediatric and adolescent patients

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Abstract

Non-classical congenital adrenal hyperplasia (NCCAH) is a late-onset, milder form of 21-hydroxylase deficiency marked by adrenal androgen excess. While endocrine aspects are well described, psychoneuro-social outcomes in pediatric and adolescent patients remain less clearly defined. A literature search of MEDLINE (PubMed) was conducted in July 2025 using "Non-Classical Con genital Adrenal Hyperplasia" with terms related to mental health, cognition, social adaptation, gender identity, sexual orientation, and heterozygous carriers. In females, androgen excess is frequently associated with anxiety, depression, body image concerns, and increased prevalence of gender nonconformity or non-heterosexual orientation, although most maintain a female gender identity. Males generally present fewer gender identity concerns, with inconsistent evidence for higher externalizing behaviors. Neurocognitive outcomes are variable, with occasional subtle deficits in working memory, executive function, or attention, alongside possible strengths in visuospatial tasks. Health-related quality of life in adequately treated pediatric NCCAH is generally comparable to that of healthy peers, though age-specific psychosocial vulnerabilities may occur. Social difficulties, particularly among females, may involve stigmatization and reduced peer acceptance. Heterozygous CYP21A2 carriers are usually asymptomatic and do not exhibit significant psychoneuro-social burden; interventions are not routinely indicated unless hyperandrogenic symptoms are present. Conclusions: Psychoneuro-social effects of NCCAH are heterogeneous and shaped by sex, age, and clinical presentation. An individualized, multidisciplinary approach integrating endocrinology, psychological support, and social resources is recommended. Longitudinal studies are needed to clarify long-term trajectories and optimize targeted interventions.

What is Known:

- *NCCAH is a common form of CAH with mild androgen excess.*
- *Its endocrine features are well described, but psychosocial aspects are often overlooked.*

What is New:

- *This review highlights cognitive, emotional, and social challenges in pediatric NCCAH.*
- *Sex-specific patterns and the role of early diagnosis in improving outcomes are emphasized.*

Keywords: Non-classical congenital adrenal hyperplasia · 21-hydroxylase deficiency · CYP21A2 · Heterozygous carriers · Pediatric endocrinology · Psychoneuro-social outcomes · Quality of life

Abbreviations

ADHD	Attention-deficit/hyperactivity disorder
CAH	Congenital adrenal hyperplasia
DSDs	Disorders of sex development
HPA	Hypothalamic-pituitary-adrenal
HRQoL	Health-related quality of life
NCCAH	Non-classical congenital adrenal hyperplasia
PCOS	Polycystic ovary syndrome
PedsQL™	Pediatric Quality of Life Inventory

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Extended author information available on the last page of the article

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A Message from the Executive Director



Dear friends,

As I reflect on the past year, I am reminded of what makes CARES Foundation so special: the people who make up our community and the connections that remind us no one has to face CAH alone. A diagnosis of congenital adrenal hyperplasia (CAH) can bring fear, uncertainty, and countless questions. At CARES, we are committed to ensuring that every person affected by CAH feels understood, supported, and connected.

This year, we created new opportunities to bring our community together through Family Fun Days at Centers of Excellence, our pilot CAH Adult Patient Retreat, and the expansion of our CAH Awareness Walks. These programs help patients and families connect with others who understand their experiences. Sometimes, a simple conversation or shared experience can make all the difference, reminding someone they are not alone.

While connection remains at the heart of our work, advancing research and improving care are equally essential to our mission. We remain committed to supporting scientific and medical research, partnering with researchers and clinicians, and ensuring that patients' needs and experiences help guide the future of CAH care.

Looking ahead to 2027, we are focused on addressing important unmet needs in our community. Our priorities include providing better tools for the transition from pediatric to adult care, expanding support for mental health and emotional well-being, and bringing education to patients, caregivers, and medical professionals in communities where CAH expertise and resources are limited.

These goals are ambitious, but we can achieve them together. CARES cannot do this work alone. To our donors, volunteers, medical professionals, patients, families, and advocates, thank you for your generosity, dedication, and belief in our mission. Your partnership allows us to reach more people, strengthen our programs, and create meaningful change.

As we approach the end of the year, I ask you to consider making a gift to CARES Foundation. Every contribution helps us expand education, support research, connect patients and families, and address unmet needs. Your generosity is an investment in a stronger, healthier, and better-supported future for everyone affected by CAH.

It is a privilege to serve this community, and I am continually inspired by the strength and compassion of the people who make CARES what it is. Thank you for being part of our family and helping us turn hope into action.

From our family to yours, I wish you a happy and healthy 2027, filled with hope, connection, and continued progress. Together, we can build a future in which no one faces CAH alone.

With heartfelt gratitude,



Dina M. Matos
Executive Director

(continued from page 1)

Introduction

Congenital adrenal hyperplasia (CAH) encompasses a group of autosomal recessive disorders resulting from enzyme deficiencies that impair cortisol biosynthesis in the adrenal glands [1].

The most common form, 21-hydroxylase deficiency, accounts for approximately 90–95% of CAH cases and can present in classical or non-classical forms depending on the severity of enzymatic impairment [2]. While classical CAH may manifest in infancy with adrenal insufficiency in both sexes and ambiguous genitalia in affected females, non-classical CAH (NCCAH) has a milder phenotype and typically presents later in childhood, adolescence, or even adulthood. NCCAH is often diagnosed incidentally or during the evaluation of symptoms such as premature pubarche, hirsutism, menstrual irregulari ties, or unexplained infertility in adults [3].

NCCAH is caused by mutations in the CYP21A2 gene, leading to partial enzyme deficiency and consequent androgen excess. Unlike classical CAH, individuals with NCCAH usually retain sufficient cortisol production to prevent adrenal crises, but they may experience significant androgen driven effects that impact growth, pubertal development, and metabolic health. In females, symptoms such as hirsutism, acne, menstrual disturbances, and virilization can affect self esteem and social interactions [4]. Males with NCCAH may exhibit subtle symptoms such as early beard growth, accelerated bone age, or subclinical testicular adrenal rest tumors that may contribute to future fertility concerns [5].

The prevalence of NCCAH varies by ethnicity and population genetics, with estimates ranging from 1 in 200 to 1 in 1000 individuals in Caucasian populations, though it is more common in certain ethnic groups such as Ashkenazi Jews, where the carrier frequency is significantly higher [6]. Given its autosomal recessive inheritance, many individuals may be asymptomatic heterozygous carriers, raising questions about potential subclinical effects on psychological and social well being even in those without overt NCCAH symptoms [7].

From a psychological perspective, NCCAH presents unique challenges, particularly in females, where androgen excess can lead to concerns related to body image, gender identity, and emotional well-being. Studies have suggested that individuals with NCCAH may be at increased risk for anxiety, depression, and social withdrawal, potentially due to the interplay between hormone exposure and psychosocial stressors [8]. Furthermore, the impact of androgens on brain development raises questions regarding potential neurocognitive differences in affected individuals, including alterations in executive functioning, attention, and behavior [9].

Socially, children and adolescents with NCCAH may face difficulties related to gender expectations, peer interactions, and self-perception. Early androgen exposure can influence play preferences, career interests, and even sexual orientation in some cases, contributing to a complex psychosocial profile [10]. Additionally, the visible physical manifestations of androgen excess, such as hirsutism and acne, may lead to stigmatization, bullying, and reduced self-confidence, particularly in adolescent females [11]. In males, while increased androgens may confer some advantages in terms of social dominance and competitive behaviors, the long-term psychosocial implications remain less well studied [12].

Another important consideration is the experience of heterozygous carriers of CYP21A2 mutations. While traditionally considered asymptomatic, emerging evidence suggests that some carriers may exhibit subtle endocrine and metabolic differences, raising the possibility of minor psychological or neurodevelopmental effects [13]. Carriers may have slightly altered androgen levels, which could impact mood regulation, stress response, and cognitive processing [14].

Understanding these nuances is critical for a comprehensive approach to NCCAH and related conditions. This review aims to synthesize available evidence on the psychological, neurocognitive, and social functioning of children and adolescents with NCCAH, and to identify potential risk and protective factors across biological and psychosocial domains.

Methods

We performed a narrative review of MEDLINE (PubMed) in July 2025 using the query: (“non-classical congenital adrenal hyperplasia” OR “NCCAH” OR “nonclassic CAH”) AND (psych* OR mental OR anxiety OR depression OR cognition OR neurocognitive OR “executive function” OR social OR “quality of life” OR “gender identity” OR “sexual orientation” OR “heterozygous”). We focused on pediatric and adolescent populations (0–18 years) and included studies reporting psychoneuro-social outcomes. Reference lists of key reviews were hand-searched. Data were qualitatively synthesized due to heterogeneity of designs and outcomes. The main characteristics of the studies assessing psychoneuro-social outcomes included in this review are summarized in Supplementary Table S1. Limitations include potential publication bias and variability in diagnostic criteria for NCCAH and carrier status. By addressing the psychological, cognitive, and social dimensions of NCCAH, this work seeks to provide a holistic understanding of the condition and inform clinical approaches to improving patient outcomes (Table 1).

Psychological implications, neurocognitive outcomes, social adaptation, and quality of life in NCCAH

Mental health disorders

Several studies and registry-based data have shown that females with NCCAH have an increased prevalence of psychiatric disorders, particularly stress-related and adjustment disorders, as well as alcohol use disorders. This risk appears more pronounced in individuals with more severe genotypes, yet remains elevated in NCCAH patients compared to unaffected controls [2, 15]. Clinical signs of androgen excess—such as hirsutism, acne, and voice deepening— have been linked to negative body image, social withdrawal, and avoidance of romantic or sexual relationships, in addition to a heightened risk of depressive and anxiety symptoms [1, 16, 17]. The Endocrine Society has emphasized that diminished quality of life and greater psychosocial burden are more common in females with CAH, including the non classical form, than in the general population [2].

In males with NCCAH, evidence of increased externalizing behaviors—such as impulsivity, aggression, hyperactivity, risk-taking, and conduct-related problems—is limited and

Table 1 Proposed psychosocial care recommendations for pediatric and adolescent patients with non-classical congenital adrenal hyperplasia (NCCAH)

Recommendation	Rationale	Suggested Implementation
Early involvement of mental health professionals with expertise in disorders of sex development (DSDs)	Ensures timely identification of psychological, social, and family concerns; promotes holistic management	Referral to psychologists or psychiatrists familiar with DSDs soon after diagnosis
Psychoeducation for patients and families	Enhances disease understanding, reduces anxiety, and promotes adherence	Age-appropriate education sessions addressing NCCAH pathophysiology, symptoms, and management
Individual and family counseling	Addresses body image concerns, stigma, and emotional distress from androgen excess	Sessions focused on coping strategies for visible symptoms (e.g., hirsutism, acne, menstrual irregularities, premature pubarche, gynecomastia)
Support for coping with chronic illness	Improves resilience and self-esteem; mitigates school and peer relationship challenges	Development of personalized coping plans and collaboration with school personnel
Facilitation of peer support and patient/family networks	Reduces isolation, fosters shared experiences and mutual support	Connection to patient advocacy groups, moderated peer meetings, or online communities
Routine psychosocial screening	Enables early detection of mental health or adjustment problems	Use of validated screening tools at regular intervals during follow-up
Low threshold for psychological or psychiatric referral	Prevents escalation of mental health concerns; ensures early treatment	Prompt referral when screening indicates emerging symptoms or when family expresses concern
Interdisciplinary care model	Integrates endocrinology, psychology, and social support for optimal outcomes	Regular multidisciplinary team meetings and coordinated care planning

**CARES Foundation does not consider CAH, in and of itself, to be a disorder of sex development (DSD). We recommend referral to a mental health professional with specific expertise in CAH.*

less consistent than in females. The majority of males with NCCAH are asymptomatic, and existing studies do not consistently report a significant increase in these behaviors when compared to control groups. However, some data suggest the presence of cognitive complaints and higher levels of autistic traits in males with CAH as a broader category [16, 18]. Currently, the literature does not clearly support a causal relationship between androgen-driven neuroendocrine alterations and externalizing behavioral outcomes in males with NCCAH.

Gender identity and sexual orientation

Females with NCCAH demonstrate a higher frequency of gender nonconforming behaviors, a modestly elevated—though still overall low—incidence of gender dysphoria, and an increased prevalence of same-sex attraction when compared to the general female population. These patterns are believed to result from mild prenatal androgen exposure, which is thought to influence gender-typical behaviors and aspects of sexual orientation in a dose-dependent manner. Empirical evidence consistently indicates that females with NCCAH tend to exhibit more traditionally male-typed preferences and behaviors, including interests aligned with male dominated careers and recreational activities. Additionally, they are more likely to report non-heterosexual orientation compared to unaffected peers, although the majority continue to identify as both female and heterosexual [19–24]. Importantly, despite the observed behavioral variations, the prevalence of gender dysphoria remains low, and most affected individuals retain a female gender identity [2].

Conversely, males with NCCAH do not appear to diverge significantly from unaffected males in terms of gender identity or sexual orientation. Current evidence suggests that prenatal and postnatal androgen exposure in these individuals does not correlate with increased rates of gender nonconformity or same-sex attraction [17, 25].

Cognitive function and executive processing

While classic forms of CAH have been associated with a masculinized cognitive profile—most notably enhanced visuospatial abilities—females with NCCAH do not consistently exhibit this cognitive shift. In contrast, some studies suggest a relative advantage in domains typically favoring females, such as episodic memory and emotion recognition, rather than in spatial performance [26].

Neuropsychological assessments in individuals with CAH, including those with milder phenotypes, have identified specific impairments—when present—in areas such as visual working memory, executive functioning, and attentional control, whereas general intellectual ability and verbal skills tend to remain preserved [27–29]. Although several of these studies included mixed cohorts or predominantly classical CAH, their applicability to NCCAH remains limited, and findings should therefore be interpreted cautiously. Adolescent females with CAH, including NCCAH, have been reported to perform less well than unaffected peers on tasks assessing visual memory span and free recall, with delayed diagnosis correlating with poorer memory performance [28]. Neuroimaging studies have revealed structural alterations in cortical regions implicated in executive functioning and working memory, particularly the prefrontal and parietal cortices, which may provide a neural basis for these observations [29, 30]. Nevertheless, the degree of impairment is typically mild and marked by considerable interindividual variability. The “brain fog” or reduced attentional efficiency occasionally reported in females with NCCAH may partly reflect secondary psychological distress rather than direct androgenic effects, as this symptom is rarely described in males.

Cognitive outcomes in NCCAH are modulated by several factors, including disease severity, age at diagnosis, cumulative exposure to glucocorticoid therapy, as well as educational, social, and environmental influences [27, 28, 31]. Earlier diagnosis and appropriately tailored medical management are generally associated with more favorable neurocognitive profiles [31]. Deficits in executive functioning and working memory may contribute to academic difficulties and hinder social adaptation, thereby amplifying the psychological burden already documented in females with NCCAH—such as mood disturbances, anxiety, and body image dissatisfaction. In contrast, current data do not demonstrate consistent cognitive differences in males with NCCAH.

Taken together, available studies reveal inconsistent findings regarding cognitive performance in NCCAH, reflecting significant methodological heterogeneity. Variability in diagnostic criteria, age at diagnosis, hormonal control, and treatment regimens—along with differences in test batteries and small sample sizes—likely contribute to divergent results. Socioeconomic background, parental education, and comorbidities may further confound these associations. Overall, the evidence supports normal cognitive functioning in most patients but highlights the need for standardized, longitudinal assessments.

Neurodevelopmental and mood disorders

There is no robust evidence for an increased prevalence of neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD) in individuals with NCCAH, particularly in males. Large-scale cohort and registry-based studies have not consistently demonstrated a significant rise in ADHD or related neurodevelopmental disorders among males with NCCAH when compared to control populations. Nevertheless, certain subgroups of males with CAH, particularly those diagnosed later in life, have shown elevated rates of psychiatric comorbidities, including psychotic disorders and substance use disorders [18, 32]. Additionally, a recent Mendelian randomization analysis has suggested a potential causal link between CYP21A2 deficiency and increased risk of autism spectrum disorder; however, this association is not specific to NCCAH and requires further investigation and replication in targeted studies [33].

With respect to mood disorders, the current body of evidence does not indicate a consistent elevation in conditions such as dysthymia or bipolar spectrum disorders in individuals with NCCAH. Instead, the literature more frequently reports increased rates of anxiety, depression, and adjustment-related psychopathologies, particularly among females. Proposed pathophysiological mechanisms include chronic androgen excess and impaired cortisol biosynthesis, which may influence central dopaminergic and serotonergic pathways, thereby affecting mood regulation, executive functioning, and attentional processes [1, 34–37]. However, direct and specific associations between these hormonal alterations and defined neurodevelopmental or mood disorders in NCCAH remain hypothetical and unconfirmed by robust empirical data. Moreover, most data on psychiatric comorbidities derive from classical CAH or unstratified cohorts; evidence specific to NCCAH is still scarce and requires confirmation in well-defined pediatric samples. The heterogeneity of reported emotional outcomes may arise from multiple factors, including variation in disease severity, hormonal control, and age at diagnosis. Differences in glucocorticoid treatment duration, psychological assessment tools, and sociocultural context can also influence results. Consequently, comparisons across studies are challenging, and findings should be interpreted cautiously.

Peer relationships and social competence

Hormonal imbalances and physical manifestations associated with NCCAH can adversely affect peer interac tions and social functioning during childhood and ado lescence, with a more pronounced impact observed in females. Androgen-related physical features—such as hirsutism, acne, and increased muscularity—are common in females with NCCAH and are frequently linked to experiences of teasing, peer rejection, and social marginalization. These physical differences can contribute to negative body image, diminished self-esteem, and difficulties initiating or sustaining friendships, as well as avoidance of social engagement and intimate relationships [10, 17, 38].

Males with NCCAH may exhibit certain socially advantageous traits—such as increased self-confidence or assertiveness—potentially related to early androgen exposure and early puberty. However, these potential benefits may be offset by tendencies toward impulsivity, heightened risk-taking, or difficulties aligning socially with age-matched peers. Despite these observations, current evidence suggests that the majority of affected males are asymptomatic, and consistent findings regarding social advantages or dis advantages are lacking [1, 17]. These observations are largely based on studies including both classical and non-classical forms of CAH. Consequently, caution is warranted when generalizing such findings to the NCCAH population.

Concerns about gender expression and societal expectations can further complicate social interactions for both sexes. Issues related to gender expression and societal norms may further complicate peer relationships in both sexes. Females with NCCAH often show preferences for male-typical interests and activities, which can lead to social friction in contexts where rigid gender roles are enforced [2]. Psychosocial support systems—including parental involvement, inclusive school environments, and targeted educational initiatives—play a key role in addressing these challenges. Interventions such as family counseling, anti-bullying programs, and psychoeducation for educators and peers have been shown to foster resilience, promote social inclusion, and enhance overall social competence in affected children and adolescents [34, 38, 39]. Conflicting results regarding social adjustment likely reflect differences in study design, sample composition, and cultural expectations surrounding gender roles and chronic disease. Many studies relied on parental reports rather than self-assessment, introducing potential reporting bias. Future research should use validated age-specific questionnaires and consider both biological and contextual moderators of social adaptation.

Academic and career implications

Educational outcomes in individuals with NCCAH are often adversely influenced by psychosocial challenges, particularly among females. Factors such as diminished self-confidence, heightened social anxiety, and body image dissatisfaction may contribute to reduced school participation and subop timal academic performance [38–40]. The chronic course of NCCAH—with its requirement for lifelong monitoring and potential hormonal instability—can further impair attention, motivation, and daily functioning. In parallel, the higher prevalence of mood disorders, including anxiety and depression, may exacerbate school absenteeism and hinder academic attainment [38–40].

Cognitive domains potentially modulated by androgen exposure, such as visuospatial processing, do not consistently show enhancement in females with NCCAH. In fact, some evidence suggests a relative advantage in abilities typically favoring females, such as episodic memory and emotional recognition, rather than improvements in spatial skills. Moreover, any putative cognitive benefit is often counterbalanced by impairments in executive functioning and working memory, which can negatively impact academic performance—particularly in cognitively demanding environments. Nonetheless, a subset of individuals may demonstrate aptitude in spatial reasoning and problem-solving, potentially facilitating engagement in STEM (science, technology, engineering, and mathematics) fields, although this is not uniformly observed [26, 41].

Long-term career outcomes are shaped by complex interactions between self-perception, sociocultural expectations, and potential workplace biases linked to visible endocrine related features. Females with NCCAH may face reduced self-efficacy and altered career trajectories due to stigma, gender nonconformity, or concerns regarding physical appearance, potentially restricting access to certain professions or limiting professional advancement [10, 40]. Epidemiological data indicate that women with milder CAH genotypes (including NCCAH) are more likely to attain higher educational qualifications, yet less likely to marry or have children, and may exhibit elevated rates of sick leave or disability benefit use—reflecting persistent psychosocial and health-related burdens [40].

Quality of life

Evidence on health-related quality of life (HRQoL) in children and adolescents with NCCAH is limited, with only a few studies employing validated instruments such as the Pediatric Quality of Life Inventory (PedsQL™). In a cross-sectional case–control study of 23 hydrocor tisone-treated patients (mean age range spanning child hood to adolescence), HRQoL scores reported by both participants and parents were comparable to those of healthy siblings, with no significant differences in total or domain scores. Anthropometric measures were within the normal range, and in NCCAH subjects, higher body mass index standard deviation scores correlated positively with total, school functioning, and psychosocial HRQoL scores, suggesting a possible influence of body composition on perceived well-being [39]. Similarly, a Portuguese single-center study including 19 patients (2–18 years old) with NCCAH found that HRQoL was generally preserved across most age groups. The only significant differences emerged in parent-proxy reports for children aged 8–12 years, where physical and emotional health scores were higher than controls, but psychosocial health and total scale scores were lower [42]. These findings suggest that, in adequately treated pediatric NCCAH populations, HRQoL is largely comparable to that of healthy peers, although specific age-related psychosocial vulnerabilities may exist, particularly in preadolescence. Both studies highlight the need for larger, longitudinal investigations to better define potential subtle impacts on HRQoL and to identify subgroups that might benefit from targeted psychosocial support.

Mechanistic pathways linking hormonal imbalance to psychoneuro-social outcomes

Several mechanisms may underlie the association between hormonal dysregulation and psychoneuro-social outcomes in NCCAH (Fig. 1). Across the various domains, apparent inconsistencies among studies should be viewed in light of methodological differences, diagnostic variability, and uncontrolled confounders. Recognizing these sources of heterogeneity provides a more coherent conceptual framework for interpreting the current evidence regarding NCCAH.

Altered prenatal androgen exposure is proposed to influence brain sexual differentiation and early programming of cognitive and emotional circuits, as demonstrated by studies in classic CAH showing masculinization of play behavior and interests in affected females, with meta-analytic evidence for robust effects on sex-typical play [43]. However, neuroimaging studies have not consistently identified corresponding structural changes, except for some findings in emotion processing and reduced white matter integrity, suggesting disease-related rather than purely androgen-driven mechanisms [44]. Postnatal androgen excess may modulate reward processing and social behavior via dopaminergic and limbic pathways, but direct evidence in non-classic CAH is sparse. Subtle dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis is present even in mild forms and may contribute to psychiatric vulnerability [1]. Chronic glucocorticoid overtreatment, as seen in classic CAH, is associated with impaired hippocampal and prefrontal function, reduced white matter integrity, and cognitive deficits such as working memory impairment and “brain-fog” complaints [30]. These effects are dose-dependent and may be relevant in non-classic CAH if overtreatment occurs. Psychosocial stress and inflammatory mediators may interact with HPA axis dysregulation, amplifying emotional vulnerability, but this remains speculative and requires further longitudinal, multimodal studies integrating hormonal, neuroimaging, and psychological data [1, 30, 44]. Overall, while these mechanisms are plausible, the evidence base in non-classic CAH is limited, and further research is needed to clarify causal pathways and clinical relevance (Table 2).

(See Figure 1 & Table 2 on the next page)

Sex-specific differences in psychosocial outcomes

Sex-related variations described across studies likely arise from an interplay of biological, clinical, and sociocultural influences. Females with NCCAH more frequently experience visible hyperandrogenic features—such as hirsutism, acne, and menstrual irregularities—that can adversely affect body image and self-esteem, particularly during adolescence [17]. In contrast, males often exhibit milder or subclinical phenotypes and may remain undiagnosed, facing fewer visible stressors but potentially different psychosocial trajectories [17]. Differences in androgen receptor sensitivity, timing and duration of hormonal exposure, and cultural gender norms may further modulate these outcomes [17, 19, 45].

Understanding these sex-specific mechanisms is crucial for tailoring psychosocial support and clinical management strategies in pediatric NCCAH [2].

Heterozygous carriers of CYP21A2 mutations

Individuals heterozygous for CYP21A2 mutations—i.e., carrying a single pathogenic allele—are generally considered phenotypically unaffected and do not meet the clinical or biochemical criteria for either NCCAH or the classical form of CAH. Nonetheless, emerging evidence suggests that a subset of heterozygous carriers, particularly females, may exhibit mild hyperandrogenic manifestations, including hirsutism, menstrual irregularities such as oligomenorrhea, or clinical

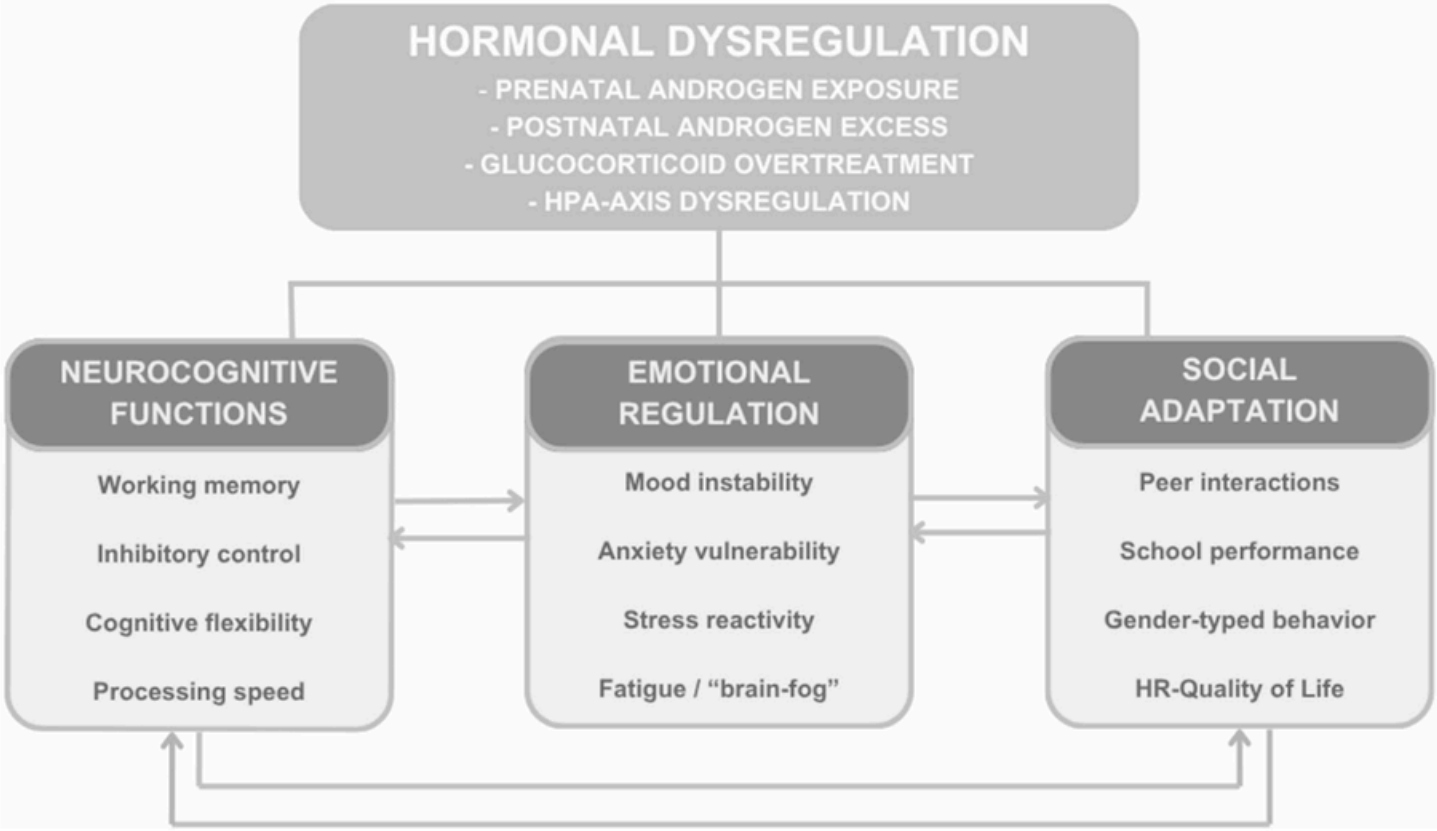


Fig. 1 Integrated psycho-neuro-social model of pediatric NCCAH

Table 2 Current evidence gaps and future research priorities in pediatric and adolescent NCCAH

Area	Main evidence gap	Research priority
Diagnostic definitions	Inconsistent criteria for NCCAH and carrier status across studies	Standardized genotype–phenotype classification
Study design	Predominance of small, cross-sectional, single-center cohorts	Multicenter longitudinal studies with harmonized outcomes
Cognitive outcomes	Heterogeneous tests and lack of normative pediatric data	Use of validated neurocognitive batteries and age-matched control
Emotional/psychiatric outcomes	Limited assessment of anxiety, depression, and stress coping	Integration of standardized psychological questionnaires
Sex-specific analyses	Insufficient attention to male cohorts	Balanced recruitment and stratified analyses by sex
HRQoL measures	Different instruments and informants used	Consensus on core HRQoL measures for pediatric CAH
Carriers	Sparse and inconsistent data	Prospective studies on psychosocial adaptation in carriers
Mechanistic studies	Limited exploration of neuroendocrine pathways	Multimodal studies combining hormonal, neuroimaging, and psychological assessments

Table 3 Summary of main characteristics in pediatric and adolescent patients with non-classical congenital adrenal hyperplasia (NCCAH) and heterozygous carriers of *CYP21A2* mutations

	Females with NCCAH	Males with NCCAH	Heterozygous ***CYP21A2*** carriers
Clinical onset and androgen excess	Often present in late childhood or adolescence; androgen excess common with hirsutism, acne, menstrual irregularities [17]	Often asymptomatic or detected via family screening; androgen excess usually mild to moderate [17]	Usually asymptomatic; rare mild hyperandrogenic features (e.g., hirsutism, menstrual irregularities in females) [13, 46, 47]
Psychological aspects	Increased prevalence of anxiety, depression, body image concerns; higher rates of gender nonconformity and non-heterosexual orientation, though female gender identity is usually maintained [17, 48, 49]	Generally fewer gender identity-related concerns; inconsistent evidence for higher impulsivity or externalizing behaviors [17, 32, 50]	No consistent evidence of increased psychiatric vulnerability; psychosocial burden minimal [13, 46, 47]
Neurocognitive outcomes	Subtle deficits in working memory or executive function; possible strengths in visuospatial skills [27, 28, 30]	Variable findings; occasional attention regulation difficulties or attention-deficit/hyperactivity disorder diagnosis [17, 32, 50]	Generally normal; isolated reports of mild mood or cognitive differences [13, 46, 47]
Social effects	Stigmatization due to physical signs; potential peer rejection; reduced self-esteem [2, 38]	Social confidence may be increased, but risk-taking behaviors can occur [17, 50]	Social functioning typically unaffected; occasional body image concerns in symptomatic carriers [13, 46, 47]

Information is based on available pediatric/adolescent data; evidence remains limited for some outcomes, and findings may vary by sex, age, and treatment status. Routine psychosocial interventions are not recommended for asymptomatic carriers

features overlapping with polycystic ovary syndrome (PCOS), especially during adolescence. The expression and severity of these features may be influenced by the specific mutation involved and possibly by the presence of regulatory polymorphisms affecting gene expression [13, 46].

Evidence regarding heterozygous CYP21A2 carriers remains limited. Although mild clinical signs may be present in some carriers, the overall psychoneuro-social burden is markedly lower than that observed in individuals with biallelic pathogenic variants (Table 3). Most pediatric carriers are asymptomatic; however, some adolescents—particularly females with mild hyperandrogenic features—may report lower self-esteem or body-image dissatisfaction. Current data do not indicate significant cognitive or emotional impairment. Nevertheless, clinicians should consider psychological support on an individual basis when clinical symptoms or psychosocial distress arise [13, 46, 47].

Conclusion

The psychoneuro-social profile of NCCAH in pediatric and adolescent patients is shaped by a complex interplay of biological, developmental, and environmental factors. While some females experience anxiety, depression, body image concerns, and gender nonconformity, many—especially when adequately treated—show preserved quality of life and social functioning. Males generally present fewer psychosocial or neurocognitive difficulties, though occasional externalizing behaviors are reported. Cognitive outcomes are variable and typically involve subtle deficits in working memory or executive processes, with early diagnosis and optimized treatment associated with better results. HRQoL studies indicate overall preservation, with isolated vulnerabilities in specific age groups. Overtreatment should be carefully avoided, as supraphysiological glucocorticoid exposure may exacerbate fatigue, mood fluctuations, and cognitive complaints. Regular dose adjustment—often to lower levels than required in simple virilizing CAH—is essential for psychological as well as somatic well-being. Heterozygous CYP21A2 carriers seldom manifest clinically relevant psychoneuro-social issues, and targeted interventions are rarely necessary unless overt hyperandrogenism is present. Given this heterogeneity, care models should be individualized, combining endocrinological management with psychological and social support when indicated. Longitudinal, multicenter studies are essential to delineate long-term neurocognitive and psychosocial outcomes and to inform tailored intervention strategies. Future research should specifically focus on NCCAH populations, as current understanding of psychological and neurocognitive outcomes often relies on extrapolations from classical or mixed CAH cohort.

Supplementary information The online version contains supplementary material available at https:// doi. org/ 10. 1007/ s00431- 025- 06673-w.

Authors' contributions RP: Conceptualization, Data Collection, Methodology, Writing—Original Draft; FPa: Conceptualization, Data Collection, Methodology, Writing—Original Draft; IP: Writing—Review & Editing; MN: Writing—Review & Editing; MS: Writing—Review & Editing; AS: Supervision—Review & Editing; FPi: Supervision— Review & Editing; IA: Supervision—Review & Editing; LT: Supervision—Review & Editing. All authors read and approved the final version of the manuscript.

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Data availability All data supporting the conclusions of this review are included within the article and its supplementary material. No addi tional datasets were generated or analyzed for this study.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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References
https://caresfoundation.org/wp-content/uploads/2026/10/Full-Sci-Article-Fall-2026-Conf.pdf

Research | Important Updates in the Community

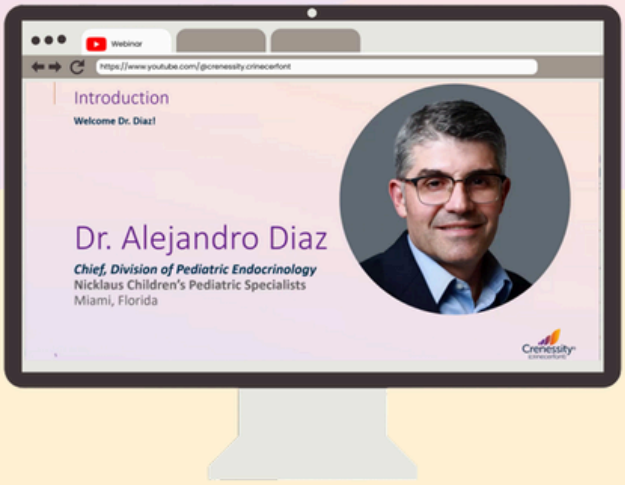


Crenessity® (crinecerfont) | NEUROCRINE® BIOSCIENCES

On-Demand Webinar: Learning More About classic CAH and CRENESSITY

Educational Webinar

An on-demand resource for patients, caregivers, and families affected by CAH



We're pleased to share an on-demand recording of an educational webinar now available on the CRENESSITY YouTube channel in the "Patient Webinars" playlist.

Whether you're new to CAH or looking to refresh your knowledge, we hope this webinar is a helpful resource for you and your loved ones.

Watch it here! →

Watch the webinar anytime on the CRENESSITY YouTube channel.

Approved Uses:
CRENESSITY (crinecerfont) is a prescription medicine used together with glucocorticoids (steroids) to control androgen (testosterone-like hormone) levels in adults and children 4 years of age and older with classic congenital adrenal hyperplasia (CAH).

IMPORTANT SAFETY INFORMATION

Do not take CRENESSITY if you: Are allergic to crinecerfont, or any of the ingredients in CRENESSITY.

CRENESSITY may cause serious side effects, including:

Allergic reactions. Symptoms of an allergic reaction include tightness of the throat, trouble breathing or swallowing, swelling of the lips, tongue, or face, and rash. If you have an allergic reaction to CRENESSITY, get emergency medical help right away and stop taking CRENESSITY.

Risk of Sudden Adrenal Insufficiency or Adrenal Crisis with Too Little Glucocorticoid (Steroid) Medicine. Sudden adrenal insufficiency or adrenal crisis can happen in people with congenital adrenal hyperplasia who are not taking enough glucocorticoid (steroid) medicine. You should continue taking your glucocorticoid (steroid) medicine during treatment with CRENESSITY. Certain conditions such as infection, severe injury, or shock may increase your risk for sudden adrenal insufficiency or adrenal crisis. Tell your healthcare provider if you get a severe injury, infection, illness, or have planned surgery during treatment. Your healthcare provider may need to change your dose of glucocorticoid (steroid) medicine.

Before taking CRENESSITY, tell your healthcare provider about all of your medical conditions including if you: are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

The most common side effects of CRENESSITY in adults include tiredness, headache, dizziness, joint pain, back pain, decreased appetite, and muscle pain.

The most common side effects of CRENESSITY in children include headache, stomach pain, tiredness, nasal congestion, and nosebleeds.

These are not all the possible side effects of CRENESSITY. Call your healthcare provider for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at www.fda.gov/medwatch or call 1-800-FDA-1088.

Dosage Forms and Strengths: CRENESSITY is available in 50 mg and 100 mg capsules, and as an oral solution of 50 mg/mL.

Please see full Prescribing Information and Patient Information.

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Saturday & Sunday - October 17 & 18, 2026

2026 ANNUAL PATIENT EDUCATION CONFERENCE

New York Presbyterian-Weill Cornell Medical Center, New York, NY

co-hosted with Weill Cornell Medicine

More than 150 individuals representing 25 states came together in New York City for our annual CARES Foundation Patient Education Conference. Over a day and a half, patients, families, medical professionals, and industry partners had the opportunity to learn from some of the leading experts in Congenital Adrenal Hyperplasia (CAH).

The feedback we received was both powerful and humbling. Participants shared that they learned more in a day and a half than they had throughout years of living with CAH. Many discovered that health concerns they had experienced were related to their condition, while others gained a better understanding of the importance of specialized care. In the days following the conference, we had already received numerous requests for referrals to CAH experts from individuals who recognized that their condition may not be optimally managed or that their care teams may lack the specialized knowledge they need.

The conference covered an incredible range of topics, including genetics, transition from pediatric to adult care, mental health, nutrition, GLP-1 medications, fertility, cardiovascular health, new treatments, and emerging research. Each presentation offered valuable insights and practical information to help individuals better understand and manage their health.

But as important as the education was, some of the most meaningful moments happened when patients and families connected with one another. They shared their experiences, their fears, their challenges, and their hopes with people who truly understood. For many, simply being in a room where they felt seen, heard, and understood was as valuable as the medical information they received. These connections are at the heart of what CARES does and remind us why creating opportunities for our community to come together matters so much.

We were also honored to host a special screening of Overlooked, a documentary that follows one individual's journey with CAH. It offered another powerful opportunity to reflect on the realities of living with this condition and the importance of making sure the CAH community is seen, heard, and understood.

We are incredibly grateful to the experts who generously shared their knowledge, time, and compassion with our community. We also extend our sincere thanks to our host institution, Weill Cornell Medicine, and to the sponsors whose support helped make this conference possible.

Thanks to the generosity of our supporters, CARES awarded approximately $45,000 in scholarships to help patients and families attend. Many scholarship recipients had never before had access to CAH specialists or experts in the field. Helping make this knowledge and expertise accessible to those who need it most is one of the most meaningful ways we can support our community.

For our team at CARES, there is nothing more rewarding than creating opportunities for individuals and families to leave feeling more informed, more confident, and less alone.



Missed this year's conference?

Conference presentations will be available via recording for anyone interested in learning more.

For additional information, please contact John@caresfoundation.org.

See more feedback on the next page...

"We learned so much in a day and a half, which shows how much thought and care was put into the program. It was so nice being able to connect with other CAH families!"

"So thankful for Dr. Su's expertise and continued support/love in the CAH community."

"I learned things that I did not know regarding what to watch for as my daughter transitions from adolescence."

"I really enjoyed the breakout session about gender & sexuality, the mental health presentation, athlete panel, and both the GLP-1 & TART education sessions."

"I wish I had the chance to take this injection training session before 2015 to inject my child. I am grateful to have been able to practice in this low-stress environment!"

"Dr. Poppas in your 30-minute presentation, you taught us more about our daughter's surgery and urology care than the doctor that performed our daughter's surgery 12 years ago, and all the doctors we have seen since. And then for you to take the time to speak individually to my husband and myself afterwards, about some individualized ideas that could help our daughter, is just above and beyond. Your help, compassion, and utmost dedication to caring for children with CAH is such a blessing. Thank you!"

"It was great meeting with others who were also learning more about CAH and ways to improve symptoms & health. We really networked and continued to build our community."

"I loved seeing the different treatments for various CAH categories."

"As someone approaching 18 years old, it was very helpful seeing expectations and the end of transition of care."

"This was such a wonderful panel. Great to hear from other athletes & share in their experiences."

"I learned so much about the aspects of CAH I would normally never think about."

"The speakers are all so knowledgeable & being able to engage with the CAH community is most rewarding."

"It was a nice mix of information for children and adults with CAH."

"I liked the focus on health, as I worry about my weight and body frequently."

"There was so much new information that I was not aware of with TART, and I should have been with an 11-year-old boy with CAH."

"To the sponsors, after almost 13 years of caring for a child with CAH we thought we had it all figured out. Then because of your generosity we were blessed with the opportunity to attend this conference. In the two days, we have learned more about certain aspects of CAH than we could have ever imagined. And as CAH advocates, our goal is to use this opportunity to share the vast knowledge learned with others. On behalf our our family and all the individuals affected, we thank you."

"Thank you to CARES for furthering my education on CAH! Life-altering experiences as always!"

Special thanks to our sponsors for helping make the event possible!

2026 CAH Partner NEUROCRINE® BIOSCIENCES

eton PHARMACEUTICALS

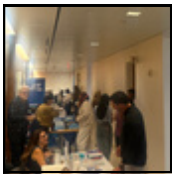
VERTEX

Crinetics Pharmaceuticals

Lundbeck

PANTHER RARE

SOLUTION










Community Events

Thank you to all of the amazing event hosts, volunteers, and attendees that helped us raise awareness for & support those with CAH.

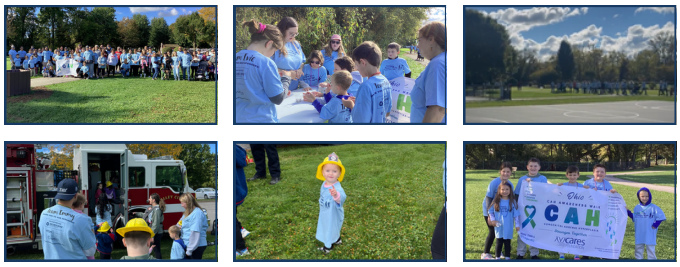


THANK YOU TO ALL WHO ATTENDED THE 1ST ILLINOIS CAH AWARENESS WALK, IN HUNTLEY, IL!

We're deeply grateful to everyone who came together to raise awareness and support the CAH community. A special thank you to our walk host, Becky, for doing such a wonderful job organizing and bringing this event to life. We also thank our generous sponsors for helping make this event possible.

THANK YOU TO OUR SPONSORS!

CAH PARTNER 2026 NEUROCRINE® BIOSCIENCES · eton PHARMACEUTICALS · Crinetics Pharmaceuticals · FOR THE PEOPLE ENTERTAINMENT · Bay Hill Dental · Snelten & Sons Well & Pump Service · ATHLETICO PHYSICAL THERAPY



THANK YOU TO THOSE THAT CAME OUT TO THE 6TH OHIO CAH AWARENESS WALK, IN VALLEY CITY, OH!

We're deeply grateful to everyone who came together to raise awareness and support the CAH community. A special thank you to our walk host, Chloe, for doing such an incredible job organizing and bringing this event to life. We also thank our generous sponsors for helping make this event possible.

THANK YOU TO OUR SPONSORS!

CAH PARTNER 2026 NEUROCRINE® BIOSCIENCES · eton PHARMACEUTICALS · Crinetics Pharmaceuticals





THANK YOU FOR SUPPORTING THE 8TH FLORIDA CAH AWARENESS WALK, IN TITUSVILLE, FL!

We're deeply grateful to everyone who came together to raise awareness and support the CAH community. A special thank you to our walk host, Gretchen, for doing such an amazing job organizing and bringing this event to life. We also thank our generous sponsors for helping make this event possible.

THANK YOU TO OUR SPONSORS!

CAH PARTNER 2026 NEUROCRINE® BIOSCIENCES · BRIDGEBIO · eton PHARMACEUTICALS · Crinetics Pharmaceuticals



INTERESTED IN HOSTING A WALK IN YOUR AREA?

If you have any interest in hosting a CAH Awareness Walk in your area, please contact Dina Matos at dina@caresfoundation.org.

CARES FOUNDATION'S FIRST EVER

CAH Family Fun Days!

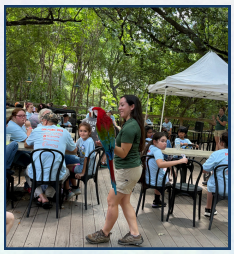
We had such a great time this year coming together, connecting & learning about CAH at our first ever Family Fun Days! Thank you to all of our participating centers of excellence, volunteers & everyone who helped make these such special events.

Make sure you are staying up-to-date with CARES Foundation's website & social media pages for more information on events like these!









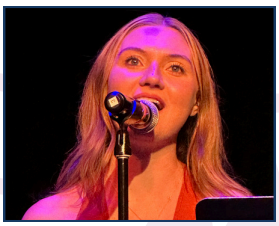

Sept. 26, 2026 in Boston, MA

CARES Cabaret Night

A Million Dreams - An Evening of Music, Storytelling & Impact

We want to extend our thanks to everyone who made it out to attend the first ever, CARES Cabaret Night! Thank you to our event host, Corrine Byrne, Club Cafe, and to all of the talented performers who helped make this such a special night!





11TH ANNUAL

CLAY SHOOT FOR CARES

LEHIGH VALLEY SPORTING CLAYS

Thank you to everyone who came out to support CARES Foundation at this year's Clay Shoot! Congratulations to all of our top performers, and a special thank you to all of those to helped to sponsor this event! In 11 years, the Clay Shoot for CARES has raised over $235k to help support those living with Congenital Adrenal Hyperplasia.







SAVE THE DATE
SATURDAY, APRIL 10, 2027

19TH ANNUAL

Everyone CARES Gala
Liberty House | Jersey City, NJ

Honorees

Ian Marshall, MD, RWJ/Barnabas Health

Jessica Margolies, Esq.

Eton Pharmaceuticals







Stay up-to-date with CARES Foundation's website & social media for more information.

xxcares
CONGENITAL ADRENAL HYPERPLASIA FOUNDATION

Eton Connect Peer Program

Has your child been prescribed Alkindi Sprinkle® (hydrocortisone) oral granules?

Starting in October, Eton is launching the Eton Connect Peer Program to connect the adrenal insufficiency community with a real caregiver like yourself. The Eton Connect Peer Program offers 1:1 calls with an AlkindiPeer mentor who will share their personal experience caring for a loved one with adrenal insufficiency and using Alkindi Sprinkle as part of their treatment.



Visit **AlkindiSprinkle.com/eton-connect** or scan QR code to register for a 1:1 call with an AlkindiPeer

The Eton Connect Peer Program is administered by an independent third party, SmithSolve, a company dedicated to healthcare communications. All information during the registration process will remain confidential and solely for the purpose of participation.

USE AND IMPORTANT SAFETY INFORMATION

USE

ALKINDI SPRINKLE is a prescription medicine used in children from birth to less than 17 years old as replacement therapy when the adrenal gland is not making enough cortisol.

IMPORTANT SAFETY INFORMATION

Always give ALKINDI SPRINKLE exactly as your doctor has directed.

Do not take ALKINDI SPRINKLE if you are allergic to hydrocortisone or any of its other ingredients.

Adrenal Crisis: giving too low a dose or stopping medication can cause low levels of cortisol, which can result in serious illness or death. Treatment with intravenous hydrocortisone should be started immediately. When switching from another type of hydrocortisone to ALKINDI SPRINKLE, watch your child closely for any changes. If your child doesn't get the entire dose of ALKINDI SPRINKLE because of vomiting or spitting some granules out, contact your doctor to see if another dose is needed.

Immunosuppression and Increased Risk of Infection with Use of a Dosage Greater Than Replacement: Use of a greater than replacement dosage can suppress the immune system and increase the risks of new infections or exacerbation of latent infections with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic infections. Monitor patients for signs and symptoms of infections.

Growth Retardation: the long-term use of corticosteroids in high doses may cause growth retardation in children.

Decrease in Bone Density: corticosteroids can affect your child's bone growth and strength.

Cushing's Syndrome Due to High Doses of Corticosteroids: treatment with high doses of corticosteroids can cause Cushing's Syndrome. Treatment should be limited to the smallest dose required, and your child's growth and development monitored appropriately.

Changes in Vision: tell your doctor if your child has blurred vision or other vision problems during treatment with ALKINDI SPRINKLE.

Psychiatric Changes: corticosteroids can change your child's behavior or mood. Tell your doctor if your child has periods of extreme happiness, extreme sadness, hallucinations, or depression.

Gastrointestinal Reactions: tell the doctor if your child has stomach pain, upset stomach, black, tarry stools, or vomiting of blood. These could be signs of ulcers or tears in the stomach or intestines. Taking anti-inflammatory nonsteroidal drugs, like ibuprofen, naproxen, or aspirin, can increase the risk of ulcers or tears.

The most common side effects of ALKINDI SPRINKLE include retaining fluids, changes in glucose tolerance, high blood pressure, behavioral and mood changes, greater appetite, and weight gain.

Vaccination: Administration of live vaccines may be acceptable in ALKINDI SPRINKLE-treated pediatric patients with adrenocortical insufficiency who receive replacement corticosteroids.

Please visit ALKINDISPRINKLE.com/patient for more information

You are encouraged to report negative side effects of prescription drugs by contacting Eton Pharmaceuticals, Inc. at 1-855-224-0233 or the U.S. Food and Drug Administration (FDA) at www.fda.gov/safety/medwatch or call 1-800-FDA-1088.

Please see full Prescribing Information for more information.

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Are You or Your Child Facing Challenges Due to CAH?

Consider Joining a Clinical Research Study

Crinetics is a pharmaceutical company that develops much-needed therapies for people with endocrine diseases. We are currently enrolling adults and children who have been diagnosed with classic congenital adrenal hyperplasia (CAH).

The Calm-CAH (adult) and Balance-CAH (pediatric) studies are looking to understand the safety and effectiveness of an investigational study drug, atumelnant, whether it may reduce the dosage needed for steroid medications like glucocorticoids (GCs), and how it may help manage symptoms of CAH.

To participate in these studies, you or your child must:

- Be 1 to 74 years of age
- Have received a diagnosis of classic CAH
- Be on a stable GC regimen (for example: modified-release hydrocortisone, cortisone acetate, prednisolone, prednisone, methylprednisolone, and dexamethasone)

Additional requirements apply, which the study team will discuss with you.

Atumelnant is an investigational study drug, which means it has not been approved by any regulatory authority and is still under investigation as a potential treatment for CAH.

Crinetics Pharmaceuticals

Balance-CAH | Calm-CAH

To learn more or to see if you or your child may qualify, scan the QR code or visit CrineticsCAH.com.

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CRN04894-12 and 13_Print Ad_V1_07/2025_NP-CAH-0114-1
CAH-ENUS-PAGAD-V1-4SEP25



Funding the future of CAH care

World's first endocrine-focused VC

As a CAH caregiver, Adriaan Brouwer knew something had to change. He saw beautiful science and technology, but no mechanism to transform that science into tangible solutions patients can actually use.

So he built Homeostasis VC, the world's first endocrine-focused venture capital firm.

Fund I: Adrenal & Pituitary patients

We back early-stage companies that meet two criteria

1. Great market and growth potential
2. Positive impact on adrenal & pituitary patients' lives

Building, researching or supporting?
Let's talk.

"I saw great science that never reached patients like my child. We fund companies that change that, and build them to scale."



Adriaan Brouwer
Founder & GP

+31 6 36 59 94 51
adriaan@homeostasis.vc
homeostasis.vc



THE DOCTOR IS IN

DR. KAREN LIN SU
CARES MEDICAL DIRECTOR

MEDICATION GUIDE

Glucocorticoids

As a class, glucocorticoids are similar to the adrenal hormone cortisol, which is deficient in patients with CAH and other forms of adrenal insufficiency. They also lower adrenal androgen production, which is increased in CAH. There are several different oral glucocorticoids commonly used for regular chronic replacement of cortisol.

- ***Hydrocortisone*** (Cortef◊): structurally identical to cortisol, it is considered to be the most physiologic of the pharmacological glucocorticoids. It has both glucocorticoid and mineralocorticoid (see below) activity. With the exception of cortisone, it is the least potent of the available glucocorticoids, and is the shortest-acting (given 2-4 times/day). It is available in tablet form, modified release (Chronocort◊), and as granules (Alkindi◊). Compounded liquid suspensions of hydrocortisone are not recommended. Solu-Cortef◊ is the injectable form of hydrocortisone and used to prevent/treat an adrenal crisis
- ***Cortisone acetate:*** slightly less potent than hydrocortisone, it must be converted to active cortisol in the body using an enzyme called 11ß-hydroxysteroid dehydrogenase type I.
- ***Prednisone/Prednisolone:*** 4-5 times as potent as hydrocortisone and longer-acting (given 2x/day). Considered to be more growth suppressive than hydrocortisone even at equivalent glucocorticoid doses, so usually not recommended in growing children. Solu-Medrol◊ is the injectable form of methylprednisolone
- ***Dexamethasone:*** 40-80 times as potent as hydrocortisone and very long-acting (given once a day). Not typically used in growing children because difficult to titrate at very small doses and tends to suppress growth.

Mineralocorticoids

Mineralocorticoids are similar to aldosterone, which is deficient in patients with salt-wasting CAH. They act on the mineralocorticoid receptor in the kidneys to reabsorb sodium and excrete potassium.

- ***Fludrocortisone:*** acts on the mineralocorticoid receptor to replace aldosterone; also has some glucocorticoid activity; comes as 0.1 mg tablets
- ***Hydrocortisone:*** acts on the mineralocorticoid receptor also, but much higher doses are needed (40 mg of hydrocortisone is roughly equivalent to 0.1 mg of fludrocortisone)

CRF1 receptor antagonist

- ***Crinecerfont:*** lowers ACTH production by blocking the CRF1 receptor; reduces adrenal androgen production and may allow GC dose reduction

Androgen receptor blocker

- ***Spironolactone:*** blocks the androgen receptor, so it prevents any androgens that are circulating in the blood from causing symptoms (such as acne, excess facial/body hair, or signs of early puberty). When the androgens are very high, though, higher doses may be required to be effective. Unfortunately, spironolactone also blocks the aldosterone receptor, so at high doses it may cause salt-wasting even in non-salt-wasters. It should not be used during pregnancy.
- ***Flutamide:*** a nonsteroidal antiandrogen that blocks testosterone from binding to the androgen receptor. It may cause liver damage that can be serious or life-threatening, so is less commonly used. It should not be used during pregnancy.

Oral contraceptive pill (OCP)

Oral contraceptive pills regulate menstrual cycles and can lower ovarian androgen production. The estrogen component increases sex hormone binding globulin, so more testosterone is bound and there is less free testosterone circulating (thereby reducing symptoms). While OCPs alone do not substantially reduce adrenal androgens in CAH, they can reduce some of the bioavailable androgens and are useful for individuals with concomitant polyendocrine metabolic ovarian syndrome (PMOS).

Aromatase inhibitors

- ***Anastrozole/Letrozole/Aromasin◊:*** reduce conversion of androgens to estrogens in order to slow bone age maturation and improve height prognos

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Novel CAH Treatments in Development

ACTH receptor antagonist (phase 3 adult, phase 2/3 pediatric)

- ***Atumelnant (CRN04894):*** once daily oral ACTH receptor (MC2R) antagonist; blocks ACTH stimulated adrenal androgen production; may allow reduction in GC dose

ACTH antibodies (phase 1/2 in adults)

- ***Asedebart:*** antibody to ACTH to lower the stimulation of adrenal androgen production and potentially allow reduction in GC dose



Preventing Adrenal Crisis Events App (iOS & Android)

PACE App

Have you downloaded it yet?

The Preventing Adrenal Crisis Events (PACE) app is available to patients, parents/caregivers, and medical professionals and is designed to provide readily accessible information and instructions for effectively managing AI (Adrenal Insufficiency). The app will include stress dosing and intramuscular injection techniques as well as other helpful tools.

SCAN TO DOWNLOAD!

(APPLE APP STORE)

This application can also be found on the Apple App Store, by searching "PACE by ChaiCore".

(GOOGLE PLAY STORE)

This application can also be found on the Google Play Store, by searching "PACE by ChaiCore".

NEUROCRINE BIOSCIENCES eTon PHARMACEUTICALS Walmart

CARES CONGENITAL ADRENAL HYPERPLASIA FOUNDATION

RESOURCES

CARES ASK THE EXPERT PROGRAM (ENGLISH/SPANISH)



ASK THE EXPERT

Dr. Karen Lin Su

CARES Medical Director

Do you need expert medical advice before your next appointment?
Do you have unanswered questions about your treatment?
Then, DON'T FORGET about our program!

CLICK HERE:
https://caresfoundation.org/ask-the-expert/ to visit this page



PREGUNTA EL EXPERTO

Dr. Alejandro Diaz

Director of the Division of Endocrinology at Nicklaus Children's Hospital in Miami, FL

¿Necesita asesoramiento médico experto antes de su próxima cita?
¿Tiene preguntas sin respuesta sobre su tratamiento?
¡NO TE OLVIDES de nuestro programa!

HAGA CLIC AQUÍ:
https://caresfoundation.org/pregunta-el-experto/ para visitar esta pagina.

IF YOU HAVE NOT ALREADY JOINED OUR COMMUNITY, please take a few moments TO JOIN and complete a free account with CARES. We ask that you provide us with vital information in order to better address your condition & needs. Once you have joined, please return to Ask the Expert and use the form to pose your question.

You must be registered with CARES to use this service. To join, visit: https://caresfoundation.org/join-the-cares-community/

Debe estar registrado en CARES para utilizar este servicio. Para unirte, haz clic en: https://caresfoundation.org/join-the-cares-community/

FUNDRAISING | Make a difference today!

NO ONE SHOULD FACE CAH ALONE

Make a difference in the lives of those living with Congenital Adrenal Hyperplasia (CAH) this holiday season!

We truly thank you for your continued support & generosity as we continue our mission to improve the lives of those living with CAH!

To make your contribuition to CARES Foundation's Year-End Giving Campaign, you can **scan the QR code or visit:**

https://caresfoundation.app.neoncrm.com/forms/cares-foundation-2026-year-end-giving

TUESDAY, DECEMBER 1, 2026

GIVING TUESDAY

ALL DONATIONS MADE TODAY, ON GIVING TUESDAY WILL BE MATCHED - UP TO $25,000!

PLEASE LOOK OUT FOR MORE INFORMATION ABOUT HOW TO DONATE AS WE APPROACH CLOSER TO DECEMBER!

CARES Foundation Endowment Fund | Securing a Future of Care and Hope

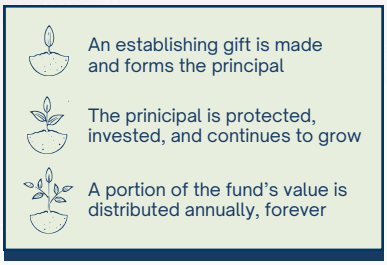
A Gift That Keeps on Giving

CARES Foundation's Endowment is designed to provide a stable, permanent source of funding. Your contribution will be carefully invested, with the annual returns supporting our mission in perpetuity. This means your single act of generosity will touch lives year after year, creating a ripple effect of positive change.

Every Gift Matters

Whether large or small, your contribution to the endowment fund is an investment in hope. It's a promise to future generations that they will have the resources, support, and opportunities they need to thrive despite CAH.

How an Endowment Grows...



Ways to Give

Bequests: Include CARES in your will or living trust.
Retirement Plan Assets: Name CARES as a beneficiary.
Life Insurance: Designate CARES as a beneficiary.
Securities: Donate stocks, bonds, or mutual funds.
Real Estate: Gift property to make a significant impact.
Cash

If you would like to name us in your Will/IRA, please add the following as a beneficiary:

Community Foundation of New Jersey
c/o CARES Foundation Congenital Adrenal Hyperplasia Fund EIN 22-2281783

If you have any questions, please do not hesitate to contact us via email or by phone:

Email: contact@caresfoundation.org **Phone:** (908) 364-0272 **Toll Free:** (866) 227-3737

CARES Foundation Donor Privacy and Confidentiality Policy

CARES Foundation respects the privacy of its donors and prospective donors and believes it is of paramount importance to maintain the trust and confidence of our community. This policy provides transparency regarding our practices for the collection, use, and protection of donor information.

To view the full CARES Foundation Donor Privacy and Confidentiality Policy, please scan the QR Code.

Interested in Fundraising with CARES Foundation?

CARES Foundation helps to co-host a variety of different events & fundraisers throughout the year. Do you have an idea for a local family fundraiser such as a walk/5K, family fun day, or another event? Learn more about how to get started with your idea by visiting the CARES Fundraising Guide. Please reach out to Dina@caresfoundation.org with more information about your idea!

You can also request a personalized donation link for birthdays, holidays, and other events! CARES Foundation will set up a personal link that will track all donations and serve as a fantastic way to get your local community involved in helping to support those with congenital adrenal hyperplasia.

If you have any questions about fundraising with CARES Foundation, please email contact@caresfoundation.org.



Adult Patient Wellness Retreat

A 3-Night Restorative Experience

September 17-20, 2026 | Canyon Ranch, Tuscon, AZ

We want to thank everyone who attended the first Adult Patient Wellness Retreat. Guests enjoyed a relaxing & rejuvenating weekend at Canyon Ranch in Tuscon, AZ.

Thank you to Canyon Ranch for an unforgettable weekend!

CARES Foundation's Podcast...

CAH Pulse

Season 3 | Episode 6: Allyson Part 2
The Good Kind of Stubborn: An Athlete's CAH Story

Can you compete in an Ironman while living with CAH? Allyson says, absolutely! In this episode of CAH Pulse, Allyson returns to share her lifelong journey as an athlete with CAH, which all began for her when she was a child as a competitive swimmer. Now, as a young adult, Allyson is training for her first half Ironman. We learn what training is like as a salt waster, the precautions she takes to stay safe, and what it means to be "Allyson stubborn."

Listen to this episode, and all previous episodes from seasons 1 & 2, by visiting: www.cahpulse.podbean.com

Do you want to be a guest on CAH Pulse?

If you have any interest on being a guest on our podcast, please contact: dina@caresfoundation.org.



Out of the Shadows

Living with CAH

by Lesley Holroyd



AVAILABLE NOW VIA AMAZON (QR CODE BELOW)

A portion of the proceeds will benefit the mission of CARES Foundation

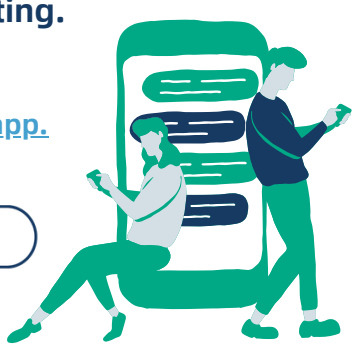
Sign-up for text updates from CARES Foundation!

Stay up-to-date with all things in the CARES Community by opting-in to receive text messages about important events, campaigns & more!

Opt-in by logging into your CARES account, and updating your profile. There will be an option to opt-in to texting.

Login here:

https://caresfoundation.app.neoncrm.com/login



www.caresfoundation.org

Support

Support Group Meetings via Zoom

Our support groups are available in a wide variety of demographics. Groups meet via Zoom for beneficial discussions that ultimately have the goal of providing necessary support in the areas that you may need! A CAH expert/medical professional will be there to answer your questions in between doctor appointments or in times of worry or concern.

Use our Event Calendar (https://caresfoundation.org/calendar/) regularly for upcoming dates for these meetings. Registration in advance is required and all you have to do to register is send an email to support@caresfoundation.org with the date of the meeting you'd like to attend.

YOU MUST BE A MEMBER OF THE CARES COMMUNITY TO JOIN ANY CARES SUPPORT GROUPS (Zoom Meetings, Facebook Groups, etc.)

Join the CARES Community here: https://caresfoundation.org/join-the-cares-community/

Upcoming Meetings

(Please contact support@caresfoundation.org to confirm your attendance at any of the listed meetings!)

Oct. 28, 2026 | 8:30PM(ET) via Zoom
Spanish Speaking Patients & Caregivers

Nov. 4, 2026 | 8:30PM(ET) via Zoom
Young Adults with CAH (17-29)

Nov. 12, 2026 | 9:00PM(ET) via Zoom
Parents of CAH Children (Newborn-Age 5)

Dec. 3, 2026 | 8:30PM(ET) via Zoom
Parents of CAH Children (School-aged/Teens/Young Adults)

Dec. 10, 2026 | 9:00PM(ET) via Zoom
Parents of CAH Children (Newborn-Age 5)

Support Group Leaders

Support Group Leaders are organized by state/topic. We appreciate our leaders and know that they are there for you when you need extra support! Please visit our website to see if there is a leader in your area. https://caresfoundation.org/support/

Support can also be found on our Facebook page by visiting Congenital Adrenal Hyperplasia Support Network.

Interested in joining any of our secret Facebook groups? Visit: Congenital Adrenal Hyperplasia Support Network on Facebook. When on our Profile, select '***More***' and then '***Groups***' to view all joinable groups. (If you are on a mobile device, select '**About**' then '*Groups*'). Click on the group(s) you would like to join, and then request access. We will then review your request, and follow-up as soon as possible.

Other social media channels

- CARES Foundation (Facebook)
- @caresfoundation (Instagram)
- CARES Foundation (LinkedIn)
- @caresfoundation (X)

Medically-Safe Camps

To learn more information about some of the medically-safe summer camps for CAH Patients offered on our website, please visit: https://caresfoundation.org/cah-medically-safe-summer-camps/.

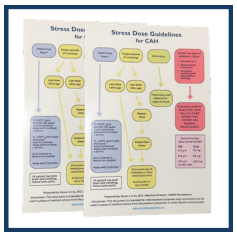
PLEASE UPDATE YOUR ACCOUNT!

Don't miss out on important information and events!

Please visit: https://caresfoundation.app.neoncrm.com/login to view your account with CARES and edit any incomplete fields in your profile.

THE CARES SHOP

Make sure to stock up on CAH awareness-related items & resources today!
View our full catalog by visiting: https://caresfoundation.org/the-cares-shop/.



STRESS DOSING GUIDELINES MAGNET

$2.50

Stress dosing guidelines in a convenient 4" x 6" magnet to be placed in your home.



CAH PULSE 17OZ. COFFEE MUG

$8.00

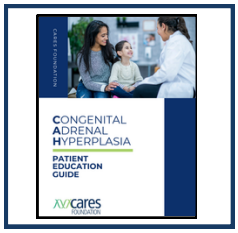
Coffee mug (17oz.) with CARES and CAH Pulse Podcast Logos, CARES Website, and Phone.



ADRENAL INSUFFICIENCY SHOE TAGS

$5.50

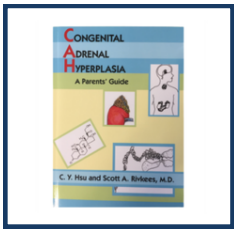
Medical ID Shoe Tags are oval tags (1"x1 1/2") with two holes (each 3/16" diameter).



CARES PATIENT EDUCATION GUIDE

DOWNLOAD

This guide is designed to help you understand and manage congenital adrenal hyperplasia (CAH).



CAH: A PARENTS' GUIDE

$15.00

A nuts-and-bolts look at CAH, what it is, how it is inherited, and how it is treated and monitored.



ADRENAL INSUFFICIENCY CAR SEAT STRAP

$12.00

Velcro pullover strap to go over seatbelts to identify adrenal insufficiency in an emergency



ADRENAL INSUFFICIENCY WINDOW CLING

$2.00

Window sticker/cling to quickly identify adrenal insufficiency in the event of a crisis



EMERGENCY SYRINGE BAG

$5.50

Durable semi-translucent carry-case for syringe or other emergency items.



EMERGENCY RESPONSE KIT (SET OF 3)

$5.00

Includes 3 semi-translucent kits, and emergency instructions brochure & checklist.



MEDICAL I.D. LUGGAGE TAGS

$6.50

Medical Alert I.D. for luggage, backpacks, and other items when traveling.

Please remember that CARES Foundation newsletters have "gone green" and are available digitally. Please make sure we have your current email address to ensure that you continue receiving newsletters and other important information from CARES. Send any updates to john@caresfoundation.org.

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www.CARESFoundation.org

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