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In This Issue

Optimizing the Timing of Highest Hydrocortisone Dose in Children and Adolescents With 21-Hydroxylase Deficiency

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INTRODUCTION

Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive diseases caused by mutations affecting adrenal steroid biosynthesis. In most cases (> 90%), CAH is caused by 21-hydroxylase deficiency (21OHD) (1), resulting in impaired cortisol and, in the most severe cases, decreased aldosterone production. Owing to the diminished cortisol production, negative feedback toward the hypothalamus and pituitary gland is decreased, resulting in increased production of pituitary adrenocorticotropic hormone (ACTH) and consequently overproduction of adrenal precursor steroids and adrenal androgens (2).

Treatment of patients with classic CAH consists of chronic glucocorticoid and, when necessary, mineralocorticoid administration, aiming to replace the relative glucocorticoid deficiency and to suppress the ACTH-mediated hyperandrogenemia (3). Usually, supraphysiological doses are required to inhibit ACTH and consequently androgen production (4). Yet, it is recommended not to completely suppress adrenal steroid production to prevent the adverse effects of glucocorticoid overtreatment (5). Overtreatment is, among other things, associated with cardiovascular complications, whereas undertreatment results in signs of chronic hyperandrogenism, and may result in the development or progression of testicular adrenal rest tumors in men (6). Therefore, the balance between overtreatment and undertreatment is a challenge for every health care provider taking care of CAH patients, and often patients may experience both periods of overtreatment and undertreatment during the day. Adequacy of treatment can be monitored by salivary levels of the precursor steroid 17-hydroxyprogesterone (17OHP) and the adrenal androgen androstenedione (A4) (7). For children with 21OHD, hydrocortisone (HC) treatment is recommended on a thrice-daily schedule (5). However, insufficient data exist regarding the best timing of the highest HC doses. In healthy individuals, cortisol levels follow a circadian rhythm with nadir cortisol levels at night, which start to rise between 2 am and 4 am, peak around 7 am, and gradually decline during the day (8). One of the treatment strategies is to give the highest dose of glucocorticoids in the morning (9, 10), mimicking this physiological circadian cortisol rhythm (11). An alternative treatment strategy is to give the highest dose in the evening, which is suggested to inhibit the increase of androgens in the early morning, when androgen levels are highest, more effectively (12, 13). A high dose of HC in the evening, however, may negatively influence sleep (14-16) and nocturnal blood pressure (BP) (17). Normally, BP drops during the night, but children and adolescents with 21OHD may experience an absence of this nocturnal dip (18, 19) and can have nocturnal hypertension (19). This may be attributed to the high evening HC dose treatment regimen (17). Several studies have focused on the number of daily doses (20, 21), or on the choice of synthetic glucocorticoid (22, 23), but studies on the best timing of highest glucocorticoid dose are limited, despite both treatment regimens being widely used (24). German et al (10) evaluated morning vs evening administration of a high HC dose with respect to disease control, sleep pattern, and daytime activity in children with CAH in a 4-week crossover study. No difference in basal hormone levels and sleep or activity measures between the 2 treatment regimens were detected. However, hormone levels were measured only at 8 am, which does not adequately reflect the hormonal status throughout the day (25, 26).

Therefore, the present study aims to evaluate 2 standard treatment timing strategies for hydrocortisone dosage either highest dosage in the morning or highest dosage in the evening—with respect to biochemical disease

Continued on pg. 3

A Message from the Executive Director

Dear Friend,

The first few months of 2023 have been fruitful ones for the CAH community. We've held several support group meetings, formed two new support groups, participated in research initiatives aimed at improving the lives of patients, and provided significant research funds to our centers of excellence.

As I look back on the last several months, I am extremely grateful for the support of our patients, families, friends, and industry partners. Thanks to this support, we were able to provide more scholarships than ever, which to allowed patients and families to participate in our patient education conference. We awarded more research funds than ever before to our Centers of Excellence and provided significant funding to update the PACE (Preventing Adrenal Crisis Events) app. While working with the international CAH community and our industry partners, we were able to provide much needed medications to patients in war-torn Ukraine.

We are proud to report that our industry partners have also made great progress. Neurocrine's CAHtalyst pediatric and adult trials are complete, and the Spruce CAHmelia trials are making progress. Many companies have been and continue to make inroads in the auto injector space. New promising trials are underway. Adrenas is making news in their promising gene therapy studies. A number of patients have already been dosed and are doing well. We have recently had the opportunity to visit the lab once again in North Carolina where researchers are working hard on potentially life-changing treatments. We are grateful to all who have and are participating in studies aimed at improving the lives of patients.

Finally, I want to thank those of you who continue to work to improve the lives of patients by spreading awareness through walks, school events, EMS advocacy; and for contributing to research through surveys, storytelling, and participating in trials. Your efforts will contribute to a brighter future for the CAH community as a whole!

With gratitude,

Continued from pg 1

control in the early morning, morning, afternoon, and evening in children and adolescents with 21OHD. Secondary objectives are the evaluation of the treatment regimens with respect to overnight BP, sleep, and daytime activity. Optimization of glucocorticoid timing efficacy, while keeping the total dose equivalent, will help prevent the overtreatment and undertreatment in children with 21OHD.

MATERIALS AND METHODS

Inclusion of Participants

Patients with CAH due to classic 21OHD aged between 4 and 20 years were invited to participate in the study. Inclusion criteria were a diagnosis of classic 21OHD confirmed by hormonal and mutation analysis and receiving treatment with HC according to standard guidelines (27). Children needed to be able to collect saliva. Patients with chronic medication use other than HC and fludrocortisone (including oral contraceptive use) or patients with other forms of CAH than 21OHD were excluded from the study.

Study Design

A prospective crossover study with a total duration of 6 weeks was performed. Patients were treated with the highest dose of HC in the evening (eg, 25%-25%-50% or 30%-30%-40% of daily dose) for 3 weeks followed by 3 weeks of treatment with the highest dose of HC in the morning (eg, 50%-25-25% or 40%-30%-30%), or the other way around, starting with their individualized regular total dose and dose distribution. In other words, patients started the study with their regular individualized dosing pattern and after 3 weeks switched their morning and evening dose. At the end of the last week of each 3-week treatment period, patients collected saliva for 2 consecutive days, 4 times a day at 5 am; 7 am; 3 pm; and 11 pm. At the latter 3 time points, saliva was collected just before the administration of hydrocortisone (at 7 am, 3 pm, and 11 pm). Hormonal control before the start of the study was documented and disease control (poor/adequate/overtreatment) during the study periods was determined using in-house reference values for 17OHP and A4 (more details below; manuscript submitted.). In case of illness or stress during the study period, patients were instructed to take an extra dose of HC or increase the glucocorticoid dose and to contact the responsible physician. In those cases, treatment periods were extended, and saliva collection was deferred.

Ethics

The study was approved by the institutional review board (CMO Radboudumc No. 2018-004802-24). Written informed consent was obtained from patients older than 12 years and from caretakers of children younger than 16 years. The study conforms to the principles set out in the World Medical Association Declaration of Helsinki.

Laboratory Measurements

The primary outcome measures of this study were salivary 17OHP and A4 levels at 4 time points during the last 2 consecutive days of each 3-week treatment period. A4 and 17OHP levels in collected saliva samples were all quantified at Radboud University Medical Center, Nijmegen, the Netherlands, using liquid chromatography–mass spectrometry (LC-MS) after solid-phase extraction. An 8-point calibration series of A4 (0.038-82.5 nmol/L) and 17OHP (0.046-100 nmol/L) were used. Samples were homogenized by sonification and internal standards (IsoSciences) were added. Solid-phase extraction was performed using Oasis MCX 1-cc cartridges (Waters Corp). Columns were preequilibrated with methanol:isopropanol (95:5) and washed with 1 mL H2O. After application of the samples, columns were washed with H2O:NH4OH (95:5) and methanol:H2O:formic acid (20:78:2). Samples were eluated in methanol, dried under a stream of N2 gas, and reconstituted in 30% methanol. Samples were injected into an Agilent Technologies 1290 Infinity UHPLC system, equipped with BEH C18 column (Waters Corp). Mobile phases were run in gradient with increasing methanol concentration. Retention time was 3.6 (A4) and 5.0 (17OHP) minutes. An Agilent Technologies 6490 Triple Quad LCMS operated in electrospray positive ion mode. Two mass transitions were monitored per analyte and internal standards. The first mass transition was used for quantification, and a second mass transition was used for confirmation. The LC-MS/MS method is described in more detail elsewhere (manuscript submitted). All collected saliva samples per patient were quantified in the same run. The intra-assay variation is 2.5% and 2.5% for A4 and 17OHP, respectively. Hormonal control during the morning, afternoon, and evening was classified based on the 17OHP and A4 levels (average of 2 days) and in-house reference values for prepubertal (Tanner of 1) and pubertal/adult patients (manuscript submitted), during each treatment period: 1) 17OHP above the upper reference limit (URL) and A4 below the URL, suggesting optimal control; 2) both 17OHP and A4 below the URL, suggesting overtreatment; and 3) both 17OHP and A4 above the URL, suggesting undertreatment.

Blood Pressure and Daily Sleep Activity Scores

To study the influence of the 2 treatment regimens on nocturnal BP, a BP measurement was performed overnight for 1 night in the last week of each treatment period using an ambulant BP monitor (Spacelabs Healthcare), with approximately 1-hour interval measurements. To study the effects of treatment regimen on daytime activity and on sleep, participants or their caretakers gave a daily sleeping score between 0 and 5 (the higher the better) and daily morning, afternoon, and evening activity scores between 0 and 10 (the higher the better), each day during the entire study period. When participants reported more than one sleeping score for a night, sleeping scores were set to "not applicable" (NA).

Statistical Analysis

For the calculation of the minimum effect of interest, G*Power software was used (28). Morning A4 levels were used as the primary outcome measure. Assuming a within-patient SD of 0.15 nmol/L, we estimated that with a sample size of 39 participants a difference of 0.07 nmol/L would be detected ($\alpha = .05$ [2-sided], power = 80%). Statistical analysis was performed in R (R Core Team; 2019). Because of nonnormality, hormone data were logarithmically transformed. The effect of treatment on averaged daily hormone levels was evaluated using linear mixed-effect models, with treatment regimen (high morning or high evening dose) and period (first or second) as fixed independent variables with a random patient effect to allow the patients' baseline values to vary. To study differences in single 17OHP and A4 levels at different time points, a time point variable (early morning, morning, afternoon, evening) and an interaction term between time point and treatment was added to the model. Evaluation of a potential interaction between treatment regimen and period confirmed the absence of a carryover effect and, therefore, the interaction was removed from the final model. Residual plots were inspected for deviations from normality or homoscedasticity. Significance of variables was evaluated using analysis of variance with Kenward-Roger approximation. In case of significant main effects or interactions, pairwise comparisons were performed using Tukey post hoc testing. Estimates with 95% CI are presented in log scale for hormonal data. To ease interpretation, raw non-transformed data are described as median with interquartile ranges. Unplanned exploratory subgroup analyses were performed to evaluate interactions between treatment regimen (high morning vs high evening) and Tanner, pubertal state (Tanner = 1 vs Tanner > 1), sex, or disease control (undertreated/optimal/overtreated) on daily average 17OHP and A4 levels. In addition, interactions between treatment regimen, time point (5 am, 7 am, 3 pm, 11 pm), and the aforementioned parameters on single 17OHP and A4 levels were evaluated. It should be noted that the study was not powered for these subgroup analyses. Differences in patients' mean nocturnal systolic and diastolic BP and differences in patients' mean activity scores (1-10) between treatment regimens were studied using linear mixed-effect models, with treatment regimen, period, and time points (for activity scores) as fixed effects and random patient effect, followed by Tukey post hoc testing. The influence of treatment regimen on sleep scores (1-5) was evaluated using cumulative link mixed-model analysis, also known as ordinal logistic regression, with treatment regimen and period as fixed effects and random patient effect. Statistical significance was considered at P values less than .05.

RESULTS

Clinical Characteristics of Participants and Adverse Events

Forty patients were enrolled in the study, of whom 39 patients (median age 12 years; range,

4-19 years) completed the study, including 22 boys and 17 girls (Table 1). One patient prematurely quit the study because of general malaise not related to the study. Thirty-six patients had the salt-wasting form of CAH and received fludrocortisone treatment. Thirteen (33% [13 of 39]) participants had prepubertal Tanner stage during the study period. Twenty-one of the 39 patients (54%) started with the highest HC dose in the morning, and the remaining 18 patients started with the highest HC dose in the evening. The median dose distribution over the day was 48% in the morning, 25% in the afternoon, and 29% in the evening, when taking the highest dose in the morning. All but one patient received HC treatment thrice daily. This one patient received hydrocortisone at 7 am, 1 pm, 6 pm, and 11 pm. For this patient, afternoon and evening steroid hormone levels were not included in the analysis. If saliva was not collected at the right time points, steroid hormone levels were also set to not applicable. In total, 68 (10.9%) 17OHP steroid hormone levels were missing (19 during the high morning regimen [HM] and 49 during high evening regimen [HE]) and 66 (10.6%) A4 steroid hormone levels were missing (19 during HM and 47 during HE). Most steroid hormone levels were missing for the 5 am saliva collection (n = 24). No severe adverse events occurred during the study period. Spontaneous abortion rates appear to be greater, as compared to healthy pregnant women, in patients with CAH, as well as in patients with NCCAH who were not treated with glucocorticoids. These rates are normalized after glucocorticoid treatment (5, 8, 9). Pregnancies of women already diagnosed with CAH seem to be normal and uneventful (9). Genetic counseling is essential (5).

Table 1

Clinical characteristics of 39 participants with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency

	Characteristics
Age, y	12 (4-19)
Sex, M/F	22/17
CAH type, SW/SV	36/3
Tanner stage, G/M	13× T1; 6× T2; 4× T3; 2× T4; 14× T5
Total daily HC dose (n = 39)	16 mg (7-30)
Total HC dose/m^2/d (n = 39)	11.7 mg (7.4-17.8)
Highest dose, morning/evening	21/18
Dose distribution, HM	48% (33-57); 25% (13-53); 29% (13-38)
Dose distribution, HE	29% (13-38); 25% (13-53); 48% (33-57)

Characteristics are summarized by median with ranges, categorical identifiers, or percentages. Abbreviations: CAH, congenital adrenal hyperplasia; F, female; HC, hydrocortisone; HE, high evening treatment regimen; HM, high morning treatment regimen; M, male; SV, simple-virilizing; SW, salt-wasting.

High Morning Dose Results in Lower Afternoon 17-Hydroxyprogesterone (17OHP) and Androstenedione Levels but Higher Early Morning 17OHP Levels

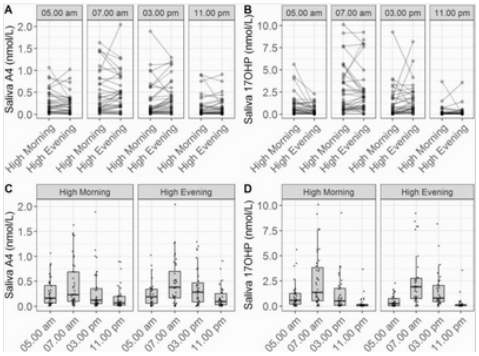
Average of salivary 17-hydroxyprogesterone and A4 concentrations (nmol/L; median and interquartile range) measured in early morning (~ 5 am), morning (~ 7 am), afternoon (~ 3 pm), and evening (~ 11 pm) the last 2 consecutive days of each treatment regimen, that is, highest dose in morning (HM) or highest dose in evening (HE), together with the median difference between treatment regimens (HM vs HE)

	17OHP				
Time	HM	HE	Difference (HM – HE)	*P*	Estimates
5 AM	0.566 (0.204 to 1.252)	0.250 (0.045 to 0.745)	0.181 (0.001 to 0.526)	< .01	0.89 (0.35 to 1.43)
7 AM	1.357 (0.537 to 3.814)	1.909 (0.738 to 2.753)	−0.062 (−0.376 to 0.731)	≥ .999	0.03 (−0.49 to 0.55)
3 PM	0.518 (0.084 to 1.748)	0.786 (0.424 to 2.045)	−0.177 (−0.565 to 0.011)	.04	−0.54 (−1.06 to −0.02)
11 PM	0.078 (0.024 to −0.167)	0.100 (0.040 to 0.164)	−0.008 (−0.064 to 0.027)	≥ .999	−0.09 (−0.61 to 0.44)
	A4				
Time	HM	HE	Difference (HM – HE)	*P*	Estimates
5 AM	0.162 (0.062 to 0.418)	0.188 (0.058 to 0.341)	0.021 (−0.051 to 0.112)	.12	0.26 (−0.03 to 0.56)
7 AM	0.232 (0.100 to 0.689)	0.381 (0.165 to 0.701)	−0.026 (−0.081 to 0.064)	≥ .999	−0.02 (−0.30 to 0.26)
3 PM	0.121 (0.055 to 0.352)	0.281 (0.088 to 0.469)	−0.050 (−0.194 to 0.010)	.01	−0.33 (−0.62 to −0.04)
11 PM	0.065 (0.022 to 0.198)	0.096 (0.031 to 0.252)	−0.013 (−0.037 to 0.018)	.99	−0.08 (−0.37 to 0.21)

Differences between single logarithmically transformed 17OHP and A4 levels at the different time points were tested using linear mixed model analysis, followed by Tukey post hoc testing of the interaction term (treatment × time point). Estimates for HM vs HE regimen with 95% CI are in log scale.
Abbreviations: 17OHP, 17-hydroxyprogesterone; A4, androstenedione; HE, high evening treatment regimen; HM, high morning treatment regimen.

Variability between patients was high (Fig. 1A and and1B).1B). No associations between Tanner stage, disease control 4 to 484 days before the study, disease control during the study period, dose/m2, or sex and treatment effect (differences in mean 17OHP or A4 levels or single 17OHP or A4 levels throughout the day between treatment regimens) were observed (data not shown). For 17OHP no statistically significant difference was observed between periods (estimate [first vs second] = –0.14 (–0.31 to 0.04); P = .13). A4 levels were slightly lower during the first study period (estimate [first vs second] = –0.14 (–0.23 to –0.04); P = .005), regardless of dosing order, compared to the second study period.

Figure 1



Two representations of the androstenedione (A4) (left panels) and 17-hydroxyprogesterone (17OHP) (right panels) data, A and B presenting the average differences (day 20 and day 21) between 2 treatment regimens at 4 time points for each patient. C and D present the pattern of A4 and 17OHP levels over the day for both treatment regimens.

Morning Hormonal Control Was Comparable Between Treatment Regimens

Based on the 17OHP and A4 levels and in-house reference values, hormonal control in the morning, afternoon, and evening was determined for each patient during both treatment periods. During the morning of the HM and HE treatment period, respectively, 19 and 18 patients were treated optimally, 4 and 3 patients were overtreated, and 16 and 15 patients were undertreated (Table 3). During the HE treatment period, 3 patients' hormonal control could not be determined. The stronger hormone suppression in the afternoon when receiving the higher HC dose in the morning vs the evening was reflected in hormonal control in the afternoon; 5 patients were optimally treated when receiving the highest dose in the morning but undertreated when receiving the highest dose in the evening (see Table 3). In addition, 2 patients were overtreated when receiving the highest dose in the morning but undertreated when receiving the highest dose in the evening, and 3 patients were overtreated when receiving the highest dose in the morning but optimally treated when receiving the highest dose in the evening. Contrarily, no patients were optimally treated during the HE treatment period but undertreated during the HM treatment period and no patients were overtreated during the HE treatment period but undertreated during the HM treatment period. Yet, one patient was optimally treated in the afternoon during the HM regimen but overtreated during the HE regimen. Hormonal control could not be determined for the 5 am time point.

Table 3

Hormonal control determined in morning, afternoon, and evening, during the high morning and high evening dose treatment periods

		Morning				
		HE				
		Undertreatment		Overtreatment	ND	
HM	Undertreatment	13	2	0	1	16
	Optimal	2	15	1	1	19
	Overtreatment	0	1	2	1	4
		15	18	3	3	
		Afternoon				
		HE				
		Undertreatment		Overtreatment	ND	
HM	Undertreatment	12	0	0	1	13
	Optimal	5	9	1	2	17
	Overtreatment	2	3	1	1	7
	ND	0	1	0	1	2
		19	13	2	5	
		Evening				
		HE				
		Undertreatment		Overtreatment	ND	
HM	Undertreatment	7	1	1	1	10
	Optimal	2	10	1	4	17
	Overtreatment	0	4	5	1	10
	ND	0	1	0	1	2
		9	16	7	7	

Hormonal control was evaluated based on 17OHP and A4 levels at 7 AM, 3 PM, and 11.00 PM (average of consecutive days) with respect to in-house reference values, where 17OHP above the URL and A4 below the URL indicates optimal control, both 17OHP and A4 below the URL suggests overtreatment, and both 17OHP and A4 above the URL suggests undertreatment. In case of missing values, hormonal control could not be

determined (ND).
Abbreviations: 17OHP, 17-hydroxyprogesterone; A4, androstenedione; HE, high evening treatment regimen; HM, high morning treatment regimen; URL, upper reference limit.

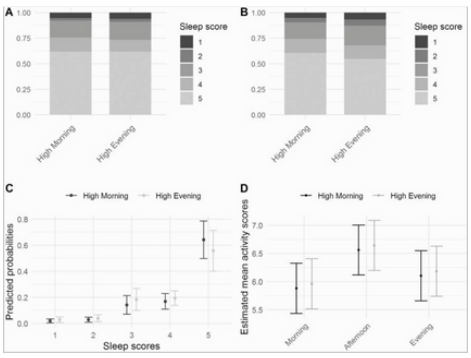
Diurnal Variation in 17-Hydroxyprogesterone and Androstenedione Levels

Patients showed a circadian rhythm of 17OHP and A4 levels, with the highest levels in the morning, lower levels in the afternoon, and lowest levels in the evening (statistically significant differences between all time points; $P < .01$). Interestingly, this circadian rhythm was observed during both treatment periods (Fig. 1C and and1D),1D), although it was less pronounced for the HE dose regimen. A4 levels were not statistically significantly higher in the morning vs the afternoon during the HE regimen (Tukey post hoc testing; $P = .053$).

Treatment Regimen Does Not Affect Sleep and Activity Scores

The secondary aim of this study was to evaluate whether the different treatment regimens affected sleep and daily activity rating. Patients reported sleep scores for each night during the entire study period. In total, 130 (7.9%) sleeping scores were missing, of which 55 were missing during the last week of the treatment periods. Overall, treatment regimen did not affect sleep rating (Fig. 2A; odds ratio [OR] = 0.93; $P = .50$). When concentrating only on the last week of each treatment period, patients seemed more likely (OR = 1.43) to give lower sleeping scores during the HE regimen, but this was not statistically significant ($P = .07$; Fig. 2B and and2C).2C). Patients reported daily activity scores (from 1 to 10) for each morning, afternoon, and evening during the entire study period. In total, 88 (1.8%) activity scores were missing. Patients' mean activity scores were highest during the afternoon (estimated marginal mean = 6.6; 95% CI, 6.2-7.0), followed by the evening (6.2 [5.7-6.6]) and the morning (5.9 [5.0-6.4]) (Fig. 2D). Patients' mean activity scores differed significantly between the morning and the afternoon (estimate = –0.68 [–0.91 to –0.45]; $P < .01$) and between the afternoon and the evening (estimate = 0.46 [0.23-0.69]; $P < .01$), but did not significantly differ between the morning and evening (estimate = –0.22 [–0.46 to 0.01]; $P = .06$). No differences were observed in mean activity scores between the treatment regimens (estimate = –0.08 (–0.239 to 0.08]; see Fig. 2D).

Figure 2



Sleep and activity scores in children and adolescents with 21-hydroxylase deficiency (21OHD) (n = 39) when either receiving the highest hydrocortisone dose in the morning (high morning) or evening (high evening). A and B present the cumulative proportions of sleep scores given during A, the complete 6-week study period, or B, during only the last week of each treatment period. C, Influence of treatment regimen on the probability (predicted probabilities with 95% CI) of sleep rating during the last week of each period was tested using cumulative link mixed model analysis. D, Differences in mean activity scores over the day (morning/afternoon/evening), presented as estimated marginal means with 95% CI, and influence of treatment regimen on mean activity scores were tested using linear mixed effect regression analysis followed by Tukey post hoc testing.

Treatment Does Not Affect Nocturnal Blood Pressure

Ambulatory overnight BP monitoring during the last week of both treatment periods was completed by 36 patients but sufficient measurements (at least 5 data points) for both treatment periods were collected for 26 patients. In addition, 6 patients obtained enough data points only during the HM dose regimen (n = 32) and 4 patients collected sufficient data points only during the HE dose regimen (n = 30). Between the HM dose and HE dose regimen, no statistically significant differences were observed in mean overnight diastolic BP (estimate = 0.45 [–1.67 to 2.57]; $P = .67$) or mean systolic BP (estimate = –0.337 [–2.69 to 2.01]; $P = .77$).

DISCUSSION

This study aimed to evaluate the timing of highest glucocorticoid dose with respect to hormonal control, overnight BP, sleep, and daytime activity in children and adolescents with 21OHD. We showed that whereas an HE dose resulted in lower levels of 17OHP in the early morning, an HM dose resulted in lower levels of 17OHP and A4 in the afternoon. Despite the early morning 17OHP suppression with the HE dose regimen, the suppressive effect was no longer observed in the morning (~ 7 am), stressing the importance of giving the evening dose as late as possible and the morning dose as early as possible. Androgen suppression by HC lasts for 6 to 8 hours after evening-dose administration, after which the levels start to rise again (9, 29), explaining why we and German et al (10) did not observe a difference in morning hormone levels (7 am or 8 am) between the 2 treatment strategies. The HM dose regimen resulted in lower androgen levels in the afternoon. Overall, no difference in mean steroid levels throughout the day was observed between the treatment regimens. Importantly, the higher evening dose, which was given relatively late in this study (~ 10.23 pm), did not substantially affect sleep rating, daily activity scores, or nocturnal BP, and thus no treatment regimen was found to be superior.
Previously, it was postulated that a higher evening dose is not expected to inhibit the early morning rise in adrenal steroid levels, even when the evening dose is given late at night (30, 31). However, here we show that a higher evening dose better suppresses the 17OHP levels in the early morning, although the inhibition of A4 was less pronounced. This discrepancy between 17OHP and A4 might be explained by differences in the half-maximal inhibitory concentration values of hydrocortisone for 17OHP and A4, described by Al-Kofahi et al (26), which suggest that HC is a more potent inhibitor of 17OHP than A4 production. Nonetheless, a higher morning dose resulted in significantly lower levels both of 17OHP and A4 in the afternoon, suggesting a variability in glucocorticoid receptor sensitivity during the day, together with the physiological decrease of ACTH during the day. It could be speculated that suppression of the hypothalamic-pituitary-adrenal (HPA) axis in the early morning is more effective to achieve optimal hormonal control compared to the afternoon since the HPA axis is more active in the early morning. The interpatient variability in 17OHP and A4 levels—both in the early morning and in the afternoon—was high. While some patients displayed differences in 17OHP and A4 concentrations when treated with the different treatment regimens, other patients did not. This variability may be due to large interindividual differences in pharmacokinetic parameters (32-34), as subgroup analysis (interaction between treatment and eg, treatment dose per meters squared, tanner staging, or sex) could not explain this variability. For patients with higher clearance of HC, a relatively higher dose (either morning or evening) may, in contrast to patients with lower clearance, not result in lower levels of 17OHP and A4 6 or 8 hours after HC administration. On the other hand, this study was not powered for these subgroup analyses. The study cohort was quite heterogeneous, and it could be speculated that a more homogeneous study cohort may present differences between the treatment regimens and that an even bigger sample size may (hypothetically) allow the identification of patients that do benefit from one of the dosing strategies. Nonetheless, we did not observe trends suggesting particular patient groups benefiting from one or the other regimen.
In healthy children, 17OHP levels follow a circadian rhythm with highest levels in the morning, lower levels at noon, and lowest levels in the evening (35). We and others (36) showed that this circadian rhythm in 17OHP and A4 is still present in patients with 21OHD treated with dexamethasone and/or HC. Interestingly, this circadian rhythm was present during both treatment strategies, which might suggest that the intrinsic circadian regulation of 17OHP and A4 production is stronger than the exogeneous effects of HC. The circadian pattern was more prominent when the highest dose was administered in the morning vs the evening. For 17OHP, this circadian pattern was clearer than for A4, which complements previous research (36). The importance of a circadian rhythm in patients with 21OHD may be deduced from the improved quality of life in poorly controlled 21OHD patients receiving subcutaneous infusion of HC that mimic the physiological levels of cortisol (37).
In this study we made use of ambulatory BP

measurement, which has been shown to be accurate and well tolerated in children, and may avoid "white-coat hypertension" (38). As we wanted to assess possible differences in cardiovascular risk between HC administration regimens, we were specifically interested in nocturnal BP because this is superior to daytime BP in predicting cardiovascular risk (38). Previously, we did not find associations between nocturnal BP and dosage of hydrocortisone or fludrocortisone (39). Elevated 24-hour diastolic and systolic BP levels and elevated overnight systolic BP were, however, reported in a small study of 6 children with 21OHD (aged 5.0-9.7 years) when patients received the highest dose in the evening (7 pm) (17), suggesting an effect on cardiovascular risk depending on HC treatment regimens. This could not be confirmed by our study presented here. Our study showed no difference in mean nocturnal BP between the treatment regimens in children with 21OHD. Although the sample size in the present study is larger, differences in relative evening dose during the HE vs HM regimens were greater in the study by Liivak and Tillmann (53% vs 17% of total dose) compared to our study (48% vs 29% of total dose) (17). Therefore, we conclude that relatively small elevations in evening HC dose do not translate into detectable differences in nocturnal BP.

Treatment regimen did not statistically significantly (P = .07) affect subjective sleep or activity rating, although sleep rating seemed lower during the last week of the HE dose regimen (OR = 1.43 for giving lower sleep score). Potentially, effects of an HE dose on sleep rating might be detected in a bigger cohort of patients. In addition, it may be argued that glucocorticoid treatment may affect sleep quality unconsciously (16), without affecting subjective sleep rating. Nonetheless, our results are in line with the study by German et al (10), who did not find differences in sleep quality and activity between either treatment regimen in children with 21OHD. It remains to be studied whether the different dosing regimens affect long-term health outcomes.

Of interest is whether administration of the highest HC dose in the morning or in the evening may be more likely to result in overexposure to HC. As overnight cortisol levels are normally low, giving a high HC dose at bedtime potentially exposes the patient to unnecessarily high levels during this time frame (29). On the other hand, it could be hypothesized that, because of the diurnal rhythmicity of glucocorticoid receptor sensitivity (40-42), harmful effects of supraphysiological cortisol doses at night may potentially be limited. However, whether an equivalent glucocorticoid dose in the evening indeed results in a lower metabolic response than in the morning has, to our knowledge, not yet been studied in children with 21OHD.

Our study addresses the same research question as the study by German et al (10), but there are important differences between the present study and the study by German and colleagues. As stated by the authors, the primary end points of German et al were sleep and activity, which resulted in a relatively small sample size for hormonal analysis (n = 15). Importantly, we have quantified hormone levels at multiple time points per day, which better reflected hormonal status throughout the day. By including the 5 am and 3 pm measurements, we were able to show that the HE regimen actually resulted in stronger suppression of 17OHP (ie, HPA axis suppression) in the early morning, and that an HM regimen resulted in stronger suppression in the afternoon.

Despite progress in the development of modified-release glucocorticoid substitutions, these are not yet available for pediatric patients with 21OHD. Therefore, until these formulations become available, we recommend that the dose distribution be individually optimized for each patient. Although overall, as a group, no treatment regimen was found to be superior, individual patients may benefit from one or the other dosing strategy. To optimize treatment, hormonal control should be monitored at multiple time points a day, preferably before taking the medication, because single measurements indicate hormonal control only at a specific time point and provide limited information on the patient's overall disease control (25, 26). The addition of an early morning salivary measurement is considered beneficial because it informs whether a higher evening dose results in better suppression of the early-morning surge in that patient. Nonetheless, it should be noted that, as the rise in ACTH starts between 2 and 4 in the morning, benefit from the HE dose in the early morning may not always be captured by the 5 am measurement. In other words, while no difference in 17OHP and A4 levels may be evident from the 5 am measurement, the HE dose may result in a period of higher androgen suppression before 5 am. If, for a patient, the HM and HE treatment regimens result in indistinguishable total androgen exposure, it can be argued that a physiological pattern of HC intake is preferable.

In this study we measured steroids in saliva, because saliva collection is less stressful for children compared to venous blood sampling and, therefore, the steroid levels are less likely to be affected by specimen sampling (43). Levels of 17OHP and A4 have been reported to highly correlate between saliva and plasma samples (44, 45). Moreover, because androgens were measured in saliva, and BP was measured using an ambulatory BP monitor, no hospitalization was required for this study design, which minimized the burden for participants. This does, however, mean that compliance to treatment is not controlled. Yet, these patients were highly motivated and explicitly instructed to adhere to treatment administration at specific time points.

We do acknowledge several limitations in this study. Although the incorporation of multiple time points of androgen measurement over the day is a strength of this study, continuous monitoring (eg, 20-minute or 1-hour interval) throughout the day or the collection of 24-hour urine might have been even more informative because it would have allowed us to compare total androgen exposure between treatment regimens. Also, whether for example a higher morning dose adjusted the morning 17OHP and A4 levels faster or better was not determined here because steroid levels were quantified only before HC administration. However, the patients' load would have been much higher and would most likely have resulted in a much lower number of participants.In healthy children, 17OHP levels follow a circadian rhythm with highest levels in the morning, lower levels at noon, and lowest levels in the evening (35). We and others (36) showed that this circadian rhythm in 17OHP and A4 is still present in patients with 21OHD treated with dexamethasone and/or HC. Interestingly, this circadian rhythm was present during both treatment strategies, which might suggest that the intrinsic circadian regulation of 17OHP and A4 production is stronger than the exogeneous effects of HC. The circadian pattern was more prominent when the highest dose was administered in the morning vs the evening. For 17OHP, this circadian pattern was clearer than for A4, which complements previous research (36). The importance of a circadian rhythm in patients with 21OHD may be deduced from the improved quality of life in poorly controlled 21OHD patients receiving subcutaneous infusion of HC that mimic the physiological levels of cortisol (37).

In conclusion, the HM dose and HE dose regimens were comparable with respect to averaged daily 17OHP and A4 levels, activity scores, sleeping scores, and nocturnal BP although they resulted in different exposure patterns to 17OHP and A4 throughout the day. We recommend individually determining the best timing of the highest HC dose based on levels of 17OHP and A4 at multiple time points during the day.

ACKNOWLEDGEMENTS

We would like to thank all patients and their caretakers for participation in this study. We acknowledge Spacelabs Healthcare and Itémedical for the use of their ambulant BP monitoring systems. We would like to thank Wendy Jansen and Nienke Sonneveld for their great support.

GLOSSARY

170HP	17-hydroxyprogesterone
210HD	21-hydroxylase deficiency
A4	androstenedione
ACTH	adrenocorticotropic hormone
BP	blood pressure
CAH	congenital adrenal hyperplasia
HC	hydrocortisone
HE	high evening treatment regimen
HM	high morning treatment regimen
HPA	hypothalamic-pituitary-adrenal
LC-MS	liquid chromatography-mass spectrometry
OR	odds ratio
URL	upper reference limit

REFERENCES

https://caresfoundation.org/wp-content/uploads/2023/04/References.pdf

RESEARCH

Adrenas

Dear CAH Community Members,

Adrenas Therapeutics, a BridgeBio affiliate, appreciates your ongoing interest in the investigational gene therapy clinical trial for adults with classic Congenital Adrenal Hyperplasia (CAH) due to 21-hydroxalyse deficiency. The ADventure phase 1/2 clinical trial continues as planned and we are pleased to share an update with you.

In this early phase clinical trial, our goals are to confirm the safety and potential effects of three dose levels (low, middle, high) of the Adrenas' investigational gene therapy, BBP-631, on adrenal-related hormones.

A total of four participants have been dosed in the ADventure clinical trial. Two participants received the investigational gene therapy at the low dose and two participants received it at the middle dose. The investigational gene therapy has been well tolerated by all participants to date, allowing for escalation to the highest dose level to proceed as planned.

As a reminder, the ADventure trial doses one participant at a time with a safety evaluation after each participant is dosed, which is standard practice for early phases of gene therapy trials. A thorough evaluation of the clinical trial safety data is conducted by a panel of independent expert physicians and clinical trial experts who comprise the Data and Safety Monitoring Committee (DSMC). At this early stage of the clinical trial, the approval of the DSMC is required for dosing additional participants at a given dosing level and advancing to higher doses.

We will soon begin dosing participants at the highest dose. Adrenas will continue to collect and review all data to guide our understanding of the potential impact of BBP-631 on the adrenal-related hormones in people living with CAH. We aim to have a more complete understanding by the second half of 2023, and we will update the community at that time.

Adrenas Therapeutics is grateful for the ongoing collaboration with the community and advocacy organizations as we work together to advance meaningful treatment options for people and families affected by CAH.

Sincerely,
The Adrenas Therapeutics Team

criteria for trial participation:
• Adults 18 years of age and older
• Diagnosed with classic CAH (simple-virilizing or salt-wasting)
• Managing CAH with glucocorticoids daily (e.g., hydrocortisone, prednisone, methylprednisolone, or dexamethasone)

For information visit http://cahgenetherapy.com and https://clinicaltrials.gov/ct2/show/NCT04783181

Abiraterone Acetate Study

Patients with the severe, classic form of congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency are unable to synthesize cortisol (stress hormone) or aldosterone (salt remaining hormone) normally. These deficiencies can be treated with hydrocortisone or fludrocortisone, respectively. In patients who are not getting enough hydrocortisone , the adrenal gland secretes large amounts of androgens (male sex hormones). Excess androgens can cause the growth plates in long bones to close too early, leading to short adult height. Controlling androgen levels may require relatively high doses of hydrocortisone that can themselves slow down growth. If androgen synthesis could be blocked in prepubertal children, this might allow us to use lower doses of hydrocortisone and eventually result in CAH patients being taller as adults.

- This study is being done to determine whether an investigational drug called abiraterone acetate, which blocks androgen synthesis, is safe to use in children with CAH, and to determine the lowest dose which works to reduce androgen levels to normal.
- This is a research study because although abiraterone has been approved by the U.S. Food and Drug Administration (FDA) for other indocations, it has not been approved by the FDA for the treatment of CAH.

To take part in this study, you must:
- Have classic CAH due to 21-hydroxylase deficiency
- Be 2 to 9 (Girls) or 2 to 10 (Boys) years old
- Be taking both hydrocortisone and fludrocortisone
- Not be in puberty

What will volunteers be asked to do?
- Have a physical exam, blood and urine tests, x-Ray of the hand, electrocardiogram (ECG) and eye exam
- Take abiraterone acetate 10 mg tablets daily by mouth for 7 days
- Attend 6 (but up to 8) study visits in person and 3 (but up to 5) telephone visits during the study

There are 4 study centers nationwide:
- South Central: Dallas, Texas at UT Southwestern Medical Center / Children's Medical Center Dallas
- East Coast: National Institute of Health, Bethesda, Maryland
- North Central: University of Michigan, Ann Arbor
- West Coast: Children's Hospital Los Angeles, Los Angeles, California

For more information on the Abiraterone in CAH study, please contact:
Principial Investigator, Perrin White, MD
Perrin.White@utsouthwestern.edu

eTon PHARMACEUTICALS

ETON CARES: HELPING YOU AND YOUR CHILD GET STARTED ON ALKINDI SPRINKLE®

Eton Cares is a support program designed for ALKINDI SPRINKLE (hydrocortisone) oral granules patients, and their families, to get access to and stay on their prescribed treatment. It's your place for answers, insurance assistance and to set convenient prescription refill reminders.

When you get an ALKINDI SPRINKLE prescription you are automatically enrolled in Eton Cares and have immediate access to: *

Insurance Specialists
Ensure you understand your benefits and help your doctor's office verify and obtain prior authorization and insurance coverage.

Pharmacists
Provide 24/7 support by phone, monthly worry-free refill reminders, and shipment alerts.

Nurse Ambassadors
Provide regular check-ins, answer questions about your child's health and medication, and support you through treatment.

- **97% of ALKINDI SPRINKLE prescriptions were successfully approved by insurance**
- **QuickStart Program provides medication in as soon as 24 hours*†**

Learn more about Eton Cares on our Website
https://www.alkindisprinkle.com/patient/support/

*Restrictions, limitations, and/or eligibility requirements apply.
†For eligible, commercially insured patients.
‡ Anovo will work with the HCP to obtain insurance coverage. I
If insurance is denied, the patient may apply to the Patient Assistance Program.

4 low-dose strengths for accurate dosing in kids
Accuracy is dependent on ensuring the entire dose is given and consumed as directed

ALKINDI SPRINKLE® (hydrocortisone) oral granules are available in 4 color-coded strengths for flexible, accurate,
Individualized dosing based on your child's specific cortisol needs as prescribed by their doctor.

See more info, dosing tips and videos, on
www.alkindisprinkle.com

USE & 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.

Infections:
all infections should be treated seriously, and stress dosing of hydrocortisone should be started early. Taking ALKINDI SPRINKLE should not stop your child from being vaccinated but let your healthcare provider know prior to vaccination.

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.

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.

*Restrictions, limitations, and/or eligibility requirements apply.
†For eligible, commercially insured patients.
‡ Anovo will work with the HCP to obtain insurance coverage. If insurance is denied, the patient may apply to the Patient Assistance Program.
*21925 W. Field Pkwy #235 Deer Park, IL 60010 (847) 787-7361

https://www.alkindisprinkle.com/patient/
See more info, dosing tips, and videos at www.AlkindiSprinkle.com

CAH AWARENESS WALKS

LACE UP, WASHINGTON!

1ST ANNUAL CAH AWARENESS WALK
Mountaineers Cascade Auditorium & Magnuson Park, Seattle, WA

https://caresfoundation.org/1st-annual-washington-cah-awareness-walk-2/

LACE UP, FLORIDA!

6TH ANNUAL CAH AWARENESS WALK
Valicente Pavillion
Titusville, FL

LINK COMING SOON

WE ARE LOOKING FOR A HOST IN SOUTHERN CALIFORNIA!

TO LEARN MORE EMAIL:
DINA@CARESFOUNDATION.ORG

STAY TUNED FOR MORE WALKS!

MARYLAND WALK

We appreciate all who walked in support of CARES Foundation at the 6th Annual Maryland CAH Walk! Despite the inclement weather, many still found the time to make advocating for CAH part of their day! Thank you to the Watson Family for hosting such a wonderful event!

STUDENT WALK

A special thank you to Silas Wood Schools for hosting this incredible event in support of the Stair Family and CARES Foundation!

June is Congenital Adrenal Hyperplasia AWARENESS month

How will you spread awareness?

The Faces of CARES

Send us your story/experiences of life with CAH for our, "Faces of CARES" campaign!

What is life like with a rare disorder?

What are your daily challenges?

How do you manage your CAH?

Who is there for you, to guide you along your journey?

& MORE

Pictures, videos, stories all welcome!

Email your contributions to us: contact@caresfoundation.org

OTHER WAYS TO SPREAD AWARENESS!

Visit your local firehouse/EMT

It is always important to alert your local emergency office(s) about your or your loved one's condition. Educate them on how to care for you/your loved one in an emergency.

Attend our 15th Annual Everyone CARES Gala

JOIN US as we celebrate the CAH Community! Take advantage of this great opportunity to bond and share your experiences! This is a great night to support CARES - a non-profit that has helped those affected by CAH for more than two decades! (See link on Page 13)

Wear an awareness ribbon or pin!

Spark interest and be a conversation starter by sporting a Tiffany-blue ribbon or pin for CAH Awareness month!

The New Brighton Middle School chapter of the National Junior Honor Society chooses a charity to raise money for every year. This year the students chose CARES Foundation because their current President, Karter Morrison, and his little brother both have congenital adrenal hyperplasia. This wonderful group of students raised $800 for CARES by holding a "Penny Wars" fundraiser for a week within their school. These young scholars display character, respect, leadership, and kindness everyday. The New Brighton School District is very proud of them.

Start spreading the news!

A Night on the Hudson

Our 15th Annual

Everyone CARES Gala

Celebrating the CAH Community and our Honorees!

Please support our event by:

-Attending
-Sponsoring
-Underwriting
-Donating Auction items/services
-Purchasing an E-Journal Ad
-Making a Donation
-Volunteering

Louise Fleming PhD, RN, MSN

spruce BIOSCIENCES

Heino Meyer-Bahlburg PhD

Learn about our Gala honorees https://one.bidpal.net/caresgala2023/custom/custom2

MAY 20, 2023

Current on Pier 59, Chelsea Piers, NYC

https://one.bidpal.net/caresgala2023/welcome

NEUROCRINE® BIOSCIENCES

Neurocrine Biosciences and Diurnal Share Continued Commitment to CAH Community

By Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences, Inc. and John Porter, M.D., Chief Medical Officer at Diurnal Ltd., a Neurocrine Biosciences Company.

Since the company's founding over 30 years ago, Neurocrine Biosciences has been dedicated to developing potential life-changing treatments for patients with unmet medical needs, including congenital adrenal hyperplasia (CAH). Our commitment can be traced back to the late Wylie Vale, PhD, a professor at The Salk Institute and one of Neurocrine's co-founders, who contributed to key Nobel Prize-winning work in endocrinology, specifically around the pathway impacted in CAH. This early discovery paved the way for current clinical trials that leverage our understanding of this pathway and formed the foundation of our driving purpose which remains true today: to meet the needs of under-addressed patients.

Last year, Neurocrine acquired Diurnal, a global pharmaceutical company focused on chronic endocrine conditions. Diurnal was also founded by a renowned endocrinologist, Professor Richard Ross, M.D. in 2004 as a spinoff company from the University of Sheffield in the U.K. to develop and commercialize pioneering endocrine replacement therapy research. It has three approved products for adrenal disorders: Alkindi® in the EU, Alkindi Sprinkle® in the U.S. (where it is marketed by Eton Pharmaceuticals), and Efmody® in the U.K. and the EU. Neurocrine and Diurnal are proud to unite our combined deep endocrinology knowledge and proven clinical development expertise to advance new therapies for endocrine disorders.

Neurocrine continues to investigate crinecerfont, a corticotropin-releasing hormone (CRF) receptor antagonist in Phase 3 studies for the potential treatment of adult and pediatric patients with CAH. There are currently no FDA-approved treatments for classic CAH besides glucocorticoids. For more than 60 years, glucocorticoids (and mineralocorticoids) have been the standard of care in treating classic CAH. However, glucocorticoids at doses to treat the cortisol deficiency alone are typically not enough to address the high adrenocorticotropic hormone (ACTH) and high androgen levels commonly found in patients with classic CAH. Thus, glucocorticoids serve a dual purpose in patients with CAH, to not only to treat the cortisol deficiency, but typically at higher doses to also reduce high ACTH and androgen levels. Long-term exposure to glucocorticoids at higher doses can cause metabolic issues, bone loss, growth impairment, and other health issues. This creates an undesirable trade-off of trying to balance the negative effects of too much glucocorticoid with the negative symptoms of too much androgen.

Crinecerfont was granted Orphan Drug Designation in the US and EU in 2019. In the second half of 2023, we plan to report results from our Phase 3 CAHtalyst Adult and CAHtalyst Pediatric clinical studies evaluating crinecerfont, an investigational medication that prevents CRF from binding to its receptor and may decrease the high ACTH and androgen levels seen in patients with classic CAH.

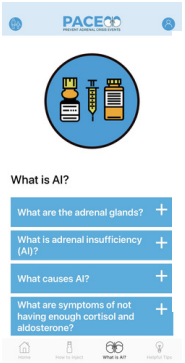
As Neurocrine and Diurnal unite, we all look forward to continuing to work closely with the CARES Foundation to keep this community informed about our investigational treatments in development for CAH and commercial offerings for other endocrine disorders. We are sincerely grateful for your active participation and partnership in this community.

You can learn more about crinecerfont, our investigational treatment in development at neurocrine.com/pipeline/, and more about Diurnal's approved treatments at diurnal.com/nonukresidents/non-hcp/home/.

PACE App

Preventing Adrenal Crisis Events

The new PACE app is now 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.



Email us at support@caresfoundation.org for the Access Code

(Apple App Store Only)
https://apps.apple.com/us/app/pace-by-chaicore/id1490431010

(Android App Store Only)
https://play.google.com/store/apps/details?id=com.jafproductions.PACEAndroidNew

Design by University of South Carolina Chapel Hill

Pinpoint Patient Recruiting, a market research recruitment company, is searching for patients and caregivers who have experience with Congenital Adrenal Hyperplasia (CAH) to participate in a 60-minute paid virtual interview to discuss their experiences with diagnosis and treatment for CAH.

If you or someone you care for has been diagnosed with classic CAH, you may be eligible to participate. Those who qualify and participate in the study will receive $145 as a thank you. All information and responses will remain confidential.

Interested?

To see if you qualify for the study or to get more information, please visit pinpointpatientrecruiting.com/cah-interview or contact Ingles Adams at ingles@pinpointpatientrecruiting.com.

Explore the possibility of changing your classic cah journey

CAHmelia 203 · 204

What is the CAHmelia Study?

Before a medication can be prescribed by a health care provider, it must be tested. Clinical trial programs are health-related research studies in humans that follow a pre-defined, detailed plan to determine the safety and effectiveness of the investigational medication for its intended use.

The primary purpose of the CAHmelia program is to assess if tildacerfont is effective in lowering androgens (testosterone-related hormones) and daily glucocorticoid doses in adults with classic CAH. The CAHmelia studies are dedicated to exploring solutions for people living with classic CAH.(1.2)

Do you live with classic Congenital Adrenal Hyperplasia (CAH)?

Currently, glucocorticoid (GC) therapy is the only treatment for classic CAH. GCs are a type of steroid treatment that can help you manage your condition by replacing deficient cortisol and reducing androgen levels. (3)

Replacing cortisol with steroids is necessary to maintain health in people with CAH. However, many people with classic CAH also need steroids to decrease their androgen production to control symptoms such as excess body hair, fertility challenges, irregular menstrual periods, and testicular adrenal rest tumors (TARTS). (2)

Steroid therapy goals are to prevent life-threatening adrenal crisis across all ages, provide balanced hormone levels and promote normal growth and development.

What is tildacerfont?

Tildacerfont is a new type of oral, once-daily investigational drug that is NOT a steroid.(4) By reducing the amount of androgens (testosterone-related hormones) your body makes, tildacerfont may improve your classic CAH symptoms.(4) This investigational drug will not replace your steroid treatment but may allow you to manage your condition with lower amounts of steroids.

Is tildacerfont safe?

Tildacerfont is generally well-tolerated in healthy volunteers and in people with classic CAH:

Generally well-tolerated at doses under evaluation

Generally well-tolerated across a diverse group of people

References: 1. ClinicalTrials.gov. NCT04544410. Available at: https://clinicaltrials.gov/ct2/show/ NCT04544410 (accessed May 23, 2022); 2. ClinicalTrials.gov.NCT04457336. Available at: https://clinicaltrials.gov/ct2/show/ NCT04457336 (accessed May 23, 2022). 3. Speiser PW, et al. J Clin Endocrinol Metab. 2018;103:4043–88; 4.Sarafoglou K, et al. J Clin Endocrinol Metab. 2021;106(11):e4666-e4679. doi:10.1210/clinem/dgab438;

Glucocorticoid related signs and symptoms to W.A.T.C.H.

- **W** — Weight Gain
- **A** — Appetite increase
- **T** — Temperament/ Mood Changes
- **C** — Circular or Moon Face
- **H** — Hair Growth & Acne (facial)

CAHmelia Clinical Studies FAQ's

Aiming to advance new treatment for classic CAH

Tildacerfont is generally well-tolerated in healthy volunteers and people with classic CAH. Tildacerfont global history includes:

Who can take part in this Study?

You may be able to take part if you*:

- Are at least 18 years of age
- Have a confirmed diagnosis of classic CAH due to 21-OH deficiency
- Take steroids daily (glucocorticoids with or without mineralocorticoids)
- Taking part is completely voluntary, and you may choose to stop at any time.

*Other criteria applies

What can I expect if I enroll?

Before the Study

Evaluations will be done (either at the clinic and/or at home) to see if you can take part in the trial.

During the Study

You will be chosen at random to receive either tildacerfont or a placebo (inactive pill). After the placebo period, everyone will receive tildacerfont. Visits and laboratory tests (blood and/or urine) will be done regularly during the study to monitor the safety of your treatment. Flexible visit schedules may allow evaluations in clinic or at home.

More information on the CAHmelia studies can be found at:
www.CAHstudy.com
or email: *CAHmelia@sprucebiosciences.com*

SCAN ME

CAHmelia 203 · 204

FAQ's

Who qualifies for the CAHmelia Studies?

18 years of age and older and diagnosed with classic congenital adrenal hyperplasia.

Can I participate if I have non-classic CAH?

At this time, only individuals with classic CAH (including salt-wasting and simple virilizing) due to 21-hydroxylase deficiency are eligible for the CAHmelia studies.

Who is conducting the CAHmelia studies?

The CAHmelia studies are sponsored by Spruce Biosciences across 20 different countries, including the United States, Canada, Europe, South America, Asia and Australia.

Where will my study visits take place?

In certain circumstances, you can choose to have home health-care visits or telemedicine appointments instead of visits that would normally be in the clinic. For some tests, you will need to visit the clinic.

Will participants stop taking steroid treatment when starting tildacerfont?

Participants will NOT stop taking steroid treatment. Tildacerfont will not replace your steroid treatment but may allow you to manage your condition with lower doses of steroids.

What if I want to stop participating in the CAHmelia study?

Participation in CAHmelia studies are completely voluntary, you can freely withdraw (discontinue participation) at any time during the clinical trial.

What does it cost?

CAHmelia participants will receive CAHmelia study-related care, including medical tests, clinical care, stress-dosing steroids, and tildacerfont at no cost.

A Personal Story

"When Eliana was 1 week old I got an urgent phone call from our pediatrician. I will never forget that call. Where I was. What I was doing. What my plans for the evening were. Fear and panic washed over me as I heard the words. I was told my daughter's newborn screening came back positive for a genetic anomaly. It was one that I had never heard of. One that was rare enough that the pediatrician hadn't seen it in at least 15 years. I was scared out of my mind. We were told we needed to come to the lab right away to get blood drawn to confirm the diagnosis. Our pediatrician met us at the hospital and talked us through what tests were going to be ran and what they were looking for. We were told those tests take about one week to come back. We were admitted to the hospital that night for observation, lab work, ultrasounds, and light therapy for her jaundice as well. Then, released the next evening with things to watch for.

"When the tests came back she was confirmed to have this genetic anomaly I now know of as Congenital Adrenal Hyperplasia (CAH). She was put on medications right away and referred to a specialist, her endocrinologist. We found out 3 weeks later that she had the salt wasting form and would need to take an additional medication as well.

"Today, 17.5 months down the road, it's not as scary. Still scary at times, but not as much as the beginning. We all have grown through the journey. Through her getting labs, and having to take medications. Us as parents learning to support her during lab work, learning to fiercely advocate for her when we think something needs attention or changed, figuring out how to deliver medications and the schedules, and so much more. She has taught me to be strong, even in some of the hardest and scariest situations in my life. She is happy. Sweet. Busy. Mischievous. She loves her family, going for walks and taking baths. She is tiny, but has a huge personality. She learns and grows more every day, and much, much more. She is my firstborn. My daughter. My sweet independent toddler. Her diagnosis is a part of her, but it doesn't define her. She is so much more than SWCAH. She is Eliana. And she is my inspiration."

Special thank you to Nikki Noble for sharing her story!

THE DOCTOR IS IN

Dr. Karen Lin Su

CARES Medical Director

Guide to CAH Medications

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.

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)

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, 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 polycystic ovarian syndrome.

Aromatase inhibitors

Anastrozole/Letrozole/Aromasin®:

reduce conversion of androgens to estrogens in order to slow bone age maturation and improve height prognosis

NOVEL CAH TREATMENTS IN DEVELOPMENT

CRF1 receptor antagonists

(in clinical trials)

Tildacerfont:

lowers ACTH production by blocking the CRF1 receptor; may allow reduction in glucocorticoid dose

Crinecerfont:

lowers ACTH production by blocking the CRF1 receptor; may allow GC dose reduction

ACTH receptor antagonist

(phase 1 clinical trials)

CRN04894:

blocks ACTH stimulated adrenal androgen production; may allow reduction in GC dose

Gene therapy

Gene therapy by Adrenas:

uses an AAV5 (type of adeno-associated virus) vector to deliver functioning copies of the CYP21A2 gene, which provides instructions for making the enzyme 21-hydroxylase. If successful, it may allow GC dose reduction or even eliminate the need for steroid treatment completely. It is administered as one intravenous dose.

ask the expert

Questions answered, worries alleviated, suggestions offered, CAH medical advice for you and your loved ones

Dr. Karen Lin Su
CARES MEDICAL DIRECTOR

Dr. Alejandro Diaz
Director of the Division of Endocrinology at Nicklaus Children's Hospital in Miami.

pregunta el experto

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

CARES CONNECTIONS 17

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

Haga clic aquí: https://caresfoundation.org/pregunta-el-experto/ para visitar esta pagina.

EDUCATION

MASTER CLASS

June 21, 2023 9PM(ET)

'WHAT WE DON'T KNOW ABOUT CAH'

Presented by:

Dr. Patricia Fechner & Dr. Richard Auchus

Join us, and learn how to better advocate for yourself and/or a family member as a rare disease patient! Do everything you can to ensure that you and your loved ones will be taken care of in the event of adrenal crisis!

Interested in attending? Contact: dina@caresfoundation.org

****OTHER SESSIONS TO FOLLOW****

Patient Advisory Summit

This October, we will be hosting our Patient Advisory Summit (Oct. 6, 2023). Email dina@caresfoundation.org if you are interested in participating!

To see our full event calendar, visit https://caresfoundation.org/calendar/

SAVE THE DATE!

PATIENT EDUCATION CONFERENCE

October 7 & 8, 2023

Washington Athletic Club, Seattle, WA

SCHOLARSHIPS WILL BE AVAILABLE

Contact:

support@caresfoundation.org

for more information!

WASHINGTON ATHLETIC CLUB

CAH AROUND THE WORLD

CANADA

Are you an adult in Newfoundland and Labrador who has Congenital Adrenal Hyperplasia (CAH)?

Do you have CAH due to 21-hydroxylase deficiency based on genetic mutation in CYP21A2 and/or elevated 17-OHP? Consider participating in our study:

What is the study about?
Most individuals with CAH require high-dose prednisone or cortisol replacement therapy, and suffer the long term consequences of that treatment as well as persistent overproduction of androgens and other steroids.

A new oral medication for CAH, Tildacerfont, acts at the level of the pituitary to reduce the production of unwanted androgens and other steroids, and enables a lower dose of prednisone or cortisol replacement to be used. It is currently being studied in two different multicenter clinical trials at the Health Sciences Centre in St. John's, Newfoundland.

Who can participate?
Adult residents of Newfoundland and Labrador who have CAH and are interested in trying a new treatment in the form of a clinical trial.

If you have questions regarding your rights as a research participant please contact the Health Research Ethics Authority at (709) 777-6974 or info@hrea.ca.

@MATES4KIDS

Have you heard about the United Nations' SDGs?

All countries of the world have committed to work together to deliver the United Nations' 17 Sustainable Development Goals (SDGs) by 2030. One of these goals, SDG 3, focuses on good health and wellbeing, with indicators that measure progress: reducing mortality for children under 5 years of age (indicator 3.2.1) and neonatal mortality (indicator 3.2.2); and reducing the preventable mortality associated with non-communicable diseases (chronic health conditions) by 30% by 2030 (SDG 3.4).

How are the SDGs relevant to our CAH Community?

Every day around the world, children born with CAH in resource poor countries of the world are either not diagnosed early enough (often due to lack of newborn screening), or struggle to survive because their parents cannot access the health care or medicines needed to help them survive and thrive. Whilst war, natural disasters, governmental financial collapse and other crises all play a role, the "everyday humanitarian disaster" of extreme poverty in resource poor countries also requires urgent attention.

What is @MATES4Kids?

The @MATES4Kids (Maximizing Access to Essential Supplies for Kids) movement unites individuals and organizations committed to collaborative and innovative action to reduce the preventable mortality associated with CAH by 30% by 2030. Every child living with CAH has a basic human right to health and life, and we are committed to saving as many lives as possible! We propose to achieve this through actions that focus on: improving access to essential medicines; strengthening CAH Communities; and improving access to newborn screening.

How does @MATES4Kids work?

@MATES4Kids facilitates a Community of Practice (a group that meets regularly), with champions from each of the six regions identified by the World Health Organisation (Africa, the Americas, the Eastern Mediterranean Region, Europe, South-East Asia and the Western Pacific Region) to share successes and solutions, and drive the change needed to save the lives of children living with CAH. @MATES4Kids works with a broad range of stakeholders. In March 2023 Paediatric Endocrinologists, CAH Community members, NGOs, multilaterals and others from around the world came together at the International Meeting of Pediatric Endocrinology (IMPE 2023) in Buenos Aires to discuss ways of working moving forward. Achievements to date are already helping to map a path forward, and stories shared from Zimbabwe, Ukraine, Pakistan, Indonesia and Sri Lanka are proving the importance of working together.

How can you get involved?

Please reach out to your national CAH Community, or the team at CARES Foundation (dina@caresfoundation.org) or CLAN (info@clanchildhealth.org) to find out how you can get more involved in the work of @MATES4Kids. We are mapping out a collective journey to 2030 and would love to have your help!

NOTEWORTHY

Pfizer Hospital

Solu-Cortef® Supply Disruption

Guidance and how to access product reserved for patient and specific emergency needs

Patients

- Pfizer can only release product to licensed health care providers for pharmacies. If you are in need of Solu-Cortef® please reach out to your physician or pharmacy to request product under the emergency request process mentioned in the full letter from Pfizer. (See link below)

Healthcare Providers & Pharmacies

- Under Pfizer's emergency request process, Pfizer will distribute Solu-Cortef® 100mg/2 ml (50mg/ml) ATC-O-VIAL Single Dose Vial, NDC 00009-0011-03 direct to healthcare providers or pharmacies only in situations in which providers or pharmacies are unable to gain access to product through direct order from Pfizer.
- Healthcare providers or pharmacies can request product under the emergency request process by completing the Emergency Request Form. Completed forms should be emailed to PISupplyContinuity@pfizer.com. Requested will be reviewed and filled in the order they are received, and only with complete documentation.
- UPDATE: SHELF LIFE EXTENDED BY 5 MONTHS

Having trouble getting Solu-Cortef®? Please let us know. Send us the name of your pharmacy, city and state support@caresfoundation.org

Emergency Request Form - https://www.pfizerhospitalus.com/sites/default/files/Solu-Cortef%20Emergency%20Request%20Form.pdf?cmp=96d9984f-b88f-494e-9567-34fe428ccac4&ttype=WEB

ADVOCACY

EMS Advocacy 2023

We can't stress enough the importance of a visit to your local EMS station. Not only will you be assuring that you as a CAH patient or parent, relative, or caregiver of a child with CAH will get the emergency care you need in a time of crisis, but you will also help pave the way, be an advocate, for other adrenal insufficient/CAH people who may be in need of the same care.

We have observed that the more EMS stations that adopt proper CAH and AI protocols, the more others take note and realize that their stations need the same protocols in place.

It's simple, and CARES provides you with the tools and tips you need for a successful visit. Please take a few moments to visit our EMS Campaign page on our website: https://caresfoundation.org/advocacy-ems-campaign/.

We continue to update our state protocols as they appear. The most recent protocols can be found on the EMS campaign page linked above.

Special thanks to Gretchen Alger-Lin for hosting our Master Class Webinars: EMS Advocacy Part I: Visit Your Local Firehouse and EMS Advocacy Part II: Advocating for Change. We are happy that they were a success!

For more information on free online webinars throughout the year, be sure to be on the lookout for any social media posts, emails, or updates to our event calendar! www.caresfoundation.org/calendar

If you need assistance, please contact our Program Coordinator, Odaly Roche: Odaly@caresfoundation.org.

Global Genes Rare Compassion Program

We are pleased to announce that our trustee, Lesley Holroyd, was invited to apply and participate in the Rare Compassion program with Global Genes. This is a global advocacy non profit organization for rare diseases.

The program is an 8 month commitment from April to November and is in two 4 month segments. Lesley is partnered with a 1st year medical student, and will be partnered with a different student for the second segment. Lesley has already met with her student and plans to meet with them monthly. The objective is for the medical student to learn about living with a rare disease from the patient's perspective. The medical student will also learn how to work and advocate for the rare disease patient.
At the end of each segment they will both do an evaluation of their experiences.

Rarely Told Stories is another part of the program, in which the pairing has to make a short video and submit it to Global Genes. They will select 3 which will be shown at their fall conference in San Diego.

This is a global program with 724 families/individuals participating; 335 are medical students. There are 35 countries with 119 medical schools with 30 unique specialties from 14 of the countries. 48 states in the US are participating.

All participants receive a completion certificate.

Support Group Leaders

CARES support groups and secret Facebook groups are available in a wide variety of demographics for any type of CAH patient or caregiver. Some groups meet for beneficial discussions that ultimately have the goal of providing necessary support in the areas you may need! Share your experience.

Leaders are also organized by topics like "Women", "Teens & Young Adults", "Parents of Newborns", "Parents of Teens & Young Adults", "Men", etc. We hope that you will take advantage of this program. We appreciate our leaders and know that they are there for you when you need extra support!

We are proud to announce two new support groups:

- ***LGBTQIA+***
- ***Grandparents of CAH Children***

Support Group Meetings

Don't forget to check out our monthly, bi-monthly, & regularly scheduled Support Group Meetings. These meetings are hosted on Zoom and there is always a CAH-expert medical professional 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 is send an email to support@caresfoundation.org with the date of the meeting you'd like to attend. To attend, you must first Join the CARES Community. (https://caresfoundation.org/join-the-cares-community/).

Please visit our support pages on our website to see if there is a leader in your area. https://caresfoundation.org/support/

Support can also be found on Facebook on our group page.

MAKE SURE TO SWITCH OVER FROM THE CAH CHAMPIONS PAGE TO CONGENITAL ADRENAL HYPERPLASIA SUPPORT NETWORK PAGE ON FACEBOOK!

DON'T FORGET TO LIKE, SHARE, AND REPOST!!

Congenital Adrenal Hyperplasia Support Network Facebook Page

Here you will find several secret groups where members share stories and experiences! Click the link below to be taken directly to our profile!

Congenital Adrenal Hyperplasia Support Network
185 likes • 280 followers

https://www.facebook.com/profile.php?id=100088886342973

We remind you not to give medical advice here. All medical questions should be addressed by a physician or other healthcare professional. We offer an Ask-the-Expert program on our website where you can email your questions/concerns to our Medical Director, Dr. Su.

https://caresfoundation.org/ask-the-expert/

FUN-RAISING!

June is Congenital Adrenal Hyperplasia (CAH) Awareness Month! Run, jog, walk, or ride every day between June 1st and June 30th. Click the link below to make your pledge!

HTTPS://CHARITY.PLEDGEIT.ORG/C/HUF8YB9DKK

8TH ANNUAL

CLAY SHOOT for CARES

Lehigh Sporting Clays, Coplay, PA

October 19, 2023

LINKS TO SPONSOR, REGISTER & DONATE COMING SOON!

COMPREHENSIVE CARE CENTERS for CAH

Centers of Excellence

Children's Health/UT Southwestern Medical Center
1935 Medical District Dr
Dallas, Texas 75235

For appointments, contact Merritt Lamm or Emily Silva, (214) 456-5980
VISIT WEBSITE

Children's Hospital Los Angeles
4650 Sunset Blvd
MS #61
Los Angeles, CA 90027

University of Southern California/Keck Medical Ctr
8700 Beverly Blvd
Los Angeles, CA 90048

For appointments contact: Janet Guerrero, Comprehensive Care Center Coordinator, 323-361-4630 janguerrero@chla.usc.edu

VISIT WEBSITE

Children's Hospital of Philadelphia/ Main Hospital
3401 Civic Center Blvd.
Philadelphia, PA 19104
Penn Med – Philadelphia, PA

For appointments, 215-590-3174
VISIT WEBSITE

Cook Children's Medical Center
801 7th Avenue
Fort Worth, TX 76104

VISIT WEBSITE

New York-Presbyterian/Weill Cornell Medical Center
525 E 68th St,
New York, NY 10065

646) 962-3442, Option 1
Email, Attn: Koree Richardson, Coordinator
kor2005@med.cornell.edu

VISIT WEBSITE

Riley Hospital for Children/ Indiana University Health
705 Riley Hospital Dr
Indianapolis, IN 46202

Comprehensive Care Center Coordinator – Heather Frady, RN - Email Heather Frady
(317) 412-1206
VISIT WEBSITE

Seattle Children's Hospital and University of Washington
Medical Center
4800 Sand Point Way NE
Seattle, WA 98105

For appointments: (206)987-0304 or toll free, (866)987-2000
VISIT WEBSITE

Rutgers-Robert Wood Johnson Medical School (RWJMS), Child Health Center of New Jersey (CHINJ)
200 Somerset Street
New Brunswick, NJ 08901

VISIT WEBSITE

If you are seeking expert CAH medical care, then plan a visit to one of 8 CARES-designated Comprehensive Care Centers for CAH. These are highly specialized care centers that offer care throughout a patient's life cycle.

VISIT OUR CENTERS OF EXCELLENCE WEBPAGE FOR MORE INFORMATION: https://caresfoundation.org/centers-of-excellence/

Ways to Support CARES

HOST A FACEBOOK FUNDRAISER!

Have you got a birthday coming up, or a wedding anniversary, retirement, or other special occasion? To honor this special event, try raising money for CARES on Facebook. It's easy to do and Facebook takes you through setting up a fundraiser step-by-step. They even published a guide for your convenience: https://tinyurl.com/pvub644a
Make sure to share your fundraiser and use hashtags to bring attention to the CARES community & others with CAH. (#caresfoundation, #congenitaladrenalhyperplasia, #CAH, etc.)

Please keep us in the know by tagging CARES Foundation in your fundraiser post!

Thank you to everyone who raised money for CARES so far!
If you've already hosted a Facebook fundraiser for CARES please let us know that too. We'd like to show our gratitude.

Walmart SPARK

CARES FOUNDATION

Every time you shop at Walmart.com, you can round up and direct Network for Good to support CARES! Visit the link below to see our Page!
https://www.walmart.com/nonprofits/5c53a68e-bace-4c07-a4d2-4ba53a91df19/profile

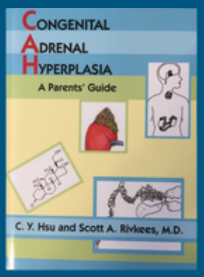
THE CARES SHOP

https://caresfoundation.org/cares-shop-ii/

In our online store you can find helpful tools and resources that can make living with CAH a little bit easier. Check out our assortment of items that promote raising awareness for CAH throughout everyday activities.

Traveling with CAH/AI Packet Printed with Shot Kit

Traveling with CAH/Adrenal Insufficiency (AI) is all about being prepared, taking the proper precautions, and most of all, having fun! CARES Foundation's "Traveling with CAH Packet" will help you plan for a safe and healthy trip.



Congenital Adrenal Hyperplasia: A Parents' Guide

A nuts-and-bolts look at CAH-what this condition is, how it is inherited, and how it is treated and monitored. This new book on CAH written for a lay audience will be welcomed by all patients, parents, caregivers, and healthcare professionals.

Medical I.D. Shoe Tags

Medical ID Shoe Tags are 2-ply red plastic oval tags (1"x1 1/2") with two holes (each 3/16" diameter). Laser engraved with medical id logo on front side and personal info on back side for privacy.

CARES Foundation Ceramic Mug

Beautiful 17 oz. ceramic mug with CARES logo, website and signature heart! Use at home or at the office - a conversation starter for CAH awareness! Price include Shipping & Handling!

Emergency Response Kit (Set of 3)

Clear, plastic, water-resistant bags just the right size for your Emergency Response Kit. Emergency wallet card and Emergency Instructions brochure are included.

CARES Emergency I.D. Luggage Tag

Luggage tag good for a purse/bag, backpack or suitcase. Includes emergency instruction card.

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 Courtney@caresfoundation.org.

www.CARESFoundation.org

CARES FOUNDATION

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