cares Connections

Improving health, connecting people, saving lives

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In This Issue

Twice Daily Compared to Three Times Daily Hydrocortisone in Prepubertal Children with Congenital Adrenal Hyperplasia

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Introduction

Congenital Adrenal Hyperplasia (CAH) refers to a group of inherited adrenocortical enzyme deficiencies. The most common form is 21-hydroxylase (P450c21) deficiency, which causes insufficient mineralocorticoid and glucocorticoid production, leading to a subsequent increase in androgen production [1,2]. The enzyme deficiency occurs on a spectrum; patients with classical CAH have a more severe enzyme deficiency while patients with non classical CAH have a milder enzyme defect [3]. Even within classical CAH, there is a spectrum of enzyme activity in which children with salt-wasting CAH present with both a glucocorticoid and mineralocorticoid deficiency while those with simple-virilizing CAH have primarily a glucocorticoid deficiency [1,3,4]. The lack of cortisol synthesis in classical CAH results in adrenal insufficiency that necessitates daily glucocorticoid replacement. It is particularly important in times of physiologic illness or stress, during which an increased stress-dose level of glucocorticoid treatment is typically warranted. The mineralocorticoid deficiency in salt-wasting CAH can present with hyponatremia and hyperkalemia as early as 5-7 days of life. Treatment includes daily fludrocortisone. Additional sodium replacement is often needed until about 1 year of age, at which point dietary intake is typically sufficient to provide daily sodium requirements [5]. In classical CAH, precursors of adrenal metabolites are shunted to the androgen pathway, causing increased production of testosterone and androstenedione. Signs of excess androgen production may include atypical genitalia in 46,XX individuals, acne, hirsutism, alopecia, premature pubarche, early epiphyseal fusion leading to poor adult height outcome, menstrual cycle irregularities, and impaired fertility [1,3,4]

Hydrocortisone is the mainstay of treatment for children with CAH [4]. It has been proven to optimize adrenal control while having the least growth suppressive impact on the pediatric patient [6]. Supraphysiologic glucocorticoid dosing lowers adrenal androgen production by suppressing ACTH. The aims of treatment are to not only replace cortisol, but to also minimize excess adrenal androgen production, thereby optimizing growth, adult height prognosis, appropriate onset of puberty, menstrual cycles and fertility. However, chronically high dose glucocorticoid treatment in the pediatric population may lead to a cushingoid appearance and growth suppression. Late onset metabolic effects, such as obesity, insulin resistance, hypertension, hyperlipidemia, atrial fibrillation, and venous thromboembolism are also seen in adult patients with CAH [7,8]. It is critical that management of CAH be balanced with known risks of prolonged steroid treatment in the pediatric population. The Endocrine Society published CAH guidelines in 2010, with an update in 2018, that have proposed glucocorticoid dosing. Data show that hydrocortisone should be given in tablet form as hydrocortisone suspension is inadequate to provide a good level of adrenal control secondary to non-uniform distribution of medication in liquid [4,9]. Guidelines also caution providers against doses exceeding 20 mg/m2/day in infants or 15-17 mg/m2/day in children secondary to concerns of growth suppression [4]. The guidelines state that hydrocortisone should be dosed three times daily in growing children and 2-3 times daily as maintenance in fully grown patients. A recent study has found that three times daily hydrocortisone is the most common pediatric CAH regimen globally[10]. However, there is no cited evidence for the superiority of three times daily over two times daily dosing of hydrocortisone in children. Our institution has used twice daily dosing of hydrocortisone as a therapeutic option for children with CAH for decades, finding that the convenience of this regimen helps patient compliance and that biochemical CAH parameters as well as clinical parameters of growth, clinical hyperandrogenism and metabolic risk are well controlled with this regimen [11-13]. We hypothesized that exposure to twice (BID) rather than three times (TID) daily hydrocortisone could reduce the total daily steroid dose and, in turn, reduce metabolic risk factors while still maintaining adequate adrenal control. Moreover, ease of administration could also lead to improved treatment consistency and compliance.

Continued on pg. 3

A Message from the Executive Director

Dear Friend,

Welcome to another edition of CARES Connections. I hope that you find the content shared in this edition informational and helpful. You will notice that we have changed our logo to better represent CAH as a genetic disorder. While we have a new look, our commitment to the CAH community remains unchanged.

Since our last newsletter, we have launched the CAHtalog patient registry in partnership with Neurocrine Biosciences. Patient registries are critical to advance CAH research. If you have not done so yet, I urge you to enroll yourself or your child today. We are also excited to announce that the new gene therapy treatment for CAH has already been administered to two classic CAH patients. This research trial holds significant promise for the future of CAH care. I had the opportunity to visit the laboratory developing this gene therapy once again and continue to be impressed by the commitment of the researchers who are working diligently on behalf of our patients.

Other CAH studies are advancing as clinical trials for Crinecerfont and Tildacerfont continue to grow. We are hopeful that these new treatments will significantly improve the lives of patients. There is also progress on the development of an auto injector for injectable hydrocortisone. A number of companies are making advances on this front thanks to input from many of you.

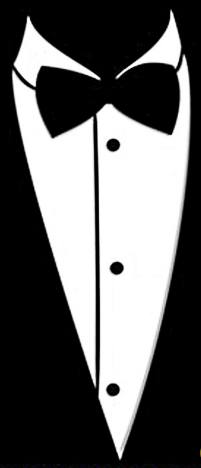
We thank all of you who have participated in focus groups, participated in clinical trials, reviewed protocols, completed surveys and wrote letters in support of treatment options. Your efforts will, undoubtedly, help improve care for patients.

We are grateful that so many of you played a part in raising awareness of CAH during the month of February and for #RareDiseaseDay. We appreciate you sharing your stories about your lives with CAH. We are looking forward to CAH Awareness Month in June and urge you to raise awareness in your own communities. Feel free to contact us for ideas and stay tuned to our website, social media platforms and monthly updates for information on how the community is celebrating.

Finally, we are very excited about our upcoming annual gala. Our 22nd Anniversary Gala will take place on June 4th at Sony Pictures Studios in Culver City, California. We hope you will join us!

With gratitude,

JOIN US for our 22ND ANNIVERSARY GALA!



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We need you! For our 22nd Anniversary Gala, we are asking for short, testimonial-style videos starring you or your child, or both! Tell us how CARES has touched your life.

Tell us what CARES Foundation has meant to you and/or your family; how your life/child's life is different because of CARES. Talk about how CARES:

- Helped you find a CAH-knowledgeable physician
- Provided you with a comprehensive website
- Connected you to a support group leader
- Gave you access to necessary educational materials and patient conferences
- Offered you in-person and online support
- Got you answers to your questions via our Ask-the-Expert program
- Helped you connect with other patients and families who are affected by CAH
- And other ways CARES has made a difference in your life!

The testimonials should be short (15-30 seconds) videos (simple mobile phone videos will work), preferably in close-up. Please do not use personal names. If referring to your favorite doctor, for instance, simply give his/her area of expertise (i.e., endocrinologist, urologist, therapist, etc.). Please be sure to speak slowly so that your message is clear. HAVE FUN WITH IT - IT'S CONTAGIOUS!

Submit your testimonial video today, email to Dina@caresfoundation.org.

DEADLINE IS MAY 12th

Thank you!

Continued from Pg. 1

Materials and Methods

A retrospective chart review (n =128 office visits of 36 individual children) of prepubertal children with classical CAH was conducted at a CAH Comprehensive Care Center at a large New York City medical center between March 2007 and February 2020. Data were extracted from one annual comprehensive visit each year between ages 4 to the onset of puberty. Onset of puberty was defined by either a pediatric LH > 0.3 IU/L or clinical exam findings of Tanner 2 breasts in females or 4 cc testes in males. Some patients had multiple visits analyzed while others had only one, depending on when care was initiated at our center and when the onset of puberty occurred. One representative annual visit in which a bone age was completed was chosen to capture metabolic, growth and adrenal endpoints. At each visit, we compared testosterone levels, androstenedione levels, annualized growth velocity (AGV), bone age, blood pressure, BMI, and total daily steroid dose in those taking glucocorticoids twice daily (n =77) versus three times daily (n = 51). Bloodwork was obtained in the morning approximately two hours after the morning hydrocortisone dose. Annualized growth velocity was measured as the difference in growth between annual visits with associated bone age and was annualized to a full 12 month period if the visits were not exactly 12 months apart. Bone age advancement was calculated as bone age minus chronological age. Annual adrenal control in both groups was also captured based on multiple 17-hydroxyprogesterone levels (17OHP) measured at visits throughout each year. Adrenal control was defined as follows for each year: Good control was defined as 17OHP < 1000 ng/dL, at least 75% of the time. Moderate control was defined as 17OHP < 1000 ng/dL more than 25% and less than 75% of the time. Poor adrenal control was defined as 17OHP < 1000 ng/dL, less than or equal to 25% of the time. IRB exemption approval status was granted by Weill Cornell Medicine Institutional Review Board for retrospective review of de-identified data under exception requirements HHS 45 CFR 46.104(d). Informed consent requirements were waived as well under IRB approval. Univariate generalized estimating equations (GEEs) models were performed to understand the effect of dose frequency on our outcomes of interest. Due to the potential correlation between visits from the same patient, GEE modeling was utilized. The models assumed an exchangeable correlation structure as we expected within-subject observations to be equally correlated. However, using an auto-regressive correlation structure also yielded similar results. All p-values are two-sided with statistical significance evaluated at the 0.05 alpha level. All analyses were performed in R 4.0.5 (R Core Team, Vienna, Austria).

Results

There were no statistically significant baseline differences between the BID and TID groups (Table > 1). (Table > 1). When analyzing biochemical parameters, there was no difference in adrenal control (92% good/fair control versus 82% good/fair control) or testosterone levels (9.65 ng/dL vs 7.62 ng/dL) between those taking hydrocortisone twice daily versus three times daily. 18% of subjects taking hydrocortisone TID had poor adrenal control compared with 7.9% of subjects taking hydrocortisone BID. However, this did not reach statistical significance (p=0.1) (Table 2). Higher androstenedione levels were observed in the BID group than the TID group (40.2 ng/dL vs. 22.5 ng/dL, p<0.05) (Table 2). When looking at growth parameters in the BID compared to the TID group, there were no significant differences in annualized growth velocity (6.86 vs. 6.32 cm per year) or bone age advancement (11.3 vs. 5.91 months) (Table 2). We were not able to detect a difference in total daily steroid doses between those taking twice daily versus three times daily hydrocortisone (12.1 vs. 11.7 mg/m2/day) in prepubertal children being treated for CAH (Table 2). When analyzing metabolic parameters, we were unable to detect a difference in BMI z-score (0.43 vs. 0.31) or systolic blood pressure percentiles (65.5%ile vs. 61.7%ile, p= 0.451) between BID and TID groups. A difference in diastolic blood pressure parameters was noted (64.3 %ile vs. 53.7%ile, p <0.05), though both groups maintained normal diastolic blood pressure percentiles for age (Table > 2)

Table 1

	BID ($n = 77$)	TID ($n = 51$)	p value
Total daily HC dose, mg/m^2/day	12.1	11.7	0.194
Adrenal control, *n* (%)			
Good/fair	70 (92)	41 (82)	0.107
Poor	6 (7.9)	9 (18)	
Androgens			
Testosterone	9.65	7.62	0.442
Androstenedione	40.2	22.5	0.041
Growth parameters			
AGV, cm/yr	6.86	6.32	0.186
Bone age advancement, months	11.3	5.91	0.380
Metabolic parameters			
BMI *Z*-score	0.43	0.31	0.479
Systolic BP, %ile	65.5	61.7	0.451
Diastolic BP, %ile	64.3	53.7	0.018

* p values were calculated using GEE modeling.

Table 2 Baseline characteristics of BID and TID hydrocortisone groups

Characteristic	BID at the first visit ($n = 20$)[1]	TID at the first visit ($n = 15$)[1]	p value[2]
Gender, *n* (%)			
Female	14 (70)	11 (73)	>0.9
Male	6 (30)	4 (27)	
Age at the first visit	6.00 (5.00, 7.00)	7.00 (5.50, 8.00)	0.6
Type of CAH, *n* (%)			
SV CAH	7 (35)	3 (20)	0.5
SW CAH	13 (65)	12 (80)	
Visits, *n*	4 (3, 5)	2 (1, 5)	0.3

[1] *N* (%); median (IQR). [2] Fisher's exact test; Wilcoxon rank sum test.

Discussion/Conclusion

Current standard of care guidelines support the use of daily glucocorticoids in the treatment of classical CAH. Dosage must be finely balanced to prevent adrenal crisis and excess androgen production while also allowing for optimization of linear growth and development [4]. There is a scarcity of studies looking into twice daily dosing regimens and its impact on the efficacy of adrenal control and its side effect profile. Overall, we have found that hydrocortisone dosing twice daily may be as effective in terms of biochemical adrenal control and clinical outcomes of growth compared to three times daily regimens. At the same time, we have demonstrated that patients who were on three times daily dosing were not on a higher steroid dose than those on twice daily dosing and did not have more metabolic compromise in the short term. Although we did not detect a statistically significant difference in adrenal control between those taking hydrocortisone twice daily versus three times daily, it should be noted that a higher percentage of those taking hydrocortisone three times daily had poor control than those taking it twice daily. A possible explanation is that some of those patients may not have consistently taken their mid-day dose, effectively reducing their total daily hydrocortisone [14]. It should be noted that compliance was not evaluated as part of this study design and thus no definitive conclusions can be drawn. It is also possible that by giving some of the total daily steroid in the afternoon (when 17OHP may be naturally lower), it precludes the clinician from giving a higher dose at bedtime or early morning, which could more effectively suppress the innate early morning rise of ACTH-driven 17OHP and androgen production [13,15].

This warrants further investigation.

We did not find any steroid sparing effect with taking hydrocortisone twice daily instead of three times daily as total daily steroid doses were similar in both groups. It should, however, be noted that the subset of patients at our institution who are on TID dosing are given a very low mid-day dose rather than evenly divided doses. Our institution's preference after infancy is to give a higher dose at bedtime to combat the overnight ACTH surge, thereby optimizing adrenal androgen suppression [16]. This regimen is different from those institutions that may choose to evenly divide hydrocortisone three times daily or to administer the lowest dose at bedtime. It is possible that dividing TID dosing evenly may lead to higher total daily doses and different metabolic outcomes. As the total daily steroid dose did not differ statistically between the BID and TID groups, it is not surprising that there were no noted metabolic differences between groups.

Current guidelines advise not to exceed hydrocortisone dose of 20 mg/m2/day in infants or 15-17 mg/m2/day in children [4]. On average, patients in both our twice and three times daily regimen groups met this recommendation with mean daily steroid doses of 12.1 mg/m2/day and 11.7 mg/m2/day, respectively. Of note, these doses are both lower than the average dose of 14.2mg/m2 reported for children ages 6 to onset of puberty in a large European cohort of 14.2mg/m2 in those taking hydrocortisone three times daily [17]. One limitation of this study is that its retrospective nature only allowed for data collected over 13 years. Literature in the adult data show that CAH patients are at increased risk of obesity, hypertension and insulin resistance. [7,8]. We cannot comment on future metabolic impacts that may become evident after puberty as a result of long-term steroid therapy or puberty itself. In our study, no difference was detected with respect to adrenal control based on 17OHP levels or with respect to testosterone levels. A small decrease in androstenedione was noted in the TID group. It remains unclear if this is clinically relevant as this biochemical parameter did not translate into any meaningful clinical differences in growth velocity or bone age advancement.

Current guidelines further note that "insufficient data exist to recommend fractional distribution of doses throughout the day or empiric dosing in the very early morning hours" [4,18]. Still, three times daily hydrocortisone is recommended for growing patients whereas 2-3 times daily hydrocortisone is recommended for fully grown patients [4].

Pharmacokinetics of hydrocortisone and diurnal variation of adrenal products are also essential to consider when understanding optimal dosing intervals. There is remarkable synchronicity in the patterns of ACTH, 17- hydroxyprogesterone, and androstenedione production, peaking at about 4 -10 am [19]. There tends to be a decline in hormones in the afternoon regardless of when hydrocortisone is given [13]. There is also a large physiologic range of half-life for hydrocortisone, which varies greatly from patient to patient. One study has proposed a mean half-life of 76.5 +/- 5.2 minutes with a remarkably large range of 40-225.3 minutes and a clearance of hydrocortisone of 578.5 +/- 1100.6 mls/minute [20]. Thus, patients may have levels of hydrocortisone remaining for longer than expected, albeit not at peak levels. The residual hydrocortisone during the middle of the day may in fact be sufficient to maintain adequate adrenal control. Furthermore, studies of diurnal variation show lowest natural 17OHP levels between the hours of 1600-2000 [13,15]. Dauber et al. has shown that some patients have a natural decline of 17OHP in the afternoon prior to any dose of HC being given [19]. Therefore, adding another hydrocortisone dose at this time with another peak may be physiologically unnecessary [15]. Other studies show that overall 17OHP may be unaffected regardless of hydrocortisone regimens once, twice or three times daily [13].

It is also important to note that there is significant variability in adrenal hormone production depending on time of day, physical activity, daily stressors, and individual patient variability [16,19]. As it is impractical to obtain multiple blood draws throughout the day in clinical practice, there must be some acknowledgement of fluctuation in 17OHP and androgen levels [19,21] . In fact, levels may fluctuate through the day as much as 40 fold [19] and steady state cortisol levels are not only very difficult to obtain [22], but are also not physiologic. Thus, clinical parameters of overall well-being, growth, bone age, and metabolic parameters remain the most important indicators of optimal treatment. These parameters are arguably more important than maintaining continuous steady state cortisol levels and suppressed androgens throughout the entire day. Our study is unique in its ability to highlight that twice daily dosing does not appear to impair any growth or metabolic parameters in children with CAH.

Limitations to our study include its single center and retrospective nature. The retrospective nature of this review limited our ability to understand important information such as dosing compliance. If patients on three times daily dosing only took their medication twice daily, this may have impacted our results. We also reviewed a relatively small number of patients. Multi-center collaborative efforts will be needed to better understand the interplay of dosing distribution and timing of dosing on adrenal, growth and metabolic parameters. In conclusion, we have shown that there is no clear advantage to three times over two times daily hydrocortisone dosing in the treatment of prepubertal children with CAH. With regards to adrenal control, twice daily dosing does not appear to detract from overall adrenal control biochemically nor does it appear to impact growth or bone age advancement.

On the other hand, patients on three times daily dosing are not on a higher glucocorticoid dose compared to patients on twice daily dosing. In addition, prepubertal children on three times daily hydrocortisone do not have apparent adverse outcomes with regard to metabolic parameters. Dosing regimens should therefore be patient-centered with consideration of individual schedules and the family's ability to consistently take the medication as prescribed.

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https://tinyurl.com/8mjpsajs

CAHtalog™
Congenital Adrenal Hyperplasia
Patient & Clinical Outcomes in Real-World Practice Settings

CARES Foundation – in Partnership with Neurocrine Biosciences and PicnicHealth – Launches the CAHtalog™ Registry, a Research Database for Classic Congenital Adrenal Hyperplasia (CAH)

By Eiry W. Roberts, Chief Medical Officer at Neurocrine Biosciences, Inc.

During the past year, CARES Foundation has worked with Neurocrine Biosciences (https://www.neurocrine.com/) and PicnicHealth (https://picnichealth.com/) to establish the CAHtalogTM (Congenital Adrenal Hyperplasia: Patient and Clinical Outcomes in Real-World Practice Settings) Registry. The goal of this remarkable joint effort is to support patient-centered research that will enhance the scientific community's foundational knowledge of CAH and ultimately improve the lives of patients who live with it every day. We are excited to announce that the CAHtalog Registry is now live, and individuals living with classic CAH can enroll and contribute to research with the click of a button.

Why is a patient registry so important? Accelerating progress in the development of treatment options for CAH requires a deep understanding of how the disease and its current standard of care impacts patients and caregivers. By participating in the CAHtalog Registry, you can contribute to the collection of important, real-world data – including disease related quality of life measures – that will form a robust, standardized database to support patients, clinicians, and researchers. Best of all, participation in the CAHtalog Registry is completely anonymous and will not interfere in any way with your current CAH care or eligibility to participate in a clinical trial.

"Patient registries for rare diseases, such as CAH, are extremely important because they strengthen our collective knowledge and provide much needed information in order to advance research for improved management as well as the development of potential new treatments," said Dr. Karen Su, Medical Director, CARES Foundation.

Adults and children living with classic CAH who have received care in the U.S. can visit https://picnichealth.com/CAH to enroll in just a few minutes. With your consent, PicnicHealth will gather and de-identify your medical history and compile it with others' information to create a valuable resource for researchers.

Not only will the CAH community benefit from your participation, but you will have ready access to your digital medical records following enrollment. Specifically, PicnicHealth will digitize and encrypt all your medical records and arrange them into one intuitive timeline, which you'll be able to access and share with your medical providers to help inform future care.

"The only way to bring new treatments to patients is through research. By participating in the CAHtalog registry, patients contribute to the important work of improving the lives of CAH patients," said Dina Matos, Executive Director, CARES Foundation. "It only takes a few minutes to register, patient confidentiality is protected, and participants will receive a copy of their fully digitized medical records."

CARES Foundation is the only non-profit organization solely dedicated to those impacted by CAH. Through their work with the CAH community, CARES recognized the need for data compilation and saw an effective pathway to establish a patient-centered registry through collaboration with a trusted partner, Neurocrine Biosciences.

Neurocrine is a biopharmaceutical company with three decades of experience developing and advancing medicines for neurological, neuroendocrine, and neuropsychiatric disorders and has sponsored and helped CARES Foundation operationalize the program. In addition to supporting the CAHtalog Registry, Neurocrine Biosciences is currently developing crinecerfont, an investigational therapy for the potential treatment of CAH (visit CAHstudies.com for more information). Neurocrine is proud to partner with CARES to launch the CAHtalog Registry and ultimately plans to turn over full ownership of the project to CARES.

Administering the CAHtalog Registry is PicnicHealth, an innovative electronic health records company with a research platform that collects, digitizes, and encrypts medical records to safeguard patient privacy and help improve the scientific and medical communities' understanding of various medical conditions, including classic CAH, to improve care and advance research.

To learn more about the CAHtalog Registry and to sign up, visit https://picnichealth.com/CAH. If you have questions, call (415) 801-0572. Once enrolled, you'll receive free lifetime access to your fully digitized medical records, as well as future updates on findings made based on your contributions as well as contributions from others with CAH.

CARES Foundation, Neurocrine Biosciences, and PicnicHealth are committed to furthering the development of treatment options for CAH, an endeavor that requires deep understanding of both the disease and its impact on the lives of patients and caregivers. Together, we extend our gratitude to you, the CAH patient community. Your participation in research initiatives like this one plays an essential role in advancing CAH treatment and care.

Diurnal

Efmody® (hydrocortisone modified-release hard capsules), which was known as Chronocort during development, was licensed across Europe in May 2021 for use in adolescents from 12 years of age and adults with Congenital Adrenal Hyperplasia. Since then, we have launched in Germany, Austria and UK. As Germany does not have a lengthy procedure for reimbursing a medicine, Efmody usage has been increasing rapidly.Feedback to date from physicians has been very positive and we will be working with physicians in Germany to capture data on how Efmody usage in clinic changes outcomes for patients.
We are also working with our investigators in Germany and the UK to study the effect of Efmody on Addison's disease, and hope that Efmody can help improve the care of patients with this condition.

CONnECT

Diurnal's CONnECT clinical study is now open for recruitment in the US

The study will be opening in four countries:

- US - where 3 sites are open and recruiting and further sites will be open in the coming months
- Japan - where 1 site is open and recruiting and further sites will be open in the coming months
- France - where sites will be open in the next few months
- Turkey - where sites are expected to be open in the early summer.

Your local endocrinologist or CARES representative will be able to find out where your nearest site is.

The CONnECT study is recruiting 150 participants with classic CAH aged 16 and over and will trial Chronocort, a modified release hydrocortisone against Cortef, an immediate release hydrocortisone. It is a blinded study (i.e. participants and their endocrinologists will not know what treatment they are on) and will last for a year.

Details of the CONnECT study can be found on the Clinicaltrials.gov website: www.clinicaltrials.gov Study ID: NCT05063994.

Additionally, at the end of this study participants can choose to continue into an open label follow-on study (the OLE study) where they will receive Chronocort.

Details of the OLE study can be found on the Clinicaltrials.gov website: www.clinicaltrials.gov Study ID: NCT05299554.

You can also get information from the Diurnal website (www.diurnal.com).

eTon PHARMACEUTICALS

Eton Pharmaceuticals Expanding Beyond ALKINDI SPRINKLE® (hydrocortisone) Oral Granules

Eton Pharmaceuticals, launched ALKINDI SPRINKLE® (hydrocortisone) oral granules in 2020, the first and only hydrocortisone adrenal insufficiency treatment designed to provide accurate and individualized dosing for newborns and children. Prior to Alkindi Sprinkle, some parents and caregivers had to use higher strength tablets that were cut, split, or crushed to equal the dose prescribed by their doctor. By choosing Alkindi Sprinkle, parents and caregivers can provide the exact dose their child needs, which can reduce the risks of over- and undertreatment that can occur from cutting and splitting adult-sized tablets. For more information, please visit https://www.alkindisprinkle.com/

Eton Pharmaceuticals has partnered with Crossject to bring the ZENEO® Hydrocortisone Autoinjector, which is under development as a potential rescue treatment for adrenal crisis. The project is on schedule to submit to the FDA in 2023. If approved, the companies are excited to provide a modern autoinjector to patients with adrenal insufficiency. ZENEO® is a proprietary needleless device developed and manufactured by Crossject. The pre-filled, single-use device propels medication through the skin in less than a tenth of a second. The device's compact form factor, two-step administration, and needle-free technology are designed to make it an appropriate delivery system for emergency medications that need to be administered in stressful situations by non-healthcare professionals.

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.
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 https://www.alkindisprinkle.com/patient/ for more information
You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/safety/medwatch, or call the FDA at 1-800-FDA-1088.
Please see Full Prescribing Information: https://tinyurl.com/yxjm4bj8 for more information.

Alkindi Sprinkle® (hydrocortisone) oral granules

NEUROCRINE® BIOSCIENCES

CAHtalyst & CAHtalyst Pediatric Clinical Trials

CAHtalyst STUDY

About the Clinical Trial

A randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of crinecerfont in adults with classic congenital adrenal hyperplasia (CAH), followed by open-label treatment with crinecerfont. The sponsor of this clinical trial is Neurocrine Biosciences, Inc.

Trial Purpose

The primary purpose of this clinical trial is to evaluate the safety and efficacy of an investigational medication called crinecerfont, compared to a placebo, in reducing daily glucocorticoid dosing and improving adrenal-related hormones in adults with classic CAH. After the initial placebo-controlled treatment period, all participants will receive treatment with crinecerfont for one year.

Population

Adults at least 18 years of age with classic CAH and a stable glucocorticoid dose regimen. Learn more: https://tinyurl.com/rmfj5dpu

CAHtalyst pediatric study

About the Clinical Trial

A randomized, double-blind, placebo-controlled clinical trial to evaluate the safety and efficacy of an investigational medication called crinecerfont compared to a placebo, in reducing daily glucocorticoid dosing and improving adrenal -related hormones in pediatric patients with classic CAH, followed by open-label treatment with crinecerfont. The sponsor of this clinical trial is Neurocrine Biosciences, Inc.

Trial Purpose

The primary purpose of this clinical trial is to evaluate the safety and efficacy of an investigational medication called crinecerfont, in children and adolescents with classic CAH. After the initial placebo-controlled treatment period, all participants will receive treatment with crinecerfont for six months.

Population

Children and adolescents between 2 and 17 years of age classic CAH and a stable glucocorticoid dose regimen.
To learn more visit https://tinyurl.com/rmfj5dpu.

SOLUtion Medical
Simplifying Adrenal Crisis Health Management

SOLUtion Medical (https://solutionmedllc.com/) is an early-stage life science company based in Philadelphia, PA developing more patient friendly drug delivery systems for reconstitutable drugs. We specifically aim to improve the administration efficacy of life-saving injectable medication with our TwistJect™ auto-injector for people living with adrenal insufficiency including Addison's Disease and Congenital Adrenal Hyperplasia.

SOLUtion has distributed a survey investigating adrenal crisis medication utilization. Please take a few minutes to participate in this important survey*: https://tinyurl.com/ycy3svvk

*This survey can be translated in to 100+ languages by using the "translate" tab, upper left

spruce BIOSCIENCES

Living with CAH: Patient Experiences with CAH Steroid Treatment

Spruce Biosciences, supported by Clara Health, conducted a confidential survey of 113 patients living with Congenital Adrenal Hyperplasia (CAH) to learn more about their experiences with CAH steroid treatment.

Respondents' Perceptions of their CAH Steroid Regimen

75% of survey respondents were satisfied with their current steroid regimen. 87% found their treatment "very effective" or "effective," 11% found it "somewhat effective," and 2% reported their treatment was "not effective at all." Respondents who were satisfied with their regimen noted that steroids:

- support their quality of life
- are a predictable and familiar treatment
- are easy to administer
- are generally accepted as an effective treatment

Some respondents noted challenges with their treatment, including side-effects. The top seven side-effects that respondents attributed to steroids were weight gain, increased appetite, fatigue, thin skin that bruises easily, a rounded face, mood changes/swings, and depression.

Participants also expressed a lack of awareness regarding the long-term risks of steroid treatment. 50% reported they have discussed the long-term risks with their healthcare provider, 37% said they have not had this discussion, and 13% were unsure. Additionally, 51% respondents have been in a situation where they were not given or able to find enough information about the risks of steroids to make an informed and empowered decision about treatment.

Willingness to Change Current CAH Steroid Regimen If Lower Dose an Option

While respondents noted steroids are effective in treating their CAH, 66% indicated they would be willing to change their current regimen if there was an opportunity to lower the dosage, 29% were unsure if they would make a change, and 5% indicated they were not willing to change their current dosage.

Respondents' openness to adjusting their steroid dosage stemmed from:

- the potential benefit of a new treatment approach
- disliking side-effects
- concerns around long-term usage

Key Takeaways from Survey:

- The majority of respondents indicated they were satisfied with their steroid regimen and found it effective. At the same time, the majority indicated an interest in lowering their steroid dosage if it was an option.
- About half of respondents said they have been in a situation where they were not given enough or able to find enough information about the risks of steroids to make an informed and empowered decision about treatment.
- Respondents' willingness to potentially use a lower steroid dose was associated with concerns around both immediate and long-term side-effects of steroid use.

Clinical Trials and Investigational Therapies For Classic CAH

At the moment, there are no non-steroidal FDA approved treatments for patients living with classic CAH. However, current clinical trials are evaluating investigational drug treatments such as CRF1 antagonists to determine if this class of medications is beneficial to patients with classic CAH. This new class of non-steroidal investigation treatments has the potential to lower the excess androgen production in patients with classic CAH.

If you or a loved one live with congenital adrenal hyperplasia, you can learn more about joining these late-stage clinical studies HERE and the Spruce sponsored study: www.CAHstudy.com

PACE
PREVENT ADRENAL CRISIS EVENTS

News about the PACE app: You are invited to take part in a research project being conducted with those affected by adrenal insufficiency (AI) and their caregivers. The purpose of this study is to provide affected adults and parents/caregivers with readily accessible information and instructions for effectively managing AI through the initial development and testing of the PACE mobile app related to stress dosing and intramuscular injection technique. Click here to take part in the research survey: https://unc.az1.qualtrics.com/jfe/form/SV_6lr4HA5hWsKt3aS

Click here for more information and invitation: https://tinyurl.com/yn7evsvn
(Note, the link at the bottom of this invitation letter will redirect you back to this page; use survey link above to participate in survey)

EDUCATION

Adrenal Crisis and Stress Dosing Videos are a Valuable Resource

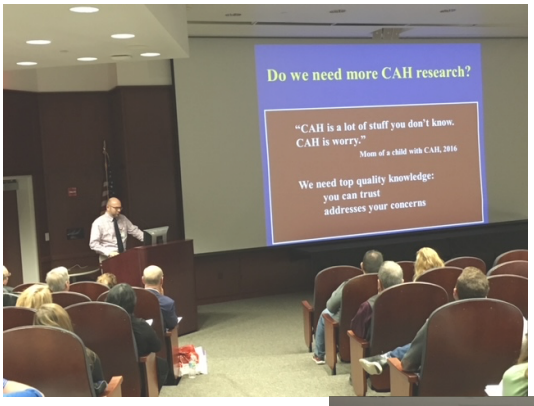
ONLINE LINK: https://caresfoundation.org/emergency-care-videos/

SHOP LINK: https://tinyurl.com/33eba7cy

cares Connections

Did you know that ALL issues of the CARES' newsletters are available on our website? There is tons of information right at your fingertips! Visit our newsletter archives page today. https://caresfoundation.org/cares-connections-newsletters-archive/

We look forward to seeing you, in person, at our 2022 Patient Education Conference in October! Please stay tuned for more information including our featured speakers, session topics, and how to attend!



THE DOCTOR IS IN

Dr. Karen Su
CARES Medical Director

Spring/Summer 2022

1. Extreme heat

Dehydration with salt loss through sweat is of particular concern for patients with CAH. If you/your child is going to be outside for an extended amount of time during extreme heat, please make sure that you have plenty of electrolyte-containing fluids available, along with snacks containing complex carbohydrates and salt (especially for salt-wasters).

Don't forget to apply sunscreen (at least SPF 30) and reapply after getting wet or every few hours (whichever comes first).

2. Increased physical activity

Once school is out, children are likely be more physically active, and they will be at risk for the same dangers that extreme heat can pose. The problems of dehydration with salt loss caused by the heat will be exacerbated by increased physical activity and exertion. Extra snacks and fluids are particularly important for patients with CAH during strenuous exercise. Water alone does not provide adequate replenishment for what is lost during copious perspiration. Gatorade (or similar) provides electrolytes and glucose along with fluid replacement, but it may not contain enough sodium for salt-wasters who are sweating profusely. In these cases, salty snacks will also be necessary to make sure that hyponatremia (dangerously low sodium) does not occur. In certain situations, it may be appropriate to give extra fludrocortisone prior to a particularly strenuous activity, but do not do so without speaking to your endocrinologist first.

3. Sodium Content in Food

In addition to taking hydrocortisone and fludrocortisone, babies with salt-wasting CAH require extra sodium supplementation during infancy because breast milk, formula, and baby food have very little sodium. The usual daily supplemental requirement for infants with salt-wasting CAH is about 1000 to 2000 mg per day of sodium chloride. It can be prescribed as a solution or as sodium chloride tablets to be dissolved in water. If neither of these forms is available, regular table salt can be used instead (one teaspoon of table salt contains 2300 mg of sodium).

Once they are eating regular table food, the sodium content is generally high enough that extra supplementation is no longer necessary, but it can be helpful to know approximately how much sodium is being consumed.

Depending on their blood pressure, older children and adults may also need to know how much sodium they are consuming.

Discuss with your physician how much sodium you or your child should aim for each day. Requirements may be higher during extreme heat or during strenuous exercise (see #1 and 2).

Item	Portion	Sodium (mg)
Apple juice	1 cup	7
Club soda	12 fl oz	75
Milk (1%)	1 cup	124
Orange juice	1 cup	2
Soy milk	1 cup	29
Tomato juice (with salt added)	1 cup	877
Butter (salted)	1 tbsp	117
Butter (unsalted)	1 tbsp	2
Cheese, cheddar	1 oz	176
Cheese, feta	1 oz	316
Cheese, parmesan, grated	1 tbsp	93
Cheese, Swiss	1 oz	74
Egg, whole	1 medium	55
Yogurt, plain, low-fat	8 oz	159
Avocado	1 oz	3
Banana	1 banana	1
Blueberries	1 cup	9
Melon, honeydew	1 cup	17
Olives, ripe, canned	5 large	192
Bagel, plain	3.5 inch bagel	379
Bread, mixed-grain	1 slice	127
Bread, whole wheat	1 slice	148
Croissant, butter	1 croissant	424
Noodles, Chinese, chow mein	1 cup	198
Pretzels, salted	10 pretzels	1029
Chickpeas, canned	1 cup	718
Refried beans, canned	1 cup	753
Beef, ground, extra lean	3 oz	60

4. Trauma

Trauma can occur at any time, but increased outdoor activity creates more opportunities for accidents to occur. Be prepared for trauma by making sure you or your child is wearing a Medical Alert bracelet and Solu-Cortef is easily accessible at all times.

5. Travel

If you decide to travel this summer, check guidelines at your destination for any testing requirements. Be sure to keep handy plenty of fluids and snacks, extra medication, Solu-Cortef, and a letter from your doctor explaining your medical condition and what treatment you require. It may be helpful to obtain the name of a local doctor and hospital in case of an emergency.

Please see our "Traveling with CAH/AI Packet" for more helpful tips: https://tinyurl.com/ypsukm7d

6. Summer Camp

In order for your child to remain safe during camp, whether it is a day camp or sleep-away camp, it is important to prepare ahead of time. If applicable, speak to the camp nurse about any medications your child requires during the day as well as when Solu-Cortef should be administered. Provide the camp with a letter from your doctor to keep on file. Also make sure that camp personnel understand the precautions detailed above under "Extreme heat" and "increased physical activity."

Please see our "Getting Ready for Camp/School" packet for additional information: https://tinyurl.com/8nh7j5cy

Have and safe and enjoyable summer!!

ADVOCACY

Patients, families and other volunteers continue to work toward changing EMS protocols across the U.S. that address adrenal crisis. This ongoing advocacy program is most successful when people get involved on a grass roots level, taking the time to visit local EMS/Fire Stations in their hometowns to illustrate the importance of carrying Solu-Cortef® medication, and to aid patients with adrenal insufficiency like CAH. CARES provides resources to help make your visit memorable.

HERE IS AN EXAMPLE OF A SUCCESSFUL EMS VISIT*. Debbie Cullen, CARES community member, fundraiser, and grandparent of an 17-yr-old granddaughter with SWCAH visits her town, West Sebring, Florida's Fire Station
Your visit can be short & sweet or involve training elements like Debbie's. The most important thing is just to go and alert them to your or your loved one's CAH status! Here are tips for your visit: https://tinyurl.com/w342m8na

I reached out to Captain Anthony Perez and he welcomed me to do a presentation at our local West Sebring Volunteer Firehouse on April 7, 2022. I talked to them about CAH and its different forms. I included poster boards showing them the adrenal glands and the connection to the CAH-absent hormones cortisol and aldosterone. I then explained my goal, and the goal of advocates across the country, to change EMS/EMT protocols for patients with adrenal insufficiency disorders. I mentioned the importance of having Solu-Cortef® on board ambulances for the treatment of adrenal crisis.

By explaining to the assembled EMT group about signs and symptoms of adrenal crisis and what actions to take, I helped to educate this group about a disorder, of which many are still not aware.

I also talked about how I and other advocates have stressed the importance of patients and parents/caregivers making sure that their local EMT/EMS personnel are aware that they and/or a child in the home has CAH. I stressed the importance of medical I.D.s and other safety measures/devices such as seatbelt covers and jewelry. This information is easily obtained via the CARES Foundation website: https://caresfoundation.org/advocacy-ems-campaign/

At the end, there was a brief question and answer period. They wanted to know if an epi-pen type device has been made.

All in all, I would say it was a successful visit. The EMTs were eager to learn how they could better aid this community. A couple of members wanted to know if I could do this for other firehouses and EMTs! I hope to do so and plan on a slideshow for my next visit.

Thank you, Debbie!

VISIT YOUR EMS PROVIDER

EMS REMINDERS:

- Always wear medical identification. ID should include: Adrenal Insufficient/Steroid Dependent - administer Solu-Cortef® at appropriate dosage
- Visit your local EMS before an emergency happens bringing local adrenal crisis protocols + information from our website https://caresfoundation.org/advocacy-ems-campaign/. Ask them to flag your address and/or phone number.
- Inject Solu-Cortef® before calling 9-1-1. Most EMS are not allowed to administer the injection and there can be delays in the ER.
- Ask for paramedics or ALS (advanced life support) to be dispatched

IAED
International Academies of Emergency Dispatch

CARES Foundation is pleased to announce a global collaborative initiative with the IAED (International Academies of Emergency Dispatch) in the development of the first adrenal crisis lesson used in the emergency dispatch setting. The IAED Council of Standards has also approved a new dispatch Determinant Code to be used specifically for a known adrenal crisis within the Medical Priority Dispatch System. This additional code will assist emergency dispatchers to triage suspected/confirmed adrenal crisis calls. Unique to the project is the extent of interaction with multiple stakeholders to achieve this outcome. CARES Foundation is pleased to be a part of this landmark initiative in healthcare. Bravo to IAED in developing and enabling this lifesaving update for EMD communities! For additional information about IAED or to inquire about ProQA software engine using the Academy's Advanced MPDS protocols for EMS/EMD in your area: https://www.emergencydispatch.org/who-we-are/contact-us

About IAED ~
"For more than 40 years, the IAED has been the standard-setting organization for emergency dispatch and response services worldwide, and is the leading body of emergency dispatch experts. We are, first and foremost, a member-driven association working to serve the public through the professional development of dispatchers. We're home to the top leaders, specialists, practitioners, and authorities of the industry. Our various boards and councils work on behalf of the membership—and in coordination with other influential public safety organizations—to ensure that the comprehensive system of emergency dispatching is as safe, fast, effective, and up to date as possible."

Looking for one-on-one support?

We have support group leaders across the US and in other countries happy to lend an understanding ear and offer their experiences. They are patients or parents, caregivers, aunts or grandparents of patients with CAH and thus have a breadth of knowledge on navigating CAH. They are happy to email, text or speak over the phone about issues you or a loved one is facing living with CAH. Email support@caresfoundation.org and we will connect you with a leader who understands.

Or, call our office during regular business hours for support from one of our staff: 866-227-3737.

More interested in online support from a group?

We have a number of secret Facebook groups under our CAH Champions Facebook account. Groups include: Women with Classical or Non-classical CAH, Men with CAH, 3 Beta, 11 Beta, 17-Hydroxylase, Adoption, Newborn, Partners/Spouses, Grandparents/Grand -caregivers, CAH Athletes, Parents/Caregivers of Teens & Young Adults, CAH-X (CAH + Ehlers Danlos Syndrome), Parents/Caregivers of College Students, Women 50+, Bereavement, Parents/Caregivers of Twins with CAH. Find CAH Champions and click on "Add Friend" to be included in a group. Please be sure to let us know if you are under a different name than in our database.

Want access to an expert and support group leaders?

Attend one of our over 20 Zoom support meetings with a CAH expert, support group leaders and others affected. This is a unique opportunity to ask doctors medical questions and get input from other patients/parents/caregivers and support group leaders. See our calendar for a complete schedule: https://caresfoundation.org/calendar/

For Physician Referrals: contact our office 866-227-3737.

For Medical Questions: utilize our ASK-THE-EXPERT form to connect with Dr. Su, our medical director: https://caresfoundation.org/ask-the-expert/

We ♥ our support group leaders! Support is the "S" in CARES and we couldn't offer that without our wonderful and dedicated support group leaders. THANK YOU for all you do!

Check out all of the amazing camp selections for 2022! These are medically-safe camps and free of charge. Spring/Summer & Fall offerings!
https://tinyurl.com/5d9s2rh2

WELCOME ABOARD!

Nicole Bollenbach

Nicole is so happy to be a new member of the CARES Foundation Board of Trustees. She is a board-certified behavior analyst (BCBA) and has been working in the field of special education for the past 20 years. She attended Rutgers University and received a B.A. in English, then went on to get an M.A. in Applied Behavior Analysis at Caldwell College.

She joined the CARES board because she had a daughter, 7 years ago, who was born with Classical CAH. Her daughter almost died when she was 5 days old. She tested positive for CAH however, doctors were not convinced with her positive test result for CAH. They kept retesting because the blood could have hemolyzed, causing a false positive result. Nicole and her husband were told several times how rare CAH is. She and her husband were fortunate to connect with a family who had been receiving support from CARES Foundation. "Our family has benefited from the CARES' support/education calls, various CAH conferences, connecting with other families, and gaining access to the best doctors in the world specializing in CAH. My family and I are forever grateful for CARES Foundation and look forward to supporting the continuation of such a powerful resource for the CAH community."

Mabel Yau, MD

Dr. Yau is an Assistant Professor of Pediatrics in the Division of Pediatric Endocrinology at Icahn School of Medicine at Mount Sinai and Mount Sinai Kravis Children's Hospital. She received a B.A. in both Biology and Economics from New York University, graduating magna cum laude and then received her medical degree from Robert Wood Johnson Medical School in New Jersey. She completed her residency in Pediatrics and fellowship in Pediatric Endocrinology at New York Presbyterian Hospital/ Weill Cornell Medical Center. Dr. Yau's clinical research focused on rare genetic endocrine disorders such as congenital adrenal hyperplasia and apparent mineralocorticoid excess. She has evaluated the quality of life in children with congenital adrenal hyperplasia, studied the genetics of congenital adrenal hyperplasia to provide prenatal counseling and studied the long-range outcomes of rare adrenal disorders. Dr. Yau also partners with a neurologist to see patients with Adrenoleukodystrophy in a combined clinic at which patients can see both providers in the same day.

Dr. Yau has written many articles for peer-reviewed publications, text book chapters, and scientific abstracts. She lectures often and holds prestigious academic positions. She is currently participating in the crinecerfont clinical trial.

She often attends CARES' support group meetings as the CAH medical expert, and we are excited to have her as member of our Scientific & Medical Advisory Board!

Comprehensive Care Centers for CAH

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
For surgical consults, please call the Urology Clinic at 214-456-2444

RESEARCH/CLINICAL TRIALS:

The following clinical trials have started or are ongoing:

- Sponsored studies of crinecerfont (a corticotropin releasing hormone receptor antagonist) in children (NCT04806451) and adults (NCT04490915). Our adult site currently has the second largest number of patients enrolled in the country.
- Sponsored study of a modified-release form of hydrocortisone (Chronocort) (NCT05063994).
- Restarting our NIH-supported trial of abiraterone acetate (NCT02574910).

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 or
VISIT WEBSITE:
https://www.chla.org/congenital-adrenal-hyperplasia-cah-clinic

RESEARCH/CLINICAL TRIALS:

Investigator-initiated Studies

- Best Starts in CAH: Neurodevelopment – We are studying neurodevelopment in young children (ages 0-8y) with classical CAH. - We would like to begin a related multi-site study examining cognitive function via iPad-based tasks with CHOP and Children's Hospital Pittsburgh that would be administered in the clinic to patients.
- 3-dimensional Facial Features in CAH – We are studying facial features in patients with CAH of all ages in 3-D. We reported our findings in 2-D last year.

Clinical Trials

- CYP21A2 Gene Therapy – Clinical trial with Adrenas
- Clinical trials with Neurocrine (Adult and Pediatric trials) and Spruce

Children's Hospital of Philadelphia
Main Hospital
3401 Civic Center Blvd.
Philadelphia, PA 19104

For appointments - (215) 590-3174. VISIT WEBSITE: https://www.chop.edu/centers-programs/adrenal-and-puberty-center

RESEARCH/CLINICAL TRIALS:

We actively enroll in the following trials

- Neurocrine trials for adult and pediatric patients
- Spruce Bioscience trials for adult patients
- Working on the regulatory aspects of upcoming Chronocort trials with Diurnal

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

VISIT WEBSITE:
https://www.cookchildrens.org/services/urology/specialty-programs/congenital-adrenal-hyperplasia

RESEARCH/CLINICAL TRIALS:

- Approved for 3 Tildacerfont studies – Spruce Biosciences CAHmelia 203 and 204.Tildacerfont is a medication that is being studied as a treatment specifically for CAH. Patients must be on a stable course of medications for 3 or more months to be eligible.
- Evaluation of the abnormalities in the 3 BHSD axis in term babies with an abnormal newborn screen
- Continued collaboration in the multi-site study on surgical outcomes

New York-Presbyterian/Weill Cornell Medical Center
525 E 68th St,
Box 103
New York, NY 10065

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

VISIT WEBSITE:
https://www.nyp.org/komansky/comprehensive-center-for-congenital-adrenal-hyperplasia

RESEARCH/CLINICAL TRIALS:

Pediatric Endocrinology:

- Retrospective chart review study comparing patients with CAH who take hydrocortisone twice daily vs those who take hydrocortisone three times daily. The study examines multiple variables including adrenal control, growth, skeletal maturation, weight gain/body mass index, and final adult height outcomes. The manuscript was submitted to Hormone Research in Paediatrics and is under review.
- Adipokines and Metabolic Parameters in CAH: Prospective cross-sectional observational study to evaluate the impact of steroid dosing on metabolic risk factors in our patient population of children and young adults with congenital adrenal hyperplasia. The primary objective of this study is to correlate adipokine levels of visfatin and adiponectin with steroid doses in patients with congenital adrenal hyperplasia, as a way to classify their future metabolic risk profile. Secondarily, we will look at inflammatory and metabolic markers (CRP, leptin, lipid panel, insulin level,
- glucose and HbA1c to better understand how steroid
- dosing impacts these measures.
- We have completed a comprehensive survey on transitioning from pediatric to adult care, which has given us insight into the challenges of the transitioning process. The survey was distributed by CARES. A medical student is reviewing and analyzing data this spring.
- Perioperative Stress Dose Management of Children with CAH: Manuscript published
- Mental Health in Children with CAH and Their Caregivers: One of our fellows is conducting a prospective cohort study to investigate the associations among anxiety and depressive symptoms in CAH children, adrenal control, and caregiver stress.
- Neurocrine Biosciences: A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Crinecerfont (NBI-74788) in Pediatric Subjects with Classic Congenital Adrenal Hyperplasia, Followed by Open-Label Treatment. Phase 3 study. Protocol number: NBI-74788-CAH2006. Weill Cornell Medicine selected as a site and we are in the final stages of IRB approval.

Pediatric Urology:

- Modeling cyp21a2 dependent steroidogenesis in zebrafish for application in Congenital Adrenal Hyperplasia
- We developed a real-time in vivo cyp21a2 reporter model and a CAH mutant zebrafish that can be used to provide new insights into CAH. Future studies utilizing our reporter fish, CAH mutant fish, and drug hits may translate to a novel treatment strategy for patients with CAH.

Comprehensive Care Centers for CAH, continued

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

(317) 412-1206
VISIT WEBSITE:
https://www.rileychildrens.org/departments/congenital-adrenal-hyperplasia-program

RESEARCH/CLINICAL TRIALS:

- Continuing to analyze and publish on the collaborative Life with CAH Study. We anticipate several additional papers will be published in 2022, including one about the experiences and preferences of North American women with CAH about disclosure of genital surgery performed in childhood.
- Life with CAH: abstract to the annual Pediatric Endocrine Society meeting
- A study looking at CRF receptor antagonist (by the company Neurocrine)
- Retrospective review of cases of classic CAH missed on the newborn screen (in process with planned abstract submission to PES)
- A Randomized, Double-BLind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Reducing Supraphysiologic Glucocorticoid Use in Adult Subjects with Classic Congenital Adrenal Hyperplasia NCT 04544410
- Paper published this year: Crinecerfont Lowers Elevated Hormone Markers in Adults with 21-Hydroxylase Deficiency Congenital Adrenal Hyperplasia. Auchus RJ, Sarafoglou K, Fechner PY, Vogiatzi MG, Imel EA, Davis SM, Giri N, SturgeonJ, Roberts E, Chan JL, Farber RH. J Clin Endocrinol Metab. 2021 Oct 15, PMID: 34653252

REGISTRIES:

- International-CAH Registry: The I-CAH registry is used by a group of clinicians and scientists who are involved in performing research as well as delivering clinical care in the field of differences of Congenital Adrenal Hyperplasia (CAH).
- Internal SCH CAH Registry: The purpose of this study is to create an internal registry for patients seen at Seattle Children's Hospital with a diagnosis of Congenital Adrenal Hyperplasia (CAH).

We hope you have the opportunity to visit one of our centers where you will receive thoughtful, expert care!

If you do visit one of our eight centers, please take a moment to complete our Patient Survey. We would be grateful for your feedback!

https://tinyurl.com/5fdcs7e3

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:
https://www.seattlechildrens.org/conditions/congenital-adrenal-hyperplasia/

RESEARCH/CLINICAL TRIALS:

- A Phase 2, Open-Label, Multiple-Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of NBI-74788 in Pediatric Subjects with Congenital Adrenal Hyperplasia NCT 04045145
- A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Crinecerfont (NBI-7488) in Pediatric Subjects with Classic Congenital Adrenal Hyperplasia, Followed by Open-Label Treatment. NCT 0480645
- A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Crinecerfont (NBI-74788) in Adult Subjects with Classic Congenital Adrenal Hyperplasia, Followed by Open-Label Treatment. NCT 04490915
- A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Adult Subjects with Classic Congenital Adrenal Hyperplasia. NCT 04457336

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

VISIT WEBSITE:
https://www.rwjbh.org/bristol-myers-squibb-childrens-hospital-at-rwjuh/treatment-care/endocrine-disease/

RESEARCH/CLINICAL TRIALS:

- A Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Study to Evaluate the Efficacy and Safety of SPR001 (Tildacerfont) in Adult Subjects with Classic Congenital Adrenal Hyperplasia, Pro2020002958
- Outcome of positive newborn screen for congenital adrenal hyperplasia, Pro2019000920

FUN-RAISING!

OUR BIGGEST FUN(D)RAISER OF THE YEAR IS RIGHT AROUND THE CORNER!

Have you decided how you would like to support our 22nd Anniversary Gala?!? Learn more: www.bidpal.net/2022CARESGala

PARTY LIKE 007

Congenital Adrenal Hyperplasia cares FOUNDATION

AWARENESS WALKS 2022

Our CAH Awareness Walks are the best way to raise awareness because this year they are LIVE and involve CAH patients, parents, healthcare professionals and CARES' supporters and friends!

FLORIDA
November 5, 2022
Sand Point Park, Titusville

We already have a commitment from our Board of Trustees' Secretary, Lesley Holroyd, to host her popular Titusville, FL walk again this year! We hope to announce more walk dates soon and look forward to some walks hosted in new areas of the country. Stay tuned for link to attend, fundraise and donate!

CALIFORNIA
October 2, 2022
Santa Anita Racetrack, Arcadia

Join us in Arcadia, California for the 9th Annual CALIFORNIA CAH AWARENESS WALK! This event was virtual the last two years and we are excited to welcome back supporters in person! Held again at the Santa Anita racetrack in beautiful Arcadia, this event is a favorite with food, raffles, auctions, kid activities and more. Links soon to attend, fundraise and donate.

WE WELCOME EVENT SPONSORS FOR ALL OUR WALKS - if interested, please contact Dina@caresfoundation.org TODAY!

If you think that you might like to host a walk in your area, please let us know. Email Dina@caresfoundation.org. WE'D LOVE TO HEAR FROM YOU!

FAMILY FUNDRAISERS

No matter the size, shape or ages of your family, it is a rewarding experience to host a family fundraiser! Fundraisers can be large or small, fancy or plain, but they are always fun! We hope that you will consider hosting a family fundraiser this year to raise much-needed funds for CARES. Bake sales, marathons, auctions, raffles, bowling, karaoke, musical performances, are all examples of ways to fundraise for CARES. Please check out our Fundraising Guide: https://caresfoundation.org/wp-content/uploads/2022/03/FUNDRAISING-GUIDE-2022.pdf for ideas and tips on how to accomplish your fundraiser. Contact Dina@caresfoundation.org to share your ideas.

We wish for sunshine, blue skies, lots of fun, and great success for this SOLD-OUT, 4th Annual Captain Jack Golf Tournament on May 9, 2022. This event, hosted by the Porter family in Massachusetts promises to be a special day!

We look forward to posting pictures of the event in our Fall newsletter, and thank the Porter family for all of their hard work in making this fun day possible.
Sponsorships are still available: https://tinyurl.com/284wddn8 and you can make a donation here: https://tinyurl.com/yckns38a

Long-time supporter of CARES and CAH parent, Sue Shirey was roasted in the style of the old Dean Martin Roasts to change up her annual James Party fundraiser. A local comedian was the Master of Ceremonies while Sue's family and friends spilled all to roast her. They shared stories with no subject off limits and the evening was marked by hilarious laughter!

There was a live auction hosted by Ken Shirey, Jr. with amazing and unique items to bid on. It was a night of glitz, glamour, and cocktails.

Sue Shirey has been involved in many community and philanthropic causes over the years. When tragedy struck in 2009 and her oldest son James passed away suddenly from CAH complications, Sue took the pain and turned it into a blessing by forming The James Shirey Foundation, Inc. so she could bless others and keep James' name and spirit alive. CARES Foundation is grateful to be one of the beneficiaries of funds raised for this annual event and we thank Sue for her tireless efforts and generous support!

THE JAMES SHIREY FOUNDATION, INC.

Simple ways to support CARES

amazonsmile
You shop. Amazon gives.

SHOPPING WITH AMAZON SMILE is the easiest way to raise funds for CARES! All you have to do is switch your Amazon shopping page from Amazon.com to AmazonSmile.com. All of your info remains the same, all of the Amazon products you know and love are still there, and the best part is, that when you switch whatever you purchase means a donation to CARES Foundation. CLICK HERE to sign-up and choose your charity (CARES Foundation, of course!): https://smile.amazon.com/charity

Become a Fundraiser on Facebook

Fundraising for CARES is beneficial and easy to do!
Share your personal stories about life with CAH, celebrate a special event, pay tribute to some one who has guided you on your CAH journey and when you do make it a fundraiser for CARES! Here is a guide on Facebook fundraisers for when you are ready to make a difference!
https://www.facebook.com/fundraisers/
AND NOW, you can link your Facebook fundraiser to your Instagram account for more exposure and even greater success. Check it out:
https://tinyurl.com/2p88azj4

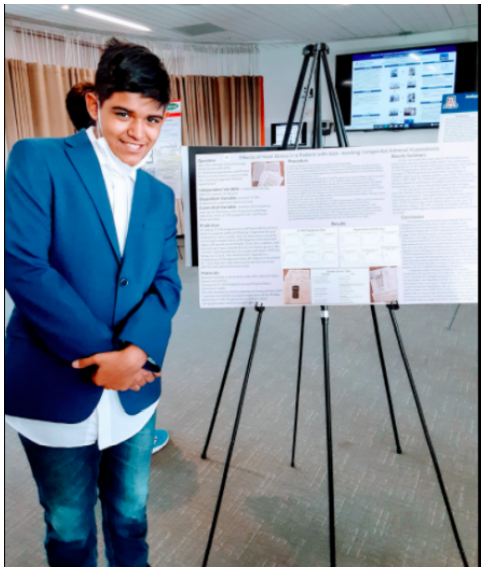
THANK YOU to Shay Lawson, March 27, and Corrine Byrne, March 30, for fundraising for CARES to celebrate their birthdays!

A PERSONAL STORY

My name is Alexis and I'm an eleven year-old boy who was born with salt-wasting Congenital Adrenal Hyperplasia. My favorite sport is football and my favorite school subjects are math and science. I think CAH does not limit me as a person, student, or athlete because I just need to manage my medication and stay extra hydrated to be safe. I live in a place where temperatures can go as high as 118 to 122 degrees. The heat can put a lot of stress on my body while playing sports. My mother and I noticed that my laboratory results were high during hot months when I was doing outdoor activities, which inspired me to do a Science Fair project. I also did this project because I want to spread awareness and encourage the Arizona Department of Health Services to make all ambulances carry a Solu-Cortef shot. My project's research question was:
"How does the heat stress from high temperatures affect the 17-hydroxyprogesterone, and plasma renin activity levels in a patient with salt-wasting Congenital Adrenal Hyperplasia?" My research question is important and unique because if scientists have not studied this topic, then endocrinologists will not be able to give accurate medical advice on stress dosing for heat stress. The idea that a CAH patient should stress dose for heat stress has not been researched and stress dosing is only suggested in times of illness or injury. I collected six years of laboratory results and divided them into six trials. My prediction was that heat stress elevates the 17-OH progesterone (OHP) and plasma renin (PR) levels in a patient with CAH. My results supported my prediction because the 17-OH progesterone was over the normal range in four of the five years. One limitation in my project was that I only had my own results, not other patients with my condition. It would help to be able to analyze data from multiple patients to see how they compare to mine. One thing I learned in research for this project was that there are only 15 out of the 50 states that make their ambulances carry a Solu-Cortef shot and Arizona isn't one of them. This information is important for anyone who has CAH, like me. I think it's important that all states should carry a Solu-Cortef shot in their ambulances because this can be a life-saving injection for people with an adrenal insufficiency disorder like mine in times of adrenal crisis and other emergency situations.

My science fair project was awarded first place in my county and third place in all of Southern Arizona. I was also invited to present my project to professionals from Arizona, New Mexico, Southern California, and Northern Mexico at the Southwest AG Summit in Arizona.

When I grow up, I want to be a chemical engineer so I can invent medicines.



Congratulations on your award, Alexis, and thank you for sharing your story and raising awareness of CAH!

June is CAH AWARENESS MONTH

How will you spread awareness?

We encourage all of those affected by CAH to do their part in spreading awareness of this disorder. When dealing with a rare condition, it's important to make sure that all are aware that CAH exists and that CAH patients get the same right to treatments and medications and their fair share of research resources that other medical conditions are afforded.

- **Visit your local firehouse/EMT station**
  This is important for raising awareness of CAH AND for alerting your local emergency office/s about your or your loved one's condition & how important it is that they are prepared in case of adrenal crisis.
- **Host an CAH event at your school, church, workplace, community center, etc.**
  Awareness is about education and informing the general public about CAH - what it is, how it effects people and why they should care.
- **Share your story with a local newspaper or online news source**
  Let your community know about CAH. People tend to help more when they read someone's personal story.
- **Post pictures, videos and your CAH story on social media**
  If ever there was a time to let everybody know what you're coping with as a CAH patient, family member or caregiver, this is it! Let's light up social media with CAH stories!
- **Attend our June 4th Gala**
  JOIN US as we celebrate the CAH community! We are stronger together and when we gather in CA for our gala it's a chance to bond, share, & support CARES - as a non-profit that has helped those affected by CAH for more than two decades. (See link on page 4)
- **Wear an awareness ribbon or pin throughout the month of June**
  Spark interest, start conversations by sporting a Tiffany-blue ribbon for CAH Awareness Month!

Every year the Geletko family goes all out for Rare Disease Day because two of their three children are affected by CAH. They celebrate by raising awareness of rare disease, showing up in blue jeans for work and school, distributing informational flyers and pamphlets, passing out #RareDiseaseDay lapel pins, sharing their stories on social media and fundraising for CARES. Colleen Geletko, mother of two CAH children, hosted a Facebook fundraiser on Rare Disease Day, February 28 2022. In fact she has been raising awareness and funds for many years. Thank you, Colleen & family for your bravery, your generosity, and for waving the #RareDiseaseDay flag!

MT. HOREB HIGH SCHOOL SENIOR HOSTS "CAH NIGHT" SOFTBALL GAME

High school senior & CAH patient, Sydnee Swiggum hopes to RAISE AWARENESS of CAH by hosting a CAH awareness event for her softball team's game on May 6, 2022. Sydnee, along with help from her sister and her teammates, have put a lot of effort into promoting this event which will feature CAH-themed t-shirts, posters, informational pamphlets, refreshments, a 50/50 raffle with proceeds donated to CARES, and lots of fun!

Thank you ALL, for spreading awareness of CAH!

Please remember that CARES Foundation newsletters have "gone green" and are now only available electronically. Please make sure we have your most current email address and contact information to ensure that you continue receiving newsletters and other important information from CARES. Send your updated information to Odaly Roche at Odaly@caresfoundation.org.
Disclaimer: any communication from CARES Foundation, Inc. is intended for informational and educational purposes only and in no way should be taken to be the provision or practice of medical, nursing or professional healthcare advice or services. The information should not be considered complete or exhaustive and should not be used in place of the visit, call, consultation or advice of your physician or other healthcare provider. You should not use the information in this or any CARES Foundation, Inc. communication to diagnose or treat CAH or any other disorder without first consulting with your physician or healthcare provider. The articles presented in this newsletter are for informational purposes only and do not necessarily reflect the views of CARES Foundation, Inc.

CONGENITAL ADRENAL HYPERPLASIA FOUNDATION

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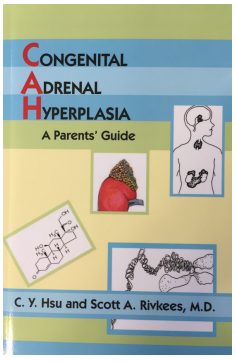
Fax: (908) 686-2019
Email: contact@caresfoundation.org
Website: www.CARESFoundation.org

THE CARES SHOP

In our online store, you will find helpful tools to make living with CAH a little bit easier as well as an assortment of items to help raise awareness of this rare disorder.

EMERGENCY RESPONSE KITS - Perfect for school, camp, clubs, sports, and leaving with the baby sitter! Clear, plastic, water-resistant bags just the right size for your Emergency Response Kit. Emergency wallet card and Emergency Instructions brochure are included. Purchase our package of 3 kits and have extra for all your needs - keep one in a purse, backpack, at Grandma's, etc.



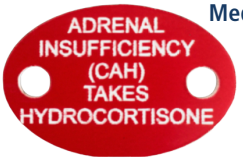
Congenital Adrenal Hyperplasia: A Parents' Guide

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.

- By C.Y. Hsu and Scott A. Rivkees, M.D.

Adrenal Insufficiency Window Cling

In case of a car accident, this sign will alert emergency medical staff that there is a passenger with adrenal insufficiency in the car. The sign "clings" to car windows and can be easily removed. Have more than 1 car? Buy extras so you don't have to worry about moving it!

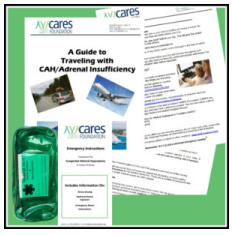


Medical ID Shoe Tags

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 medical info on back side for privacy.
Tell First Responders how best to care for you in an event of an emergency. Perfect for active kids and adults!

***"BUZZY"* PAIN MANAGEMENT DEVICE**

Buzzy is a palm-sized device combining cold and vibration that when placed between the brain and the pain, decreases sharp pains. His wings are icy cold, and his tummy vibrates when you touch his head. This confuses your body's nerves to block sharp feelings, just like rubbing a bumped elbow helps stop the hurt, or cool running water soothes a burn. Buzzy is ideal for blood draws, vaccinations, flu shots, dental procedures and more.



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! Whether you or your loved one is staying overnight, leaving for a couple of days, or traveling to a foreign country, CARES Foundation's "Traveling with CAH Packet" will help you plan for a safe and healthy trip.

ALL CARES SPECIALTY ITEMS REDUCED!

T-Shirts

Luggage Tags

CAH Awareness Pins

Mugs

Car Magnets

Bracelets

AND MORE!

VISIT THE CARES SHOP TODAY!

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