CARESFoundation
research, education and support for CAH
Improving health...connecting people...saving lives

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CAH Comprehensive Care Centers

Imagine the possibilities...

Have you ever had trouble locating an endocrinologist well versed in CAH? Have you needed care from other specialties, but the physicians do not communicate with each other? ***We are working with experts in the CAH healthcare arena to change that.***

CARES has engaged the world's leading clinicians in CAH as well as individuals and families affected by this condition to develop guidelines for the establishment of CAH Comprehensive Care Centers (centers of excellence for CAH) throughout the US. The overarching goal of these centers is to improve care for those affected by CAH throughout their life span. The centers will be comprised of multi-disciplinary teams of healthcare professionals. The teams will include pediatric and adult endocrinologists, urologists, surgeons, gynecologists, fertility experts, psychologists, primary care physicians, geneticists, nurses, nutritionists, and other specialists who will care for CAH patients from birth through adulthood.

Background:

As diagnosis and clinical care improves, there is a growing population of adolescent and adult patients with CAH. However, at present there are no centers in the United States recognized as specializing in the care of teens and adults with this disorder.The result is significant disparity in the quality and comprehensiveness of care that patients receive. CAH Comprehensive Care Centers will ensure a continuum of care throughout the lifecycle of the CAH patient that will lead to better treatment practices and improve health outcomes. The centers will also serve as a resource for research opportunities which one day may lead to a cure. **...Together we can make it a reality**

For more information on this initiative, click on:
http://www.caresfoundation.org/productcart/pc/comprehensive_care_cah.html

An Evidence Based Recommendation for Hydrocortisone Dosing during Puberty in Classical Adrenal Hyperplasia (CAH)

Walter Bonfig, MD

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Management of children with CAH is a challenge with regard to growth outcome: the children are at risk for early pubertal development with decreased pubertal growth. When regular timing of puberty is achieved by glucocorticoid treatment, there is the risk of too tight control, which might also result in short stature. Traditional treatment consists of substitution of cortisol to reduce excessive androgen production and its consequences. Undertreatment with glucocorticoids leads to androgen excess with advancement of bone age, and reduced final height. In overtreatment growth is suppressed by growth inhibiting effects of glucocorticoids. Further side effects of overtreatment are obesity and osteoporosis. Alternate approaches in the treatment of CAH have been investigated recently,

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IN THIS ISSUE

A Message from the Executive Director

Dear Friends:

This is a very exciting, as well as, challenging time for our organization. Exciting because, we are working on projects that will have a significant impact on the lives of those living with CAH—namely preparing to establish CAH Comprehensive Care Centers and advocating for EMS protocols during an adrenal crisis. Our greatest challenge is doing this while funding, both public and private, continues to decrease. Both of these projects will have a tremendous impact on CAH patients, but we need your help to move forward. Your support is critical to the success of our new endeavors, as well as to our ability to continue existing programs such as research, physician referral, one on one support, and education.

Our last newsletter included two pages of fun and easy ways that individuals can raise funds for CARES. If you missed it, it's on our website. Try using social networks such as Facebook and Twitter to raise awareness and funds. The holidays provide a perfect opportunity to raise funds for CARES. Teachers get plenty of mugs, candy, ornaments and other knick knacks. Why not show your appreciation with a CARES cookbook or with a donation in honor of your child's teacher this year? You will help raise funds and spirits. If every CARES family raises $500, it will total one million dollars. Imagine what we can do with that… Together, we can do it.

CARES Charity Cookbook

The CARES Foundation Charity Cookbook is here! It's filled with many wonderful recipes sent in by CARES families and friends. 100% of the profits raised by this book will fund CAH support, education, advocacy and research. Consider purchasing extra copies for friends, family and special occasions, such as: birthday, anniversary, wedding shower, hostess, Mother's or Father's Day, teachers, thank you, house-warming, or just because. The book can be purchased through our website (*www.caresfoundation.org*) for the low cost of $20. Get yours today!

No-Sweat Run for a Cure

It's not too late to make a donation for the No-Sweat Run for a Cure! You can still contribute through the CARES website. Proceeds from this year's campaign are significantly lower than previous years and will impact the services and programs that we can provide going forward. Please help us get closer to our goal by making your donation today at *www.caresfoundation.org*!

CAH Comprehensive Care Centers (Centers of Excellence)

If you are an adult who has experienced a lack of quality care, you understand the significance of having a place where you can access care that will encompass all your needs, provided by a leading CAH expert. If you are the parent of a child with CAH, remember that as your child grows, his or her needs will also grow and when they reach adulthood, they will require continued specialized care.

CARES is working with a group of top, international experts in the care of CAH to create guidelines to establish CAH Comprehensive Care Centers. In September, these professionals gathered together at a meeting in Bethesda, MD to write these guidelines. We look forward to publishing and presenting the guidelines and to begin the process of opening the first Comprehensive Care Center.

We are very excited about a future that includes the best and most comprehensive care for those affected by CAH and hope that you will support us as we work hard to make this a reality.

CARES Education Series

It is with much regret that we announce the cancelation of the CARES Education Series (formerly the CARES Family Conference). Canceling the Series was a difficult decision, but the lack of funding and the high cost of financing it made it impossible for us to continue with our plans. We are looking at cost-effective ways to provide patient education and will notify you of our efforts in the future.

Personal Stories

Many of our newsletters have included inspirational personal stories about living with CAH. We would love to be able to include a personal CAH story in each and every newsletter, so I'm inviting you to tell yours. We are especially interested in stories about your experience during an adrenal crisis. These will help CARES demonstrate the need for EMS protocols for adrenal insufficiency. If you'd like to share your experience with the rest of our membership, please send your story, with a picture or two, to Suzanne Levy at *suzanne@caresfoundation.org*. We look forward to reading your story!

Thank you for supporting our efforts as we meet the needs of the CAH community.

Warm regards,

Dina

Welcome Aboard!

Please join us in welcoming Dr. Heather Applebaum to the CARES Foundation Scientific & Medical Advisory Board.

An obstetrician and gynecologist, Dr. Heather Applebaum has a special interest in congenital anomalies of the reproductive tract, pediatric pelvic reconstructive surgery, pediatric and adolescent gynecologic surgery, minimally invasive/laparoscopic surgery, ovarian cysts, endometriosis, and polycystic ovarian syndrome. A graduate of Emory University School of Medicine in Atlanta, Georgia, she completed her post-doctorate training at the Mt. Sinai School of Medicine in New York.

Dr. Applebaum currently holds academic appointments at the Albert Einstein College of Medicine and Long Island Jewish Center/Schneider Children's Hospital and sees patients at the Ann and Jules Gottlieb Women's Comprehensive Health Center and Long Island Jewish Medical Center/Schneider Children's Hospital in New York.

KIND WORDS

On a happy note, Abby, our CAH daughter, has been asked by People to People to travel to Australia for 20 days next summer as a Student Ambassador. I truly believe that without the information received from CARES, Dr. Migeon, Dr. Merke and Carol Van Ryzin and the support from Kelly that I received after she was diagnosed, that Abby would not be able to take advantage of this opportunity.

Abby Breeding

I want to tell you that I truly appreciate all that you have done for our family. When Abby was first diagnosed we were told that she would be lucky to reach 5'2"—thanks to the medical care that we were able to contact through CARES, she is now just over 5"6", which I think is a dramatic example of how good her care has been. Thank you.

Krista Breeding

This newsletter is published 4 times a year.

Family Fundraisers are a significant source of support for CARES.

Many families have found creative ways to raise money. We are highlighting two examples of how families turned asking for donations into fun-filled events. Our profound appreciation goes to all of the wonderful families who help us fulfill our mission.

The Harpers' Family Fundraiser

CARES,

We couldn't be more pleased to tell you that our **First Annual Cook Out For A Cause** raised $1800! We decided to do something different this year with our annual donation to your foundation. Instead of simply mailing you a check, we used that money and put it towards making an elaborate, mostly homegrown and made dinner for our friends. Using vegetables and fruit from our garden, plus fresh caught Halibut, Salmon and Elk, we made appetizers, dinner and dessert for our 50+ guests. Drinks and entertainment were provided as well including a rubber duck race down the creek. People paid $1 per duck; winner took half and CARES received half. In lieu of making contributions to the meal, we asked people to make donations to you. Our $250 was turned into $1800 in one night-great return! We hope this contribution helps your organization, individuals with CAH and their families.

Thanks for all you do for us,

Dawn, Mark, Luke & Wyatt Harper

Thanks to the wonderful work of our community, more than $45,000 has been raised to date through the 2009 No-Sweat Run for a Cure! Congratulations to all of our teams!

Thank you for taking time out of your busy lives to make a difference!

HIGHEST FUNDRAISERS

Kimura/Ohana Team raised $6,790

Team Racin' Jason raised $3,265

GREATEST NUMBER OF DONORS

Elizabeth Shaker & Nick Araujo—36 donors raised $4,145 ***New team!***

Ray & Emily Harmer—27 donors raised $2,207

Two CARES Foundation board members deserve special recognition for leading outstanding teams and making tremendous contributions:

Rhonda & Gregory Kraff raised $4,772

Jessica & Matthew Upchurch—raised $4,452

YOUR NAME AND PHOTO HERE

We will happily publicize your fundraising event and its success in our upcoming newsletter. (With your permission of course.) Just email info and photo to: *suzanne@caresfoundation.org*

Creative fundraisers are the key to surviving in this challenging economy. Please keep us posted on your results!

Kraff Family Chili Cook-Off

Friends, family and neighbors gathered on September 26th for the *1st Annual Kraff Family Chili Cook-Off* in support of the Cares' *2009 No-Sweat Run for a Cure.* Gregory, Rhonda & Ally Kraff hosted sixty-five guests with promises of savoring some yummy south-west eats. Fourteen Chilis were submitted to the gaggle of eager tasters, with names like "Cha Cha Chili," "Mini-Mall Chili" & "CARESili Chili for Cares".

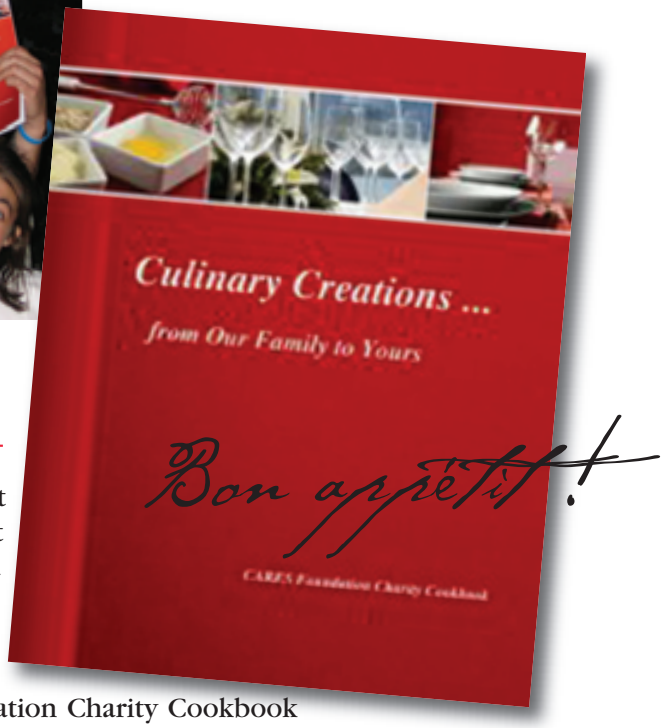
Bragging rights were at stake for the 14 chili chefs in the categories of *People's Choice, Most Original* and *Most Likely to Make You Sweat!* One would think with a name like "Pit Viper", this chili would pack a punch comparable to a viper's bite. Luckily for Chef Joseph Taffurelli, his Pit Viper Chili had just the right amount of spice to win over the voters and snag the *People's Choice* award.

Da' Best Chili (Seafood Version) was awarded *Most Original*, an honor for the 13 year old cook, Timothy Feyrer. Da' Best Chili was filled with the flavors of the sea, including delicious scallops which won over the hostess of the night, Rhonda Kraff.

"CARESili Chili for Cares," a white chili made from a very secret recipe, was voted *Most Likely to Make You Sweat*, which was a fitting win for the hot-headed Kevin Kraff! The sweetest chili of all was submitted by Ally Kraff & her cousin Maggie Feyrer. This delectable Chocolate Chili was the perfect desert to cap off a spicy competition.

In addition to having a family-fun-filled fiesta, the Kraff Family Chili Cook-Off raised over $2000.00 for CARES Foundation! Now that is a healthy portion we can all appreciate!

People's Choice Winner—*Joseph Tafurelli (pictured with his winning apron and Allyson); they also received CARES Cookbooks.*



IN THE SPIRIT OF THE HOLIDAY SEASON...

A delicious holiday gift that is sure to delight family, friends, and colleagues is *Culinary Creations…from Our Family to Yours*, a one of-a-kind CARES Foundation Charity Cookbook filled with favorite recipes from CARES families and friends around the world. 100% of the proceeds from each book will go to support CARES and its efforts to serve those touched by CAH. *Price: $20.00*

To order online: *www.caresfoundation.org* Click on CARES Shop

A contribution to CARES—in honor of family, friends, associates and those to whom you'd like to show your appreciation—is a wonderful gift that will resonate throughout the year! We will be delighted to send a personal card to the folks you wish to honor, telling them of your gift. For Tribute Donation info, please visit:

https://www.caresfoundation.org/productcart/pc/tribute.asp

CAH and Osteoporosis Screening Study UNC

Chapel Hill, North Carolina

WHO: Children with CAH who are 8-12 years old (bone age 14 years) and are still growing. Siblings (6-14 years old, bone age 14 years old) of those children with CAH who otherwise meet the same eligibility criteria except that they do not have CAH and are not on glucocorticoids.

WHY: Although cortisol replacement is essential to treat children with CAH, there is the potential risk of over-treatment with glucocorticoids that can result in abnormal weight gain, decreased linear growth and, more recently reported in adults, the risk of osteoporosis. We are now testing if there exists a risk for osteoporosis in children with CAH and if this risk is related to the dosing of glucocorticoid used, as would be expected with any medical condition in which steroids are required for long-term treatment. We are also examining if the subtype of CAH contributes to the risk for osteoporosis.

WHERE: Children will be enrolled in the study at the General Clinical Research Center at the University of North Carolina, Chapel Hill.

WHAT: Your child would have:

1. Bone Age X-ray
2. DXA scans (to screen for osteoporosis and for subtle spine fractures)
3. Special X-ray of his/her arm to look at the effects of glucocorticoid dosing (Cortef, for example) on bone structure itself
4. Blood and urine tests to determine the degree of his/her "control" of CAH
5. Blood test for genotyping for all children in the study. In this way, "control" siblings can find out if they are "unaffected" or "carriers"

WHEN: This would all occur in a one-time visit (3 hours) for your child with CAH and/or sibling.

HOW MUCH:: The clinical visit, including laboratory testing, radiologic evaluation and physical exam will be paid for by this protocol. Overnight accommodations can be arranged, a rental car to/from the airport and parking at UNC will be covered. Travel assistance is possible (please inquire for details). There is a $50 compensation provided for incidental costs for each child enrolled.

For more information, please contact:

Karen J. Loechner, M.D./Ph.D.
Director, UNC Pediatric Osteoporosis Clinic,Assistant Professor,
Pediatric Endocrine Unit
919.216.5946 • 919.966.2423 (fax)
karen_loechner@med.unc.edu (email)

NCAH Study at Children's Hospital of Los Angeles

The Division of Endocrinology at Children's Hospital Los Angeles is currently recruiting subjects for a research study aimed at determining the stress-fighting ability in subjects with Non-classical Congenital Adrenal Hyperplasia (NCAH) and comparing these responses to those in subjects with Classical Congenital Adrenal Hyperplasia (CAH) and those in carriers of either disorder. If you have NCAH, CAH or are a family member (parent or sibling) of someone with either disease, and are interested in participating in this study, please contact:

Bhavna Bali, MD at 323.361.8705
bbali@chla.usc.edu
or
Mitchell Geffner, MD at 323.361.7032
mgeffner@chla.usc.edu

Identifying the Unmet Needs of Individuals with CAH

WHO: Women (18 & older) with CAH.

WHY: Due to the sensitive nature of the issues associated with CAH, it is likely that individuals with CAH will have needs that are not met in the management and treatment of the disorder. If so, genetic counselors may be in a position to fulfill some of the needs of these individuals. The purpose of this study is to identify the unmet needs of women with CAH, and to investigate how genetic counselors may expand their role in the management of this disorder to better meet women's needs. The results of this study could also have implications for the role of other health care providers in the management of this disorder.

WHERE: Participants will be enrolled through e-mail or telephone contact. To set up an interview or request more information, please contact me or my faculty sponsor. Contact information is provided below.

WHAT: The study will consist of one telephone interview.

WHEN: The interview will last approximately 30-45 minutes.

HOW MUCH: There will be no costs involved with participation. There will be no compensation for participating in this study. If interested, please contact:

Kristin Zelley, principal investigator
kzelley@arcadia.edu
Kathleen Valverde, faculty sponsor
valverdk@arcadia.edu
215-572-4058)

Please pass this information on to any women you know with CAH who'd be interested in participating in this study. Thank you.

Blood Spot Sample Study

While significant advancements to improve newborn screening for CAH have been made in recent years, there remains considerable room for improvement. Currently, CAH has been fully implemented into newborn screening programs across all 50 states. Newborn screening has been most effective in detecting the cases of CAH caused by 21-hydroxylase deficiency, but current methods have not proven as reliable in detecting less common forms, including 11-ß-hydroxylase deficiency.

Based on previous work, Dr. Dietrich Matern and colleagues in the Biochemical Genetics Laboratory at Mayo Clinic are working to further improve current screening strategies by determining the analyte ranges that correspond to CAH caused by other enzyme deficiencies, in addition to 21-hydroxylase. In order to accomplish this, the Biochemical Genetics Laboratory aims to collect and analyze leftover newborn screening samples of patients diagnosed with any form of CAH. The results from this study are expected to enhance newborn screening for CAH two-fold: a) by allowing for the identification of individuals with less common forms of CAH; and b) by reducing the number of false positive results through steroid profile analysis. Early detection and diagnosis allows for treatment of affected infants prior to the onset of symptoms.

Call for Samples—Participate in Ongoing Research at Mayo Clinic

Members of CARES Foundation may be able to help in this effort by allowing Mayo Clinic to analyze any leftover newborn screening samples that may still be available in the newborn screening lab of the state where a CAH patient (less than 8 years old) was born (see chart to determine if your blood spot sample may still be available or call the respective screening laboratory to determine if a sample may still be available). Analysis of such precious samples would allow Mayo Clinic's Biochemical Genetics Laboratory to accelerate the completion of this study and achieve more quickly the ultimate goal of improving newborn screening for CAH.

http://genes-r-us.uthscsa.edu/resources/consumer/statemap.htm

If you would like to participate and a newborn screening sample may still be available, please contact a biochemical genetic counselor by e-mail at *biochemicalgenetics@mayo.edu* or phone at 507-266-8158 for assistance in requesting this sample from the respective newborn screening laboratory. If you have any questions or concerns, Dr. Matern or a member of his research team would be happy to discuss the study with you in more detail. Please call with any inquiries or to assist with initiating participation in the study. Thank you in advance for considering this request. We greatly appreciate your time and cooperation.

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See the chart below to find out if your Newborn Screening card is available

STATE	NBS CARD STORAGE TIME
Alabama	3 months
Alaska	3 years
Arkansas	2 years
Arizona	3 months
California	Indefinitely
Colorado	3 months
Connecticut	6 months
Delaware	4 months
District of Columbia	2 years min.
Florida	Indefinitely
Georgia	6 wks-10 yrs
Hawaii	1 year
Idaho	Not Given
Illinois	2–4 months
Iowa	1 month
Indiana	23 years
Kansas	1 month
Kentucky	6 months
Louisiana	2–4 weeks
Maine	5 years
Maryland	6 months
Massachusetts	1991-present
Michigan	21.5 years
Minnesota	7 years
Missouri	6 months
Mississippi	2 year minimum
Montana	2-6 months
Nebraska	3 months
Nevada	1 year
New Hampshire	Indefinitely
New Jersey	23 years
New Mexico	3 months
New York	27 years
North Carolina	Indefinitely
North Dakota	10 years
Ohio	21 years
Oklahoma	1 month
Oregon	1 year
Pennsylvania	3 months
Rhode Island	23 years
South Carolina	Parent's choice
South Dakota	2 months
Tennessee	3 months
Texas	6 months
Utah	3 months
Vermont	Indefinitely
Virgin Islands	1 year
Virginia	6 months
Washington	21 years
West Virginia	3 months
Wisconsin	1 year
Wyoming	Not Given

PERSONAL STORY

Adrenal Crisis and EMS: One Family's Story

Jessica Hall-Upchurch

As the parent of a child with SWCAH, you know the day will come when you have to give your child his first injection. What you don't know is where you will be, will you be able to calm down to do it and will you have someone there to help you. Here is how it happened for me.

I was a trainer at a workshop in Denver when my son, Clay, became ill with the stomach flu. And as we know, the stomach flu for a child with SWCAH can be serious—this time it was, as we ended up in the ER in an adrenal crisis. I got the call that he had thrown-up so I immediately left the workshop and headed to the hotel room. We followed the oral stress dose protocol but he continued to vomit—and that is when it hit and it took all of twenty minutes but it felt like a second. He was limp, eyes rolling into the back of his head, pale and cold—and I was scared to death!

I called 911 as my fear was coming alive in front of me, my son was in dire need and I had to act fast. The paramedics and hotel staff arrived in minutes—so quickly in fact, I had just pulled his injection and solu-cortef from the medical bag I carry with us. Oh help me, give me the strength to slow this down because I knew I had to give him a shot—and this was the first time.

At that point they put an oxygen mask on my angel, he was only three years old at the time, and started asking lots of questions. Of course, they told me they could not give him his injection. Imagine, here we were with trained personnel surrounding us and they couldn't "legally" give my son a shot that would save his life. Reason being "the attending doctor at the hospital to which we were being transported didn't prescribe it." It was up to me!

Literally, I had to tell them to "stop" as they were trying to load he and I onto the gurney and I still hadn't given him his shot. I got them to stop, and with a kind paramedic next to me, he coached me through it. The injection was completed and within 10 minutes, my little angel was blinking his big brown eyes, color was back in his skin and I was in tears of relief and gratitude. If it wasn't for CARES, I wouldn't have been as prepared and informed when it came to saving my own child's life. And that is what I did that day, I saved his life.

Thank you CARES for providing me with the knowledge and skills to save my son. I am forever grateful for the guidance and support you provide our family!

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including the use of antiandrogens and aromatase inhibitors. Adequacy of treatment is best evaluated by monitoring growth rate and skeletal maturation. In addition, urinary and serum analysis of steroid hormones and determination of 17-hydroxy-progesterone in saliva are used for evaluation of therapy.

Reports on long-term follow-up and final height outcome in patients with CAH are heterogeneous. Previously we found that total pubertal growth is significantly reduced in patients with CAH, who have received traditional steroid treatment with hydrocortisone or prednisone (Bonfig et al, J Clin Endocrinol Metab 2007;92(5):1635-9). In the present study we tried to determine an evidence based hydro- cortisone dose recommendation during puberty by evaluating data from 92 patients with CAH—all followed in our clinic—who have reached final height and who have been treated with hydro-cortisone exclusively since diagnosis of CAH until final height.

In conclusion, maintenance of normal growth velocity is a very important variable in the assessment of control of CAH, especially during the first six months of life and during puberty, when growth velocity is fastest.

Patients and Methods

The effects of glucocorticoid treatment for classical CAH were retrospectively analyzed in 92 patients (57 females, 35 males) with 21-hydroxylase deficiency. Growth pattern, final height and mean daily hydrocortisone dose were recorded. All patients were exclusively treated with hydrocortisone. The patients were born between 1969 and 1987.The diagnosis of CAH was based on both clinical symptoms and signs, and on hormonal analysis and genotyping later on. At the time of diagnosis newborn-screening for CAH was not yet available. 54 patients had salt-wasting CAH (32 females, 22 males), and 38 patients had the simple virilizing form (25 females, 13 males). Patients with nonclassical forms of CAH were not included in this study. All patients were continuously cared for in our clinic, with follow-up appointments every three months during the first two years of life, and every six months in childhood and adolescence. All 92 patients had received hydrocortisone (three times daily) for glucocorticoid substituition and patients with salt-wasting CAH received fludrocortisone in addition. None of the patients had received GnRH analog treatment to delay onset of puberty. Since patients were followed at a single center, we present data on a homogeneously treated group of patients with CAH.

A logistic regression model and a receiver operating curve analysis (ROC-analysis) were assessed to estimate a hydrocortisone dose recommendation during puberty. ROC analysis and logistic regression were performed with the statistical computing package "R", version 2.7.1, R, Development Core Team (2008), R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria. (ISBN 3-900051-07-0, URL *http://www.R-project.org*). The ROC-curve was smoothed using the LOWESS ("locally weighted least squares") method.

Results

Patients with salt-wasting CAH (n=54, 32f, 22m) were diagnosed early at a mean age of 0.2 years [range 0-2.7 yr, median 0 yr], whereas patients with the simple virilizing form (n=38, 25f, 13m) were diagnosed at a mean age of 2.2 years [range 0-6 yr, median 2 yr]. None of the patients had suffered from adrenal crisis once salt-wasting CAH was diagnosed.

Pubertal growth was significantly reduced in all patients: salt-wasting females 13.8±7.4 cm, simple virilizing females 13.1±6.2 cm vs. reference population 20.3±6.8 cm, $p<0.05$, and salt-wasting males 17.7±6.7 cm, simple virilizing males 16.2±5.7 cm vs. reference population 28.2±8.2 cm, $p<0.05$. Decreased pubertal growth resulted in final height (FH) at the lower limit of genetic potential (corrected FH in salt-wasting females -0.6±0.9 height standard deviation score, simple virilizing females -0.3±0.9 height standard deviation score, salt-wasting males -0.8±0.8 height standard deviation score and simple virilizing males -1.0±1.0 height standard deviation score). Overall corrected FH in our patients with 21-hydroxylase deficiency was within one standard deviation of target height.

During puberty mean daily hydrocortisone dose was 17.2±3.4 mg/m² body surface area in females (salt-wasting females 17.0±3.3, simple virilizing females 17.4 ±3.5) and 17.9±2.5 mg/m² body surface area in males (salt-wasting males 17.4±2.0, simple virilising males 18.7±3.1). In a logistic regression model a significant correlation between the mean daily hydrocortisone dose and FH was found ($p<0.01$, Figure 1) and in a Receiver Operating Curve (ROC) analysis the positive predictive value for short stature rose from <30% to >60%, when a hydrocortisone dose >17 mg/m² body surface area was administered (Figure 2).

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Body mass index (BMI) was found to be above average in CAH patients irrespective of the sex. At onset of puberty males had a mean BMI standard deviation score of 1.2±0.9, which decreased to 0.9±0.9 when FH was reached. Males with simple virilizing CAH had significantly higher BMI standard deviation score than males with salt-wasting CAH ($p<0.05$). In females there was no change of mean BMI standard deviation score with 0.6±1.2 at start of puberty and 0.6±1.3 at FH. There was no significant difference between females with simple virilizing or salt-wasting CAH.

Discussion

We conclude from our results that an optimal hydrocortisone dose during puberty should not exceed 17 mg/m² body surface area. To our knowledge this is the first study to prove the correlation between pubertal glucocorticoid dose and FH and also to suggest a cut-off for the maximum hydrocortisone dose during puberty in patients with CAH. Of course this is just a general recommendation and individual patients may have different sensitivity to glucocorticoids, which has to be considered. In previous studies the growth suppressant effects of glucocorticoid overtreatment during the first two years of life have been demonstrated (Manoli et al, 2002 Clin Endocrinol;57:669-676, Stikkelbroeck et al, 2003 J Clin Endocrinol Metab;88:3525-3530, Kirkland et al, 1978 J Clin Endocrinol Metab;47:1320-1324). In contrast in a retrospective study with 54 patients no association between glucocorticoid dose and adult height was found (Muirhead et al, 2002 J Pediatr;141:247-252).

According to the consensus statement on 21-hydroxylase deficiency from the Lawson Wilkins Pediatric Endocrine Society and The European Society for Pediatric Endocrinology typical hydrocortisone doses during infancy range between 10-15 mg/m² body surface area, but higher doses up to 25 mg/m² body surface area may be necessary initially. No specific hydrocortisone dose recommendations are mentioned for the pubertal age (Joint LWPES/ESPE CAH Working Group 2002 J Clin Endocrinol Metab;87(9): 4048-4053). Especially in boys during puberty the androgen secretion from the adrenals is relatively low compared to that of the testes and therefore it is less critical to suppress adrenal androgens in boys than in girls during puberty.

With regard to growth potential puberty is an extremely critical period in the treatment of CAH. Total pubertal growth was significantly decreased in both forms of classical CAH, irrespective of the sex. An explanation for the decreased pubertal growth spurt could be a too tight control of the disease at the onset of puberty, so that the influence of sex hormones on growth is suppressed, resulting in a less profound growth spurt. The pubertal growth was not poor due to prepubertal undertreatment with an advanced bone age at the onset of puberty (except for males with simple virilizing CAH), since bone age was within one year of chronological age in more than two thirds of the patients at that time. Acceleration of bone age in males with simple virilizing CAH used to be caused by delayed diagnosis, but is no longer a problem since newborn screening is available by now.

In conclusion, maintenance of normal growth velocity is a very important variable in the assessment of control of CAH, especially during the first six months of life and during puberty, when growth velocity is fastest.

In summary, final height in CAH patients receiving traditional therapy is within the lower range of genetic potential. Total pubertal growth is significantly decreased in this cohort. Accuracy of treatment should not be monitored only by biochemical assessment, but also by careful follow-up of growth velocity especially during puberty. Thus glucocorticoid doses should be adjusted (below 17 mg hydrocortisone per m² body surface area) in this rapid phase of growth.

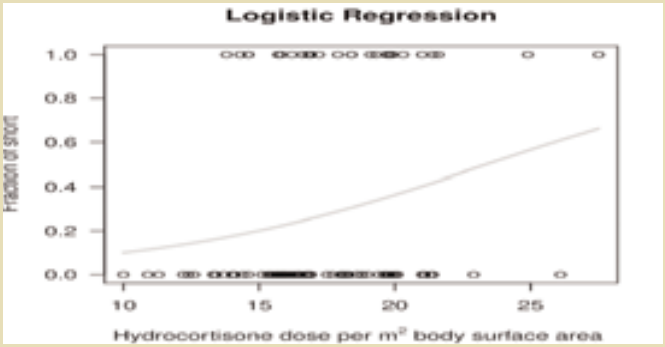

***Figure 1**. Logistic regression model. Each circle represents one patient and patients with normal stature are plotted at 0.0, patients with short stature are plotted at 1.0. The line represents the fitted logistic model and represents the predicted fraction of short patients at the mean daily hydrocortisone dose during puberty.*

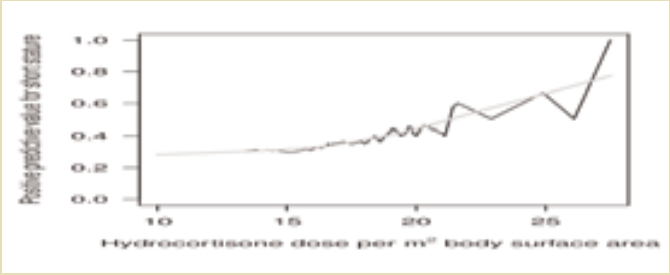

***Figure 2:** ROC Analysis. The positive predictive value for short stature rises from below 30% to 40-60%, when the mean daily hydrocortisone dose exceeds 17 mg/m² body surface area. The grey line is a LOWESS smoother curve.*

EMSC: A Piece of the EMR Puzzle

In both of our last two newsletters, we have written about Emergency Medical Services for Children (EMSC) and its pivotal role in CARES Foundation's campaign for immediate, appropriate emergency medical treatment of adrenal insufficiency. In the Spring '09 newsletter we wrote of CARES and our EMS initiative being introduced to the EMSC community across the nation through a story in FAN Mail. Then in our Summer '09 issue, we reported that two CARES family members had the unique opportunity to represent CARES and the adrenal insufficient community at the EMSC national conference this past June in Washington DC.

What is EMSC?

As noted on the EMSC website (*www.childrensnational.org/emsc*), EMSC is a federally funded program "designed to ensure that all children and adolescents, no matter where they live, attend school, or travel, receive appropriate care in a health emergency." The Program is administered by the U.S. Department of Health and Human Services, Health Resources and Services Administration (HRSA), Maternal and Child Health Bureau (MCHB). The Program provides grant funding to EMSC programs in all 50 states, the District of Columbia, and five U.S. territories.

In 1991, the EMSC Program established the EMSC National Resource Center (NRC) which is housed within the Children's National Medical Center in Washington, DC. Among the many responsibilities of the NRC is overseeing the EMSC Family Advisory Network (FAN).

Created by the NRC in 1999, FAN is committed to ensuring the inclusion of family voices in every state EMSC Program. EMSC State Family Representatives serve on EMSC advisory committees, assist with special community outreach programs and work on developing and implementing EMSC policy objectives and educational opportunities within their state. The NRC also distributes FAN Mail, a semi-annual newsletter distributed to the EMSC community.

What is the importance of EMSC and FAN to CARES' EMS initiative?

EMSC is vital to introducing CARES' campaign for emergency medical treatment of adrenal insufficiency to EMS leaders across the nation. It was through the NRC's introduction that CARES was featured in the Winter '09 issue of FAN Mail and CARES family representatives were invited to the EMSC national conference. EMSC's involvement in our campaign now continues at the state level where EMSC program managers and family representatives are playing pivotal roles in having our request placed before state EMS medical advisory boards. A complete list of state EMSC program managers and family representatives can be found at:
http://www.childrensnational.org/files/PDF/EMSC/GrantPrograms/State_Grantee_List.pdf

Emergency Medical Response for CAH—Update

The New York State Emergency Medical Advisory Committee (SEMAC) met on September 2, 2009. The committee considered a motion brought forward by the State Emergency Medical Services Council (SEMSCO) to add Solu-Cortef® to the state formulary based on the strong recommendation of the Emergency Medical Services for Children (EMSC) Advisory Committee. Despite unanimous agreement by committee members present to add Solu-Cortef® to the formulary, no formal vote could be taken due to lack of a quorum. These recommendations will go before the committee again in December 2009. If the recommendations are adopted at this time, they will then go out to the various regions of New York in the form of an advisory. Each region will then have to formally adopt the new protocols. To make EMR for CAH and other adrenal insufficiencies a reality in New York, our

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EMR *continued from page 11*

efforts will switch from a state-wide to region-by-region campaign at that time. If you live in New York and would be interested in representing your region in this campaign, please contact CARES Support Group Leader Deborah Brown at *ny3.support@caresfoundation.org*.

In Maryland, Support Group Leader Debbie Ham met with the State Protocol Development Committee in August. A medical director was assigned as a sponsor to our request for the addition of Solu-Cortef® to the formulary and associated protocols for emergency treatment of adrenal insufficiency. CARES Foundation is working on the protocol request submission application with the assigned medical director.

Families and healthcare professional members continue work on EMS campaigns in the states of Arkansas, Colorado, Massachusetts, Michigan, Nebraska, Nevada, North Carolina, Tennessee and Virginia. To learn more about CARES EMS Campaign visit: *http://www.caresfoundation.org/productcart/pc/ems_cah.html*

If you are interested in adding your voice to that of CARES Foundation and our family and healthcare professional members in any of these arenas or wish to learn more about organizing an initiative in your own state, please contact Gretchen Alger Lin at *gretchen@caresfoundation.org*.

Please note that our phone and fax numbers have changed.

Our new phone number is (908) 364-0272 and our new fax number is (908) 686-2019 Our toll-free number is still 1-866-227-3737

CANCELLATION NOTICE

2009 CARES Foundation Education Series

CARES is feeling the effects of the poor economy as both private donations and corporate grants have decreased significantly. As a result, we were forced to cancel the 2009 Education Series (formerly CAH Family Conference) which was to take place on November 1, 2009. In lieu of the Education Series, we plan to offer some regional events in the coming year and will notify you of those in your area.

Despite our financial challenges, we continue to work hard to improve the lives of those living with CAH. Currently, we are engaged in two critical initiatives—the establishment of comprehensive care centers for CAH (multi-disciplinary clinics) and EMS protocols for adrenal insufficiency.

Please remember

that CARES Foundation has "Gone Green" and that our newsletters are now only available electronically. Please make sure we have your most current e-mail address and contact information to ensure that you receive newsletters and other important information from CARES.

Send your updated information to Odaly Roche at *Odaly@caresfoundation.org*.