



CARES Foundation

research, education and support for CAH

2414 Morris Avenue, Suite 110

Union, NJ 07083

In New Jersey: 973-912-3895

Toll Free: 1-866-CARES37

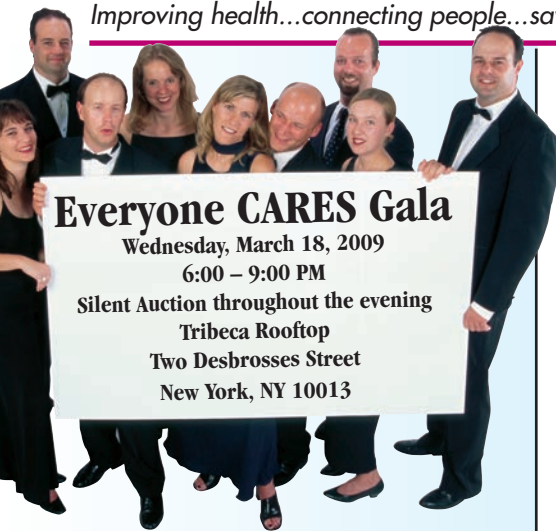
Fax: 973-912-8990

Email: info@caresfoundation.org

Web: www.caresfoundation.org

Improving health...connecting people...saving lives

Volume 9 • Winter 2009



Everyone CARES Gala

Wednesday, March 18, 2009

6:00 – 9:00 PM

Silent Auction throughout the evening

Tribeca Rooftop

Two Desbrosses Street

New York, NY 10013

On Wednesday, March 18th, CARES Foundation, Inc. will present its **Everyone CARES Gala** at Tribeca Rooftop in Manhattan. The evening event will recognize the tremendous contributions of our distinguished honorees, Pfizer Corporation and Dix P. Poppas, M.D.

Our **Everyone CARES Gala** promises to be a memorable evening. There will be a silent auction, welcome reception, buffet dinner and dessert. Please consider helping to make this event a success by purchasing tickets, becoming an event sponsor, purchasing an ad in our tribute journal, or donating an item for our silent auction. Visit www.caresfoundation.org for more details and to download our sponsor and silent auction forms.

Please save the date for this special evening. Hope to see you there!

CARES Foundation's Continuing Medical Education Workshop for physicians coming to Washington, DC on June 9, 2009. See page 3 for details.

PREVENTING FEMALE VIRILIZATION IN CONGENITAL ADRENAL HYPERPLASIA

FEMALE PRENATAL TREATMENT of CLASSIC CAH with DEXAMETHASONE: **PRO VS. CON**

From: *The Endocrine Society's Research Affairs Core Committee*

Edited by: *Ellen W. Seely, M.D. and David A. Ehrmann, M.D.*

Introduction

Congenital Adrenal Hyperplasia (CAH) is an autosomal recessive disorder causing absent or deficient cortisol production. The most common form of CAH, 21-hydroxylase deficiency, has an incidence of about 1 in 16,000 births, or even more in specific populations. Severely affected female fetuses undergo virilization. Treating the mother with the glucocorticoid dexamethasone during pregnancy has been shown to decrease or even prevent this virilization. However, the current approach to prenatal treatment means that unaffected as well as affected fetuses are exposed to dexamethasone and this treatment may have side effects, particularly on the central nervous system. This article presents a pro and con view from two experts on prenatal treatment of CAH with dexamethasone.

Presenting the pro perspective is Phyllis W. Speiser, M.D., chief of pediatric endocrinology at Schneider Children's Hospital in New Hyde Park, New York, and professor of pediatrics at New York University School of Medicine.

Presenting the con perspective is Walter L. Miller, M.D., professor of pediatrics, director of the Pediatric Endocrinology Training Program, and chief of endocrinology at the University of California, San Francisco.

Article continued on page 7



IN THIS ISSUE

CAH Article	1, 7-9
Female Prenatal Treatment of Classic CAH with Dexamethasone: Pro VS. Con	
Everyone Cares Gala	1
Message from the Acting Executive Director	2
New Addition to Board of Trustees	3
Continuing Medical Education	3
Founders, Board, Staff	3
Fundraising	4, 5
Kelly's Holiday Boutique	4
Lemonade Stand	4
Oops!	4
Why I Run	5
CAH Studies	6
NCAH Study at Los Angeles	
Classical Adult Women's Quality of Life Study	
CAH & Osteoporosis in NC	
Advocacy	10-11
EMR for CAH-RI	10
Newborn Screening Act	10
Go Vietnam!	11
WHO's Essential Drug List	11
Fun and Games!	12
White Post Farms	
Wisconsin Get-Together	

© 2009 CARES Foundation, Inc. All rights reserved. Republication or redistribution of CARES newsletter content, including by framing or similar means, is prohibited without prior written consent of CARES Foundation, Inc.

A Message from the Acting Executive Director



Dear Friends,
Happy New Year!
I hope all of you and your loved ones enjoyed a magical holiday season and are looking forward to good things in the new year. CARES

Foundation certainly is, as we've got many exciting events coming up in 2009.

Everyone CARES Gala

On March 18, CARES Foundation is honoring Dix P. Poppas, M.D. and Pfizer Corporation for their contributions to CARES and the CAH community. Dr. Poppas is Chief of Pediatric Urology at the Children's Hospital of New York-Weill Medical College of Cornell University. Dr. Poppas' practice is limited to pediatric urology with special interest in genital reconstruction, laparoscopy and intersex disorders. He serves as Director of the Laboratory for Minimally Invasive Urologic Surgery. Pfizer has, over the years, played a pivotal role in the treatment and management of CAH by making Solu-Cortef available to those affected by CAH and as a generous corporate sponsor to CARES. CARES Foundation and the CAH community are truly grateful for the contributions and commitment of Dr. Poppas and Pfizer Corporation.

CME Workshop for Physicians

CARES Foundation's first ever continuing medical education (CME) workshop is scheduled for June 9, 2009 in Washington, DC. The workshop is for physician education and will last a full day. The main focus of the workshop is on CAH throughout the lifespan with information on other adrenal disorders as well. Our co-sponsor for the workshop is The University of Texas Southwestern Medical Center. Please don't forget to tell your doctors about this opportunity.

Family Conference

Mark your calendars! The next CARES Family Conference is scheduled for Sunday, November 1, 2009 at the College of St. Elizabeth's in Madison, NJ. This will be an all day event. We look forward to sharing more of the details with you soon and hope to see you there.

Chevron Houston Marathon Run for a Reason

This year, CARES Foundation was included for the first time on the list of charities taking part in the Run for a Reason. This is a wonderful opportunity for CARES to raise more awareness about CAH and we are thrilled to be included. For more information on our registered runner, Gary Russell, and how to donate, see page 5.

We're on Facebook!

CARES Foundation now has a Facebook page. All you need to do to join our cause is download the "Causes" application to your own Facebook page and plug CARES Foundation into the search option. Facebook is a great way to stay connected and build your own network, so join today!


Personal Stories

Many of our newsletters have included inspirational personal stories about living with CAH. You may remember the one about our race car driver from the last issue. It would be really wonderful if we were able to include a personal CAH story in each and every newsletter, so I'm inviting you to tell yours. If you'd like to share your experience with the rest of our membership, please send your story, with a picture or two, to me at suzanne@caresfoundation.org. I look forward to reading your story!

Best Wishes for a Happy and Healthy
New Year,

All my best,

Suzanne

© CARES Foundation, Inc.  Winter 2009

Welcome Aboard!

New Addition to Board of Trustees

CARES would like to extend a warm welcome to the newest addition to our Board of Trustees, Jodi Mandell. Please join us in welcoming Jodi.

Jodi Mandell

Jodi is an associate at Cullen and Dykman LLP in Garden City, New York where she works in the firm's Banking Department, focusing on both commercial lending and real estate financing. Prior to attending law school, Ms. Mandell was a Compliance Manager at an online financial services company and a Senior Consultant at PricewaterhouseCoopers LLP, where she designed and implemented compliance, ethics and corporate governance programs for Fortune 500 companies. Jodi graduated from St. John's University School of Law, magna cum laude, and received a BA, cum laude, in Economics from Brandeis University.



FOUNDERS

Kelly and Adam Leight

Staff & Consultants

Suzanne R. Levy, *Acting Executive Director*
Suzanne@caresfoundation.org

Meryl I. Stone, *Chief Operating Officer*
Meryl@caresfoundation.org

Mazal Wolfskehl, *Bookkeeper*
Mazal@caresfoundation.org

Odaly Roche, *Administrative Assistant*
Odaly@caresfoundation.org

Camela Cruz, *Intern*
Camela@caresfoundation.org

Gretchen Alger Lin, *Public Affairs*
Gretchen@caresfoundation.org

Stephanie Erb, *Parent/Family Support*
Stephanie@caresfoundation.org

BOARD OF TRUSTEES

Gregory Kraff, *Acting President*

Jessica Hall Upchurch,
Acting Vice President

Vivian Altman Quintanilla, *Treasurer*

Stephanie R. Fracassa, *Secretary*

Deborah Brown, R.N.

Louise Fleming, R.N.

Monica L. Heinze

Tonya Judson, R.N.

Kelly Rosso Leight, Esq., *President Emeritus*

Alan Macy

Stephen Maebius

Jodi Mandell

Catherine Peterson

Karthik Radhakrishnan

Victoria Shenderovich

Diane Snyder, M.D.

Daniel Taylor

Michael P. Wajnrajch, M.D.

SCIENTIFIC & MEDICAL ADVISORY BOARD

Henry Anhalt, D.O.

Richard J. Auchus, M.D., Ph.D.

Ricardo Azziz, M.D.

Susan W. Baker, Ph.D.

Sheri A. Berenbaum, Ph.D.

Felix A. Conte, M.D.

Alejandro Diaz, M.D.

Walter Futterweit, M.D.

Mitchell E. Geffner, M.D.

Karen J. Loechner, M.D., Ph.D.

Claude Migeon, M.D.

Walter L. Miller, M.D.

Maria I. New, M.D.

Sharon E. Oberfield, M.D.

Dix P. Poppas, M.D.

Richard C. Rink, M.D.

Scott A. Rivkees, M.D.

Richard Ross, M.D.

David E. Sandberg, Ph.D.

Ellen Seely, M.D.

Phyllis W. Speiser, M.D.

Bradford L. Therrell, Ph.D.

Maria Vogiatzi, M.D.

Garry Warne, M.D.

Selma Feldman Witchel, M.D.

This newsletter is published 4 times a year.

Advances in CAH & Adrenal Disorders

Endocrine Society Satellite Meeting

Tuesday, June 9, 2009

Renaissance Washington DC Hotel

999 9th Street, NW, Washington, DC 20001

CARES FOUNDATION, INC. is jointly sponsoring this activity with THE UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER, the accredited sponsor.

This program will inform and educate participants about the latest advances regarding diagnosing and treating CAH and other adrenal disorders. It is appropriate for all medical professionals who diagnose and treat adrenal disorders.

The University of Texas Southwestern Medical Center designates this educational activity for a maximum of 7.5 AMA PRA Category 1 Credits™

Physicians should only claim credit commensurate with the extent of their participation in the activity.

Kelly's Holiday Boutique

On December 6, CARES Foundation's Founder and President Emeritus, Kelly Leight, opened her home for a holiday boutique fundraiser.

Holiday shoppers could choose from designer jewelry, pashmina scarves, high quality skin-care products, and designer handbags. Over \$2,000 was raised for CARES!

Way to go Kelly!

Left to right: Meryl Stone, Suzanne Levy, Kelly Leight



Lemonade Stand

Over the summer, Tara Hewes and her family had a yard sale. Not wanting to feel left out, Tara's youngest daughter, Paris, along with her sister and cousins, opened a lemonade stand. They raised \$101 and donated all of it to CARES! Many thanks to Paris and her family!

Left to right: Summer Hewes, Janessa Mowrery, Keyaira Travis, Paris Hewes, Tara Hewes

No-Sweat Run for a Cure

No-Sweat Run for a Cure honorable mention was omitted in our last newsletter: We want to acknowledge and thank Dick Pendino for his very generous donation this year to our No-Sweat campaign. Dick has been a "trailblazer" and generously donated \$5,000 again this year. Many thanks!





Gary Russell

WHY I RUN

By Gary Russell

I have been a distance runner since high school. My first race event was the Crescent City Classic 10K in New Orleans (my hometown) in 1984. Since that time, I've run in numerous 5K & 10K events.

In Jan 1997, I completed the Chevron Houston Marathon (my only marathon to date) in 4:11:33, missing my 4:00:00 goal. I decided then that I would do another marathon and achieve or surpass my original goal.

Twelve years later, at the age of 41, I'm finally back to keep that commitment to myself. Barring injury or setback, I'm on track to complete the 2009 Chevron Houston Marathon at approximately an 8:30 pace or 3:42:00 total time.

Unfortunately, within the past 2-1/2 years, I lost 2 close relatives. In Oct '05, my cousin, Nicole Chasson, died from complications resulting from Congenital Adrenal Hyperplasia (CAH) at the age of 31. And in Nov '06, her father (my uncle), Nolan Chasson, died from throat and stomach cancer.

Last year, I completed the Houston Half Marathon. In doing so, I raised approximately \$3,500 for each of two charities which provide support to victims of the two diseases that took my relatives. The two charities are: **CARES Foundation** (Congenital Adrenal Hyperplasia Research Education and Support), and the **American Cancer Society**. To learn more, go to www.caresfoundation.org, and www.cancer.org.



Nicole Chasson

Now I am hoping to build on last year's half marathon success and run the full marathon. I am also hoping to build on last year's fundraising success and increase my fundraising goal to raise at least \$5,000 for each of the two charities.

Moreover, the Run for a Reason team was nice enough to include **CARES Foundation** as one of 47 charities officially supported by the Chevron Houston Marathon. ACS has long been one of the supported charities of the Houston Marathon. I hope that will help increase awareness about CARES Foundation and CAH.

Anyone wishing to help with fundraising efforts can do so via the websites below:

www.active.com/donate/CARESFoundation/GRussell2009

www.active.com/donate/ACS09/GRussell2009

Any and all support is greatly appreciated! Thank you!

UPDATE: Gary successfully completed the full marathon and, as of this printing, has raised \$4,000 for CARES. Thank you Gary!

Classical Adult Women's Quality of Life Study

CARES Foundation and Dr. Sheri Berenbaum from Pennsylvania State University have launched a quality of life study of women with classical CAH. It is open to women with classical CAH (Salt wasting and simple virilizing forms) over the age of 18 and entails answering a written survey.

If you have questions about the study or require additional information, please contact Suzanne Levy:

1-866-227-3737 or
suzanne@caresfoundation.org

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:

Mitchell Geffner, MD
at 323.361.7032
or mgeffner@chla.usc.edu

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 (pager) • (919) 966-4435 ext. 224 (voice mail)

(919) 966-2423 (fax); or

Roxanne Schock, CDE/RN, Study Coordinator

(919) 966-0428 (voice mail) • (919) 966-0971 (fax)

FROM DR. SPEISER

(Summary of the pro perspective)

- CAH females are born with disfiguring genital ambiguity.
- Genital ambiguity can largely be prevented by administering dexamethasone to the pregnant mother at risk for carrying a CAH female fetus.
- Dexamethasone has not been proven seriously harmful in humans to either mother or fetus.
- Long-term observation for safety concerns based on animal studies is warranted.

DEFINING THE PROBLEM

Virilizing CAH requires inheritance of a mutation from both parents. When both parents are carriers, there is a 1 in 4 risk of having a CAH-affected child and a 1 in 8 risk of an affected girl. In the virilizing forms of CAH, females are exposed in utero to elevated levels of fetal adrenal androgens (male hormones), leading to ambiguity in the external genitalia and more masculine behavior. Ideally, one would want to minimize or eliminate these anomalies because they cause distress to the parents and the daughter.

TREATMENT TRACK RECORD

More than twenty years of clinical experience have shown that prenatal maternal administration of dexamethasone improves or prevents genital ambiguity in affected females compared to their older affected sisters who were not treated, if dexamethasone is reliably and continuously administered before 9 weeks gestation.¹ Prenatally treated females and their families avoid psychosexual difficulties associated with genital ambiguity and the possible need for surgical reconstruction.

CONTROVERSIES

Unnecessary treatment

Dexamethasone treatment for at-risk pregnancies remains controversial. To prevent female genital virilization, treatment must be started early in the first trimester, before it is possible to determine sex and whether or not the child is CAH-affected; therefore 7 of 8 pregnancies will be treated unnecessarily, albeit briefly, to prevent one case of ambiguous genitalia. Families must therefore be fully informed when they consent to the diagnostic and recognized therapeutic interventions.^{2,3}

To minimize the duration of unnecessary dexamethasone treatment for male or unaffected female fetuses, prompt and accurate diagnostic studies are crucial. Most often, chorionic villus sampling is performed at 10-12 weeks gestation. Finding an XY karyotype (male) permits discontinuation of prenatal treatment because males with 21-hydroxylase deficiency do not suffer from genital ambiguity, and thus prenatal dexamethasone serves no therapeutic purpose. If the karyotype is XX (female), CYP21A2 genotyping must be performed to determine whether the female fetus is affected. In unaffected females, treatment may be stopped. However, by the time the genotype is known, the fetus has been exposed to dexamethasone for up to 7 weeks. For CAH-affected females, treatment continues to term; termination of therapy even for a few days has been associated with genital ambiguity.

Future methods for obtaining fetal tissue for diagnosis may include analysis of fetal cells collected from the maternal circulation in the mid-first trimester and pre-implantation genetic

diagnosis (PGD). Theoretically, if done early enough, the former test could prevent prenatal treatment of male fetuses, regardless of CAH status. PGD could help couples select either male or female embryos unaffected by the disease in question. The ethics of PGD itself and the relative cost and benefit of each approach are beyond the scope of this discussion.

TERATOGENICITY AND LATE EFFECTS

To date, glucocorticoids have not been linked causally with any congenital malformations in humans.^{1,4} The drugs are used in pregnancy most often to promote fetal lung maturation before impending premature delivery. In this use, betamethasone is given for only a few days rather than for several weeks to months as in CAH prenatal therapy. The U.S. Food and Drug Administration classifies corticosteroids as Category B, indicating that there are no controlled studies in human pregnancy. However, animal data show some risk.⁵ Adverse outcomes in rodents and primates have included low placental weight, low birth weight, small head circumference, cleft palate, adrenal hypoplasia, thymic hypoplasia, hepatomegaly, late-onset hypertension, and impaired glucose tolerance.⁶ High-dose glucocorticoid administration or manipulation of endogenous glucocorticoid metabolism has produced fetal growth retardation, and has led to speculation that adverse outcomes for fetuses exposed to first trimester dexamethasone may be seen primarily beyond middle age in humans.⁷ As yet, no long-term data exist to support this concern in children who have been treated prenatally for CAH, most of whom are now teens or young adults. Some limited data suggest mild adverse cognitive or behavioral effects in these children,⁸ yet larger

continued on page 8

studies have not confirmed such findings.⁹ Masculine behavior was, in fact, less prominent in the prenatal treatment group than in controls.¹⁰ Genital reconstructive surgery need not be considered when the degree of virilization is mild or absent.

MATERNAL EFFECTS

The incidence of maternal complications varies, but is generally estimated at about 10%-20%. Overt Cushing's syndrome and hypertension have been reported in approximately 1%-2% of all treated pregnancies, usually with subjects treated throughout pregnancy.¹¹ Treated women gain excessive weight during the first trimester, but stabilize during continued treatment. No significant differences have been observed between treated and untreated pregnant mothers in blood pressure, proteinuria, gestational diabetes, or placental weight.¹² Monitoring of urinary estriol to assess compliance, dosing, and efficacy has been sporadic, and a proposed decrease in the dexamethasone dose in later pregnancy has not been systematically tested.

CONCLUSION

Prenatal treatment of pregnancies at risk for CAH is effective in improving or preventing genital ambiguity. The long-term safety of prenatal dexamethasone should be monitored prospectively, preferably in an international database comprising data from specialized centers with approved protocols. Women must be fully informed of the potential risks for themselves and the fetus and the possible lack of benefit in an affected female.

FROM DR. MILLER (Summary of the con perspective)

- Prenatal treatment of CAH improves the genital virilization in affected females, but must be started before a diagnosis of CAH can be made.
- Only 1 in 8 treated fetuses, the affected females, will potentially gain from the treatment; 7 of 8 fetuses will be treated needlessly.
- Prenatal treatment with dexamethasone delivers glucocorticoids at 60-100 times the physiologic level for the fetus.
- Glucocorticoids are neurotoxic in fetal animal studies, and accumulating evidence is showing mildly adverse neurodevelopmental outcomes in treated human fetuses.
- It does not seem ethical to submit 7 of 8 fetuses to any risk whatsoever when the treatment cannot benefit them, but instead potentially benefits the 1 in 8 affected females.

Prenatal treatment of CAH has been advocated by a small number of vigorous proponents since the 1980s, but has not been widely accepted by the pediatric or reproductive endocrine communities. Concerns about the safety of prenatal treatment have been voiced for over ten years.¹ The issues are clear. As described by Dr. Speiser, prenatal treatment can improve or eliminate the genital virilization of female fetuses with CAH by treating the pregnant mother with dexamethasone or other glucocorticoids that cross the placenta. To be effective, treatment must be started very early in pregnancy, essentially as soon as the pregnancy test becomes positive.

UNANSWERED PROBLEMS

There are two overriding issues that raise serious questions about the ethics

of this experimental treatment. First, because treatment must be initiated before the time when androgens (male hormones) will direct genital development toward a male phenotype, one cannot make a prenatal diagnosis before the time when therapy must be started. If a woman has had a previous child with CAH and is pregnant again (with the same father), only one in 8 pregnancies will be a female fetus with CAH who might be helped by the treatment (4 of 8 will be male, 3 of 8 will be females who are unaffected). Thus, for each fetus that might be helped by the treatment, 7 others are needlessly exposed to dexamethasone. If paternity is uncertain, a far smaller portion of fetuses will be affected, and vastly more will be treated needlessly. Second, the doses of dexamethasone used are grossly above normal. Measurements of fetal cortisol levels (by cordocentesis) and simultaneous measurement of maternal levels show that the ratio of maternal to fetal cortisol concentrations are about 10:1.² However, estimations of dexamethasone's biopotency based on suppression of adrenal C-19 steroid secretion⁴ and suppression of growth⁵ suggest the ratio is closer to 80:1. Thus, assuming a materno-fetal dexamethasone partition coefficient of 1, i.e., that dexamethasone freely crosses the placenta, the effective glucocorticoid doses reaching the fetus are 60-100 times the normal amount.

ETHICS OF TREATING 7 OF 8 FETUSES NEEDLESSLY

Little of what is summarized above is controversial; the real question is whether or not exposure of 7 of 8 normal fetuses to grossly above normal concentrations of glucocorticoids is harmful. If any harm at all can be demonstrated, then it would clearly be

unethical to subject a normal fetus to potential harm in order to help an affected one. Glucocorticoids are toxic to the developing central nervous system.^{6,7} Prenatal exposure to betamethasone to induce pulmonary surfactant in threatened early delivery may result in hyperactivity and attention deficit disorder.⁸ Post-natal dexamethasone therapy for broncho-pulmonary dysplasia adversely affected motor development and intelligence.⁹ Although these studies have employed short-term, high-dose treatment, it is important to remember that there are no 'safe doses' of teratogenic agents; rather, lower doses usually translate to a lower incidence or milder problems, rather than an absence of problems.¹⁰ The doses of dexamethasone used in CAH cause hypertension when rats treated in utero reach adulthood.¹

Other animal studies have found decreased birth weight and placental weight, impaired glucose tolerance, and adrenal and thymic hypoplasia. Studies with children treated with dexamethasone in utero for CAH show the treated children have greater emotionality and shyness and less sociability.¹¹ The only controlled prospective trial found that treated children have poorer verbal working memory, poorer self-perception of scholastic competence and increased self-rated social anxiety.¹²

PRENATAL TREATMENT OF CAH SHOULD BE ABANDONED

We will not know the real outcome of prenatal treatment of CAH until large numbers of the needlessly treated fetuses reach adulthood and are studied in detail. The only proven benefit of

prenatal treatment of CAH is that it can eliminate the need for plastic reconstructive surgery of the virilized genitalia in 1 out of 8 treated fetuses. Recent advances in genital reconstruction that permit complete repair in a single operation before 6 months of age have now reduced the motivation to employ prenatal pharmacology of unproven safety. The accumulating evidence that prenatal exposure to dexamethasone has mild but harmful effects on the developing brain of the 7 of 8 fetuses treated needlessly should clearly indicate that prenatal treatment of CAH is fraught with ethical (and possibly legal) problems. It is this author's opinion that this experimental treatment is not warranted and should not be pursued, even in prospective clinical trials.

Pro References

1. Nimkarn S, New MI. Prenatal diagnosis and treatment of congenital adrenal hyperplasia. *Pediatr Endocrinol Rev*, 2006; 4:99-105.
2. Consensus Statement on 21-Hydroxylase Deficiency from the European Society for Paediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society. *Horm Res*, 2002; 58:188-195.
3. Clayton PE, Miller WL, Oberfield SE, Ritzen EM, Sippell WG, Speiser PW. Consensus statement on 21-hydroxylase deficiency from the Lawson Wilkins Pediatric Endocrine Society and The European Society for Pediatric Endocrinology. *J Clin Endocrinol Metab*, 2002; 87:4048-4053.
4. Gluck PA, Gluck JC. A review of pregnancy outcomes after exposure to orally inhaled or intranasal budesonide. *Cur Med Res Opin*, 2005; 21:1075-1084.
5. Janssen NM, Genta MS. The effects of immunosuppressive and anti-inflammatory medications on fertility, pregnancy, and lactation. *Arch Intern Med*, 2000; 160:610-619.
6. Seckl JR, Miller WL. How safe is long-term prenatal glucocorticoid treatment? *JAMA*, 1997; 277:1077-1079.
7. Seckl JR, Cleasby M, Nyirenda MJ. Glucocorticoids, 11beta-hydroxysteroid dehydrogenase, and fetal programming. *Kidney Int*, 2000; 57:1412-1417.
8. Hirvikoski T, Nordenstrom A, Lindholm T et al. Cognitive functions in children at risk for congenital adrenal hyperplasia treated prenatally with dexamethasone. *J Clin Endocrinol Metab*, 2007; 92:542-548.
9. Meyer-Bahlburg HE, Dolezal C, Baker SW, Carlson AD, Obeid JS, New MI. Cognitive and motor development of children with and without congenital adrenal hyperplasia after early-prenatal dexamethasone. *J Clin Endocrinol Metab*, 2004; 89:610-614.

10. Meyer-Bahlburg H, Dolezal C, Baker S, et al. Diminished behavioral masculinization in girls with congenital adrenal hyperplasia after prenatal dexamethasone exposure. *Horm Behav*, 2003; 44:64.
11. Forest MG, Dorr HG, E.S.P.E. Prenatal therapy in congenital adrenal hyperplasia due to 21-hydroxylase deficiency: retrospective follow-up study of 253 treated pregnancies in 215 families. *The Endocrinologist*, 2003; 13:252-259.
12. Lajic S, Wedell A, Bui TH, Ritzen EM, Holst M. Longterm somatic follow-up of prenatally treated children with congenital adrenal hyperplasia. *J Clin Endocrinol Metab* 1998; 83:3872-3880.

Con References

1. Seckl JR, Miller WL. How safe is long-term prenatal glucocorticoid treatment? *JAMA*, 1997; 277:1077-1079.
2. Kari MA, Raivio KO, Stenmann UH, Voutilainen R. Serum cortisol, dehydroepiandrosterone sulfate, and steroid-binding globulins in preterm neonates: effect of gestational age and dexamethasone therapy. *Pediatr Res*, 1996; 40:319-324.
3. Kerrigan JR, Veldhuis JD, Iranmanesh A, Rogol AD. Estimation of daily cortisol production and clearance rates in normal pubertal males by deconvolution analysis. *J Clin Endocrinol Metab*, 1993; 76:1505-1510.
4. Rivkees SA, Crawford JD. Dexamethasone treatment of virilizing congenital adrenal hyperplasia: the ability to achieve normal growth. *Pediatrics*, 2000; 106:767-773.
5. Styne DM, Richards GE, Bell JJ, et al. Growth patterns in congenital adrenal hyperplasia—correlation of glucocorticoid therapy with stature. In Lee P, Plotnick L, Kowarski A, Migeon C, eds. *Congenital adrenal hyperplasia*. Baltimore: University Park Press, 1977; 247-261.

6. Uno H, Eisele S, Sakai A, et al. Neurotoxicity of glucocorticoids in the primate brain. *Horm Behav*, 1994; 28:336-348.
7. Matthews SG. Antenatal glucocorticoids and the developing brain: mechanisms of action. *Semin Neonatol*, 2001; 6:309-317.
8. French NP, Hagan R, Evans SF, Mullan A, Newnham JP. Repeated antenatal corticosteroids: effects on cerebral palsy and childhood behavior. *Am J Obstet Gynecol*, 2004; 190:588-595.
9. Yeh TH, Lin YJ, Lin HC, et al. Outcomes at school age after postnatal dexamethasone therapy for lung disease of prematurity. *N Engl J Med*, 2004; 350:1304-1313.
10. Holms LB. Commentary. *Pediatr Res*, 1999; 45:286-287.
11. Trautman PD, Meyer-Bahlburg HE, Postelnek J, New MI. Effects of early prenatal dexamethasone on the cognitive and behavioral development of young children: results of a pilot study. *Psychoneuroendocrinology*, 1995; 20:439-449.
12. Hirvikoski T, Nordenstrom A, Lindholm T, et al. Cognitive functions in children at risk for congenital adrenal hyperplasia treated prenatally with dexamethasone. *J Clin Endocrinol Metab*, 2007; 92:542-548.

Reprinted with permission.

Complete article can be found at www.endo-society.org/endo_news/tri_point_series.cfm/

Click Prenatal Treatment of Classic CAH: Pro vs. Con (Part 1 and Part 2)

EMERGENCY MEDICAL RESPONSE FOR CAH Rhode Island First in the Nation



Did you know that having medical ID that says, "Adrenal Insufficiency" on it, doctor's orders that detail medical treatment protocols for adrenal crisis, or properly labeled medications may not be enough if emergency medical responders do not have the necessary training, medications or permissions to give "the shot" to individuals affected by CAH?

Over the past eight years, CARES Foundation has worked tirelessly to ensure that every baby in America has a chance at a healthy start through advocating for expanded newborn screening including testing for CAH. Having achieved this goal, CARES Foundation is now beginning work to make sure we keep our children healthy throughout their lives. We are saving our babies and learning to care for our children. We are working toward better treatments and a cure, but those affected by the severe form of CAH are still always at risk of adrenal crisis which requires immediate, appropriate medical response in times of illness or severe physical stress.

CARES Foundation is looking to accomplish this through the inclusion of injectable glucocorticoids ("the shot") on Emergency Medical System (EMS) medication lists as well as in EMS treatment protocols for individuals with adrenal insufficiency. The only state where EMS response for CAH does exist at this time is Rhode Island.

We have started campaigns for immediate, appropriate EMS response for CAH in New York and Nevada. It is through our combined voices that we can ensure individuals affected by CAH receive the emergency medical care they need. If you are interested in adding your voice to that of CARES Foundation and our family and healthcare professional members in either of these states, or wish to start an initiative in your own state, please contact Gretchen Alger Lin at gretchen@cares.foundation.org.

Newborn Screening Saves Lives Act of 2007

"To amend the Public Health Service Act to establish grant programs to provide for education and outreach on newborn screening and coordinated follow-up care once newborn screening has been conducted, to reauthorize programs under part A of title XI of such Act and for other purposes"

While CARES Foundation is celebrating the fact that every baby in the United States is being tested for CAH at birth, there are still huge inconsistencies in screening programs and follow-up from state to state, making whether a baby dies or lives, survives or thrives largely dependent on where they are born. On April 24, 2008, all that changed when President Bush signed the Newborn Screening Saves Lives Act (S.1858/H.R. 3825) into law. ***Our work, however, is far from done.***

The Bill provides funding necessary for states to expand and improve their newborn screening programs as well as ensure appropriate follow-up, treatment and education. In particular, the Newborn Screening Saves Lives Act:

- Finally requires a uniform panel for tests across the nation eliminating state to state disparities in NBS screens
- Puts as much emphasis on what happens after screening as the screen itself, most especially all follow-up activities
- Gives strong financial incentives for states to bring their programs up to national standards

- Gives more power to the Secretary's Advisory Committee to make policy and to help states implement programs that meet national standards
- Will help states deal with natural disasters and other emergency situations
- Creates an unfunded program for research into new technologies and better treatments
- Ties all funding to compliance with national screening program standards as set forth by the Sec. Advisory Committee

Thank you to all who helped pass this monumental bill! Now we need to make sure it is implemented and Congress funds it appropriately. To make this a reality, CARES Foundation has been attending strategy meetings with other major stakeholders such as March of Dimes, Save Babies Through Screening Foundation, National Organization of Rare Disorders (NORD), Hunter's Hope, Cystic Fibrosis Foundation, Cerebral Palsy Foundation and others. If you live in the DC Metro area and are interested in spending a little time on "The Hill" advocating for our babies, please contact CARES Foundation Public Affairs

Gretchen Alger Lin, at
gretchen@caresfoundation.org.

GO VIETNAM!

On December 15, 2008, Dr. Nguyen Ba Thuy, Deputy Minister of Health in Vietnam, announced plans to expand his country's newborn screening program covering 24 provinces and cities nationwide. Wonderful news for families across the country, all babies will now be tested for four conditions including CAH.



From September 29 to October 3, 2008, the World Health Organization (WHO) Subcommittee of the Expert Committee on the Selection and Use of Essential Medicines held a meeting at which they considered an application to add hydrocortisone and fludrocortisone to WHO's essential drug list. While the report is still only available in draft form (www.who.int/selection_medicines/committees/expert/17/DRAFT_2nd_SC_TRS.pdf), the application submitted by CARES Foundation advocacy partner and President & Founder of Caring & Living As Neighbours (CLAN), Dr. Kate Armstrong, has met with approval. The draft report notes that in addition to expert testimony, "Numerous external comments in support of the proposal were received from health professionals, associations and individuals." It concludes, "The Sub-committee agreed that fludrocortisone and hydrocortisone are both essential medicines for children in the management of congenital adrenal hyperplasia and adrenal insufficiency, and included them on the EMLc." Thank you to all who submitted letters and joined this effort!

Just as with the Newborn Screening Saves Lives Act, getting these medications included in the List is only the first step to making these drugs available to families around the world. We now need to translate this to reality. If anyone is interested in working on this, please contact Gretchen Alger Lin: gretchen@caresfoundation.org.



CARES Meet-up at White Post Farms

This past June, CARES Foundation's New York City Metro Area Support Group held a "Meet-up at White Post Farms" in Melville, NY. Although it was a very hot day, a fun time was had by all.

Left to right: Greg Kraff, Rhonda Kraff, Allyson Kraff, Debbie Brown, Isabelle Brown, David Brown, and Dave Brown

Wisconsin Get-Together

On November 8, 2008 the Wisconsin and Northern Illinois CAH support group got together in the Wisconsin Dells for an afternoon of fun! Close to 35 people came and there were quite a few new families joining in the fun as they swam in the indoor water park, ate some pizza and talked about their experiences with CAH. The next Get-Together will be April 18, 2009 at Vilas Park, next to the Vilas Zoo in Madison, Wisconsin. They are looking forward to having a couple of endocrinologists and residents join them as well as a urologist from the University Children's Hospital in Madison. Mark your calendars!



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.

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.

2009 CARES Foundation, Inc. All rights reserved. Reproduction or redistribution of CARES newsletter content, including by framing or similar means, is prohibited without prior written consent of CARES Foundation.