THE CAHOOT

CAH ORGANIZATION OF TEXAS

VOLUME 4 TEXAS NEWBORN SCREENING PROGRAM SPRING 2003

CAH FAMILY WORKSHOP, HOUSTON, April 27, 2002

I would like to thank all the families that attended the workshop. I hope we can continue to meet on a yearly basis to chat and discuss any new advances in the treatment or cure for CAH.

It was wonderful meeting all of you and your beautiful children. The workshop turned out better than I had hoped. There is always room for improvement but all in all it was wonderful!

I wanted to thank Dr. Gunn, Dr. Berenbaum and Dr. New for their support in bringing this workshop to you. I would also like to thank the Cares Foundation for supporting this workshop. They are a wonderful organization with many resources and help to offer CAH families. I would also like to thank Starbucks and Kinkos. Their sponsorship of the workshop was a great gift. From the wonderful coffee and treats to the paper goods, we really appreciated it.

I hope you all enjoyed meeting and chatting with each other. I hope you will use the networking list I sent or emailed to those that attended or responded. It is nice to know that we are not alone and that together our children will benefit from our desire to continually improve the way we deal with CAH.

—Sandra Billings

TDH TO OFFER GENETIC TESTING FOR CAH

Susan M. Tanksley, Ph.D.
DNA Diagnosis Section Chief

The Texas Department of Health DNA Diagnosis Laboratory in Austin will soon offer additional testing services for individuals diagnosed with congenital adrenal hyperplasia (CAH).

CAH is a homozygous recessive disorder. Thus, an individual must possess two defective copies of the gene in order to exhibit disease symptoms. Prior research has indicated that there is a good correlation between the types of mutations present in the gene that causes CAH and the severity of the disease. Physicians armed with knowledge from a DNA analysis can more accurately predict whether a child will be a salt waster, a simple virilizer, or have non-classical CAH and can thus provide better treatment to these patients.

In addition, DNA testing may be beneficial to family members of patients with CAH to determine if they have a defective copy of the gene (referred to as a "carrier") for family planning purposes. Unaffected siblings of CAH patients have a 2/3 chance of being a carrier. In the general population, a random individual has a 1 in 50 chance of possessing a defective copy. Therefore, two individuals from the general population would have a 1 in 10,000 chance of having a child with CAH. However, if an individual is a known carrier, the chance of having a child with CAH increases to 1 in 200.

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The DNA test will identify defects (mutations) in the gene for 21-hydroxylase, which is responsible for 95% of CAH cases. Newborns in Texas who are diagnosed with CAH will receive the analysis as a confirmatory test as part of the Newborn Screening Program. The results will be reported to the submitting physician.

Fee-for-service testing will be available at a later date to provide complete analysis of the 21-hydroxylase gene in individuals with CAH not detected through the Texas NBS Program or to determine carrier status in family members of CAH patients. Specimens must be submitted to the Texas Department of Health by a physician to whom test results will be reported.

The TDH Laboratory staff is pleased to be able to add this service to our existing Newborn Screening Program.

HI ALL,

by Laura Kovalcik

Sandra has asked me to write a bit on the idea of circadian rhythm dosing. I'm not a physician. I'm a mom with two CAH children. Always check with your doctor before making changes to your child's medication schedule or amounts.

There have been many questions lately regarding dosing to mimic the cortisol circadian rhythm. For me, a picture was worth a thousand words. I couldn't believe it when I first saw the cortisol circadian rhythm chart. One brief glance told me that we had never dosed efficiently. Dosing to mimic cortisol circadian rhythm is not a new idea at all. Back at least as far as 1985, research was done using dosing schedules to achieve this goal.

Dosing to mimic circadian rhythm is not hard to understand, but implementing it can be tedious. If your child is doing well on a traditional 3x a day dosing schedule, it may not be worth it to your family to change. Quality of life is important. Quality of sleep is important. Meds shouldn't get in the way of living. However, if your child has control problems or cannot achieve acceptable control without cushingoid symptoms (decreased growth velocity, weight gain, abdominal fat pad, moon face), dosing with consideration to the cortisol circadian rhythm may be worth it to you.

A healthy endocrine system follows a very predictable pattern every day. CAH children can't do this, so medication must do it for them. Giving the meds in a way that mimics a healthy body should result in the most effective use of the medication. This means less side effects and better overall control.

A fairly typical dosing schedule of equal doses of Cortef given at 7am, 3pm, and 11pm. There are big areas of under-replacement and big areas of over-replacement. This schedule results in a period of under-replacement during the early morning hours and the early afternoon hours. It guarantees a period of over-replacement in the early sleep hours, during the time when growth hormone is trying to peak.

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EDITOR'S NOTE

We are so thankful that Sandra Billings, a CAH parent, agreed to gather articles for the CAHOOT in order that we could print/mail one out at this time, and hopefully, more frequently in the future. And "thank you" to all of you who contributed articles.

The Texas Department of Health Newborn Screening Program will continue to edit, print and mail the CAHOOT to Texas CAH families.

Please remember to keep us informed of future changes in your address/phone number, so that we can mail you the CAHOOT and let you know about special events such at the CAH Family Workshop in Houston in April.

Now I'll discuss a dosing schedule that considers the cortisol circadian rhythm. It is based on an article by Moeller from 1985. It adds a dose (and requires you to get up at night). The total dose is less, and coverage overall is far superior to conventional dosing. The apparent lack in coverage during the hours before 3am was not considered a problem in either the Moeller article or a more recent Charmandari study.

For a concrete example, a schedule of 3.75mg/3am, 3.75mg/7am, 2.5mg/noon, and 1.25mg/5:30pm would give you less Cortef (less side effects) and get better coverage (less androgen breakthrough). It's a win-win proposition, if you don't consider the darn alarm clock. I've had several parents report that their endo thinks this approach is not necessary. I agree. My girls would have survived on the old schedule. In our case, I had to decide how bad I was going to let it get before I did something. How much growth do our children need to lose before it becomes "necessary"? How many summers do they need to spend reluctant to put on a bathing suit because the tummy roll is embarrassing?

—Laura K.

REFERENCES:

1: Eur J Pediatr 1985 Nov;144(4):370-3

Chronopharmacology of hydrocortisone and 9 alpha-fluorhydrocortisone in the treatment for congenital adrenal hyperplasia.

Moeller H.

The conventional treatment of CAH with hydrocortisone (16-19 mg/m2 per day) and 9 alpha-F-cortisol (just enough to normalise renin concentrations, started at 07:00 h) was ineffective in suppressing the early morning rise of 17-OH-progesterone and in turn androgens in about 20% of our patients. The present work explored the effect of a modified dosage regimen of the drug in five patients. The schedule was: 03:00 h F 33% + 9 alpha-F-F 33%; 07:00 h F 30%; 12:00 h F 22% + 9 alpha-F-F 33%; 17:30 h F 15% + 9 alpha-F-F 33%. Monitored levels of circulating 17-OH-progesterone, testosterone, and individual urinary 17-ketosteroids showed significant improvement, which was not achieved by giving higher or later evening doses. Menarche was induced in two girls (bone age 15 years). The modified dosage schedule offers on the one hand the possibility of better management of CAH, and on the other, cuts down the risk of enhanced Cushing-like effects, which in animal models have been related frequently to dosage schedules not corresponding to the circadian rhythm. The difficulty of administering the drugs at 03:00 h should be overcome by the development of a late-releasing preparation.

PMID: 4076253 [PubMed - indexed for MEDLINE]

2. J Clin Endocrinol Metab 2001 Oct;86(10):4679-85

Serum cortisol and 17-hydroxyprogesterone interrelation in classic 21-hydroxylase deficiency: is current replacement therapy satisfactory?

Charmandari E, Matthews DR, Johnston A, Brook CG, Hindmarsh PC.

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One of the main aims in the management of patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency is to achieve adequate suppression of the adrenal cortex with the smallest possible dose of glucocorticoid substitution. To evaluate the administration schedule of current replacement therapy regimens, we investigated the cortisol-17-hydroxyprogesterone interrelation in 36 patients (13 males and 23 females; median age, 12.3 yr; range, 6.1-18.8 yr) with salt-wasting congenital adrenal hyperplasia. As sufficient variation in 17-hydroxyprogesterone concentrations was required to allow analysis of the cortisol-17-hydroxyprogesterone interrelation, patients were divided into 2 groups depending on the adequacy of hypothalamic-pituitary-adrenal axis suppression. The first group consisted of 17 patients with suppressed 17-hydroxyprogesterone concentrations (group 1), and the second group consisted of 19 patients with nonsuppressed 17-

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hydroxyprogesterone concentrations (group 2). We determined serum cortisol and 17-hydroxyprogesterone concentrations at 20-min intervals for a total of 24 h while patients were receiving their usual replacement treatment with hydrocortisone and 9alpha-fludrocortisone. We also determined the lowest dose of dexamethasone required to suppress the 0800 h serum ACTH concentrations when administered as a single dose (0.3 or 0.5 mg/m(2)) the night before. Mean 24-h cortisol and 17-hydroxyprogesterone concentrations were 3.9 microg/dl (SD = 2.1) and 66.2 ng/dl (SD = 92.7), respectively, in group 1 and 4.1 microg/dl (SD = 2.5) and 4865.7 ng/dl (SD = 6951) in group 2. The 24-h 17-hydroxyprogesterone concentrations demonstrated circadian variation, with peak values observed between 0400-0900 h. In group 2, 17-hydroxyprogesterone concentrations decreased gradually in response to the rise in cortisol concentrations during the day, but remained low during the night despite the almost undetectable cortisol concentrations between 1600-2000 h. Mean 0800 h androstenedione concentrations correlated strongly with integrated 17-hydroxyprogesterone concentrations ($r = 0.81$; $P < 0.0001$), but not with integrated cortisol concentrations. There was a significant negative correlation between cortisol and 17-hydroxyprogesterone at lag time 0 min ($r = -0.187$; $P < 0.0001$), peaking at lag time 60 min ($r = -0.302$; $P < 0.0001$), with cortisol leading 17-hydroxyprogesterone by these time intervals. Finally, 0800 h serum ACTH concentrations were sufficiently suppressed after a dexamethasone dose of 0.3 mg/m(2) in all but three patients. These findings indicate that in classic 21-hydroxylase deficiency, hydrocortisone should be administered during the period of increased hypothalamic-pituitary-adrenal axis activity, between 0400-1600 h, with the biggest dose given in the morning. Blood investigations performed as part of monitoring of congenital adrenal hyperplasia patients should include androstenedione and 17-hydroxyprogesterone concentrations determined in the morning before the administration of hydrocortisone. It should also be emphasized that blood investigations are only complementary to the overall assessment of these patients, which is primarily based on the evaluation of growth and pubertal progress.

PMID: 11600525 [PubMed - indexed for MEDLINE]

3. J Endocrinol 2001 Apr;169(1):65-70

Bioavailability of oral hydrocortisone in patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency.

Charmandari E, Johnston A, Brook CG, Hindmarsh PC.

London Centre for Paediatric Endocrinology, University College London, London, UK.

The management of congenital adrenal hyperplasia due to 21-hydroxylase (CYP21) deficiency requires glucocorticoid substitution with oral hydrocortisone given twice or thrice daily. In paediatric practice little is known of the bioavailability of oral hydrocortisone tablets used in these patients. The aim of this study was to assess the bioavailability of oral hydrocortisone and to evaluate current replacement therapy in the light of cortisol pharmacokinetic properties. We determined the bioavailability of hydrocortisone following oral and intravenous administration in sixteen (median age: 10.9 years, range: 6.0-18.4 years) adequately controlled CYP21 deficient patients. Serum total cortisol concentrations were measured at 20-min intervals for 24 h while patients were on oral substitution therapy, and at 10-min intervals for 6 h following an intravenous bolus of hydrocortisone in a dose of 15 mg/m(2) body surface area. The area under the serum total cortisol concentration versus time curve (AUC) following oral and intravenous administration of hydrocortisone was calculated using the trapezoid method. The bioavailability was estimated by dividing the corrected for dose AUC after oral hydrocortisone administration by the corrected for dose AUC after the intravenous hydrocortisone administration and was exemplified as a percentage. After oral administration of hydrocortisone in the morning, median serum total cortisol concentrations reached a peak of 729.5 nmol/l (range: 492-2520 nmol/l) at 1.2 h (range: 0.3-3.3 h) and declined monoexponentially thereafter to reach undetectable concentrations 7 h (range: 5-12 h) after administration. Following administration of the evening hydrocortisone dose, median peak cortisol concentration of 499 nmol/l (range: 333-736 nmol/l) was attained also at 1.2 h (range: 0.3-

3.0 h) and subsequently declined gradually, reaching undetectable concentrations at 9 h (5-12 h) after administration of the oral dose. After the intravenous hydrocortisone bolus a median peak serum total cortisol concentration of 1930 nmol/l (range: 1124-2700 nmol/l) was observed at 10 min (range: 10-20 min). Serum cortisol concentrations fell rapidly and reached undetectable levels 6 h after the hydrocortisone bolus. The absolute bioavailability of oral hydrocortisone in the morning was 94.2% (90% confidence interval (CI): 82.8-105.5%) whereas the apparent bioavailability in the evening was estimated to be 128.0% (90% CI: 119.0-138.0%). We conclude that the bioavailability of oral hydrocortisone is high and may result in supraphysiological cortisol concentrations within 1-2 h after administration of high doses. The even higher bioavailability in the evening, estimated using as reference the data derived from the intravenous administration of hydrocortisone bolus in the morning, is likely to reflect a decrease in the hydrocortisone clearance in the evening. Decisions on the schedule and frequency of administration in patients with congenital adrenal hyperplasia should be based on the knowledge of the bioavailability and other pharmacokinetic parameters of the hydrocortisone formulations currently available.

PMID: 11250647 [PubMed - indexed for MEDLINE]

GROWING UP WITH CAH

by Penny Halloin
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Growing up different for a kid, any kid, presents a unique set of challenges for all involved. CAH involves extra doctor visits, daily medication, and more understanding on a parent's part.

I was diagnosed with Congenital Adrenal Hyperplasia at age 3 1/2 by a pediatric endocrinologist in Michigan. My parents noticed the development of secondary sexual characteristics and took me to be treated. At that time, I was placed on daily doses of Cortisone to control the problem. My parents were briefed on the importance of the daily medication and to double or triple it if trauma occurred.

As a small child, I do not remember CAH affecting my daily activities in any way. I was actually taller than many of my playmates, as I received much of my growth early. My early childhood was no different from any other, except for the fact I had to take my medicine daily, and had to double it anytime I ran a fever. I had the usual run of childhood maladies and was never made to feel that I could have anything but "normal" activities.

When I grew older, around 9-11 years of age, I started to notice that I was developing earlier than many of my peers. I had breasts and other sexual characteristics that they didn't, and this caused a large amount of stress in my life. I received a lot of teasing at school and, as a result, began to have panic attacks. However, again, my parents helped me through this by helping me to understand that, at some point in their lives, EVERYONE gets teased. As I grew older, and my peers caught up to me physically, the teasing lessened. It's very tough for a child to have these types of problems because its not something that is talked about in every day conversation in most households.

Now that I am 26 years old, I realize that I was very lucky to have understanding parents and doctors who emphasized that CAH was something that needed to be treated, but that I did not need to curtail any of my physical activities or think that I couldn't have a full life as an adult. I battle my weight due to the prednisone and the fact that I like to eat junk food. I might have difficulty conceiving when I'm ready to have children. I'm very short (4'11") and have to get a step stool to reach things. But, all of these are challenges that other people face as well, and have met and overcome them.

CAH is a life threatening disease. It requires understanding, vigilance on the part

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of the patient and the parent, and lifelong treatment. However, the disease does not have to run the patient's entire life. My advice to any parent of a CAH kid is let them know you are there for them and that they can talk to you about anything that they have questions about. I am a happy, well adjusted woman and plan to enjoy my life to the fullest.

JACKSON'S CAH DIAGNOSIS

by Sandra Billings
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My pregnancy was pretty uneventful. It was my third one and I was feeling the usual pregnancy pains. I made sure to take my vitamins, avoid junk food and sodas. I tried to eat healthy and stay away from anything that I thought was harmful. I had a perfect, beautiful baby boy on June 18th 2001! He weighed 8lbs, 12oz and we decided to name him Jackson. He was perfect in every way. He was a little jaundiced but my other two sons had also been jaundiced at birth. I didn't worry about it. We took our little guy home and started to adjust to life with three boys!

One week or so after we had been home, I get a call from the nurse for the pediatrician that saw my son in the hospital. She left a message saying to call her back right away. Before I had time to call her back, my husband was calling me to tell me that he had also gotten a call at work and to call the nurse back to find out what was going on. That phone call changed my life. The nurse explained to me that the first newborn screen they did had come back slightly elevated for 17OHP and that he could have Congenital Adrenal Hyperplasia. I couldn't believe what she was saying. She asked me to take him to get a repeat test. She told me not to worry too much because it would probably clear up on the rescreen. It didn't. After a few visits to the pediatrician to check Jackson's electrolytes, a referral to a pediatric endocrinologist and a stimulation test, Jackson was diagnosed as having Classical Salt Wasting Congenital Adrenal Hyperplasia. That was the most terrifying moment of my life! I didn't know what to think or do. I had always been able to find a way out of problems in my life but this one seemed unbelievable, unmanageable. I had never heard of CAH. What was it? What would happen to Jackson? What did I do wrong? I sat in the doctor's office with tears running down my face and the doctor telling me not to worry that it wasn't so bad. I was looking at her in amazement. How could she tell me it wasn't so bad?

I went through the usual fear that comes along with ignorance. I wondered what I had done, what I could have done. I couldn't believe that something like this had happened. I had never dreamed that it could happen to us. I started reading everything I could about CAH and found a great online support group. I say it was great because I found a mom or two that could relate and helped me out tremendously. My husband was also a wonderful support. He dealt with the diagnosis completely differently than I did. He was much more calm and collected. He approached the whole CAH diagnosis with an "it could have been worse" attitude. As a mother though, I felt so guilty. I felt that maybe I had done something wrong.

Carolyn Scruggs was also wonderful at helping me through the initial first few weeks. She told me something that I will never forget. She said that out of all the disorders their office screens for, if she had to pick one for her child to have, she would pick CAH. It helped me realize that there were others who were dealing with even more serious disorders or problems. This had such an impact on me that I started to realize that maybe we could deal with this. Carolyn sent me the back issues of the CAHOOT Newsletter. I wanted to know how kids with CAH did as they grew. I wanted to know how

they dealt with CAH. I wanted to know what they looked like. I felt so much fear and pain and disbelief for what my son had that I felt that seeing other kids with CAH would set my fears at ease.

I began to learn so much about CAH that I started to wonder if my son really did have CAH after all. He had never had a crisis and he never had abnormal electrolytes yet his ACTH stimulation test showed that he did have CAH. During my reading I came across other types of CAH and I began to wonder if he didn't have another form of CAH. Maybe he had the Non Classical kind. Of course, deep down I was wishing that I could find another explanation for his high 17OHP, like immature adrenals or something like that but I knew I couldn't deny what he had. Yet it bothered me that he didn't have any weight loss or problems eating or sleeping that other saltwasting (SW CAH) babies seemed to suffer from. Jackson didn't even start his meds until he was 30 days old. At that point he wasn't even close to being in a crisis. I found out that many endocrinologists lump the salt wasters and simple virilizers (SV CAH) together into one group since it is still within the Classical kind. I am assuming they do this because they don't want to take the chance of any kids having a salt wasting crisis. I questioned my endocrinologist and she assured me that Jackson was a saltwaster and that he needed the florinef. His renin was a little on the high side but all other lab work was normal.

I decided to have his DNA tested. Our local endocrinologist informed me that DNA testing was not offered. I told her that maybe not in Texas but it was in New York. I had my son's blood sent to Dr. Maria News' DNA Lab at Cornell in the NY Presbyterian Hospital. Jackson's DNA showed that he was not a saltwaster after all but that he was a simple virilizer. I felt a little bit better that I was able to improve his diagnosis. The poor kid hated the taste of salt and cried every time I tried to supplement him with sodium.

I was so excited about this new diagnosis that I wanted to go see Dr. New. It took me a few months to get an appointment with Dr. New but Jackson and I were soon off to New York. This was a month after the September 11th attacks. I was terrified to go alone but my husband had to stay with the other two boys.

Dr. New, in my opinion, was wonderful. She took one look at Jackson and saw that he was cushingoid. She cut his cortef in half, took him off of Florinef and watched him. Actually, he was on a pharmacy-made liquid cortef. Dr. New was disgusted that he had been put on this. She told me to only use the pills.

Jackson and I spent two weeks in the hospital. Dr. New wanted to make sure that his phenotype (what he presents with) and his genotype (what his DNA shows) matched. He did great and all of his test results concluded that he did have simple virilizing CAH, not the saltwasting kind. To some this may seem trivial but to me it meant so much. I had made it better for my son. I am not saying that kids that have SW CAH are doomed but I was relieved that he nor I would most likely never have to deal with any saltwasting crisis.

We returned home with some sense of accomplishment. I felt for the first time in a long time that he would be OK. Of course we have only been dealing with CAH for a short time but we have come a long way. He has been sick only twice with common childhood illnesses. Both times he did wonderful with some extra meds. He now takes only Cortef.

The most frustrating part of the CAH is that every doctor has their own way of treating CAH. There is no consensus. Our local endocrinologist, to this day, wants Jackson on Florinef. Dr. New and her fellows assured me that he produces sufficient aldosterone and that his electrolytes

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are fine. His renin was slightly over the mean for his age group but all CAH kids, according to Dr. New, are going to have higher renins. All CAH patients have a tendency to waste salt. I just don't want to give my son any more medication that he really doesn't need. Yes, it's true that some kids use florinef to try to keep the total amount of Cortef down but in my son's case he is on a very low dose of cortef to begin with. I also had my two older sons tested with the ACTH stimulation test. They both did not have CAH. When they get older and get ready to have kids of their own, we will get genetic testing done to see if they are carriers.

My goal now, as an advocate for my son, is to stay educated about CAH and it's treatment, and to stay involved in funding research for a cure. I want to be a support for other parents. I would like to repay the kindness of those that helped me through a tough time.

The most wonderful thing I am grateful for is that we were in Texas when Jackson was born. We had moved from California just two years prior to having Jackson. They do not screen for CAH in California. We would not have known that Jackson had CAH if he would have been born there. If he were a saltwaster, the only way we would have found out was when he presented with a saltwasting crisis. Since he is a SV, we probably wouldn't have found out about his CAH until he started presenting with problems like early puberty not to mention the potential for an adrenal crisis. I thank God for somehow directing us to Texas. I thank God that Texas screens for CAH. I can't imagine why some states don't.

So, almost a year later, we are getting ready to celebrate Jackson's 1st birthday. I don't feel worried or scared for him any more. I thought I would never feel this way but just in his first year he has shown me that he is just as normal as any other kid. He started walking when he was 10 1/2 months old. He has hit every developmental milestone early and above average. I have learned so much about CAH that now I really do believe what the doctor was telling me that first day, "CAH is not that bad". It really isn't. It is manageable and the kids grow up to be just as normal as any other kid. My husband and I are talking about trying again for a 4th. With three beautiful boys, a girl would be a nice addition. I feel that no matter what, CAH or not, girl or boy, we will be so much more prepared and comfortable. CAH has just become part of our lives but not our entire life. I will try to instill this in Jackson too. CAH is a part of him, not him.

JUNE 4TH

by Karon Watson
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As I was leaving my children at my parents house on April 26, 2002, I had many feelings going on. My husband and I were on our way to Houston. We were going to the first CAH Workshop.

We had many concerns and questions for the meeting. What would we learn about the condition? Was there new medicine? How did other families deal with the same problems we do? As I sat and listened to the guest speakers, I found out that we all had the same concerns. The one thing that needs to be addressed is the insurance companies. Many of us deal with the insurance company on a daily or monthly basis. What will happen if we loose our jobs? What happens when we start getting older?

I would like to see a children's workshop come about. My son has talked to other children a few times but as parents we need to know how they feel, their thoughts about their condition. As parents this may help us to know how to deal with their feelings more.

I would like to thank Sandra Billings for her hard work and the love she has for her son. She was not happy with what her doctor was saying. She

went the extra mile and that's how we got our 1st CAH workshop. Thank you, Sandra. And as I always say, "Keep the faith and an eye on your CAH Children."

Thanks Again,
Karon

KROGER GROCERY STORE SHARE CARD

by Sandra Billings
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I have asked Dr. New's office for permission to sign up for the Kroger Grocery Store Share Card. How does it work? The brochure explains it like this:

"Members of your group carry their Share Card to Kroger each time they shop. The Card has an account number exclusively assigned to your organization. Members simply ask the cashier to scan the card before their groceries are scanned. The purchase price of their groceries is automatically recorded to your organization's Kroger Share Card Account. Kroger Keeps a running total of your account, and reimburses a percentage (1%) of your total purchases directly to your organization." The card is good at any Kroger location in Texas and Louisiana.

I chose to apply for a Share Card to help Dr. New's research for a cure for CAH. At our Houston CAH Workshop, Dr. New said that she did think that there would be a cure in her lifetime. This was very encouraging to me and I want to help support that research, not only for my child but for all the other CAH people out there.

Krogers sent me 500 cards at no cost to me. I handed out cards at the Houston CAH Worshop. Please contact me if you lost yours or you would like more to hand out to family and friends. You can contact me at 281 861-6043 or at billprop@aol.com.

If you don't think it will add up to much just look at this example: 50 participating members with average quarterly purchases at $75.00 per week at 1% refund we could potentially earn $488.00 per quarter for CAH Research. If we could double that, it would be almost $3,000 a year. This is a great way to contribute considering it is money that is waiting to be donated. Please help if you can. If you are interested in finding out if other grocery stores do this type of program, I encourage you to do so. I did this on my own and you can find ways to help also!

Considering that CAH is considered an Orphan Disease, we need to become more effective in supporting research for new and better treatments along with researching for a cure.

PARENTING A SON WITH CAH

by Nancy Manning

The amazing thing to me is that I have not written my story before this. Of course, I have told it many times, although less frequently as the years have gone by. Recently, however, my son has been giving a lot of thought to his congenital adrenal hyperplasia, and he has honored me by suggesting that we write our stories together.

Twenty-eight years ago, Rick was born at Homestead Air Force Base in Florida. Following an easy pregnancy and delivery, my beautiful, towheaded baby boy entered the world weighing 7 pounds 3 ounces. He had some problems right from the beginning. I tried to breastfeed Rick, but he had a feeble sucking response. Whatever milk he managed to swallow was soon forcefully vomited. He was quite jaundiced, so he was placed under fluorescent light to break down the excess bilirubin. Then he developed a belly button infection. Sadly, I was sent home without my baby, as he needed observation for the infection and bilirubin count, which went high, but

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eventually dropped without causing permanent damage. Meanwhile, I visited him daily but was still having no success feeding him. I was worried, but expected to bring him home in a matter of days. As it turned out, I will be forever thankful that Rick stayed in the hospital. If I had brought him home with me, I believe that he could have suffered an adrenal crisis, shock, or worse before I sought medical treatment. This of course was in the days before routine testing of newborns for CAH, and I was an inexperienced new mother.

On his tenth day, with his weight down to under 6 pounds, Rick was transferred by ambulance to the Newborn Intensive Care Unit at Jackson Memorial Hospital in Miami. This came as a shock to me, as I had been told he might be coming home soon. On this day I understood for the first time that something was seriously wrong with my baby. My mother, who had come from New York State to be with me but had to fly home that very day, later told me that she was afraid she would never see her new grandson again. Maybe it was my naiveté, or my faith, or both, but I can honestly say I never considered my baby's life to be in danger. Looking back, I know that he could not have survived much longer without appropriate treatment. What I did feel at the time was the nightmare of being home without my baby in my arms. It felt so unnatural after nine months of being together, and I had no idea when he would finally come home.

The fine staff at Jackson Memorial took good care of my son. I was soon told that they suspected a hormonal deficiency – this was the first mention of congenital adrenal hyperplasia. This diagnosis was confirmed after several lab tests, including a 24-hour urine collection which had to be sent to California for analysis. When Rick was three weeks old I moved into the hospital's care-by-parent unit. There I was able to live with my baby around the clock while the doctors closely monitored his progress. Now that he was receiving cortisone acetate and the needed salt retaining hormone he was finally gaining weight. I was taught to give him injections, which I continued to do every third day for his first year. I had to add a teaspoon of salt to his daily formula. Sadly, breastfeeding was no longer an option, although looking back I think I could have made it work with supplemental feedings if I had been given the proper support and encouragement. When Rick was six weeks old he was finally released and we went home. Living for those three weeks among other parents and children with much greater health problems, including cancer and multiple birth defects, put CAH into perspective for me. I wouldn't have traded places with any of them.

Life with my CAH child became fairly routine. My confidence grew as did my experience in carefully monitoring his health. We made frequent trips to the doctors for checkups and the periodic "episodes" when he developed a fever, began vomiting, or became lethargic. I learned to recognize when to increase his cortisone, when to increase his salt intake, when to administer the monthly shot of mineralcorticoid, and especially when to see his doctor. I learned to ask lots of questions but I never networked with other parents of CAH babies. We were so few and far between in those days that it just didn't happen. Of course there was no Internet to bring us together and no world wide web to surf for information as there is today. I am so pleased to see the plentiful resources available today to families dealing with this disease.

My husband and I wanted to have another child. We knew the chances of having a CAH baby, but that did not deter us. We were forewarned this time, and the doctors knew to watch the baby carefully for any sign of adrenal insufficiency. Our second son was born without CAH just a year after Rick.

Twice Rick experienced adrenal crises that required hospitalization. This happened when he was 9 months and 18 months old. While these events were very scary to me, each time he rapidly improved and was able to come home in two or three days. As he grew, we were fortunate to have access to excellent doctors who managed his care wisely. The worst was behind us, and from his toddler-hood on, managing Rick's CAH was a constant yet basically uneventful part of our lives.

I was very interested to read Rick's own account of living with CAH, and I consider it a real testimony to his doctors and upbringing that he feels CAH has had limited impact on his life. Indeed, I know that if he in turn has a child with CAH, he and his wife will give him or her that same gift.

I think my tale was waiting for the day when Rick and I would write our stories together. Our wish is to bring hope and encouragement to families facing the unknown. It definitely gets better, and you too will be able to smile as you write your own story.

GROWING UP WITH CAH

by Rick Buswell

I am a 28-year-old male with salt losing congenital adrenal hyperplasia and I'm writing this article to relate first hand what I dealt with growing up with CAH. I was actually a little hesitant when first presented with this opportunity because I didn't think I'd have much to write about, but then I realized the limited significance of CAH to me growing up may be of interest by itself, especially to new male CAH parents. In my case, I think CAH was more troubling for my parents than for me while I was growing up so I have also asked my Mother to write about her own perspective.

I do not have any memory of sickness episodes as a baby or toddler, although I know I went through a few, and was probably near death at least at the time of my initial diagnosis. I did not get sick very often as a kid, and still don't, although I have always known to take extra cortisol if I do. I can only remember one episode that may have been an adrenal crisis when I was about 13. I was riding my bike one summer in Texas and suddenly felt very weak and dizzy, which at the time I thought was heat stroke because it went away after lying down for a while in the shade.

I'm not sure if it was good fortune, good medical care, or both, but I also did not have any developmental problems. I went through puberty at a normal age and ended up an average height of 5'9", which I think is probably my natural height anyway since my non-CAH brother is about the same height.

I was aware that I had the disease as a kid, but I was always told that I would live a normal life as long as I took my medicine, and so that's what I did. I was not told to limit strenuous activities or anything like that, and although I was not very into sports, I was always very active and did not feel any different than my friends in that regard.

The CAH-related "problems" that I experienced growing up were merely minor annoyances looking back, and even at the time never felt like serious issues. For instance, one time my brother and I were visiting an aunt without our parents and she freaked out when I got a fever. She knew that I had CAH and that a fever could be a problem but I felt like she was over-reacting making me take a bath in ice water. I was sometimes embarrassed when friends would ask what my medic alert bracelet was for but I would usually just say that I had to take medicine to retain enough salt and wouldn't have to go

continued on next page

into it any further. The most embarrassing moments were when my brother would try getting to me by blurting out to friends, "Ricky has a disease". As a teenager, the frequent doctor visits and lab work (especially the 24-hour urine collections) started to feel like a nuisance but I dealt with it fine.

I have taken florinef and cortisol (in one form or another: hydrocortisone, prednisone, dexamethasone) for as long as I can remember and never had a problem with taking my pills, other than forgetting the occasional dose. My dosages have always been prescribed as morning and night, so I never had to worry about taking medicine during school. I usually get a headache by the afternoon if I forget my morning dose so I have never tried to go without medicine on purpose. Taking my pills actually became more of a nuisance as an adult when I went away to college and had to start buying them myself. Even now, I think of the monthly refill trip to the pharmacy as more of an inconvenience than taking the pills twice a day since taking them is so routine.

The CAH concerns I've dealt with as an adult have been somewhat more serious than what I experienced as a kid but are still far from unbearable. In my senior year of college I briefly contemplated going into the military until I talked to a recruiter and was told that they do not take anyone who is medicine-dependent. Also, in my jobs as a mechanical engineer I have had to move several times, and finding an endocrinologist that I'm comfortable with has always been tough. None of them seem as familiar with CAH as the pediatric endocrinologists I saw as a kid; most of the adult endocrinologists I've found deal mainly with diabetes patients. Another more recent concern is the possible implications for having children. My wife and I have been married for 2 1/2 years and are planning to start a family soon. Since CAH is a genetic disease, we know there is a chance of having CAH children. We were informed that the chances of her being a carrier, or anyone in the general population, is about 1 in 57. This is fairly small, but we were happy to learn that there is testing available to see if she is a carrier (we are currently waiting on the test results). Thankfully, if she is a carrier, there are precautions we can take to prevent masculinized genitalia in a CAH daughter.

All in all, growing up with, and now living with CAH has never really been too big of a deal to me, certainly not enough that I ever felt emotionally or psychologically affected by it. And, based on my experience, I believe that with proper diagnosis and care, most CAH baby boys will grow up feeling the same way, as I'm sure many already have.

ORPHAN DRUG ACT ALERT – REQUEST FOR ACTION

by Calvin and Tricia Luker

The Orphan Drug Act (ODA) promotes development of medications for people who have rare diseases. The ODA was passed because there was no financial reason for drug companies to pay out huge research and development costs to create drugs that would help only a small number of patients. The pharmaceutical companies could not expect that they would be able to recover their development costs. The ODA mandated that if a drug company created a medication used for rare diseases and disorders, then the company would have the exclusive right to sell the drug for seven years. No "generic" sales would be permitted during that seven-year period. The Federal Drug Administration (FDA) grants the exclusivity when it approves the drug's use for a specific condition. The ODA has inspired drug companies to spend the money up front to create the medicines so desperately needed by people

who have rare diseases and disorders.

The ODA is under attack in a very subtle way. Medicare or Medicaid pays for many drugs protected under the ODA. The Department of Health and Human Services administers Medicare/Medicaid payments through the Center for Medicare & Medicaid Services (CMS). Recently the CMS has started paying for generic drugs for certain diseases and disorders even though the drug company that developed the medication has the right to exclusive sales under the ODA.What the CMS has said, in effect, is that it does not have to follow the FDA's approval of ODA exclusivity when it administers Medicare/Medicaid programs. The result is that the companies who developed the medication are being cheated out of their right to recover their research and development costs.

The CMS payment practice is dangerous to the Orphan Drug Act for several reasons:

First, it undermines and possibly destroys the economic incentive for drug companies to create new medicines to treat rare diseases and disorders. Why should a company work to develop a drug for a specific use if CMS is going to ignore the company's right to exclusivity?

Second, it imperils drug development for the people who have rare diseases and disorders. What hope can they have for pharmaceutical help if there is no incentive for the drug companies to develop the medication?

Third, it creates an administrative veto of a law that people with disabilities and their families and advocates worked their hearts out to get passed. What faith can we in the disability community place in government if HHS/CMS can ignore the FDA's decision to grant drug exclusivity under the ODA?

Finally, it undermines our efforts to be sure treatment and medications are made available at the earliest possible time to the people who need them. For example, what good does it do to implement comprehensive newborn screening if there is no incentive or mechanism to be sure that the drugs needed to treat the identified rare disorders are created and available.

The HHS/CMS practice of ignoring FDA drug exclusivity determinations under the Orphan Drug Act must be stopped, or the Orphan Drug Act itself will be stopped. THERE IS NO TIME TO WASTE. We cannot let this happen. WE MUST ACT NOW. Please call, write or email your US Senator, Congress member, and HHS Secretary Tommy Thompson and tell them to save the Orphan Drug Act before it's too late. This is about our children and our future. We must be sure that the incentive to develop drugs for rare diseases and disorders is preserved. We have seen ODA drugs save our children's and other family member's lives. We cannot let the ODA get away. Please forward this email to all disability related listserves, friends and relatives you can think of. PLEASE ACT IMMEDIATELY TO SAVE THE ORPHAN DRUG ACT.

Please email or call Calvin and Tricia Luker at calvinluker@inetmail.att.net or 248-544-7223 if you have questions about this email.

Thank you very much.

The contact information for Secretary Tommy Thompson is:

Honorable Tommy Thompson
Secretary, US Department of Health and Human Services
200 Independence Avenue,SW,
Washington, DC 20201
Tel: 202-690-7000
Fax: 202-690-7203
Email: hhsmail@os.dhhs.gov

We hope this information is helpful. If families do not respond right away our children have the most to lose. This is not about lobbying — this is about advocacy for our children.

—Tricia and Calvin Luker

MOM OF A CAH CHILD

by Shaji

1. CAH makes me wonder about the complexity of life which we all often take for granted, and a greater awe and respect for the creator God.
2. CAH creates a sense of gratitude to the medical community for their inventions and their tireless efforts to find a solution (inspite of some failures here and there).
3. CAH makes the parents and the children tougher in facing greater challenges in life.
4. It makes me feel more sympathetic towards not only those who have CAH, but also towards those with other congenital or acquired problems.

DAD OF A CAH CHILD

by Andrew

One <u>really</u> positive thing about CAH is that the potentially fatal aspect of this condition can now be treated successfully.

LIVING WITH CAH - A NEWSLETTER

No. 5, January 2002

This newsletter is a collaborative project of professionals from diverse disciplines of New York Presbyterian, the combined University Hospitals of Cornell and Columbia.

What Does Prenatal diagnosis and treatment of CAH Involve?

(We elected to combine newsletters for classical and non-classical CAH in this issue. Whenever appropriate, we will provide separate newsletters.)

<u>Prenatal Diagnosis in General</u>

Prenatal diagnosis can be accomplished using one of two tests: amniocentesis or chorionic villus sampling (CVS). First let's go over these two tests and then we'll review the laboratory methods used to detect CAH in a fetus.

Amniocentesis is a procedure that has been around for over 20 years. It is usually performed at around 16 week's gestation. This means that it is performed 16 weeks after the first day of your last period (LMP) or 14 weeks after the most likely date of conception if your periods are irregular. A sonogram or ultrasound (same thing) is performed to check the fetus and to identify a safe position for the amniocentesis needle. While the sonogram is still on and tracking the fetal movements, amniocentesis is performed by inserting a needle through the abdomen of the pregnant woman and into the fluid-filled space surrounding the fetus. In this fluid are floating some of the fetus' cells that have sloughed off. Once a small amount of amniotic fluid (about an ounce) is withdrawn, the fluid is sent to a specialized laboratory that can culture the fetal cells. Some of the cells floating in the fluid are still living and will grow and divide in the culture dish and form colonies of cells. A cell from each of several colonies is studied. Within each cell are the chromosomes. For more on chromosomes, see the December newsletter on genetics.

Chorionic Villus Sampling (CVS) is done at approximately 10 1/2 weeks of gestation. Chorionic villi are like interlaced fingers that anchor the placenta in place. Some villi are of maternal origin and some are of fetal origin. Fetal villi cells will have the same chromosomes and genes as the fetus. During CVS, ultrasound is performed to check the fetus and continues throughout the procedure to keep track of fetal movements. Depending on the location of the placenta, CVS can be done by either inserting a needle through the abdomen or cervix of the pregnant woman. Once inside the uterus, a small amount of the chorionic villi is aspirated through the needle. The villi of fetal origin are separated from those of maternal origin, and those fetal cells are cultured.

The two main differences between amniocentesis and CVS are timing and risk. Because CVS is performed earlier in pregnancy, a pregnant woman can potentially discontinue the dexamethasone at an earlier stage of her pregnancy. Amniocentesis is performed later in the pregnancy but has a comparatively lower risk of miscarriage. Note however that neither procedure involves a high risk of miscarriage. These relative risk values are relevant when making a decision between the two tests. Genetic counseling should always be offered before you make a decision about prenatal diagnosis. Genetic counselors are trained to explain all the information while leaving the decision to the parent.

Prenatal Diagnosis of CAH

The Prenatal diagnosis of CAH began in 1965 through measurement of the levels of 17-hydroxyprogesterone (17OHP) in amniotic fluid. This method was only effective in diagnosing salt wasters. A fetus with simple virilizing CAH or non-classical CAH usually could not be detected this way. At that time, prenatal diagnosis was indicated when a couple with a previously affected child, who were therefore known to be carriers, were expecting another baby (see previous newsletter on genetics). Testing for carrier status was not possible.

In 1978 it was discovered that the gene for CAH is located within the HLA complex of genes on the number 6 chromosome. HLA stands for Human Leukocyte Antigen. Each person carries a unique constellation of HLA genes; this is the basis for tissue-typing donors for transplants, for determining paternity, and for forensic DNA analysis. Related individuals carry a higher proportion of similar HLA genes. Finding the connection between the HLA complex and the CAH gene allowed for a new type of prenatal diagnosis: the CAH gene could be identified by its linkage to one particular parental HLA gene. Linkage via HLA typing was an improvement over the earlier method but only worked within families with affected individuals and could also be inaccurate.

In 1988 the gene for 21-hydroxylase deficiency CAH was first discovered. Within two years the process of direct molecular analysis was refined so that prenatal diagnosis could be accomplished by looking for the exact point mutations within the 21-hydroxylase gene. Evaluating the CAH gene directly was a big improvement as it allowed prenatal diagnosis to be accomplished for all types of CAH, and it made possible carrier testing for an unrelated person.

Prenatal Treatment

Prenatal treatment for CAH is geared toward eliminating the genital ambiguity found in classically affected girls. In 1984 it was discovered that if a pregnant at risk mother is given dexamethasone (a synthetic replacement for the naturally occurring cortisol) during her pregnancy, it can reduce or eliminate the genital ambiguity found in classically affected girls. There are some

continued on next page

difficulties, however. Ideally, one would want to treat only the affected female fetuses since all others will not benefit by this therapy. However development of the external genitalia begins by 8 weeks gestation (8 weeks after the first day of the last period). This means that dexamethasone must be started by 8 weeks gestation; this is a time point before a woman knows whether she is carrying an affected female fetus. If CVS is performed at 10 1/2 weeks, it is at least 11 1/2 weeks before a mother will know if the fetus is male (via chromosome analysis) and at least 14 weeks before results of DNA analysis are available to indicate whether a female fetus is affected.

A Summary of the Process of Prenatal Treatment

If you find you are at risk to have an affected child (see the December newsletter on genetics), prenatal treatment is an option. After you and your spouse are DNA tested, discuss with your endocrinologist whether you should consider prenatal treatment when you get pregnant. If he or she recommends treatment, and you elect to have treatment, the following are the steps involved:

1. You alert your endocrinologist and obstetrician that you are trying to get pregnant. At the first suspicion that you might be pregnant you get a pregnancy test (as immediate treatment is very important).
2. As soon as you get a positive pregnancy test you inform your endocrinologist so you can immediately be put on the proper dose of dexamethasone.
3. Now it is time to see a genetic counselor, so you can discuss the options for prenatal testing, CVS or amniocentesis. You select the option you prefer and arrange for the test (you are on treatment during this period.)
4. If the test (CVS or Amnio) comes back that your baby is a girl you continue taking the medication. If your baby is a boy you stop taking the dexamethasone.
5. When the DNA analysis comes back, if it says your baby girl is affected you continue taking the dexamethasone until your daughter is born, then you stop. If your baby is an unaffected female you should stop the dexamethasone as soon as you get the DNA results.

Safety of dexamethasone for the fetus

Dexamethasone has been around for a long time and is used in pregnancy to treat lots of maternal conditions like asthma and lupus. While it has a good reputation for use during pregnancy, we continue to perform studies to look at the safety of dexamethasone for the offspring, from birth weight to birth defects and from head circumference to IQ. Studies are still ongoing but, to date, we have no strong evidence that dexamethasone use during pregnancy causes significant problems.

Side effects on the pregnant mother

In terms of mother's symptoms while on dexamethasone, weight gain is a common complaint and purple stretch marks called striae are reported by a small number of women. For women taking dexamethasone until term, hypertension and gestational diabetes are a concern but rarely occur. It is important to let the treating MD know if side effects occur. We do keep track of the side effects experienced by the treated women and report on them periodically. We continue to get lots of calls from women inquiring about the safety of dexamethasone and hope that you would feel free to call us for the latest information if you need it.

UPDATE REPORT
June 5, 2002

by Karon Watson
817 923-4723

As my son, Fredrick went to his first day of middle school, I was upset. I just knew he would have trouble adjusting. Was I wrong! He went through the school year with flying colors. He plays the drums in the school band. Some of his friends want to start up a band. His grades were good and the phone rang off the wall. Talk about a normal kid. 13 years ago, when the doctors said, he would have a normal life, I thought they had lost their minds. Here's a baby on three medicines and a mother who didn't understand what went wrong.

Well, 13 years later and many sleepless nights, trips to the doctors office, just because I was frightened, he is happy, well adjusted and busy.

Frederick is taking Tae Kwon Do, plays in the school band, skate boards and talks on the phone.

So, as you can see the children can have a normal life, as long as they get their medicines and care they need.

As I always say, keep the faith and your eyes on your CAH child.

P.S. I would like to say farewell to Carolyn Scruggs, as she is leaving her job. She has done a great job with the CAH families in Texas. She will truly be missed.

Newborn Screening

Approximately 34 states include screening for 21-hydroxylase deficiency CAH as a part of their newborn screening profiles. The major objectives of newborn screening for CAH due to 21-OHD are to identify infants at risk for developing a life-threatening adrenal crisis and to prevent the male sex assignment of affected female infants with ambiguous genitalia. Early identification also allows the monitoring and early treatment of affected infants to prevent the postnatal (after birth) exposure to excessive androgens and the accompanying clinical problems. Data from almost 6.5 million newborns screened in the general population worldwide has demonstrated an overall incidence of between 1:13,000 and 1:15,000 live births for the classical form of 21-hydroxylase deficiency CAH.

INFORMATION CONSENT FORM

PLEASE ADD MY NAME TO YOUR CAH NEWSLETTER MAILING LIST

NAME: _____

ADDRESS: _____

_____

TELEPHONE: _____

NAME OF PERSON WITH CAH: _____

DATE OF BIRTH: _____

PLEASE CIRCLE ONE: MALE FEMALE

1. WHAT WOULD YOU LIKE TO SEE IN FUTURE NEWSLETTERS? _____

_____

_____

_____

2. COMMENTS:

_____

_____

_____

_____

WOULD YOU LIKE TO HAVE A LIST OF CAH FAMILIES IN TEXAS? YES NO

IF YES, PLEASE PRINT YOUR NAME ON THE LINE, AND SIGN BELOW:

I, _____ , give the Newborn Screening Program, Texas Department of Health, permission to share our family's names, address, telephone number, and date of birth and gender of my child with CAH with other CAH parents in Texas.

SIGNED: _____

DATE: _____

NAME OF COUNTY IN WHICH YOU RESIDE: _____

PLEASE RETURN TO:
NEWBORN SCREENING PROGRAM T-602
BUREAU OF CHILDREN'S HEALTH
TEXAS DEPARTMENT OF HEALTH
1100 W. 49TH ST
AUSTIN, TX 78756-3199

Newborn Screening CAH Information Newsletter

Readers are encouraged to submit articles for publication. Submissions should be typed and double spaced. The acceptance of information to be published is at the discretion of the "CAHOOT" Newsletter editorial staff. For additional information, write the CAH Newsletter, Managing Editor, Texas Department of Health, Bureau of Children's Health, 1100 West 49th St., Austin, Texas 78756-3199 or call 1-800-422-2956, ext. 2128.

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