CARES FOUNDATION

CONGENITAL ADRENAL HYPERPLASIA

PATIENT EDUCATION GUIDE

cares FOUNDATION

CARES Foundation dedicates this patient guidebook to all of the patients, their families, the doctors, nurses, researchers, and donors who support them in their journey to find a cure.

For more information about CAH, visit
www.caresfoundation.org
or call: (866) 227-3737

Welcome to Your CAH Patient Guide

We're pleased to welcome you and your family to our care community. This guide is designed to help you understand and manage congenital adrenal hyperplasia (CAH). While it provides valuable information, it is not intended to replace guidance from your healthcare team.

Whether your child is newly diagnosed or you are seeking trustworthy resources, we hope this guide helps you feel informed, supported, and more confident in navigating your CAH journey.

A resource from CARES Foundation—the only U.S.-based organization solely dedicated to individuals and families affected by CAH. Inside, you'll find practical information on daily management, treatment options, emergency preparedness, and long-term planning.

For more support, community connections, and the latest updates, we invite you to visit our website: www.caresfoundation.org.

If you have any questions, our team is here to support you every step of the way.

We'd also like to thank our generous sponsors—Neurocrine Biosciences, Eton Pharmaceuticals, and Crinetics Pharmaceuticals—whose support made this project possible.

Warm regards,

Dina M. Matos
Executive Director

TABLE OF CONTENTS

1. WHAT IS CAH?

The Pituitary Gland 11
Adrenal Glands 12
Salt-wasting CAH 13
Aldosterone 14

2. TYPES OF CAH

CLASSICAL 16
Salt-wasting 17
Simple Viralizing (non-salt-wasting) 18
NON-CLASSICAL 19

3. CAH SYMPTOMS

Classical CAH Symptoms 21
External Symptoms at Birth 22
Non-classical Symptoms 23
- *Females* 24
- *Males* 25

4. DIAGNOSIS

Prenatal
- *Genetic Testing* 27
- *Chorionic Villus Sampling /* 28
  Amniocentesis 29

Birth
- *Newborn Screening* 31
- *Genetic Testing* 33

TABLE OF CONTENTS

4. DIAGNOSIS

After Birth

- *Physical Examination* **35**
- *Physical Signs* **37**
- *Bone Age* **38**
- *Blood Tests* **39**
- *Hormone Level in A.M.* **40**
- *Genetic Testing* **41**

5. CAH TREATMENTS

Medication - Classical CAH **44**
Salt-wasting CAH Patients **44**
Medication - Non-classical CAH **44**
Infancy Symptoms **45**
Older Children & Adult Symptoms **46**
Stress Dosing **47**
Vomiting **53**
Adrenal Crisis and Illness Surgery **55**
Psychological Support **56**

6. LIVING WITH CAH: AGES INFANT- 5

Support for Parents **59**
Giving SAlt to Children **60**
Pearls of Wisdom **61**

7. LIVING WITH CAH: AGES 5 - 12

School & Camping Considerations **63**
Puberty & Growth **66**
Growth & Height Potential **67**
Obesity, Stature, Early Puberty **68**
Psychological Support **69**
Pearls of Wisdom **70**

TABLE OF CONTENTS

8. LIVING WITH CAH: AGES 12 - 18

School & Camping Considerations **72**
Missed Doses & Injuries at School **73**
School & Camping Considerations (Part 2) **74**
Puberty and Growth **75**
Psychological Support **76**
Obesity & Stature **77**
Special Considerations Female Patients **78**
Special Considerations Male Patients **79**
Support Groups **81**
Pearls of Wisdom **82**

9. LIVING WITH CAH: AGES 18 - 24

Teens & Young Adults Overview **84**
Reproductive Issues: Females & Males **85**
Adult Considerations: Glucocorticoids **86**
Medical Treatment for Adults **86**
Obesity **87**
Genetic Counseling **88**
Bone Health & Density **88**
Considerations: Male Patients (TART) **89**
Female Reproductive Development **91**
Polycystic Ovary Syndrome (PCOS) **93**
Psychological Support **94**
Pearls of Wisdom **95**

TABLE OF CONTENTS

10. LIVING WITH CAH: AGES 25 - 50

Adult Considerations Overview **97**
Minimizing Glucocorticoids **98**
Mineralcorticoid & Adernal Masses **99**
Reproductive Function **100**
Female Reproductive Development **101**
Obesity **103**
Excessive Hair Growth & Acne **103**
Bone Health **103**
Genetic Counseling **104**
Considerations: Male Patients (TART) **105**
Psychological Support **107**
Pearls of Wisdom **108**

11. LIVING WITH CAH: AGES 50+

Minimizing Glucocorticoids **110**
Mineralcorticoid Medication Dosing **111**
Cardiovasular Disease **113**
Insulin Resistance **113**
Obesity **113**
Adernal Masses **113**
Considerations: Male Patients (TART) **114**
Psychological Support **116**
Pearls of Wisdom **117**

12. CAHTALOG & RESOURCES

CAHtalog Registry **119**
Emergency Instructions **123**
How to Give a Hydrocortisone Injection **124**

About CARES Foundation and Support for CAH

CARES Foundation leads in the effort to improve the lives of the Congenital Adrenal Hyperplasia community and seeks to advance quality health care through support, advocacy, education, and research.

The Foundation serves families and individuals with Congenital Adrenal Hyperplasia (CAH), an orphan condition that is historically under-served, supported, and funded. We also strive to increase the awareness of CAH within the healthcare community.

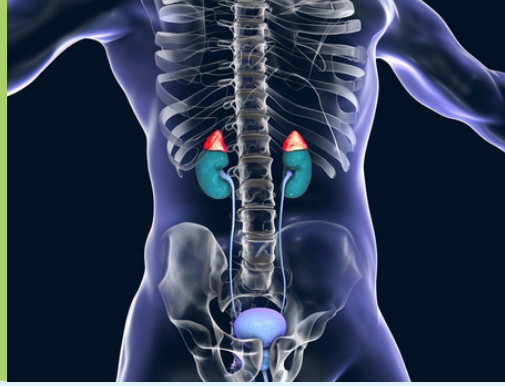
Because the disorder can be so rare, there are few CAH specialists and many medical professionals who are not even familiar with the general description of the disorder. Non-classic patients often go undiagnosed. CARES programs benefit more than 8,000 families and medical professionals across the United States and abroad. Our community includes every state in the United States and over 70 countries outside the US.

1

CHAPTER

WHAT IS CAH?

What is CAH?



CONGENITAL ADRENAL HYPERPLASIA (“CAH”)
refers to a family of inherited enzyme deficiencies that cause decreased cortisol production by the adrenal glands. Cortisol is an essential hormone that regulates blood pressure and blood sugar levels and is critical during times of stress. CAH is inherited as an autosomal recessive disorder and affects males and females equally.

THE MOST COMMON FORM OF CAH
is 21-hydroxylase deficiency (21-OHD), which can be severe (classical) or mild (non-classical). Classical CAH is usually detected in the newborn period or in early childhood while non-classical CAH (NCAH) may cause symptoms at any time from infancy through adulthood. The prevalence of classic CAH has been estimated at 1:15,000. The prevalence of NCAH may be as high as 1:100 in some populations. Both can be managed with proper medication and monitoring, enabling affected individuals to lead normal lives.

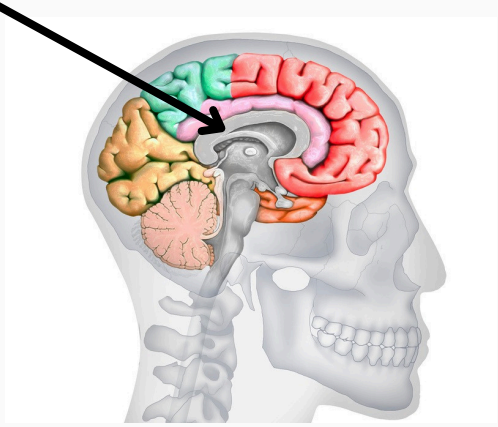
OTHER RARE ENZYME DEFICIENCIES THAT BELONG TO THE CAH FAMILY ARE:

- 3ß-hydroxysteriod dehydrogenase (3BHSD) deficiency
- 11B-hydroxylase deficiency (11B-OHD)
- 17a-hydroxylase deficiency (17a-OHD)
- StAR deficiency
- Cholesterol side chain cleavage (CYP11A) deficiency
- P450c11AS deficiency
- POR deficiency

ALL OF WHICH ARE MUCH LESS COMMON
This guide will focus on 21-OHD deficiency, the most common form of the disorder.

Pituitary Gland

The pituitary gland
is a small pea-sized gland at the base
of the brain that controls the adrenal glands



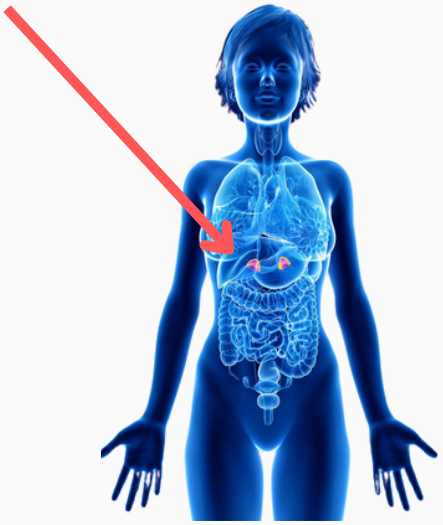
When the pituitary gland
senses there is not enough cortisol in the blood, it releases a hormone called ACTH (adrenocorticotropic hormone), which stimulates the adrenals to produce more cortisol.

However, individuals with CAH
have insufficient amounts of the enzyme 21-hydroxylase, which is necessary for converting a precursor molecule called 17-hydroxyprogesterone (17OHP) into cortisol.

As a result,
the pituitary gland continues to sense the need for cortisol and pumps out more ACTH. This leads to an excess of 17OHP (hormone that is measured both for diagnosis and to monitor treatment).

Adrenal Glands

The adrenals then convert the excess 17OHP into excess androgens



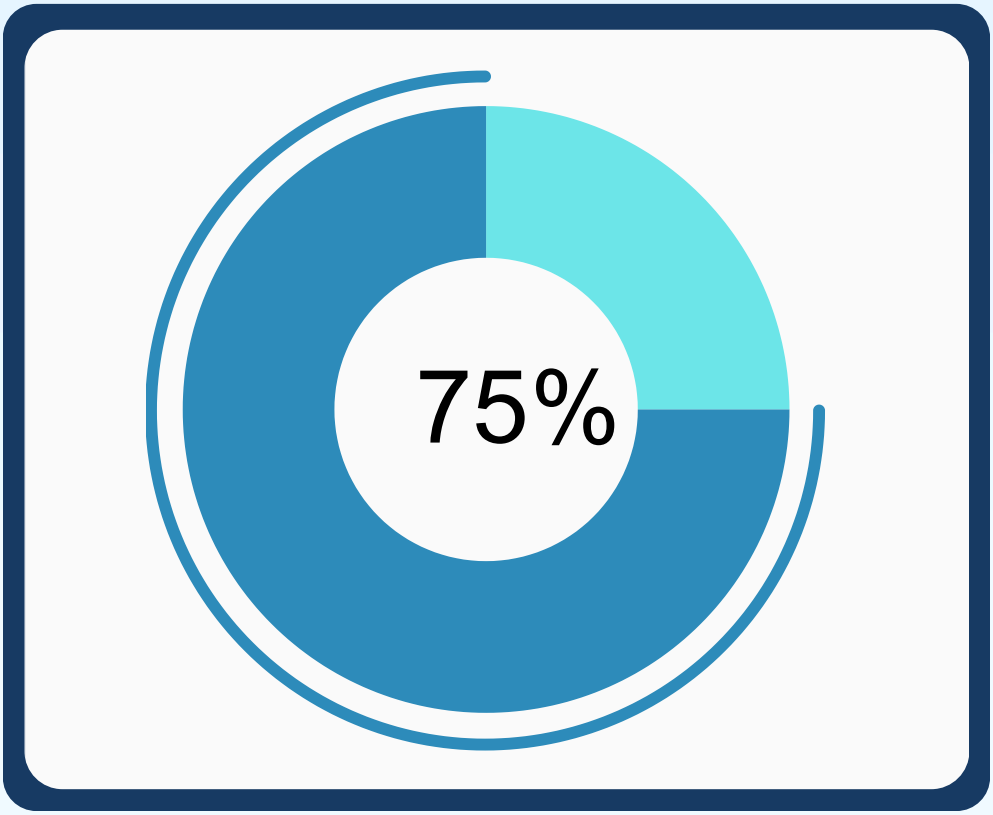
In females,
this leads to virilization in utero.

In both males and females,
insufficient cortisol also hinders the body's ability to properly metabolize sugar and responding to physical stress.

The lack of a proper
stress response can result in an adrenal crisis.

Salt-Wasting CAH

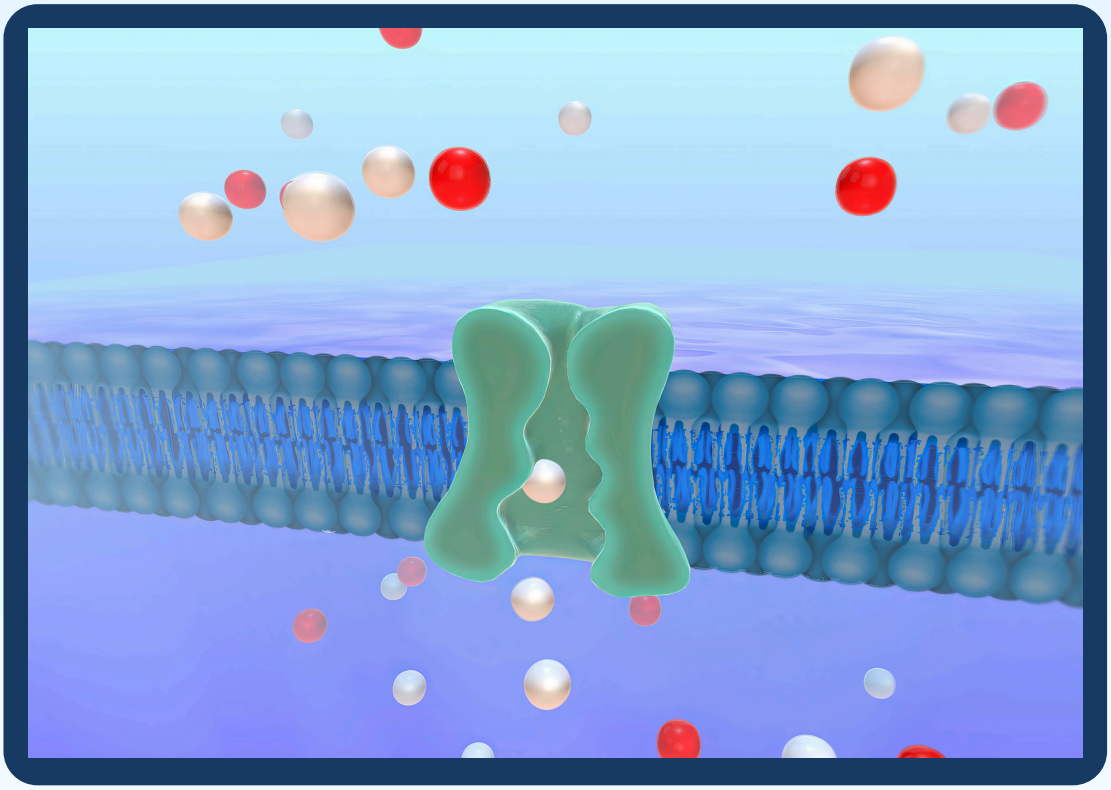
Salt-wasting CAH (SW-CAH) affects approximately 75% of individuals with classical CAH



These individuals do not make adequate cortisol and aldosterone.

Aldosterone

Aldosterone is another essential hormone made by the adrenal glands and helps to maintain normal fluid balance and normal levels of sodium and potassium.



Abnormal levels of sodium
or potassium can affect proper functioning of the brain and heart.

The remaining 25%
of those with classical CAH who produce sufficient aldosterone have “simple-virilizing” CAH (SV-CAH).

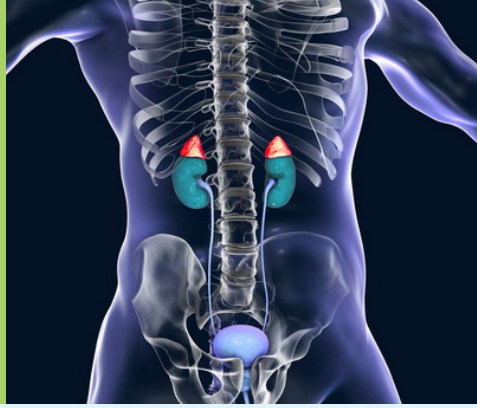
2

CHAPTER

TYPES OF CAH:

Classical & Non-Classical

Classical CAH



CLASSICAL CAH IS THE MORE SEVERE FORM OF CAH
(further divided into salt-wasting or simple-virilizing), leading to a range of symptoms that can impact an individual's physical development and overall health.

CLASSICAL CAH MUST BE DETECTED
soon after birth to avoid an adrenal crisis, which can be fatal.

DUE TO THE SEVERITY OF THE CONDITION,
all 50 states in the U.S. and many other countries now include newborn screening for classic CAH.

FAMILIES ARE NOTIFIED BY
their Department of Health or primary care physician that their newborn's screening test shows a positive result for CAH, and immediate medical evaluation is required.

EARLY DETECTION THROUGH NEWBORN SCREENING
can ensure timely treatment for both male and female infants, preventing the occurrence of an adrenal crisis. Without newborn screening for CAH, the child is at a higher risk of experiencing a life-threatening adrenal crisis, especially newborn males, who do not exhibit any outward physical manifestations.

Salt-Wasting

Approximately 75% of individuals with classical CAH also lack another adrenal hormone called aldosterone, necessary for maintaining sodium and potassium balance.

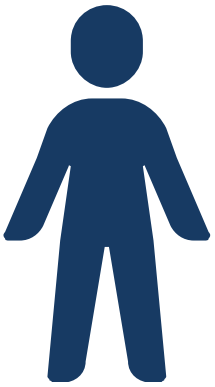
When the adrenals cannot make sufficient aldosterone, too much sodium and water are lost in the urine, leading to dehydration and salt deficiency. High levels of potassium can cause serious disturbances of heart rhythm and may lead to cardiac arrest.

These babies become very ill soon after birth (usually 10-20 days after birth in most cases) if not diagnosed and treated. When this deficiency occurs, it is called **“Salt-Wasting CAH”** (SW-CAH).

Simple Virilizing

(non salt-wasting)

25%



The remaining 25 percent of those with Classical CAH who produce some aldosterone are referred to as "Simple Virilizers" (SV-CAH).

Non-Classical CAH

Non-classical Congenital Adrenal Hyperplasia (NCAH), also known as “late-onset” CAH, is a milder form of CAH that can lead to a build-up of androgens resulting in a range of symptoms affecting physical development and reproductive health.

Unlike classical CAH, there are no symptoms of NCAH at birth.
NCAH is a variation of CAH that, though not immediately life-threatening, can begin to cause noticeable changes at any time from early childhood through early adulthood. There can be a range of symptoms that overlap with other disorders and may not be easily diagnosed, so it is less likely to be diagnosed promptly.

Newborn girls and boys with NCAH have no external symptoms
at birth. Because the symptoms begin later in life, it is sometimes called late-onset CAH, adult-onset CAH, or the attenuated form of CAH. Importantly, NCAH does not progress to classic CAH, the more severe form, in affected individuals. It is occasionally picked up in infants through newborn screening tests, but they do not necessarily require treatment. Parents should be aware of the potential symptoms of the disorder and seek treatment if it becomes necessary.

Only those children and adults who are symptomatic
should be treated. Those without symptoms do not require treatment. Symptoms for both classic and NCAH will be discussed in further detail in the next section.

3

CHAPTER

CAH SYMPTOMS

Classical CAH

External Symptoms at Birth

At birth, female infants
with classical CAH may have atypical genitalia, such as the presence of urogenital sinus (single opening for urethra and vagina) an enlarged clitoris, due to excess androgen exposure during fetal development.

They are usually identified at birth,
leading to prompt treatment for adrenal crisis and salt-wasting. Only the external genitalia appear atypical.

The female reproductive internal organs,
including ovaries, fallopian tubes, uterus, and cervix, are not affected.

Some parents may consider
restorative genitourinary surgery for their daughters.

(See our section on Surgery for more in depth discussion of this issue.)

Classical CAH

External Symptoms at Birth

Infant males with classic CAH
have typical male genitalia at birth and show no external signs of the disorder.

In the absence of newborn screening
and early treatment, most babies present with vomiting or life-threatening shock within the first few weeks of life.

In addition, infants who are missed by newborn screening
(especially males) might present as toddlers with early pubic hair and a growth spurt if they make enough aldosterone to prevent a salt-wasting crisis as a newborn.

Non-Classical CAH Symptoms

In the case of non-classical CAH (NCAH), symptoms vary from person to person and over time.

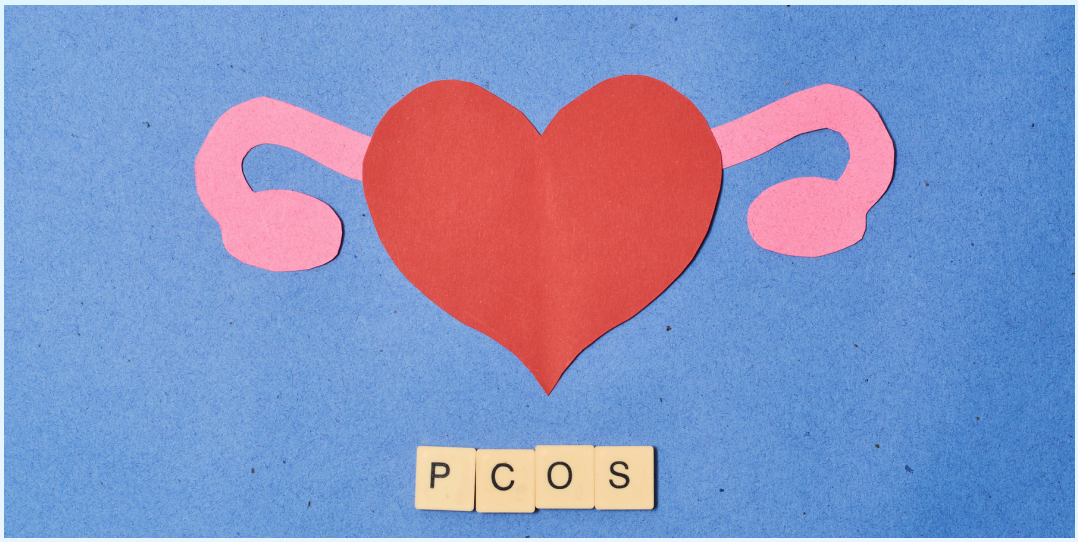
These symptoms can begin at any time in life and may start in early childhood. They often are mistaken for precocious puberty – girls with signs of puberty before age 8 years and boys before age 9 years.

NCAH is progressive, meaning that the untreated symptoms may become worse over time. Both males and females with NCAH may show the following:

Symptoms

- Premature development of body hair (pubic and underarm)
- Body odor (young children's perspiration normally has no odor)
- Early, rapid growth spurt, but ultimately short stature as adult
- Oily hair and skin
- Severe acne
- Mood swings
- Infertility in women

Non-Classical CAH Symptoms



In women, symptoms most frequently become apparent shortly after the onset of menstruation and may include the following:

Symptoms

- Early age of first menstrual period
- Menstrual irregularities
- Thinning hair on head, especially at the temples (male pattern baldness)
- Excessive facial hair on chin and upper lip and/or body hair may be thick, coarse, and dark
- Previous diagnosis or symptoms of Polycystic Ovarian Syndrome (PCOS)

(as well as those symptoms mentioned on the previous page)

Non-Classical CAH Symptoms

In NCAH adult males, there are typically no symptoms. If there are early symptoms, they include:

Symptoms

- Premature development of body hair (pubic and underarm) and/or body odor
- Early, rapid growth spurt, but ultimately short stature as adult
- Oily hair and skin
- Severe acne

4

CHAPTER

DIAGNOSIS

Prenatal

Genetic Testing

CAH is an autosomal recessive genetic disorder that affects males and females equally.

The CYP21A2 gene provides
the necessary instructions for the enzyme 21-hydroxylase, which is used by the adrenal glands to produce cortisol, a hormone that is essential for life. Both parents must carry a CAH-causing change in the CYP21A2 gene for their child to be born with 21- hydroxyase deficiency CAH.

Notably, the parents of an affected child
do not necessarily have CAH, but one of their two copies of the gene contains a CAH-causing change in the CYP21A2 gene. Offspring born to the same parents each carrying one copy of a CAH-causing gene will have a 1 out of 4 chance of having CAH.

DNA testing is available
for both the diagnosis of CAH and to detect carriers of CAH-causing genes, but should not be done without first consulting a genetic counselor.

Prenatal

Chorionic Villus Sampling / Amniocentesis

Prenatal testing can be performed by two methods.

The first method is called chorionic villus sampling (CVS) which is a procedure that obtains fetal cells by sampling cells from the developing placenta.

The procedure is usually done with ultrasound guidance to see the physical structures of the patient and fetus.

CVS is typically offered at 10-12 weeks from the last known menstrual period.

As with any prenatal procedure, CVS carries with it a small risk of miscarriage.

CVS is a procedure that takes place in the first trimester so genetic test results can be obtained early in the pregnancy. The cells are taken to a laboratory and grown so that the DNA can ultimately be obtained and tested.

Prenatal

Amniocentesis is another technique that can be used to obtain a sample of fetal cells for genetic testing.

This method is typically performed at 15-20 weeks from the last menstrual period. This procedure requires that a thin needle is passed through the abdomen, under ultrasound guidance, into the fluid filled sac that surrounds the fetus. A few tablespoons of the fluid are taken from the sac. This fluid contains cells from the baby that are then grown in a laboratory.

As is the case with CVS, amniocentesis is not a risk-free procedure. With amniocentesis, there is a small risk that the procedure **may** cause a miscarriage.

The risks and benefits must be taken into consideration when considering prenatal testing. Your doctor and genetic counselor are good resources for additional information regarding these procedures.

Prenatal

If prenatal genetic testing for CAH is to be accurate and reliable, it is very important to think about genetic testing in advance.

Due to the complexities in testing previously described,
it is recommended that both parents have genetic testing completed prior to getting pregnant. If the fetus alone is tested first, it may not be possible for a lab to issue a final report without requesting blood specimens from the parents and, if present, any previously affected children. This may delay the results by a few weeks while the lab compares the genetic pattern present in the fetus with that of the rest of the family.

Some laboratories recommend
that another genetic test called maternal cell contamination studies be ordered at the same time as the prenatal test. Maternal cell contamination studies ensure that the fetal DNA being tested is in fact from the fetus and not contaminated with the mother's DNA, thus ensuring an accurate analysis and result.

For example, if the DNA being tested
were actually the mother's DNA and not the baby's, then the result would be incorrectly reported that the baby was a carrier just like the mother, when in fact the baby could be affected, not a carrier at all, or a carrier of the father's pathogenic variant. Anyone considering genetic testing for CAH, for whatever reason, should meet with a genetic counselor to discuss the various options available.

You can find a genetic counselor near you at www.nsgc.org.

A genetic counselor can also assist in coordinating your testing as well as help explain and interpret your results.

At Birth

Newborn Screening

Newborn screening (NBS) is the most common way infants affected by classical CAH are first identified.

NBS is a series of tests done on blood samples
from newborns between 24 and 72 hours of life for a number of different disorders that can result in severe mental/physical impairment or death if not detected and treated before signs and symptoms of the disease appear. Screening is the first step in a two-step process. The first screening test indicates a problem may be present, and then a second diagnostic test confirms whether or not the baby has the disease.

The screening test for CAH
is sensitive, simple and inexpensive. It involves taking one additional drop of blood from the heel of a newborn at birth, along with the other drops taken for the screens for other disorders. The blood is collected on filter paper and allowed to dry, and then sent to a laboratory for testing.

The newborn screening laboratory
is looking for 17-hydroxyprogesterone (17OHP) levels, an indicator of 21-hydroxylase deficiency (21-OHD) CAH.

At Birth

Infant females with classical CAH
usually receive prompt evaluation and treatment because they are born with atypical genitalia.

However, newborn males with classical CAH
show no outward signs of the disorder and are sent home. Newborn screening allows for these children to be identified as possibly having CAH before they go into adrenal crisis. A second confirmatory diagnostic test is then ordered and the diagnosis of CAH either confirmed or excluded.

Babies with SW-CAH and SV-CAH
are detected through this process. It is rare that a child with NCAH will be picked-up through this type of testing because 17OHP levels will not be high enough to meet testing criteria.

At Birth

Genetic Testing

Genetic testing can be used to confirm the diagnosis of CAH and identify the specific changes in the CAH gene present in a person who is suspected of having CAH.

For example, genetic testing can help confirm the diagnosis in infants that have a positive newborn screen for CAH. Adults with suspected CAH due to infertility problems or women who have symptoms of androgen excess might also have their diagnosis confirmed through genetic testing.

Genetic testing can also be used to screen an unaffected person who has no family history of CAH to determine if they carry CAH. This can be especially useful for the partners of individuals who are either affected by CAH, or are planning and are known carriers of CAH, for the purpose of family pregnancy management.

If both members of a couple are known carriers, prenatal treatment with dexamethasone aims to reduce female genital atypia and its associated risk of social stigma, but is considered experimental, should only be done in research study setting, and long-term side effects are not known. Genetic screening for Y-chromosomal DNA in maternal blood should be done to exclude male fetuses from potential treatment.

At Birth

For couples that have no known personal or family history of CAH, but are currently pregnant with a female fetus that has atypical genitalia detected by prenatal ultrasound, genetic testing for CAH may be appropriate after other causes have been ruled out.

The advanced knowledge can help the family and physicians prepare for the medical, social and emotional issues related to the diagnosis and birth of an affected child.

Parents of a child with CAH may want to know which pathogenic variants are present in their affected child. The parents themselves can be tested to determine what pathogenic variant they carry.

After Birth

Physical Examination

Height and weight: In general, with proper treatment, children with CAH should grow approximately along the percentile according to their genetic potential (based on parental heights).

Between 2-3 years of age,
the average child grows about 3 inches per year; between 3-4 years of age, average growth is about 2.75 inches year. From 4 years of age until puberty, the average child grows about 2 inches per year and gains 2-3 pounds for every inch of height gain.

During infancy and puberty,
growth velocity is even faster than during childhood. In general, a child with proper treatment should grow along the same percentile on growth charts from early childhood through adolescence. Thus, height and weight need to be both monitored and plotted on standard growth charts to assess growth in CAH.

Looking at growth charts
and following changes in height and weight, one can detect signs of over- and undertreatment. If glucocorticoid (hydrocortisone) doses are too high, growth will slow and weight will increase. It takes about 3-6 months to appreciate changes in growth velocity. Changes in weight, though, can be seen much sooner. Increases in weight, above and beyond that which are normally expected, can be a sign of overtreatment.

After Birth

Whereas slowing of growth can represent signs of overtreatment, an increase in growth velocity can reflect undertreatment.

With undertreatment, there is increased androgen production, which can stimulate excessive growth. Undertreated children may therefore climb to higher height percentiles on growth charts. Undertreated children are also at risk for early puberty.

To assess physical changes in CAH and be able to respond to signs of over- or undertreatment in a timely manner, many practitioners will see children with CAH every 3-4 months on average, but may differ based on age and adrenal control.

After Birth

There are additional physical signs that clinicians can see that suggest either over- or undertreatment.

With overtreatment, the face can become round (“moon-like”). With significant overtreatment, striae (purple “stretch-marks”) can occur.

Features of undertreatment include:

- Dark or hyperpigmented knuckles, elbows, and knees
- Darkening of gums, tongue, palate and scars caused by excessive ACTH secretion.
- Stomach pain and excessive fatigue are also symptoms of undertreatment.

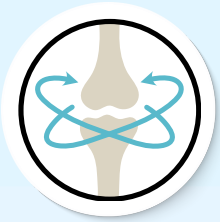
Blood pressure can provide clues about the sufficiency of mineralocorticoid (Florinef, fludrocortisone) treatment. If blood pressure is elevated, this may indicate that the mineralocorticoid dose or salt supplementation is too high and should be reduced.

Signs of pubertal development are also monitored.

- In girls, the earliest sign of puberty is breast development.
- In boys, enlargement of the size of the testes is the earliest sign that puberty has started.

If puberty begins before eight years of age in girls and before nine years of age in boys, it is said to be early or “precocious”. Because the adrenal hormones can affect the pituitary gland, precocious puberty is seen in CAH and warrants attention.

After Birth



One of the best tools for monitoring changes in physical maturation is the "bone age."

The growth plates, which can be easily visualized with an x-ray of the left hand, provide a marker of long-term androgen/estrogen secretion. As children get older, the shape of the growth centers changes and has characteristic appearances at each age.

By comparing the size and shapes of the growth plates in the child's hand to those found in a book of standards, a "bone age" can be determined. Because there is variability from practitioner to practitioner in bone age interpretation, it is useful to have bone ages interpreted by the same individual. Also, some pediatric endocrinologists may be more experienced in interpreting bone ages than general radiologists.

When there is excessive androgen/estrogen secretion, the skeleton matures at a more rapid pace than usual. This will result in an advanced bone age (the bone age is older than chronological age). Those with advanced bone age typically have an early growth spurt, but then stop growing at an earlier age, eventually leading to a shortened final stature. Thus, an undertreated child at 6 years of age may have a bone age of 9 years of age.

The bone age also reflects hormone secretion over the preceding 6-12 months. Changes in the bone age may lag behind recent periods of excess androgen/estrogen secretion. Many practitioners therefore obtain bone ages every 6 to 12 months.

After Birth

Blood Tests

Assessing control from a single blood test is very commonly used due to its convenience. However, a single test may not always reflect if there is adequate control of adrenal gland activity.

One also needs to consider the time of day and the timing of doses in interpreting blood levels. Some hormone levels are also better than others in assessing treatment.

A number of hormones that reflect adrenal gland activity can be measured in the blood.

Laboratory tests may include:

- 17-hydroxyprogesterone (17OHP)
- Androstenedione
- Testosterone

Electrolytes (sodium and potassium) and renin are used to assess mineralocorticoid replacement.

After Birth

Of these different hormones, androstenedione and testosterone most closely reflect adrenal androgen production. These hormones are especially useful in prepubertal children and females.

Because testosterone levels rise in puberty in males, testosterone levels are not as useful in adolescent or adult males. In comparison with androstenedione and testosterone, 17OHP levels can fluctuate widely and may be elevated even when there is good control.

Treating CAH to “normalize” all hormone levels, especially 17OHP levels, requires an excessive amount of glucocorticoid and can result in growth suppression and weight gain. Thus, many clinicians aim for androstenedione and testosterone levels that are normal for age and sex, but will accept 17OHP levels above normal for an unaffected individual, but safe in a CAH population.

Early morning 17OHP levels prior to taking medication will be higher because the adrenal glands are more active in the early morning hours and the medication from the day before is wearing off.

Therefore, it is important to be consistent in the timing of blood draws and to know what time the blood sample was drawn as well as the timing relative to medication.

To measure if the child is getting enough salt and/or fludrocortisone, renin and electrolyte levels are measured. An elevated renin level indicates a need for more salt and/or fludrocortisone. A suppressed or undetectable renin suggests that the dose of salt and/or fludrocortisone is too high.

After Birth

Genetic Testing

Finding the specific changes in the CAH genes present in an affected child allows testing of other family members, such as the aunts and uncles of an affected child, for the specific pathogenic variant(s) identified.

This allows other relatives to know if they are carriers so that they can use the information in the way that is best for them and their own family planning. If an affected child has not been tested and a relative decides to pursue their own testing, problems with interpretation of the results can occur.

It is always best to test the affected individual. For example, if the relative is negative, it is still possible that the family carries a pathogenic variant that cannot be detected with current methods, and that would not be known unless the affected individual was also tested and was negative.

Genetic testing can also be used to screen an unaffected person who has no family history of CAH to determine if they carry CAH.

After Birth

This can be especially useful for the partners of individuals who are either affected by CAH, or are known carriers of CAH, for the purpose of family planning and pregnancy management.

If both members of a couple are known carriers, prenatal treatment with dexamethasone aims to reduce female genital atypia and its associated risk of social stigma, but is experimental and long-term side effects are not known. Genetic screening for Y-chromosomal DNA in maternal blood should be done to exclude male fetuses from potential treatment.

For couples that have no known personal or family history of CAH, but are currently pregnant with a female fetus that has atypical genitalia detected by prenatal ultrasound, genetic testing for CAH may be appropriate after other causes have been ruled out.

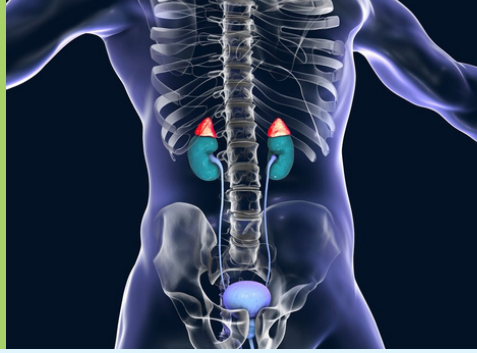
The advance knowledge can help the family and physicians prepare for the medical, social and emotional issues related to the diagnosis and birth of an affected child.

5

CHAPTER

CAH TREATMENTS

CAH Treatments



MEDICAL-CLASSICAL CAH

All individuals affected by classical CAH require glucocorticoid replacement. Examples of glucocorticoids include:

- Hydrocortisone
- Prednisone/Prednisolone
- Dexamethasone
- Methylprednisolone

SALT-WASTING CAH PATIENTS

Should additionally be treated with fludrocortisone (a mineralcorticoid) as well as sodium chloride during infancy

- Fludrocortisone requirements typically range between 0.05 to 0.2 mg per day
- Sodium chloride supplementation is often needed during infancy, approximately 1-2 grams (17-34 mEq) per day distributed over several feedings

MEDICATION NON-CLASSICAL CAH

In children and adolescents with inappropriately early onset and rapid progression of pubarche or bone age advancement or in adolescent patients with overt virilization:

- Glucocorticoid treatment is recommended

CRENESSITY™ (crinecerfont) is now available for adults and children with classical CAH. www.crenessity.com

CAH Treatments

Illness and Emergency

CAH-affected patients (all classical and some non-classical)

are not able to produce the extra cortisol needed for the body to be able to cope with times of stress, illness, injury, or during surgery.

During such times, affected individuals may require stress-dosing, which is extra hydrocortisone in addition to their daily dose. Left untreated or inadequately treated, a CAH individual may go into adrenal crisis, a potentially life-threatening condition.

Symptoms and signs of adrenal crisis are varied, nonspecific and vary among different age groups.

Doctors may mistake these problems for formula intolerance or inadequate lactation, or alternatively, primary infectious or gastrointestinal disorders.

In infancy, these symptoms may include:

- **Lethargy**
- **Vomiting**
- **Poor appetite**
- **Failure to thrive**

CAH Treatments

Illness and Emergency

In older children and adults, symptoms may include:

- Chronic fatigue
- Salt-craving
- Headache
- Skin hyperpigmentation
- Gastrointestinal symptoms
- Mucosal pigmentation

Stress dosing and seeking appropriate medical care at times of adrenal crisis is essential especially for CAH-affected individuals.

CAH Treatments

Stress Dosing

WHAT IS STRESS DOSING?

Stress dosing is extra hydrocortisone (in addition to a daily maintenance dose) that people with CAH take when they are sick, injured, and/or before any kind of surgery.

WHY DO PEOPLE WITH CAH HAVE TO STRESS DOSE?

Remember…normally functioning adrenal glands produce up to 5-10 times (depending on the degree of stress) the amount of cortisol when the body is under the physical stress of illnesses such as:

- **Fever (over 100.5°F)**
- **Vomiting**
- **Diarrhea**
- **Infection, surgery, trauma with loss of consciousness**

SINCE PEOPLE WITH CLASSICAL CAH CANNOT PRODUCE

more cortisol, stress doses of hydrocortisone are necessary when they are sick. It is also important for them to drink plenty of sugar and salt-containing fluids to prevent low blood sugar or dehydration. If a child with CAH is sick with a fever, infection, vomiting, or diarrhea, it is important to administer extra hydrocortisone and call the health care provider right away.

STRESS DOSING FOR CHILDREN TYPICALLY INVOLVES

doubling or tripling the dose of hydrocortisone until they feel better and symptoms are gone. Oral stress dosing is typically done with hydrocortisone tablets or hydrocortisone sprinkles (Alkindi Sprinkles®) (even if a person is on dexamethasone or prednisone). The dose of fludrocortisone will not change with illness.

CAH Treatments

Child Dosage

HOW DO I KNOW HOW MUCH INCREASED HYDROCORTISONE TO GIVE WHEN SOMEONE WITH CAH IS SICK?

This is a really good question that can sometimes be variable. Always check with your healthcare provider in advance on how he/she handles "sick day rules." Below are general guidelines to follow from the National Institutes of Health.

Child

Child has a minor illness or low grade fever (100.5°F – 102°F)

- Double the usual daily dose of glucocorticoids divided into 4 doses to be given every 6 hours (some providers recommend 3 doses given every 8 hours).
- If your child looks ill and seems lethargic, consider giving a triple dose when the fever is in this range. Give 15 grams of simple carbohydrates (e.g. ½ cup of juice, regular soda, applesauce, 3-4 glucose tablets) regularly. Give extra fluids.
- If your child is taking a very low dose of glucocorticoids, consider giving triple dose with consultation with your healthcare provider.

Child has a major illness or high grade fever (> 102°F)

- Triple the usual daily dose of glucocorticoids divided into 4 doses to be given every 6 hours (some providers recommend 3 doses given every 8 hours)
- Give 15 grams of simple carbohydrates (e.g. ½ cup of juice, regular soda, applesauce, 3-4 glucose tablets) regularly. Give extra fluids.

CAH Treatments

Child Dosage

Here is an example:

Joey is an eight-year-old child that receives:

10 mg of hydrocortisone in the morning

5 mg of hydrocortisone in the afternoon

5 mg of hydrocortisone at night

This means that Joey receives a daily dose of 20 mg of hydrocortisone. At 11 a.m., Joey has a fever of 101°F and says his throat hurts. He looks fine and is eating and drinking well.

You give Joey a medication to lower his fever (e.g. ibuprofen (Advil) or acetaminophen (Tylenol) as you have been directed to in the past by your healthcare provider. You determine, based on guidelines from your provider, that it is best to give Joey a double dose of hydrocortisone. This means that Joey should receive **40mg per day divided in 4 doses (10mg per dose).**

- You give Joey his first dose of 10 mg around 11:15 a.m.
- His next doses will be due around 5 p.m., 11 p.m., 5 a.m., etc. until he is feeling better and is fever free.
- Then go back to regular dosing.

CAH Treatments

Child Dosage

What if the stress dose needs to be rounded?

Round up. Let's say the child needs a triple dose, and a triple daily dose is 75 mg divided into 4 doses of 18.75 mg.

- A good rule of thumb is to round up to the nearest ¼ of a tablet (either 5 mg or 10 mg – whatever you have on hand).
- So if you have 10 mg tablets of hydrocortisone to use for stress dosing, this would be rounded up to 20 mg (two 10 mg tablets) for each dose.

Now, let's say the child's triple daily dose is 67.5 mg divided into 4 doses of 16.88 mg.

- If you have both 5 mg and 10 mg tablets on hand, you would round up to the nearest ¼ of a tablet.
- This would be 17.5 mg (a 10 mg tablet, a 5 mg tablet, and ½ a 5 mg tablet)

A child is between the ages of 12 and 18. Should they use adult or child stress dosing guidelines?

If you do the math, most children in this age range do weigh similarly to an adult and both adult and child stress dosing guidelines are appropriate. Please consult your provider.

CAH Treatments

How does a parent/caregiver explain stress dosing to adults that care for a child with CAH when they are not present (eg. teachers, babysitters, day care workers)?

- If a child is in school or daycare, you need to provide a school letter explaining stress dosing and how to respond if it is discovered that the child has a fever or illness while in their care.
- The best approach is to be clear and direct to minimize any confusion.
- It is recommended that there is a **pre-calculated triple dose** available at the child's school or daycare that you instruct the nurse or designee to give the child when ill as you are enroute to get them.
- Even if the child only needed a double dose based on the guidelines, to simplify instruction, go with a one-time triple dose for instruction during these circumstances.
- Remember that this triple dose will likely increase over time as the child grows and might need to be adjusted during the school year.

CAH Treatments

Adult Dosage

Adult

Person has a minor illness or low grade fever (100.5°F – 102°F)

- Take 10mg of hydrocortisone three times a day in addition to your usual glucocorticoid regimen.
- Take in 30g (grams) of simple carbohydrates (1 cup of juice or regular soda) regularly.
- Increase fluid intake.
- Go to a healthcare provider for an evaluation if lethargic with decreased oral intake and urine output.

Person has a major illness or high grade fever (> 102°F)

- Take 20mg of hydrocortisone three times a day in addition to usual glucocorticoid regimen.
- Take in 30g (grams) of simple carbohydrates (1 cup of juice or regular soda) regularly.
- Increase fluid intake.
- Go to a healthcare provider for an evaluation if lethargic with decreased oral intake and urine output.

CAH Treatments

Vomiting

What if a person with CAH is vomiting?

Repeat oral dose if someone with CAH vomits within one hour of giving the medication.

- If the person with CAH vomits again, give the appropriate dose of injectable hydrocortisone (Solu-Cortef®) into a large muscle.
- Call the patient's healthcare provider and consider getting emergency care (after injection), especially if unable to tolerate fluids.
- Remember that for children, the dose of Solu-Cortef® may vary so always check with your healthcare provider.
- **Children 0-3 years** of age will receive 25 mg of Solu-Cortef®
- **Children 3-12 years** of age will receive 50 mg of Solu-Cortef®
- **Adults** and children greater than 12 years of age will receive 100 mg (entire vial) of Solu-Cortef®

How do you stress dose if the person with CAH takes daily prednisone or dexamethasone and not hydrocortisone?

As always, check with your healthcare provider. In this case, it may be possible to stress dose using adult guidelines depending on the age of the child. No matter which glucocorticoid an individual with CAH is on, when stress dosing, hydrocortisone is best to use.

Other points to remember:

- When a person with CAH is sick, they should drink sugar- and salt- containing liquids (e.g. non diet soda, 7-UP, Gatorade, popsicles, soup) to prevent dehydration.

- If a person with CAH needs to have surgery, extensive dental work, or has been in an accident, a larger dose of hydrocortisone will be needed:

    - Notify the physician or dentist performing the procedure that the person has cortisol deficiency, so proper amounts of hydrocortisone can be given. For surgery or dental work requiring anesthesia (regular dental work, even under local anesthesia, does not require stress dosing). This will generally be an increased dose prior to the procedure. For an injury, and sometimes with surgery, more than one increased dose may be recommended.

- It is essential that people with CAH wear a medical identification tag/bracelet/necklace to alert people in times of emergency with the words: **ADRENAL INSUFFICIENCY and STEROID-DEPENDENT**

- Do not increase the dose or take “extra” pills for emotionally stressful days, common cold, regular exercise, or airline flights.

- People with CAH need to let those around them know to seek medical help on their behalf if there is a change in behavior, they are unresponsive or difficult to arouse.

- Family members and/or friends of people with CAH need to learn how to give the emergency injection of hydrocortisone (Solu-Cortef®). If a person with CAH is very sick, they may not be able to give themselves the injection and will need help.

How to give injection of hydrocortisone (Solu-Cortef®)
https://youtu.be/VY9m25Hcsao

Download the PACE App, which helps provide timely information on how to stress dose and give emergency medications. Information can be found here:

https://caresfoundation.org/pace- app/.

CAH Treatments

Surgery

CARES recognizes that any surgical decision, including timing, for some girls born with CAH is a deeply personal one to be made by the family in consultation with a multi-disciplinary team of CAH experts and evidence-based data.

In the past, surgery for atypical genitalia was considered urgent. Current thinking and practice are evolving to allow the families to play a greater decision-making role in situations that do not require immediate attention. After careful consideration, decisions should be based on the specific medical situation of each individual and family values.

Due to the high complexity of these surgeries, CARES recommends that they be performed at a CAH Center of Excellence. It is very important that the surgeon specializes in this type of surgery and commonly performs these types of procedures. In some Centers of Excellence, a concerted surgical repair may be performed in a single stage in early life, while others will delay vaginal restoration until nearer the time a girl is mature enough to become sexually active.

The decision of whether, when, and what type of genital surgery is desirable needs to be decided by the family and/or patient, experienced surgeons, and endocrinologist. Surgery is not necessary in some cases. CARES Foundation does not endorse any specific course of action, but supports the option for all medical interventions, including surgery.

CAH Treatments

Psychological Support

Psychological support may come in different forms, including individual psychological support, counseling, and peer support groups.

Peer support groups, including peer parent social support or parent mentors, can help patients and families adjust to cope with a CAH diagnosis by offering emotional support, compassion, and specific information relating to the diagnosis and caregiving advice.

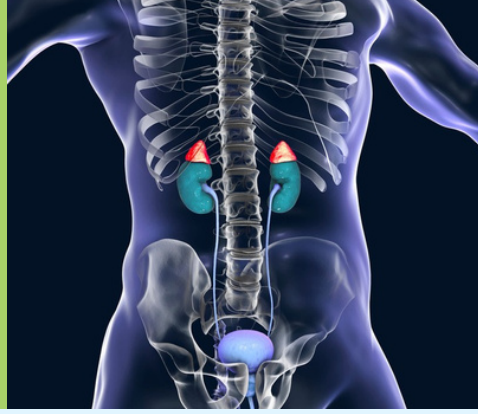
CARES provides a resource for specific information for CAH patients and peer groups for caregivers and patients alike. Support groups have been shown to provide patients and caregivers an increased sense of control over their disease, increased self- acceptance, decreased isolation, and improved education to help them advocate for themselves particularly at medical visits.

6

CHAPTER

Ages Infant – 5

Living with CAH



CLASSICAL CAH IS A CONGENITAL CONDITION

with far-reaching ramifications in childhood, adolescence and adult life. Much progress has been made in understanding various aspects of CAH, but several areas remain to be studied.

NON- CLASSICAL CAH IS OF VARIABLE SEVERITY,

and should only be treated in cases with overt clinical evidence of androgen excess. Whereas treatment duration is lifelong for classic CAH patients, this is not necessarily so for the non-classical CAH. Patients, parents and family members should be aware of the changing needs of CAH patients throughout life, and seek appropriate medical care.

CLASSICAL CAH IS A CHRONIC ILLNESS

that requires lifelong medication and, in some cases, hospitalizations. It is reasonable to expect a multitude of potential stressors during various stages of life, which can impact physical and emotional issues for CAH patients.

THE FOLLOWING "LIVING WITH CAH" SECTIONS

break down groups of CAH patients based on their ages and attempts to address relevant health issues, quality of life issues, and provide practical tips from current patients. It is not possible to address each and every factor that is relevant for a CAH patient and therefore, it is essential to seek professional medical care at every stage of a CAH patient's life. In this section, we divide CAH patients into the following age groups:

- **Ages Infant - 5**
- **Ages 5 - 12**
- **Ages 12 - 18**
- **Ages 18 - 24**
- **Ages 25 - 50**
- **Ages 50 +**

Living with CAH

Ages: Infant - 5

Support for Parents

Upon diagnosis and during a child's early years, parents and caregivers seek specific information about the CAH diagnosis, how to care for their CAH child, and to attain emotional support from other parents caring for CAH patients. CARES offers multiple specialized support groups that provide support from experienced parents and caregivers who are able to draw from their own experiences.

Medication for Infants and Babies

Medications for infants and babies may include:

- Hydrocortisone tablets
- Hydrocortisone granules (Alkindi Sprinkle®)
- Cortisone acetate
- Fludrocortisone Sodium
- Chloride for salt-wasters

CARES further provides access to Secret Facebook Groups

Safe environments where those affected by CAH are able to ask questions, share experiences with others who are in the same situation.These groups are by invitation via our *Congenital Adrenal Hyperplasia Support Network Facebook page**. Please follow this page and request entry into the group you are interested in.

Alternatively, email *support@caresfoundation.org* to see a list of these private groups or to request an invitation.

Ages: Infant - 5

Giving Salt to Children

Infants and young children with CAH are at risk for salt-wasting due to the lack of aldosterone production. Infants require fludrocortisone as well as additional salt in their diet to compensate for this deficiency. In infants with Classical CAH, extra sodium chloride is needed because breast milk and formula do not contain adequate sodium.

- Sodium chloride can be prescribed as a solution or as tablets.
- The tablets are easily dissolved in water and can be administered using a syringe (squirt into the cheeks to avoid the tongue)
- Tablets can be added to breast milk, formula, or food (once child is eating solids).
- Sometimes mixing it into a sweet solution (juice or Pedialyte®) can mask the saltiness and make it easier to take.
- Once eating solid food, salt can easily be added to food.

"Pearls of Wisdom"

Recommendations
from
CAH parents

Ages: Infant - 5

Always carry at least one day's supply of:

- ✔ Medicine
- ✔ Stress dose medicine and Solu-Cortef®
- ✔ With syringes and needles for administering

- Get a medical alert identification for your child with wording that includes: **ADRENAL INSUFFICIENCY and STEROID DEPENDENT**
- Tape emergency medical alerts on small children's car seats. Frequently check the expiration dates of Solu-Cortef®

Download the PACE App, which helps caregivers and medical professionals obtain timely information on how to stress dose and give emergency medications. Information can be found here:

https://caresfoundation.org/pace-app/.

CARES is a great resource for CAH-affected individuals at all ages.

Visit your local firehouse and/or EMS/EMT station and inform them of your child's status and the emergency protocol needed in the event of an adrenal crisis.

Living With CAH

7

CHAPTER

Ages 5 - 12

Ages: 5 - 12

School and Camping Considerations

As the primary caregiver for a child affected by CAH, one of the most difficult transitions can be handing over that care to others while your child attends school. There are medications to keep track of, signs and symptoms of illness to look for, and the need for appropriate and immediate action in case of emergency.

Find out what is required in your area concerning daily medication.

A doctor's order is generally required detailing:

- The time, dose, reason for medication
- The diagnosis of disorder, side effects, if any, etc.
- May require doctor's signature and parent's authorization.
- Requirements vary from state-to-state, and from county-to-county
- Some jurisdictions are extremely rigid and others flexible.

While this might be a source of stress for parents, rest assured that as time passes, you will quickly learn how to best support your CAH-affected child. Managing CAH in schools is a partnership between you, the teacher, and the administration (school nurse, if available, and the principal). While the focus of this is on public school, many of these ideas and strategies can be used in preparing for daycare, preschool, private school and camp.

Here are a few pointers to help parents about to send off their child with CAH:

- Meet with the school nurse (or person in charge of medication administration).
- Discuss CAH with them and try to convey the seriousness of the condition without too much drama.
- In addition, request that they keep the health information of your child private.

School and Camping Considerations

Please note: A separate doctor's order might be required for medication administration outside of the daily dose. This is called a PRN (Latin for 'as needed') and simply covers for medication to be given under other circumstances. This could include if you have forgotten the morning meds and you'd like the school to administer them, if your child has had a serious injury during the school day and you'd like hydrocortisone to be administered orally, if your child develops a high fever during the school day and you'd like extra hydrocortisone to be administered orally. A PRN will usually include wording such as, "to be administered in times of injury, fever, and/or illness and/or at the parent's discretion" and should include a dosage limit, i.e. "up to X mgs".

Meet with your child's teacher(s).
This is where your child will be spending their day. Meet with the teachers to give them a brief rundown of what CAH is and why your child might have special needs. Many parents have their CAH child carry a water bottle to prevent dehydration, but be prepared that a doctor's order might be required. Discuss falls on the playground and whether or not you would like to be called for any and all mishaps.

Meet with your principal.
Most principals want to be aware of any child at their school who might have unique needs or disorders. This is a good failsafe for an emergency situation if the nurse is unavailable. The principal is in charge of everything that happens at that school; attempting to explain CAH in an emergency to the person in charge results in wasted time.

Try to schedule meds at times that are
the least disruptive or outside of school hours. Fitting in a trip to the nurse's office during a break (perhaps on the way in or out for recess) or in between classes is generally the best way to allow for a school day that is as normal as possible. If there are no breaks in between classes near the needed time, discuss with the teacher the best time to allow your child to leave the classroom.

Create a written health plan
with the school for monitoring and treating your child while they are at school including agreed upon policies and procedures for everything from medication distribution to monitoring your child for signs of illness and access to water in the classroom. In the public school system accommodations and modifications can be obtained under Section 504 of the Rehabilitation Act of 1973.

School and Camping Considerations

One issue that might be a difficult one for some of you:
Discuss with your doctor whether or not s/he considers Solu-Cortef® a necessity for school. While this may seem like an obvious necessity to you, remember that you are dealing with legal issues concerning an intramuscular injection and you may find yourself in a struggle with the school system.

Most of us carry the Solu-Cortef® kit with us everywhere.
However, to require the school to do so can get tricky. Consider field trips, for example. Depending on the rigidity of the school system you are in, many areas will require an RN to be available to give an injection. If this means hiring an RN to accompany your child on all field trips, many school systems will balk.

Here's what the American Disabilities Act states:
"Public entities are not required to take actions that would result in undue financial and administrative burdens. They are required to make reasonable modifications to policies, practices, and procedures where necessary to avoid discrimination, unless they can demonstrate that doing so would fundamentally alter the nature of the service, program, or activity being provided." (www.ada.gov ADA Title II: State and Local Government Activities).

In other words, this is an issue that will vary
greatly throughout the municipalities. This is also an area where those in private schools might be told that their child is too great a "risk" to have in their school. Again, carefully consider bringing up the Solu-Cortef® issue. If you live or work close to the school, or if you have family or friends versed in intramuscular injections and who can arrive at the school quickly in an emergency, this may be an area where you would want to maintain 100% control. Talk to your pediatric endocrinologist about the best course of action for your CAH child.

To assist parents in this process, CARES Foundation has created a Getting Ready for School/Camp packet including:

- Getting Ready for School/Camp Parent Tips
- Medical Information – Sample Letter (aka doctor's note)
- What is a 504 Plan and How Can it Help My Child?
- 504 Accommodation Plan Request – Sample Letter
- Medical Supply Kit Checklist
- Health Plan Worksheet
- Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency: A guide for affected individuals and their families
- CARES Foundation Emergency Instructions brochure

Living with CAH

Puberty, Precocious Puberty, and Growth

Puberty

Puberty may occur
early, late, or on time in CAH patients. Since pubertal hormones contribute to growth and height attainment, it is important for puberty to be properly timed. A child whose hormone levels are poorly controlled may grow rapidly, then abruptly stop growing.

Girls who are not receiving enough hydrocortisone tend to have delayed onset of their menstrual periods. In some cases, additional treatment may be necessary to induce periods.

Boys should be examined for normal pubertal development as well. One particular concern in boys is the development of testicular masses due to poor hormonal control (see below, Reproductive function in CAH males).

Growth and Height Potential

Although children with CAH grow too rapidly,
they may finish growth prematurely, so that adult height is shorter than expected. Balancing medical treatment to maintain appropriate blood hormone levels is often complicated in CAH.

Untreated or inadequately treated children
grow rapidly and may not reach their height potential; on the other hand, those treated with excessive glucocorticoid will have slowed growth and may not reach their height potential.

Since overzealous medical treatment
is a major cause of poor growth, it is important to treat CAH children with the lowest dose effective in maintaining adrenocortical hormones in a reasonable range. Optimal levels of these hormones will change with age and sex.

Another experimental treatment program
involves standard medication combined with daily injections of growth hormone and monthly injections of Lupron, a gonadotropin-releasing hormone (GnRH) analog that suppresses puberty. Clearly, these experimental regimens are complex and would be difficult to manage for many patients.

Thus, such regimens are not the current standard
of care and are not covered by insurance. The heights of individuals with non-classical CAH are usually not significantly different from family heights, and thus they would seldom be candidates for extreme forms of height-enhancing treatment.

In all, it is best to work with your medical provider to monitor your child's height and growth, pubertal developments, and CAH medications to optimize care.

Obesity

Weight gain in CAH
can be a side effect of glucocorticoid treatment, especially for women. Monitoring weight is important to prevent weight gain and avoid harsh weight reducing diets. Careful attention to diet and exercise in conjunction with precisely monitoring treatment should help most adults with CAH avoid obesity. Many adults with CAH find regular sustained exercise of an hour several times per week is essential in keeping weight down and fitness levels up. Exercise also helps with maintaining bone density.

Stature

Growth: children with CAH
Although children with CAH grow too rapidly, they may finish growth prematurely, so that adult height is shorter than expected. Balancing medical treatment to maintain appropriate blood hormone levels is often complicated in CAH. Untreated or inadequately treated children grow rapidly and may not reach their height potential; on the other hand, those treated with excessive glucocorticoid will have slowed growth and may not reach their height potential. Since overzealous medical treatment is a major cause of poor growth, it is important to treat CAH children with the lowest dose effective in maintaining adrenocortical hormones in a reasonable range.

Early Puberty

Children may begin to show symptoms
At this age, some children may begin to show symptoms of precocious puberty. Such symptoms may include voice changes, severe acne and early pubic, armpit and facial hair. A gonadotropin-releasing hormone (GnRH) analog, such as Lupron, may be used to suppress early central puberty. It is important to talk to your healthcare provider if early symptoms are presented.

Living with CAH

Psychological Support

Having gotten through your child's early years,
parents may continue seeking support as their CAH-affected child prepares for school and for being outside the direct care of their caregiver for extended periods. This can be a stressful time and patient advocate groups and support groups can be useful to learn about how best to navigate this period. CARES is one of a number of patient advocacy groups that provides a great resource on preparing for school, meeting with teachers, and advocating for your child.

Peer support groups, including peer patient social support

CARES further provides access to
Secret Facebook Groups that are safe environments where those affected by CAH are able to ask questions, share experiences with others who are in the same situation.

These groups are by invitation via our Congenital Adrenal Hyperplasia Support Network Facebook page*. Please follow this page and request entry into the group you are interested in.

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"Pearls of Wisdom"

Recommendations
from
CAH parents

Ages: 5 - 12

Always carry at least one day's supply of:

- ✔ Medicine
- ✔ Stress dose medicine and Solu-Cortef®
- ✔ With syringes and needles for administering

- → Ensure that your child consistently wears medical alert identification with wording that indicates: **ADRENAL INSUFFICIENCY and STEROID DEPENDENT**
- → Tape emergency medical alerts to backpacks and lunch boxes.
- → Frequently check the expiration dates of Solu-Cortef®. Save expired Sold-Cortef® vials to assist training school administration on how to giver the emergency shot.

Download the PACE App,
which helps caregivers and medical professionals obtain timely information on how to stress dose and give emergency medications. Information can be found here:
https://caresfoundation.org/pace- app/.

Keep your lines of communication open with school administrators and staff to ensure an appropriate response in emergency situations for your child; be patient with schools as they learn about CAH and how best to handle medications and emergency situations under their own regulations.

CARES is a great resource for CAH-affected individuals at all ages.

Visit your local firehouse and/or EMS/EMT station and inform them of your child's status and the emergency protocol needed in the event of an adrenal crisis.

Living With CAH

8 CHAPTER

Ages 12 – 18

Ages: 12 - 18

School and Camping Considerations

As the primary caregiver for a child affected by CAH, you have already gotten through the early years of school. As your child enters their middle school and high school years, there is yet another transition. Your child may want more independence, but you still need to monitor medications, signs and symptoms of illness, and the emergency care, as needed.

Continue to manage CAH in schools as a partnership between you, the teacher, and the administration (school nurse, if available, and the principal). While the focus of this is on public school, many of these ideas and strategies can be used in preparing for daycare, preschool, private school and camp.

Find out what is required in your area concerning daily medication

A doctor's order is generally required detailing:

- The time, dose, reason for medication
- The diagnosis of disorder, side effects, if any, etc.
- May require doctor's signature and parent's authorization.
- Requirements vary from state-to-state, and from county-to-county
- Some jurisdictions are extremely rigid and others flexible

Here are a few pointers to help parents about to send off their child with CAH:

- Meet with the school nurse (or person in charge of medication administration).
- Discuss CAH with them and try to convey the seriousness of the condition without too much drama.

Missed Doses/Sickness or Injuries at School

Please note: A separate doctor's order might be required for medication administration outside of the daily dose. This is called a PRN (Latin for 'as needed') and simply covers for medication to be given under other circumstances.

Please note: It is necessary to have your school be authorized to administer your child's medications at school. If your child misses their morning meds, you should ensure that your school is able to administer them. In addition, if your child gets sick (low or high fever) or has a serious injury during the school day, you will want the school to administer hydrocortisone orally. A PRN (meaning "as needed") will usually include wording such as, "to be administered in times of injury, fever, and/or illness and/or at the parent's discretion" and should include a dosage limit, i.e. "up to X mgs".

Meet with your child's teacher(s). This is where your child will be spending his day. Meet with the teachers to give them a brief rundown of what CAH is and why your child might have special needs. Many parents have their CAH child carry a water bottle to prevent dehydration, but be prepared that a doctor's order might be required. Discuss falls on the playground and whether or not you would like to be called for any and all mishaps.

Meet with your principal.
Most principals want to be aware of any child at their school who might have unique needs or disorders. This is a good failsafe for an emergency situation if the nurse is unavailable. The principal is in charge of everything that happens at that school; attempting to explain CAH in an emergency to the person in charge results in wasted time.

Try to schedule meds at times that are
the least disruptive or outside of school hours. Fitting in a trip to the nurse's office during a break (perhaps on the way in or out for recess) or in between classes is generally the best way to allow for a school day that is as normal as possible. If there are no breaks in between classes near the needed time, discuss with the teacher the best time to allow your child to leave the classroom.

Create a written health plan
with the school for monitoring and treating your child while they are at school including agreed upon policies and procedures for everything from medication distribution to monitoring your child for signs of illness and access to water in the classroom. In the public school system accommodations and modifications can be obtained under Section 504 of the Rehabilitation Act of 1973.

School and Camping Considerations

One issue that might be a difficult one for some of you:
Discuss with your doctor whether or not she/he considers Solu-Cortef® a necessity for school. While this may seem like an obvious necessity to you, remember that you are dealing with legal issues concerning an intramuscular injection and you may find yourself in a struggle with the school system.

Most of us carry the Solu-Cortef® kit with us everywhere.
However, to require the school to do so can get tricky. Consider field trips, for example. Depending on the rigidity of the school system you are in, many areas will require an RN to be available to give an injection. If this means hiring an RN to accompany your child on all field trips, many school systems will balk.

Here's what the American Disabilities Act states:
"Public entities are not required to take actions that would result in undue financial and administrative burdens. They are required to make reasonable modifications to policies, practices, and procedures where necessary to avoid discrimination, unless they can demonstrate that doing so would fundamentally alter the nature of the service, program, or activity being provided." (www.ada.gov ADA Title II: State and Local Government Activities).

In other words, this is an issue that will vary
greatly throughout the municipalities. This is also an area where those in private schools might be told that their child is too great a "risk" to have in their school. Again, carefully consider bringing up the Solu-Cortef® issue. If you live or work close to the school, or if you have family or friends versed in intramuscular injections and who can arrive at the school quickly in an emergency, this may be an area where you would want to maintain 100% control. Talk to your pediatric endocrinologist about the best course of action for your CAH child.

To assist parents in this process, CARES Foundation
has created a Getting Ready for School/Camp packet including:

- Getting Ready for School/Camp Parent Tips
- Medical Information – Sample Letter (aka doctor's note)
- What is a 504 Plan and How Can it Help My Child?
- 504 Accommodation Plan Request – Sample Letter
- Medical Supply Kit Checklist
- Health Plan Worksheet
- Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency: A guide for affected individuals and their families
- CARES Foundation Emergency Instructions brochure

Living with CAH

Puberty, Precocious Puberty, and Growth

Puberty

Puberty may occur
early, late, or on time in CAH patients. Since pubertal hormones contribute to growth and height attainment, it is important for puberty to be properly timed. A child whose hormone levels are poorly controlled may grow rapidly, then abruptly stop growing.

Girls who are not receiving enough hydrocortisone tend to have delayed onset of their menstrual periods. In some cases, additional treatment may be necessary to induce periods.

Boys should be examined for normal pubertal development as well. One particular concern in boys is the development of testicular masses due to poor hormonal control (see below, Reproductive function in CAH males).

Living with CAH

Ages: 12 - 18

Psychological Suppport :

During puberty,
both parents and CAH-affected teenage children may want to seek psychological support. Adolescents are particularly vulnerable during this time due to their changing hormones. Children with CAH are more prone to having anxiety disorder. Adolescent girls are prone to developing a negative body image.

One key to supporting teenagers
during puberty is patient education and disclosure of relevant medical information to the child. This should be a combined strategy with parents and medical professionals. Additionally, development of coping strategies and increased self-management of their treatment should be encouraged. One-on-one or group counseling as well as support groups can aid in providing the psychological support for CAH-affected families.

Obesity

Weight gain in CAH
can be a side effect of glucocorticoid treatment, especially for women. Monitoring weight is important to prevent weight gain and avoid harsh weight reducing diets. Careful attention to diet and exercise in conjunction with precisely monitoring treatment should help most adults with CAH avoid obesity. Many adults with CAH find regular sustained exercise of an hour several times per week is essential in keeping weight down and fitness levels up. Exercise also helps with maintaining bone density.

Stature

Growth: children with CAH
Although children with CAH grow too rapidly, they may finish growth prematurely, so that adult height is shorter than expected. Balancing medical treatment to maintain appropriate blood hormone levels is often complicated in CAH. Untreated or inadequately treated children grow rapidly and may not reach their height potential; on the other hand, those treated with excessive glucocorticoid will have slowed growth and may not reach their height potential. Since overzealous medical treatment is a major cause of poor growth, it is important to treat CAH children with the lowest dose effective in maintaining adrenocortical hormones in a reasonable range. Optimal levels of these hormones will change with age and sex.

Another experimental treatment program
involves standard medication combined with daily injections of growth hormone and monthly injections of Lupron, a gonadotropin-releasing hormone (GnRH) analog that suppresses puberty. Clearly, these experimental regimens are complex and would be difficult to manage for many patients. Thus, such regimens are not the current standard of care and are not covered by insurance.

The heights of individuals with nonclassical CAH
are not significantly different from family heights, and thus they would seldom be candidates for extreme forms of height-enhancing treatment. In all, it is best to work with your medical provider to monitor your child's height and growth, pubertal developments, and CAH medications to optimize care.

Special Considerations for Female Patients

Polycystic Ovary Syndrome (PCOS)

Females with poorly controlled CAH
are at high risk for developing polycystic ovary syndrome (PCOS). Polycystic ovaries are physically larger, but have smaller, dysfunctional follicles and produce excess testosterone. PCOS may cause the egg not to develop as it should or not be released during ovulation as it should. It can further cause irregular menstrual periods, which can lead to infertility or the development of small fluidfilled sacs (cysts) in the ovaries.

In many women with CAH,
irregular periods and ovulation problems can be helped with more aggressive glucocorticoid treatment. However, finding a balance between over-treatment and achieving fertility is sometimes challenging. Women with CAH with PCOS would be best served seeing a reproductive endocrinologist experienced with disorders of androgen excess.

For help finding a board certified endocrinologist, please call CARES Foundation's office toll free at 866-227-3737.

Males 12 - 18

Special Considerations for Male Patients Testicular Adrenal Rest Tumors (TART) and Testicular Issues

The testicles and adrenal glands are made of similar tissue.
Within the testicles there is a normal amount of adrenal cells that do not typically affect fertility. However, without adequate medication or treatment, men with Classical CAH may develop testicular masses (usually benign) called adrenal rest tumors and, in rare cases, enlarged testes.

When treatment is inadequate or sporadic in a male with CAH,
the adrenal cells may grow into masses that release hormones hindering sperm production. This happens when cortisol levels are too low and there is over secretion of ACTH by the pituitary. Just as ACTH stimulates the adrenal glands and causes them to enlarge (hyperplasia) it also stimulates the adrenal cells in the testicles.

It is important to note that in patients with known CAH,
adrenal rest tissue is not usually malignant and can be clinically differentiated from Leydig cell tumors by virtue of the fact that it is usually bilateral and common in men who show other evidence of poor adrenal suppression. Also, if the mass is located near the mid-center line of the testes and does not distort the contour of the testes it is likely an adrenal rest and not a malignancy.

Special Considerations for Male Patients Testicular Adrenal Rest Tumors (TART) and Testicular Issues

Fortunately, adrenal rest tissue usually regresses
with increased glucocorticoid treatment to reestablish optimal cortisol levels and suppress ACTH secretion. Once the correct cortisol levels have been restored, the body may be able to return to normal levels of sperm production. It may take several months to achieve normal sperm production after the increased glucocorticoid dosages have been initiated.

Enlarged adrenal tissue in the testes in men with CAH
The enlargement is due to increased ACTH and usually recedes when ACTH is adequately suppressed. The enlargement normally recedes once the cortisol levels are increased, through increased glucocorticoid therapy or potentially with crinecerfont (reduces ACTH). The doctor may recommend to perform a biopsy of the enlarged testicle to ensure that there is no cancer present.

CAH does not cause cancer,
but it is good practice ensure that there are not other reasons for the enlargement. It may seem counterintuitive to experience low testosterone in a disorder where the primary symptoms occur as a result of androgen excess, but this can be a frequent cause of infertility in men with uncontrolled CAH.

Men with Classical CAH
who are not well suppressed will have uncontrolled adrenal androgen secretion. When too much testosterone is made by the adrenal glands over a long period of time, the body aromatizes (converts) the androgens to estrogen. The estrogen then feeds back to the pituitary which, sensing the body has enough testosterone, stops secreting the hormones that stimulate the testicles to make testosterone. This is called hypogonadotropic hypogonadism (HH), where the testes “shut down,” stop producing sperm and even shrink. As with adrenal rests, this condition can also (usually) be reversed with increased glucocorticoid therapy.

Men with CAH who are interested in fertility
should pay special attention to their endocrine care. Compliance (taking medicine as prescribed) is essential in avoiding adrenal rests and fertility problems. It is a good idea to establish a baseline picture of the testes during puberty with a testicular ultrasound. If no problems are found, the endocrinologist may recommend follow-up ultrasounds every few years. Men with adrenal rests that do not respond to glucocorticoid suppression can consider testis-sparing surgery with malignancy being ruled out.

Living with CAH

Support Groups

Teens with CAH may seek emotional support through one-on-one or group counseling in their treatment or seek out support groups.

Peer support groups, including peer patient social support

CARES further provides access
to Secret Facebook Groups that are safe environments where those affected by CAH are able to ask questions, share experiences with others who are in the same situation.

These groups are by invitation via our Congenital Adrenal Hyperplasia Support Network Facebook page*. Please follow this page and request entry into the group you are interested in.

*Alternatively, email **support@caresfoundation.org** to see a list of these private groups or to request an invitation.*

“Pearls of Wisdom”

Recommendations
from
CAH parents

Ages: 12 - 18

Always carry at least one day’s supply of:

- ✔ Medicine
- ✔ Stress dose medicine and Solu-Cortef®
- ✔ With syringes and needles for administering

- → Ensure that your child consistently wears medical alert identification with wording that indicates: **ADRENAL INSUFFICIENCY and STEROID DEPENDENT**
- → Tape emergency medical alerts to backpacks and lunch boxes.
- → Frequently check the expiration dates of Solu-Cortef®. Save expired Sold-Cortef® vials to assist training school administration on how to giver the emergency shot.

Download the PACE App, which helps caregivers and medical professionals obtain timely information on how to stress dose and give emergency medications. Information can be found here: **https://caresfoundation.org/pace- app/.**

Keep your lines of communication open with school administrators and staff to ensure an appropriate response in emergency situations for your child; be patient with schools as they learn about CAH and how best to handle medications and emergency situations under their own regulations.

CARES is a great resource for CAH-affected individuals at all ages.

Visit your local firehouse and/or EMS/EMT station and inform them of your child’s status and the emergency protocol needed in the event of an adrenal crisis.

9

CHAPTER

Ages 18 – 24

Living with CAH

Ages: 18 - 24

Transitioning for Teens/Young Adults
During the transition from childhood to adolescence to adult care, growth and puberty remain important, but additional new concerns develop. The transitioning process for CAH-affected individuals should occur over time and not at one specific age. During such time, such individuals should become educated on their condition and learn how to self-manage their condition and treatment.

Other issues that may arise include
psychosexual development, but mental and behavioral health conditions are not diagnosed more frequently in individuals with CAH than in the general population. The vast majority of girls with classic CAH retain a female gender identity well into adulthood. Psychological support from professionals experienced in treating gender-related problems should be sought by families on an as-needed basis.

Young adults should become educated on:

- Their prior medical history
- Their medication regimen
- Work directly with their medical professionals.

This is particularly important
at the time of diagnosis in severely affected females, andin adolescence, especially if genital surgery is performed. It is important to know that overt psychiatric disturbances are not common among CAH patients.

Young adults should eventually learn
how to manage their care during emergency situations Including learning how to stress dose and self-administer their emergency hydrocortisone injection.

Reproductive Issues for Females

Reproductive problems for women
are with classical CAH usually become apparent in adolescents who have poor hormonal control. Some patients have a clinical picture similar to polycystic ovarian syndrome:

- multiple ovarian cysts
- irregular menstrual bleeding
- excess facial and body hair
- acne

Removal of both adrenal glands
(adrenalectomy) is the last resort when medical therapies are unsuccessful in achieving adrenal suppression in severely affected CAH women. In some cases, this may allow conception and fertility. Adrenalectomized patients must still be followed with medical treatment since they are more vulnerable to adrenal crisis and death if lifelong glucocorticoid treatment is interrupted.

Reproductive function in non-classic CAH
is more consistently normal. In fact, many cases of mild 21-hydroxylase deficiency (21-OHD), both male and female, go undiagnosed for lack of clinically important symptoms. At present, there is no test to predict which individuals affected with non-classical CAH will progress and suffer adverse consequences of their hormonal imbalance.

Reproductive Function in CAH Males

Impaired reproductive function
is less frequent among men with classical CAH compared with affected women. Most CAH males are able to father children, or at least have adequate sperm counts. Low sperm counts, observed in both classical and non-classical CAH, do not preclude fertility.

Testicular adrenal rest tumors (TART)
(also referred to as “testicular tumors of adrenogenital syndrome”) may occur in CAH males, especially if they are inadequately treated salt-wasters. For this reason, it is recommended that by adolescence, all CAH boys have careful testicular examinations and a baseline testicular sonogram. The preferred treatment consists of effective adrenal hormone suppression. Male infertility and TART are very rare in non-classical CAH.

Adult Considerations

Glucocorticoids have only been used to treat CAH
for the last 70 years or so. While we have gained considerable knowledge and expertise about the treatment of CAH in children, there is much less information about the treatment of adults with CAH. Optimal treatment for the adult continues to challenge the healthcare community. What we do know is: People with CAH have a normal life expectancy, and for most who are well managed and receiving adequate treatment, there is little interference in every day life.

Adults with CAH require life-long follow-up
to maintain correct medical care, and it is becoming increasingly clear that adults with CAH benefit from a multidisciplinary approach that includes primary care physicians, endocrinologists, gynecologists, urologists, fertility specialists and psychologists. Even when well-controlled, adults with CAH should continue with medical check-ups.

For women,
endocrine visits should be made two to three times per year. Good management and regular visits for women brings control of androgen levels and improved fertility and overall health.

For men,
endocrine visits should be at least once per year, and again, good control is essential in maintaining fertility.

Men and women with CAH
obviously, important long-term health issues affect both men and women with CAH. Earlier studies focused on bone density, but more recently, questions have been raised concerning cardiovascular health and weight management.

Medical Treatment for Adults:

With the completion of growth,
adult CAH patients may continue to be managed with hydrocortisone, but may also be managed with longer-acting glucocorticoids, such as prednisone or dexamethasone. These drugs are not often used routinely in children because of their greater tendency to cause growth suppression.

Living with CAH

Ages 18 - 24

Obesity

Weight gain in CAH
can be a side effect of glucocorticoid treatment, especially for women. Monitoring weight is important to prevent weight gain and avoid harsh weight reducing diets. Careful attention to diet and exercise in conjunction with precisely monitoring treatment should help most adults with CAH avoid obesity.

Many adults with CAH
find regular sustained exercise of an hour several times per week is essential in keeping weight down and fitness levels up. Exercise also helps with maintaining bone density.

Genetic Counseling

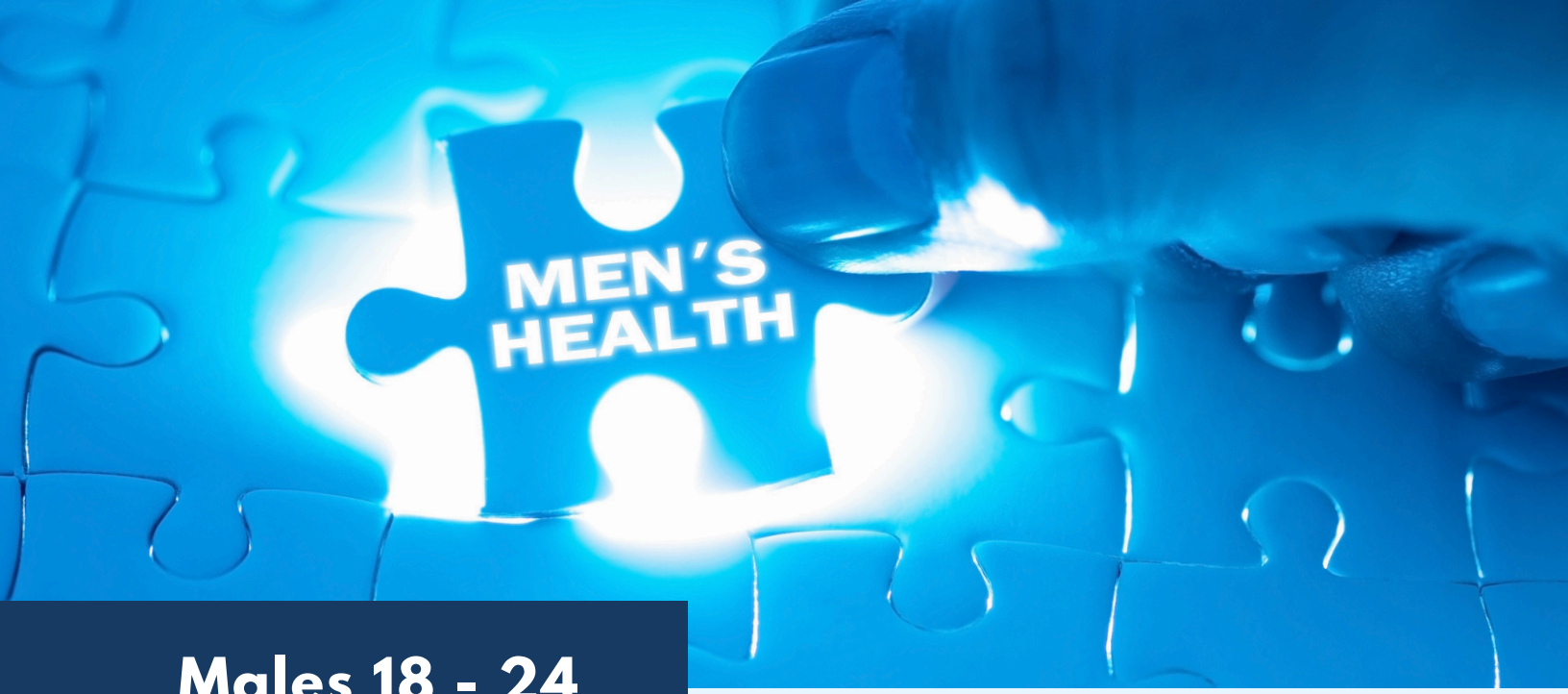
The diagnosis of CAH
is most often made on clinical grounds and on the basis of hormone measurements. Genetic counseling is useful in helping the family understand the implications of the diagnosis. There are several circumstances when genetic testing is important, especially, prenatal diagnosis and newborn screening with questionable results. Another common situation arises when a woman has been told she has “CAH” and is treated with glucocorticoids, but the hormonal measurements upon which the diagnosis was made are either unavailable or in doubt.

Since hormonal diagnosis
can be is unreliable during or immediately following glucocorticoid treatment or during pregnancy, genetic testing is a viable alternative. Genetic testing may also be done for those who have been diagnosed with non-classical CAH who wish to know whether they carry a classical trait or allele. Their partner should also undergo genetic testing to determine if they carry a pathogenic variant. If both partners carry a severe pathogenic variant, their offspring will have a 1 in 4 risk of having classic CAH.

Bone Health and Density

Osteoporosis is an understandable concern
for adults with CAH who are glucocorticoid-dependent and have been treated for a long time. It is known that glucocorticoid therapy inhibits osteoblastic (bone building) activity which could potentially lead to decreased bone density. This is of particular concern to individuals who were treated with high doses of glucocorticoids and whose 17-hydroxyprogesterone (17-OHP) levels were consistently kept in low- to mid-normal ranges (signaling oversuppression). If there is evidence of glucocorticoid over-treatment, routine bone density measurements are warranted in the young adult.

An initial bone mineral density scan
is recommended starting at 30 in women and 40 in men and subsequent scans will depend on the results and according to your provider. Fortunately, medications are now available to stop and reverse bone loss due to glucocorticoid therapy.



Males 18 - 24

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with increased glucocorticoid treatment to reestablish optimal cortisol levels and suppress ACTH secretion. Once the correct cortisol levels have been restored, the body may be able to return to normal levels of sperm production. It may take several months to achieve normal sperm production after the increased glucocorticoid dosages have been initiated.

Body Enlarged testes in men with CAH
are generally a result of inadequate treatment over the course of many years. The enlargement normally recedes once the cortisol levels are increased, through aggressive glucocorticoid therapy. The doctor may recommend to perform a biopsy of the enlarged testicle to ensure that there is no cancer present.

CAH does not cause cancer,
but it is good practice ensure that there are not other reasons for the enlargement. It may seem counterintuitive to experience low testosterone in a disorder where the primary symptoms occur as a result of androgen excess, but this can be a frequent cause of infertility in men with uncontrolled CAH.

Men with Classical CAH
who are not well suppressed will have uncontrolled adrenal androgen secretion. When too much testosterone is made by the adrenal glands over a long period of time, the body aromatizes (converts) the androgens to estrogen. The estrogen then feeds back to the pituitary which, sensing the body has enough testosterone, stops secreting the hormones that stimulate the testicles to make testosterone. This is called hypogonadotropic hypogonadism (HH), where the testes “shut down,” stop producing sperm and even shrink. As with adrenal rests, this condition can also (usually) be reversed with aggressive glucocorticoid therapy.

Men with CAH who are interested in fertility
should pay special attention to their endocrine care. Compliance (taking medicine as prescribed) is essential in avoiding adrenal rests and fertility problems. It is a good idea to establish a baseline picture of the testes during puberty with a testicular ultrasound. If no problems are found, the endocrinologist may recommend follow-up ultrasounds every few years. Men with adrenal rests that do not respond to glucocorticoid suppression can consider testis-sparing surgery with malignancy being ruled out.

Females 18 - 24

Female Reproductive Development

Women with CAH
There is a lot of speculation about the reasons for reduced fertility rates in women with CAH. Very early reports were pessimistic about the fertility rates in women with CAH and NCAH, but most specialists are beginning to agree that, with adequate, modern treatment, the fertility prospects for women with CAH are much better than outdated figures would indicate. Anecdotal evidence from CARES members also indicates higher levels of reproduction than past (and some current) literature would suggest.

Precise fertility rates are difficult to obtain
for a number of reasons. Because we cannot accurately quantify the number of women attempting reproduction, we cannot quote precise ovulation and pregnancy rates. Additionally, especially in the US, many of the girls initially followed at pediatric centers are lost to follow-up once they “age out” of the pediatric care system. As adults these women are followed by internists, gynecologists and adult endocrinologists, if at all. Moreover, unless there is a “problem,” many of these women do not seek treatment from the centers conducting studies. Hopefully, evidence from natural history studies will provide more tangible data about fertility rates.

Female Reproductive Development

Fertility for women with CAH

Several researchers and clinicians have hypothesized and written about the barriers to fertility for women with CAH. These barriers include:

- poor adrenal suppression
- a high prevalence of polycystic ovaries
- implantation failure
- unsatisfactory intercourse due to an inadequate vaginal introitus

The combination of these biological factors with additional psychological factors culminating in decreased heterosexual activity. High levels of androgen from the adrenal gland may cause irregular or absent periods, and high levels of progesterone and 17-OHP may prevent ovulation.

Polycystic ovaries

Additionally, it is thought that high levels of androgen in childhood might lead to the development of polycystic ovaries (ovaries that are physically larger but have smaller, dysfunctional follicles). Polycystic ovaries are also associated with irregular periods and ovulation problems. In many women with CAH, irregular periods and ovulation problems can be helped with more aggressive glucocorticoid treatment. However, finding a balance between over treatment and achieving fertility is sometimes challenging.

Ovulation is not a problem

In cases where ovulation is not a problem, implantation may be the barrier to fertility. Many women with CAH experience elevated progesterone levels during the follicular phase of the menstrual cycle. Sometimes this results in an endometrium (uterine lining) that is too thin for implantation. Even though fertilization can occur, the uterus is not ready to accept or hold the fertilized egg.

Therapies available to women with CAH

There are many therapies available to women with CAH who are experiencing problems with fertility, such as different (or increased) glucocorticoid therapy, clomiphene citrate for ovulation, and metformin for insulin resistance and androgen excess, to name a few. Women with CAH interested in pregnancy would be best served seeing a reproductive endocrinologist experienced with disorders of androgen excess.

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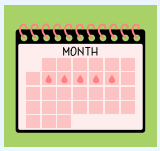
Special Considerations for Female Patients

Polycystic Ovary Syndrome (PCOS)

Females with poorly controlled CAH
are at high risk for developing polycystic ovary syndrome (PCOS). Polycystic ovaries are physically larger, but have smaller, dysfunctional follicles and produce excess testosterone. PCOS may cause the egg not to develop as it should or not be released during ovulation as it should. It can further cause irregular menstrual periods, which can lead to infertility or the development of small fluidfilled sacs (cysts) in the ovaries.



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Adrenal Masses

The incidence of adrenal masses
increases with age, and is higher in CAH patients than in the general population. Most adrenal masses associated with CAH are benign, including benign adrenocortical adenomas and myelolipomas. Adrenal incidentalomas can be the presentation of non-classic CAH.

Thus it is important to get screened by your doctors as an adult.

Living with CAH

Psychological Support

Adults with CAH may seek emotional support through one-on-one or group counseling in their treatment or seek out support groups.

Peer support groups, including peer patient social support

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to Secret Facebook Groups that are safe environments where those affected by CAH are able to ask questions, share experiences with others who are in the same situation.

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Recommendations
from
CAH patients
and parents

Ages: 18 - 24

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- Medicine
- Stress dose medicine and Solu-Cortef®
- With syringes and needles for administering

- Get and consistently wear a medical alert identification with wording that indicates: **ADRENAL INSUFFICIENCY and STEROID DEPENDENT**
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Download the PACE App, which helps caregivers and medical professionals obtain timely information on how to stress dose and give emergency medications. Information can be found here: **https://caresfoundation.org/pace- app/.**

CARES is a great resource for CAH-affected individuals at all ages.

Seek out an adult endocrinologist early prior to turning 18 years of age so that you can seamlessly transition your medical care, preferably one experienced with CAH

10

CHAPTER

Ages 25 - 50

Living with CAH

Ages: 25 - 50

Adult Considerations

Glucocorticoids have only been used to treat CAH for the last 70 years or so. While we have gained considerable knowledge and expertise about the treatment of CAH in children, there is much less information about the treatment of adults with CAH. Optimal treatment for the adult continues to challenge the healthcare community. What we do know is: People with CAH have a normal life expectancy, and for most who are well managed and receiving adequate treatment, there is little interference in every day life.

Medical Treatment for Adults:

With the completion of growth, CAH patients may continue to be managed with hydrocortisone, but may also be managed with longer-acting glucocorticoids, such as prednisone or dexamethasone. These drugs are not often used routinely in children because of their greater tendency to cause growth suppression.

Adults with CAH require life-long follow-up to maintain correct medical care

CAH adults benefit from a multidisciplinary approach that includes:

- Primary care physician
- Endocrinologists
- Gynecologists
- Urologists
- Fertility specialists
- Psychologists
- Continue with medical check-ups

Living with CAH

Ages: 25 - 50

Minimizing Glucocorticoids

Thus, the goals for treating CAH adults relate more to the consequences of long-term glucocorticoid use. The common strategy being used by many adult endocrinologists is to find the **minimum effective dose of glucocorticoids for maintenance.**

This is determined by a combination of clinical (physical) and biochemical (blood) evidence. Treatment must be adjusted according to individual needs and goals, as there is no uniform or “perfect” regimen. The patient and physician must take into account the whole picture of physical and biochemical evidence.

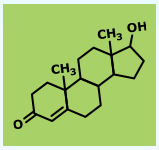
Long-term glucocorticoid use can result in:

- Bone loss (osteoporosis)
- Weight gain
- Increased risk of cardiovascular disease
- Insulin resistance
- Hypertension

Ages: 25 - 50

Factors Relating to Mineralcorticoid Medication Dosing:

Concerning 17-hydroxyprogesterone (17-OH)
researchers and clinicians have found that complete suppression to “normal” (CAH unaffected) levels results in over suppression and side effects of glucocorticoid excess (Cushingoid symptoms). Often, symptoms of over-suppression signal the need for dose adjustment or reduction.



Androstenedione and testosterone
concentrations move on a longer time-scale and can indicate longer periods of under-or over-suppression by glucocorticoids. Optimal dosing is that which does not fully suppress 17-hydroxyprogesterone (17-OH) to normal/CAH unaffected levels and maintains androgen levels in the mid-to high-normal range.

Adrenal Masses

The incidence of adrenal masses
increases with age, and is higher in CAH patients than in the general population. Most adrenal masses associated with CAH are benign, including benign adrenocortical adenomas and myelolipomas. Adrenal incidentalomas can be the presentation of non-classic CAH.
Thus it is important to get screened by your doctors as an adult.

Reproductive Function:

Reproductive function in non-classic CAH
is more consistently normal. In fact, many cases of mild 21-hydroxylase deficiency (21-OHD), both male and female, go undiagnosed for lack of clinically important symptoms. At present, there is no test to predict which individuals affected with non-classical CAH will progress and suffer adverse consequences of their hormonal imbalance.

Pregnancy outcome in women with CAH:
A recent review found that up to about 80% of simple virilizers and 60% of salt-wasters can bear children. French investigators found that about 50% of women affected with non-classical CAH became pregnant before the diagnosis of mild 21-hydroxylase deficiency (21-OHD) was made, without receiving any specific treatment. Among the other 50%, those who desired pregnancy conceived during hydrocortisone treatment; and only one in twenty women required additional treatment with Clomid, a standard fertility drug, to conceive. Despite high levels of maternal testosterone (male hormone) during pregnancy, unaffected female offspring, even of classical CAH mothers, show no genital ambiguity. This is because the placental aromatase enzyme prevents maternal testosterone from reaching the fetus.

Reproductive function in CAH males:
Impaired reproductive function is less frequent among men with classical CAH compared with affected women. Most CAH males are able to father children, or at least have adequate sperm counts. Low sperm counts do not preclude fertility. Testicular adrenal rest tumors (TART) (also referred to as “testicular tumors of adrenogenital syndrome”) may occur in CAH males especially if they are inadequately treated salt-wasters. For this reason, it is recommended that by adolescence, all CAH boys have careful testicular examinations and a baseline testicular sonogram.The preferred treatment consists of effective adrenal hormone suppression. Male infertility and TART are very rare in non-classical CAH.

Patients treated for non-classical CAH
before or during the child-bearing years may not require treatment throughout adult life, if symptoms abate. Patients on long term glucocorticoid should be carefully monitored for potential development of excess weight gain, hypertension, high blood glucose, and bone density problems.

Females 25 - 50

Female Reproductive Development

Women with CAH
There is a lot of speculation about the reasons for reduced fertility rates in women with CAH. Very early reports were pessimistic about the fertility rates in women with CAH and NCAH, but most specialists are beginning to agree that, with adequate, modern treatment, the fertility prospects for women with CAH are much better than outdated figures would indicate. Anecdotal evidence from CARES members also indicates higher levels of reproduction than past (and some current) literature would suggest.

Precise fertility rates are difficult to obtain
for a number of reasons. Because we cannot accurately quantify the number of women attempting reproduction, we cannot quote precise ovulation and pregnancy rates. Additionally, especially in the US, many of the girls initially followed at pediatric centers are lost to follow-up once they "age out" of the pediatric care system. As adults these women are followed by internists, gynecologists and adult endocrinologists, if at all. Moreover, unless there is a "problem," many of these women do not seek treatment from the centers conducting studies. Hopefully, evidence from natural history studies will provide more tangible data about fertility rates.

Female Reproductive Development

Fertility for women with CAH

Several researchers and clinicians have hypothesized and written about the barriers to fertility for women with CAH. These barriers include:

- poor adrenal suppression
- a high prevalence of polycystic ovaries
- implantation failure
- unsatisfactory intercourse due to an inadequate vaginal introitus

The combination of these biological factors with additional psychological factors culminating in decreased heterosexual activity. High levels of androgen from the adrenal gland may cause irregular or absent periods, and high levels of progesterone and 17-OHP may prevent ovulation.

Polycystic ovaries

Additionally, it is thought that high levels of androgen in childhood might lead to the development of polycystic ovaries (ovaries that are physically larger but have smaller, dysfunctional follicles). Polycystic ovaries are also associated with irregular periods and ovulation problems. In many women with CAH, irregular periods and ovulation problems can be helped with more aggressive glucocorticoid treatment. However, finding a balance between over treatment and achieving fertility is sometimes challenging.

Ovulation is not a problem

In cases where ovulation is not a problem, implantation may be the barrier to fertility. Many women with CAH experience elevated progesterone levels during the follicular phase of the menstrual cycle. Sometimes this results in an endometrium (uterine lining) that is too thin for implantation. Even though fertilization can occur, the uterus is not ready to accept or hold the fertilized egg.

Therapies available to women with CAH

There are many therapies available to women with CAH who are experiencing problems with fertility, such as different (or increased) glucocorticoid therapy, clomiphene citrate for ovulation, and metformin for insulin resistance and androgen excess, to name a few. Women with CAH interested in pregnancy would be best served seeing a reproductive endocrinologist experienced with disorders of androgen excess.

For help finding a board certified endocrinologist, please call CARES Foundation's office toll free at 866 -227-3737

Obesity

Weight gain in CAH
can be a side effect of glucocorticoid treatment, especially for women. Monitoring weight is important to prevent weight gain and avoid harsh weight reducing diets. Careful attention to diet and exercise in conjunction with precisely monitoring treatment should help most adults with CAH avoid obesity. Many adults with CAH find regular sustained exercise of an hour several times per week is essential in keeping weight down and fitness levels up. Exercise also helps with maintaining bone density.

Excessive Hair Growth and Acne

Treatments for excessive hair growth and acne
It is not uncommon that men and women with CAH are prone to excessive acne and unwanted hair growth. In some cases, where the CAH is untreated, it can lead to hair loss. To avoid this, the goal is to get the right balance of glucocorticoid therapy. However, practically, many CAH patients prefer to use additional treatments to treat the unwanted hair growth, such as using cosmetic hair removal, including laser treatment, bleaching, shaving, waxing, or electrolysis, for example. For acne, some CAH patients use topical and oral anti-acne medications, and drugs that either reduce production (e.g., oral contraceptives) or block action (e.g., spironolactone) of male hormones.

Bone Health

Is an understandable concern for adults
with CAH who are glucocorticoid-dependent and have been treated for a long time. It is known that glucocorticoid therapy inhibits osteoblastic (bone building) activity which could potentially lead to decreased bone density. This is of particular concern to individuals who were treated with high doses of glucocorticoids and whose 17-OH levels were consistently kept in low- to mid-normal ranges (signaling over-suppression). If there is evidence of glucocorticoid over-treatment, routine bone density measurements are warranted in the young adult.

An initial bone mineral density scan is recommended starting at 30 in women and 40 in men and subsequent scans will depend on the results and according to your provider. Fortunately, medications are now available to stop and reverse bone loss due to long-term glucocorticoid therapy.

Genetic Counseling

The diagnosis of CAH
is most often made on clinical grounds and on the basis of hormone measurements. Genetic counseling is useful in helping the family understand the implications of the diagnosis. There are several circumstances when genetic testing is important, especially, prenatal diagnosis and newborn screening with questionable results. Another common situation arises when a woman has been told she has “CAH” and is treated with glucocorticoids, but the hormonal measurements upon which the diagnosis was made are either unavailable or in doubt.

Since hormonal diagnosis
can be is unreliable during or immediately following glucocorticoid treatment or during pregnancy, genetic testing is a viable alternative. Genetic testing may also be done for those who have been diagnosed with non-classical CAH who wish to know whether they carry a classical trait or allele. Their partner should also undergo genetic testing to determine if they carry a pathogenic variant.

Carriers or Heterozygotes

Family members
often wish to know their risk of transmitting CAH. If both parents are carriers of a CAH pathogenic variant, their offspring have a 50% (1 in 2) chance of being a carrier, 25% (1 in 4) chance of being genetically unaffected, and 25% (1 in 4) chance of having a CAH. The risk is the same in each successive pregnancy. Carriers of CAH do not usually exhibit any significant symptoms or hormone imbalance, and hormone treatment is not generally recommended.

Males 25 - 50

Special Considerations for Male Patients Testicular Adrenal Rest Tumors (TART) and Testicular Issues

The testicles and adrenal glands are made of similar tissue.
Within the testicles there is a normal amount of adrenal cells that do not typically affect fertility. However, without adequate medication or treatment, men with Classical CAH may develop testicular masses (usually benign) called adrenal rest tumors and, in rare cases, enlarged testes.

When treatment is inadequate or sporadic in a male with CAH,
the adrenal cells may grow into masses that release hormones hindering sperm production. This happens when cortisol levels are too low and there is over secretion of ACTH by the pituitary. Just as ACTH stimulates the adrenal glands and causes them to enlarge (hyperplasia) it also stimulates the adrenal cells in the testicles.

It is important to note that in patients with known CAH,
adrenal rest tissue is not usually malignant and can be clinically differentiated from Leydig cell tumors by virtue of the fact that it is usually bilateral and common in men who show other evidence of poor adrenal suppression. Also, if the mass is located near the mid-center line of the testes and does not distort the contour of the testes it is likely an adrenal rest and not a malignancy.

Special Considerations for Male Patients Testicular Adrenal Rest Tumors (TART) and Testicular Issues

Fortunately, adrenal rest tissue usually regresses
with increased glucocorticoid treatment to reestablish optimal cortisol levels and suppress ACTH secretion. Once the correct cortisol levels have been restored, the body may be able to return to normal levels of sperm production. It may take several months to achieve normal sperm production after the increased glucocorticoid dosages have been initiated.

Body Enlarged testes in men with CAH
are generally a result of inadequate treatment over the course of many years. The enlargement normally recedes once the cortisol levels are increased, through aggressive glucocorticoid therapy. The doctor may recommend to perform a biopsy of the enlarged testicle to ensure that there is no cancer present.

CAH does not cause cancer,
but it is good practice ensure that there are not other reasons for the enlargement. It may seem counterintuitive to experience low testosterone in a disorder where the primary symptoms occur as a result of androgen excess, but this can be a frequent cause of infertility in men with uncontrolled CAH.

Men with Classical CAH
who are not well suppressed will have uncontrolled adrenal androgen secretion. When too much testosterone is made by the adrenal glands over a long period of time, the body aromatizes (converts) the androgens to estrogen. The estrogen then feeds back to the pituitary which, sensing the body has enough testosterone, stops secreting the hormones that stimulate the testicles to make testosterone. This is called hypogonadotropic hypogonadism (HH), where the testes “shut down,” stop producing sperm and even shrink. As with adrenal rests, this condition can also (usually) be reversed with aggressive glucocorticoid therapy.

Men with CAH who are interested in fertility
should pay special attention to their endocrine care. Compliance (taking medicine as prescribed) is essential in avoiding adrenal rests and fertility problems. It is a good idea to establish a baseline picture of the testes during puberty with a testicular ultrasound. If no problems are found, the endocrinologist may recommend follow-up ultrasounds every few years. Men with adrenal rests that do not respond to glucocorticoid suppression can consider testis-sparing surgery with malignancy being ruled out.

Living with CAH

Psychological Support

Adults with CAH may seek emotional support through one-on-one or group counseling in their treatment or seek out support groups.

Peer support groups, including peer patient social support

CARES further provides access
to Secret Facebook Groups that are safe environments where those affected by CAH are able to ask questions, share experiences with others who are in the same situation.

These groups are by invitation via our Congenital Adrenal Hyperplasia Support Network Facebook page*. Please follow this page and request entry into the group you are interested in.

*Alternatively, email **support@caresfoundation.org** to see a list of these private groups or to request an invitation.*

"Pearls of Wisdom"

Recommendations
from
CAH patients
and parents

Ages: 25 - 50

Always carry at least one day's supply of:

- ✔ Medicine
- ✔ Stress dose medicine and Solu-Cortef®
- ✔ With syringes and needles for administering

- → Get and consistently wear a medical alert identification with wording that indicates: **ADRENAL INSUFFICIENCY and STEROID DEPENDENT**
- → Frequently check the expiration dates of Solu-Cortef®.

Download the PACE App, which helps caregivers and medical professionals obtain timely information on how to stress dose and give emergency medications. Information can be found here: **https://caresfoundation.org/pace- app/.**

CARES is a great resource for CAH-affected individuals at all ages.

Adults with CAH that have children without CAH should educate them about being a carrier and what this means for their future children

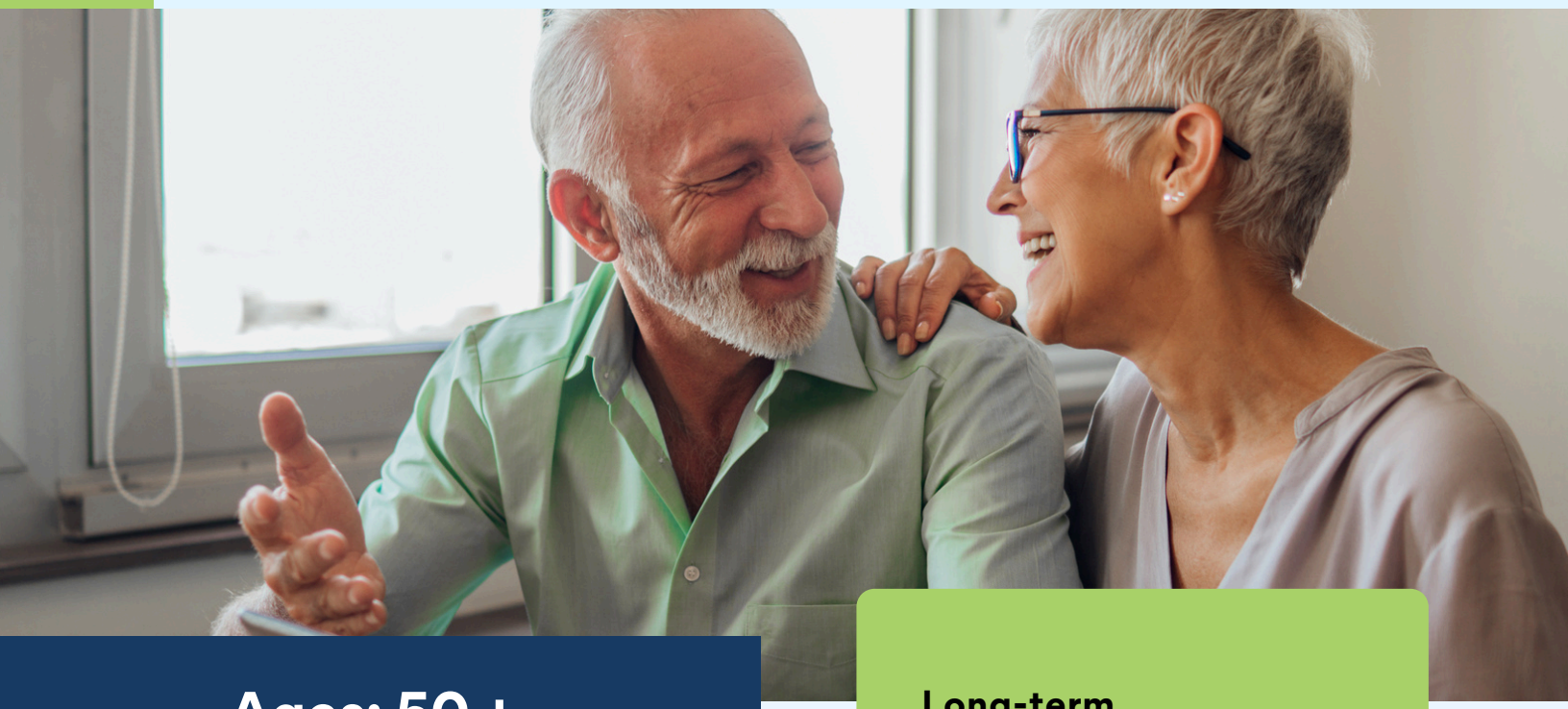
Living With CAH

11

CHAPTER

Ages 50 +

Living with CAH



Ages: 50 +

Minimizing Glucocorticoids

Thus, the goals for treating the 50+ adult relate more to the consequences of long-term glucocorticoid use and the common strategy being used by many adult endocrinologists is to find the **minimum effective dose of glucocorticoids for maintenance.**

This is determined by a combination of clinical (physical) and biochemical (blood) evidence. Treatment must be adjusted according to individual needs and goals, as there is no uniform or “perfect” regimen. The patient and physician must take into account the whole picture of physical and biochemical evidence.

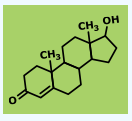
Long-term glucocorticoid use can result in:

- Bone loss (osteoporosis)
- Weight gain
- Increased risk of cardiovascular disease
- Insulin resistance
- Hypertension

Ages: 50 +

Factors Relating to Mineralcorticoid Medication Dosing:

Concerning 17-hydroxyprogesterone (17-OHP)
researchers and clinicians have found that complete suppression to “normal” (CAH unaffected) levels results in over-suppression and side effects of glucocorticoid excess (Cushingoid symptoms). Often, symptoms of over-suppression signal the need for dose adjustment or reduction.



Androstenedione and testosterone
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In contrast to the child with CAH
the adult’s range of acceptable 17-hydroxyprogesterone (17-OHP), androstenedione and testosterone may be higher.

Mineralcorticoid Medication Dosing

Mineralocorticoid (Florinef or fludrocortisone) treatment also requires monitoring in the adult. There is some anecdotal evidence that sensitivity to salt loss diminishes with age and that salt-wasting crises are far less common and less precarious in adults. However, optimal treatment suggests that adults should continue mineralocorticoid therapy with careful monitoring of hypertension and renin activity by the endocrinologist. In both salt-wasters and simple-virilizers, mineralocorticoid treatment may allow for a lower dose of glucocorticoids to maintain good control.

Osteoporosis

Is an understandable concern for adults with CAH who are glucocorticoid-dependent and have been treated for a long time. It is known that glucocorticoid therapy inhibits osteoblastic (bone building) activity which could potentially lead to decreased bone density. This is of particular concern to individuals who were treated with high doses of glucocorticoids and whose 17-OH levels were consistently kept in low-to-mid-normal ranges (signaling over-suppression). If there is evidence of glucocorticoid over-treatment, routine bone density measurements are warranted in the young adult.

Bone Density Scans

An initial bone mineral density scan is recommended starting at 30 in women and 40 in men and subsequent scans will depend on the results and according to your provider. Fortunately, medications are now available to stop and reverse bone loss due to long-term glucocorticoid therapy.

Cardiovascular Disease/ Insulin Resistance

Those receiving long-term glucocorticoid therapy for CAH are now reaching the age where cardiovascular disease becomes an issue. Theoretically, people with CAH may be at an increased risk of cardiovascular disease due to insulin resistance related to chronic hyperandrogenism. It is thought that increased levels of insulin over a long period of time may confer an increased long-term cardiovascular risk. Additionally, chronic glucocorticoid therapy has been linked to dyslipidemia, disruptions in blood lipid (cholesterol) levels. So far, only a few preliminary studies have addressed this health issue and there is much that remains to be discovered.

Obesity

Weight gain in CAH can be a side effect of glucocorticoid treatment, especially for women. Monitoring weight is important to prevent weight gain and avoid harsh weight reducing diets. Careful attention to diet and exercise in conjunction with precisely monitoring treatment should help most adults with CAH avoid obesity. Many adults with CAH find regular sustained exercise of an hour several times per week is essential in keeping weight down and fitness levels up. Exercise also helps with maintaining bone density.

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from
CAH patients
and parents

Ages: 50+

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- With syringes and needles for administering

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- Keep medic alert information in your wallet/purse/phone with information about your current medications and emergency contacts.

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CAH-affected individuals at all ages.

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12

CHAPTER

CAHtalog Registry & Resources

How HCP's Can Help with CAHtalogTM Recruitment

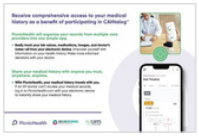
Sharing the opportunity to participate in CAHtalog™ with your patients is easy:

1. **Identify:** You can identify eligible participants through a variety of ways:
   a. General recollection
   b. Database query
   c. Review of notes
2. **Share:** Educate eligible patients about the registry leveraging IRB-approved patient materials, whichever you prefer:
   a. Physical brochure
   b. Digital message (via EHR portal, email, etc.)
3. **Sign Ups**
   a. Patients sign up on their own within 10 minutes via virtual landing page at www.CAHtalog.com.

Central IRB Approved Physical Brochure

Front side:

Back side:



Brochures can be shared directly with patients in person or mailed. Pre-paid postage envelopes are available upon request (to be filled out and mailed directly by yourself). Please email help@picnichealth.com for brochures and envelopes.

Digital Messages

If you'd like to digitally message (via email, EHR portal, etc.) your patients about the study, the following messaging has been approved by central IRB:

Dear [Patient Name], I wanted to inform you about an opportunity to participate in the CAHtalog

You can learn more and sign up here: www.CAHtalog.com. ™ Registry. Please see below for more information.

Sincerely,

[Insert HCP Name and/or email signature.]

Help improve treatment and care for CAH patients by participating in the CAHtalog ™ Registry.

CAHtalogTM is a comprehensive collection of medical records from patients living with classic congenital adrenal hyperplasia (CAH), specifically curated to drive advancements in CAH research.

Sign up on CAHtalog.com in less than 10 minutes. Here's what you can expect:

- ***After signing up, sit back and relax. Nothing else is required. PicnicHealth will collect your medical records on your behalf.***
- ***We take your privacy seriously. All personal identifying information will be removed from your medical records before sharing with researchers.***
- ***Get your medical records organized into one simple app. Upon enrollment, you'll receive comprehensive access to your health records as a benefit of participating.***
- ***Potential Earnings. You can be compensated for your time to complete optional short surveys twice a year.***

Have questions or need help signing up? Email PicnicHealth at help@picnichealth.com

CAHtalogTM is open to adults and caregivers on behalf of their children living with classic CAH and who receive medical care in the United States.

CAHtalogTM is collaborative partnership between CARES Foundation, PicnicHealth, and Neurocrine Biosciences.

Visit CAHtalog.com today to learn more and sign up!

Patient recruitment materials (brochures, envelopes, and digital messages) have been approved by a central IRB. By simply sharing IRB approved recruitment patient materials you are generally not conducting any human subject research. However, some institutions may need additional local research and/or privacy approvals in addition to central IRB approval before sharing information. PicnicHealth can assist with the preparation of submissions and/or questions upon request.

The following script can be used to contact your IRB to seek offline approval to share patient recruitment materials:

Subject: Request for Guidance on Sharing Patient Materials for Observational Research Study Attachment: Attach copy of digital message and/or picture of patient brochure to this email.

Dear [IRB Contact],
I am writing to seek guidance regarding referring patients for a virtual, observational research study currently underway. To support this research, I would like to share with some of my patients certain patient materials, including a patient brochure and/or a digital message through our provider portal or email. These materials have already been approved by a central IRB, and would refer patients to a virtual landing page, from which they will separately and individually sign up and consent to be considered for the study.
I wanted to inquire whether any specific approvals or waivers from IRB are required before proceeding to share these materials. I would appreciate any guidance on if there are any forms or processes I should follow.
Thank you for your attention to this request. I look forward to your guidance.
Best regards,
<Your Name and Email Signature>

Upon request to help@picnichealth.com we are ready to support:

- Sending copies of brochures and postage-paid envelopes
- Sending copy of email templates
- Support with IRB queries and submissions
- Answering any questions you may have

NEUROCRINE BIOSCIENCES · PicnicHealth · CARES CONGENITAL ADRENAL HYPERPLASIA FOUNDATION

For more information, visit www.CAHtalog.com or contact help@picnichealth.com.

Overview of the CAHtalog™ Registry

Study Title

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

A Patient Registry Collecting Longitudinal Data of Patients With Congenital Adrenal Hyperplasia (CAH)

Study Objectives

Study objectives include characterizing the natural history, treatment patterns, and real-world burden of illness of CAH

Study Design

CAHtalogTM is an observational, rolling retrospective study of patients living with Classical CAH in the United States. Patients provide their consent to have PicnicHealth act as a proxy to collect their electronic health records on their behalf. Records are processed to abstract large-scale real-world data, resulting in a de-identified dataset reflective of real-world treatment use, outcomes, and natural history.

Study Inclusion/Exclusion Criteria

The CAHtalogTM registry is open to adults and caregivers on behalf of their children living with classic CAH. Participants must receive medical care in the U.S.

of Participants

The enrollment target is ~300 patients. The registry launched in 2022 and as of July 2024, there are currently ~150 participants enrolled.

How to participate

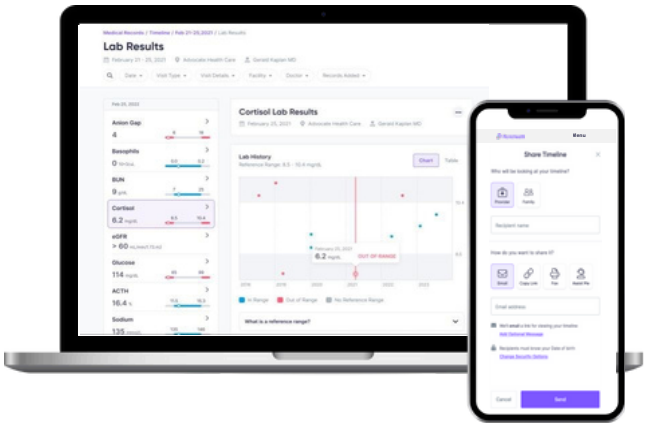
Participants can sign up, consent, and participate in CAHtalogTM online in less than 10 minutes from their own home*. No visits to any sites are necessary.*

- PicnicHealth will ask for screener questions, such as sharing contact info of patient's most recent PCP and endocrinologist.
- Patients may participate in **optional** surveys

No additional effort is required on behalf of patient

- PicnicHealth will collect medical records on behalf of patients
- Patients are not required to undergo site visits
- No data entry is required by physicians or staff

Patient Benefit



- Patients can contribute to CAH research from home with **minimal effort**.
- Earn up to **$150 a year** by completing ***optional* short surveys**.
- **Patients will have their medical records organized into one simple app as a benefit of participating.**
  - Includes records from not just one, but nearly all sites of a patient's care over last 5+ years.
  - Patients can share their medical history with anyone they trust, anywhere, anytime.
  - With PicnicHealth, patients' medical histories travel with them. If an ER doctor cannot access their medical records, patients can log in to PicnicHealth.com with their electronic device to instantly share their medical history.

KOL Testimonial

"CARES Foundation is collaborating with Neurocrine Biosciences on the development of the CAHtalog™ Registry. Utilizing PicnicHealth's research platform, this first-of-its-kind registry will enable patients and their families to easily share their real-world data for the advancement of CAH research. We're excited to participate in the project and see the positive impact of the registry."

- Dr. Karen Lin Su, CARES Medical Director

CAHtalog™ is a partnership between:

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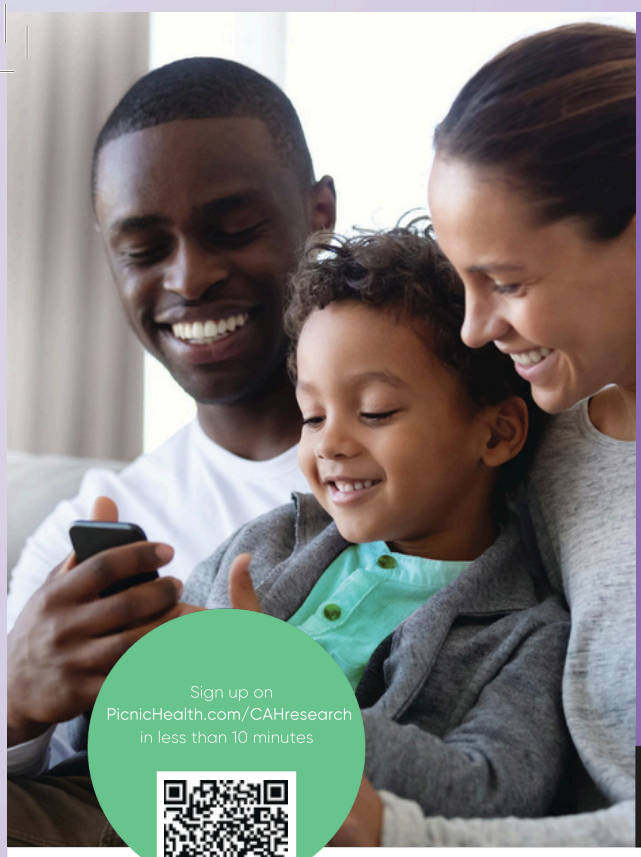


Sign up on
PicnicHealth.com/CAHresearch
in less than 10 minutes

Be a hero for the CAH community!

Help improve treatment and care for fellow CAH patients by participating in the CAHtalog™ Registry

CAHtalog is a comprehensive collection of clinical data from medical records from patients living with classic congenital adrenal hyperplasia (CAH), designed to drive advancements in CAH research.

Sign up on PicnicHealth.com/CAHresearch in less than 10 minutes.

Here's what you can expect:

- After signing up, sit back and relax. Nothing else is required. PicnicHealth will collect your medical records on your behalf.
- We take your privacy seriously. All personal identifying information will be removed from your medical records before sharing with researchers.
- Get your medical records organized into one app. Upon enrollment, you'll receive comprehensive access to your health records.
- Potential earnings. You can be compensated for your time to complete optional short surveys twice a year.

Have questions or need help signing up? Email us at help@picnichealth.com

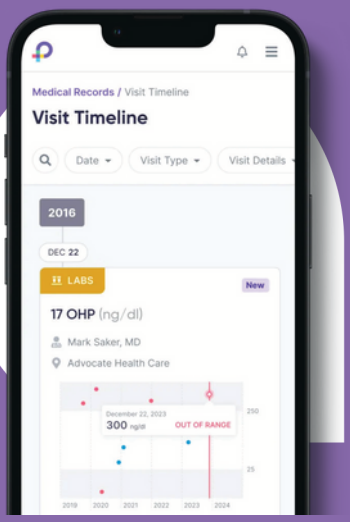
CAHtalog is open to adults and caregivers on behalf of their children living with classic CAH and who receive medical care in the United States.

CAHtalog is a collaborative partnership between PicnicHealth NEUROCRINE BIOSCIENCES XXcares FOUNDATION

Receive comprehensive access to your medical history as a benefit of participating in CAHtalog™.

PicnicHealth will organize your records from multiple care providers into one simple app.

- Easily track your lab values, medications, images, and doctor's notes—all from your electronic device. Empower yourself with information on your health history. Make more informed decisions with your doctor.



Share your medical history with anyone you trust, anywhere, anytime.

- With PicnicHealth, your medical history travels with you. If an ER doctor can't access your medical records, log in to PicnicHealth.com with your electronic device to instantly share your medical history.

PicnicHealth NEUROCRINE BIOSCIENCES XXcares FOUNDATION

Emergency Instructions

Treatment for Congenital Adrenal Hyperplasia in times of stress

Includes Information on:

- Stress Dosing
- Hydrocortisone Injection
- Emergency Room Instructions

Your or your child's body does not make enough of certain essential hormones: cortisol, and in salt-wasting CAH, aldosterone. Cortisol, which is produced by the adrenal glands, has many purposes in the body such as maintaining energy supply, fluid, electrolyte balance, blood pressure, normal blood sugar levels, and controlling the body's reaction to physical stress. Aldosterone is used by the kidneys to maintain a normal blood sodium and fluid balance (salt and water). When cortisol and aldosterone are not produced by the body they must be replaced by medication.

Extra hydrocortisone must be given during times of extreme physical stress such as fever, vomiting and diarrhea, surgery, and traumatic injuries (e.g., broken bones and concussions).

The extra hydrocortisone is called a "stress dose." The Florinef dose does not change. Make sure you discuss stress dosing with your or your child's physician and you know how to proceed in the event of illness.

If ill, call physician to alert him/her of your or your child's condition. Typically, stress dosing is required when . . .

*FEVER IS GREATER THAN 100.5°F : DOUBLE the hydro-cortisone dose for the entire day

*FEVER IS GREATER THAN 102°F : TRIPLE the hydrocortisone dose for the entire day

*VOMITING: Triple dose with vomiting with or without a fever. If you vomit less than 30 minutes after taking the hydrocortisone stress dose, the medication likely was not absorbed and the dose should be repeated. Wait 10-15 minutes after you/your child vomit(s) and repeat triple stress dose of hydrocortisone. If you/your child vomit(s) again, give the injectable hydrocortisone (brand name Solu-Cortef® in the U.S.) and contact your physician.
DO NOT DELAY in giving the injectable hydrocortisone.

*DIARRHEA: Injection may also be needed in the event of diarrhea due to loss of fluids. If diarrhea, no fever and feeling fine, no need to stress dose. If not feeling well, double dose of hydrocortisone recommended.

*Try small amounts of clear liquids that contain SUGAR (not artificial sweetener) frequently, at least 1 ounce every 15 minutes.

Signs of acute adrenal crisis from cortisol:

- Headache
- Abdominal pain
- Pale skin
- Dehydration
- Nausea
- Confusion
- Listlessness
- Dizziness

If these occur and continue after oral stress dosing, call your or your child's physician and go to the nearest emergency room immediately.

Again, do NOT wait to give the injectable hydrocortisone. It should be given BEFORE a trip to the emergency room or activating 911 if those actions become necessary

Remember, stress dose with:

Fever of 100.5°F or higher ● Vomiting ● Diarrhea

Physical trauma (broken bone, concussion, etc.)

EXAMPLE STRESS DOSING:

Normal dose: 1 tab + 1/2 tab + 1 tab (total of 2.5 pills)

Double dose: 5 total tablets (divide into 1.5 tablets every 8 hours)

Triple dose: 7.5 total tablets (divide into 2.5 tablets every 8 hours)

HOW TO GIVE AN INJECTION OF HYDROCORTISONE INSTRUCTIONS

1. STAY CALM. Wash your hands and gather equipment: needle, syringe, alcohol pad, and vial of hydrocortisone (Solu-Cortef® Act-O-Vial).

Steps 2-3

Steps 4-5

2. Mix the medication by pushing down on top of the vial to release the cork into the vial.

3. Shake the vial to mix medicine, take off the top of the vial, and wipe down the rubber stopper with alcohol.

Steps 6-7

Steps 8-10

4. Take the cap off the syringe needle and insert into the vial through the rubber stopper.

5. Draw up the medication and replace the needle cap.

6. Select the site for the intramuscular injection, typically the outer portion in the middle of the thigh.

7. Use the alcohol to clean the skin at the injection site.

Step 11

Step 12

8. Take off the cap of the needle and hold the syringe like a dart.

9. Using your thumb and first two fingers, spread the skin by pushing down lightly.

10. Dart the needle into the thigh, going at a 90° angle.

11. Hold the syringe in place and pull back the plunger to make sure you don't see blood, (seeing blood means you are in a blood vessel, but this is rare). If you do see blood, withdraw syringe and discard*. Prepare another syringe with medication and inject in a slightly different site.

(*However, if this is the only dose you have, continue with the same syringe, injecting in a slightly different site).

12. Inject medicine then place tissue or cotton ball near the needle. Pull the needle out quickly.

13. Place the needle and syringe in a hard, unbreakable container.

14. Call doctor, 911, or go to hospital, (if necessary).

EMERGENCY ROOM INSTRUCTIONS

We recommend filling out this form with your/your child's name, then giving it to your/your child's physician (whichever physician you would like contacted in case of emergency). Have the doctor read over, complete & sign. You and your child's caregiver should always carry a copy of these signed instructions.

I/my child, _____, have/has a rare, inherited, genetic disorder called Congenital Adrenal Hyperplasia (CAH). I am/my child is adrenally insufficient and steroid dependent. I/my child must be seen by a physician IMMEDIATELY because life threatening electrolyte disturbances/adrenal crises are possible with febrile illnesses, fluid depletion from vomiting and diarrhea, surgery, and serious injuries.

Time in a waiting area or triage situation is not appropriate.

Signs of adrenal crisis include, but are not limited to weakness, dizziness, nausea and vomiting, hypotension, hypoglycemia, pallor, and lethargy.

Treatment should include:

*IV fluids-D5 normal saline at 20cc/kg for at least one hour then continuous fluid replacement for dehydration and hypotension.

*STAT basic metabolic panel (sodium, potassium, chloride, carbon dioxide, glucose, BUN, creatinine, and calcium)

*Initial hydrocortisone IV bolus can be administered IM if IV access an issue

- 25mg for children under age 3
- 50mg for children aged 3-10
- 100mg for children older than 10 years or weighing more than 40kg
- 100mg for teens and adults

*Hydrocortisone as a continuous drip (if necessary) or in 4 divided doses IV bolus

- 5mg/day for ages 0-37
- 75mg/day for ages 3-10
- 100mg/day for children older than 10 years or weighing more than 40kg
- 100mg/day for teens and adults

NOTE FROM PHYSICIAN: Please follow the above treatment instructions and contact me as soon as possible. (See contact info below). Patient's health issues include:

_____

_____

_____

Thank you. Please call if additional information is needed.

_____ (Physician signature)

Physician Contact Information

Endocrinologist: _____

Phone Number _____ Fax Number _____

Primary Care Provider/Pediatrician: _____

Phone Number _____ Fax Number _____

These are the medications I/my child take(s) daily: _____

_____

These are the medications I have/my child has taken today (includes any stress dosing), including approximate time(s) medication(s) was/were taken:_____

_____

_____

_____

We extend our gratitude to our sponsors whose support made this patient guide possible.

www.caresfoundation.org