

PARENTAL MANAGEMENT OF ADRENAL CRISIS
IN CHILDREN WITH CONGENITAL ADRENAL HYPERPLASIA

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ABSTRACT

Louise Kathleen Fleming: Parental Management of Adrenal Crisis in
Children with Congenital Adrenal Hyperplasia
(Under the direction of Marcia Van Riper and Kathleen Knafl)

Background: Life-threatening conditions in children change the meaning of parenting. Classical congenital adrenal hyperplasia (CAH), a rare, endocrine disorder, requires caregivers to inject a child with hydrocortisone intramuscularly during illness and adrenal crisis. The inability to effectively respond to a crisis prevents parents from optimally managing the condition. Few studies have examined parental education on managing crises or parental management strategies. Identifying gaps in parent education by healthcare providers, especially concerning times of crisis, is necessary to promote positive outcomes, for children and family members.

Purpose: This is a three-manuscript dissertation. Chapter 2 presents a systematic review of the literature surrounding CAH management. Chapter 3 presents the results of a two-phase, mixed methods study examining parental management of adrenal crisis in children with CAH. Chapter 4 compares the family experiences of parents of girls versus boys with CAH.

Methods: Chapter 2 is a systematic literature review examining the management and care related to children with CAH. Chapter 3 presents the results of a mixed methods study. In phase 1, parents completed online questionnaires about family life in the context of having a child with CAH. Results from Phase 1 were used to select a purposive sample for interviews in Phase 2 to elicit descriptions of parents' experiences of managing CAH-related crises and their perceptions of the consequences of living with CAH. Chapter 4 compares the family experiences of parents of girls versus boys with CAH.

Results: Four distinct themes emerged from the literature regarding family management of CAH. As parents' management ability increases, CAH has less impact on the family. Additionally, parents feel better able to manage the condition after their child turns 5 years old. Families having a daughter with CAH experience significant, additional challenges such as stigmatization, surgery, and disclosure about their daughter's CAH.

Conclusion: Healthcare providers should deliver increased and more frequent education regarding adrenal crisis management and offer more in-depth, emotional assistance to parents of children with CAH. Furthermore, providers need to create a network of support specifically for families of girls born with CAH that addresses both surgical decisions and the stigmatization often associated with ambiguous genitalia.

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LIST OF ABBREVIATIONS

17OHP	17 hydroxyprogesterone
AQ	Autism spectrum questionnaire
BMI	Body mass index
cIMT	Carotid intima media thickness
CAH	Congenital adrenal hyperplasia
CARES	Cares Foundation
DEX	Dexamethasone
DSD	Disorders of sex development
EAI	Epinephrine auto-injector
EMS	Emergency medical services
ESPE	European Society for Pediatric Endocrinology
FaMM	Family Management Measure
FMSF	Family Management Style Framework
GH	Growth hormone
HRQoL	Health related quality of life
IM	Intramuscular
LHRHa	Leutinizing hormone releasing antagonist
PedsQL	Pediatric quality of life
U.K.	United Kingdom
U.S.	United States
UTI	Urinary tract infection

CHAPTER 1: INTRODUCTION

Background and Significance

Classic congenital adrenal hyperplasia (CAH) is a life-long, life threatening endocrine condition that has the potential to negatively affect the lives of children diagnosed with it as well as their families. CAH is inherited in an autosomal recessive pattern and affects approximately 1 in 15,000 live births (Speiser et al., 2010). Management of this condition requires parents to administer steroids, typically oral hydrocortisone, up to three times daily. In addition, parents need to supplement maintenance doses with oral “stress dosing” during times of illness and intramuscular (IM) injections of hydrocortisone when a child is unable to tolerate oral medications and/or if signs of adrenal crisis are present (Merke & Bornstein, 2005, Speiser et al., 2010, Witchel & Azziz, 2011). Children with CAH are at significant risk for adrenal crisis, defined as an abrupt, life threatening state with symptoms including hypotension, pallor, fatigue, headache, tachycardia, and vomiting, due to glucocorticoid and mineralocorticoid deficiency (Speiser, 2011). The need for stress dosing, either orally or by injection, related to simple viral and bacterial childhood illnesses is frequent and unpredictable, requiring parents to make life or death complex treatment decisions (Merke & Bornstein, 2005). The looming threat of an adrenal crisis is ever present, and the knowledge that improperly responding to such a threat can result in a fatal outcome creates an environment of uncertainty, stress, and potential dysfunction within the family (Fleming, Rapp, & Sloane, 2011).

Despite the importance of being able to effectively respond to an adrenal crisis episode, a 2011 study showed that only half of the 60 parents of children with CAH surveyed reported ever having received a demonstration from a health care professional on

how to administer the emergency injection of hydrocortisone (Fleming, Rapp, & Sloane, 2011). Additionally, although these children experienced adrenal crisis one to two times per year, 39% of parents had not received a prescription for injectable hydrocortisone at the time of diagnosis, despite that being the standard of care (Speiser et al., 2010). The study further found that the type of emergency education given to parents by health care providers varied considerably, with some parents receiving no formal instruction from providers while others receiving both oral and written instruction as well as an actual injection demonstration from a provider on when and how and to correctly administer the injection (Fleming et al., 2011). Adrenal crisis events are inherently stressful for parents and a lack of detailed, ongoing, thorough education from health care providers to parents on how to best handle such occurrences increases parental stress regarding ability to respond effectively in an emergency.

CAH shares characteristics of episodic, life-threatening crises with other, more prevalent, chronic childhood conditions (Harris et. al, 2002; Barnard et. al., 2010; Sicherer et. al, 2010). For example, during times of hypoglycemia in children with Type 1 diabetes, defined as a serum blood glucose level less than 70 mg/dL, parents are instructed to administer IM glucagon to prevent further declining blood glucose and the health hazards associated with hypoglycemia such as confusion, tachycardia, tremors, and even death (NIDDK, 2008). As with CAH, prior research in the pediatric diabetes community suggests that parental fear over their ability to properly handle times of a life threatening hypoglycemic crisis in their child is related to a lack of thorough and repeated education from health care providers (Harris et. al, 2002; Barnard et. al., 2010; Sullivan-Bolyai et. al, 2010). In a descriptive study of parents of school-age children with diabetes who were attending a summer education camp, over half (69%) of parents reported experiencing hypoglycemic management difficulties, such as opening the IM injection kit and removing the needle and syringe. Moreover, approximately a fourth of the parents injected an

incorrect dose of glucagon during a simulation (Harris et. al, 2002). Parental stress is not only a challenge for parents of diabetic children, but can also negatively affect children's health outcomes, as parents report maintaining slightly elevated blood glucose levels in their children in an effort to avoid hypoglycemia (Barnard et. al, 2010).

Another childhood chronic condition that requires an IM injection during times of crisis is life threatening, or anaphylactic, food allergies, which affect approximately 5% of children--and that number is rising (Liu et al., 2010). Management of food allergies depends on strict allergen avoidance and ready availability of injectable epinephrine for emergency management (LeBovidge et al., 2008). Emergency IM epinephrine administration is crucial in managing anaphylaxis, but epinephrine auto-injectors (EAI) are underused by providers, patients, and their families (Chad et al., 2013). Studies have described a lack of parental knowledge regarding indications and technical aspects of EAI administration (Kapoor et al., 2004; Hayman, Bansal & Bansal, 2003). A 2013 study asked parents of children who had been prescribed an EAI whether they were fearful of using it and, if so, what factors that may contribute to that fear. Over half of the 1209 parents surveyed expressed fear regarding the use of the EAI, which they attributed to hurting the child, using the EAI incorrectly, or a negative outcome. Parents whose child had been diagnosed with anaphylactic food allergies longer or had experienced a severe reaction in the past and parents who were satisfied with the EAI training were less likely to be afraid (Chad et al., 2013). Studies exploring the impact of food allergies on families' quality of life and parental stress have found significant links between increased levels of parental distress and worry and family tension compared with normative families (Sicherer, Noone & Munoz- Furlong, 2000; King, Knibb & Hourihane, 2008). A 2008 study with a primary aim of investigating the impact of peanut allergies on quality of life and anxiety for children and their immediate family members showed significant findings when comparing children with food allergies and their unaffected siblings. Children with peanut allergies reported greater separation anxiety than their siblings, likely

from a fear of having to manage an anaphylactic reaction to a food by themselves with no family help (King, Knibb & Hourihane, 2008). Having to carry medication, or a “shot kit” at all times, and the isolation associated with not being able to eat school lunches at the same table as their peers further contributes to these children feeling stigmatized and different (King, Knibb & Hourihane, 2008).

In addition to being able to respond effectively to the life threatening aspect of CAH, parents must also handle day-to-day condition management. If a child is prescribed too much hydrocortisone, side effects can include growth suppression, obesity, and other cushingoid features. If the dose of hydrocortisone is not sufficient, children with CAH are at a high risk for precocious puberty, which can also lead to stunted growth and adrenal crisis. Daily management typically includes replacing deficient levels of cortisol and/or aldosterone, while attempting to: minimize androgen excess, prevent virilization, optimize linear growth (which is often compromised) and protect future fertility (Merke & Bornstein, 2005). Determining the proper dosage of steroids is typically achieved by obtaining routine laboratory work and measuring the height, weight and bone age, typically every 3-6 months, in a growing child (Merke & Bornstein, 2005).

Parents of girls born with CAH face additional challenges, as girls born with CAH have a significant risk of experiencing virilization, resulting in ambiguous genitalia at birth, due to elevated testosterone levels (Witchel & Azziz, 2011). This has the potential to profoundly affect both the child and family, as gender assignment of the infant can initially be uncertain. Reconstructive feminizing genitoplasty is often recommended at an early age and can involve multiple surgeries into adolescence (Witchel & Azziz, 2011). Although the majority of girls with CAH have a female gender identity (Dessens, Slijper, & Drop, 2005), they often show increased preference for male toys and activities (Pasterski et al, 2005), increased aggression (Pasterski et al., 2007), increased male-typical sexual orientation

(Nordenstrom et al., 2010), and differences when compared to non-CAH girls in spatial abilities (Berenbaum et al., 2012).

Aims

The aims for this study include:

AIM 1. Describe circumstances surrounding adrenal crises in children with CAH by examining:

- 1.1) Parents' actual experiences (e.g., what they did, how they used information)
- 1.2) Parental perceptions of sources of information related to managing time of crisis (e.g., education from healthcare professionals, support groups, Internet, etc.);
- 1.3) How such information was delivered (written guidelines, demonstration, etc.);
- 1.4) Strategies and approaches parents take to inform other family members (siblings, grandparents, etc.), schools, and others in their social network (friends, babysitters, etc.) about the management of adrenal crises and their perceptions of effective versus ineffective strategies to manage them.

AIM 2. Explore parents' perceptions of the consequences, for themselves and their family, of living with the possibility that their child with CAH will experience a life-threatening adrenal crisis

AIM 3. Examine a possible relationship between parents' management ability and the impact CAH has on the family (Table 1)

Theoretical Framework

There are many reasons to use a theoretical model as a guide when conducting family research. The interface between theory and research has been described as a mutual relationship in which research supports theory and theory brings about research questions (Young et al. 2001). Theories provide a clear focus for research, including interventional work; help in the organization of large amounts of information; and provides a systematic way of understanding events, behaviors and/or situations. This study was guided by the Family Management Style Framework (FMSF), which is grounded in the originators' research and syntheses of studies of family life in the context of childhood chronic conditions (Knafl, Deatrick, & Havill, 2012). (Figure 1) It has been used in studies with families exploring the overall response to the child's condition as well as studies of selected aspects of their response (e.g., information management) (Knafl et al., 2012).

The framework is comprised of three components (with 8 dimensions total): *definition of the situation* (child identity, illness view, management mindset, parental mutuality), *management behaviors* (parenting philosophy, management approach), and *perceived consequences* (family focus, future expectations) (Knafl, Deatrick, & Havill, 2012; Knafl et al., 2013). According to the latest revision of the FMSF, individuals in the family contribute to developing a family management style or pattern of response that can influence both individual and family outcomes (Knafl, Deatrick, & Havill, 2012; Knafl et al., 2013). The FMSF has been used widely in family nursing research to date. Some examples of its use include studies investigating families of children with brain tumors (Deatrick et al., 2006); families of children with cancer (Nelson et al., 2006; Thibodeaux & Deatrick, 2007); families with children in the NICU (Bernaix, 2006); and families with genetic conditions (Van Riper, 2007).

Prepared Manuscripts

This is a three-manuscript dissertation. Chapter 1 is an introduction to the challenges associated with family management of congenital adrenal hyperplasia with particular attention to crisis management. Chapter 2 is a systematic review, with an initial intent of focusing on family management of CAH; however, results of a preliminary scoping study conducted to examine the extent, nature, and range of research related to this focus indicated that few, if any, studies had addressed family response (Arksey & O'Malley, 2005; Levac, Colquhoun & O'Brien, 2010). Hence, the aims of the review were expanded to focus on the management and care related to children with CAH in order to better understand the full extent of chronic condition related management challenges children with CAH and their families may face.

Chapters 3 and 4 are two manuscripts that comprise the dissertation project. Chapter 3 presents the results of a two-phase, mixed methods study. In Phase 1, parents were asked to complete online questionnaires about selected aspects of experiences of family life in the context of having a child with CAH. Results from the Phase 1 survey were used to select a purposive sample of parents for follow-up interviews. In Phase 2, descriptive, qualitative interviews were conducted to elicit more detailed descriptions of parents' experiences of managing CAH-related crises and their perceptions of how the consequences of living with the threat of crisis influences their child's and their family's life.

Chapter 4 compares the experiences of parents of girls versus boys with CAH. Parents of girls born with CAH often feel the need to keep their child's diagnosis of CAH more private due to their daughters' ambiguous genitalia, which can create a feeling of stigmatization and bring additional challenges to a condition that is already complex to manage for both genders.

Chapter 5 is a discussion regarding the synthesis of the results of the study, the implications of the study, and directions for future research studies to continue this program of research. The titles of the chapters are as follows:

Chapter 2: Management of Congenital Adrenal Hyperplasia-A Systematic

Review of the Literature

Chapter 3: Parental Management of Adrenal Crisis in Children with Congenital

Adrenal Hyperplasia

Chapter 4: Gender Matters in Families Having a Child with Congenital Adrenal

Hyperplasia

Chapter 5: Discussion

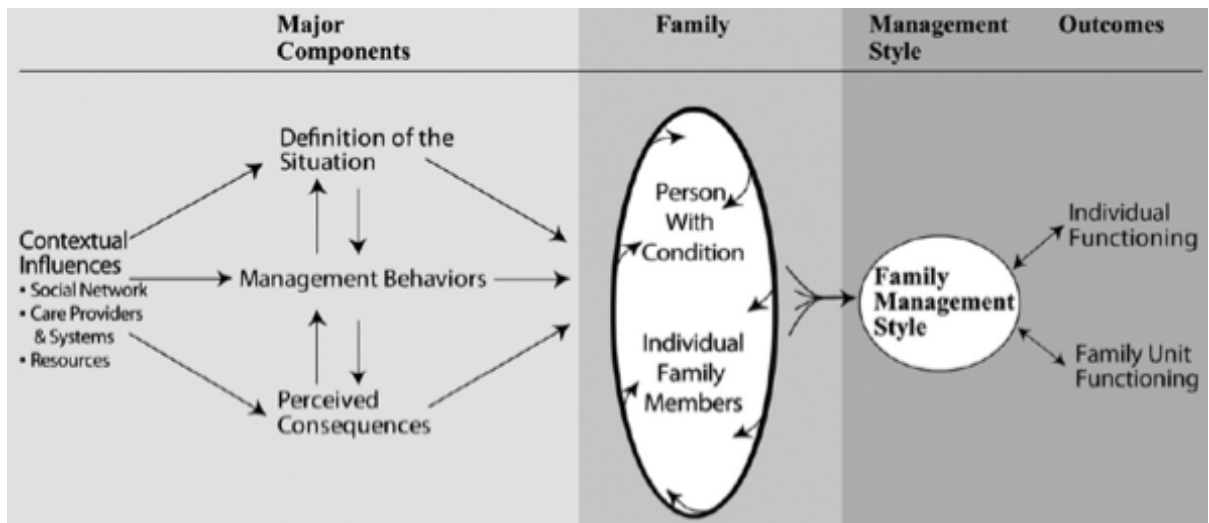


Figure 1.1. Family Management Style Framework

Table 1.1. Outline of Study Aims and FMSF

Aim of the Study	Component of Framework	Topic(s) of Interest	Data Collection Method
Describe circumstances surrounding adrenal crises in children with CAH by examining: 1.1) Parents' actual experiences (e.g., what they did, how they used information) 1.2) Parental perceptions of sources of information related to managing time of crisis (e.g., education from healthcare professionals, support groups, internet, etc.); 1.3) How such information was delivered (written guidelines, demonstration, etc.); 1.4) Strategies and approaches parents take to inform other family members (siblings, grandparents, etc.), schools, and others in their social network (friends, babysitters, etc.) on how to manage adrenal crises and determine which strategies parents perceive to be effective versus ineffective.	Definition of the Situation, Management Behaviors	Parental perceptions and interpretations of adrenal crisis events and their beliefs about their ability to manage the event Parents' assessment of the extent to which they have an established approach for responding to an adrenal crisis and their strategies for accessing and conveying information about crisis management	Semi-structured Interview; Family Management Measure – View of Condition Impact and Management Ability Scales; PedsQL-Family Impact Module
Explore parents' perceptions of the consequences, for themselves and their family, of living with the possibility that their child with CAH will experience a life-threatening adrenal crisis	Perceived Consequences	Parents' perceptions of the ways in which the life threatening nature of the condition affects everyday life for their child and family	Semi-structured Interview; Family Management Measure – View of Condition Impact and Management Ability Scales; PedsQL-Family Impact Module
Examine a possible relationship between parents' management ability and the impact CAH has on the family	Definition of the Situation, Management Behaviors	The relationship between parents' management ability and the impact CAH has on the family (e.g. does increased ability to manage CAH lead to decreased impact of the condition on the family?)	Family Management Measure – View of Condition Impact and Management Ability Scales; PedsQL-Family Impact Module

REFERENCES

- Arksey H & O'Malley L. (2005). Scoping studies: Towards a methodological framework. *International Journal of Social Research Methodology*, 8,19-32.
- Barnard, K., Thomas, S., Royle, P., Noyes., K. Waugh, N. (2010). Fear of hypoglycemia in parents of young children with type 1 diabetes: a systematic review. *BMC Pediatrics*, 10(50), 1-8.
- Berenbaum, S., Bryk, K., & Beltz, A. (2012). Early androgen effects on spatial and mechanical abilities: evidence from congenital adrenal hyperplasia. *Behavioral Neuroscience*, 126(1), 86-96. Doi: 10.1037/a0026652
- Bernaix, L. W., Schmidt, C. A., Jamerson, P. A., Seiter, L., & Smith, J. (2006). The NICU experience of lactation and its relationship to family management style. *MCN: The American Journal of Maternal/Child Nursing*, 31(2), 95-100.
- Chad, L., Ben-Shoshan, M., Asai, Y., Cherkaoui, S., Alizadehfar, R., St-Pierre, Y., ... & Clarke, A. (2013). A majority of parents of children with peanut allergy fear using the epinephrine auto-injector. *Allergy*, 68(12), 1605-1609. doi: 10.1111/all.12262
- Deatrick, J. A., Thibodeaux, A. G., Mooney, K., Schmus, C., Pollack, R., & Davey, B. H. (2006). Family management style framework: A new tool with potential to assess families who have children with brain tumors. *Journal of Pediatric Oncology Nursing*, 23(1), 19-27.
- Dessens, A., Slijper, F., & Drop, S. (2005). Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. *Archives of Sexual Behavior*, 34(4), 389-397. Doi: 10.1007/s10508-005-4338-5
- Fleming, L., Rapp, C. & Sloane, R. (2011). Caregiver knowledge and self-confidence of stress dosing of hydrocortisone in children with congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 26, 55-60. Doi: 10.1016/j.pedn.2011.03.009
- Harris, G., Diment, A., Sulway, M., & Wilkinson, M. (2002). Glucagon administration undervalued and undertaught. *Practice Diabetes International*, 18(1), 22-25.
- Hayman, G. R., Bansal, J. A., & Bansal, A. S. (2003). Knowledge about using auto-injectable adrenaline: review of patients' case notes and interviews with general practitioners. *BMJ*, 327(7427), 1328. Doi: 10.1136/bmj.327.7427.1328
- Kapoor S., Roberts G., Bynoe Y., Gaughan M., Habibi P. & Lack, G. (2004). Influence of a multidisciplinary paediatric allergy clinic on parental knowledge and rate of subsequent allergic reactions. *Allergy* 15(59), 185–191. Doi:10.1111/all.12262
- King, R. M., Knibb, R. C., & Hourihane, J. B. (2009). Impact of peanut allergy on quality of life, stress and anxiety in the family. *Allergy*, 64(3), 461-468. Doi: 10.1111/j.1398-9995.2008.01843.
- Knafl, K. and J. Deatrick. (2003). Further refinement of the family management style framework. *Journal of Family Nursing*, 9(3), 232-256.

- Knafl, K., Deatrick, J., & Havill, N. (2012). Continued development of the family management style framework. *Journal of Family Nursing*, 18(1), 11-34. Doi: 10.1177/1074840711427294
- Knafl, K., Deatrick, J., Knafl, G., Gallo, A., Grey, M., & Dixon, J. (2013). Patterns of family management of childhood chronic conditions and their relationship to child and family functioning. *Journal of Pediatric Nursing*, 28, 523-535. Doi: 10.1016/j.pedn.2013.03.006
- Levac, D., Colquhoun, H., & O'Brien, K. (2010). Scoping studies: Advancing the methodology. *Implementation Science*, 5:69.
- LeBovidge, J. S., Timmons, K., Rich, C., Rosenstock, A., Fowler, K., Strauch, H., ... & Schneider, L. C. (2008). Evaluation of a group intervention for children with food allergy and their parents. *Annals of Allergy, Asthma & Immunology*, 101(2), 160-165. doi:10.1016/S1081-1206(10)60204-9
- LWPES/ESPE CAH Working Group. (2002). Consensus statement on 21-hydroxylase deficiency from the Lawson Wilkins pediatric endocrine society and the European Society for Paediatric Endocrinology. *The Journal of Clinical Endocrinology & Metabolism*, 18(9), 4048-4053.
- Merke, D. & Bornstein, S. (2005). Congenital adrenal hyperplasia. Retrieved from http://www.utp.edu.co/libproxy.lib.unc.edu/~maternoinfantil/Hiperplasia%20suprarrenalLancet_2005_review.pdf
- National Institute of Diabetes and Digestive and Kidney Disease (NIDDK). (2008). Hypoglycemia. Retrieved from <http://www.niddk.nih.gov/health-information/health-topics/Diabetes/hypoglycemia/Pages/index.aspx>
- Nelson, A. E., Deatrick, J. A., Knafl, K. A., Alderfer, M. A., & Ogle, S. K. (2006). Consensus statements: The Family Management Style Framework and its use with families of children with cancer. *Journal of Pediatric Oncology Nursing*, 23(1), 36-37.
- Nordenstrom, A., Frisen, L., Falhammer, H., Filipsson, H., Holmdahl, G., Janson, P. . . . Nordenskjold, A. (2010). Sexual function and surgical outcome in women with congenital adrenal hyperplasia due to CYP21A2 deficiency: clinical perspective and the patients' perception. *Journal of Clinical Endocrinology & Metabolism*, 95(8), 3633-3640. Doi: 10.1210/jc.2009-2639
- Pasterski, V., Geffner, M., Brain, C., Hindmarsh, P., Brook, C., & Hines, M. (2005). Prenatal hormones and postnatal socialization by parents as determinants of male-typical toy play in girls with congenital adrenal hyperplasia. *Child Development*, 76(1), 264-278.
- Pasterski, V., Geffner, M., Brain, C., Hindmarsh, P., Brook, C., & Hines, M. (2007). Increased aggression and activity level in 3- to 11-year-old girls with congenital adrenal hyperplasia. *Hormones and Behavior*, 52(3), 368-374. Doi: 10.1016/j.yhbeh.2007.05.015

- Pearson, T. (2008). Glucagon as a treatment of severe hypoglycemia: safe and efficacious but underutilized. *The Diabetes Educator*, 34(1), 128-134. Doi: 10.1177/0145721707312400
- Sicherer, S. et al. (2012). Development and validation of educational materials for food allergy. *The Journal of Pediatrics*, 160(4), 651-656. Doi: 10.1016/j.jpeds.2011.09.056
- Speiser, P., Azziz, R., Baskin, L., Ghizzoni, L., Hensle, T., Merke, D. . . . White, P. (2010). Congenital adrenal hyperplasia due to 21-hydroxylase deficiency: An endocrine clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*, 95(9), 4133-4160. Doi:10.1210/jc.2009-2631
- Speiser, P. (2011). During illness and emergency. Retrieved from CARES Foundation website: http://www.caresfoundation.org/productcart/pc/Adrenal_Crisis.html
- Sullivan-Bolyai, S., Bova, C., Leung, K., Trudeau, A., Lee, M. & Gruppuso, P. (2010). Social support to empower parents (STEP): An intervention for parents of young children newly diagnosed with type I diabetes. *The Diabetes Educator*, 36, 88-97. Doi: 10.1177/0145721709352384
- Thibodeaux, A. G., & Deatrick, J. A. (2007). Cultural influence on family management of children with cancer. *Journal of Pediatric Oncology Nursing*, 24(4), 227-233.
- Van Riper, M. (2007). Families of children with down syndrome: responding to a change in plans with resilience. *Journal of Pediatric Nursing*, 22(2), 116-128. doi: 10.1016/j.pedn.2066.07.004
- Witchel, S. & Azziz, R. (2011). Congenital adrenal hyperplasia. *Journal of Pediatric Adolescent Gynecology*, 24, 116-126. Doi: 10.1016.j.jpag.2010.10.001
- Young A., Taylor S.G.. & McLaughlin-Renpenning K. (2001) *Connections: Nursing Research, Theory and Practice*. Mosby, St. Louis, MO.

CHAPTER 2: MANAGEMENT OF CONGENITAL ADRENAL HYPERPLASIA-A SYSTEMATIC REVIEW OF THE LITERATURE

Introduction

Childhood chronic illness can be defined as lasting, or expected to last, more than three months and likely producing one or more of the following conditions: a limitation in function and/or activity level; a dependency on specific medications, diets, medical technology or personal assistance; and/or a need for medical care beyond what is usual for a child of the same age (Perrin et al., 1993; Stein et al., 1993; Newacheck & Halfon, 1998). Families having a child with a chronic illness face many challenges related to the child's condition such as parental conflict, strained parent-child bond, and sibling-child relationship difficulties, which puts them at risk for poor family functioning (Hall et al., 2011; Barlow & Ellard, 2006; Cabizuca, Marques-Portella, Mendlowicz, & Coutinho, 2009; Popp et al., 2014; van Oers et al., 2014). Families' having a chronically ill child whose condition is *also life threatening* face the same challenges and often more problematic ones. The need for constant vigilance, especially with younger children who do not yet have the ability to recognize and respond to crisis events (e.g., hypoglycemic episodes in diabetic children and adrenal crisis events in children who are adrenal insufficient), is ever present (Grey et al., 2011). Families who struggle to cope with the life threatening aspect of their child's chronic condition often have children who report lower quality of life and parents with increased psychological distress (Whittemore, Urban, Tamborlane, & Grey, 2003; Streisand, Wickmark, Chen, & Holmes, 2005).

One such episodically life threatening condition is classic congenital adrenal hyperplasia (CAH), a rare, genetic, endocrine disorder that requires caregivers to inject

hydrocortisone intramuscularly (IM) during times of illness and adrenal crisis (Merke & Bornstein, 2005). Management requires parents to not only inject IM hydrocortisone when a child is unable to tolerate oral medications and/or if signs of adrenal crisis are present, but to also administer oral steroids up to three times daily, supplementing maintenance doses with oral “stress dosing” during times of illness (Merke & Bornstein, 2005; Speiser et al., 2010; Witchel & Azziz, 2011). The need for stress dosing, either orally or by injection, related to simple viral and bacterial childhood illnesses is frequent and unpredictable, often requiring parents to make life or death complex treatment decisions (Merke & Bornstein, 2005).

Moreover, girls born with CAH often experience virilization, which can result in ambiguous genitalia at birth due to elevated testosterone levels related to adrenal dysfunction (Witchel & Azziz, 2011). This means some families having a child with CAH face multiple surgeries into adolescence should reconstructive feminizing genitoplasty be recommended (Witchel & Azziz, 2011). These features of the disease have the potential to profoundly affect the family, as adrenal crisis events can be fatal, and gender ambiguity brings both physical and emotional challenges.

There are multiple challenges for practitioners and families regarding the treatment and monitoring of children with CAH including achieving optimal glucocorticoid replacement, height and weight difficulties, excess androgen exposure leading to ambiguous genitalia in females, and the need for stress dosing during times of illness and when signs and symptoms of adrenal crisis are present (Kim, Ryabets-Lienhard & Geffner, 2012; Merke & Bernstein, 2005; Schaeffer et al., 2010; Speiser et al., 2010). In addition to these physiological concerns, children and families with CAH must also manage the psychosocial aspects of chronic illness, such as dealing with school personnel who are often unfamiliar with the condition, the challenges associated with future family planning due to the autosomal recessive nature of the condition, decisions related to reconstructive surgery for girls with ambiguous genitalia, and the possible stigma associated with the consequences of

excess androgens (Schaeffer et al., 2010; Speiser et al., 2010). The primary purpose of this systematic review was to explore the management and care, including treatment modalities, associated health issues, and growth and developmental consequences, for children with CAH. Examination of family life in the context of CAH is needed to better understand the scope of chronic condition-related management challenges these families face. The review is intended to provide an evidence base for the development testing of interventions that will support optimal family management of CAH.

Methods

Four web-based literature indexes were searched for peer reviewed journal articles published from January 2000 to June 2015. It was decided to go back fifteen years to obtain a sufficient number of articles, as this is the first review exploring multiple aspects of care management related to children with CAH and their families and a comprehensive review was needed. Databases searched included PubMed, CINAHL, PsycINFO, and Family and Society Studies Worldwide. After consultation with a university health science librarian, the following search terms were used: congenital adrenal hyperplasia and family (or parents or siblings) as well as adrenal crisis and parents. The words family, parents, and siblings were truncated for maximum results.

To be included in this review, the studies needed to: 1.) concern CAH management, experience, and challenges for children under 18 years, 2.) be written in the English language and published between 1/1/2000 and 6/1/2015, and 3.) be peer reviewed. Exclusion criteria included: 1.) a primary pathological focus with little detail regarding management of the condition, 2.) other adrenal disorders or other disorders that may result in ambiguous genitalia, and 3.) articles that focused on non-classical or rare types of CAH. This search resulted in 470 articles (Figure 2). After further review of the article titles, 389 were then excluded, leaving 81 articles from the initial search. Additional review of the

abstracts and full text excluded 55 articles leaving 26. Thirteen other manuscripts that met the criteria were added based on review of the reference lists of relevant research articles, resulting in a total of 39 empirical reports meeting the search criteria. A defined template was used that included information obtained from each report (author/title, research purpose, location of study, participant information, data collection methods, and findings). Data analysis was completed using a systematic approach consisting of sorting, categorizing, and summarizing data in an effort to create meaningful conclusions (Whittemore & Knafl, 2005).

Results

Thirty-nine empirical research studies met the criteria and were included in this review. Thirty-four studies used a quantitative design, four used a mixed methods design, and one study used a qualitative design. These studies had global representation with North America, South America, Europe, Australia and Asia all having reported research on children with CAH. Of the 39, fifteen were conducted in the United States (U.S.), thirteen in Europe (with the majority of European studies coming from the United Kingdom (U.K.)), eight in Asia (Jordan, Turkey, India, and Malaysia), three from Brazil, and one from Australia. One study was conducted jointly in the U.K. and the U.S. In the United States, studies were primarily conducted in Bethesda, Maryland (at the National Institutes of Health), in Los Angeles, New York, and in states described by the authors as in the “mid-western region.”

Four themes emerged from the 39 studies: 1.) health and development issues associated with a diagnosis of CAH (n=10); 2.) physical and psychosocial consequences for the child resulting from exposure to excess androgens (n=18); 3.) the life experience of having CAH for those affected and their families (n=7); and 4.) acute illness and managing and averting adrenal crisis (n=4).

Health and Development Issues Associated with CAH

Children with CAH are steroid dependent for life, and the goal of daily maintenance treatment is to replace deficient levels of cortisol and/or aldosterone while minimizing androgen excess, preventing virilization, optimizing linear growth, and protecting future fertility. If children are prescribed excess hydrocortisone, side effects can include growth suppression, obesity, and other cushingoid features. If the dose of hydrocortisone is not sufficient, these children are at a high risk for precocious puberty, which can also lead to stunted growth and adrenal crisis (Merke & Bornstein, 2005).

Ten studies focused on aspects of CAH that lead or have the potential to lead to negative health outcomes (Table 2.1). Of the ten, five articles focused on growth issues, both height and weight, in these children. Obesity was found to be a significant problem in children with CAH (Volkl, Simm, Beier, & Dorr, 2006; Mendes-dos-Santos et al., 2011; Cetinkaya & Kara, 2011; Moreira et al., 2013). Mendes-dos-Santos et al. (2011) concluded in their cross sectional, retrospective study that height in these children was similar to unaffected children of the same age, yet children with CAH had higher body fat, which tended to be visceral. Volkl et al. (2006), in a cross-sectional study, examined Bavarian children with CAH and found that steroid dosing, age, advanced bone age maturation, and parental obesity all contributed to elevated body mass indexes (BMI); while birth height and weight, the types of glucocorticoids prescribed, and mineralocorticoid use were not associated with obesity. Similarly, Moreira et al. (2013) found that CAH children presented with a higher prevalence of obesity and metabolic syndrome, and like Volkl et al., child weight did not seem to be correlated with glucocorticoid treatment. Cetinkaya and Kara evaluated the effects of glucocorticoid doses on bone mineral density in their 2011 study and found that children with CAH have higher BMIs than healthy controls. The bone ages of the poorly controlled (when looking at 17 hydroxyprogesterone (17-OHP) levels) and late-diagnosed groups were higher than tightly controlled, early-diagnosed groups. Additionally,

treatment of glucocorticoids did not appear to influence bone mineral density in CAH children.

Using a descriptive design, Bonfig, Schmidt, and Schwartz analyzed linear growth patterns in children with CAH treated with low doses of hydrocortisone during their first three years of life (2011). In their cohort of fifty-one children, birth length was above average in boys and girls, possibly due to increased androgens in utero, which correlated with Bonfig's 2007 study results as well. Treating these children with lower levels of glucocorticoids in infancy did not accelerate bone age and growth, and they were able to achieve height within the target range as they grew. However, final height in these children was still decreased (Bonfig et al., 2007). Lin-Su, Harbison, Lekarev, Vogiatzi, and New (2011) evaluated whether growth hormone (GH) alone or in combination with a leutinizing hormone releasing hormone agonist (LHRHa) would improve final height in children with CAH, as LHRHa can effectively suppress puberty, preserving the ability for continued growth. These findings indicate that for CAH children experiencing precocious puberty and short stature, GH alone or in combination with LHRHa is an effective therapy for improving final height; however, males experience somewhat less height benefit than females.

Due to a variety of factors, children with CAH are at risk for vascular problems (Harrington, Pena, Gent, Hirte, & Couper, 2012); hence a study was designed to establish whether children with CAH have reduced vascular function and increased carotid intima media thickness (cIMT) when compared to healthy children. The findings of this cross-sectional study suggest that CAH children have significant vascular and smooth muscle dysfunction when compared to healthy controls, and this level of dysfunction was comparable to the healthy subjects that were mild to moderately obese. Risk factors that were identified with the potential to cause such vascular dysfunction in these children include obesity, insulin resistance, hypertension, dyslipidemia, hypercortisolism, and hyperandrogenism (Harrington et al., 2012). The authors conclude that these children are at

risk for cardiovascular problems later in life and education related to healthy lifestyle choices such as exercise and proper nutrition for these families is needed to diminish possible negative health outcomes as these children age (Harrington et al., 2012).

A 2006 retrospective, descriptive study was conducted to determine the incidence of urinary tract infections (UTIs) in children with CAH (Nabhan, Rink, & Eugster). Since girls with CAH often experience ambiguous genitalia that may result in structural genitourinary anomalies, the authors hypothesized these girls may be at higher risk for such infections. Both boys and girls with CAH were included in the study. The incidence of UTIs in children with CAH was similar to the general population; furthermore, there was not a significant increase in UTIs if genital surgery was delayed in affected girls.

Finally, one study investigated the behavioral health of children with CAH. Idris et al. (2014) studied behavioral outcomes in children with CAH compared to a non-affected, control group. They found a higher incidence of parent reported child problems including anxiety, depression, somatic complaints, social and attention problems, and aggressive behavior when compared to controls. Internalizing behavior problems were seen more often in boys with CAH compared with control boys, and CAH girls had similar psychosocial adjustment to their non-affected girl control counterparts. Idris et al. further found a relationship between increased parent reported child problem behavior and higher glucocorticoid doses and/or lower family income (2014).

Physical and Psychosocial Consequences from Exposure to Excess Androgens

Both female and male children born with CAH are exposed to high concentrations of androgens in utero; while males do not show any outward physical signs of this exposure (except possibly subtle hyperpigmentation and penile enlargement), females typically have ambiguous genitalia at birth to varying degrees, which often leads to a diagnosis in females shortly after delivery. The degree of virilization is graded according to the Prader score (with a 0 appearing as a typical female and a 5 appearing as a typical male). Gender assignment

in these affected females can pose both a medical and family crisis (Merke & Bornstein, 2005). The majority of the studies reviewed (18) addressed the potential impact of excess androgen exposure on the physical genitalia characteristics and psychosocial presentations of children with CAH. (Table 2.2)

The aim of a 2004 retrospective study in Turkey was to report on the experience of gender (re) assignment in genotypical female patients with CAH. Seventy female patients were studied with 21 of them having been reared “male.” Nine of them were surgically reassigned as females, with a mean age of seven months at the time of surgery. The study found significant difficulties, both in surgical complications as well as family emotional strain, in attempting to correct the gender of female patients with CAH when they present at greater than 2.5 years of age (Ozbey, Darendeliler, Kayserili, Korkmazlar & Salman, 2004).

Another study (Al-Maghribi, 2007), based in Jordan, evaluated the clinical features of all patients with CAH treated at a major medical center from 1996-2006. Among the 39 females born with CAH, 27 had problems with external genitalia. Seven of these chose not to have reconstruction surgery and six of these had hysterectomies and gonadectomies to keep their “male genders.” Although the majority of these female children did have reconstructive surgery and were raised as girls, fifteen percent were genetically identified as female, but physically reconstructed, and raised as male. There were no other studies found that described these types of surgical measures to preserve male identity, which could be based on cultural differences related to gender roles in middle eastern countries. In addition, in areas where there are universal newborn screenings such as in the U.S. and most of Europe, incorrect gender assignment after the first few weeks is uncommon (Servin, Nordenstrom, Larsson & Bohlin, 2003). Although there is controversy regarding early reconstructive surgery for females with regards to eventual sexual satisfaction, it remains the recommendation by most pediatric endocrinologists in Europe and the U.S. (Schaeffer et al., 2010; Merke & Bernstein, 2005; Ozbey et al, 2004).

A 2002 study in Germany (Woelfle et al.) examined sixteen completely virilized females in an effort to better understand specific problems these girls face. In this study, gender identity was defined as “an individual’s internalized sense of males or femaleness and the acceptance of the gender role of that sex as appropriate” (Woelfle et al., 2002, p. 233). The authors of this study define the circumstance of a female born with ambiguous genitalia due to CAH as “female pseudohermaphroditism,” which is a term that would likely not be accepted or welcomed in the general CAH population, nor medical communities that treat CAH globally (Matos, 2015). The authors concluded that there are five main concerns experienced in this population: 1.) delayed diagnosis (due to an assumption of the child being a male rather than female), 2.) gender assignment, 3.) surgical procedures, 4.) short stature, and 5.) precocious puberty. All of these issues, with the exception of gender assignment and related subsequent surgical procedures, also affect males with CAH. Similarly, a 2010 study in India used a case study approach to report the effect of steroid therapy during infancy and early childhood on the appearance of the external genitalia of girls with CAH (Kulshreshtha et al., 2010). It is unclear as to whether the three girls in the study had a definitive diagnosis of CAH, as steroids were not initiated until after two months of age in one and as late as 2.5 years in another. However, the authors concluded that there is improvement in the external appearance of the girls’ genitalia with post-natal steroid therapy.

Four cross-sectional studies examined toy preferences in children with CAH from the first year of life to young adulthood. In both the Servin et al. and Wong et al. (2003, 2013) studies, girls with CAH were more interested in masculine toys such as cars and construction toys versus feminine toys such as dolls and tea sets. In the Wong study, which also looked at parental encouragement of sex-typical toy play, parents of girls in both CAH and control groups encouraged girl-typical toy play; however, parents reported encouraging less girl-typical, and more boy-typical, toy play in girls with CAH than in control females. The

authors suggest that this could be due to the fact that parents simply encourage their children to play with toys that the child naturally prefers. Servin et al. (2003) examined the degree of masculinization for girls with CAH in regards to play behavior and attempted to identify playmates by asking the girls whom their “best friends” were. Two thirds of girls with severe masculinization reported a boy as their best friend, where most of the girls with milder forms of CAH and all of the control girls reported girls as their best friend. In addition, the group of girls with CAH who had the most masculinization spent significantly more time playing with masculine toys than girls with less masculinization.

A 2005 study by Pasterski investigated 65 CAH children, both male and female, as well as controls, to assess toy choices. As in the Servin and Wong studies, Pasterski et al. found that girls with CAH, aged 3-10, displayed more male-typical toy choices than controls, whereas boys with and without CAH did not differ. Similarly, a 2002 study (Nordenstrom et al.) not only investigated toy preference in girls with CAH, but also explored a relationship between the degree of disease severity, reflected in CYP21 genotype, and the degree of masculinization with toy play and preference. They too found that girls with CAH played more frequently with masculine type toys than controls; additionally, the higher degree of androgen exposure in utero did correlate with an increased preference of masculine toys.

A 2004 study explored if school aged girls with CAH had problems with gender identity due to increased androgen exposure prenatally and hypothesized that if the gender identity of CAH females was determined by prenatal androgens, one would expect indications of increased gender confusion or gender dysphoria to be evident in childhood (Meyer-Bahlburg et al., 2004). As expected based on previous studies, girls with CAH scored significantly more masculine than control girls on all scales used when looking at gender behavior; however, there was an absence of gender confusion/dysphoria. This varies slightly from Berenbaum and Bailey’s 2003 study that showed that the vast majority of girls with CAH had similar scores (on a nine-question interview) to those of control girls, but

the average score was in between control girls and “tomboys,” which is not defined. However, girls with CAH, as also reflected in Meyer-Bahlburg’s study, did not express true gender confusion and articulated no discomfort in being a girl. Beltz, Swanson, and Berenbaum (2011) explored the contribution of androgens on occupational interests in males and females with CAH compared to their same gender, unaffected siblings in an effort to better comprehend women’s lack of representation in careers focused on science and technology. The framework used was “Things versus People,” which stipulates that males prefer occupations related to objects and females prefer occupations related to people. Females with CAH did have more interest in “things” over “people” when compared to unaffected females and variations among females were significant to the degree of androgen exposure in utero (Beltz, Swanson, and Berenbaum, 2011).

Pasterski et al. (2015) studied 153 children total (43 females and 38 males with CAH as well as unaffected relative controls) to investigate potential cross gender identification in girls who were exposed to androgens prenatally. This was one of four studies evaluating the physical and psychosocial consequences of exposure to excess androgens that used a mixed methods approach in which standardized measures as well as a short parent and child interview were conducted. In this study, *gender role behavior* “refers to behaviors which, on average, are more typical of one gender or the other and includes preferences for specific toys, playmates and play styles” while *gender identity* was defined as “the sense of self as male, female, or a category that is neither male nor female” (Pasterski et al., 2015, p.1364). The study found that girls exposed to high levels of androgens in utero due to CAH show increased cross gender identification as well as cross gender role behavior, when compared to female controls (Pasterski et al., 2015).

Spatial ability is typically described as the ability to understand and remember the spatial relations among objects. The largest cognitive sex difference is in spatial ability, with males outperforming females in most aspects (Berenbaum, Bryk, & Beltz, 2012). Spatial

abilities in males with CAH show inconclusive results. A 2003 study showed that males with CAH have unaltered performance on targeting tasks and impaired performance on internal rotation tasks compared to unaffected males, yet a 2012 study showed males with CAH scoring lower than their unaffected brothers in spatial ability (Hines et al., 2003; Berenbaum et. al., 2012). For females however, both studies suggest that females with CAH perform better than unaffected females on spatial ability measures and resemble unaffected males and males with CAH in this respect (Hines et al., 2003; Berenbaum et. al., 2012).

Knickmeyer et al. (2006) investigated whether autistic traits among boys and girls with CAH are increased as a result of exposure to excess androgens. The Autism Spectrum Questionnaire (AQ) was given, and females with CAH scored significantly higher than unaffected females, in large part due to increased scores on subscales measuring social skills and imagination. However, none of the females in the study had AQ scores that met the cut off for suspicion of a clinical diagnosis of autism among the general population. Males with CAH did not differ from unaffected males on the total AQ or on any of its subscales.

Finally, four studies evaluated possible personality differences in children with CAH due to excess androgen exposure. Females with CAH tend to display increased aggressive behavior and activity levels in childhood (Pasterski et al., 2007; Mathews, Fane, Conway, Brook & Hines, 2009). However, such results in males is less conclusive with one study reporting no significant differences in either aggressive behavior or activity level (Paterski et. al, 2007) while another showed males tend to display less dominant, less rough and tumble play and show increased “tender minded” characteristics (Mathews et al., 2009). The rationales offered by the authors as to why males with CAH might display less dominant behavior than unaffected males is based the possibility of non-hormonal factors, particularly illness, associated with CAH or that testosterone levels may be initially elevated, but due to

neural feedback mechanisms, may readjust to normal or even lower than normal levels (Mathews et al., 2009).

Prenatal treatment of dexamethasone (Dex) in pregnant women at risk for having a child with CAH was introduced decades ago (Nimkarn & New, 2009) with the understanding that taking steroids during pregnancy reduces the risk of virilization in the unborn female fetus with CAH by reducing the level of circulating adrenal androgens. Maryniak et al. (2014) studied 33 females in Poland ranging from 6-23 years of age from at-risk CAH families; 17 girls treated prenatally with Dex (9 affected and 8 unaffected after birth) and 16 CAH affected females that were not treated prenatally. The purpose of the study was to assess cognitive development and social and emotional function in girls treated with dexamethasone prenatally compared to female CAH patients who were not treated prenatally. The authors found that prenatal treatment with Dex was significantly associated with better cognitive functioning (based on measures including an intelligence scale as well as memory and verbal learning tests) in girls with CAH; however, treating unaffected CAH girls (in utero prior to knowing if they will have CAH or not) can cause the risk of unfavorable influence on the development of certain cognitive functions. Hence, prenatal Dex treatment in mothers should be discontinued immediately after determination of the unborn child's CAH status and/or gender. As reflected in other studies (Beltz et al., 2014; Maryniak et al., 2014; Nordenstrom et al., 2002; Pasterski et al., 2005; Servin et al., 2003; Wong et al., 2013), prenatally untreated CAH girls had more male "interests" than unaffected and CAH affected/treated prenatally with Dex girls.

The Life Experience of Having CAH for Those Affected and Their Families

Families having a child with CAH often experience challenges such as missed school and work, frequent times of illness, isolation, and a decreased quality of life (Fleming et al., 2011; Boyse et al., 2011; Yau et al., 2015). Seven studies, one of which was qualitative, focused on the experience of having CAH from the perspective of either the child with CAH,

family members, or both (Table 2.3). Three of the studies focused on parents of children with CAH in developing countries: Sri Lanka, Vietnam and India (de Silva et. al., 2014, Armstrong, Henderson, Hoan & Warne, 2006; Bhakhri & Jain, 2011). Children's perspectives were not given; however parents in the three countries reported misconceptions and confusion with medication administration and general knowledge of the disorder. Other similar concerns expressed by parents from these countries included surgical options and care for their daughters with CAH as well as the financial burden associated with having a chronically ill child. Authors concluded that there is a strong need for more support groups in helping parents deal with such struggles as well as more universal newborn screenings (Armstrong, Henderson, Hoan & Warne, 2006; Bhakhri & Jain, 2011). The de Silva study (2014) examined depressive symptoms in parents of children with CAH and found over half of the parents of children with CAH were classified as having symptoms of depression that did not subside with the passage of time.

In the United States, Boyse et al. (2014) conducted a small, qualitative study (6 parents from 4 families) examining the experience of having CAH for children and their families and identified multiple challenges facing families having a child recently diagnosed with CAH. These included communication problems with health care providers, especially regarding parents' understanding of the diagnosis and treatment options and the need for decision making regarding genital surgery in girls, as well as a lack of social support. These challenges left parents feeling overwhelmed and isolated as well as concerned that their knowledge of how to manage the condition was insufficient (Boyse et al., 2014).

Three additional studies examined aspects of families' quality of life related to their child's CAH diagnosis. Sanches et. al (2012) investigated the physical, social, and societal functioning of children with CAH and their parents in The Netherlands through parent report. Parents reported that their child with CAH experienced few negative effects from the condition, with children participating (as unaffected children would) in typical school and

leisure activities, but also noted needed improvements in parental preparation for adrenal crisis events in their children. Gilban, Alves and Beserra (2014) evaluated the health related quality of life (HRQoL) of children and adolescents with CAH in Brazil. This was one of the few studies that used measures completed by both parents and affected children. They found a loss of HRQoL in children and teens with CAH, especially in the physical dimension (when compared with unaffected controls), which was in agreement with the assessment made by their parents. There were no statistically significant differences in quality of life between boys and girls with CAH however. Finally, Yau et al. (2015) evaluated the HRQoL in children with CAH, with a specific focus of comparing children with CAH and children with other endocrine conditions (hypothyroidism). Hypothyroidism was chosen because it too “requires the administration of daily medication and continuous medical assessment throughout childhood” (Yau et al., 2015, p.2). Based on both parent and child reports, children with CAH had an overall decrease in HRQoL compared to both healthy children and children with hypothyroidism in school functioning. Furthermore, CAH children more frequently reported peers not wanting to be friends.

Acute Illness and Managing and Averting Adrenal Crisis

Four studies focused on acute illness, stress dosing, and adrenal crisis experiences and management in children with CAH (Table 2.4). Three of the four examined the role that physical stress, such as exercise and acute illness, had on metabolic processes such as glucose regulation in children with CAH. In a randomized, double blind, crossover study from 2004, Weise et al. examined whether an extra dose of hydrocortisone would help normalize blood glucose levels in patients with CAH during exercise, as children with CAH do not mount the normal exercise-induced glucose response due to lack of cortisol production with physical activity (Weise et al., 2004; Green-Golan et al., 2007). The authors concluded that children with CAH do not benefit from additional hydrocortisone during short-term exercise, as the extra hydrocortisone did not increase blood glucose levels. Supporting

these findings, a 2010 study examined blood glucose levels and physical symptoms during typical acute viral or bacterial illnesses at home (Keil, Bosmans, Van Ryzin & Merke). Children with CAH who were being “stress dosed” appropriately during common childhood illnesses are at risk for hypoglycemia during the illness course. This suggests the need for additional glucose supplementation in addition to “stress dosing” during times of acute illness (Keil et al., 2010). Finally, a 2011 study assessed 60 caregivers’ knowledge of CAH, adrenal crisis, and stress dosing as well as their confidence in responding to adrenal crises (Fleming, Rapp & Sloane). The majority of caregivers responded that their child experiences a “crisis” situation an average of one to two times per year. Caregivers seemed to have a strong, basic understanding of the disorder; moreover, those that received both a written instruction guideline and a demonstration by clinicians on how to stress dose, both orally and via an injection, scored significantly higher when looking at self-efficacy (Fleming et al., 2011).

Discussion

Studies that met the inclusion criteria for this systematic review were primarily conducted using quantitative methods and were cross-sectional and descriptive in nature, with the sample population coming from either one institution or one city. Studies that use only samples from within one institution typically have the same group of pediatric endocrinologists treating children with CAH in a similar manner regarding medication dosing, family education, etc., which has the potential to affect the results, especially when looking at factors such as growth patterns. Many of the studies used structured measures, but did not report on their reliability and validity. Only one out of 39 studies involved an intervention (Lin-Su et al., 2011). This study examined the effect of growth hormone on final height in children with CAH, but was not a randomized, controlled study. Since most children

with CAH do not require growth hormone treatment, its applicability to the general CAH population is limited.

All of the investigators whose research focused on acute illness, stress dosing, and adrenal crisis either acknowledged having a small sample size (Keil et al., 2010; Fleming et al., 2011) or had a sample size less than 10 (Weise et al., 2004; Green-Golan et al., 2007). There were five studies that investigated body weight in children with CAH; however, only the Volkl et al. study accounted for parental BMIs and inquired about daily dietary intake for these children, making it difficult to know if the child's weight was directly influenced simply by the child having CAH and not environmental or familial factors.

Two of the studies dealing with the family experience were in developing countries where steroids were reported to be expensive based on the typical amount of family income, and parents in these studies reported that medication cost was a significant concern (Armstrong, Henderson, Hoan & Warne, 2006; Bhakhri & Jain, 2011). This particular difficulty is likely not to be as prevalent in more developed countries such as those in Europe or in Canada and the U.S.; thus, it is probable that a similar study conducted in these countries would yield different results.

Overall, there is a heavy emphasis placed on gender behavior and identity, yet very little research on how families manage the social challenges associated with girls born with ambiguous genitalia. With the exception of the Wong et al. and Nordenstrom et al. studies (2013, 2002) which involved the use of some observational methods, investigators relied on parents' reports of their child's play preferences over the course of their development. In addition, very few confounding variables (e.g. gender of other siblings) were addressed in the majority of studies investigating the effects of androgens on gender-related play and toy preferences. For example, a girl with CAH having three older brothers might be living in an environment where most toys were boy-typical. In addition, the observers who were interpreting the play behavior of the children in the studies and their training were not

described. Again, as reflected in previously discussed studies, investigators rarely collected data on aspects of family life such as marital status or parenting competence that could potentially influence child personality traits such as aggression and activity level. Since these studies focused on children, the lack of longitudinal studies, especially with regards to child preferences, is significant. The effects of excess prenatal androgens on both males and females with CAH have been studied in depth over the last fifteen years; however, there are few qualitative or mixed method studies on this issue. Ambiguous genitalia and the physical and emotional struggles associated with it are likely sensitive topics for research and the related effects might not be adequately represented in questionnaires and surveys completed by parents and children with CAH.

As stated, studies were focused primarily on potential health complications associated with CAH, emergency management of the disorder, and potential consequences of excess androgen exposure; however, few studies examined the implications of these significant problems on families managing their child's CAH. The lack of knowledge in this area limits the conclusions that can be made about family management and experience with CAH.

Future Implications for Practice and Research

While CAH has similarities to other chronic, life threatening illnesses such as type 1 diabetes and asthma, which have previously been studied through a family lens, more research is needed to identify the ways having a child with CAH intersects with family life. For example, when parents are not properly instructed on how to handle the emergency aspects of CAH management, the result can be not only improper use of emergency medical services (EMS) services and emergency departments in hospitals, but also, and more significantly, serious injury and possible death of the child. Understanding and identifying gaps in parent education by healthcare professionals, especially concerning

times of adrenal crisis, is necessary to promote positive outcomes, both from an emotional and physiological family perspective (Fleming, Rapp & Sloane, 2011). In addition, parents of girls born with CAH likely feel the need to keep their child's diagnosis of CAH more private due to potential stigmatization, which adds another challenge to a disorder that is already complex to manage. Acknowledging this difference and studying the effects of support systems designed specifically for girls born with CAH that address both the surgical procedures often associated with ambiguous genitalia as well as possible long-term complications resulting from being born with elevated testosterone is critical to promoting a healthy family response to the disorder. Future studies with an emphasis on family experience and management would enhance the current state of the science and provide a much-needed window into prospective interventions aimed at improving the lives of families and children with CAH.

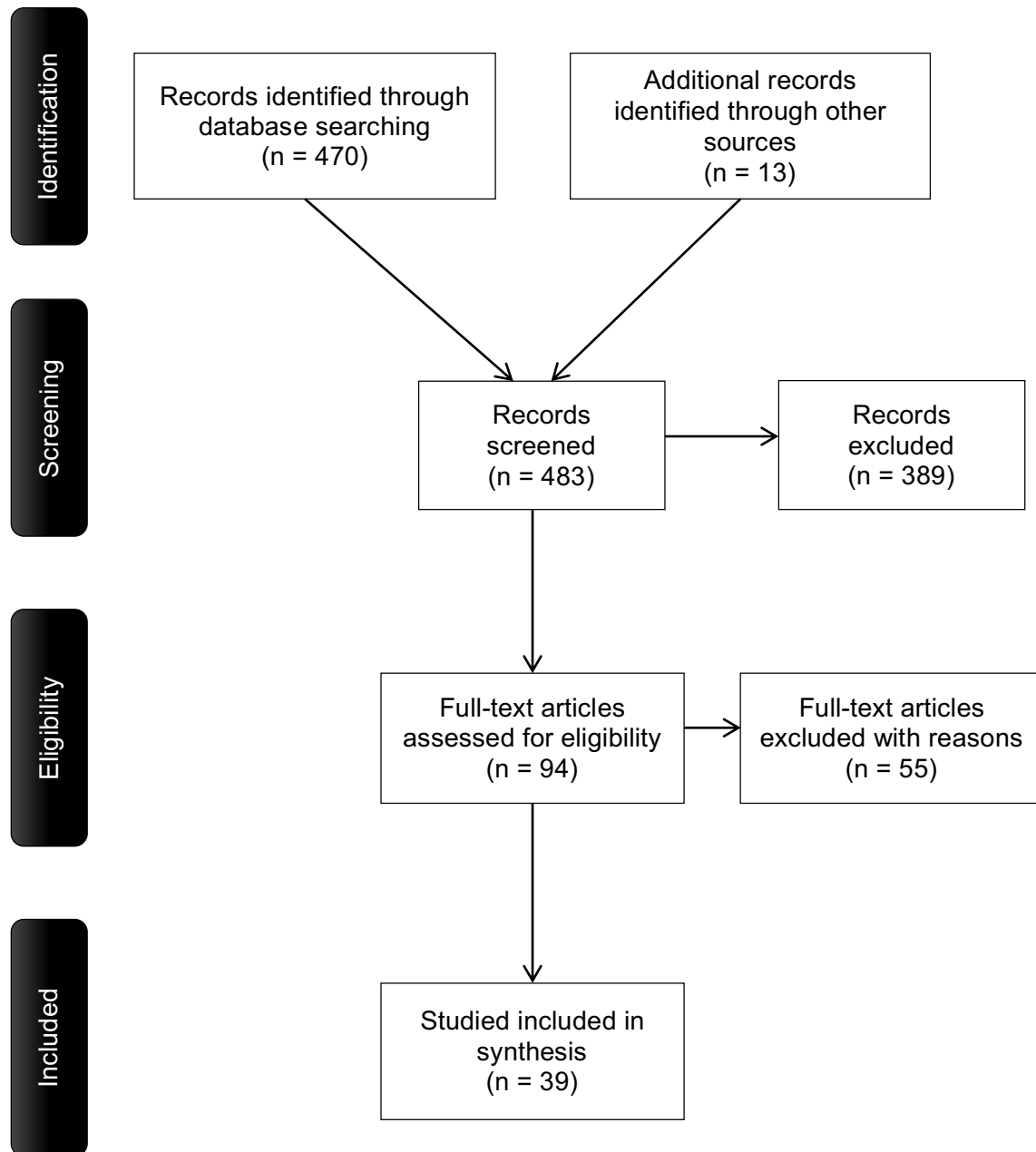


Figure 2.1. PRISMA flowchart

Table 2.1. Summary of Articles: Health Related Issues Associated with CAH Diagnosis

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Bonfig et al. (2007)	68 patients with salt-wasting CAH in one clinic	To determine final height outcome and influences of steroid treatment	Retrospective	Patients with CAH are able to achieve adequate final height with conventional therapy. Total pubertal growth is significantly decreased and treatment with prednisone results in decreased final height.
Bonfig et al. (2011)	51 patients with CAH ages birth to 3 years in Bavaria. Both genders.	To analyze growth patterns in children with CAH diagnosed by newborn screening and treated with relatively low doses of hydrocortisone during the first year of life.	Cross sectional/ Descriptive	Birth length is above average in children with classical CAH, which might be the result of untreated hyperandrogenism in utero. Relatively low doses of hydrocortisone treatment in the first 3 years results in heights that achieve genetic height potential.
Centinkaya & Kara (2011)	26 children with CAH and 11 healthy controls ages 2-15 years in Turkey. Both genders.	To evaluate the effects of glucocorticoid doses on bone mineral density (BMD) in children with CAH and to investigate other factors influencing BMD	Cross sectional/ Descriptive	Children with CAH have higher BMIs than healthy controls. The bone age of the poorly controlled group (looking at 17ohp), late diagnosed groups and male patients were higher than the tightly-controlled group, early diagnosed group and female patients.
Harrington et al. (2012)	14 patients with CAH and 28 obese and 53 healthy controls ages 9-20 in Australia. Both genders.	To establish whether children with CAH have reduced vascular function and increased carotid intima media thickness (cIMT) when compared to healthy and obese children.	Cross sectional/ Descriptive	CAH children have significant vascular endothelial and smooth muscle dysfunction when compared to healthy controls. The vascular dysfunction was comparable to the subjects with mild to moderate obesity.

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Idris et al. (2014)	49 patients between the ages of 6-18 that attend a medical center in Malaysia. Both genders.	To determine the status of the behavioral outcome in children with CAH compared to a control group of children without CAH and to identify the risk factors that may influence it	Cross sectional/ Descriptive	There was a higher incidence of parent reported problems of anxious/depressed and withdrawn/depressed behaviors, somatic complaints, social, thought, and attention problems and rule-breaking, aggressive, internalizing and externalizing behavior among CAH children compared to controls. Internalizing behavior problems were higher in CAH boys compared with controls; CAH girls had similar psychosocial adjustment to the control group. Family income (the lower the income, the more behavior problems) and glucocorticoid dose (the higher the dose, the more behavior problems) were significantly related to parent reported problem behavior.
Lin-Su et al. (2011)	34 patients with CAH treated with GH with a mean age of 8 yrs in New York, USA. Both genders.	Examine whether growth hormone (GH) alone or in combination with leutinizing hormone releasing hormone antagonist (LHRHa) improved the final adult height in patients with CAH	Non randomized/ Prospective with an intervention	GH alone or in combination with LHRHa improves final adult height in patients with CAH.
Medes-dos-Santos et al. (2011)	21 pre-pubertal patients ages 2-10 years old with CAH and 67 healthy controls in Brazil. Both genders.	To evaluate growth and body composition of patients with CAH and to compare them with healthy children	Cross sectional/ Retrospective/Descriptive	Patients had growth recovery with mean height similar to the general population; however, they had higher body fat, which seemed to be visceral, since there was not difference between the skinfolds of both groups.
Moreira et al. (2013)	33 patients ages 6-17 who attend a clinic in Sao Paulo, Brazil. Both genders.	To investigate the prevalence of obesity and metabolic syndrome in young patients with CAH and to correlated this prevalence with glucocorticoid treatment and family history	Cross sectional/ Comparative	CAH patients presented a higher prevalence of obesity and metabolic syndrome, which were not correlated with the glucocorticoid treatment suggesting that obesity and familial predisposition are significant determining factors for an adverse metabolic profile in CAH patients.
Nabhan et al. (2006)	71 patients with CAH ages 15 and younger in Indianapolis, USA. Both genders.	Investigate the incidence of urinary tract infections (UTIs) in children with CAH and to determine whether there was a correlation between timing and type of genital surgery in girls	Cross sectional/ Descriptive/Retro spective	The incidence of UTIs in children with CAH is similar to the general population. There is not a suggested increase in UTIs if genital surgery in girls is delayed.

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Volkl et al. (2006)	89 children and adolescents with ages birth through 17 in Bavaria. Both genders.	Analyze BMI values, compared with population-based references, for children and adolescents with CAH	Cross sectional/ Retrospective	Children and adolescents with CAH have a higher risk of obesity. Glucocorticoid dosage, chronologic age, advanced bone age maturation, and parental obesity contributed to elevated BMI SDS, whereas birth weight and length, serum leptin levels, used glucocorticoid, and mineralocorticoid dosage were not associated with obesity.

Table 2.2. Summary of Articles: Physical and Psychosocial Consequences from Exposure to Excess Androgens

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Al-Maghribi (2007)	The records of 73 children (39 were genetic females and 34 were genetic males) with CAH ages five months to 18 years in Jordan. Both genders	To evaluate the clinical features of all of the patients with CAH who were followed at the King Hussein Medical Center in Jordan from 1996-2006.	Descriptive/ Retrospective	Among the 39 females with CAH, 27 had developed anomalies of the external genitalia; 20 of them underwent surgical interventions of their external genitalia. Fourteen genetically female patients were wrongly diagnosed as 'male sex' at birth due to severe virilization. Seven of them were reassigned 'female sex' socially, legally, and surgically; the parents of one of them (a four-year-old girl) wanted the surgical intervention postponed for two to three years. Hysterectomy and gonadectomy were carried out for 6 of the other 7 patients who chose to keep the male genders.
Beltz et al. (2011)	125 individuals: 46 females with CAH; 21 without and 27 males with CAH; 31 without ages 9-26 years in Mid-western USA. Both genders.	To explore the contribution of sex hormones on occupational interests in females and males with CAH compared to their same gender, unaffected siblings.	Cross sectional/ Descriptive	Females with CAH had more interest in "things" versus "people" than unaffected females and variations among females were congruent with degree of exposure to androgens.
Berenbaum & Bailey (2003)	43 girls with CAH, 7 tomboys, and 29 sister/cousin controls ages 3-18 years in USA. All girls.	To study gender identity in girls with CAH in relation to characteristics of the disease and treatment, particularly genital appearance and surgery	Mixed Methods/ Descriptive	Gender identity in girls with CAH was not related to degree of genital virilization or age at which genital reconstructive surgery was done.
Berenbaum et al. (2012)	58 males and females with CAH and 27 unaffected siblings ages 16-30 in mid-western USA. Both genders.	To study effects of early androgens on spatial and mechanical abilities in adolescents and young adults with CAH	Cross sectional/ Descriptive	Increased spatial ability was enhanced for females with CAH compared to their unaffected sisters. Males with CAH showed reduced spatial abilities compared to their unaffected brothers.
Hines et al. (2003)	128 participants: 40 females and 29 males with CAH and 29 unaffected female and 30 unaffected male relatives of individuals with CAH ages 12-45 years in London. Both genders	To investigate the androgen influences on spatial abilities	Cross sectional/ Descriptive	Females with CAH performed better than unaffected females on spatial ability tests and resembled unaffected males and males with CAH. Males with CAH showed unaltered performance on the targeting tasks, and impaired performance on the mental rotations tasks.

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Knickmeyer et al. (2006)	60 individuals with CAH (34 females, 26 males), and 49 unaffected relatives age 12-45 years in London. Both genders.	To examine the hypothesis that autistic traits are increased following prenatal exposure to abnormally high levels of testosterone caused by CAH	Cross sectional/ Descriptive	Females with CAH scored significantly higher than unaffected females on the total Autism Spectrum Quotient questionnaire, largely due to enhanced scores on subscales measuring social skills and imagination.
Kulshreshtha et al. (2010)	3 individuals with CAH age 2 to 4 years that attend a clinic in India. Females	To report on the effect of steroid therapy during infancy and early childhood on the appearance of the external genitalia of girls with CAH.	Longitudinal/ Case Study	Unclear if patients in the study suffered from classical CAH, although that is the determination of the authors, despite none of the 3 children beginning steroid treatment until after the age of 2 months. There is improvement in the external appearance of genitalia with post-natal steroid therapy.
Maryniak et al. (2014)	33 females ranging from 6-23 years old from 19 at-risk CAH families (17 girls treatment prenatally with dexamethasone (9 affected; 8 non affected)) and 16 CAH affected females prenatally untreated. Poland.	To assess cognitive development and social and emotional function in girls prenatally treated with dexamethasone compared to female CAH patients who were not subjected to prenatal therapy	Mixed Methods/Cross sectional	Prenatal treatment with dexamethasone in CAH unaffected girls can cause the risk of unfavorable influences on the development of some cognitive functions.
Mathews et al. (2009)	128 participants belonging to 1 of 4 groups: 1. Females with CAH 2. Unaffected female relatives 3. Males with CAH and 4. Unaffected male relatives ages 12-44 in the London area. Both genders.	To investigate influences of early androgen exposure on personality	Cross sectional/ Descriptive	There are alterations in males and females with CAH in some personality facets that show sex differences. Females: tendencies to physical aggression and less tender minded. Males: less dominant, less rough and tumble play, more tender minded.
Meyer-Bahlberg et al. (2004)	Dexamethasone unexposed girls (15 with CAH and 30 without) and the dexamethasone unexposed boys without CAH ages 5-12 years old in the U.S. Both genders	To test in CAH girls of middle childhood the assumption that prenatal androgens determine the development of gender identity	Mixed Methods/ Descriptive	Prenatal androgenization female fetuses lead to marked masculinization of later gender-related behavior, but the absence of any increased gender-identity confusion/dysphoria. This concludes that a direct determination of gender identity by prenatal androgens does not support a male gender assignment at the birth of the most markedly masculinized girls.

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Nordenstrom et al. (2002)	40 females (from 35 families) with CAH in Sweden between the ages of 1-10.	To investigate the possible influence of disease severity (degree of fetal androgen exposure) on toy play and toy preference in girls with CAH.	Cross sectional/ Observational	Girls with CAH played more frequently with masculine toys than controls. Additionally, the degree of disease severity reflected in CYP21 genotype (ie. degree of fetal androgen exposure) contributed to the degree of masculinization of toy play and preference, with a higher degree of fetal androgen exposure correlating to increased likelihood of preferring masculine toys.
Ozbey et al. (2004)	70 female patients with CAH were counseled for gender assignment and had reconstructive surgery in Istanbul Turkey. Girls only.	To report experience of gender (re)assignment in genotypical female patients with CAH	Descriptive/ Retrospective	49 were reared as female and 21 as male. Only 9 of these "males" could be reassigned as females (mean age 7.87 months). It is extremely difficult to correct the gender of patients with female CAH when they present > 2.5 years of age.
Pasterski et al. (2005)	117 children (34 females and 31 males with CAH; 27 unaffected sisters and 25 unaffected brothers) ages 3-10 and parents. Los Angeles, USA.	To assess the toy choices of young children with CAH and their unaffected siblings as well as the parental encouragement of sex-typed toy play.	Cross sectional/ Observational	Girls with CAH displayed more male-typical toy choices than did their unaffected sisters, whereas boys with and without CAH did not differ. Mothers and fathers encouraged sex-typical toy play in children with and without CAH. Girls with CAH received more positive feedback for play with girls' toys than did unaffected girls.
Paterski et al. (2007)	113 children (36 girls, 29 boys with CAH; 25 unaffected sisters, 21 unaffected brothers) ages 3-11 and their mothers from the U.S and U.K. Both genders	To provide more definitive information on the effects of early androgen exposure on aggression and activity level by using a larger sample than in prior studies and by using a standardized questionnaire measure of current behavior	Cross Sectional/ Descriptive	Prenatal elevation in androgen that is experienced by females with CAH is associated with increased aggressive behavior and activity level in childhood. There were no significant differences in either aggressive behavior or activity level for boys with versus without CAH.

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Pasterski et al. (2015)	153 children total. 43 females and 38 males with CAH and 41 unaffected female and 31 unaffected male relatives, aged 4-11, living in the United Kingdom (England, Northern Ireland, Wales, and Scotland)	To investigate potential cross-gender identification in girls exposed prenatally to high concentrations of androgens due to classical CAH.	Cross sectional/ Mixed Methods	Girls with CAH had more cross-gender responses than female controls on all three measures of cross-gender identification as well as on a composite measure of gender identity independent of gender role behavior. Parent report showed 12.8% of the girls with CAH exhibited cross-gender behavior in all 5 behavioral domains compared to 0% of the children in the other three groups combined. The researchers concluded that prenatal androgen exposure could play a role in gender identity development in healthy children, and may be relevant to gender assignment in cases of prenatal hormone disruption.
Servin et al. (2003)	26 girls affected with CAH and 26 unaffected girls ages 2-10 years in Sweden. Girls only	3 aims: 1.to replicate and extend previous findings of masculinization of behavior in girls affected by CAH. 2.to investigate a possible relationship between disease severity and toy play 3. to explore possible parental influences on the behavior of the girls	Cross sectional/Observational	Girls with CAH were more interested in masculine toys and less interested in feminine toys and were more likely to report having male playmates and to wish for masculine careers. Parents of girls with CAH rated their daughters' behaviors as more boy like than did parents of unaffected girls. A relationship was found between disease severity and behavior indicating that more severely affected CAH girls were more interested in masculine toys and careers. No parental influence could be demonstrated on play behavior.
Woelfle et al. (2002)	16 completely virilized females in Germany between the ages of 8-49 years	To better understand specific problems of female CAH patients with complete virilization and male sex assignment	Cross sectional/ Descriptive	Patients with CAH and complete virilization have a high risk of being diagnosed late. There are significant negative challenges associated with gender reassignment. Gender identity is disturbed in some patients. Multiple surgical procedures are necessary and challenges with stature and precocious puberty are likely. Neonatal screening is of great importance to avoid some of these concerns.

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Wong et al. (2013)	The adolescent–adult sample included 40 females and 29 males with CAH and 29 female and 30 male unaffected relatives age 12–45 years recruited from UK. The child sample included 37 females and 31males with CAH and 27 female and 21 male unaffected relatives ages 3–10 years. Twenty-nine children with CAH and 13 unaffected relatives were recruited in the UK and 39 children with CAH and 35 unaffected relatives were recruited in Los Angeles, USA.	To assess parental encouragement of sex-typical toy play, as well as encouragement of spatial activities, in offspring with and without CAH. To evaluate the relationships between parental encouragement and offspring toy play and spatial ability.	Cross sectional/ Observational	Females with CAH showed more boy-typical toy play and better targeting performance than control females, but did not differ in mental rotations performance. Males with CAH showed worse mental rotations performance than control males, but did not differ in sex-typical toy play or targeting. Reported parental encouragement of girl-typical toy play correlated with girl-typical toy play in all four groups.

Table 2.3. Summary of Articles: The Lived Experience of Having CAH for Those Affected and Their Families

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Armstrong et al. (2006)	58 parents of children age 1 month -17 years with CAH in Hanoi Vietnam. Both genders.	To provide more specific insights into difficulties faced by families with CAH living in Vietnam	Cross sectional/ Descriptive	A child with CAH is a huge financial concern for parents. There is a need for both support groups and universal screening.
Bhakhri & Jain (2011)	28 individuals (17 males and 11 females) who are parents of 22 affected children aged < 5 years in New Delhi India.	To explore the perceptions and misconceptions of parents of children with CAH in India	Cross sectional/ Descriptive	There is a great deal of misconceptions, practices and concerns prevalent among the parents of children in India affected with CAH. These include gaps in knowledge concerning CAH, steroid use, medication, and ambiguous genitalia.
Boyse et al. (2014)	4 mothers and 2 fathers from four separate families having a child with CAH (children's ages were 5-11 with 2 males and 2 females). USA.	To characterize early parent caregiver experiences and needs in CAH with a focus on contextual factors that can be modulated through education and support delivered by health care providers or via the newborn screening system.	Qualitative/ Descriptive	Several themes emerged from the interviews including health communication problems, a lack of medical home and decision support, and a desire for parent-to-parent social support.
de Silva et al. (2014)	37 parents (26 mothers and 11 fathers) of children (both genders) with CAH who attended an endocrinology center in Sri Lanka.	To determine the depressive symptoms in parents of children with CAH	Cross sectional/ Descriptive	59% of the parents of children with CAH were classified as having symptoms of depression, and these depressive symptoms did not abate with the passage of time.
Gilban, Alves, & Beserra (2014)	25 patients (age 5-18 years) with CAH in Brazil as well as their parents. There were 19 female patients and 6 were male. Among the 19 female patients, 2 identified as male. Brazil.	To evaluate the health related quality of life of children and adolescents with CAH	Cross sectional/ Descriptive	There is a loss of health related quality of life in children and adolescents with classical CAH. The self-assessment was concordant in key areas with the assessment made by their parents. No differences were observed between genders or clinical presentation of the disease.
Sanches et al. (2012)	104 parents of children with CAH age 0-18 years as	To investigate the physical, social, and societal functioning of children with CAH and their parents in a	Cross sectional/ Descriptive	Children with CAH, according to their parents, experience few negative effects of the condition and they participate well in several areas such as school

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
	well as 24 adolescents with CAH living in The Netherlands. Both genders.	Dutch population.		and leisure time. Improvements can be made concerning the measures parents and children must take to prevent an adrenal crisis.
Yau et al. (2015)	Children with CAH (n=33) as well as children with hypothyroidism (n=14) and their parents were recruited from a university based pediatric endocrinology clinic in Los Angeles, USA. Both genders.	To evaluate health related quality of life in children with CAH and investigate whether CAH poses an additional burden compared to other endocrine disorders.	Cross sectional/ Descriptive	Compared to subjects with hypothyroidism, children with CAH self-reported lower health related quality of life in school domain scores. CAH children more frequently reported peers not wanting to be friends. There was a strong correlation between child self report and parent proxy report.

Table 2.4. Summary of Articles: Acute Illness, Stress Dosing, and Adrenal Crisis Experiences and Management

Author (Year)	Sample/Setting	Purpose	Study Design	Conclusions
Fleming et al. (2011)	60 caregivers of children ages 0-16 with CAH in Los Angeles, CA. Both genders.	To assess caregiver knowledge of CAH, adrenal crisis, and stress dosing and to assess their confidence in managing adrenal crisis and stress dosing of children with CAH. Further the relationship between caregiver knowledge and self-efficacy was examined.	Cross sectional/ Descriptive	Caregivers had a good understanding of CAH but those that received both a written instruction guideline and a demonstration on how to give the hydrocortisone injection scored higher on both self efficacy of stress dosing and self efficacy of how to give the injection
Green-Golan et al. (2007)	6 adolescents with CAH ages 16-20yrs were compared with 7 age sex and BMI matched controls (16-23yrs) using a 90 min standardized ergometer test. National Institutes of Health in Bethesda, MD. Both genders.	To assess hormonal, metabolic, and cardiovascular response to prolonged moderate intensity exercise comparable to brisk walking in adolescents with classic CAH	Cross sectional/ Observational	Patients with CAH have defective glycemic control evident in prolonged moderate intensity exercise. CAH patients have difficulty maintaining glucose levels as exercise duration increases.
Keil et al. (2010)	20 patients with CAH ages 3-10 enrolled in a long-term study at National Institutes of Health in Bethesda, MD. Both genders.	Examine blood glucose levels and symptoms of children with CAH during a physical stressor, such as a typical acute illness managed at home, and prospectively determine the frequency of hypoglycemia	Longitudinal	Children with CAH, despite receiving adequate glucocorticoid and mineralocorticoid supplementation, are at risk for hypoglycemia during common childhood illnesses.
Weise et al. (2004)	9 adolescent children with CAH and 9 adolescent children without CAH-done at National Institutes of Health in Bethesda MD	To examine whether an extra dose of hydrocortisone, similar to that given during other forms of physical stress, would normalize blood glucose levels during exercise in patients with CAH	Cross sectional/ Observational	Patients with classical CAH do not benefit from additional hydrocortisone during short-term, high intensity exercise.

REFERENCES

- Al-Maghribi, H. (2007). Congenital adrenal hyperplasia: Problems with developmental anomalies of the external genitalia and sex assignment. *Saudi Journal of Kidney Diseases and Transplantation : An Official Publication of the Saudi Center for Organ Transplantation, Saudi Arabia*, 18(3), 405-413.
- Armstrong, K. L., Henderson, C., Hoan, N. T., & Warne, G. L. (2006). Living with congenital adrenal hyperplasia in vietnam: A survey of parents. *Journal of Pediatric Endocrinology & Metabolism : JPEM*, 19(10), 1207-1223.
- Barlow, J., & Ellard, D. (2006). The psychosocial wellbeing of children with chronic disease, their parents and siblings: An overview of the research evidence base. *Child: Care Health & Development*, 32(1), 19-31.
- Beltz, A. M., Swanson, J. L., & Berenbaum, S. A. (2011). Gendered occupational interests: Prenatal androgen effects on psychological orientation to things versus people. *Hormones and Behavior*, 60(4), 313-317. doi:10.1016/j.yhbeh.2011.06.002; 10.1016/j.yhbeh.2011.06.002
- Berenbaum, S. A., & Bailey, J. M. (2003). Effects on gender identity of prenatal androgens and genital appearance: Evidence from girls with congenital adrenal hyperplasia. *The Journal of Clinical Endocrinology and Metabolism*, 88(3), 1102-1106.
- Berenbaum, S. A., Korman Bryk, K., Duck, S. C., & Resnick, S. M. (2004). Psychological adjustment in children and adults with congenital adrenal hyperplasia. *The Journal of Pediatrics*, 144(6), 741-746. doi:10.1016/j.jpeds.2004.03.037
- Berenbaum, S., Bryk, K., & Beltz, A. (2012). Early androgen effects on spatial and mechanical abilities: evidence from congenital adrenal hyperplasia. *Behavioral Neuroscience*, 126(1), 86-96. Doi: 10.1037/a0026652
- Bhakhri, B. K., & Jain, V. (2011). Congenital adrenal hyperplasia: As viewed by parents of affected children in india--a pilot study. *Journal of Pediatric Endocrinology & Metabolism*, 24(11-12), 959-963.
- Bonfig, W. (2007). Reduced final height outcome in congenital adrenal hyperplasia under prednisone treatment: Deceleration of growth velocity during puberty. *The Journal of Clinical Endocrinology and Metabolism*, 92(5), 1635; 1635-1639; 1639.
- Bonfig, W., Schmidt, H., & Schwarz, H. P. (2011). Growth patterns in the first three years of life in children with classical congenital adrenal hyperplasia diagnosed by newborn screening and treated with low doses of hydrocortisone. *Hormone Research in Paediatrics*, 75(1), 32-37. doi:10.1159/000316973
- Boyse, K. L., Gardner, M., Marvicsin, D. J., & Sandberg, D. E. (2014). "It was an overwhelming thing": Parents' needs after infant diagnosis with congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 29(5), 436-441. doi:10.1016/j.pedn.2014.01.007

- Cabizuca, M., Marques-Portella, C., Mendlowicz, M., Coutinho, E., & Figueira, I. (2009). Posttraumatic stress disorder in parents of children with chronic illnesses: A meta-analysis. *Health Psychology, 28*(3), 379-388. doi 10.1037/a0014512
- Cetinkaya, S., & Kara, C. (2011). The effect of glucocorticoid replacement therapy on bone mineral density in children with congenital adrenal hyperplasia. *Journal of Pediatric Endocrinology & Metabolism : JPEM, 24*(5-6), 265-269.
- de Silva, K. S., de Zoysa, P., Dilanka, W. M., & Dissanayake, B. S. (2014). Psychological impact on parents of children with congenital adrenal hyperplasia: A study from sri lanka. *Journal of Pediatric Endocrinology & Metabolism : JPEM, 27*(5-6), 475-478. doi:10.1515/jpem-2013-0267
- Everhart, R. S., Fiese, B. H., & Smyth, J. M. (2008). A cumulative risk model predicting caregiver quality of life in pediatric asthma. *Journal of Pediatric Psychology, 33*(8), 809-818. doi: 10.1093/jpepsy/jpn028
- Fleming, L. K., Rapp, C. G., & Sloane, R. (2011). Caregiver knowledge and self-confidence of stress dosing of hydrocortisone in children with congenital adrenal hyperplasia. *Journal of Pediatric Nursing, 26*(6), e55-60. doi:10.1016/j.pedn.2011.03.009; 10.1016/j.pedn.2011.03.009
- Gilban, D. L., Alves Junior, P. A., & Beserra, I. C. (2014). Health related quality of life of children and adolescents with congenital adrenal hyperplasia in brazil. *Health and Quality of Life Outcomes, 12*, 107-014-0107-2. doi:10.1186/s12955-014-0107-2
- Goldbeck, L. (2006). The impact of newly diagnosed chronic paediatric conditions on parental quality of life. *Quality of Life Research, 15*(7), 1121-1131.
- Green-Golan, L., Yates, C., Drinkard, B., VanRyzin, C., Eisenhofer, G., Weise, M., & Merke, D. P. (2007). Patients with classic congenital adrenal hyperplasia have decreased epinephrine reserve and defective glycemic control during prolonged moderate-intensity exercise. *Journal of Clinical Endocrinology & Metabolism, 92*(8), 3019-3024.
- Grey, M., Jaser, S. S., Whittemore, R., Jeon, S., & Lindemann, E. (2011). Coping skills training for parents of children with type 1 diabetes: 12-month outcomes. *Nursing Research, 60*(3), 173. Doi: 10.1097/NNR.0b013e3182159c8f
- Hall, D. E. (2011). The care of children with medically complex chronic disease. *The Journal of Pediatrics, 159*(2), 178-180. doi: 10.1016/j.jpeds.2011.03.031
- Harrington, J., Peña, A. S., Gent, R., Hirte, C., & Couper, J. (2012). Adolescents with congenital adrenal hyperplasia because of 21-hydroxylase deficiency have vascular dysfunction. *Clinical Endocrinology, 76*(6), 837-842.
- Hines, M., Fane, B. A., Pasterski, V. L., Mathews, G. A., Conway, G. S., & Brook, C. (2003). Spatial abilities following prenatal androgen abnormality: Targeting and mental rotations performance in individuals with congenital adrenal hyperplasia. *Psychoneuroendocrinology, 28*(8), 1010-1026.

- Idris, A. N., Chandran, V., Syed Zakaria, S. Z., & Rasat, R. (2014). Behavioural outcome in children with congenital adrenal hyperplasia: Experience of a single centre. *International Journal of Endocrinology*, 2014, 483718. doi:10.1155/2014/483718
- Keil, M. F., Bosmans, C., Van Ryzin, C., & Merke, D. P. (2010). Hypoglycemia during acute illness in children with classic congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 25(1), 18-24. doi:10.1016/j.pedn.2008.06.003
- Kim, M. S., Ryabets-Lienhard, A., & Geffner, M. E. (2012). Management of congenital adrenal hyperplasia in childhood. *Current Opinion in Endocrinology, Diabetes, and Obesity*, 19(6), 483-488. doi:10.1097/MED.0b013e32835a1a1b; 10.1097/MED.0b013e32835a1a1b
- Knickmeyer, R., Baron-Cohen, S., Fane, B. A., Wheelwright, S., Mathews, G. A., Conway, G. S., ... & Hines, M. (2006). Androgens and autistic traits: A study of individuals with congenital adrenal hyperplasia. *Hormones and Behavior*, 50(1), 148-153.
- Kulshreshtha, B., Khadgawat, R., Eunice, M., & Ammini, A. C. (2010). Congenital adrenal hyperplasia: Results of medical therapy on appearance of external genitalia. *Journal of Pediatric Urology*, 6(6), 555-559. doi:10.1016/j.jpuro.2010.01.001
- Lin-Su, K., Harbison, M. D., Lekarev, O., Vogiatzi, M. G., & New, M. I. (2011). Final adult height in children with congenital adrenal hyperplasia treated with growth hormone. *Journal of Clinical Endocrinology & Metabolism*, 96(6), 1710-1717. doi:10.1210/jc.2010-2699
- Ludder-Jackson, P. & Vessey, J. (1996). *Primary Care of the Child with a Chronic Condition*. (2nd edition). St. Louis: Mosby.
- Maryniak, A., Ginalska-Malinowska, M., Bielawska, A., & Ondruch, A. (2014). Cognitive and social function in girls with congenital adrenal hyperplasia -- influence of prenatally administered dexamethasone. *Child Neuropsychology : A Journal on Normal and Abnormal Development in Childhood and Adolescence*, 20(1), 60-70. doi:10.1080/09297049.2012.745495
- Mathews, G. A., Fane, B. A., Conway, G. S., Brook, C. G., & Hines, M. (2009). Personality and congenital adrenal hyperplasia: Possible effects of prenatal androgen exposure. *Hormones and Behavior*, 55(2), 285-291. doi:10.1016/j.yhbeh.2008.11.007; 10.1016/j.yhbeh.2008.11.007
- Matos, D., personal communication, January 16, 2016.
- Mendes-Dos-Santos, C. T., Lemos-Marini, S. H., Baptista, M. T., Guerra-Junior, G., De-Mello, M. P., Paulino, M. F., & Morcillo, A. M. (2011). Normalization of height and excess body fat in children with salt-wasting 21-hydroxylase deficiency. *Journal of Pediatrics*, 87(3), 263-268. doi:doi:10.2223/JPED.2095; doi:10.2223/JPED.2095
- Merke, D. P., & Bornstein, S. R. (2005). Congenital adrenal hyperplasia. *Lancet*, 365(9477), 2125-2136. Retrieved from https://auth.lib.unc.edu/ezproxy_auth.php?url=http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=2009043786&site=ehost-live&scope=site

- Meyer-Bahlburg, H. F., Dolezal, C., Baker, S. W., Carlson, A. D., Obeid, J. S., & New, M. I. (2004). Prenatal androgenization affects gender-related behavior but not gender identity in 5-12-year-old girls with congenital adrenal hyperplasia. *Archives of Sexual Behavior*, 33(2), 97-104. doi:480175
- Moreira, R. P., Villares, S. M., Madureira, G., Mendonca, B. B., & Bachega, T. A. (2013). Obesity and familial predisposition are significant determining factors of an adverse metabolic profile in young patients with congenital adrenal hyperplasia. *Hormone Research in Paediatrics*, 80(2), 111-118. doi:10.1159/000353762
- Nabhan, Z. M., Rink, R. C., & Eugster, E. A. (2006). Urinary tract infections in children with congenital adrenal hyperplasia. *Journal of Pediatric Endocrinology and Metabolism*, 19(6), 815-820.
- Newacheck, P. W., & Halfon, N. (1998). Prevalence and impact of disabling chronic conditions in childhood. *American Journal of Public Health*, 88(4), 610-617.
- Nimkarn, S. & New, M. (2009). Prenatal diagnosis and treatment of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Molecular and Cellular Endocrinology*, 300, 192-196. doi: 10.1016/j.mce.2008.11.027
- Nordenstrom, A., Servin, A., Bohlin, G., Larsson, A., & Wedell, A. (2002). Sex-typed toy play behavior correlates with the degree of prenatal androgen exposure assessed by CYP21 genotype in girls with congenital adrenal hyperplasia. *The Journal of Clinical Endocrinology and Metabolism*, 87(11), 5119-5124. doi:10.1210/jc.2001-011531
- Ozbey, H., Darendeliler, F., Kayserili, H., Korkmazlar, U., & Salman, T. (2004). Gender assignment in female congenital adrenal hyperplasia: A difficult experience. *BJU International*, 94(3), 388-391. doi:10.1111/j.1464-410X.2004.04967.x
- Pasterski, V. L., Geffner, M. E., Brain, C., Hindmarsh, P., Brook, C., & Hines, M. (2005). Prenatal hormones and postnatal socialization by parents as determinants of male-typical toy play in girls with congenital adrenal hyperplasia. *Child Development*, 76(1), 264-278. doi:CDEV843
- Pasterski, V., Hindmarsh, P., Geffner, M., Brook, C., Brain, C., & Hines, M. (2007). Increased aggression and activity level in 3- to 11-year-old girls with congenital adrenal hyperplasia (CAH). *Hormones and Behavior*, 52(3), 368-374. doi:10.1016/j.yhbeh.2007.05.015
- Pasterski, V., Zucker, K. J., Hindmarsh, P. C., Hughes, I. A., Acerini, C., Spencer, D., . . . Hines, M. (2015). Increased cross-gender identification independent of gender role behavior in girls with congenital adrenal hyperplasia: Results from a standardized assessment of 4- to 11-year-old children. *Archives of Sexual Behavior*, 44(5), 1363-1375. doi:10.1007/s10508-014-0385-0
- Perrin E., Newacheck P., Pless I., et al. (1993). Issues involved in the definition and classification of chronic health conditions. *Pediatrics* (93), 787-793.
- Popp, J. M., Robinson, J. L., Britner, P. A., & Blank, T. O. (2014). Parent adaptation and family functioning in relation to narratives of children with chronic illness. *Journal of*

- Sanches, S. A., Wiegers, T. A., Otten, B. J., & Claahsen-van der Grinten, H. L. (2012). Physical, social and societal functioning of children with congenital adrenal hyperplasia (CAH) and their parents, in a dutch population. *International Journal of Pediatric Endocrinology*, 2012(1), 2-9856-2012-2. doi:10.1186/1687-9856-2012-2
- Schaeffer, T. (2011). The role of the nurse educator in a multidisciplinary clinic for patients and families affected by congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. *Journal of Pediatric Nursing* 26(3), 275-276. doi:10.1016/j.pedn.2011.04.007
- Servin, A., Nordenström, A., Larsson, A., & Bohlin, G. (2003). Prenatal androgens and gender-typed behavior: A study of girls with mild and severe forms of congenital adrenal hyperplasia. *Developmental Psychology*, 39(3), 440-450. doi:10.1037/0012-1649.39.3.440
- Speiser, P. (2011). During illness and emergency. Retrieved from CARES Foundation website: http://www.caresfoundation.org/productcart/pc/Adrenal_Crisis.html
- Speiser, P. W., Azziz, R., Baskin, L. S., Ghizzoni, L., Hensle, T. W., Merke, D. P., . . . White, P. C. (2010). A summary of the endocrine society clinical practice guidelines on congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency. *International Journal of Pediatric Endocrinology*, 2010. doi:10.1155/2010/494173; 10.1155/2010/494173
- Speiser, P. (2011). During illness and emergency. Retrieved from CARES Foundation website: http://www.caresfoundation.org/productcart/pc/Adrenal_Crisis.html
- Stein, R., Bauman, L., Westbrook, L., Coupey, S., & Ireys, H. (1993). Framework for identifying children who have chronic conditions: the case for a new definition. *The Journal of Pediatrics*, 122(3), 342-347.
- van Oers, H. A., Haverman, L., Limperg, P. F., van Dijk-Lokkart, E. M., Maurice-Stam, H., & Grootenhuys, M. A. (2014). Anxiety and depression in mothers and fathers of a chronically ill child. *Maternal and Child Health Journal*, 18(8), 1993-2002. doi 10.1007/s10995-014-1445-8
- Völkl, T., Simm, D., Beier, C., & Dörr, H. (2006). Obesity among children and adolescents with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Pediatrics*, 117(1), e98-105. Retrieved from https://auth.lib.unc.edu/ezproxy_auth.php?url=http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=2009115275&site=ehost-live&scope=site
- Weise, M., Mehlinger, S. L., Drinkard, B., Rawson, E., Charmandari, E., Hiroi, M., ... & Merke, D. P. (2004). Patients with classic congenital adrenal hyperplasia have decreased epinephrine reserve and defective glucose elevation in response to high-intensity exercise. *Journal of Clinical Endocrinology & Metabolism*, 89(2), 591-597.
- Whittemore, R., Knafl, K., (2005). The integrative review: updated methodology. *Journal of Advanced Nursing* 52, 546–553.

- Witchel, S. F., & Azziz, R. (2011). Congenital adrenal hyperplasia. *Journal of Pediatric and Adolescent Gynecology*, 24(3), 116-126. doi:10.1016/j.jpag.2010.10.001; 10.1016/j.jpag.2010.10.001
- Woelfle, J., Hoepffner, W., Sippell, W. G., Bramswig, J. H., Heidemann, P., Deiss, D., . . . Albers, N. (2002). Complete virilization in congenital adrenal hyperplasia: Clinical course, medical management and disease-related complications. *Clinical Endocrinology*, 56(2), 231-238. doi:1463
- Wong, W. I., Pasterski, V., Hindmarsh, P. C., Geffner, M. E., & Hines, M. (2013). Are there parental socialization effects on the sex-typed behavior of individuals with congenital adrenal hyperplasia? *Archives of Sexual Behavior*, 42(3), 381-391. doi:10.1007/s10508-012-9997-4
- Yau, M., Vogiatzi, M., Lewkowitz-Shpuntoff, A., Nimkarn, S., & Lin-Su, K. (2015). Health-Related Quality of Life in Children with Congenital Adrenal Hyperplasia. *Hormone Research in Paediatrics*, 84(3), 165-171. doi: 10.1159/00043585

CHAPTER 3: PARENTAL MANAGEMENT OF ADRENAL CRISIS IN CHILDREN WITH CONGENITAL ADRENAL HYPERPLASIA

Introduction

Chronic conditions in children dramatically change the meaning of parenting and have varied impacts on family life (Knafl et. al, 2013). Classic congenital adrenal hyperplasia (CAH) is a rare, genetic, endocrine disorder that affects approximately 1 in 15,000 live births annually (Speiser et al., 2010) and is one such condition. Management of CAH requires parents to administer steroids, typically oral hydrocortisone, up to three times daily, supplementing maintenance doses with oral “stress dosing” during times of illness and an emergency intramuscular (IM) injection of hydrocortisone when a child is unable to tolerate oral medications and/or if signs of adrenal crisis are present (Merke & Bornstein, 2005; Speiser et al., 2010; Witchel & Azziz, 2011). The need for stress dosing, either orally or by injection, related to simple viral and bacterial childhood illnesses is frequent and unpredictable, often requiring parents to make complex treatment decisions (Merke & Bornstein, 2005).

Despite the importance of being able to effectively respond to an adrenal crisis episode, a 2011 study by the author showed that only half of the 60 parents of children with CAH surveyed reported ever having received a demonstration from a health care professional on how to administer the emergency injection of hydrocortisone (Fleming, Rapp, & Sloane, 2011). Additionally, although parents reported that these children experienced adrenal crisis one to two times per year, 39% of parents had not received a prescription for injectable hydrocortisone at the time of diagnosis, though that is the standard of care (Fleming et al., 2011; Speiser et al., 2010). Moreover, the type of

emergency education given to parents by providers, such as written instructions, injection demonstration, and when to go to an emergency department of a hospital varied considerably (Fleming et al., 2011). Adrenal crisis events are inherently stressful for parents and a lack of detailed, ongoing, thorough education from health care providers to parents on how to best handle such occurrences increases parental stress regarding ability to respond effectively in an emergency (Fleming et al, 2011).

CAH shares characteristics of episodic, life-threatening crises with other, more prevalent, chronic childhood conditions such as type I diabetes, asthma, and anaphylactic food allergies (Harris et. al, 2002; Barnard et. al., 2010; Sicherer et. al, 2010). As with CAH, prior research in the pediatric diabetes community suggests that parental fear over times of crisis is related to a lack of thorough and repeated education from health care providers on how to best handle these crises (Harris et. al, 2002; Barnard et. al., 2010; Sullivan-Bolyai et. al, 2010). In a descriptive study of parents of school-age children with diabetes who were attending a summer education camp, over half (69%) of parents reported experiencing crisis management difficulties such as opening the injection kit and removing the sheath. Moreover, approximately a fourth of the parents injected an incorrect dose during simulation (Harris et. al, 2002).

In addition to the life-threatening aspect of CAH, parents must also handle day to day maintenance, which includes replacing deficient levels of cortisol and/or aldosterone, while attempting to minimize androgen excess, prevent virilization, optimize linear growth (which is often compromised) and protect future fertility (Merke & Bornstein, 2005). If a child is prescribed too much hydrocortisone, side effects can include growth suppression, obesity, and other cushingoid features. If the dose of hydrocortisone is not sufficient, children with CAH are at a high risk for precocious puberty, which can also lead to stunted growth and adrenal crisis. Determining the proper dosage of steroids is typically achieved by obtaining

routine laboratory work and measuring the height, weight and bone age, typically every 3-6 months, in a growing child (Merke & Bornstein, 2005).

The aims of this study involve acute management of the condition. They include describing circumstances surrounding adrenal crisis events in children with CAH (ie. causes and frequency, parental preparation, preparation of others caring for the child); exploring parents' perceptions of the consequences of having a child with a life threatening condition; and examining the relationship between parents' management ability and the impact CAH has on the family.

Methods

Guiding Framework

This study was guided by the Family Management Style Framework (FMSF), which provides a structure for understanding family responses to a child's chronic condition (Knafl, Deatrick, & Havill, 2012) (Figure 3.1). The FMSF is grounded in the originators' research and syntheses of studies of family life in the context of childhood chronic conditions. It has been used in studies with families exploring the overall response to the child's condition as well as studies of selected aspects of their response (e.g., information management) (Knafl et al., 2012). According to the FMSF, individuals in the family contribute to developing a family management style or pattern of response that can influence both individual and family outcomes (Knafl et al., 2012, Knafl et al., 2013). The framework is comprised of three components: *definition of the situation* (the ways in which the child and child's condition is viewed by the parent(s), management mindset, and parental mutuality), *management behaviors* (parenting goals, strategies, and behaviors linked to caring for a chronically ill child), and *perceived consequences* (actual or expected family, child, and illness outcomes that shape management behaviors) (Knafl et al., 2012; Knafl et al., 2013). Table 3.1 outlines how the study aims are linked to the FMSF.

Design

This descriptive, mixed methods study was conducted in two phases. In Phase 1, parents were asked to complete online questionnaires about selected aspects of their experiences of family life in the context of having a child with CAH. In Phase 2, semi-structured qualitative interviews were conducted to elicit more detailed descriptions of parents' experiences in managing CAH-related crises and their perceptions of how the consequences of living with the threat of crisis influenced their child's and their family's life. The purposive intent of the Phase 2 interview sample was to achieve maximum variation in terms of both the demographic profile of families (e.g., parents of boys and girls, families having children of varying ages, families from different geographic areas of the U.S, etc.) and their experiences managing adrenal crisis events. Scores on the structured measures in Phase 1 were also examined so that parents reporting both high and low impact of the condition on their family as well as management ability were included in Phase 2. This design allowed for comparison and corroboration of the quantitative results with qualitative findings (Creswell & Clark, 2010) and provided a rich, comprehensive description of parents' crisis management strategies and their perceptions of the adrenal crisis education they had received from health care providers.

Participants

Parents were recruited through the CARES Foundation (CARES), a non-profit organization, based in New Jersey, which provides support to families having a child with CAH (CARES (Congenital Adrenal hyperplasia-Research, Education, and Support) Foundation, 2014). To be included in the study, the parent needed to be over the age of 18, English speaking, and have a child between the ages of birth and 18 years diagnosed with classic, salt-wasting CAH and free from any other complex health conditions. Furthermore, parents needed to have access to a telephone, computer, and email account. A parent was defined as a person who lived in the same household with the child and had the

responsibility of caring for the child and managing the child's CAH, even if the parent was not the biological mother or father. Recruitment for the study consisted of an "Invitation to Participate" letter that CARES emailed to its members who had previously expressed an interest in participating in research. In addition, CARES provided a brief description of this research study within the research section of their website.

Measures

Data were collected through a demographic/family information questionnaire, the Pediatric Quality of Life-Family Impact Module (PedsQL-FIM), two scales from the Family Management Measure (FaMM)-- View of Condition Impact and Management Ability, and an individual semi-structured interview using an interview guide (with each parent participating separately). The demographic/family information questionnaire included information about the family, the child's health status, and the frequency of adrenal crisis experience(s). The demographic/family information questionnaire was also used to gather data about the provider the child saw to manage CAH as well as how and when, if ever, the parent was instructed about management of an adrenal crisis. The PedsQL-FIM and the FaMM-View of Condition Impact and Management Ability scales provided additional information on the effects of living with a child who has a life threatening illness. Varni's 36-item Peds QL-FIM is designed to measure parent self-reported perceptions of the impact of the condition on their physical, emotional, social and cognitive functioning; communication; and worry. The measure also examines parent-reported family daily activities and family relationships (Varni, Sherman, Burwinkle, Dickinson, & Dixon, 2004). In prior studies, the Peds QL-FIM internal consistency reliability coefficients have ranged from .82-.97 (Varni et al., 2004). Additionally, the 10-item FaMM-View of Condition Impact scale is designed to address parents' perceptions of the seriousness of the condition and its implications for their child's and their family's future (Knafl et al., 2012). The scale has well established validity and reliability. In a study of over 400 families in which a child had a chronic condition, the internal

consistency reliability coefficients for the scale were .73 for mothers and .77 for fathers (Knafl et al., 2012). The 12-item FaMM-Management Ability scale addresses parents' perceptions of the overall manageability of the child's condition, including knowing what needs to be done to take care of the condition and their ability to competently carry out the management of their child's condition (Knafl et al., 2012). The internal consistency reliability coefficients for this scale were .72 for mothers and .73 for fathers (Knafl et al., 2012). Use of these measures contributed to a more complete understanding of parents' perceptions of the impact of their child's CAH on themselves and family life.

Phase 2 of the study entailed qualitative telephone interviews with the subsample of parents who participated in Phase 1. Topics for the interview guide focused on parents' description of their crises management experiences and their perceived competence and ability to manage crises based on the three components of the FMSF. (Figure 3.2)

Data Collection

Phase 1. In Phase 1, following IRB approval, parents of children with CAH were recruited via an email from the CARES Foundation and interested participants then contacted the author via telephone, email, or text message. After consent was obtained, the demographic/family information questionnaire and the three measures were made available to the participants in one document via an online survey using Qualtrics software. Each person participating in the survey (including parents in the same family) received a secure, individualized electronic link.

Phase 2. After the survey information was completed and analyzed, a purposive sample was generated for Phase 2, and the author contacted the selected parent(s) who were willing to be interviewed. When both parents were participating, parents were asked to complete the questionnaires separately so that one parent did not influence the other's responses. Each parent in Phase 2 was interviewed separately to provide a full accounting

of their individual experiences. Data collection continued during Phase 2 until common themes repeatedly emerged to the point of saturation (Bowen, 2008).

Data Analysis

Phase 1. Using the family information questionnaire, descriptive statistics were computed for both parents and children including variables such as age, gender, household income, as well as examining the timing of when, or if, providers gave parents the prescription for injectable hydrocortisone. Then, six separate analyses were done using linear mixed models allowing for the variance to be different for fathers and mothers (compound symmetry heterogeneous covariance). The first relationship examined was between parental management ability and whether providers had demonstrated to parents how to give the injection. The second analysis investigated the relationship between parental management ability and child age. Next, the relationship between the impact the condition has on the family (FaMM-View of Condition Impact and PedsQL-Family Impact Module) and management ability (FaMM-Management Ability Scale) was examined.

Finally, the relationship between age of the child and the number of adrenal crisis events was examined. In the family information questionnaire, parents were asked to categorize the number of adrenal crisis events their child had experienced to date (no crisis events; 1-2 crisis events; 3-5 crisis events; or 5 or greater crisis events). The lowest number in each category was normalized (to obtain a minimum number of adrenal crisis events) with the current age of the child (to obtain a minimum number of adrenal crisis events per year) and modeled as a function of age less than or equal to five years or greater than five years. The age of five was chosen based on several factors including the child beginning school and being able to better articulate how they are feeling as well as parental responses when asked how their view of the condition has changed over the years in the Phase 2 interviews. Then, the relationship between the minimum number of adrenal crises per year and age of

the child was modeled as possibly non-linear using adaptive regression (Knafl & Ding, in press).

Phase 2. A professional transcriptionist transcribed the audio recordings verbatim, and the transcriptions were checked against the tape for accuracy in an effort to gain a full understanding of the tone and emotion elicited from the parents. Following transcription, all interviews were coded using a combination of a start list of codes based on the FMSF and the online measures and codes inductively derived from interview data. Qualitative data analysis was supported using MAXQDA (Verbi Software, 2015), a software program that facilitates coding of qualitative data and retrieval of coded material. The analysis of interview data first focused on developing a thematic summary of each parent's interview (Ayres, Kavanaugh & Knafl, 2003; Sandelowski, 2011a). In order to balance the inherently reductionist nature of coding, a second analytic strategy entailed completion of narrative family case summaries of each interview. Case summaries are a useful strategy for grounding the analysis of individual codes in the context of the respondent's overall experience (Sandelowski, 2011b). In families where both parents participated, the analysis addressed the extent to which parents had a shared or discrepant thematic profile to look for varying patterns of family management. Additionally, comparisons were made across all parents' thematic summaries and across all families to provide a greater understanding of the nature and range of perceived consequences, for a variety of families, of having a child with CAH (Sandelowski, 2011a). Finally, quantitative scores from the measures' were included in the summary matrices for further comparison within and across families based on all data sources. Using a within and across case analysis approach (Ayres et al., 2003; Sandelowski, 2011a) that included all data sources contributed to a thorough description of how participating parents perceived and managed their child's CAH in the context of everyday family life.

Results

Phase 1 Results

Seventy-seven parents participated in Phase 1 (60 mothers, 2 grandmothers, and 15 fathers). Of those parents, nine were dyads (8 mother/father; 1 grandmother/father). (Tables 3.2, 3.3) There was very little missing data; however, certain analyses were computed with varying data sets when this occurred. The majority of the parents who participated in Phase 1 were Caucasian (95%). This is not surprising, as in the United States the incidence of CAH is much lower in the African American, Hispanic, and Asian populations (Pass & Neto, 2009). The mean parent age ($n=75$) was 41.9 years for mothers and 40.7 years for fathers (two grandmothers participated as well-- ages 75 and 44 years); the mean child age ($n=68$) was 8.4 years. Forty-four parents reported having a girl with CAH (57%) and 33 parents (43%) a boy. The parents who participated in Phase 1 lived in 28 states within the U.S. as well as four parents from Ghana, Australia, United Kingdom and Puerto Rico, which indicates that a large sample of healthcare providers were represented in terms of providers' efforts to prepare parents for managing adrenal crisis events. Of the 73 parents who shared household income information, about half ($n=36$) had a yearly income greater than \$100,000 (US) per year.

Of the 68 parents who responded to a question inquiring when their child's provider gave them a prescription for intramuscular hydrocortisone, ten parents stated they received the prescription one month after diagnosis, three responded between 6-12 months, and four stated it took over one year to receive it, meaning that 25% of parents surveyed did not receive the prescription within one month of diagnosis, despite that being the standard of care (Speiser et al., 2010). How parents perceived providers' instructions about how to give the injection (eg. written guidelines, injection demonstration) varied; however, there was a significant relationship ($p=.02$) between parents having directly been shown by a provider

how to correctly administer the injection and higher scores on the FaMM Management Ability scale, indicating a stronger ability to manage the condition.

When examining adrenal crisis event occurrences in Phase 1, there was a significant, non-linear relationship between the age of child and the average number of adrenal crisis events experienced each year, with the number of crises decreasing over time. (Figure 3.3) Parents reported children having 0.77 adrenal crisis events per year (a minimum number of one adrenal crisis episode every 1.3 years) in the first five years of life; however, after the age of five, parents reported 0.27 adrenal crisis events per year (a minimum of one adrenal crisis episode every 3.7 years). There was a significant difference in the mean number of adrenal crisis events in children under the age of five and greater than or equal to the age of five ($p=.01$). (Figure 3.3) Additionally, mean ability to manage the condition was significantly lower (40.9 v 44.1; $p=.009$) for parents of children five and under compared to parents of children older than five years of age. This indicates that parents feel better able to manage the condition as the child gets older.

Furthermore, when examining parental management ability and the impact the condition has on the family using both family impact measures, as management ability increased, there was a decrease in the impact CAH has on the family ($p<.001$).

Phase 2 Results

In Phase 2, 16 parents purposively selected from Phase 1 were interviewed, seven mother/father dyads and two single mothers. Of the nine families, four had boys with CAH and five had girls with CAH. Ages of the children at the time of the interviews ranged from 2 years to 15 years, which highlighted varied parent experiences such as school encounters and age-dependent child care needs. The parents interviewed were heterogeneous in nature when examining demographic variables such as family income, age of the child, and where in the United States they resided.

Contextual influences on family management. There were multiple contextual influences that parents discussed in the interviews that they perceived as affecting family management of CAH. These contextual influences included healthcare providers, school personnel, babysitters, extended family, and extracurricular activities in which the child participated in, primarily sports.

Interchanges healthcare providers and school personnel. Parents stated that although they were satisfied with the relationships they had with their current pediatric endocrinologists, providers did not offer support to them emotionally and did not refer them to family support groups---local nor national.

“[The doctor] sat down, and he explained the medical terms of it all ... And then basically he re-described the whole scenario to us in terms that I can understand.”

“As far as [providers] being there emotionally, I don’t know if his doctors ever really played that role. I think - I just don’t see them – or I can’t site an example where there’s the pat on the back or the hug. Nothing like that.”

The management of CAH, especially during times of illness, remains complicated and stressful for parents. Although parents reported feeling pleased with their current pediatric endocrinologists, parents from five families described not being appropriately prepared by their initial providers for adrenal crisis events, which prompted them to change health care providers. Parents stated that their current providers have educated them on how to administer the emergency injection of hydrocortisone; however, the process had been demonstrated only one time by either their pediatric endocrinologists or their staff members (ie. nurses, physician assistants, medical assistants). Four parents voiced concern that one-time instruction was insufficient in terms of feeling confident in their ability to effectively manage an adrenal crisis.

“They [initial pediatric endocrinologist office] did not demonstrate anything. They actually could not even give us a correct dosage of how much to put in the syringe. They gave us a piece of paper that had instructions on it and sent us on our way.”

“We actually asked for it [prescription for injectable hydrocortisone] at our doctor’s visit. I knew about it from the websites I had looked at. And we had a written piece of

paper they [pediatric endocrinologist's office] gave us on how to give it. So basically, we watched a You-Tube video on our own [to learn how to give the injection]."

Consistent with the significant relationship between parents having been shown how to given the injection by health care providers and an increased perception of management ability in Phase 1, parents who expressed satisfaction in the interviews regarding how their providers have prepared them to handle adrenal crisis events described being taught how to administer the injection by a nurse or doctor face-to-face.

Parents described educating their child's school nurse or daycare provider on CAH and reviewing injection instructions with school nurses on a yearly basis. Overall, parents reported favorable experiences with school personnel regarding nurse preparation and teacher understanding of the condition; however, several parents describe an often lengthy and repetitive process of nurse/staff education as well as anxiety whenever a new nurse joined the school staff or when the child changed schools.

"From very early on when she was getting ready to start a new school, my wife would go and make an appointment before school started with the school nurse, bring the shot kit and spare meds and all of the other stuff to leave with them in their medicine cabinet during the school year. Bring them a letter that our pediatric endocrinologist would write to explain what was going on, warning signs, how to react, who the emergency contacts are, that's been something she's done you know every year. But each time when she has change schools, you know moved up from you know kindergarten to first grade to elementary, we have to start all over with the nurse and how is that nurse going to respond. But it's usually gone well."

Social network.

Babysitters. Parents in seven of the families interviewed discussed specific management challenges related to times when babysitters were needed for their child with CAH. These challenges were related to fear over their child becoming ill while under the care of the babysitter, not knowing how much instruction to give the babysitter regarding the injection (ie. is a demonstration on how to give the injection necessary?), and misgivings that teenage babysitters would be unable to handle an adrenal crisis event. Parents stated that they preferred to use family members who had been taught how to

respond to a crisis as babysitters; furthermore, they described varying strategies to educate babysitters on their child's condition.

"I have taught the babysitter how to give the injection. And I write it down on a piece of paper ... like really simple steps if they would have to. But I would always emphasize to just call 911."

"This is my son, so if you're going to be around my son, you're going to know what to do. You're going to know what to look for. You're going to understand. Now what might happen to him if I leave the room, if I run to the store, if whatever. If you're with my child you're going to know what he has and how to do the basic treatment of it."

Extended family. Parents from six families described their extended families as supportive and helpful, especially with regards to child care. However, other parents relayed struggles with how their extended families dealt with the diagnosis initially, expressed concern over extended family members' inability to fully understand the challenges associated with CAH management, and stated that their families were too afraid to help with their child's care. These struggles created tension within the family.

"Some of the other people, like my mom and our friends that watch him for short periods of time ... I don't think they understand the severity of the condition. They just see him, and to them he's a normal kid."

"I tried to educate my family and his but they're just not interested-- they don't understand it. And I guess me and my husband both have felt a little bit of animosity towards them because they don't. I guess they don't show the worry or see the seriousness in it. And that's kind of made us a little bit mad."

Extracurricular Activities/Coaches/Sports. Parents in seven families had children who were actively participating in at least one school or community based sport including soccer, volleyball, hockey, track, and t-ball. The two children not participating in sports were the two youngest -- ages 2 and 3. Parents relayed how sports participation was a source of concern and described fears that physical exertion might trigger an adrenal crisis; however, parents also stated that they wanted their children with CAH to participate in sports because of the benefits, both socially and physically, associated with being on a sports team. Parents discussed the importance of instructing coaches about the signs and management of a crisis. Of the seven children currently playing sports, parents in one family had chosen not to

inform the coach about the condition; however, one of those parents brings the emergency injection kit to every practice and competition and stays near the child. Parents in only one family had instructed their child's coaches about how to give the injection and confirmed that the coach was willing to administer an injection if needed.

"Because there is a lot of explaining that needs to go on [for the coaches]. We have to say if you don't do the right thing, he's going to go into a death spiral so it's a fine line."

Access to resources. Parents in five of the families reported leaving their initial pediatric endocrinologists soon after the time of diagnosis because of dissatisfaction with the provider's level of knowledge about CAH as well as a lack of education on adrenal crisis from the provider. Two different mothers stated:

"Because what I was finding was that it could be fatal if not treated correctly. And the endocrinologist we had at the time was not somebody we liked at all and did not explain this to us."

"I didn't feel like she [the pediatric endocrinologist] had much experience... I think it's rare and there's not very many cases period. But she couldn't put us at ease basically."

For parents in four of the families, this required finding a pediatric endocrinologist in another state and a far distance from their homes. Parents reported having to drive long distances to see pediatric endocrinologists two to three times per year.

"Yeah now we've been stable now for I think two years with the one we got but we still have to drive three and a half hours away [to see new pediatric endocrinologist]."

"There's not one [a pediatric endocrinologist] –the closest one to us is about three hours. And we did actually start out with that endocrinologist but she started him on the prednisolone instead of the hydrocortisone, and he wasn't growing. She blamed us, said it was our fault and diagnosed him as failure to thrive and pretty much told us to prepare ourselves. So I called the CARES Foundation and got a list of good doctors, and I made an appointment at Vanderbilt and that's where we went and we just stayed there ever since. It is a 8-9 hour drive."

Overall, parents detailed certain challenges related to managing the contextual influences on the family with regards to their child's CAH. These included a lack of detailed and thorough adrenal crisis preparation from health care providers, repeated adrenal crisis

education needs for people in their child's social network such as teachers, babysitters, and coaches, as well as interactions with their extended family related to their child's condition.

Definition of the situation. Definition of the situation includes how parents view the condition and the child, their management mindset, and parental mutuality (Knafl et al., 2012). Parents stated certain aspects of their child's CAH management were going very well such as administering daily medication, their child's current height and weight, and their child's performances in school. All felt that, overall, their child was thriving, happy, and well-adjusted. However, there were some clear distinctions made by parents between their family and others without a child with CAH. For example, the decision for one parent not to work outside the home because of the extra attention needed for the CAH child, not allowing grade school aged children to play at friends' houses, and not allowing non-family members to babysit were linked to the CAH and described as unique challenges faced by the family. When asked what was the most important information to relay to parents having a child just diagnosed with the condition, the majority of parents responded that being prepared to manage an adrenal crisis event was paramount.

"So knowing that if you are going to be outdoors on hot summer days you need plenty of fluids and salt tablets and you always need to have your shot kit with you. You need to know if you're going to be away from the home all day that you need to have all of your different medicines with you. You can't get caught not prepared for the situation."

Parents in seven dyads described a strong sense of "being on the same page" regarding how they managed their child's CAH. None of the dyads expressed any discrepant management views, nor any significant tension in their relationship related to their child's CAH. Parents described a dramatic difference in how they initially viewed CAH at the time of diagnosis and how they viewed it now, with an emphasis on the condition becoming easier to manage over time. All of the parents having a child over the age of five reported that their view of the condition began to change around the time their child turned five years old, which supports the Phase 1 finding that parents find the condition more

manageable when their child becomes school age. According to parents, one reason for this change in their view of the condition was their child being able to articulate how he/she was feeling physically and emotionally. Additionally, by the time the child was four, all of the parents had successfully managed an adrenal crisis. At the time of the interview, their management mindset was one of confidence.

“Now we know what to look for more. We know the signs and symptoms [of adrenal crisis]... like when she was a baby we didn’t know what it would look like.”

“In the first few months [after diagnosis] it was trying to understand it. It was educating. It was learning about it. It was researching. It was trying to understand how it happened, why it happened ... The first couple of years were the roughest but as he’s grown and gotten better, it is easier.”

Parents in all nine families had experienced an adrenal crisis event, with parents in eight of the nine families describing multiple crisis episodes. Parents acknowledged that these life threatening events contributed greatly to how they viewed the illness and their management capacity. Parental accounts of adrenal crisis episodes were most often linked to gastrointestinal illnesses involving repeated vomiting as well as trauma related to accidental injuries related to outdoor activities. Adrenal crisis events were described as inherently stressful, and parents stated that knowing that their child could die if their response was not effective was both overwhelming and terrifying.

“And the doctors would explain to you ‘Now he’s not going to die as long as you just do what you’re supposed to do.’”

“It [adrenal crisis event] was the most terrifying thing I’ve ever experienced. It was because we did not have all of the information, so we weren’t prepared.”

“One day my wife and him they were outside, and he was playing normal and fine. He wasn’t sick, he didn’t have a cold, he didn’t have anything that would have caused it. He was running across the yard and the next thing you know he was face down in the yard.”

With few exceptions, parents labeled their child’s life and their family life as “normal,” and the parents that were partnered described a strong sense of agreement in their approach to managing the condition. Over time, parents developed a daily routine for

condition management that they viewed as manageable. However, during illness and adrenal crisis, there were management challenges, and during these times, the parental view of the condition and the child would temporarily change

Management behavior. The Management Behavior Component of the FMSF includes parenting philosophy and management approach, including management routines (Knafl et al., 2012). Parents described daily management of CAH as relatively straightforward, consisting of giving their child oral steroids two to three times a day. However, four dyads described a highly structured routine that could not be compromised in any way when discussing the exact timing of administering the medication.

“Going back to us being super science-based we’re very, very strict on like eight hours, her medication every eight hours. So we do follow this one hundred percent, and she has her medication at like eight, four and midnight.”

Across families, one parent, either the mother or the father, was usually responsible for daily management including medication administration, communicating their child’s special health needs to others in their child’s social network, and taking their child for healthcare provider visits. However, both parents reported being trained and capable of giving the hydrocortisone injection when needed. Although parents in the seven dyads described a shared view of the condition, several parents expressed that they felt they and their partner had differing management approaches. For example, regarding stress dosing and giving the IM injection, one parent might feel more anxious and take the “better safe than sorry” approach of giving the stress dose, while the other parent was more willing to “wait it out;” however, none of the parents described this as a source of significant conflict.

“I’d say when it comes to time ... when he gets a little bit sick, sometimes she’ll get into a mentality of ‘oh it’s not that big of deal,’ and I have a much quicker trigger finger. I am ready to start stress dosing.”

“He constantly worries. He is just always worried about what we did [stress dosing]. I’m more like, well, I always felt like we could get him help you know what I mean? There are hospitals everywhere is how I feel. But he’s like, he’s very anxious.”

Regarding parenting philosophy, every parent interviewed discussed making a conscious choice to treat their child normally and not unnecessarily restrict activities because of the condition. They also described their family life in general as similar to that of other families.

“I think it’s extremely important to make these children feel that they’re really not that different. That everybody has something and this happens to be what you have, what your child has. And they can do anything they want to do you shouldn’t limit them.”

Perceived consequences. Perceived consequences are the extent to which family life is focused on the child and future expectations for the child and how the family is viewed as linked to the condition (Knafl et al., 2012). Parents described how efforts to incorporate CAH management as part of the usual family routine were successful; however, unpredictable, acute illnesses and the possibility of adrenal crisis could dramatically disrupt that routine. Parents remained hopeful regarding their child’s future, but also expressed concerns for their child’s health and wellbeing in regards to puberty/adolescence as well as their anticipation that they would have less control over the treatment regimen and response to crises as the child becomes a young adult.

“My expectation is she’s going to have a normal life. And she’s got a pretty good head on her shoulders.”

“We all worry about him being by himself or somebody not knowing he’s sick or not knowing what’s going on and that bothers me. I think I want him to live next door to me.”

“Yeah and I think about that when she goes to college, you know? Is she going to be equipped? Are the medical centers going to be equipped if she gets hurt or if she drinks too much and she’s vomiting the next day? You know I think about those things.”

Parents in eight of the nine families interviewed had children other than their child with CAH child. When asked, parents stated they felt CAH had minimal impact on the siblings; however, parents also noted that siblings experienced distress during a CAH crisis. Parents expressed concern that some of the events experienced by siblings, especially related to paramedics at the home and hospitalizations of the child with CAH, would be long

lasting negative childhood memories for siblings. Additionally, parents in three families stated that siblings exhibited jealous behavior regarding the extra attention that CAH children received because of special care needs, illness, or crisis.

Finally, for some parents, having a child with CAH resulted in challenging reproductive decisions. Six parents interviewed described making a decision to not have other children after their CAH child because they did not feel capable of managing the care of more than one child with an episodically life threatening condition. Parents in one family did have subsequent children, but opted for prenatal treatment of dexamethasone (the baby she was carrying was a girl) in an effort to prevent virilization, while parents in another family chose to have another child but not take dexamethasone and knowingly risk having another girl with possible virilization. Parents in another family chose to do a pre-implantation genetic diagnosis to determine if CAH was present in any of the embryos produced through in-vitro fertilization prior to implantation in an effort to ensure their subsequent child did not have the condition. A recurrent theme concerning the perceived consequences families having a child with CAH experience involves planning. Family planning after having one child with CAH, planning for potential adrenal crisis events, and planning for their child's health and safety as they grow into adolescents and young adults are all important issues and decisions for these families.

Discussion

This study provided evidence that over time parents adapt to the management challenges of having a child with CAH, but the threat of a crisis remains an ongoing concern. Parents believe that their children are, for the most part, living normal lives despite having CAH; however, living with the uncertainty of an adrenal crisis is challenging for parents, especially in the context of not being properly prepared by healthcare providers to manage adrenal crisis events. When parents are not properly prepared on how to manage the life

threatening aspects of CAH, the result can be a reliance on EMS services and emergency departments to manage crisis events. Due to the need for an immediate effective response to the signs and symptoms of adrenal crisis, this reliance on outside emergency services can lead to serious injury and possible death of the child if the response is not swift or treatment is misunderstood. Additional stressors for these families include finding appropriate child care, which includes care providers trained to give a hydrocortisone injection, as well as feeling emotionally unsupported by health care providers. The CAH child's social environment such as school, daycare, and extracurricular activities also produce challenges regarding parental fear of adrenal crisis episodes when they are not present.

Understanding and identifying gaps in parent education by healthcare providers, especially concerning times of adrenal crisis, is necessary to promote positive family outcomes, both from an emotional standpoint as well a child health perspective. Provider support is needed for these parents throughout childhood, but especially in the first five years of life when parents are adjusting to having a child with a life-threatening condition and children frequently acquire common childhood illnesses that require stress dosing of hydrocortisone as well as associated hospitalizations (Rushworth et al., 2016). Developing interventions that encourage appointments with health care providers to include a focus on the nonmedical aspects of life with CAH in an effort to increase emotional support from providers to families is needed. For example, regular appointments and check ups with providers should include discussions about how families are handling the child's extra-curricular activities, school environment, height and weight difficulties, and child care when a parent is unavailable, as these are all aspects of CAH management that have the potential to disrupt family life. Additionally, detailed and uniform education from providers on how to effectively handle adrenal crisis episodes has great potential in preventing costly emergency room visits and providing peace of mind to caregivers of children with CAH.

Table 3.1. Outline of Study Aims and FMSF

Aim of the Study	Component of Framework	Topic(s) of Interest	Data Collection Method
<p>Describe circumstances surrounding adrenal crises in children with CAH by examining:</p> <p>1.1) Parents' perceptions of the experience (e.g., what they did, how they used information)</p> <p>1.2) Parents' descriptions of sources (e.g., education from healthcare professionals, support groups, internet, etc.) of information related to managing times of crisis;</p> <p>1.3) Strategies and approaches parents used to inform other family members (siblings, grandparents, etc.), school personnel, and others in their social network (friends, babysitters, etc.) on how to manage adrenal crises about adrenal crisis management including parents' perceptions of their effectiveness</p>	Definition of the Situation, Management Behaviors	<p>Parental perceptions and interpretations of adrenal crisis events and their beliefs about their ability to manage the event</p> <p>Parents' assessment of the extent to which they have an established approach for responding to an adrenal crisis and their strategies for accessing and conveying information about crisis management</p>	Semi-structured Interview; Family Management Measure – View of Condition Impact and Management Ability Scales; PedsQL-Family Impact Module
Explore parents' perceptions of the consequences, for their child with CAH, themselves, and their family, of living with the possibility that their child with CAH will experience a life threatening crisis	Perceived Consequences	Parents' perceptions of the ways in which the life threatening nature of the condition affects everyday life for their child and family	Semi-structured Interview; Family Management Measure – View of Condition Impact and Management Ability Scales; PedsQL-Family Impact Module
Examine a possible relationship between parents' management ability and the impact CAH has on the family	Definition of the Situation, Management Behaviors, Perceived Consequences	The relationship between parents' management ability and the impact CAH has on the family (e.g. does increased ability to manage CAH lead to decreased impact of the condition on the family?)	Semi-structured Interview; Family Management Measure – View of Condition Impact and Management Ability Scales; PedsQL-Family Impact Module

Table 3.2. Phase 1 Parent Participant Characteristics

Parenting Role	<u>n (%)</u>
Mother	60 (78)
Father	15 (19)
Grandmother	2 (3)
Racial Identification	<u>n (%)</u>
American Indian/Alaskan Native	1 (1.3)
Asian	2 (2.7)
Black	1 (1.3)
Hawaiian/Pacific Islander	0
White	71 (94.7)
Ethnicity	<u>n (%)</u>
Hispanic	4 (5.3)
Non-Hispanic	72 (94.7)
Yearly Family Income	<u>n (%)</u>
<\$50,000	10 (13.7)
\$50,000-80,000	12 (16.4)
\$80,000-100,000	15 (20.6)
\$100,000-150,000	14 (19.2)
>\$150,000	22 (30.1)
Age of Mother	
Mean (SD)	41.98 (7.4)
Range	26-54
Age of Father	
Mean (SD)	40.71 (4.9)
Range	33-47
Age of Grandmother	
Mean (SD)	59.5 (21.9)
Range	44-75

Table 3.3. Phase 1 Parent Reported Child Characteristics

Racial Identification	<u>n (%)</u>
American Indian/Alaskan Native	1 (1.3)
Asian	2 (2.7)
Black	1 (1.3)
Hawaiian/Pacific Islander	0
White	71 (94.7)
Ethnicity	<u>n (%)</u>
Hispanic	6 (7.9)
Non-Hispanic	70 (92.1)
Wears Medical Alert Tag	<u>n (%)</u>
Yes	51 (66)
No	26(34)
Gender of Child	<u>n (%)</u>
Male	33 (43)
Female	44 (57)
Age of Child	
Mean (SD)	8.4 (5.3)
Range	1 month-18 years

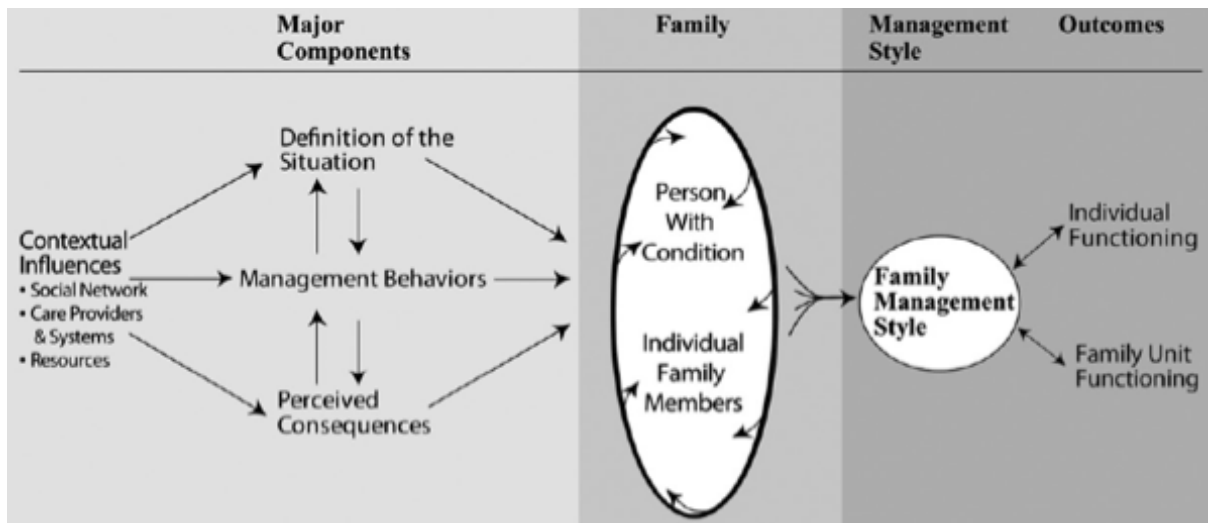


Figure 3.1. Family Management Style Framework

Contextual Influences on Family Management	Definition of the Situation	Management Behavior	Perceived Consequences
Care providers; Resources; Social support; Community	View of the condition; Choice to live a “normal” life; Management mindset; Parental mutuality; Uncertainty in times of acute illness	Parenting philosophy; Management approach	Family focus; Future expectations; Family planning

Figure 3.2. Data codes and major components of FMSF

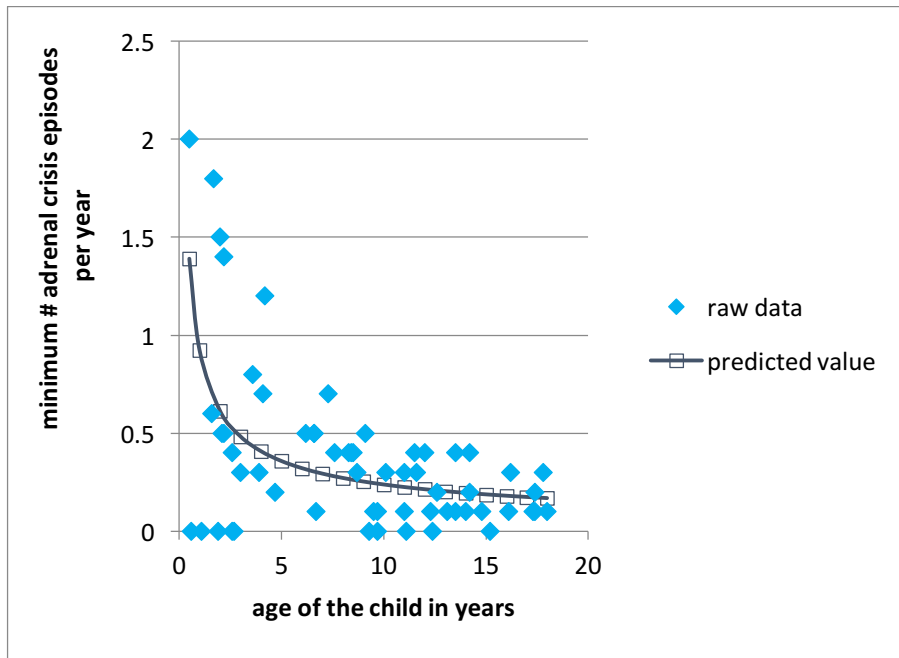


Figure 3.3. Phase 1-Minimum Number of Adrenal Crisis Episodes and Age of the Child

REFERENCES

- Ayres, L., Kavanaugh, K., and Knafl, K. (2003). Within-case and across-case approaches to qualitative data analysis. *Qualitative Health Research*, 13(6), 871-883.
- Barnard, K., Thomas, S., Royle, P., Noyes, K. Waugh, N. (2010). Fear of hypoglycemia in parents of young children with type 1 diabetes: a systematic review. *BMC Pediatrics*, 10(50), 1-8.
- Bowen, G. A. (2008). Naturalistic inquiry and the saturation concept: a research note. *Qualitative research*, 8(1), 137-152.
- CARES Foundation (2014). Retrieved from <http://www.caresfoundation.org>
- Creswell, J. W., & Clark, V. L. P. (2010). *Designing and Conducting Mixed Methods Research*. Thousand Oaks, CA: Sage Publications.
- Fleming, L., Rapp, C. & Sloane, R. (2011). Caregiver knowledge and self-confidence of stress dosing of hydrocortisone in children with congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 26, 55-60. Doi: 10.1016/j.pedn.2011.03.009
- Harris, G., Diment, A., Sulway, M., & Wilkinson, M. (2002). Glucagon administration undervalued and undertaught. *Practice Diabetes International*, 18(1), 22-25.
- Knafl, G. J., & Ding, K. (in press). Adaptive regression for modeling nonlinear relationships. New York: Springer Verlag.
- Knafl, K., Deatrck, J., & Havill, N. (2012). Continued development of the family management style framework. *Journal of Family Nursing*, 18(1), 11-34. Doi: 10.1177/1074840711427294
- Knafl, K., Deatrck, J., Knafl, G., Gallo, A., Grey, M., & Dixon, J. (2013). Patterns of family management of childhood chronic conditions and their relationship to child and family functioning. *Journal of Pediatric Nursing*, 28, 523-535. Doi: 10.1016/j.pedn.2013.03.006
- Knafl, K. et al. (2012). Family Management Measure (FaMM). Retrieved from <http://nursing.unc.edu/research/office-of-research-support-consultation/resources/family-management-measure-famm/>
- Merke, D. P., & Bornstein, S. R. (2005). Congenital adrenal hyperplasia. *The Lancet*, 365(9477), 2125-2136.
- Pass, K. & Neto, U. (2009). Update: newborn screening for endocrinopathies. *Endocrinology Metabolism Clinics of North America*, 38, 827-837.
- Rushworth, R. L., Falhammar, H., Munns, C. F., Maguire, A. M., & Torpy, D. J. (2016). Hospital admission patterns in children with CAH: Admission rates and adrenal crises decline with age. *International Journal of Endocrinology*, 2016. Doi:10.1155/2016/5748264

- Sandelowski, M. (1995). Qualitative analysis: what it is and how to begin. *Research in Nursing & Health*, 18, 371-375. Doi:10.1002/nur.4770180411
- Sandelowski, M. (2011a). "Casing" the research case study. *Research in Nursing and Health*, 34(2), 153-159.
- Sandelowski, M. (2011b). Parallelism in constant comparison analysis. *Research in Nursing and Health*, 34(6), 433-434.
- Sicherer, S. et al. (2012). Development and validation of educational materials for food allergy. *The Journal of Pediatrics*, 160(4), 651-656. Doi: 10.1016/j.jpeds.2011.09.056
- Speiser, P., Azziz, R., Baskin, L., Ghizzoni, L., Hensle, T., Merke, D. . . . White, P. (2010). Congenital adrenal hyperplasia due to 21-hydroxylase deficiency: An endocrine clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*, 95(9), 4133-4160. Doi:10.1210/jc.2009-2631
- Sullivan-Bolyai, S., Bova, C., Leung, K., Trudeau, A., Lee, M. & Gruppuso, P. (2010). Social support to empower parents (STEP): An intervention for parents of young children newly diagnosed with type I diabetes. *The Diabetes Educator*, 36, 88-97. Doi: 10.1177/0145721709352384
- Varni, J., Sherman, S., Burwinkle, T., Dickinson, P., & Dixon, P. (2004). The PEDsQL family impact module: Preliminary reliability and validity. *Health and Quality of Life Outcomes*, 2, 55-60. Doi: 10.1186/1477-7525.2-55
- VERBI Software (2015). MAXQDA 12 Reference Manual (v1.0), available at: [http://www.maxqda.com/download/manuals/ ... al_eng.pdf](http://www.maxqda.com/download/manuals/...al_eng.pdf)
- Witchel, S. & Azziz, R. (2011). Congenital adrenal hyperplasia. *Journal of Pediatric Adolescent Gynecology*, 24, 116-126. Doi: 10.1016.j.jpag.2010.10.001

CHAPTER 4: GENDER MATTERS IN FAMILIES HAVING A CHILD WITH CONGENITAL ADRENAL HYPERPLASIA

Overview

Congenital adrenal hyperplasia (CAH) is an inherited, endocrine disorder that occurs in approximately 1 in 15,000 live births and affects males and females equally (Speiser et al., 2010). Both boys and girls born with CAH are exposed to high concentrations of androgens in utero; while boys typically do not show any outward physical signs of this exposure (except possibly subtle hyperpigmentation and penile enlargement), girls often have ambiguous genitalia to varying degrees, which typically leads to a diagnosis in girls shortly after birth (Witchel & Azziz, 2011). The degree of virilization is graded according to the Prader score (with a 0 appearing as a typical female and a 5 appearing as a typical male). Gender assignment in these affected females can pose both a medical and family crisis (Merke & Bornstein, 2005; Speiser et al., 2010). A surgical procedure called reconstructive feminizing genitoplasty is recommended by some providers at an early age and can involve multiple surgeries into adolescence (Witchel & Azziz, 2011; Karkazis, 2008). Although girls with CAH identify as female (Berenbaum & Bailey, 2003; Dessens, Slijper, & Drop, 2005), they often show increased preference for male toys and activities (Nordenstrom et al., 2002; Pasterski et al, 2005; Wong et al., 2013), increased aggression (Pasterski et al., 2007; Mathews et al, 2009), increased male-typical sexual orientation (Nordenstrom et al., 2010), and differences when compared to non-CAH girls in spatial abilities (Hines et al., 2003; Berenbaum et al., 2012).

All children with CAH are at significant risk for adrenal crisis, defined as an abrupt, life-threatening state with symptoms including hypotension, pallor, fatigue, headache,

tachycardia, and vomiting, due to steroid deficiency (Speiser et al., 2010). Parents must administer steroids, typically oral hydrocortisone, up to three times daily to replace deficient levels of cortisol, and “stress dose,” meaning give additional oral steroid doses or an intramuscular injection of hydrocortisone, during times of acute physical illnesses due to common viral and bacterial causes as well as during surgeries or traumas. Despite the complex nature of CAH management, both during times of maintenance and emergency, as well as the unique struggles that girls born with CAH and their families can experience, very few studies have explored the impact CAH has on families in which a daughter has the condition.

The purpose of this analysis, which draws on data from a larger, mixed methods study, was to examine, based on the gender of the child, the varying family experiences of having a child with CAH. This cross-sectional, qualitative study was the second phase of a larger mixed-methods (phase 1, quantitative; phase 2, qualitative) study conducted by the primary author. The purposes of the larger study were to examine parental management of adrenal crisis in children with CAH as well as the consequences of having a child with a life threatening condition; however, during the qualitative, Phase 2 portion of the study, it became evident that certain aspects of the family experience of having a child with CAH were profoundly different based on the gender of the child.

Methods

Participants

In order to be included in the study, the parent needed to be over the age of 18, English speaking, and have a child between the ages of birth and 18 years diagnosed with classic, salt-wasting CAH and free from any other complex health conditions. Furthermore, parents needed to have access to a telephone, computer, and email account. Parents were recruited through the CARES Foundation (CARES), a non-profit organization, based in New

Jersey, which provides support to families in which there is a member with CAH (CARES Foundation, 2014). Recruitment for the study consisted of an “Invitation to Participate” letter that CARES emailed to its members who had previously expressed an interest in participating in research. In addition, CARES provided a brief description of this research study within the research section of their website.

Sixteen parents, seven mother/father dyads and two single mothers, were successfully contacted and agreed to participate in the qualitative portion of the study. There were five families having a girl with CAH and four having a boy. Child age ranged from 2-15 years and geographical location, family income, marital status of the parents, and scores on the Phase 1 quantitative measures examining family management ability and impact of the condition, varied. All of the parents that were interviewed and their children were Caucasian. In the United States, the incidence of CAH is much lower in the African American, Hispanic, and Asian populations (Pass & Neto, 2009).

Analysis of Data

A professional transcriptionist transcribed the audio recordings verbatim, and the transcriptions were reviewed multiple times to get a broad understanding of the content. MAXQDA (VERBI Software, 2015), a qualitative software program, was used to aid with the coding and retrieval of coded data. Directed content analysis was used to identify descriptive and/or conceptual categories to organize the inquiry (Vaismoradi, Turunen, & Bondas 2013). Comparisons were made across all themes reflected in the parents’ interviews to provide a richer understanding of the impact having a child with CAH has on the family (Sandelowski, 2011). Data collection continued until common themes repeatedly emerged to the point of saturation (Bowen, 2008; Morse, 2015). During the analysis of the interviews in Phase 2, it was noted that the way parents viewed the condition and the impact CAH had on the family differed based on the gender of the child, and additional investigation ensued examining these variations.

Findings

There were some clear and important distinctions in the family experiences of parents of boys and girls with CAH. Of the 16 parents from nine families interviewed, five had a girl with CAH ranging in age from 2-14, and all five girls were born with ambiguous genitalia. These parents, four mother/father dyads and one single mother, detailed experiences much different than the four families having a boy between the ages of 3-15. These differences included parents' descriptions of the time of diagnosis, their accounts of challenging surgical, treatment-related decisions (feminizing genitoplasty), and a sense of a pervasive stigma surrounding CAH.

Timing of Diagnosis

For boys, the CAH diagnosis was made within two weeks of birth, after the child had been discharged from the hospital setting, via newborn screening. Three boys were diagnosed within ten days of being born. One boy was born in a state where newborn screening wasn't done at the time of his birth and was diagnosed after a month of age. Parents of boys reported feeling shocked and devastated when hearing of the diagnosis. None of the parents of the boys stated they were dissatisfied with the manner in which health care providers informed them of the diagnosis.

"I guess the very first thing was the newborn screening. I remember vividly the day. I remember exactly what I was wearing. What I was doing. It shattered our whole world basically."

"[After diagnosis] It was educating. It was learning about it. It was researching. It was trying to understand how it happened, why it happened ..."

Whereas the parents of boys first learned that their child had CAH after their son had been discharged from the hospital, parents of girls experienced an extended hospital stay after birth because of the child's ambiguous genitalia and learned of the condition during the hospitalization. Providers suspected a diagnosis of CAH or some other condition from the beginning, and these parents stayed in the hospital with their daughters until a definitive

diagnosis was made. For parents of girls, the news was somewhat of a relief, as parents were searching for reasons as to why their daughter had ambiguous genitalia and had concerns over other possible explanations. The news of CAH provided an answer after several hours or days of confusion, which was welcomed.

“So when she was first diagnosed I think that I was...I was relieved mostly. The testing confirmed that the condition was something that the doctors understood and that it was something that could be treated.”

“We knew something was wrong the minute she was born because of the very ambiguous genitalia. It was a whirlwind five days in the NICU where she was misdiagnosed as a male instead of a female until we got our test back and everything was verified. It was pretty crazy.”

Four families of girls expressed frustration with the way in which the healthcare providers in the delivery room (obstetricians, nurses, pediatricians, nurse midwives) as well as pediatric endocrinologists responded to and explained their daughters' ambiguous genitalia. Two mothers stated that, despite hearing their daughters' immediate afterbirth cries, providers refused to allow them to see their babies, leaving them in extreme distress and confusion.

“I just wanted the baby on my chest and somebody to just like cut the crap and tell me what was going on. And I said, ‘okay that’s fine can I have the baby? Like can you just bring the baby? It doesn’t have like any immediate medical needs can I have the baby?’”

“They [healthcare providers] seemed to be much more preoccupied about her genitalia in a way that my partner and I absolutely were not... So it was really intimidating. And you know I just had a baby. I was feeling awful and it was, you know, a pediatric gynecologist, a pediatric social worker, pediatric psychologist....”

Only one family was satisfied with the way providers shared the news of their daughter's diagnosis. The father remembers this positive encounter:

“He could tell by doing some sonograms what the internal physiology was because the outside physiology could have gone either way... He said it could be – it was ambiguous enough that he could not make a call from that. So they set up, even on a Sunday morning, they set up the sonogram for us. It was probably like around nine thirty, ten o'clock in the morning, with a big smile on his face and said you have a beautiful, healthy daughter and this is what we need to do.”

All five of the parents were told that their child's gender was uncertain immediately after birth, but the terminology varied. For some parents, the terminology used to describe their daughter from the midwife in the delivery room was painful and traumatizing.

"My husband is in the room, and our nurse takes a peek and says it's a boy! Then the midwife turns her over, looks at me and says 'I'm not so sure.' The NICU doctor and my midwife turned to me and said 'we need to talk about the white elephant-- that this child might be a "hermaphrodite." Oh my God! It was awful, the shock. All I could think was "hermaphrodite." I'm lying in the hospital thinking can I raise this baby? It was so traumatic."

A father added:

"One of the things one of the nurses said when my daughter was first born ... We thought maybe she was a boy and then like one of the nurses was like, 'oh maybe this is a transvestite?' And you hear that and you're like, really?"

Following the diagnosis and within the first month, parents of boys did not report any concerns regarding telling family and friends of their child's birth and condition. Most described extended family as an initial source of support providing childcare for the baby and/or siblings as well as accompanying the parents to doctor appointments. However, for families having a girl with CAH, the experience of who to tell after their daughter's birth was much more complicated. Parents explained that deciding whether or not to tell friends was difficult, as they were concerned that as their daughter grew, she might feel uncomfortable with others knowing that she was born with ambiguous genitalia. One father stated that he didn't tell certain family members about his daughter's ambiguous genitalia initially because he felt like they would never change her diaper so they didn't need to know. A mother described not wanting to announce the birth of her daughter on social media because she was unsure at that time if her child was a boy or a girl. Keeping the birth so quiet for the first week, especially when family and friends knew she had gone to the hospital to have the baby, was very stressful and awkward for her and her husband and created an environment of secrecy regarding an occasion that she thought would be joyous and open.

“But talking about the ambiguous genitalia with our friends and family... pretty much we decided in the beginning we would not tell everybody because what if she didn’t want anyone to know?”

For parents of girls, the way the condition was initially described to them by healthcare providers was, for the most part, traumatizing and began to shape the way they viewed CAH. A prolonged hospital stay combined with confusion over the condition and stigmatizing language differentiated the time surrounding the diagnosis of CAH for parents of girls versus boys.

Surgical Decisions

Of the five families having a daughter with ambiguous genitalia, parents in four families decided in favor of surgical intervention within the first year. The goals of feminizing genitoplasty are to facilitate genital appearance compatible with gender, relieve urinary obstructions that result in episodes of incontinence and infections, and to preserve adult sexual and reproductive function (Speiser et al., 2010). All parents described this as a very difficult decision, although none of them currently expressed regret. One mother and father of a teenage daughter who has had two surgeries to date and continues to require daily vaginal dilating interventions at home stated:

“We talked about it ... we went over it a million times in our head and we said you know she may hate us for it later, but we feel this is the best decision we can make for our child.”

The mother went on to describe how she and her husband explained the decision to have the surgery to their daughter:

“We told her about her surgery and the reason she had it primarily was because her urethra and her vagina were fused together and there was some backflow causing infections. She knew about that from pretty early on. We’re very upfront with her. I can’t tell you when we told her but I know it’s been early and it’s been an open conversation.”

Another mother of a pre-teen daughter with CAH explained that her and her husband voiced their concerns regarding trying to preserve later sexual function to their daughter’s pediatric urologist.

“We, you know, had read about the doctors that focused more on the aesthetic of it and then these ... children grow up and don’t have the nerve endings there because they were cut to make it look perfect and they have no sexual satisfaction. So we expressed to him several times, and got our point across, that we wanted her to look normal, but we wanted her to have sexual satisfaction.”

Finally, another mother of a teenage daughter with CAH shared that although she was currently satisfied with the results of the surgery from a cosmetic standpoint, her daughter had undergone three surgeries and will need at least one more. These surgeries were extremely stressful for this mother and contributed to her decision not to have any more children.

“Oh yeah it’s really been a struggle for me. I’m not the same person, but it was worth it to me. It was absolutely worth it. I was a wreck. She had to be put to sleep a total of three times for that. Each time I thought I was going to lose my mind with worry so I couldn’t do that again.”

One family of a three year old girl made the decision not to have feminizing genitoplasty. Both parents agreed that it was better to wait until their daughter could make the decision as to whether or not to have surgery on her own. They felt strongly that there were too many potential problems later in life related to genital surgery and believed that waiting until their daughter was a young adult and could make an informed decision herself was a better approach. They were disappointed in the way in which their daughter’s initial pediatric urologist explained the surgical option to them.

“He said ‘well you know this is just the time to do it.’ And I said wouldn’t you have to have like revisions later? And he said ‘yeah but, you know, it’s better now.’ He ended up like kind of divorcing us from his practice because we kept saying no to surgery, and he said ‘well fine then we’ll see you in five years.’”

These parents went on to explain that, for their daughter, there was no medical reason to have the surgery. Therefore, it was frustrating and upsetting to them that they felt the medical team did not honor or respect their opinion to forego the procedure, at least until their daughter was older.

“Unless there is a medical reason like she was having ... which I don’t foresee, I would never touch her genitalia because she might need it ... I don’t know. I think

it's a challenge because you kind of could delay some of these things until even like five or six or when your kid can articulate what they're feeling, you know?"

The decision of whether to or not to have reconstructing feminizing genitoplasty is complex and challenging for parents. A lack of support from providers at the time of the decision as well as follow-up support is evident.

Stigma

Parents of both boys and girls with CAH described experiencing some degree of stress and stigmatization involving their child's condition. Wearing a medic alert tag identifying their child as "different," taking medication during school hours, and having to explain a rare condition that is complex to manage to others in their child's social circle were mentioned by all parents. However, the stigma for families having a daughter with ambiguous genitalia was pervasive and intense and contributed to how these families viewed CAH in general.

"We decided in the beginning we would not tell everybody because what if she didn't want anyone to know? But then we thought that kind creates an atmosphere that there's something wrong if we keep it a secret ..."

"We don't want to create a freak show environment ... where people are talking about it all the time because people don't really talk about their own genitalia all the time. So we kind of want to normalize it, and it's really hard to know how to do that. ... There's nobody to ask."

When parents of both boys and girls were asked what they felt the most important topic to discuss at a support group meeting for families having a child newly diagnosed with CAH, parents of the boys overwhelmingly focused on preparation for times of illness and adrenal crisis. Parents of girls mentioned this as well, but focused heavily on trying to normalize, gender identity, and handling stigma. The life-threatening aspect of CAH appears to be something that parents of girls are clearly aware of and concerned about, but view as something that is clear-cut and manageable, which is distinctly different than parents of boys. Parents of girls described potential adrenal crisis events as somewhat in the

background of daily life. For these parents, issues related to ambiguous genitalia were the predominant concern.

“How to deal with the ambiguous genitalia is something that’s very much on-going and not as cut and dry as the adrenal condition as it stands because we’re sort of constantly running this risk of providing private information about our child. You know we can’t un-tell people. On the other hand we’re also cognitive of the fact that there’s nothing to be ashamed about this condition and we have to treat it like we would treat anything else. There’s nothing to be ashamed of.”

Additionally, several parents of girls described stress dosing or giving the injection during times of illness as daunting, but easier to manage and explain to others when compared to ambiguous genitalia. For stress dosing, there are clear treatment guidelines such as tripling the oral dose if their daughter has a high fever but there were few, if any, guidelines for parenting a child with ambiguous genitalia. On the other hand, parents of boys all remarked on how the fear of adrenal crisis has impacted family life and shaped their view of the condition.

Finally, whether or not society would accept and understand their daughter’s past and/or present ambiguous genitalia was unknown to parents and described as a major worry. This concern was evident from birth for parents of girls and is reflected in their hesitancy to announce the birth, share information about the diagnosis, and in deliberate attempts by parents to protect their child from possible embarrassment or ridicule (Sanders et al., 2012).

“We were somewhat beholding to how mean kids can be, and you know not wanting her to ever have to deal with it in a locker room or whatever.”

“I don’t know who this person was [on Twitter], but the person he was talking about was a transgender, and he called her the face of Congenital Adrenal Hyperplasia. And I remember being so angry I almost tweeted back at him. I didn’t know what to say. I decided to put down the computer and walk away.”

Discussion

Rare childhood conditions, such as CAH, are often misunderstood, which can create isolation and stress for those affected as well as their families (Zurynski, Frith, Leonard & Elliott, 2008; Dellve, Samuelsson, Tallborn, Fasth, & Hallberg, 2006). Family-related challenges such as access to care, stress during times of acute illness, and school and work disruptions also contribute to parental feelings of loneliness and exclusion (Zurynski et al., 2008). Families having a daughter with CAH experience significant, additional challenges associated with the condition when compared to families having a son with CAH. These include the fear of intense stigmatization, challenging surgical decisions, and concerns regarding disclosure to others of their daughter's condition.

The initial time period following the diagnosis of CAH, whether that is in the delivery room or by a newborn screening days later, produced varied parental responses based on the gender of the child. How the child's condition is initially portrayed to the family from healthcare providers is critical in shaping the lens through which the family views the condition. For parents of girls with CAH, the view of the condition begins to emerge shortly after birth and can be related to healthcare providers' responses to the condition and associated ambiguous genitalia and what terminology is used to communicate the diagnosis to parents. Several parents interviewed voiced disappointment over the way healthcare providers responded to their daughters' genital appearance and the language providers used as they discussed differential diagnoses.

Seven out of nine parents having a daughter with CAH who were interviewed expressed concern and disappointment regarding how healthcare providers discussed their daughters' ambiguous genitalia. This echoes concerns raised by patient advocacy groups in the last ten years over the use of terms such as "intersex," "pseudo hermaphroditism," and "hermaphroditism." Recently, these terms have been replaced in the medical community, particularly in Europe, by the more acceptable term of disorders of sex development (DSD)

(Pasterski et al., 2010; Hughes, 2008). The intent in changing this nomenclature was that the term DSD would be both medically appropriate as well as sensitive to needs of the patients and parents (Lin-Su, Lekarev, Poppas & Vogiatzi, 2015). A large number of CAH patients, parents, and other relatives of patients with CAH were surveyed on their response to the term DSD last year (Lin-Su et al., 2015). Although DSD was developed with a primary objective of better representing affected individuals, most surveyed believed DSD had a negative effect on the CAH community, which stems from concern that DSD contributes to stigmatizing CAH and implies some sort of “sexual disorder” in the population labeled as having it. Furthermore, there is concern that classifying CAH as a DSD lessens the significance of the important medical issues surrounding adrenal insufficiency (Lin-Su et al., 2015). Of the 486 participants who took the survey, the most favored term, endorsed by 35% of the respondents, was “non-typical genitalia” (Lin-Su et al., 2015). Healthcare providers need to refrain from using terms to describe children born with ambiguous genitalia that may be viewed by parents as insensitive or stigmatizing and focus more directly on the anatomical presentation, possibility of life threatening salt wasting crisis if the child does have CAH, and providing reassurance that CAH is manageable and emphasizing the many ways the child is normal.

Parents of daughters with ambiguous genitalia struggle with sharing information about their child’s condition with others, not only at birth, but throughout their child’s life (Crissman et al., 2011; Sanders et al., 2012). For parents having a child with ambiguous genitalia, the decision of whether or not to disclose information and to whom is based on: the likelihood of stigmatization, who they felt had a “right” to the information, a personal ease with the terminology associated with the affected anatomy, and parents’ perceptions of their ability to accurately describe the condition. If parents decide to share information with others, they often choose to limit the amount and details due to the fear of stigmatization, which can be taxing on the family (Crissman et al., 2011).

Parents of both genders described difficulties in how much information to provide to individuals in their child's social life such as family and friends. They explained not wanting to "scare" others about the possibility of adrenal crisis events when the likelihood of them occurring is relatively small. For example, determining if injection training is needed for adults watching their child for an occasional, brief period of time was problematic as was apprising their child's adolescent friends of condition management. However, fear that not informing others might result in a life threatening situation if their child became ill or sustained a traumatic injury was also distressing. Despite these concerns, parents of boys did not describe concerns about stigma surrounding disclosure decisions, unlike parents of girls. As in previous studies, the parents in this current study guarded the knowledge that their daughter was born with ambiguous genitalia very closely in an effort to protect their child's relationships now and in the future and shield them from potential embarrassment and stigmatization (Sanders et al., 2012). However, in doing so, parents worried that keeping this part of their child's life a secret was, in and of itself, stigmatizing.

For families of girls with CAH considering feminizing genitoplasty, perceptions of stigma were described as a major factor in parental surgical decision making. If the degree of virilization is less, meaning minimal clitoromegaly with the junction between the vagina and urethra near the perineum, surgery might not be necessary. However, parents may still opt for surgical intervention from a more cosmetic perspective (Speiser et al., 2010). Parents are typically told that if they opt for surgery, it is best to do so between two months to one year of age due to the assumed child psychological benefits associated with having normal genitalia, less likelihood of associated stigma related to ambiguous genitalia, and the inability for the child to remember the surgery as a traumatic childhood event (Gollu et al., 2007). Early surgery is also thought to reduce parental anxiety associated with having a child with a disorder of sex development (DSD) (Crawford, Warne, Grover, Southwell & Hutson, 2009).

However, any type of surgery that reduces clitoral size is a delicate one, as without preservation of the neurovascular bundle, the glans, and the preputial skin associated with the glans, sensitivity in the genital area may be comprised, which has the potential to permanently affect sexual satisfaction in adulthood (Gollu et al., 2007). Additionally, some of these girls will need additional, corrective surgery as they age into adulthood in order to successfully wear tampons and have sexual intercourse. Having repeated clitoral surgery has the potential to cause increased damage to sexual functioning and some providers recommend waiting to make the decision to have surgery until the child is old enough to participate in the decision making process (Gollu et al., 2007; Creighton, Minto & Steele, 2001). Certain studies on adult women who have had cosmetic surgery for genital ambiguity as children report feeling dissatisfied with having had the surgery, not necessarily related to ultimate cosmetic appearance, but rather sexual satisfaction (Gollu et al., 2007; Creighton, Minto & Steele, 2001; Rangecroft, 2003). Parents of daughters with ambiguous genitalia report a struggle between wanting to protect their child and do “what is right,” but realizing that their decision for their child may be in conflict with what their child as an adolescent or adult may have chosen for themselves (Carter & Goodacre, 2012). It is evident in this study and others that the decision regarding whether or not their daughters should have corrective, genital surgery is a very difficult one for parents, filled with concerns over stigmatization, future sexual satisfaction, and gender identity (Sanders et al., 2012; Crissman et al., 2011; Lundberg et al., 2016). Health care providers must be aware of this significant family struggle from social, ethical, and practical perspectives and provide not just informative, but also compassionate and supportive, care to families having a daughter with CAH. Additionally, this care should not just be focused on the time surrounding the surgery and the eventual surgical decision. Thoughtful care should continue throughout the child’s life, as early surgical intervention may alleviate some concerns surrounding genital

appearance initially, but over time, parents continue to worry about their child's future sex development and function as well as whether additional surgeries will be needed.

Conclusion

Although there were some limitations to this study including a small sample size and that the children's perspectives were not included, it is evident that family management is different, and more complex, for families of girls when compared to boys with CAH. Acknowledging the significant different experiences for families having a boy versus families having a girl with CAH and creating support systems specifically for girls born with CAH that address both the surgical procedures often associated with ambiguous genitalia as well as possible long-term complications resulting from being born with elevated testosterone is critical to promoting a healthy family response and child adaptation to the disorder. Healthcare providers, especially pediatric endocrinologists and pediatric endocrine nurses, need to evaluate not only the physical aspects of health for girls with CAH such as growth and endocrine lab values, but also the psychosocial effects related to being born with ambiguous genitalia. Conducting further research into the possible relationship between parents of girls deciding to keep the condition confidential in an effort to protect the child and family's privacy and the risk of people in the child's social environment not knowing of the diagnosis, thus not responding appropriately during times of acute illness and/or adrenal crisis, is warranted. In summation, future studies with an emphasis on family experiences and management, including differences between families having a boy versus a girl, would enhance the current state of the science and provide a much-needed window into needed prospective interventions aimed at improving the lives of all families and children with CAH.

REFERENCES

- Berenbaum, S. A., & Bailey, J. M. (2003). Effects on gender identity of prenatal androgens and genital appearance: Evidence from girls with congenital adrenal hyperplasia. *The Journal of Clinical Endocrinology and Metabolism*, 88(3), 1102-1106.
- Berenbaum, S., Bryk, K., & Beltz, A. (2012). Early androgen effects on spatial and mechanical abilities: evidence from congenital adrenal hyperplasia. *Behavioral Neuroscience*, 126(1), 86-96. Doi: 10.1037/a0026652
- Bowen, G. A. (2008). Naturalistic inquiry and the saturation concept: a research note. *Qualitative research*, 8(1), 137-152.
- CARES Foundation (2014). Retrieved from <http://www.caresfoundation.org>
- Crawford, J. M., Warne, G., Grover, S., Southwell, B. R., & Hutson, J. M. (2009). Results from a pediatric surgical center justify early intervention in disorders of sex development. *Journal of Pediatric Surgery*, 44(2), 413-416.
- Creighton, S. M., Minto, C. L., & Steele, S. J. (2001). Objective cosmetic and anatomical outcomes at adolescence of feminizing surgery for ambiguous genitalia done in childhood. *The Lancet*, 358(9276), 124-125.
- Dessens, A. B., Slijper, F. M., & Drop, S. L. (2005). Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. *Archives of Sexual Behavior*, 34(4), 389-397.
- Dellve, L., Samuelsson, L., Tallborn, A., Fasth, A., & Hallberg, L. R. M. (2006). Stress and well-being among parents of children with rare diseases: a prospective intervention study. *Journal of Advanced Nursing*, 53(4), 392-402.
- Gollu G, Yildiz RV, Bingol-Kologlu M, et al. (2007). Ambiguous genitalia: an overview of 17 years' experience. *Journal of Pediatric Surgery*, 42(5), 840-844.
- Hines, M., Fane, B. A., Pasterski, V. L., Mathews, G. A., Conway, G. S., & Brook, C. (2003). Spatial abilities following prenatal androgen abnormality: Targeting and mental rotations performance in individuals with congenital adrenal hyperplasia. *Psychoneuroendocrinology*, 28(8), 1010-1026.
- Hughes, I. A. (2008). Disorders of sex development: a new definition and classification. *Best Practice & Research Clinical Endocrinology & Metabolism*, 22(1), 119-134.
- Karkazis, K. (2008). *Fixing Sex: Intersex, Medical Authority, and Lived Experience*. Duke University Press.
- Knafl, K., Deatrack, J., & Havill, N. (2012). Continued development of the family management style framework. *Journal of Family Nursing*, 18(1), 11-34. Doi: 10.1177/1074840711427294
- Lin-Su, K., Lekarev, O., Poppas, D., & Vogiatzi, M. (2015). Congenital adrenal hyperplasia-patient perception of disorders of sex development nomenclature. *International Journal of Pediatric Endocrinology*, 1. Doi: 10.1186/s13633-015-0004-4

- Lundberg, T., Lindström, A., Roen, K., & Hegarty, P. (2016). From knowing nothing to knowing what, how and now: Parents' experiences of caring for their children with congenital adrenal hyperplasia. *Journal of Pediatric Psychology*, 1-10. Doi: 10.1093/jpepsy/jsw001
- Mathews, G. A., Fane, B. A., Conway, G. S., Brook, C. G., & Hines, M. (2009). Personality and congenital adrenal hyperplasia: Possible effects of prenatal androgen exposure. *Hormones and Behavior*, 55(2), 285-291. doi:10.1016/j.yhbeh.2008.11.007; 10.1016/j.yhbeh.2008.11.007
- Merke, D. P., & Bornstein, S. R. (2005). Congenital adrenal hyperplasia. *The Lancet*, 365(9477), 2125-2136.
- Morse, J. M. (2015). Data were saturated... *Qualitative Health Research*, 25(5), 587-588. doi: 10.1177/1049732315576699
- Nordenstrom, A., Servin, A., Bohlin, G., Larsson, A., & Wedell, A. (2002). Sex-typed toy play behavior correlates with the degree of prenatal androgen exposure assessed by CYP21 genotype in girls with congenital adrenal hyperplasia. *The Journal of Clinical Endocrinology and Metabolism*, 87(11), 5119-5124. doi:10.1210/jc.2001-011531
- Nordenstrom, A., Frisen, L., Falhammar, H., Filipsson, H., Holmdahl, G., Janson, P. O., ... & Nordenskjold, A. (2010). Sexual function and surgical outcome in women with congenital adrenal hyperplasia due to CYP21A2 deficiency: clinical perspective and the patients' perception. *The Journal of Clinical Endocrinology & Metabolism*, 95(8), 3633-3640. Doi: <http://dx.doi.org.libproxy.lib.unc.edu/10.1210/jc.2009>
- Pass, K. & Neto, U. (2009). Update: newborn screening for endocrinopathies. *Endocrinology Metabolism Clinics of North America*, 38, 827-837.
- Pasterski, V. L., Geffner, M. E., Brain, C., Hindmarsh, P., Brook, C., & Hines, M. (2005). Prenatal hormones and postnatal socialization by parents as determinants of male-typical toy play in girls with congenital adrenal hyperplasia. *Child Development*, 76(1), 264-278. doi:CDEV843
- Pasterski, V., Hindmarsh, P., Geffner, M., Brook, C., Brain, C., & Hines, M. (2007). Increased aggression and activity level in 3- to 11-year-old girls with congenital adrenal hyperplasia (CAH). *Hormones and Behavior*, 52(3), 368-374. doi:10.1016/j.yhbeh.2007.05.015
- Pasterski, V., Prentice, P., & Hughes, I. A. (2010). Consequences of the Chicago consensus on disorders of sex development (DSD): current practices in Europe. *Archives of Disease in Childhood*, 95(8), 618-623. Doi: 10.1136/adc.2009.163840
- Rangecroft, L. (2003). Surgical management of ambiguous genitalia. *Archives of Disease in Childhood*, 88(9), 799-801.
- Sandelowski, M. (2011). Parallelism in constant comparison analysis. *Research in Nursing and Health*, 34(6), 433-434.

- Sanders, C., Carter, B., & Goodacre, L. (2012). Parents need to protect: influences, risks and tensions for parents of prepubertal children born with ambiguous genitalia. *Journal of Clinical Nursing*, 21(21-22), 3315-3323. Doi: 10.1111/j.1365-2702.2012.04109.x
- Speiser, P., Azziz, R., Baskin, L., Ghizzoni, L., Hensle, T., Merke, D. . . . White, P. (2010). Congenital adrenal hyperplasia due to 21-hydroxylase deficiency: An endocrine clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*, 95(9), 4133-4160. Doi:10.1210/jc.2009-2631
- Vaismoradi, M., Turunen, H., & Bondas, T. (2013). Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nursing & Health Sciences*, 15(3), 398-405. Doi: 10.1111/nhs.12048
- VERBI Software (2015). MAXQDA 12 Reference Manual (v1.0), available at: [http://www.maxqda.com/download/manuals/ ... al_eng.pdf](http://www.maxqda.com/download/manuals/al_eng.pdf)
- Witchel, S. & Azziz, R. (2011). Congenital adrenal hyperplasia. *Journal of Pediatric Adolescent Gynecology*, 24, 116-126. Doi: 10.1016.j.jpag.2010.10.001
- Wong, W. I., Pasterski, V., Hindmarsh, P. C., Geffner, M. E., & Hines, M. (2013). Are there parental socialization effects on the sex-typed behavior of individuals with congenital adrenal hyperplasia? *Archives of Sexual Behavior*, 42(3), 381-391. doi:10.1007/s10508-012-9997-4
- Zurynski, Y., Frith, K., Leonard, H., & Elliott, E. (2008). Rare childhood diseases: how should we respond?. *Archives of Disease in Childhood*, 93(12), 1071-1074. Doi: 10.1136/adc.2007.134940

CHAPTER 5: DISCUSSION

This dissertation sets the stage for a program of research that will contribute to the development of evidenced-based, family-centered interventions for children with congenital adrenal hyperplasia (CAH). The analysis reported in Chapter 2 synthesized the existing literature examining the care and management of children with CAH over the last fifteen years. To date, most investigators have addressed health and developmental issues for children with CAH and the unique physical and psychosocial challenges for girls with CAH. Relatively few studies have examined the contextual factors influencing child wellbeing or the family response to having a child with CAH.

The primary physiological health issues children with CAH face include obesity, short stature, vascular abnormalities, feminizing genitoplasty surgery for girls, and potential adrenal crisis events. Obesity was found to be a significant problem in children with CAH (Volkl, Simm, Beier, & Dorr, 2006; Mendes-dos-Santos et. al, 2011; Cetinkaya & Kara, 2011; Moreira et al., 2013). However, decreased height was more difficult to predict. Medes-dos-Santos et al. (2011) concluded in their cross sectional study that height in children with CAH was similar to unaffected children of the same age, yet final height appeared decreased in other studies (Bonfig, 2007; Bonfig, Schmidt & Schwartz, 2011). The only intervention study found concerning children with CAH was a 2011 study by Lin-Su, Harbison, Lekarev, Vogiatzi, and New, which evaluated whether growth hormone (GH) alone or in combination with a leutinizing hormone releasing hormone agonist (LHRHa) would improve final height in children with CAH. They concluded that specifically for children with CAH experiencing precocious puberty and short stature, GH alone or in combination with LHRHa is an

effective therapy for improving final height; however, males experienced somewhat less height benefit than females.

Due to a variety of factors, children with CAH are at risk for vascular problems (Harrington, Pena, Gent, Hirte, & Couper, 2012). A 2012 study showed that children with CAH have significant vascular and smooth muscle dysfunction when compared to healthy controls, and this level of dysfunction was comparable to the healthy subjects that were mild to moderately obese, suggesting that it may be obesity rather than adrenal insufficiency that places these children at risk. However, more research is needed to evaluate if other risk factors such as insulin resistance, hypertension, dyslipidemia, hypercortisolism, and hyperandrogenism play a role in reduced vascular function (Harrington et al., 2012).

Very few studies focused on acute illness, stress dosing, and adrenal crisis prevention, despite the fact that parents in the current study expressed much concern about these events. Three of the four studies investigating illness and adrenal crisis examined the role that physical stress had on glucose regulation in children with CAH. Children with CAH do not mount the normal exercise-induced glucose response due to lack of cortisol production with physical activity (Weise et al., 2004; Green-Golan et al., 2007) and are at risk for hypoglycemia during acute viral or bacterial illnesses (Keil, Bosmans, Van Ryzin & Merke, 2010). These studies suggest the need for additional glucose supplementation in addition to “stress dosing” during times of acute illness (Keil et al., 2010) as well as possibly before strenuous exercise (Weise et al., 2004; Green-Golan et al., 2007). A 2011 study by the author investigated parents’ knowledge of CAH, adrenal crisis, and stress dosing as well as their confidence in responding to adrenal crises (Fleming, Rapp & Sloane, 2011). As with this dissertation study, parents stated that their children experience adrenal crisis events an average of one to two times per year and described having a clear understanding of the condition and the need for stress dosing/injection; however, they felt that there was a lack of repeated instruction and demonstrations from providers on how to give the injection

Fleming, Rapp & Sloane, 2011. Parental difficulties in effective and detailed communication with their CAH child's health care providers, especially surrounding the time of diagnosis and in adrenal crisis management, were found in this study as well as a 2014 study (Boyse et al.).

The studies that explored health related quality of life (HRQoL) for children with CAH had mixed results. Parents in the Netherlands reported no negative effects on their child's quality of life (Sanches et. al, 2012); however a Brazilian study (Gilban, Alves and Beserra, 2014) found a loss of HRQoL in children and teens with CAH, especially in the physical dimension (when compared with unaffected controls), and a study based of out Los Angeles (Yau et al., 2015) found that children with CAH had an overall decrease in HRQoL with regard to school functioning.

The majority of the studies found in the systematic review concerned the consequences of androgen exposure on child behavior in girls born with CAH, not surgical decision making by parents, nor possible stigma associated with being born with ambiguous genitalia. Although reconstructive feminizing genitoplasty is recommended by some providers at an early age and can involve multiple surgeries into adolescence (Witchel & Azziz, 2011; Karkazis, 2008), there is not an accepted recommendation by providers on this issue. Girls with CAH identify as female (Berenbaum & Bailey, 2003; Dessens, Slijper, & Drop, 2005), but they often show increased preference for male toys and activities (Nordenstrom et al., 2002; Pasterski et al, 2005; Wong et al., 2013), increased aggression (Pasterski et al., 2007; Mathews et al, 2009), increased male-typical sexual orientation (Nordenstrom et al., 2010), and differences when compared to non-CAH girls in spatial abilities (Hines et al., 2003; Berenbaum et al., 2012).

In the systematic review, it is evident that more research examining CAH from a family perspective as well as different research methodologies is needed to better understand the challenges these families face so that interventions can be developed to

improve their daily lives. The studies reviewed used quantitative methods for the most part and were cross-sectional and descriptive in nature. Additionally the studies that used structured measures did not report their reliability and validity. Since these studies focused on children, the lack of longitudinal studies is a notable gap in the literature. Moreover, there are few qualitative or mixed method studies on the issue of how families are coping with having a child with CAH, which is surprising as ambiguous genitalia and the life threatening nature of CAH along with the related physical and emotional struggles are sensitive topics that are likely difficult to adequately address in questionnaires and surveys.

Chapter 3 of this dissertation comprised the primary, mixed methods study that investigated parental management of adrenal crisis in children with CAH. This study had findings that point to a clear and distinct need for increased healthcare provider education related to supporting parents of children having CAH. The most important findings from the analysis of Phase 1 include that 25% of parents surveyed did not receive the prescription for injectable hydrocortisone within one month of diagnosis, despite that being the standard of care (Speiser et al., 2010). Additionally, there were significant relationships between parents having directly been shown by a provider how to correctly administer the injection and a stronger perceived ability to manage the condition as well as between the age of child and the average number of adrenal crisis events experienced each year, with the number of crises decreasing over time. Regarding frequency of adrenal crisis events, parents reported children having 0.77 adrenal crisis events per year (a minimum number of 1 adrenal crisis episode every 1.3 years) in the first five years of life; after the age of five, parents reported 0.27 adrenal crisis events per year (a minimum of 1 adrenal crisis episode every 3.7 years). Moreover, there was a significant, positive relationship between the age of the child and perceived management ability by parents. Finally, there was a significant, negative relationship between perceived management ability by parents and the impact CAH has on the family.

In Phase two of the study, it was evident that there are multiple contextual influences that affect family management of CAH including interchanges with schools and healthcare providers, the child and family's social network (extended family, sports and extracurricular activities, babysitters), and access to resources. One half of the parents interviewed (five families) switched healthcare providers within the first two years of their child's life due to a perceived lack of provider knowledge of CAH treatment and/or lack of provider education on adrenal crisis management. Furthermore, parents don't feel they have received frequent enough instruction from health care providers on how to administer intramuscular hydrocortisone and would benefit from repeated demonstrations. In addition, parents don't feel they receive meaningful emotional support from their child's healthcare providers.

Despite the challenges associated with the condition, all of the parents interviewed felt day-to-day management of their child's condition is going very well and that their children are thriving overall. Partnered parents did not express any discrepant views of the illness, nor any significant tension in their relationship related to their child's CAH; however, parents did express some differences in management of the condition. One example is how quickly a parent decides to stress dose with steroids when their child is ill.

Parents of children with CAH feel a pervasive worry about possible adrenal crisis events, their CAH child's transition into young adulthood/adolescence and "letting go," and the experiences for siblings of watching the CAH child have an adrenal crisis and witnessing the extra attention the CAH child requires. Additionally, because CAH is autosomal recessive, future family planning decisions are challenging for these families

Chapter 4 examined the differences in management experiences for families having a girl with CAH versus families having a boy. The time period surrounding the child's diagnosis and the consequences of ambiguous genitalia including the related fear or actual stigmatization, who to disclose the situation to, and the often necessary difficult surgical decisions parents must make show the unique, additional struggles families having a girl

with CAH face. Acknowledging these important differences and how these differences affect the family is crucial. Support systems specifically for girls born with CAH that address both the surgical procedures often associated with ambiguous genitalia as well as possible long-term complications resulting from being born with elevated testosterone is needed and should be encouraged by health care providers. Additionally, pediatric endocrinologists and pediatric endocrine nurses need to assess both the physical health for girls with CAH as well as the emotional aspects related to being born with ambiguous genitalia and make referrals as need to mental health professionals equipped to handle these concerns.

Future Implications for Practice and Research

There is a clear need for additional research to identify the ways in which having a child with CAH intersects with family life. From a research methodology perspective, additional studies that are longitudinal in nature, have a larger number of participants, and are qualitative or use mixed methods would be beneficial in providing a richer and more meaningful understanding family management challenges over time.

Additionally, intervention studies addressing parental knowledge of effective response to adrenal crisis events are warranted. The problem of ineffective preparation regarding how to manage an adrenal crisis for parents of children with CAH by providers is likely multi-factorial. Limited time during the provider-patient encounter, the episodic nature of adrenal crises, and necessity to discuss management issues such as lab values, growth, and weight rather than crisis management may be the focus in encounters with providers. During routine office visits, health care professionals may not recognize the importance of emergency management and assessing parents' current level of competency. Although parents of children with CAH must deal with aspects of the disease other than adrenal crisis, it is the life threatening aspect of the disorder that is the focal concern identified by parents based on the results of both the current study and others (Merke & Bornstein, 2005;

Fleming, Rapp, & Sloane, 2011). When parents are not properly educated on how to respond to adrenal crisis events, the result can lead to parental stress as well as serious injury and possible death of the child. An intervention study addressing these gaps in provider education is critical. One such intervention could include the use of a training video that discusses the condition and walks through the injection process in detail, with the intervention involving parental review of the video at six-month intervals coinciding with their child's required lab draws. This video could also be used by parents to train others who care for their children in the parents' absence, such as babysitters and teachers.

From this study, it appears there is room for improvement in the interactions between pediatric endocrinologists and parents, especially surrounding parental adrenal crisis preparation and the potential stigma associated with ambiguous genitalia. Studies that investigate how pediatric endocrinologists view adrenal crisis events themselves might be helpful in addressing the disconnect parents feel regarding a lack of thorough, detailed provider instruction on adrenal crisis management. Perhaps pediatric endocrinologists have not witnessed these crisis events firsthand, as by the time they are likely notified, many of the children experiencing adrenal crisis have been stabilized post-injection, either in their homes or in the emergency departments. The lack of provider involvement in the actual adrenal crisis event might account for some of the decreased emphasis placed on parental preparation.

Moreover, pediatric endocrinologists are in a challenging position regarding long term care of ambiguous genitalia, both for their female CAH patients that have had corrective surgery as well as those that have not. Stigmatization, repeated genital surgeries, and sexual satisfaction are sensitive topics, especially during adolescence. It is likely that these children and their parents are interacting more regularly over the course of childhood with a pediatric endocrinologist, rather than a surgeon, and perhaps frequent guidance and discussion of these complex topics from pediatric endocrinologists would be beneficial for

families. For example, the relationship between parents of girls deciding to keep the condition confidential in an effort to protect the child and family's privacy and the risk of people in the child's social environment not knowing of the diagnosis, thus not responding appropriately during times of acute illness and/or adrenal crisis, warrants addressing.

Finally, hearing from children with CAH themselves would be helpful in understanding the individual, as well as the family, effects of this episodically life threatening condition. Such a study would need to include both boys and girls with the condition as well as children that are varied ages, as the experience and concerns of a younger child is likely significantly different from an adolescent, especially with regards to social support.

REFERENCES

- Berenbaum, S. A., & Bailey, J. M. (2003). Effects on gender identity of prenatal androgens and genital appearance: Evidence from girls with congenital adrenal hyperplasia. *The Journal of Clinical Endocrinology and Metabolism*, 88(3), 1102-1106.
- Berenbaum, S., Bryk, K., & Beltz, A. (2012). Early androgen effects on spatial and mechanical abilities: evidence from congenital adrenal hyperplasia. *Behavioral Neuroscience*, 126(1), 86-96. Doi: 10.1037/a0026652
- Bonfig, W. (2007). Reduced final height outcome in congenital adrenal hyperplasia under prednisone treatment: Deceleration of growth velocity during puberty. *The Journal of Clinical Endocrinology and Metabolism*, 92(5), 1635; 1635-1639; 1639.
- Bonfig, W., Schmidt, H., & Schwarz, H. P. (2011). Growth patterns in the first three years of life in children with classical congenital adrenal hyperplasia diagnosed by newborn screening and treated with low doses of hydrocortisone. *Hormone Research in Paediatrics*, 75(1), 32-37. doi:10.1159/000316973
- Boyse, K. L., Gardner, M., Marvicsin, D. J., & Sandberg, D. E. (2014). "It was an overwhelming thing": Parents' needs after infant diagnosis with congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 29(5), 436-441. doi:10.1016/j.pedn.2014.01.007
- Cetinkaya, S., & Kara, C. (2011). The effect of glucocorticoid replacement therapy on bone mineral density in children with congenital adrenal hyperplasia. *Journal of Pediatric Endocrinology & Metabolism : JPEM*, 24(5-6), 265-269.
- Dessens, A. B., Slijper, F. M., & Drop, S. L. (2005). Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. *Archives of Sexual Behavior*, 34(4), 389-397.
- Fleming, L. K., Rapp, C. G., & Sloane, R. (2011). Caregiver knowledge and self-confidence of stress dosing of hydrocortisone in children with congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 26(6), e55-60. doi:10.1016/j.pedn.2011.03.009; 10.1016/j.pedn.2011.03.009
- Gilban, D. L., Alves Junior, P. A., & Beserra, I. C. (2014). Health related quality of life of children and adolescents with congenital adrenal hyperplasia in Brazil. *Health and Quality of Life Outcomes*, 12, 107-014-0107-2. doi:10.1186/s12955-014-0107-2
- Green-Golan, L., Yates, C., Drinkard, B., VanRyzin, C., Eisenhofer, G., Weise, M., & Merke, D. P. (2007). Patients with classic congenital adrenal hyperplasia have decreased epinephrine reserve and defective glycemic control during prolonged moderate-intensity exercise. *Journal of Clinical Endocrinology & Metabolism*, 92(8), 3019-3024.
- Harrington, J., Peña, A. S., Gent, R., Hirte, C., & Couper, J. (2012). Adolescents with congenital adrenal hyperplasia because of 21-hydroxylase deficiency have vascular dysfunction. *Clinical Endocrinology*, 76(6), 837-842.
- Hines, M., Fane, B. A., Pasterski, V. L., Mathews, G. A., Conway, G. S., & Brook, C. (2003). Spatial abilities following prenatal androgen abnormality: Targeting and mental

- rotations performance in individuals with congenital adrenal hyperplasia. *Psychoneuroendocrinology*, 28(8), 1010-1026.
- Karkazis, K. (2008). *Fixing Sex: Intersex, Medical Authority, and Lived Experience*. Duke University Press.
- Keil, M. F., Bosmans, C., Van Ryzin, C., & Merke, D. P. (2010). Hypoglycemia during acute illness in children with classic congenital adrenal hyperplasia. *Journal of Pediatric Nursing*, 25(1), 18-24. doi:10.1016/j.pedn.2008.06.003
- Lin-Su, K., Harbison, M. D., Lekarev, O., Vogiatzi, M. G., & New, M. I. (2011). Final adult height in children with congenital adrenal hyperplasia treated with growth hormone. *Journal of Clinical Endocrinology & Metabolism*, 96(6), 1710-1717. doi:10.1210/jc.2010-2699
- Mathews, G. A., Fane, B. A., Conway, G. S., Brook, C. G., & Hines, M. (2009). Personality and congenital adrenal hyperplasia: Possible effects of prenatal androgen exposure. *Hormones and Behavior*, 55(2), 285-291. doi:10.1016/j.yhbeh.2008.11.007; 10.1016/j.yhbeh.2008.11.007
- Mendes-Dos-Santos, C. T., Lemos-Marini, S. H., Baptista, M. T., Guerra-Junior, G., De-Mello, M. P., Paulino, M. F., & Morcillo, A. M. (2011). Normalization of height and excess body fat in children with salt-wasting 21-hydroxylase deficiency. *Journal of Pediatrics*, 87(3), 263-268. doi:doi:10.2223/JPED.2095; doi:10.2223/JPED.2095
- Merke, D. P., & Bornstein, S. R. (2005). Congenital adrenal hyperplasia. *Lancet*, 365(9477), 2125-2136. Retrieved from https://auth.lib.unc.edu/ezproxy_auth.php?url=http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=2009043786&site=ehost-live&scope=site
- Moreira, R. P., Villares, S. M., Madureira, G., Mendonca, B. B., & Bachega, T. A. (2013). Obesity and familial predisposition are significant determining factors of an adverse metabolic profile in young patients with congenital adrenal hyperplasia. *Hormone Research in Paediatrics*, 80(2), 111-118. doi:10.1159/000353762
- Nordenstrom, A., Servin, A., Bohlin, G., Larsson, A., & Wedell, A. (2002). Sex-typed toy play behavior correlates with the degree of prenatal androgen exposure assessed by CYP21 genotype in girls with congenital adrenal hyperplasia. *The Journal of Clinical Endocrinology and Metabolism*, 87(11), 5119-5124. doi:10.1210/jc.2001-011531
- Pasterski, V. L., Geffner, M. E., Brain, C., Hindmarsh, P., Brook, C., & Hines, M. (2005). Prenatal hormones and postnatal socialization by parents as determinants of male-typical toy play in girls with congenital adrenal hyperplasia. *Child Development*, 76(1), 264-278. doi:CDEV843
- Pasterski, V., Hindmarsh, P., Geffner, M., Brook, C., Brain, C., & Hines, M. (2007). Increased aggression and activity level in 3- to 11-year-old girls with congenital adrenal hyperplasia (CAH). *Hormones and Behavior*, 52(3), 368-374. doi:10.1016/j.yhbeh.2007.05.015

- Sanches, S. A., Wiegers, T. A., Otten, B. J., & Claahsen-van der Grinten, H. L. (2012). Physical, social and societal functioning of children with congenital adrenal hyperplasia (CAH) and their parents, in a dutch population. *International Journal of Pediatric Endocrinology*, 2012(1), 2-9856-2012-2. doi:10.1186/1687-9856-2012-2
- Speiser, P. W., Azziz, R., Baskin, L. S., Ghizzoni, L., Hensle, T. W., Merke, D. P., . . . White, P. C. (2010). A summary of the endocrine society clinical practice guidelines on congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency. *International Journal of Pediatric Endocrinology*, 2010. doi:10.1155/2010/494173; 10.1155/2010/494173
- Völkl, T., Simm, D., Beier, C., & Dörr, H. (2006). Obesity among children and adolescents with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Pediatrics*, 117(1), e98-105. Retrieved from https://auth.lib.unc.edu/ezproxy_auth.php?url=http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=2009115275&site=ehost-live&scope=site
- Weise, M., Mehlinger, S. L., Drinkard, B., Rawson, E., Charmandari, E., Hiroi, M., ... & Merke, D. P. (2004). Patients with classic congenital adrenal hyperplasia have decreased epinephrine reserve and defective glucose elevation in response to high-intensity exercise. *Journal of Clinical Endocrinology & Metabolism*, 89(2), 591-597.
- Witchel, S. F., & Azziz, R. (2011). Congenital adrenal hyperplasia. *Journal of Pediatric and Adolescent Gynecology*, 24(3), 116-126. doi:10.1016/j.jpag.2010.10.001; 10.1016/j.jpag.2010.10.001
- Wong, W. I., Pasterski, V., Hindmarsh, P. C., Geffner, M. E., & Hines, M. (2013). Are there parental socialization effects on the sex-typed behavior of individuals with congenital adrenal hyperplasia? *Archives of Sexual Behavior*, 42(3), 381-391. doi:10.1007/s10508-012-9997-4
- Yau, M., Vogiatzi, M., Lewkowitz-Shpuntoff, A., Nimkarn, S., & Lin-Su, K. (2015). Health-Related Quality of Life in Children with Congenital Adrenal Hyperplasia. *Hormone Research in Paediatrics*, 84(3),

APPENDIX A: INVITATION TO PARTICIPATE LETTER

“Parents Managing Adrenal Crisis in Children with Congenital Adrenal Hyperplasia”

We are inviting you to take part in a research project that we are conducting with parents (or primary caregivers) of children with classic congenital adrenal hyperplasia (CAH). The purpose of this study is to better understand how parents view and manage adrenal crisis episodes in their children with CAH. Additionally, how parents are prepared by health care providers on managing their child's adrenal crisis and the impact on the family of having a child with a life threatening condition will be explored.

Who can participate? If you are the parent of a child with classic CAH age 0-18, you are invited to participate. Your child must not have any other complex medical conditions. If your child is not between the ages of 0-18 or has additional complex medical conditions, you are not eligible for this study at this time. In addition, you must speak English, be at least 18 years old, have an email account, and have access to the internet. Please contact Louise Fleming at lkfleming@email.unc.edu with any questions.

What will we ask you to do? We will ask you to complete four online questionnaires, ***and may interview you, if you are willing***. The questionnaires include one with general family information (such as where you live, how old your child(ren) is, etc.) as well as the Family Management Measure (FaMM)-View of Condition Impact scale, which has 10 items; ***the FaMM Management Ability Scale, which as 12 items***; and the PedsQL-Family Impact Module, which has 36 items. They will measure the impact that you feel your child's CAH has on your family, how well you feel you manage your child's CAH, and they should take about 15-20 minutes to complete. The interview will be a telephone interview at a time that is convenient for you. The interview will take approximately 45-60 minutes.

The project has been approved institutional review board for human subjects research at University of North Carolina at Chapel Hill and is supported by the CARES Foundation. If you agree to take part, all information you give will be confidential. No one except the research team, which includes the chair of my dissertation committee, Marcia Van Riper, PhD, RN, FAAN, will have access to your information. If you wish to be involved in this research or have any questions, please contact Louise Fleming. Email is lkfleming@email.unc.edu or telephone (919) 272-7174. Many thanks for your kind consideration.

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APPENDIX B: INTERVIEW GUIDE

Opening:

I would like to thank you for taking the time to talk to me about your child's CAH and how you (and partner, spouse, etc. if applicable) manage the condition, especially during times of adrenal crisis. The questions I will ask are to learn how you (and your partner) feel about the preparation you have received regarding how to handle times of adrenal crisis, how such information was given to you by providers, and how you then prepare others that care for your child, when you are not present, to handle possible crises. Additionally, I will ask you some questions about how having child with a life-threatening condition have affected you and your family, if at all.

If I will also be, or have already interviewed your partner, please know that both of your responses will be kept confidential. I will not share what you say with them, or what they say with you.

Definition of the Situation:

Tell me how you felt soon after your child was diagnosed with CAH and has that changed in the [XX] years since diagnosis?

How would you describe your child's day and typical activities in comparison to other children his (or her) age?

How much would you say you and your partner have in common with how you view and manage your child's CAH?"

Tell me about how confident you feel to take care of your child's CAH.

If you were to make support group topics for families of children with CAH, what do you think would be most important to discuss?

Management Behavior :

Tell me about some of the aspects of managing the life threatening components of your child's condition that you believe are going well.

Tell me about how your provider has prepared you, if at all, to handle a potential adrenal crisis and are you satisfied with the instruction? Have you sought such instruction from sources other than your child's healthcare providers such as the internet or support groups, and if so, tell me to what extent you have found that to be helpful.

Who in your social network, such as schools, babysitters, family members, etc., have you discussed your child's CAH with and how, if at all, have you prepared them to care for your child if an adrenal crisis episode were to occur when you are not present?

Perceived Consequences:

Tell me how many times a day you think about your child's CAH.

How would you describe the impact of the life threatening nature of CAH on day-to-day family life?

How do you see CAH impacting your child and family in the future?

If your child with CAH has siblings, what impact, if at all, do you consider having a brother (or sister) with CAH has on them?

APPENDIX C: FAMILY INFORMATION FORM

Family Information Form--Parental Management of Adrenal Crisis in Children with Classical Congenital Adrenal Hyperplasia (CAH)

We are interested in finding out more information about the care of your child with classic CAH and your family as well as your experiences with adrenal crisis. These questionnaires should only take approximately 20 minutes to complete. Your answers will be combined with those of other parents. Please answer the questions to the best of your knowledge and remember that the answers to this survey are confidential. Thank you.

I understand that by completing these surveys, I consent to participate in this study.

If you are interested in being interviewed please check yes. The interview will be conducted at a time and time or your choice. Yes ___ No ___

If you choose Yes to be potentially being interviewed, please provide your first name, child's first name, your relationship to the child with CAH, and your preferred contact information (phone number, email address, etc.). Depending on the number of willing participants, there is the possibility that not every parent willing to participate in an interview will be asked to participate in one.

This survey is intended for caregivers/parents/guardians of children between the ages of birth-18 years of age with classic (salt-wasting) CAH only.

1. Is your child between the ages of 0-18 years of age? ___ Yes ___ No
2. Does your child have classic (salt-wasting) Congenital Adrenal Hyperplasia (CAH)? ___
Yes ___ No
3. Does your child have any other complex medical conditions? ___ Yes ___ No
4. To the best of your knowledge, how often does your child have an adrenal crisis?

5. Do you have a prescription for injectable hydrocortisone (also known as Solu-Cortef)?
If No, check here ___ and go to question 7 on the bottom of this page. If yes, please answer the questions 6a-6h below.

6a. Have you filled the prescription? ___ Yes ___ No
6b. How long after your child's diagnosis did you receive the prescription for injectable hydrocortisone? ___ at diagnosis or ___ days/month/years (circle correct length).
6c. Which statement best fits how you got your child's prescription for injectable hydrocortisone: My doctor prescribed it at diagnosis without me saying anything ___

<p>Sometime after diagnosis I had to ask my child's physician for the prescription of injectable hydrocortisone_____ or</p> <p>My physician prescribed injectable hydrocortisone for my child eventually without my asking for it_____</p>
<p>6d. Did you change physicians in order to receive the prescription for injectable hydrocortisone? _____Yes_____No</p>
<p>6e. Does your child consistently have a vial of injectable hydrocortisone readily available for an emergency? (for example, at their school, in the home, at daycare, in the car, etc.) _____Yes_____No</p>
<p>6f. Have you ever given your child a shot of injectable hydrocortisone? _____Yes_____No</p>
<p>6g. Do you have a written instruction guideline sheet for stress-dosing during adrenal crisis via an injection that was given to you by your physician? _____Yes_____No.</p> <p>If you answered yes, please check all information that is listed on the instruction sheet:</p> <p>_____dose of injectable hydrocortisone</p> <p>_____under what circumstances to give the injection</p> <p>_____how and where to give the injection</p>
<p>6h. Has your physician OR one of his/her staff (such as a nurse or medical assistant) ever demonstrated to you how to correctly administer a shot of injectable hydrocortisone to your child? _____Yes_____No</p>

Go to Question 7

7. Does your child wear a medical identification tag specifying that he/she has CAH or is adrenal insufficient? _____Yes_____No

8. Does your child see a pediatric endocrinologist to manage and treat his/her CAH? _____Yes_____No.

If no, what type of healthcare provider treats your child's CAH?

_____ (ex. general pediatrician, family practice physician, nurse practitioner, etc).

8a. Is the health care provider who manages and treats your child's CAH affiliated with a medical school? _____Yes_____No

Please list the medications your child is currently taking:

9. Parent gender: _____M _____F

10. Parent age: _____

11. Gender of child with CAH: _____M _____F

12. Age of child with CAH: _____years_____months

13. Race of you and your child (ex. American Indian, Asian, Native Hawaiian, Black/African American, White, other-please specify): You_____ Your Child_____

14. Ethnicity of you and your child (Hispanic/Latino or Not Hispanic/Latino):

You _____ Your Child_____

15. Please list all family members that live in your home. Simply list their relationship to your child with CAH, their age, and their gender. Example: 5 year old sister. No names are necessary.

16. Family Type:

_____ 2 parent family

_____ Single parent family (only mother)

_____ Single parent family (only father)

_____ Single parent family (mother figure only) living with partner

_____ Single parent family (father figure only) living with partner

_____ Other relative(s)

_____ Foster family

_____ Other: please specify _____

17. Approximate gross yearly family income (before taxes):

___ Less than \$20,000 _____ \$60,000 to \$69,999

___ \$20,000 to \$29,999 ___ \$70,000 to \$79,999

___ \$30,000 to \$39,999 ___ \$80,000 to \$89,999

___ \$40,000 to \$49,999 ___ \$90,000 to \$99,999
___ \$50,000 to \$59,999 ___ Over \$100,000

18. What city and state do you live in? _____

19. Approximately how many hours do you travel to see the physician who currently manages and treats your child's CAH? _____

20. How far from your home is the hospital where you would take your child if he/she were in adrenal crisis? _____

Thank you very much for your time.

APPENDIX D: PEDIATRIC QUALITY OF LIFE-FAMILY IMPACT MODULE

For each statement in this questionnaire, you are asked to rate your response to the statement on a scale of 0 to 4, with 0 indicating “Never,” 1 indicating “Almost Never,” 2 indicating “Sometimes,” 3 indicating “Often,” and 4 indicating “Almost Always”. Please respond to each statement in this questionnaire based on what you think, not on how you think others might respond.

DIRECTIONS: In the past *ONE MONTH*, as a result of your child’s health, how much of a problem have *YOU* had with....

PHYSICAL FUNCTIONING (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. I feel tired during the day	0	1	2	3	4
2. I feel tired when I wake up in the morning	0	1	2	3	4
3. I feel too tired to do the things I like to do	0	1	2	3	4
4. I get headaches	0	1	2	3	4
5. I feel physically weak	0	1	2	3	4
6. I feel sick to my stomach	0	1	2	3	4

EMOTIONAL FUNCTIONING (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. I feel anxious	0	1	2	3	4
2. I feel sad	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I feel frustrated	0	1	2	3	4
5. I feel helpless or hopeless	0	1	2	3	4

SOCIAL FUNCTIONING (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. I feel isolated from others	0	1	2	3	4
2. I have trouble getting support from others	0	1	2	3	4
3. It is hard to find time for social activities	0	1	2	3	4
4. I do not have enough energy for social activities	0	1	2	3	4

COGNITIVE FUNCTIONING (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. It is hard for me to keep my attention on things	0	1	2	3	4
2. It is hard for me to remember what people tell me	0	1	2	3	4
3. It is hard for me to remember what I just heard	0	1	2	3	4
4. It is hard for me to think quickly	0	1	2	3	4
5. I have trouble remembering what I was just thinking	0	1	2	3	4

COMMUNICATION (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. I feel that others do not understand my family's situation	0	1	2	3	4
2. It is hard for me to talk about my child's health with others	0	1	2	3	4
3. It is hard for me to tell doctors and nurses how I feel	0	1	2	3	4

WORRY (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. I worry about whether or not my child's medical treatments are working	0	1	2	3	4
2. I worry about the side effects of my child's medications/treatments	0	1	2	3	4
3. I worry about how others will react to my child's condition	0	1	2	3	4
4. I worry about how my child's illness is affecting other family members	0	1	2	3	4
5. I worry about my child's future	0	1	2	3	4

DIRECTIONS: Below is a list of things that might be a problem for ***your family***. Please tell us ***how much of a problem*** each one has been for ***your family*** during the ***past ONE month***.

DAILY ACTIVITIES (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. Family activities taking more time and effort	0	1	2	3	4
2. Difficulty finding time to finish household tasks	0	1	2	3	4
3. Feeling too tired to finish household tasks	0	1	2	3	4

FAMILY RELATIONSHIPS (problems with...)	Never	Almost Never	Sometimes	Often	Almost Always
1. Lack of communication between family members	0	1	2	3	4
2. Conflicts between family members	0	1	2	3	4
3. Difficulty making decisions together as a family	0	1	2	3	4
4. Difficulty solving family problems together	0	1	2	3	4
5. Stress or tension between family members	0	1	2	3	4

APPENDIX E: FAMILY MANAGEMENT MEASURE-VIEW OF CONDITION IMPACT SCALE

This questionnaire is about how your family manages caring for a child with a chronic condition, and for this study, the condition is congenital adrenal hyperplasia (CAH).

DIRECTIONS:

For each statement in this questionnaire, you are asked to rate your response to the statement on a scale of 1 to 5, with 1 indicating “Strongly Disagree” and 5 indicating “Strongly Agree”. Please respond to each statement in this questionnaire based on what you think, not on how you think others might respond. Many of these questions use the word “family”. This refers to those people living in your household who you think of as family.

Please check the boxes with your answers.

	<i>Strongly Disagree</i> 1	2	3	4	<i>Strongly Agree</i> 5
1. Our child’s condition is the most important thing in our family.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Because of the condition, we worry about our child’s future.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. We expect to be devoting less time to our child’s condition in the future.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Our child’s condition requires frequent hospital stays.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. People with our child’s condition have a normal length of life.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Our child’s condition will be harder to take care of in the future.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. We think about the way our child’s condition all the time.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Many conditions are more	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	<i>Strongly Disagree</i> 1	2	3	4	<i>Strongly Agree</i> 5
serious than the ones our child has.					
9. It is hard to know what to expect of our child's condition in the future.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. We are confident that we can take care of our child's condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

APPENDIX F: FAMILY MANAGEMENT MEASURE-MANAGEMENT ABILITY SCALE

This questionnaire is about how your family manages caring for a child with a chronic condition, and for this study, the condition is congenital adrenal hyperplasia (CAH).

DIRECTIONS:

For each statement in this questionnaire, you are asked to rate your response to the statement on a scale of 1 to 5, with 1 indicating “Strongly Disagree” and 5 indicating “Strongly Agree”. Please respond to each statement in this questionnaire based on what you think, not on how you think others might respond. Many of these questions use the word “family”. This refers to those people living in your household who you think of as family.

Please check the boxes with your answers.

	<i>Strongly Disagree</i> 1	2	3	4	<i>Strongly Agree</i> 5
1. In the future, we expect our child to take care of the condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. We have some definite ideas about how to help our child live with the condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Despite the condition, we expect our child to live away from home in the future.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. We have enough money to manage our child's condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. We are looking forward to a happy future for our child.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. When something unexpected happens with our child's condition, we usually know how to handle it.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. We feel we are doing a good job taking care of our child's condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. We have goals in mind to	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	<i>Strongly Disagree</i> 1	2	3	4	<i>Strongly Agree</i> 5
help us manage our child's condition.					
9. It is difficult to know when our child's condition must come first in our family.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. It is often difficult to know if we need to be more protective of our child	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. We often feel unsure about what to do to take care of our child's condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12. We have not been able to develop a routine for taking care of our child's condition.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>