



DSHS - School Nurse Notes | February 2017

Adrenal Insufficiency and the Use of Solu-Cortef®

To address the needs of school nurses, the Texas Department of State Health Services (DSHS)–School Health Program has developed this repository of information. With each issue of *School Nurse Notes*, DSHS brings you the latest research, evidence-based practices, and resources in school nursing related to a topic of interest. If you have any questions or comments about this publication, please contact Anita Wheeler, School Nurse Consultant, at (512) 776-2909 or at anita.wheeler@dshs.state.tx.us.

Background

The Medication

Solu-Cortef® is the product name for hydrocortisone sodium succinate, of the corticosteroids drug class. ^{1, 2} The medication comes as powder and must be mixed with liquid to be administered via the IV or IM route or with Act-O-Vial®. ^{1, 2} Solu-Cortef® is approved for pediatric anti-inflammatory or immunosuppressive uses. ¹ It works by replacing steroids in people whose natural level of corticosteroids is low. ² Solu-Cortef® is indicated for endocrine disorders such as primary or secondary adrenocortical insufficiency; acute adrenocortical insufficiency; preoperatively and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful; and congenital adrenal hyperplasia. ¹

The Condition

Adrenal insufficiency can be caused by hormonal imbalances that originate in the adrenal glands (one sits atop each kidney), pituitary gland, or hypothalamus. **Primary adrenal insufficiency**, also called Addison's disease, refers to conditions in which the adrenal glands are damaged and not producing sufficient levels of cortisol. Most cases of Addison's disease are caused by autoimmune disorders. ³ **Secondary adrenal insufficiency** refers, most commonly, to conditions in which hormone imbalances of the pituitary gland impact cortisol production in the adrenal glands. Secondary adrenal insufficiency is much more common than Addison's disease. ³

Regardless of the type of adrenal insufficiency or its cause, life-

threatening adrenal crisis may result if the adrenal insufficient patient is not given a Solu-Cortef® injection during times of physiological stress, such as illness or a severe injury. Sudden, severe worsening of adrenal insufficiency symptoms is called adrenal crisis. ³

Research

The following articles have been compiled from a review of the scientific literature. For assistance in obtaining an article, please contact the DSHS Library at library@dshs.state.tx.us and mention inclusion of the requested article in the *School Nurse Notes*. The articles are presented on a continuum, ranging from those that address adrenal insufficiency and adrenal crisis in general to those that relate to specific forms of the condition, such as Addison's disease or Congenital Adrenal Hyperplasia (CAH). Following each citation is a portion of the article's abstract.

1. Moloney S, Murphy N, Collin J. **An overview of the nursing issues involved in caring for a child with adrenal insufficiency.** *Nurs Child Young People*. 2015;27(7):28-36.
Adrenal insufficiency is an endocrine condition defined as the inadequate production or action of glucocorticoids While rare in childhood, it carries the risk of adrenal crisis in the event of a child becoming unwell as a result of inter-current illness, injury or surgery. Children's nurses must be vigilant in caring for a child with adrenal insufficiency and have a clear understanding and awareness of the principles of emergency management at home and in hospital.
2. Bornstein, SR. **Predisposing Factors for Adrenal Insufficiency.** *N Engl J Med*. 2009;360:2328-2339.
Adrenal insufficiency—the clinical manifestation of deficient production or action of glucocorticoids—is a life-threatening disorder that may result from either primary adrenal failure or secondary adrenal disease due to impairment of the hypothalamic-pituitary axis. This article focuses on providing the practicing clinician with new insights into predisposing factors for adrenal insufficiency. . . . The cardinal clinical symptoms of adrenocortical insufficiency, as first described by Thomas Addison in 1855, include weakness, fatigue, anorexia, and abdominal pain, with orthostatic hypotension, salt craving, and characteristic hyperpigmentation of the skin occurring with primary adrenal failure.
3. Elder CJ, Dimitri P. **Hydrocortisone for adrenal insufficiency.** *Arch Dis Child Educ Pract Ed*. 2015;100:272-276.
Thomas Addison first described Addison's disease in 1855 in patients who had adrenal tuberculosis, highlighting the importance of the adrenal cortex to

survive. In 1952, a decade after the medical landmark discovery of cortisone as a treatment for inflammatory conditions, the first case of adrenal crisis and death in a patient on glucocorticoid therapy undergoing surgery was described A knowledge of how to treat adrenal insufficiency during times of (patho) physiological stress is paramount to prevent complications and death.

4. Shulman DI, Palmert MR, Kemp SF. **Adrenal insufficiency: Still a cause of morbidity and death in childhood.** *Pediatrics*. 2007;119(2):e484-e494. If unrecognized adrenal insufficiency may present with life-threatening cardiovascular collapse. Adrenal crisis continues to occur in children with known primary or secondary adrenal insufficiency during intercurrent illness because of failure to increase glucocorticoid dosage. . . . Suggestions for prevention of adrenal crisis in patients at risk are provided for health care professionals and families.
5. Puar TH, Stikkelbroeck NM, Smans LC, et al. **Adrenal crisis: Still a deadly event in the 21st century.** *Am J Med*. 2016;129:339.e1-339.e9. Gastrointestinal illness is the most common precipitant for an adrenal crisis. Although most patients are educated about "sick day rules," patients, and physicians too, are often reluctant to increase their glucocorticoid doses or switch to parenteral injections, and thereby fail to avert the rapid deterioration of the patients' condition. . . . There is generally a paucity of studies on adrenal crisis. Hence, we will review the current literature, while also focusing on the incidence, presentation, treatment, prevention strategies, and latest recommendations in terms of steroid dosing in stress situations.
6. Bornstein SR, Allolio B, Arlt W, et al. **Diagnosis and treatment of primary adrenal insufficiency: An endocrine society clinical practice guideline.** *J Clin Endocrinol Metab*. 2016;101(2):364-389. This clinical practice guideline addresses the diagnosis and treatment of primary adrenal insufficiency. . . . We recommend diagnostic tests for the exclusion of primary adrenal insufficiency in all patients with indicative clinical symptoms or signs. In particular, we suggest a low diagnostic (and therapeutic) threshold in acutely ill patients, as well as in patients with predisposing factors. . . . We recommend a short corticotropin test (250 µg) as the "gold standard" diagnostic tool to establish the diagnosis. . . . Diagnosis of the underlying cause should include a validated assay of antibodies against 21-hydroxylase. . . . In children, hydrocortisone (~8mg/m²/d) is recommended. (See Resources and Tools section for PDF.)
7. Moloney S, Dowling M. **Early intervention and management of adrenal insufficiency in children.** *Nurse Child Young People*. 2012;24(7):25-28. The endocrine disorder adrenal insufficiency includes inadequate production of the steroid hormone cortisol. This results in poor physiological responses

to illness, trauma or other stressors and risk of adrenal crisis. Management is based on administration of hydrocortisone. . . . A steroid therapy card for adrenal insufficiency containing personal information on a patient's condition was developed for use by families and their specialist centres.

8. Malikova J, Flück CE. **Novel insight into etiology, diagnosis, and management of primal adrenal insufficiency.** *Horm Res Paediatr.* 2014;82:142-157.

Primary adrenal insufficiency (PAI) is a rare condition in childhood which is either inherited (mostly) or acquired. . . . The most common form in children is 21-hydroxylase deficiency, which belongs to the steroid biosynthetic defects causing PAI. . . . Other forms of PAI include metabolic disorders, autoimmune disorders and adrenal dysgenesis, e.g. the IMAGe syndrome, for which the underlying genetic defect has been recently identified. Newer work has also expanded the genetic causes underlying isolated, familial glucocorticoid deficiency (FGD).

9. Perry R, Kecha O, Paquette J, et al. **Primary adrenal insufficiency in children: Twenty years experience at the Sainte-Justine Hospital, Montreal.** *J Clin Endocrinol Metab.* 2005;90:3243-3250.

Primary adrenal insufficiency (PAI) in the pediatric population (0-18 yr.) is most commonly attributed to congenital adrenal hyperplasia (CAH), which occurs in about 1 in 15,000 births, followed by Addison's disease, with an assumed autoimmune etiology. . . . All patients with a diagnosis of PAI followed by the Endocrinology Service at our institution between September 1981 and September 2001 were studied. One hundred three patients (48 boys) were identified, primarily by the Endocrinology Clinic case registry. CAH was the most frequent etiology (71.8 percent. However, non-CAH etiologies accounted for 28.2 percent, of which 55 percent were non-autoimmune in etiology.

10. Michels A, Michels N. **Addison disease: Early detection and treatment principles.** *Am Fam Physician.* 2014;89(7):563-568.

Primary adrenal insufficiency, or Addison disease, has many causes, the most common of which is autoimmune adrenalitis. Autoimmune adrenalitis results from destruction of the adrenal cortex The clinical manifestations before an adrenal crisis are subtle and can include hyperpigmentation, fatigue, anorexia, orthostasis, nausea, muscle and joint pain, and salt craving. . . . During times of stress (e.g., illness, invasive surgical procedures), stress-dose glucocorticoids are required because destruction of the adrenal glands prevents an adequate physiologic response.

11. Øksnes M, Ross R, Løvås K. **Optimal glucocorticoid replacement in adrenal insufficiency.** *Best Pract Res Clin Endocrinol Metab.* 2015;29:3-15. Adrenal insufficiency (glucocorticoid deficiency) comprises a group of rare diseases, including primary adrenal insufficiency, secondary adrenal

insufficiency and congenital adrenal hyperplasia. . . . Over the past decade, systematic cohort and registry studies have described reduced health-related quality of life, an unfavourable metabolic profile and increased mortality in patients with adrenal insufficiency, which may relate to unphysiological glucocorticoid replacement. . . . Here, evidence for the inadequacy of conventional glucocorticoid therapy and recent developments in treatment are reviewed, with an emphasis on primary adrenal insufficiency.

12. Webb EA, Krone N. **Current and novel approaches to children and young people with congenital adrenal hyperplasia and adrenal insufficiency.** *Best Pract Res Clin Endocrinol Metab.* 2015;29:449-468. Congenital adrenal hyperplasia (CAH) represents a group of autosomal recessive conditions CAH is the most common cause of adrenal insufficiency (AI) in the pediatric population. The majority of the other forms of primary and secondary adrenal insufficiency are rare conditions. Following the introduction of life-saving glucocorticoid replacement 60 years ago, steroid hormone replacement regimes have been refined leading to significant reductions in glucocorticoid doses over the last 2 decades. . . . However, despite optimization of existing glucocorticoid replacement regimens fail to mimic the physiologic circadian rhythm of glucocorticoid secretion, current efforts therefore focus on optimizing replacement strategies. In addition, in recent years novel experimental therapies have been developed which target adrenal sex steroid synthesis in patients with CAH (congenital adrenal hyperplasia) aiming to reduce co-morbidities associated with sex steroid excess.
13. Merke DP, Poppas DP. **Management of adolescents with congenital adrenal hyperplasia.** *Lancet Diabetes Endocrinol.* 2013;1(4):341-352. The management of congenital adrenal hyperplasia (CAH) involves suppression of adrenal androgen production, in addition to treatment of adrenal insufficiency. Management of adolescents with CAH is especially challenging because changes in the hormonal milieu during puberty can lead to inadequate suppression of adrenal androgens, psychosocial issues often affect adherence to medical therapy, and sexual function plays a major part in adolescence and young adulthood. . . . Extensive patient education is key during transition from pediatric care to adult care and should include education of females with classic CAH regarding their genital anatomy and surgical history. . . . Education of health-care providers on how to successfully transition patients is greatly needed.
14. Zöllner EW, Lombard CJ, Galal U, et al. **Hypothalamic-pituitary-adrenal axis suppression in asthmatic school children.** *Pediatrics.* 2012;130(6):e1512-e1519. Hypothalamic-pituitary-adrenal axis suppression (HPAS) when treating children with corticosteroids is thought to be rare. Our objective was to

determine the prevalence of and predictive factors for various degrees of HPAS. Clinical feature of HPAS, doses, adherence, asthma score, and lung functions were recorded in 143 asthmatic children. . . . Two-thirds of children on corticosteroids may have hypothalamic-pituitary-adrenal axis dysfunction. In one-third, central function had recovered but adrenal suppression persisted. Predictive factors for HPAS are nasal steroid (NS) use, BMI, and adherence to inhaled corticosteroid (ICS) and NS.

15. de Lind van Wijngaarden RF, Otten, BJ, Festen DA, et al. **High prevalence of central adrenal insufficiency in patients with Prader-Willi syndrome.** *J Clin Endocrinol Metab.* 2008;93(5):1649-1654.

The annual death rate of Prader-Willi syndrome (PWS) patients is very high (3 percent). Many of these deaths are sudden and unexplained. Because most deaths occur during moderate infections and PWS patients suffer from various hypothalamic insufficiencies, we investigated whether PWS patients suffer from central adrenal insufficiency (CAI) during stressful conditions. Overnight single-dose metyrapone tests were performed. . . . Morning salivary cortisol levels and diurnal profiles were normal in all children, suggesting that CAI becomes apparent only during stressful conditions. Strikingly, 60 percent of our PWS patients had CAI.

16. Corrias A, Grugni G, Crino A, et al. **Assessment of central adrenal insufficiency in children and adolescents with Prader-Willi syndrome.** *Clin Endocrinol.* 2012;76:843-850.

A recent study evidenced by metyrapone test a central adrenal insufficiency (CAI) in 60 percent of Prader-Willi syndrome (PWS) children. . . . We extended the research by Low-Dose Tetracosactrin Stimulation Test (LDTST) in pediatric patients with PWS. . . . Responses were correlated with the patients' clinical and molecular characteristics to assess genotype-phenotype correlation. . . . Our results support the hypothesis that, albeit rare, CAI may be part of the PWS in childhood.

Resources and Tools

Adrenal Insufficiency: A Condition with Many Causes

- ✓ National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK): [Adrenal Insufficiency and Addison's Disease Fact Sheet](#) ³
 - Basic drawing of Hypothalamic-Pituitary-Adrenal Axis
 - Broad summary under "Points to Remember"
- ✓ National Adrenal Diseases Foundation (NADF) [Website](#) (Includes the following resources.)
 - Potentially Life-Preserving Information Packet for Adrenal Insufficient Patients (downloadable from home page)

- Articles Tab
 - [Hydration “Salt Wasters” And Dehydration](#)
- [Tools for Life](#) Tab (numerous PDFs; 4 research articles)
 - [Adrenal Crisis Alert Poster](#)
- Links & Resources Tab
 - [Kids Pen-Pal Network](#)
- ✓ [Endocrine Society website](#): Membership primarily includes doctors, scientists, researchers, and educators.

Primary Adrenal Insufficiency: Adrenal Glands Damaged

- ✓ National Adrenal Diseases Foundation (NADF) [Website](#) (Includes the following resources.)
 - Potentially Life-Preserving Information Packet for Adrenal Insufficient Patients (including Addison’s disease)
 - Diagnosis and Treatment of Primary Adrenal Insufficiency: [An Endocrine Society Clinical Practice Guideline](#) (#6 in Research section)
 - Adrenal Diseases Tab
 - [Addison’s Disease: The Facts You Need To Know](#) (downloadable fact sheet)

Secondary Adrenal Insufficiency: Commonly Pituitary Gland Failure

- ✓ National Adrenal Diseases Foundation (NADF) [Website](#) (Includes the following resources.)
 - Adrenal Diseases Tab
 - [Secondary Adrenal Insufficiency: The Facts You Need To Know](#) (downloadable fact sheet)
 - [Congenital Adrenal Hyperplasia \(CAH\): The Facts You Need To Know](#) (downloadable fact sheet)
 - Potentially Life-Preserving Information Packet for Congenital Adrenal Hyperplasia (CAH) Patients
- ✓ Texas Department of State Health Services (DSHS): [Congenital Adrenal Hyperplasia, A Handbook for Parents](#)
- ✓ CARES Foundation—Supporting the Congenital Adrenal Hyperplasia (CAH) community: [Website](#)
 - [Glossary of Terms Related to CAH](#)
 - [How to Talk About Your Child’s CAH](#)

Medication

- ✓ MedlinePlus: [Hydrocortisone Injection](#) ²
- ✓ Nevada (Clark County): [Administration of Solu-Cortef® Policy & Procedure](#) (The following links are included within.)
 - Pediatric Endocrinology Nursing Society (PENS): [Cortisol Dependent School Instructions / Solu-Cortef® Injection Handout/ Adrenocorticoid Medication instructions](#)
 - University of Texas, MD Anderson Cancer Center: [Act-O-Vial® Instructions](#) (search in Patient Education)
 - Plano Independent School District [Adrenal Crisis Action Plan](#) (2013)
- ✓ Oregon Department of Education: [Medication Administration in Oregon Schools—A Manual for School Personnel](#)

References

For assistance in obtaining any resources, please contact the DSHS Library at library@dshs.state.tx.us and mention inclusion of the requested resource in the *School Nurse Notes*.

1. Hydrocortisone Sodium Succinate Injection. Facts and Comparisons [database online]. Hudson, OH: Wolters Kluwer Clinical Drug Information. Updated November 2016. Accessed December 9, 2016.
2. U.S. National Library of Medicine. Hydrocortisone Injection: <https://medlineplus.gov/druginfo/meds/a682871.html>. Updated May 15, 2016. Accessed December 9, 2016.
3. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Adrenal insufficiency and Addison's disease: <https://www.niddk.nih.gov/health-information/health-topics/endocrine/adrenal-insufficiency-addisons-disease/Pages/fact-sheet.aspx>. Updated May 2014. Accessed December 12, 2016.

External links to other sites appearing here are intended to be informational and do not represent an endorsement by the DSHS. These sites may also not be accessible to people with disabilities. External email links are provided to you as a courtesy. Please be advised that you are not emailing the DSHS and DSHS policies do not apply should you choose to correspond. For information about any of the initiatives listed, contact the sponsoring organization directly. Copyright free. Permission granted to forward or make copies in its entirety as needed.