

**Incidence and Preventative Strategies  
of Adrenal Crisis in Congenital Adrenal  
Hyperplasia**

**Padmasree Veeraraghavan<sup>1</sup>,Diala El-Maouche<sup>1</sup>,  
Deborah P. Merke<sup>1,2</sup>**

<sup>1</sup>National Institutes of Health Clinical Center,

<sup>2</sup>*Eunice Kennedy Shriver* National Institute of  
Child Health and Human Development,  
Bethesda, MD 20892

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- Other authors: None

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**Objectives**

- Understand adrenal crisis and adrenal crisis prevention
- Characterize the rates and causes of stress dosing and associated factors in a cohort of CAH patients
- Review nurses' role in patient and family education for adrenal crisis prevention
- Propose new guidelines for stress dosing in patients with adrenal insufficiency

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## Congenital Adrenal hyperplasia(CAH)

- Congenital adrenal hyperplasia (CAH) is a rare, autosomal recessive disease
- It is caused by an enzyme deficiency in the steroid synthesis pathway, which occurs in the adrenal glands.
- It is mainly characterized by cortisol and aldosterone deficiency and androgen excess

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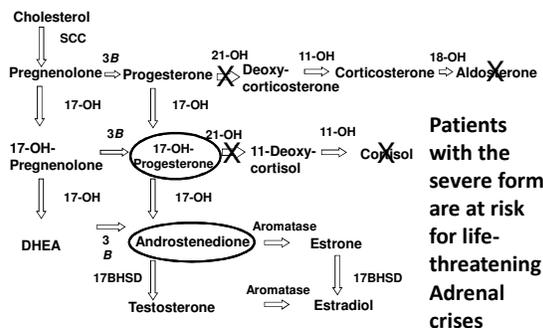


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## Steroidogenesis pathway and CAH




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## Adrenal Insufficiency in CAH

- Patients with CAH have adrenal insufficiency (AI)
- AI: Inability to produce cortisol from adrenal glands
- AI can lead to life-threatening adrenal crisis.
- Signs and symptoms of AC: Hypotension, electrolyte abnormalities (hyperkalemia, hyponatremia), hypoglycemia, nausea and vomiting , loss of consciousness

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### Adrenal Crises Findings

- Incidence of Adrenal Crisis 5-10/100PY
- Mortality 0.5/100PY
- AC deaths contribute to 15% of all deaths in autoimmune AI and 42% of those in CAH
- There is no widely accepted definition of adrenal crises.
- Prevention through education

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### Adrenal Crisis Prevention

- At NIH, we use patient education as one of the methods to prevent adrenal crisis
- We teach self-administration of IM hydrocortisone injection at each clinic visit
- Both adult patients and parents of pediatric patients receive teaching



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### “Sick Day Rules” at NIH Prior to 2018

- Children
  - T> 100.5°F: Double HC dose
  - T> 102°F: Triple HC dose
- Adults:
  - Minor Illness: 10 mg tid HC in addition to their usual glucocorticoid regimen
  - Major Illness: 20 mg tid HC in addition to their usual glucocorticoid regimen

(HC= Hydrocortisone)

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## Methods

- Longitudinal analysis of 156 patients with CAH followed at NIH Clinical Center for over 23 years
- Children were evaluated every 6 months, and adults annually
- We analyzed the rates of illnesses and stress-dose days, ER visits, hospitalizations and adrenal crises

El-Maouche D, et al. *J Clin Endocrinol Metab.* 2018; *Epub ahead of print.*

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## Main Outcomes

- Total Illnesses (events)
- Total days stress dosed
- ER visits
- Hospitalizations
- Adrenal crises

El-Maouche D, et al. *J Clin Endocrinol Metab.* 2018; *Epub ahead of print.*

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## Results

- Cohort consisted of 156 patients and 2298 visits
  - 29 adults and 127 children (<18 years of age)
  - 58% male, 42% female
  - 97.4% had 21-hydroxylase deficiency and 2.6% had other rare types of CAH
  - Patients followed for an average of  $9.3 \pm 6$  years

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## Results

- Children had significantly **more total illnesses** and **greater** number of **days of stress dosing** compared to adults
- However, children had significantly **fewer ER** and **fewer hospitalizations** compared to adults
- Data suggests successful home management of illness was achieved in childhood

El-Maouche D, et al. *J Clin Endocrinol Metab.* 2018; Epub ahead of print.

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## Incidence of Adrenal Crises

- The incidence of adrenal crises was 7.55/100 patient-years: rates were lower in children than adults (7.2/100 vs. 10.2/100 patient years), however the difference was not statistically significant
- Adrenal crisis with probable hypoglycemia occurred in 11 pediatric patients (ages 1.1 -11.3 years), including 2 with seizures

El-Maouche D, et al. *J Clin Endocrinol Metab.* 2018; Epub ahead of print.

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## Differences by sex and phenotype

- For pediatric patients with classic CAH, females reported higher rates of illnesses and stress dosing than males ( $1.9 \pm 2.9$  vs.  $1.4 \pm 2$  days/year,  $p < 0.0001$ )
- During adulthood for patients with classic CAH, females had more stress-dose days than males
- Patients with SW had more ER visits than patients with SV during childhood and no phenotype differences found during adulthood

El-Maouche D, et al. *J Clin Endocrinol Metab.* 2018; Epub ahead of print.

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### Causes of stress dosing

- Upper respiratory tract illness, followed by gastrointestinal illness were the main causes of stress dosing and adrenal crisis across all ages as shown in the next two graphs
- URI includes sinusitis, otitis media, pharyngitis

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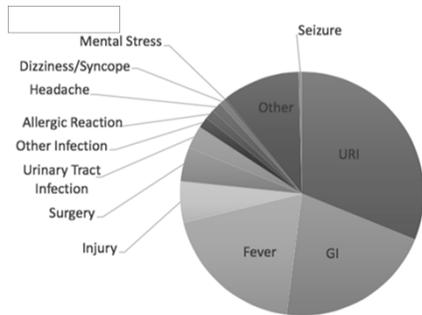
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### Causes of Illness in Children



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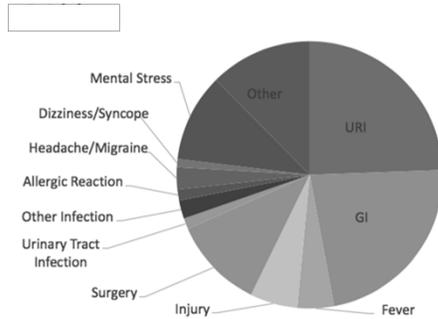
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### Causes of Illness in Adults



El-Maouche D, et al. *J Clin Endocrinol Metab.* 2018; *Epub ahead of print.*

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### Conclusions

- In this large cohort of patients with CAH who received extensive and repeated adrenal insufficiency education, stress dosing was mostly done according to our teaching protocol, but hospitalizations and hypoglycemic events still occurred
- Special attention should be given to the youngest patients, who may be more susceptible to illnesses and hypoglycemia. Revised stress dose guidelines are recommended.

El-Maouche D, et al. J Clin Endocrinol Metab. 2018; Epub ahead of print.

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### Proposed Sick Day Rules for children

Types of illness	Proposed Guideline
<b>Minor illness or low-grade fever (&gt; 38°C children)</b>	Double the dose of glucocorticoids, divided into 4 doses (to be given every 6 hours, round up)
<b>Major illness or high-grade fever (&gt; 39°C children) or severe diarrhea (with or without fever)</b>	Triple the dose of glucocorticoids, divided into 4 doses (take every 6 hours). Increase fluid intake and frequent ingestion of simple & complex carbs

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### Proposed Sick Day Rules for children

Types of illness	Proposed Guideline
<b>All illnesses</b>	15 grams of simple carbohydrates (1/2 cup juice or regular soda or apple sauce or 3-4 glucose tablets) for lethargy. Increase fluids. Simple and complex carbohydrates every 4 to 6 hours. Hospital/physician evaluation for lethargy and decreased oral intake and urine output.

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### Proposed Sick Day Rules for children

Types of illness	Proposed Guideline
Vomiting	Repeat oral dose if child vomits within 1 hour of medication. If vomits again, administer intramuscular injection of hydrocortisone 50-100 mg/m <sup>2</sup> . If unable to tolerate fluids, call emergency services (911) for evaluation following intramuscular injection.

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### Proposed Sick Day Rules for Adults or Patients on Long-acting Glucocorticoids

- Take hydrocortisone 10 mg (≈ 2X daily dose) or 20 mg (≈ 3X daily dose) three times a day **in addition to** usual glucocorticoid regimen
- IM injection: hydrocortisone 100 mg

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### Clinical Implications for Nurses

- Prevention of hypoglycemia should be incorporated into adrenal insufficiency patient education
- Interventions include stress dosing every 6 hours, in addition to increased emphasis on fluid and glucose intake during illness to prevent severe adrenal crises with hypoglycemia in children

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THANK YOU !!!  
Questions?

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