

# Early Identification of Cushing's Syndrome in Children

Meg Keil, MS, CNP, Dalia Batista, MD, Constantine A. Stratakis, MD, DSc  
 NICHD, The National Institutes of Health, Bethesda, MD

## Cushing's Syndrome in Children

- ❖ The incidence of endogenous Cushing's syndrome is approximately 2 to 5 new cases per million people per year, and approximately 10% of these new cases occur in children.
- ❖ The most common cause of endogenous Cushing's syndrome in children is an ACTH-secreting pituitary adenoma (accounts for approximately 75% of all cases of endogenous Cushing's syndrome in children older than 7 years).
- ❖ The most common cause of Cushing's syndrome in infants and toddlers is an adrenal tumor (adenoma, carcinoma, or bilateral hyperplasia).
- ❖ Bilateral nodular adrenal disease is an ACTH-independent cause of Cushing's syndrome. Children and adolescents with bilateral nodular adrenal disease may have periodic or "cyclic" Cushing's syndrome. Bilateral nodular adrenal

## Symptoms & Signs of Cushing's in Children

In many children the onset of Cushing's syndrome may be insidious. Growth failure (or deceleration) associated with weight gain is a hallmark feature of Cushing's syndrome in children. Other sign and symptoms often seen in children and adolescents with Cushing's syndrome include facial plethora, increased fine downy hair on the face, body and extremities, a temporal fat pad, round face, diabetes and other symptoms listed below

Normal



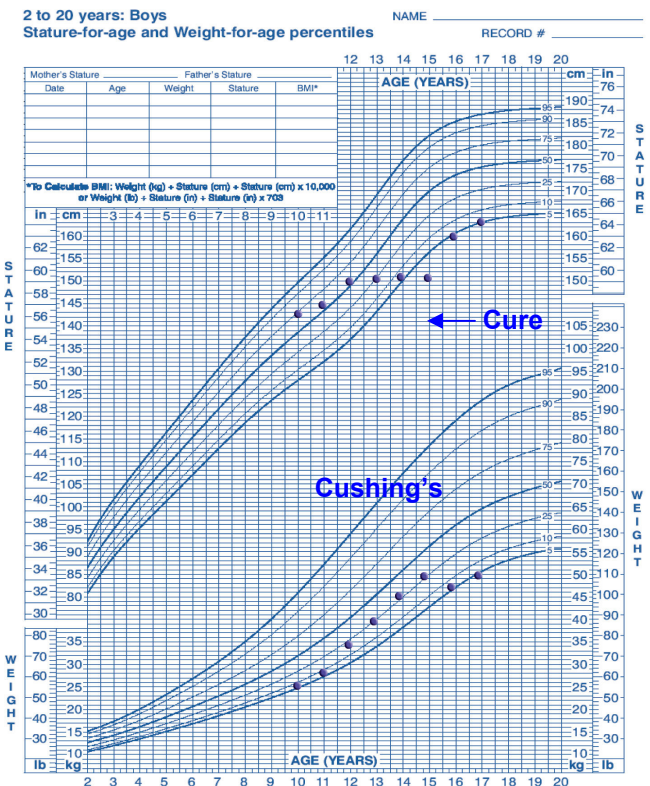
Cushing's



## Presenting Symptoms & Signs of Cushing's

Symptom	Frequency
Weight Gain	90
Growth Retardation	83
Menstrual Irregularities	81
Hirsutism	81
Obesity (BMI > 85th percentile)	73
Violaceous skin striae	63
Acne	52
Hypertension	51
Fatigue-weakness	45
Precocious puberty	41
Bruising	27
Mental Changes	18
"Delayed" bone age	14
Hyperpigmentation	13
Muscle weakness	13
Acanthosis nigricans	10
"Accelerated" bone age	10
Sleep disturbances	7
Pubertal delay	7
Hypercalcemia	6
Alkalosis	6
Hypokalemia	2
Slipped femoral capital epiphysis	2

## Delayed Growth with Weight Gain—Boys



Adapted from Magiakou M, Mastorakos G, Oldfield EH, et al. Cushing's Syndrome in Children and Adolescents: Presentation, Diagnosis and Therapy. *New England J Med* 1994;331:629-36.

## Testing

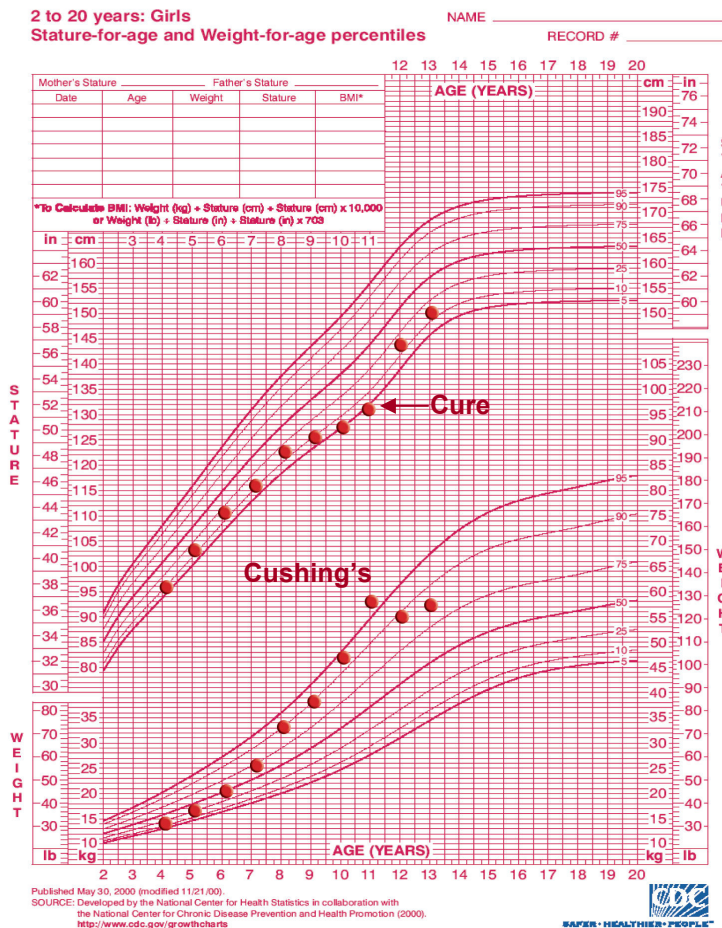
- ❖ It is important for children to be evaluated by a pediatric Endocrinologist who is experienced with Cushing's Syndrome, since some tests require adjustment for the child's size.
- ❖ The best screening test for Cushing's Syndrome in children is a collection for urinary free cortisol (UFC). The results must be adjusted for the child's size.
- ❖ Diurnal cortisol: Normally, the cortisol level is very low at midnight, but with Cushing's Syndrome, the midnight are levels are usually higher than expected; often not very different from the early AM cortisol. Diurnal cortisol measurements can be obtained by blood draws or salivary cortisol<sup>1</sup> measurements collected at 7:30-8:00 AM and 11:30-12 PM. The FDA recently approved a salivary cortisol assay<sup>2</sup> however this test has not been validated in children. The FDA approved assay is available from ACL Labs (800-877-7016), Salimetrics (800-790-2258), or Esoterix (800-444-9111).
- ❖ Low-dose dexamethasone test: This test involves giving one milligram of dexamethasone (adjusted for the child's weight) and measuring the AM cortisol level in blood. The low-dose dexamethasone test has not been validated extensively in children, but results of a study done at N.I.H. show that AM cortisol should be less than 5mcg/dL.

### References:

1 Gafni RI, Papanicolaou DA, Nieman LK. Nighttime salivary cortisol measurement as a simple, non-invasive outpatient screening test for Cushing's syndrome in children and adolescents. *J. Pediatr.* 2000 July 137(1):30-35.

2 Raff H, Homar PJ, Skoner DP. New enzyme immunoassay for salivary cortisol (Letter) *Clin Chem.* 2002;48:207-8.

## Delayed Growth with Weight Gain—Girls



Normal



Cushing's



Growth Charts: Courtesy of N.I.H. Photos: Courtesy of CSRF Fall, 2004

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website: [www.CSRF.net](http://www.CSRF.net) email: [cushinfo@csrf.net](mailto:cushinfo@csrf.net)