Objectives:

• Describe appropriate treatment for adrenal insufficiency due to congenital adrenal hyperplasia.

• Distinguish between primary and secondary adrenal insufficiency.

• Identify screening tests used in the evaluation for Addison disease and Cushing syndrome.

• Name 3 things that differentiate obesity from Cushing syndrome.
Case 1: Question 1

• You are called into a delivery. The family is expecting a boy. You find ambiguous genitalia and no palpable gonads in the labioscrotal folds. An ultrasound shows a uterus. Karyotype is pending. What lab evaluation will help with diagnosis?

A. 17-OH Pregnenolone
B. 17-OH Progesterone
C. DHEA-S
D. Anti-Müllerian Hormone
E. Testosterone
Ambiguous genitalia
Ambiguous genitalia: Assessment

<table>
<thead>
<tr>
<th></th>
<th>Length (Pubic ramus – tip of phallus)</th>
<th>Width (At mid-shaft)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>≥ 25 mm</td>
<td>≥ 9 mm</td>
</tr>
<tr>
<td>Female</td>
<td>≤ 9 mm</td>
<td>2-6 mm</td>
</tr>
</tbody>
</table>
Phallic length
### External genitalia development

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
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</thead>
<tbody>
<tr>
<td>Genital tubercle</td>
<td>Corpus cavernosa</td>
<td>Clitoris</td>
</tr>
<tr>
<td></td>
<td>Glans penis</td>
<td></td>
</tr>
<tr>
<td>Urogenital folds</td>
<td>Corpus spongiosum</td>
<td>Labia minora</td>
</tr>
<tr>
<td></td>
<td>Penile urethra</td>
<td></td>
</tr>
<tr>
<td>Labioscrotal folds</td>
<td>Scrotum</td>
<td>Labia majora</td>
</tr>
</tbody>
</table>

[https://pedclerk.bsd.uchicago.edu/page/ambiguous-genitalia](https://pedclerk.bsd.uchicago.edu/page/ambiguous-genitalia)
Urethral opening

https://pedclerk.bsd.uchicago.edu/page/ambiguous-genitalia
http://www.uofmchildrenshospital.org/healthlibrary/Article/40095
## Prader scale: Virilization grading

<table>
<thead>
<tr>
<th>Grade</th>
<th>Phallus</th>
<th>Fusion of labioscrotal folds</th>
<th>Urogenital sinus</th>
<th>Opening</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female appearance, slightly enlarged</td>
<td>None</td>
<td>None</td>
<td>Normal female</td>
</tr>
<tr>
<td>2</td>
<td>Further enlargement</td>
<td>Posterior</td>
<td>None</td>
<td>Normal female</td>
</tr>
<tr>
<td>3</td>
<td>Significant increase</td>
<td>Almost complete</td>
<td>Present</td>
<td>Perineal</td>
</tr>
<tr>
<td>4</td>
<td>Penile appearance</td>
<td>Complete</td>
<td>Present</td>
<td>Base or ventral surface of phallus</td>
</tr>
<tr>
<td>5</td>
<td>Well-developed penis</td>
<td>Complete</td>
<td>Present</td>
<td>Body of phallus/balanic area</td>
</tr>
</tbody>
</table>
Anogenital ratio

Anogenital ratio = Center of anus – Posterior fourchette
Center of anus – Base of phallus

> 0.5 = virilized

Ambiguous genitalia assessment: Summary

• Phallic dimensions:
  – Female: Length (≤ 9 mm), width (2-6 mm)

• Gonads: Palpable, likely testes

• Urethral opening: Location, location, location

• Virilization grading: Prader scale

• Anogenital ratio: > 0.5 = virilized
17-OH Pregnenolone

17-OH Progesterone
Glucocorticoid deficiency

Virilization

Adrenal crisis
Mineralocorticoid deficiency

Electrolyte abnormalities

Most common cause

21-hydroxylase

CYP21A2

Mineralocorticoids

Glucocorticoids

Androgens

Zona glomerulosa

Zona fasciculata

Zona reticularis

ACTH

Cholesterol

StAR

17α-hydroxylase

CYP17A1

17α-hydroxylase

17,20-lyase

170H-pregnenolone

170H-progesterone (170HP)

11-deoxycortisol

11-deoxycorticosterone

180H-corticosterone

Aldosterone

Mineralocorticoid synthesis

Electrolyte abnormalities

3β-HSD2

HSD3B2

Aldosterone synthase

CYP11B2

17β-HSD5

AKR1C3

11β-hydroxylase

CYP11B1

DHEA

Androstenedione

Testosterone

Zona glomerulosa

Zona fasciculata

Zona reticularis

Mineralocorticoids

Glucocorticoids

Androgens

Han TS et al. Nat Rev Endocrinol, 2014, 10: 115-124
Case 1

- Newborn with ambiguous genitalia. An ultrasound shows a uterus. Karyotype is pending.
- You contact the pediatric endocrinologist. They ask for a 17-OHP.  
  (= 17-OH Progesterone, not Pregnenolone)  
  - Does she have CAH?

<table>
<thead>
<tr>
<th>Date</th>
<th>17-OHP (ng/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOL 2</td>
<td>3130</td>
</tr>
<tr>
<td>DOL 4</td>
<td>&gt; 15,000</td>
</tr>
</tbody>
</table>
Case 1

• Newborn with ambiguous genitalia. An ultrasound shows a uterus. Karyotype is pending.
• You contact the pediatric endocrinologist. They ask for a 17-OHP.
  – Other labs they may ask for:
    • BMP
    • Plasma renin activity
    • ± Androstenedione, aldosterone, cortisol, testosterone
      (per PES: Limited value in diagnosis)
21-hydroxylase deficiency CAH: Diagnosis

**Baseline 17-OHP**

- > 300 nmol/L [10,000 ng/dL]
  Likely Classic CAH
- 6 - 300 nmol/L [200 - 10,000 ng/dL]
  Likely Non-classic CAH
- < 6 nmol/L [< 200 ng/dL]
  Likely unaffected or NCCAH

**17-OHP post-ACTH stimulation test**

- > 300 nmol/L [10,000 ng/dL]
  Classic CAH
- 31 - 300 nmol/L [1,000 - 10,000 ng/dL]
  Non-classic CAH
- < 50 nmol/L [< 1,666 ng/dL]
  Likely unaffected or heterozygote

Speiser PW et al. JCEM, 2010, 95: 4133-4160
Case 1: Question 2

- You are concerned the baby has salt-wasting CAH. What lab abnormalities would you expect?

<table>
<thead>
<tr>
<th>Plasma renin activity (PRA)</th>
<th>Sodium</th>
<th>Potassium</th>
<th>Bicarbonate</th>
<th>BUN</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>B</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>nL</td>
</tr>
<tr>
<td>C</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>D</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>E</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
</tbody>
</table>
Adrenal gland physiology:
Normal – Renin-angiotensin-aldosterone (mineralocorticoids)
Adrenal insufficiency:
Primary – Renin-angiotensin-aldosterone

Mineralocorticoid defect, Electrolyte abnormalities
Aldosterone action

Figure 1 Classical MR-mediated effects of aldosterone in the principal cells of the kidney, resulting in increased potassium excretion and sodium reabsorption

ALDO, aldosterone; Hsp, heat-shock protein; SRE, steroid-response element; CHIF, corticosteroid-hormone-induced factor. Reproduced from [128] with permission.


Booth RE et al. Advances in Physiology Education, 2002, 26: 8-20
Aldosterone action

**Blood**
- Aldosterone
- Angiotensin-2

**Urine**
- Na reabsorption
- K secretion
- HCO3 secretion

**Channels**
- ENaC
- ROMK
- HK-ATPase

**Transport**
- Na
- K
- H+
Aldosterone deficiency:
Electrolyte abnormalities - Summary

- ↓ Na⁺ reabsorption → ↓ Na⁺ in blood
  → ↑ urinary Na⁺ loss
  → ↓ H₂O reabsorption → ↓ TBW → ↑ urea (BUN)

- ↓ K⁺ excretion → ↑ K⁺ in blood

- ↓ Cl⁻ reabsorption → ↓ Cl⁻ in blood

- ↓ H⁺ excretion → ↑ H⁺ reabsorption (acidosis = ↓ HCO₃⁻)
Case 1: Question 3

- Newborn with classic congenital adrenal hyperplasia. How are you going to treat the glucocorticoid deficiency in CAH?

A. Hydrocortisone tablet ÷ TID
B. Hydrocortisone suspension ÷ TID
C. Prednisolone ÷ BID
D. Prednisone ÷ BID
E. Dexamethasone ÷ once daily
Han TS et al. Nat Rev Endocrinol, 2014, 10: 115-124

**Glucocorticoid deficiency**

- **Treatment** Glucocorticoid Rx

**Adrenal crisis**

**Virilization**

**Ongoing**

- CYP11A1
- 3β-HSD2
- HSD3B2
- 21-hydroxylase CYP21A2
- Aldosterone synthase CYP11B2

- ACTH
- Cholesterol
- Pregnenolone
- Progesterone
- 11-deoxycorticosterone
- Corticosterone
- 180H-corticosterone
- Aldosterone
- 17α-hydroxylase CYP17A1
- 17α-hydroxylase
- 17,20-lyase
- 170H-pregnenolone
- 170H-progesterone (170HP)
- 11-deoxycorticosterone
- 11-deoxycortisol

- DHEA
- Androstenedione
- Testosterone

- 17β-HSD5 AKR1C3
- 11β-hydroxylase CYP11B1

- Zona glomerulosa Mineralocorticoids
- Zona fasciculata Glucocorticoids
- Zona reticularis Androgens

**Glucocorticoid deficiency**

- Glucocorticoid Rx

- Ongoing Virilization

- Adrenal crisis
Exogenous corticosteroids: Growth suppression

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Anti-inflammatory activity</th>
<th>Growth suppression activity</th>
<th>HPA axis suppression activity</th>
<th>Mineralocorticoid activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cortisone acetate</td>
<td>0.8</td>
<td>0.08</td>
<td>?</td>
<td>0.8</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4</td>
<td>?</td>
<td>4</td>
<td>0.5-0.8</td>
</tr>
<tr>
<td>Prednisone</td>
<td>3.5-4</td>
<td>5</td>
<td>?</td>
<td>0.5-0.8</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>25-80</td>
<td>80</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Fludrocortisone</td>
<td>14-15</td>
<td>?</td>
<td>12</td>
<td>125-200</td>
</tr>
</tbody>
</table>

HPA. Hypothalamic-adrenal axis
CAH: Treatment

• Glucocorticoid deficiency: Hydrocortisone
  – Endogenous production: 6-8 mg/m²/day
  – Treatment dose: 10-15 mg/m²/day ÷ TID (tablet only)
    • To prevent virilization
    • Gastric acid/1st pass in the liver

Not suspension
- Not bioequivalent
- Uneven distribution
CAH: Treatment

- Glucocorticoid deficiency: Hydrocortisone
  - Endogenous production: 6-8 mg/m²/day
  - Treatment dose: 10-15 mg/m²/day ÷ TID (tablet only)
  - Medical alert ID
  - Stress-dosing
    - Fever > 101°F, vomiting
    - Not for mental/emotional stress, minor illness
    - Triple each dose (~ 30-50 mg/m²/day)
    - Teach Solu-Cortef
Most common cause
Mineralocorticoid deficiency
Electrolyte abnormalities

Treatment
CAH: Treatment

• Mineralocorticoid deficiency
  – Per Endocrine Society and PES guidelines
    • Treat all infants with classic CAH
    • In newborn, early infancy period. Lab-based dose adjustment.
CAH: Treatment

- Mineralocorticoid deficiency
  - Fludrocortisone: 0.05-0.2 mg/day
  - NaCl: 1-2 gram/day ÷ over several feeds
CAH: Treatment

• Monitoring
  – Diagnostic evaluation
    • Labs:
      – 17-OHP, androstenedione, BMP, plasma renin activity
        » Infancy: q3mo → Later: q4-12mo
    • Radiography: Bone age q1yr after 2 years old
  – Physical exam
    • Vitals: Height, weight, blood pressure
    • GU: Not needed unless
      – Concern for poor control
      – Monitoring pubertal pace, clitoral size
Congenital adrenal hyperplasia: Summary

• Methodical evaluation of ambiguous genitalia.

• CAH evaluation: Serum 17-OH Progesterone

• CAH $\rightarrow$ Glucocorticoid (+ mineralocorticoid) deficiency

• Treatment
  – Hydrocortisone tablet: Start 10-15 mg/m2/day $\div$ TID
  – Fludrocortisone: Start 0.05 – 0.2 mg/day
  – NaCl supplement: 1-2 g/day $\div$ over several feeds

• Monitoring
  – Labs: 17-OHP, androstenedione, BMP, renin
  – Physical exam: Height curve may show over/under-Rx
Case 2: Question 1

• You see a 10 yo male with history of Type 1 diabetes mellitus for a routine physical. You notice that he has a coppery tan. You suspect Addison disease. How should you obtain the cortisol level?

A. 8 AM serum cortisol
B. Midnight serum cortisol
C. Midnight salivary cortisol
D. 24 hour urinary free cortisol
E. It does not matter what time of day.
Adrenal gland physiology:
Normal physiology – HPA axis (glucocorticoids)
Adrenal gland physiology:
Normal – Renin-angiotensin-aldosterone (mineralocorticoids)
Adrenal insufficiency: Primary – HPA axis
Adrenal insufficiency:
**Primary** – Renin-angiotensin-aldosterone
Adrenal insufficiency: 
**Secondary** – HPA axis
1° vs 2° adrenal insufficiency: Summary

<table>
<thead>
<tr>
<th>Hormonal insufficiency</th>
<th>1° (e.g., CAH, Addison)</th>
<th>2°</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucocorticoid</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Mineralocorticoid</td>
<td>✔</td>
<td></td>
</tr>
</tbody>
</table>
Addison disease (Primary adrenal insufficiency): Clinical features

- Glucocorticoid deficiency
  → ↓ BP, ↑ HR
  → ↓ glucose
  → ↑ ACTH → hyperpigmentation

- Mineralocorticoid deficiency (i.e. aldosterone)
  → ↑ K, ↓ Na → Salt craving
  → Hypovolemia → ↓ BP, ↑ HR
  → Shifts in muscle electrolyte concentrations
    → Weakness, myalgias
    → GI symptoms: N/V/abdominal pain

- Anorexia, weight loss
- Apathy, confusion
- Fatigue

http://dxline.info/img/new_ail/addisons-disease.jpg
Addison disease:
Screening lab evaluation

- Glucocorticoid deficiency
  - 8 AM cortisol
  - ACTH
- Mineralocorticoid deficiency
  - Electrolytes (e.g. BMP)
  - Plasma renin activity
- Other evaluation
  - Suspect autoimmunity: Anti-21 hydroxylase antibodies
  - In a male: Very long-chain fatty acids (r/o ALD)
1° adrenal insufficiency: Treatment

- Glucocorticoid deficiency: Hydrocortisone
  - Treatment dose: 6-10 mg/m$^2$/day ÷ TID (tablet only)
  - Medical alert ID
- Stress-dosing
  - Fever > 101°F, vomiting
  - Not for mental/emotional stress, minor illness
  - Triple each dose (~ 30-50 mg/m$^2$/day)
  - Teach Solu-Cortef
1° adrenal insufficiency: Treatment

- Mineralocorticoid deficiency
  - Fludrocortisone: 0.05-0.2 mg/day
Adrenal Crisis: Treatment - Summary

- Presentation:
  - Glucocorticoid deficiency $\rightarrow$ ↓ BP $\rightarrow$ NS bolus  
    $\downarrow$ glc $\rightarrow$ D10 or D25

- Give Hydrocortisone IM/IV (Goal: To give too much)
  - Newborn: 15 mg $\rightarrow$ 15 mg/d $\div$ q6h
  - Infant: 25 mg $\rightarrow$ 25 mg/d $\div$ q6h
  - Child: 50 mg $\rightarrow$ 50 mg/d $\div$ q6h
  - Adult: 100 mg $\rightarrow$ 100 mg/d $\div$ q6h

- Mineralocorticoid deficiency $\rightarrow$ ↑ K$^+$ ↓ Na$^+$
  - Fludrocortisone: Only available PO
  - Hydrocortisone has some mineralocorticoid activity
    - Thus, no need to replace mineralocorticoid immediately
Adrenal insufficiency: Treatment

- **Primary adrenal insufficiency**
  - Glucocorticoid: Hydrocortisone
    - Stress-dosing: Solu-Cortef
  - Mineralocorticoid: Fludrocortisone

- **Secondary adrenal insufficiency**
  - Glucocorticoid: Hydrocortisone
    - Stress-dosing: Solu-Cortef
Addison disease: Summary

• Pathophysiology
  – 1° adrenal gland insufficiency
    → Glucocorticoid + mineralocorticoid deficiency

• Clinical features
  – Glucocorticoid: Hypotension, hypoglycemia, hyperpigmentation
  – Mineralocorticoid: Electrolyte abnormalities, dehydration

• Evaluation
  – Glucocorticoid: 8 AM cortisol, ACTH
  – Mineralocorticoid: Electrolytes, plasma renin activity
  – In a male → screen for X-linked ALD

• Treatment
  – Glucocorticoid: Hydrocortisone (tablet only); Solu-Cortef
  – Mineralocorticoid: Fludrocortisone
Case 3: Question 1

- A 15 yo M complains of fatigue, depression, and nausea. He has a history of persistent asthma. He was on prednisolone 40 mg daily for several weeks and is now on a steroid wean.

What is the hydrocortisone equivalent of prednisolone 40 mg daily?

A. 20 mg/day of hydrocortisone
B. 40 mg/day of hydrocortisone
C. 160 mg/day of hydrocortisone
D. 800 mg/day of hydrocortisone
Exogenous corticosteroids: HPA axis

<table>
<thead>
<tr>
<th>Steroid</th>
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<th>HPA axis suppression activity</th>
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<td>125-200</td>
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HPA. Hypothalamic-adrenal axis
Case 3: Question 1

- A 15 yo M complains of fatigue, depression, and nausea. He has a history of persistent asthma. He was on prednisolone 40 mg daily for several weeks and is now on a steroid wean.

Weight: 48.8 kg, height: 162.1 cm, BSA: 1.5 m²

Prednisolone 40 mg/day = 40 x 4
= 160 mg/d hydrocortisone
Hydrocortisone (mg/m²/day) = 160/1.5
= 106.7 mg/m²/d
Endogenous cortisol production: 6-8 mg/m²/d
A 15 yo M complains of fatigue, depression, and nausea. He has a history of persistent asthma. He was on prednisolone 40 mg daily for several weeks and is now on a steroid wean.

Is this primary or secondary adrenal insufficiency?

A. Primary adrenal insufficiency
B. Secondary adrenal insufficiency
Exogenous steroids: Adrenal insufficiency

Exogenous steroids $\rightarrow$ 2° Adrenal insufficiency
Case 3: Question 3

• A 15 yo M complains of fatigue, depression, and nausea. He has a history of persistent asthma. He was on prednisolone 40 mg daily for several weeks and is now on a steroid wean.

When would you consider a steroid wean?

A. 5 days
B. 7 days
C. 10 days
D. 14 days
E. 21 days
Exogenous corticosteroids: Wean

• Steroid wean if on exogenous steroids $x \geq 2$ weeks
  – Otherwise, at risk for glucocorticoid withdrawal symptoms

• Steroid wean schedule
  – Empiric: Many different ways to get to the same goal
  – Supraphysiologic $\rightarrow$ physiologic doses
    • Decrease by 25% weekly
    • Decrease based on underlying illness
  – If on other steroid, switch to hydrocortisone equivalent dose
  – Monitor 8 AM cortisol to decide when to discontinue replacement
    • Usually Cortisol $\geq 10$
    • Still need stress-dosing coverage
  – ACTH stimulation test to determine if stress-dosing needed
Exogenous steroid therapy: Summary

- Prolonged exogenous steroids $\rightarrow$ risk for 2° adrenal insufficiency

- Exogenous steroids $x \geq 2$ weeks $\rightarrow$ Steroid wean

- Signs and symptoms of glucocorticoid withdrawal
  - $\downarrow$ BP, malaise, lethargy, anorexia, HA, nausea, fever

- Steroid wean: Empiric (hydrocortisone)
  - Go slow
  - Monitor 8 AM cortisol
  - ACTH stimulation test to determine if stress-dosing needed
Case 4: Question 1

• The mother of an obese 14 yo F is convinced that her daughter has Cushing syndrome. She has continued to gain weight despite reported changes in her diet and physical activity. Your patient has stretch marks and a bump on her neck.

What additional history or sign would concern you that she has true Cushing syndrome?

A. Depression
B. Pictorial evidence of rapid weight gain
C. PCOS
D. Moon facies
E. Hypothyroidism
Cushing syndrome: Clinical features

“Lemon on a toothpick”

- Moon face
- Red cheeks
- Bruises easily
- Thin limbs
- Poor wound healing
- Abdominal striae
- Central fat deposition

Hypothalamus produces releasing factor
Anterior pituitary produces ACTH
ACTH travels through blood
ACTH causes adrenal cortex to produce cortisol

Cushing’s syndrome

https://s-media-cache-ak0.pinimg.com/236x/cf/53/20/cf5320d99c75ebf2955cc382d51f105c.jpg
Cushing syndrome: Clinical features

- “Classic signs”: Features of advanced disease

- Emotional disturbance
- Osteoporosis
- Buffalo hump
- Muscle weakness

http://www.physio-pedia.com/Cushing's_Syndrome
Weight gain and growth arrest

Cushing syndrome: Clinical features

• Earliest signs: Weight gain and growth arrest
Case 4: Question 2

• The mother of an obese 14 yo F is convinced that her daughter has Cushing syndrome. She has continued to gain weight despite reported changes in her diet and physical activity. Your patient has stretch marks and a bump on her neck.

You explain to Mom why you do not think her daughter has Cushing syndrome, but she remains unconvinced.

What screening diagnostic evaluation might you consider?

A. 8 AM serum cortisol
B. Low dose dexamethasone suppression test
C. High dose dexamethasone suppression test
D. Midnight salivary cortisol
E. It does not matter what time of day.
Cortisol secretion: Diurnal variation
Cushing syndrome: Loss of diurnal variation
Cushing syndrome: Loss of diurnal variation

- Midnight salivary cortisol
- 24h urine free cortisol (+ 24h urine creatinine)

Should have ≥ 2 elevated tests.
# Obesity vs. Cushing syndrome

<table>
<thead>
<tr>
<th></th>
<th>Obesity</th>
<th>Cushing syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight distribution</td>
<td>Generalized</td>
<td>Centripetal</td>
</tr>
<tr>
<td>Linear growth</td>
<td>Normal - ↑</td>
<td>Poor</td>
</tr>
<tr>
<td>Striae</td>
<td>Narrow, pink</td>
<td>Wide, violaceous</td>
</tr>
<tr>
<td>24h urine free cortisol</td>
<td>Normal - ↑</td>
<td>↑</td>
</tr>
<tr>
<td>MN salivary cortisol</td>
<td>Normal</td>
<td>↑</td>
</tr>
</tbody>
</table>
Cushing syndrome: Summary

• Earliest signs of Cushing syndrome: Poor growth, ↑ weight

• Classic signs of Cushing syndrome = Advanced disease

• Screening for Cushing syndrome:
  – Midnight salivary cortisol
  – 24h urinary free cortisol + creatinine
Take home points

1. Congenital adrenal hyperplasia (CAH)
   A. 1° adrenal insufficiency
   B. Screen with 17-OHP (= 17-OH Progesterone)

2. Adrenal insufficiency
   A. Screening labs: 8AM cortisol, ACTH ± electrolytes, plasma renin activity
   B. 1° versus 2° adrenal insufficiency
      1°: Glucocorticoid + mineralocorticoid deficiency
      2°: Glucocorticoid deficiency
   C. Treatment:
      1. Glucocorticoid deficiency: Hydrocortisone
      2. Mineralocorticoid deficiency: Fludrocortisone

3. Exogenous steroids for ≥ 2 weeks → wean

4. Cushing syndrome:
   A. Earliest signs: Growth arrest and weight gain
   B. Screening labs: 2 elevated screening tests → positive
      1. 24h urinary free cortisol + creatinine
      2. Midnight salivary cortisol