Common Adrenal Diseases

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Outline

• Pre-test Questions
• Cases
• Anatomy/physiology
• Symptoms/Signs
• Diagnosis/Treatment
• Post-test Questions
• Questions

• Topics:
  • Primary AI
  • Central AI
  • Cushing’s syndrome
  • Incidentaloma
  • Pheochromocytoma
  • Primary Aldosteronism
The primary cause of central adrenal insufficiency is

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>1. Pituitary adenoma</td>
</tr>
<tr>
<td>20%</td>
<td>2. Sheehan’s syndrome</td>
</tr>
<tr>
<td>20%</td>
<td>3. Exogenous glucocorticoids</td>
</tr>
<tr>
<td>20%</td>
<td>4. Tuberculosis</td>
</tr>
<tr>
<td>20%</td>
<td>Metastatic cancer</td>
</tr>
</tbody>
</table>
Case #1

- Mr. Smith is a 34 yo wm presents to your office to establish care. He is a manual laborer and has noticed worsening fatigue that is interfering with his job. He also reports nausea, decreased appetite and progressive, unintentional weight loss. No night sweats, diarrhea, or blood in his stool. No chest pain or SOB. He admits to some recent problems with memory and depression.
- He has no known medical problems and is a non-drinker, never smoker.
- His family history is unknown as he is adopted.
- He takes no prescribed medications.
Case #1 continued

- On physical exam you note a blood pressure of 100/60, and general, diffuse tenderness on palpation of his abdomen
- He has some areas of vitiligo and otherwise looks tan
Case #1 Continued

- Laboratory evaluation shows a normal TSH, normal LFTs, normal CBC except for eosinophilia
- His BMP shows mild hyponatremia and hyperkalemia
Primary Adrenal Insufficiency

- AKA Addison’s Disease
- First described by Thomas Addison in 1855
- First synthesized cortisone did not become available until 1949
- Most common cause at the time was tuberculosis infiltration of the adrenals
- Most common cause today is autoimmune adrenalitis
- 60-120 per million in Caucasians, women > men
- Peak age of diagnosis in fourth decade of life
Stress activates the hypothalamus, which in turn stimulates neurosecretory cells to produce hypothalamic-releasing hormone. This hormone activates the anterior pituitary gland, which secretes ACTH. ACTH stimulates the adrenal cortex to produce glucocorticoids and mineralocorticoids.
Primary Adrenal Insufficiency
Autoimmune adrenalitis (most common)
Infection
   Tuberculosis
   Mycosis
   Bacterial
   HIV associated
Metastatic cancer
Medications
   Etomidate
   Ketoconazole
   Metyrapone
Adrenal hemorrhage
Primary Adrenal Insufficiency

- Secretion of all adrenal corticosteroids is impaired
  - Aldosterone
  - Cortisol
  - Dehydroepiandrosterone (DHEA)
  - DHEA sulfate
- Acute vs chronic presentation
Primary AI: Chronic Symptoms/Signs

- Chronic malaise, fatigue, generalized weakness, myalgias
- Nausea, vomiting, anorexia, abdominal pain, weight loss
- Salt wasting with resultant salt craving
- Psychiatric symptoms (impairment of memory, depression, psychosis)
- Other autoimmune disease (hyper or hypothyroidism, DM 1, vitiligo)
- Hyperpigmentation of skin and mucosa
- Volume depletion/hypotension
- Hyponatremia
- Hypokalemia
### Clinical manifestations of chronic adrenal insufficiency

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency, percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness, tiredness, fatigue</td>
<td>100</td>
</tr>
<tr>
<td>Anorexia</td>
<td>100</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>92</td>
</tr>
<tr>
<td>Nausea</td>
<td>86</td>
</tr>
<tr>
<td>Vomiting</td>
<td>75</td>
</tr>
<tr>
<td>Constipation</td>
<td>33</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>31</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16</td>
</tr>
<tr>
<td>Salt craving</td>
<td>16</td>
</tr>
<tr>
<td>Postural dizziness</td>
<td>12</td>
</tr>
<tr>
<td>Muscle or joint pains</td>
<td>6-13</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sign</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>100</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>94</td>
</tr>
<tr>
<td>Hypotension (systolic BP &lt;110 mmHg)</td>
<td>88-94</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>10-20</td>
</tr>
<tr>
<td>Auricular calcification</td>
<td>5</td>
</tr>
</tbody>
</table>
## Clinical and laboratory findings suggesting adrenal crisis

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydration, hypotension, or shock out of proportion to severity of current illness</td>
</tr>
<tr>
<td>Nausea and vomiting with a history of weight loss and anorexia</td>
</tr>
<tr>
<td>Abdominal pain, so-called &quot;acute abdomen&quot;</td>
</tr>
<tr>
<td>Unexplained hypoglycemia</td>
</tr>
<tr>
<td>Unexplained fever</td>
</tr>
<tr>
<td>Hyponatremia, hyperkalemia, azotemia, hypercalcemia, or eosinophilia</td>
</tr>
<tr>
<td>Hyperpigmentation or vitiligo</td>
</tr>
<tr>
<td>Other autoimmune endocrine deficiencies, such as hypothyroidism or gonadal failure</td>
</tr>
</tbody>
</table>

*Adapted from: Burke CW. Adrenocortical insufficiency. Clin Endocrinol Metab 1985; 14:947.*
Adrenal Crisis Treatment

- IV normal saline
- Dexamethasone 4mg IV q 6 or hydrocortisone 50-100 mg IV q 6-8
- Taper to oral dosing over 1-3 days
Primary AI Diagnosis

- Cosyntropin stimulation test:
  - 250mcg cosyntropin given IV or IM
  - Plasma cortisol at baseline and 30min, 60min, 90min
  - Plasma cortisol >20mcg/dL
- Plasma ACTH distinguishes primary from secondary adrenal failure
- CT adrenal glands
- If autoimmune adrenalitis, can measure antibodies against 21 hydroxylase (80%)
  - Evaluate other endocrine gland dysfunction (calcium, glucose, TSH, gonadal function)
Primary AI Treatment

• Prednisone or hydrocortisone
• Fludrocortisone 0.1mg daily, adjust dose to maintain blood pressure and K within normal range
• Replacement therapy with DHEA is not essential for survival
• Patient education:
  • Steroid adjustment for illness, injury
  • Vial IM dexamethasone or hydrocortisone or pre-filled dexamethasone syringes
  • Medical ID tag or bracelet
Secondary/Central Adrenal Insufficiency

- Secondary adrenal insufficiency = loss of ACTH from the pituitary
- Tertiary adrenal insufficiency = loss of CRH from the hypothalamus
- 150-280 per million
- Peak age of diagnosis sixth decade of life, women > men
- Decreased production of ACTH-dependent corticosteroids (cortisol, DHEA, and DHEA sulfate)
Central Adrenal Insufficiency

Exogenous corticosteroid administration (most common)

Hypothalamic/pituitary disease, such as:

- Pituitary adenoma
- Rathke cyst or craniopharyngioma
- Hypothalamic tumors
- Sarcoidosis
- Cranial irradiation

Chronic administration of drugs with corticosteroid activity

- Megestrol acetate
Pre-Test Question #2

Which of the following medication regimens is least likely to cause resultant adrenal insufficiency?

1. Prednisone 10mg daily, given at 9am for one week
2. Hydrocortisone 40mg daily, given at 9am for one week
3. Prednisone 10mg daily, given at 9pm for one week
4. Hydrocortisone 40mg daily, given at 9pm for one week
5. Dexamethasone 1.5mg daily for one week
Pre-Test Question #2

Which of the following medication regimens is least likely to cause resultant adrenal insufficiency?

| 20%  | 1. Prednisone 10mg daily, given at 9am for one week |
| 20%  | 2. Hydrocortisone 40mg daily, given at 9am for one week |
| 20%  | 3. Prednisone 10mg daily, given at 9pm for one week |
| 20%  | 4. Hydrocortisone 40mg daily, given at 9pm for one week |
| 20%  | Dexamethasone 1.5mg daily for one week |
Central Adrenal Insufficiency

- Exogenous steroid administration highest risk:
  - >10mg prednisone
  - Long half life > short half life
  - Night time administration
  - Length of treatment
Secondary adrenal Insufficiency

Hypothalamus

CRH↑

Pituitary

ACTH↓

Adrenal

Cortisol↓

Pituitary disease

---

Hypothalamus

CRH↓

Pituitary

ACTH↓

Adrenal

Cortisol↓

Hypothalamic disease
Central AI Symptoms

- Malaise, fatigue, myalgias, arthralgias, weight loss
- Loss of other pituitary hormones- amenorrhea, decreased libido, cold intolerance
- Mass effects (headache or visual field defects)
- NO hyperpigmentation (ACTH is not elevated)
- RAS is usually intact, aldosterone secretion is normal
  - Less prominent volume depletion and no hyperkalemia
Central AI Diagnosis

- Cosyntropin stimulation test, ACTH
- Withhold glucocorticoids for 24 hours
- Chronic partial secondary AI requires ITT or metyrapone stimulation test
- Brain MRI with coned down views of the pituitary
- May be normal in recent-onset secondary AI, takes several weeks for adrenal atrophy
  - Test 4-6 weeks after pituitary injury or surgery
AI Testing Considerations

- Current assays measure total cortisol (free and protein bound)
- Pregnancy, estrogen therapy (HRT, OCP) increase serum cortisol through an increase in binding proteins
  - Increased serum cortisol levels without altering the physiologically important free hormone concentrations
- Patients with hypoproteinemia have lower total serum cortisol levels but may have normal serum free cortisol levels
  - Critically ill patients
Case #1 Continued

- Mr Smith has been started on glucocorticoid and mineralocorticoid replacement and has had a great improvement in his symptoms over the course of a few months.

- He follows up with you today to discuss pre-operative clearance, now that he is feeling better and back at his job his right knee is causing him increased pain. He has seen an orthopedist and wants to pursue arthroscopy.
Corticosteroid coverage for surgery in patients taking exogenous corticosteroids

For minor procedures or surgery under local anesthesia (eg, inguinal hernia repair) take usual morning steroid dose. No extra supplementation is necessary.

For moderate surgical stress (eg, lower extremity revascularization, total joint replacement) take usual morning steroid dose. Give 50 mg hydrocortisone intravenously just before the procedure and 25 mg of hydrocortisone every 8 hours for 24 hours. Resume usual dose thereafter.

For major surgical stress (eg, esophagogastrrectomy, total proctocolectomy, open heart surgery) take usual morning steroid dose. Give 100 mg of intravenous hydrocortisone before induction of anesthesia, and 50 mg every 8 hours for 24 hours. Taper dose by half per day to maintenance level.
Perioperative Glucocorticoids

• Patients who should be assumed to have functional suppression of HPA axis:
  • Currently taking prednisone >20 mg/day for > 3 weeks
  • Any patient on glucocorticoids who has clinical Cushing's syndrome
• Treat with supplemental glucocorticoids in the perioperative period
Perioperative Glucocorticoids

• Not considered to have HPA suppression:
  • Any patient who has been taking any dose of glucocorticoid for < 3 weeks
  • Patients who have received morning doses of < 5 mg/day of prednisone for any length of time
  • Patients being treated with <10 mg of prednisone or its equivalent every other day
• These patients can be safely maintained on their normal daily dose of glucocorticoids in the perioperative period and monitor for any evidence of hemodynamic instability peri-operatively
Perioperative Glucocorticoids

• For patients who are currently off glucocorticoids, but used them in the past year:
  • Patients who received regimens that would not be expected to suppress the HPA axis do not require testing
  • All other patients who received regimens of either longer duration or higher doses of glucocorticoids that could have potentially suppressed the HPA axis should undergo preoperative assessment of their HPA axis beginning with a morning serum cortisol
Case #2

• The patient is a 50 yo wf presenting to your office to establish care as she has recently signed up for Obama Care. She has a history of rheumatoid arthritis and has been maintained on prednisone 20mg daily for a number of years as she was previously unable to afford other medications for treatment.

• On ROS she admits to progressive weight gain, muscle weakness and difficulty sleeping.

• On exam she has Stage 1 HTN and a fingerstick glucose is 205. She has central obesity and hirsuitism
Cushing’s Syndrome

- Results from prolonged exposure to excessive glucocorticoids
- Exogenous vs Endogenous
- ACTH dependent vs ACTH independent
- Cushing's disease, originally described in 1932 by Harvey Cushing
  - ACTH secreting pituitary adenoma
  - Annual incidence of 5-25 per million
  - Women of reproductive age, 25-45
- Pseudo-Cushing’s syndrome
<table>
<thead>
<tr>
<th>Cause</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endogenous Cushing syndrome</strong></td>
<td></td>
</tr>
<tr>
<td>ACTH-dependent</td>
<td>75-80</td>
</tr>
<tr>
<td>ACTH-secreting pituitary adenomas</td>
<td>60-65</td>
</tr>
<tr>
<td>Ectopic ACTH secretion by tumors</td>
<td>10-15</td>
</tr>
<tr>
<td>CRH-secreting tumors</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td><strong>ACTH-independent</strong></td>
<td></td>
</tr>
<tr>
<td>Adrenal adenoma</td>
<td>20-25</td>
</tr>
<tr>
<td>Adrenal carcinoma</td>
<td>10-15</td>
</tr>
<tr>
<td><strong>Exogenous Cushing syndrome</strong></td>
<td></td>
</tr>
<tr>
<td>Administration of corticosteroids (prednisone, dexamethasone, hydrocortisone)</td>
<td>—</td>
</tr>
<tr>
<td>Administration of drugs with corticosteroid activity (progestational agents, such as megestrol acetate)</td>
<td>—</td>
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</tbody>
</table>
Cushing’s Syndrome

• Establishing the diagnosis is often difficult because none of the symptoms or signs are pathognomonic of the syndrome

• An important clinical clue to the presence of glucocorticoid excess is the simultaneous development and increasing severity of several of these symptoms

• Wide spectrum of manifestations, depending on the duration and intensity of excess glucocorticoid excess and cause of the hypercortisolism
Cushing’s Syndrome Symptoms/Signs

- Progressive central obesity
- **Metabolic complications**
- Dermatologic complications
- Reproductive changes
- Musculoskeletal manifestations
- Neuropsychiatric changes
- Other

- Glucose intolerance
- Hyperglycemia/DM 2
- Increased albinuria
- HTN
- HLD
- Increased risk of death from CV disease (MI, CVA, Thromboembolism)
Cushing’s Syndrome Symptoms/Signs

• Progressive central obesity
• Metabolic complications
• **Dermatologic complications**
  • Reproductive changes
  • Musculoskeletal manifestations
  • Neuropsychiatric changes
  • Other
• Skin atrophy
• Easy bruising
• Striae
• Fungal infections
• Hyperpigmentation
• Acanthosis nigricans
• Pigmented scars
Cushing’s Syndrome Symptoms/Signs

- Progressive central obesity
- Metabolic complications
- Dermatologic complications
- **Reproductive changes**
  - Musculoskeletal manifestations
  - Neuropsychiatric changes
  - Other
- Menstrual irregularities
- Hirsutism
- Oily facial skin, acne
- Increased libido
- Virilization
Cushing’s Syndrome Symptoms/Signs

- Progressive central obesity
- Metabolic complications
- Dermatologic complications
- Reproductive changes
- **Musculoskeletal manifestations**
- Neuropsychiatric changes
- Other
- Weakness
- Proximal muscle wasting
- Osteoporosis
Cushing’s Syndrome Symptoms/Signs

- Progressive central obesity
- Metabolic complications
- Dermatologic complications
- Reproductive changes
- Musculoskeletal manifestations
- Neuropsychiatric changes
- Other

- Emotional lability/ Irritability
- Agitated depression
- Anxiety/Panic attacks
- Mild paranoia
- Insomnia
- Learning, cognition, memory impairment
- Decreased hippocampal volume/brain volume
Cushing’s Syndrome Symptoms/Signs

<table>
<thead>
<tr>
<th>Symptoms/Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive central obesity</td>
</tr>
<tr>
<td>Metabolic complications</td>
</tr>
<tr>
<td>Dermatologic complications</td>
</tr>
<tr>
<td>Reproductive changes</td>
</tr>
<tr>
<td>Musculoskeletal manifestations</td>
</tr>
<tr>
<td>Neuropsychiatric changes</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Increased frequency of infections</td>
</tr>
<tr>
<td>Increased intraocular pressure</td>
</tr>
<tr>
<td>Cataracts</td>
</tr>
<tr>
<td>Central serous chorioretinopathy</td>
</tr>
</tbody>
</table>
Cataracts
Ulcers
Skin: striae, thinning, bruising
Hypertension/ Hirsutism/ Hyperglycemia
Infections
Necrosis, avascular necrosis of the femoral head
Glycosuria
Osteoporosis, obesity
Immunosuppression
Diabetes
<table>
<thead>
<tr>
<th>Symptoms and signs of Cushing's syndrome</th>
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</thead>
<tbody>
<tr>
<td><strong>Symptom or sign</strong></td>
</tr>
<tr>
<td>Centripetal obesity</td>
</tr>
<tr>
<td>Facial plethora</td>
</tr>
<tr>
<td>Glucose intolerance</td>
</tr>
<tr>
<td>Weakness, proximal myopathy</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Psychological changes</td>
</tr>
<tr>
<td>Easy bruisingability</td>
</tr>
<tr>
<td>Hirsutism</td>
</tr>
<tr>
<td>Oligomenorrhoe or amenorrhea</td>
</tr>
<tr>
<td>Impotence</td>
</tr>
<tr>
<td>Acne, oily skin</td>
</tr>
<tr>
<td>Abdominal striae</td>
</tr>
<tr>
<td>Ankle edema</td>
</tr>
<tr>
<td>Backache, vertebral collapse, fracture</td>
</tr>
<tr>
<td>Polydipsia, polyuria</td>
</tr>
<tr>
<td>Renal calculi</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Exophthalmos</td>
</tr>
<tr>
<td>Tinea versicolor infection</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
</tbody>
</table>
Cushing’s Syndrome Diagnosis

- Biochemical diagnosis should proceed imaging studies
  
- 1. Document the presence of hypercortisolism
  
- 2. Determine if the cortisol excess is ACTH dependent or independent
  
- 3. Determine the source of the ACTH (in the ACTH dependent form)
Cushing’s Syndrome Diagnosis

- Dexamethasone suppression test
  - 1mg dexamethasone at 11pm
  - Plasma cortisol at 8am
  - Plasma cortisol <2mcg/dL
- 24 hour urine cortisol
  - >4x ULN
- Late night salivary cortisol
Cushing's Syndrome Diagnosis

- Once endogenous Cushing’s syndrome is confirmed, check plasma ACTH level
- Undetectable or low levels (<5 mcg/dL) characterizes a primary adrenal source
  - Thin section CT or MRI of adrenals
- ACTH levels >15 mcg/dL indicates an ACTH dependent cause
  - Cranial MRI
- ACTH 5-15 mcg/dL is indeterminate and should be repeated
Cushing’s Disease Diagnosis

- Midnight plasma cortisol/late evening salivary cortisol
- Low dose dexamethasone suppression test
- CRH stimulation test
- High dose dexamethasone test
- CRH after dexamethasone test
- Petrosal sinus sampling
Treatment

- Exogenous – Taper off steroids
- Adrenal adenoma or carcinoma – Unilateral adrenalectomy
- Cushing’s disease- Transphenoidal microadenectomy, radiation, bilateral adrenalectomy
- Pharmacologic control:
  - Ketoconazole
  - Mitotane
  - Metyrapone
  - Aminoglutethimide
Pre-Test Question #3

All functioning tumors and those larger than ___ in diameter should be considered for surgical removal

20%  1.  2 cm
20%  2.  4 cm
20%  3.  6 cm
20%  4.  8 cm
20%  5.  10 cm
Case #3

- A 65 yo female presents with complaints of general abdominal pain which she describes as dull and intermittent. She reports diarrhea and hematochezia. Denies fever, weight loss.
- On exam she has abdominal distention and mild ttp throughout, worst in the lower quadrants.
- You obtain a CT abdomen/pelvis in evaluation and her GI system is reunremarkable.
- However, she is found to have a 4cm right adrenal nodule.
Adrenal Incidentaloma

- 2% to 3% of the scanned population older than 50 years and in up to 7% of those older than 70 years
- 10% are functioning
- Functioning vs non-functioning
- Benign vs malignant
- Primary vs metastatic
Adrenal Incidentaloma DDx

- Lipoma, cyst, hematoma, infection (TB, fungal)
- Benign adrenocortical tumors
- Adrenal adenoma causing Cushing’s syndrome or primary hyperaldosteronism
- Pheochromocytoma
- Adrenocortical carcinoma
- Metastatic cancer
- Lymphoma
Adrenal Incidentaloma Evaluation

• H&P:
  • HTN, headache, palpitations, sweating
  • Signs of Cushing’s
  • Signs or history of malignancy elsewhere

• Labs:
  • Plasma potassium, aldosterone, renin
  • Plasma or 24 hour urinary catecholamines, metanephrines
  • Cortisol or overnight dexamethasone suppression test
  • Dehydroepiandrosterone sulfate (DHEA S)
Adrenal Incidentaloma Evaluation

- Up to 15% of adrenal incidentalomas are bilateral, differential includes:
  - Bilateral adrenal hyperplasia, metastatic cancer and adrenocortical carcinoma
- The risk of primary or metastatic cancer:
  - 2% for tumors less than 4 cm in diameter
  - 25% for tumors 6 cm or larger
Adrenal Incidentaloma Treatment

• All functioning tumors and those > 6 cm should be considered for surgical removal
• Non-functioning tumors smaller than 4 cm are often followed
• Tumors 4 to 6 cm can be either surgically removed or clinically observed, depending on the presence or absence of other suspicious clinical and radiographic features
• A follow-up CT scan should be obtained in 6 to 12 months for non-functioning masses
Case #4

• Patient is a 32 yo who presents for follow up and refills of her 4 blood pressure medications. She continues to have episodes of severe headache, palpitations and diaphoresis that resolve on their own after about an hour.

• Her blood pressure is 180/100 and she reports compliance with her medications. She denies alcohol, tobacco or over the counter supplement use.
Pheochromocytoma

- Relatively rare tumors that occur in 0.1% to 0.6% of persons with hypertension
- Occur at any age, starting in infancy and peaking in third and fourth decades of life
- Chromaffin cells derived from the neural crest, secrete biogenic amines (epinephrine, norepinephrine, and dopamine) and their metabolites
  - Most predominantly secrete norepinephrine, which results in sustained or episodic hypertension
- 90% arise in the adrenal medulla
- 25% are familial
- 10% bilateral, 10% are extra-adrenal and occur along the sympathetic chain, 10% are asymptomatic, and 10% are malignant
Pheochromocytoma Symptoms/Signs

- The clinical manifestations are variable
- “Classic triad” = severe headache, diaphoresis, and palpitations
- 90% Hypertension (episodic or sustained)
- Diaphoresis, pallor, palpitations, and headaches
- Hyperglycemia, weight loss
- Arrhythmias (atrial and ventricular fibrillation)
- Catecholamine-induced cardiomyopathy
Pre-Test Question #4

All the following may interfere with biochemical testing for pheochromocytoma except:

- 20% tricyclic antidepressants
- 20% labetalol
- 20% theophylline
- 20% caffeine
- 20% lisinopril
Pheochromocytoma Diagnosis

- Plasma metanephrines and catecholamines typically elevated more than 2 fold (often >2000 ng/L)
- Lower levels are equivocal and require further biochemical confirmation, such as with a clonidine suppression test
  - Milder elevations in plasma norepinephrine levels (600-1000 ng/L) can be seen with stress and essential hypertension
  - Clonidine suppression test – decrease by 50% is expected response, consistently elevated levels suggest pheochromocytoma
  - Stress, caffeine, alcohol, and certain drugs
Pheochromocytoma Diagnosis

- Urine catecholamines and metanephrines in the urine
- CT or MRI
- Scintigraphic localization with iodine-131–metaiodobenzylguanidine ($^{131}$I-MIBG) is used when CT scans and MRIs are negative
Pheochromocytoma Treatment

- Surgical resection
- Avoid β-blockers until patient has adequate α-adrenergic blocker therapy
- Phenoxybenzamine used peri-operatively
- α-antagonists, calcium channel blockers, and labetalol should be used and BP titrated for a SBP 150 for more than 7 days prior to procedure
Case #5

• Patient is a 34 yo female who presents with complaints of muscle spasms and hand cramps. She also reports a seven year history of episodic muscle weakness that often caused near paralysis of her legs. She otherwise denies all other complaints, has no known past medical history and takes no medications.

• Initial laboratory evaluation shows hypokalemia, metabolic alkalosis
Primary Aldosteronism

• AKA Conn’s syndrome
• Defined as renin-independent HTN with non-suppressable hypersecretion of aldosteronism
• Reported first in 1955 by Jerome W Conn
• 10% prevalence among HTN patients, increases with severity of HTN
  • More common among younger patients with HTN
• Causes:
  • Idiopathic hyperaldosteronism
  • Aldosterone-producing adenomas
Primary Aldosteronism Symptoms/Signs

- Muscle weakness and cramping
- Headache, fatigue, palpitations, polyuria
- No specific physical findings
- HTN, more severe end organ damage
- Hypokalemia, metabolic alkalosis, mild hypernatremia, hypomagnesemia
Pre-Test Question #5

An aldosterone-to-renin ratio greater than 20 is highly suggestive of primary hyperaldosteronism.

1. True
2. False
Primary Aldosteronism Diagnosis

1. Screening
   - Draw plasma aldosterone and renin levels
   - PAC/PRA Ratio >20 to >50 are supportive of primary aldosteronism

2. Confirmation
   - Document non-suppression of aldosterone during sodium loading
   - Oral, IV options

3. Localization
   - CT or MRI of the adrenal glands
Primary Aldosteronism Treatment

• Unilateral laparoscopic adrenalectomy
  • Aldosterone producing adrenal adenoma
  • Primary adrenal hyperplasia

• Medical management
  • Idiopathic hyperaldosteronism
  • Familial hyperaldosteronism
  • Refuse surgery/poor candidate

• Spironolactone
  • Eplerenone
  • Amiloride and triamterene

• Therapeutic goals:
  • Normalization of BP
  • Resolution of hypokalemia
  • Normal aldosterone level
Post-Test Question #1

The primary cause of central adrenal insufficiency is:

- **Pituitary adenoma** (20%)
- **Sheehan’s syndrome** (20%)
- **Exogenous glucocorticoids** (20%)
- **Tuberculosis** (20%)
- **Metastatic cancer** (20%)
The primary cause of central adrenal insufficiency is:

- Pituitary adenoma: 20%
- Sheehan’s syndrome: 20%
- Exogenous glucocorticoids: 20%
- Tuberculosis: 20%
- Metastatic cancer: 20%
Post-Test Question #2

Which of the following medication regimens is least likely to cause resultant adrenal insufficiency?

| 20% | 1. Prednisone 10mg daily, given at 9am for one week |
| 20% | 2. Hydrocortisone 40mg daily, given at 9am for one week |
| 20% | 3. Prednisone 10mg daily, given at 9pm for one week |
| 20% | 4. Hydrocortisone 40mg daily, given at 9pm for one week |
| 20% | Dexamethasone 1.5mg daily for one week |
Which of the following medication regimens is least likely to cause resultant adrenal insufficiency?

- Prednisone 10mg daily, given at 9am for one week
- Hydrocortisone 40mg daily, given at 9am for one week
- Prednisone 10mg daily, given at 9pm for one week
- Hydrocortisone 40mg daily, given at 9pm for one week
- Dexamethasone 1.5mg daily for one week

20% for each option.
All functioning tumors and those larger than ___ in diameter should be considered for surgical removal.

- 2 cm
- 4 cm
- 6 cm
- 8 cm
- 10 cm
All functioning tumors and those larger than ___ in diameter should be considered for surgical re...
Post-Test Question #4

All the following may interfere with biochemical testing for pheochromocytoma except:

| 20% | 1. tricyclic antidepressants |
| 20% | 2. labetalol                  |
| 20% | 3. theophylline               |
| 20% | 4. caffeine                   |
| 20% | lisinopril                    |
All the following may interfere with biochemical testing for pheochromocytoma except:

- tricyclic antidepressants
- labetalol
- theophylline
- caffeine
- lisinopril
An aldosterone-to-renin ratio greater than 20 is highly suggestive of primary hyperaldosteronism.

1. True
2. False
An aldosterone-to-renin ratio greater than 20 is highly suggestive of primary hyperaldosteronism.

- True: 50%
- False: 50%
References

- MKSAP 15
- Up To Date Online
References

References

- Images/Tables:
- http://ts2.explicit.bing.net/th?id=H.4832152983569449&pid=1.7
Questions?

- Thank you!