Endocrine Excitement

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Objectives

At the end of this presentation the participant will be able to describe the hypothalamic-pituitary adrenal axis.

At the end of this presentation the participant will be able to discuss anesthetic considerations for 5 disorders related to the hypothalamic-pituitary adrenal axis.
Endocrine System Review

ROLE:

- Regulate cellular and organ functions with hormone messengers that affect target cell activity
- Closely regulated to maintain homeostasis
Endocrine System Review

Three basic components:
- Endocrine Glands
- Hormones
- Target Organ
Endocrine System Review

GLANDS

- Hypothalamus
- Pituitary
- Thyroid
- Pancreas
- Adrenal
- Thymus
- Reproductive: ovaries and testes
Hormones

Classified by their chemical structure

- Protein or Peptide Hormones (e.g. insulin, glucagon, ACTH)
- Steroid Hormones (e.g. testosterone)
- Amino acid derivatives (catecholamines)

Structure dictates hormone receptor location
Structure influences half-life of hormone
Endocrine System Review

- Control of hormone release
  - Neural Control
  - Hormonal Control
Endocrine System Review

- Nutrient or Ion Control
Abnormal Endocrine function

- Abnormal production of hormone
- Decreased receptor number or function
## Interpretation of Hormone Levels

<table>
<thead>
<tr>
<th>Pituitary Hormone Level</th>
<th>Target Hormone Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>High</td>
</tr>
<tr>
<td>High</td>
<td>Primary failure of target endocrine organ</td>
</tr>
<tr>
<td></td>
<td>Autonomous secretion of pituitary hormone or resistance to target hormone action</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal range</td>
</tr>
<tr>
<td>Low</td>
<td>Pituitary failure</td>
</tr>
<tr>
<td></td>
<td>Autonomous secretion by target endocrine organ</td>
</tr>
</tbody>
</table>
Endocrine System Review

- Hypothalamus
- New “Master” gland
Endocrine System Review
Endocrine System Review

Pituitary Gland

During embryonic development, forms from a fusion of endocrine and neural tissue
Endocrine System Review

Pituitary Gland

Adenohypophysis – anterior pituitary
- ACTH – adenocorticotropic hormone or corticotropin
- GH – growth hormone
- TSH – thyroid stimulating hormone
- FSH – follicle stimulating hormone
- LH – luteinizing hormone
- Prolactin
- MSH – melanocyte stimulating hormone

Neurohypophysis – posterior pituitary
- Oxytocin
- ADH – anti-diuretic hormone
Feedback Loops
Hypothalamic-Pituitary Axis

**Hypothalamus**
- GnRH
- GHRH
- SS
- TRH
- DA
- CRH

**Anterior Pituitary**
- FSH and LH
- Growth Hormone
- Liver and Other cells
- Thyroid
  - Secretes thyroxine, triiodothyronine
- TSH
- Prolactin
- ACTH

**Gonads**
- Germ Cell Development
  - Female: Estradiol
  - Male: Testosterone, Progesterone

**Gonads**
- Female: Ovum, Sperm
- Male: Sperm, Progesterone

**Many organs and tissues**
- Protein synthesis, carb. and lipid metabolism

**Breasts**
- Breast development and milk production.
  - In males may facilitate reproductive function

**Adrenal cortex**
- Secretes cortisol
Thyroid Gland

Located in the neck, anterior to and straddling the trachea, just below the larynx

Produces hormones

- Thyroxine (T4)
- Triiodothyronine (T3)
- Calcitonin
Thyroid Gland

Actions of thyroid hormones

- Metabolic actions
  - Increases metabolic rate
  - Heat production

- Permissive actions
  - Catecholamines

- Growth and development
  - Production of growth hormone
  - Nerve/muscle reflexes
  - Normal cognition
  - Fetal life – CNS development
Hypothalamus-Pituitary-Thyroid Axis
Adrenal Glands

- Located at the superior pole of each kidney
- Contains 2 endocrine organs
  - Adrenal medulla --- “fight or flight”
    - Secretes Catecholamines
      - Epinephrine
      - Norepinephrine
      - Dopamine
  - Adrenal Cortex
    - Secretes Steroid Hormones
      - Cortisol
      - Corticosterone
      - Aldosterone
      - Androgens
Adrenal Medulla

Effects of Epinephrine and Norepinephrine

Metabolic effects
- Increase alertness
  - Epinephrine - anxiety and fear
- Increase secretion of insulin and glucagon

Myocardial effects
- Norepinephrine – vasoconstriction
- Epinephrine – total PVR drops
Adrenal Cortex

- Zona glomerulosa
- Zona fasciculata
- Zona reticularis
Aldosterone

- Sodium retention
- Potassium secretion
- Maintains intravascular volume
- Renin-angiotensin-aldosterone system
Glucocorticoids

Physiologic effects

- Increased protein catabolism
- Increased hepatic glycogenesis and gluconeogenesis
- Anti-inflammatory actions
- Anti-immune functions

In fetal and neonatal life:

- Proper differentiation of tissues and glands
- Surfactant production
Glucocorticoids

Physiologic effects

Permissive actions

- For glucagon and catecholamines to exert their calorogenic effects
- For catecholamines to exert their lipolytic effects
- For catecholamines to produce pressor responses and bronchodilation
Glucocorticoid

- Resistance to Stress
Hypothalamic-Pituitary-Adrenal Axis
First case of the day:

- 4 year old boy
- 109 cm, 18.6 kg
- 6 month history of diaphoresis and reddening of skin as day goes on
- Tachypnea and tachycardia
- Referred to your facility
- Any guesses???
Pheochromocytoma

Catecholamine-secreting tumors
Arise from chromaffin cells of the sympathoadrenal system
80% located in adrenal medulla
Potentially lethal
  - Malignant hypertension
  - Cerebrovascular accidents
  - Myocardial infarctions
One of the few curable causes of hypertension
Most secrete norepinephrine alone or more commonly combined with smaller amount of epinephrine – ratio of 85/15
Pheochromocytoma

Signs and Symptoms

- Triad
  - Hypertension
  - Headache
  - Sweating
- Pallor
- Palpitations
- Orthostatic hypotension
- Catecholamine-induced cardiomyopathy may occur

Diagnosis

- Urine testing
Pheochromocytoma
Anesthetic Considerations – Preoperative

- $\alpha$ – adrenergic blockade
  - Phenyoxybenzamine
    - Allows re-expansion of intravascular volume
- Delay $\beta$-blockade until $\alpha$-blockade effective
  - Unopposed $\alpha$ stimulation
    - Dangerous vasoconstriction, hypertension
  - $\beta$-blockade useful to treat dysrhythmias or tachycardia
- Correct hypovolemia
Pheochromocytoma
Anesthetic Considerations

Monitoring
- Standard monitors
- Arterial line
- CVP or PAC
- Urinary catheter

Fluids
- Large positive fluid balance is usually required to keep intravascular volumes within a normal range
Pheochromocytoma
Anesthetic Considerations – Intraoperative

Optimal preparation essential

Goals

- Avoid drugs or maneuvers that provoke catecholamine release or potentiate catecholamine actions
- Maintain cardiovascular stability
Pheochromocytoma

Anesthetic Considerations

Avoid

- Drugs that cause histamine release
- Sympathomimetic or vagolytic drugs
- Succinylcholine (fasciculations stimulate tumor, may stimulate autonomic ganglia)
- Agents that cause an indirect increase in catecholamine levels
- Anything that stimulates catecholamine release: fear, stress, pain, shivering, hypoxia, and hypercarbia
Pheochromocytoma
Anesthetic Considerations – Intraoperative Periods of Greatest Danger

**Hypertension/Arrhythmias**
- Induction
- Intubation
- Surgical incision
- Tumor manipulation/abdominal exploration

**Hypotension**
- Ligation of tumor’s venous drainage
Pheochromocytoma
Anesthetic Considerations – Intraoperative

- Hypertension
  - Sodium Nitroprusside
  - Phentolamine
  - Nicardipine
- Arrhythmia
  - Esmolol
  - Lidocaine
Pheochromocytoma
Anesthetic Considerations – Intraoperative

- Hypotension
  - Volume expansion
  - Phenylephrine
  - Decrease anesthetic depth

- Hypoglycemia
  - Occurs in 10-15% of patients
  - May need glucose infusion
Next up:

- 18 year old male
- Skateboarding injury
  - Complex left closed femur fracture
- Urgent, not emergent repair
- Nervous, agitated, restless
- VS: 160/90, HR 130, Temp 37.6°C
- Past Medical History
  - Polysubstance Abuse
    - ETOH
    - THC
    - Tobacco
<table>
<thead>
<tr>
<th>Endocrine</th>
<th>Range</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH, Sensitive</td>
<td>0.3-5.0 mlU/L</td>
<td>0.01</td>
</tr>
<tr>
<td>Thyroxine, Total</td>
<td>5.0-12.5 ug/dL</td>
<td>25.3</td>
</tr>
<tr>
<td>Thyroxine, Free</td>
<td>0.8-1.8 ng/dL</td>
<td>10.3</td>
</tr>
<tr>
<td>Triiodothyronine</td>
<td>80-190 ng/dL</td>
<td>627</td>
</tr>
<tr>
<td>Free T3</td>
<td>2.0-3.5 pg/mL</td>
<td>27.5</td>
</tr>
</tbody>
</table>
Thyroid Storm

- Exaggeration of hyperthyroidism symptoms
- Unrecognized and untreated is fatal
- Adult mortality - 10-20%
- Abrupt onset of signs of hyperthyroidism from sudden release of T4 and T3
Thyroid Storm – Signs/Symptoms

- Tachycardia
- Hyperthermia
- Agitation
- Skeletal muscle weakness
- CHF
- Shock
- Abdominal Pain
- Goiter
- Hepatic Failure
- Anxiety
- Delirium
- Psychosis
- Stupor
- Coma
- Nausea
- Vomiting
- Diarrhea
### Diagnostic criteria for thyroid storm

<table>
<thead>
<tr>
<th>Thermoregulatory dysfunction</th>
<th>Cardiovascular dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Temperature (°F</td>
<td>°C)**</td>
</tr>
<tr>
<td>99 to 99.9</td>
<td>99 to 109</td>
</tr>
<tr>
<td>100 to 100.9</td>
<td>110 to 119</td>
</tr>
<tr>
<td>101 to 101.9</td>
<td>120 to 129</td>
</tr>
<tr>
<td>102 to 102.9</td>
<td>130 to 139</td>
</tr>
<tr>
<td>103 to 103.9</td>
<td>≥140</td>
</tr>
<tr>
<td>≥104.0</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>&gt;40.0</td>
<td>Heart failure</td>
</tr>
<tr>
<td></td>
<td>Mild edema</td>
</tr>
<tr>
<td></td>
<td>Pedal edema</td>
</tr>
<tr>
<td></td>
<td>Bibasilar rales</td>
</tr>
<tr>
<td></td>
<td>Pulmonary edema</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>Precipitant history</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Central nervous system effects</td>
<td></td>
</tr>
<tr>
<td><strong>Mild</strong></td>
<td></td>
</tr>
<tr>
<td>Agitation</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td></td>
</tr>
<tr>
<td>Delirium</td>
<td></td>
</tr>
<tr>
<td>Psychosis</td>
<td></td>
</tr>
<tr>
<td>Extreme lethargy</td>
<td></td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td></td>
</tr>
<tr>
<td>Seizure</td>
<td></td>
</tr>
<tr>
<td>Coma</td>
<td>30</td>
</tr>
<tr>
<td>Gastrointestinal-hepatic dysfunction</td>
<td></td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td></td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td></td>
</tr>
<tr>
<td>Unexplained jaundice</td>
<td></td>
</tr>
</tbody>
</table>

* A score of 45 or more is highly suggestive of thyroid storm; a score of 25 to 44 supports the diagnosis; and a score below 25 makes thyroid storm unlikely.
Thyrotoxic Crisis

Treatment

- β-blocker
- Thionamide (propylthiouracil or methimazole)
- Iodine solution (SSKI or Lugol’s solution)
- Iodinated radiocontrast agent (not available in US)
- Glucocorticoids
- Infusion of cooled crystalloid solutions
- Tylenol
- Avoid Aspirin
  - Displaces thyroid hormones from thyroglobulin and could aggravate the disease
- ICU care
Later in the day:

- 19 year old male
- 3 week history of:
  - Fatigue
  - Muscle weakness
  - Dizziness
- Fainted this am when went out to exercise
  - Fell down stairs – fractured humerus, requires ORIF
- BP 95/60, P 110
- Skin: cool, dry, tanned
- Labs: Hct 36%, glucose 62 mg/dL, Na 120 mmol/L, K 6.7 mmol/L, Cr 1.4 mg/dL, BUN 36 mg/dL
Addison’s Disease
Primary Adrenal Insufficiency

Destruction of the adrenal cortex, manifested by absence of cortisol and aldosterone

Signs and Symptoms
- Hyperpigmentation over palmar surfaces and pressure points
- Psychiatric symptoms
- Arthralgias
- Myalgias
Addison’s Disease
Primary Adrenal Insufficiency

Signs and Symptoms

**Aldosterone Deficiency**
- Hyponatremia
- Hypovolema
- Hypotension
- Hypokalemia
- Metabolic Acidosis

**Cortisol Deficiency**
- Weakness
- Fatigue
- Hypoglycemia
- Hypotension
- Weight loss
Addison’s Disease

- Physiology
Addison’s Disease

- Preoperative tests: CBC, electrolytes, and glucose level
- Provide corticosteroid supplementation for those patients that have been treated with corticosteroids for more than 1 month within the 6-12 months prior to surgery
- Cortisol 25 mg IV at induction, then 25 mg every 4 hours
- Daily maintenance dose should be given the day of surgery
Secondary Adrenal Insufficiency

- ACTH dependent
- Loss of glucocorticoid function
- Intact mineralocorticoid function
- Uncommon
Caused by hypothalamic/pituitary depression or absence
Most common form
Glucocorticoid deficiency
Commonly caused by use of synthetic glucocorticoids
Lack cutaneous hyperpigmentation
Mild electrolyte abnormalities
ACTH suppression from steroid treatment leads to adrenal atrophy
Adrenal Insufficiency
Activation of HPA Axis

Surgery

Activation depends on:

- Magnitude and duration of surgery
- Type and depth of anesthesia
Endogenous Glucocorticoids

Daily secretion estimated at 5 - 10 mg/m$^2$
- 5 to 7 mg/day of oral prednisone
- 20 to 30 mg/day of hydrocortisone

Cortisol synthesis can increase under conditions of stress to 100 mg/m$^2$/day.
# Adrenal Supplementation Therapy

<table>
<thead>
<tr>
<th>Surgical Stress</th>
<th>Corticosteroid Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minor</strong></td>
<td>25 mg of hydrocortisone or 5 mg of methylprednisolone IV day of procedure only</td>
</tr>
<tr>
<td>Inguinal Hernia Repair</td>
<td>Colonoscopy</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>50-75 mg of hydrocortisone or 10-15 mg of methylprednisolone IV day of procedure. Taper quickly over 1-2 days to usual dose.</td>
</tr>
<tr>
<td>Open cholecystectomy</td>
<td>Hemicolecctomy</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td>100-150 mg hydrocortisone or 25-30 mg of methylprednisolone IV day of procedure. Rapid taper to usual dose over next 1-2 days</td>
</tr>
<tr>
<td>Major cardiothoracic surgery</td>
<td>Whipple procedure</td>
</tr>
<tr>
<td>Liver resection</td>
<td></td>
</tr>
</tbody>
</table>

## Relative Potencies of Steroid Formulations

**TABLE 30-2.**

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>PHYSIOLOGIC REPLACEMENT DOSE (MG)</th>
<th>GLUCOCORTICOID ACTIVITY, † RELATIVE TO HYDROCORTISONE</th>
<th>MINERALOCORTICOID ACTIVITY, RELATIVE TO HYDROCORTISONE</th>
<th>DURATION OF ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone*</td>
<td>15-25</td>
<td>1</td>
<td>1.0</td>
<td>Short</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4</td>
<td>4</td>
<td>0.5</td>
<td>Short</td>
</tr>
<tr>
<td>Prednisone</td>
<td>5</td>
<td>4</td>
<td>0.75</td>
<td>Longer</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>4</td>
<td>0.75</td>
<td>Longer</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.25-0.50</td>
<td>30-50</td>
<td>0.0</td>
<td>Long</td>
</tr>
</tbody>
</table>

* Hydrocortisone is the synthetic form of cortisol.

† Suppression of hypothalamo-pituitary-adrenal axis.
Recovery after long term glucocorticoids
Adrenal Crisis

- High fever
- Apathy
- Confusion
- Anorexia
- Nausea
- Vomiting

- Hyponatremia
- Hyperkalemia
- Lymphocytosis
- Eosinophilia
- Hypoglycemia

Untreated – coma, severe hypotension, or shock unresponsive to vasopressors may rapidly lead to death

Under anesthesia: catecholamine-resistant hypotension
Adrenal Crisis

Management

- Treat aggressively
- Dexamethasone 4 mg IV
- Empiric treatment with IV hydrocortisone
- IV hydration
- Glucose
Adrenal Insufficiency
Anesthetic Considerations

- Glucocorticoid replacement
- Avoid Etomidate
- Untreated AI and Emergency Surgery
  - Invasive monitoring (arterial line, CVC or PAC)
  - IV corticosteroids
  - Fluid and electrolyte resuscitation
  - Minimal doses of anesthetic agents and drugs
Next up:

- 26 y.o. female
- 170 cm
- 110 kg
- Thin limbs, truncal obesity
- Buffalo hump
Cushing’s Syndrome

Problem = too much cortisol

Two types
- Corticotropin-dependent Cushing’s syndrome
  - Pituitary adenomas
- Corticotropin-independent Cushing’s syndrome
  - Adrenocortical tumors

Signs and Symptoms
- Sudden weight gain
- Moon face
- HTN
- Glucose intolerance
- Muscle weakness
Cushing’s Syndrome
Cushing’s Syndrome

Anesthetic Considerations

- Preoperative
  - Evaluate BP, electrolytes, blood glucose
- Positioning: consider osteoporosis
- Choice of drugs or anesthetic technique is not influenced
- Skeletal muscle weakness
  - Mechanical ventilation
  - Hypokalemia – influence response to NDMRs
- Continuous cortisol infusions may be initiated intraoperatively
The End!