Steroid Therapy and Stress Dose Steroids

Dan Roke, MD

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Stress Dose Steroids

- Hydrocortisone
- 100 mg
- IV

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Questions?

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Steroid Therapy and Stress Dose Steroids

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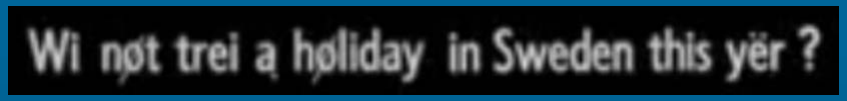

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Disclosures

- No financial disclosures
- There will be graphic elements from a British documentary on the legend of King Arthur

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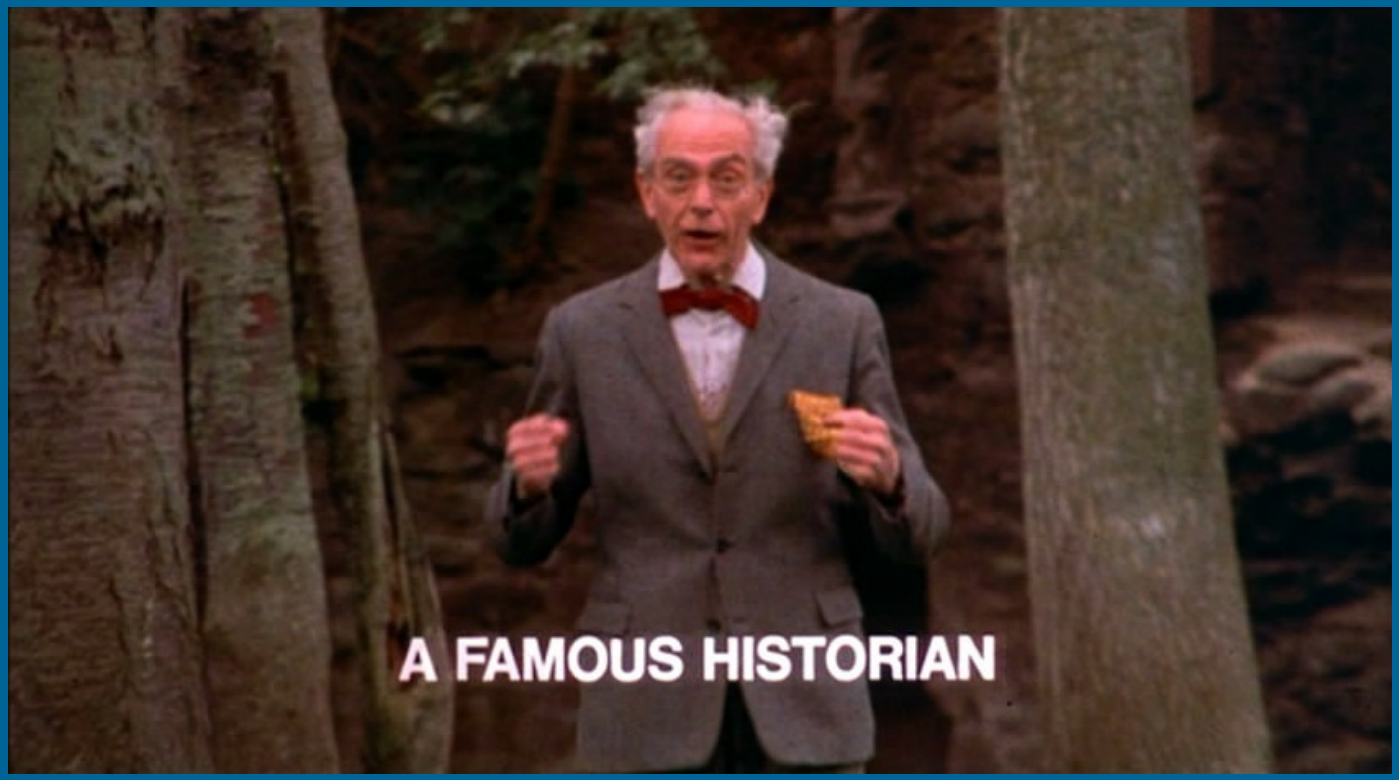
It must be a good documentary – this guy is in it



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What are we going to discuss?

- Steroid overview
- Perioperative Adrenal Insufficiency
- Cortisol
- Perioperative Stress Response
- Steroid Side Effects
- Recommendations

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Steroids

- Adrenal cortex synthesizes two classes of steroids:
  - –Corticosteroids
  - –Androgens

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Corticosteroids

- Corticosteroids divided into:
  - Glucocorticoids
  - Mineralocorticoids

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Corticosteroids

- Glucocorticoid vs Mineralocorticoid based on:
  - Carbohydrate metabolism
  - Sodium retention
  - Inflammation

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Corticosteroid Division

Some do all three

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Glucocorticoids

- Glucocorticoid effects:
  - Carbohydrate metabolism – INCREASE
  - Inflammation - DECREASE

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Mineralocorticoids

- Mineralocorticoid effect:
  - Sodium retention - INCREASE

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Adrenal Gland Physiology

- Adrenal glands are made up of:
  - Cortex
    - Glucocorticoids, mineralocorticoids, androgens
  - Medulla
    - Epinephrine, norepinephrine
- Adrenal glands are part of Hypothalamic-Pituitary-Adrenal Axis
  - HPA axis is critical to the stress response

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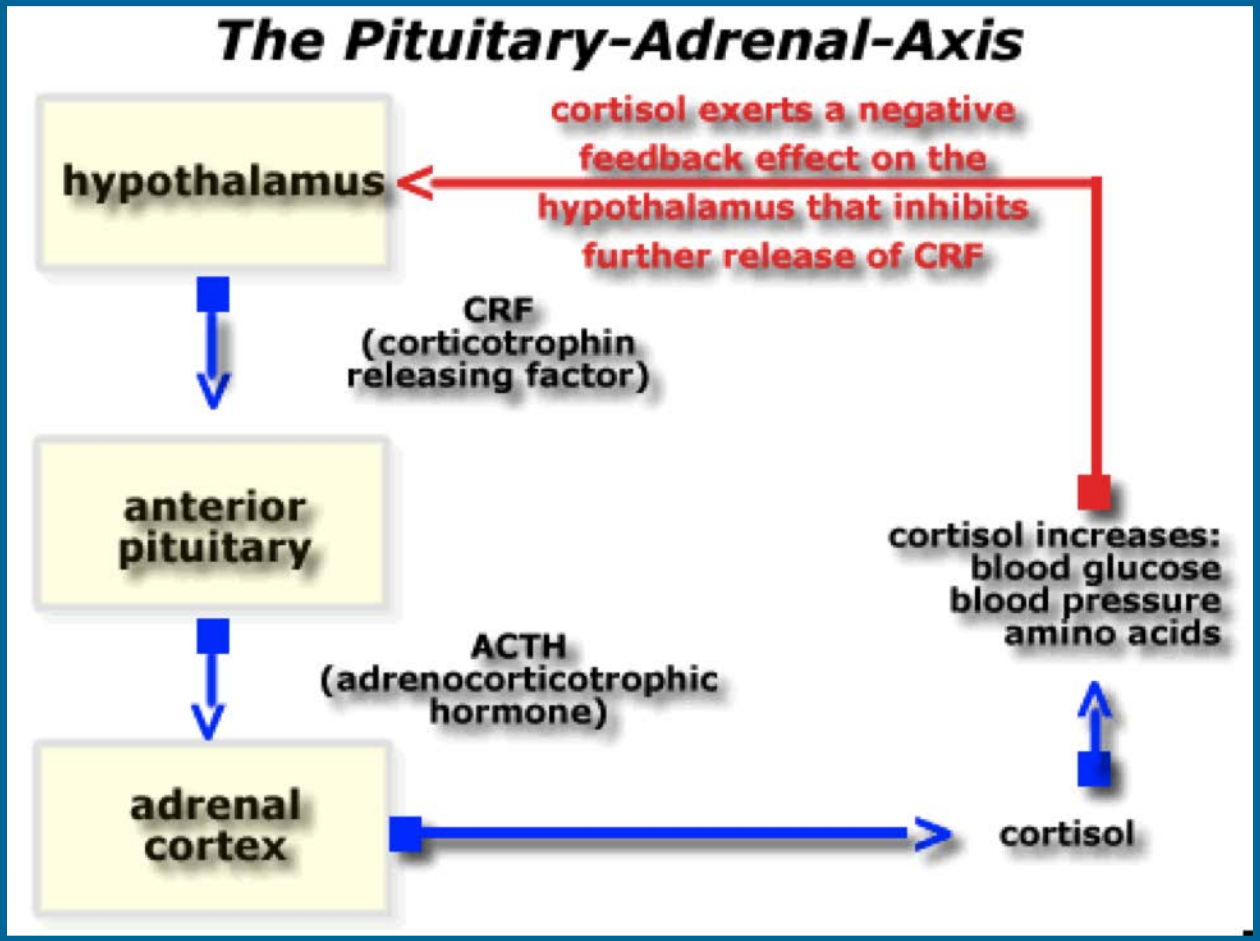
Adrenal Gland Physiology



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Perioperative Adrenal Insufficiency

- 1949 – Cortisone developed – Adrenal insufficiency can be treated

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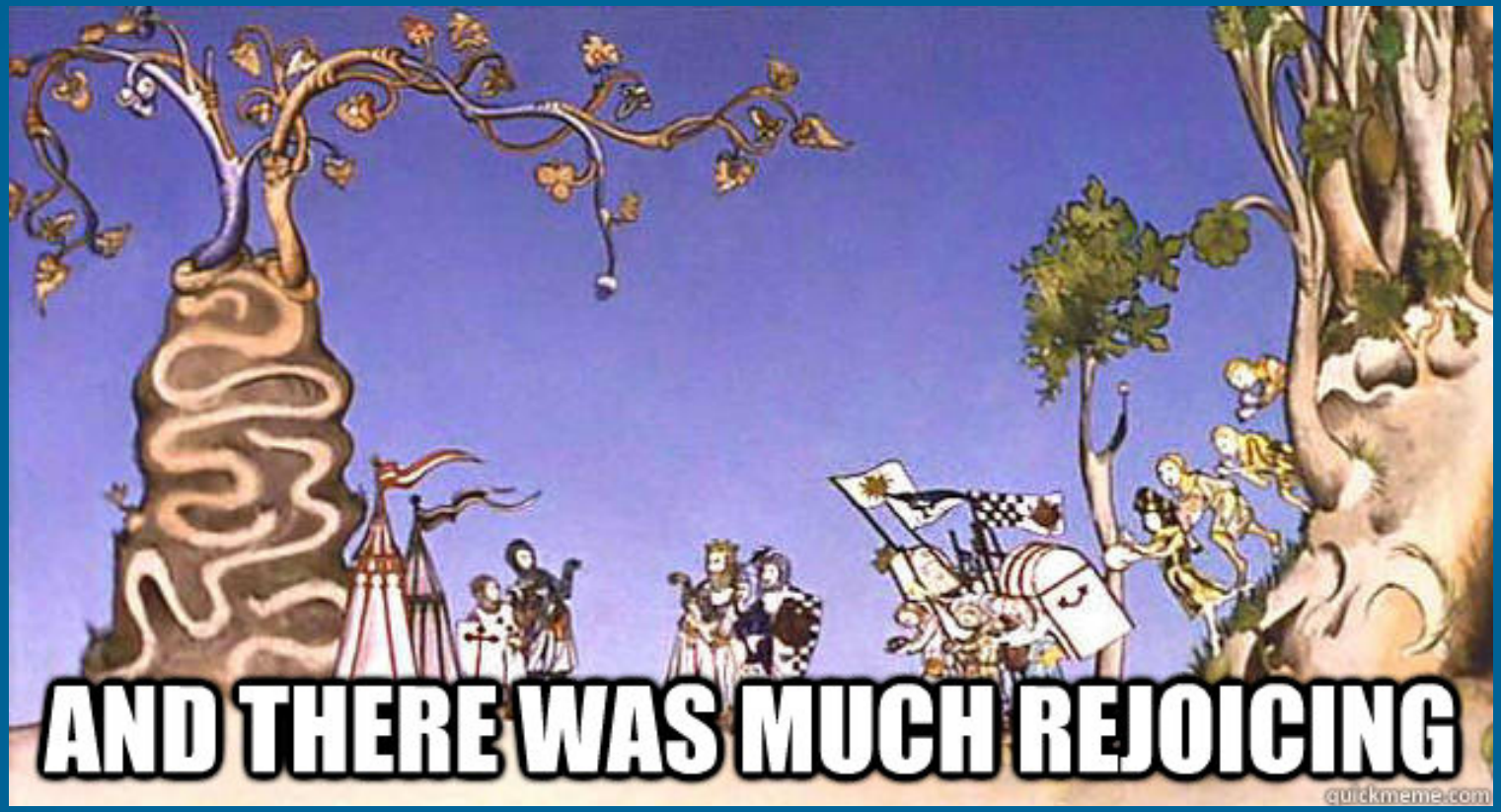
Perioperative Adrenal Insufficiency



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Perioperative Adrenal Insufficiency

- 1952 – 34 year old man being treated with cortisone for rheumatoid arthritis is anesthetized for a hip arthroplasty
  - Hemodynamic collapse immediately following the operation
  - Autopsy revealed bilateral adrenal atrophy

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Perioperative Adrenal Insufficiency

- 1953 – 20 year old woman treated with cortisone is anesthetized for knee surgery
  - Hemodynamic collapse and death 5 hours postoperatively
  - Autopsy revealed adrenal atrophy

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Perioperative Adrenal Insufficiency

- SUPRAPHYSIOLOGIC STEROID ADMINISTRATION RECOMMENDED PREOPERATIVELY
  - Up to 4 times the baseline dose
  - Baseline dose: 25 mg BID
  - **Thus Hydrocortisone 100 mg**

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Perioperative Adrenal Insufficiency

- True incidence of perioperative adrenal insufficiency is unknown
  - Many studies identify adrenal insufficiency via signs and symptoms
    - Hypotension, Tachycardia, Fever, Lethargy, Arthralgias, Myalgias, Nausea, Emesis, Mental status changes
  - Few studies identify adrenal insufficiency via laboratory results

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Cortisol

- A glucocorticoid
- Actions
  - Gluconeogenesis
  - Protein breakdown
  - Release of fatty acids
  - Anti-inflammatory
  - Has some mineralocorticoid effect
- Hydrocortisone is synthetic cortisol

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But what about Dexamethasone?

- Also a glucocorticoid
- Much longer duration of action so doesn't mimic the surge seen in the stress response
- No mineralocorticoid effect

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Normal Cortisol Secretion

- Studies have cited cortisol secretory rates in children of:
  - 12 mg/m^2/day
  - 6 mg/m^2/day
- So, using the highly scientific method of averaging these we arrive at:
  - 9 mg/m^2/day

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And after some really complicated math requiring a great deal of mental acuity

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Assuming cortisol secretion of 9 mg/m^2/day

- Unstressed cortisol secretion per day (approximate) for the average male:
  - Birth: 3.6 kg, 50 cm, 0.22 m^2 = **2 mg**
  - 6 month old: 7.8 kg, 67 cm, 0.38 m^2 = **3.5 mg**
  - 1 year old: 10.4 kg, 76 cm, 0.46 m^2 = **4 mg**
  - 2 year old: 13 kg, 87 cm, 0.56 m^2 = **5 mg**
  - 5 year old: 18 kg, 109 cm, 0.74 m^2 = **7 mg**
  - 10 year old: 32 kg, 139 cm, 1.1 m^2 = **10 mg**

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Perioperative Stress Response

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Perioperative Stress Response

- HPA axis stimulated via:
  - Direct afferent signaling
  - Cytokine release from tissue at surgical site
  - Baroreceptor signaling as a result of hypovolemia
  - Psychological stress

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So, What's A Typical Stress Response?

- Taylor et al. 2013
  - 30 healthy patients, 5 months to 6 years of age
  - Elective urologic procedures
  - Blood sampled at 5 time points
    - IV placement, intubation, 50% of surgery completed, anesthesia reversal, 1 hour postoperatively
  - No significant differences between cortisol levels at any of the time points
    - Peak cortisol noted 1 hour postoperatively

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So, What's A Typical Stress Response?

- Hsu et al. 2012
  - 110 patients between 1 month to 17 years of age
  - Routine sedated procedures
  - Salivary cortisol measured at baseline, every 30 minutes during procedure, at completion, and in recovery

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So, What's A Typical Stress Response?

- Hsu et al. 2012 continued
  - All patients had a 3 times elevation in cortisol
  - 25% of patients had a 4 times elevation in cortisol
  - No differences in cortisol based on type of sedation or procedure
  - **Highest cortisol levels in recovery**

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But If A Little Is Good…

- Steroids – They help you handle stress – like a little white rabbit…

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Then How Can More Be Bad?

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“That’s no ordinary rabbit. That’s the most foul, cruel, and bad tempered rodent you ever set eyes on.”

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Steroid Side Effects

- Acute, supraphysiologic dosing of steroids can cause:
  - Hyperglycemia
  - Hypertension
  - Fluid retention
  - Increased risk of infection

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Steroid Side Effects

- Chronic dosing of steroids can lead to HPA axis suppression

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Steroid Side Effects

- Chronic dosing of steroids can lead hypothalamic-pituitary-adrenal axis suppression
- Or does it?...

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Chronic Steroid Dosing And HPA Suppression

- Multiple studies showing no apparent suppression with chronic steroid usage
- Can it happen? Yes
- Does it ALWAYS happen? No

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Chronic Steroid Dosing And HPA Suppression

- Likelihood of suppression increases with:
  - Dose
  - Duration
  - Decreasing time between cessation and anesthetic
- Laboratory testing can be expensive, slow, and unreliable

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Recommendations

- Per Smith 8th edition (2011)
  - Brief and/or minimally invasive procedures
    - Hydrocortisone 50 mg/m^2 (5.5 times normal daily production)
    - As a single dose
  - Prolonged and/or significantly invasive procedures
    - Hydrocortisone 100 mg/m^2 (11 times normal daily production)
    - As continuous infusion or split into 4 doses per day
    - Taper may be needed

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Recommendations

- Per Cote 5th Edition (2013)
  - For fever, illness, or minor procedures
    - Replacement dosing of 3-5 times oral maintenance dose
  - For critical illness or major procedures
    - Replacement dosing of 5-10 times oral maintenance dose

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Recommendations

- Taking what we've covered:
  - Minor procedures – 4 times maintenance dose
  - Major procedures – 6 times maintenance dose with 1-2 day taper
- **Consider dosing after surgery and prior to recovery**
- But there's work to do before this issue is definitively settled

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- Chapman G, Cleese J, Idle E, Gilliam T, Jones T, Palin M. Monty Python and the Holy Grail. Python (Monty) Pictures Ltd. 1975
- And for further reading if you are really interested in swallow airspeed velocity: http://style.org/unladenswallow/

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Steroid Equivalents

- From Smith 8th ed (2011)

Generic Name	Trade Name	Glucocorticoid Effect (= 100 mg Cortisol)	Sodium Retention Effect (= 0.1 mg Fludrocortisone [Florinef])	Duration of Action
Hydrocortisone	Hydrocortisone Solu-Cortef	100	20	S
Cortisone	Cortone	125	20	S
Prednisolone	Delta-Cortef	20	50	I
Prednisone	Deltasone Meticorten	25	50	I
Methylprednisolone	Medrol Solu-Medrol	15	No effect	I
Triamcinolone	Aristacort Kenacort	10	No effect	I
Dexamethasone	Decadron Hexadrol	1.5	No effect	L
Betamethasone	Celestone	3	No effect or salt loss	L
Aldosterone	NCA	300	0.1-0.04	—
9-Fluorocortisol	Florinef	6.5	0.1	I
Desoxycorticosterone acetate	NCA	0	1 (IM)	I

S, Short (8-12 hr biological half-life); *I,* intermediate (12-36 hr biological half-life); *L,* long (36-72 hr biological half-life); *IM,* intramuscularly; *NCA,* not commercially available.

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