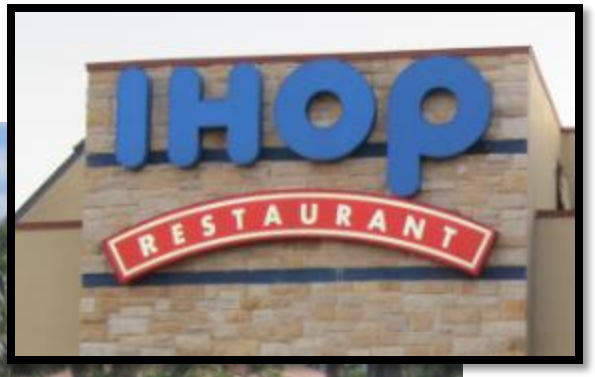
Adrenal Disorders for the USMLE, Step One:

Abnormalities of the Fasciculata: Hypocortisolism

Howard Sachs, MD
Patients Course, 2017
Associate Professor of Clinical Medicine
UMass Medical School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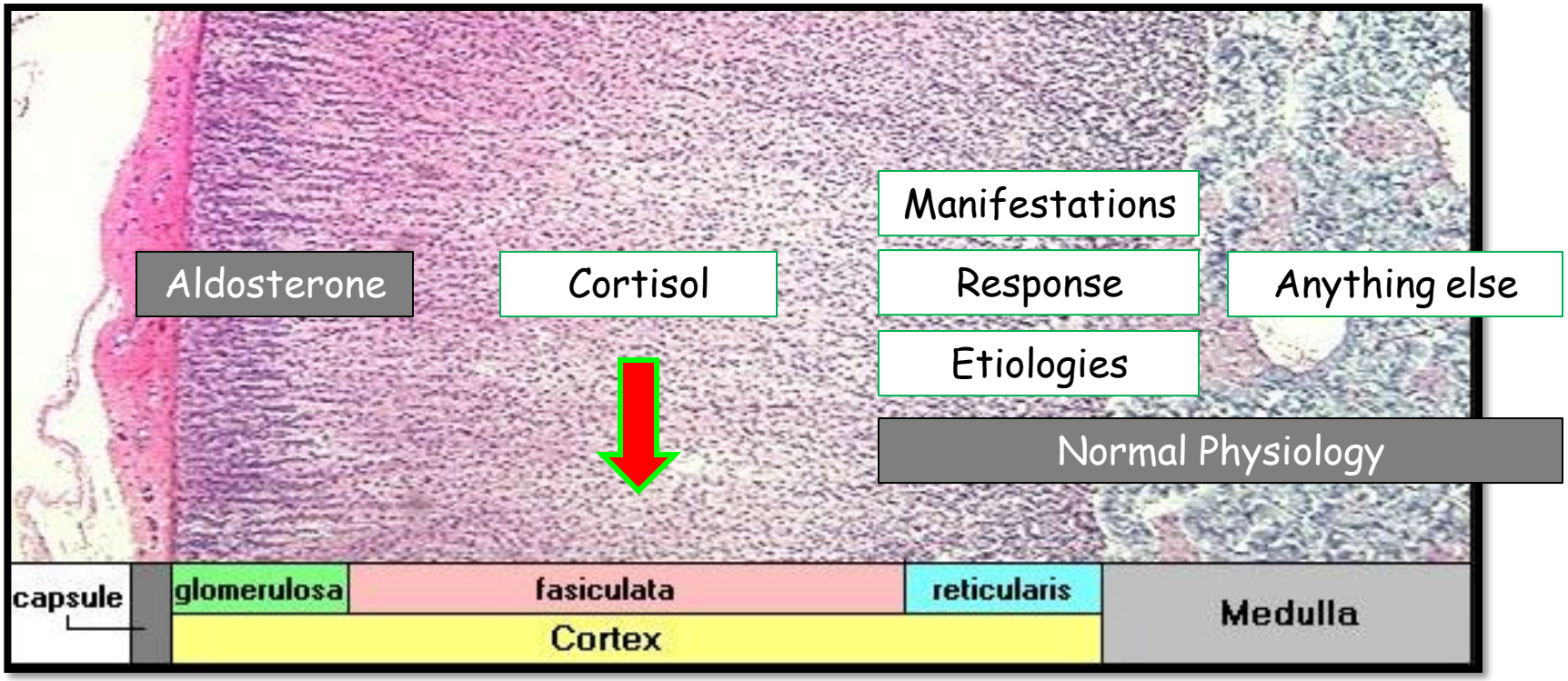
Aldosterone
Cortisol
Manifestations
Response
Etiologies
Anything else
Normal Physiology
capsule
glomerulosa
fasiculata
reticularis
Cortex
Medulla

Etiololgy of Hypocortisolism

Acute, Shock

- Pituitary
  - Apoplexy
- Adrenal
  - Hemorrhage
- HPA Failure
  - Acute cessation+

Chronic: HPA axis failure

- Hypothalamus
  - Infiltrative disorders
- Pituitary
  - Sheehan's
  - Adenoma/Mass effect
- Adrenal
  - Autoimmune
  - Infiltrative (bait-switch)
    - Tumor
    - Infection
  - CAH (enzyme deficiency)
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  - Cessation: exogenous CCS

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Adrenalitis
(Addison's Disease)

Infiltrative Disorders

Adrenal Hemorrhage
Sepsis

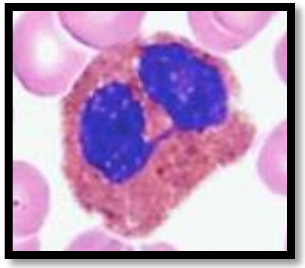
TB, Histo, Mets

Primary Adrenal Failure: High CRH and ACTH

Manifestions of Insidious Hypocortisolism (Hypoadrenalism)

- Cardiovascular
  - Hypotension (↓ α-1 tone)
- GI
  - Nausea, anorexia
- Endo
  - Weight loss,fatigue, weakness, hypoglycemia

- Heme
  - Eosinophilia
- Derm (if 1° adrenal failure)
  - Hyperpigmentation



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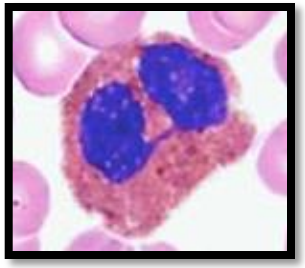

CRH → Proopiomelanocortin (POMC) → ACTH and MSH

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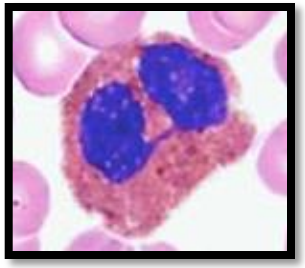


- Renal (if adrenal failure → hypoaldosteronism)
  - Type IV, RTA
  - Failure of aldosterone stimulation of H+-ATPase pump
    - Both contribute to metabolic acidosis, NAG
  - Hyponatremia (aldosterone failure, non-osmotic ADH release)
    - Salt cravings
  - Hyperkalemia (aldosterone failure)

↑↑ ACTH

21-hydroxylase deficiency

Cholesterol

desmolase

Pregnenolone

3βHSD

Progesterone

17α-hydroxylase

↑↑ 17-OH Progesterone

21-OH

Mini-Aldosterone

11-OH

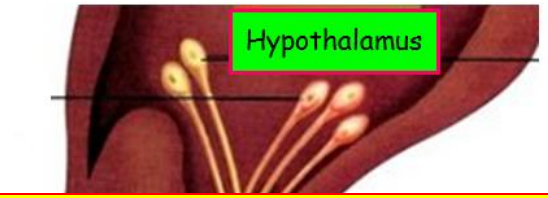
Aldosterone

Hypoaldosteronism
(Adrenal Insufficiency)

Hypotension
Hyponatremia (Low aldo/high ADH)
Hyperkalemia
NAG Metabolic Acidosis

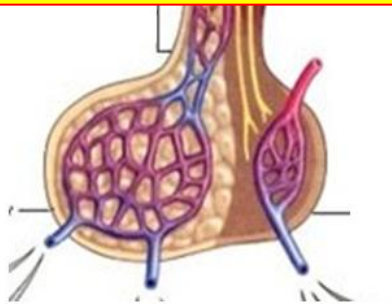
What is renin level? → elevated
(kidney is unaffected by adrenal enyzme deficiency)

CRH



If indolent central failure, only cortisol fails.
The Renin-Angiotensin-Aldosterone system is intact

ACTH



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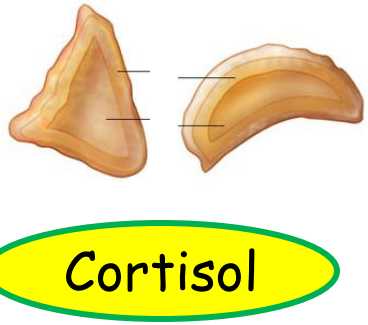
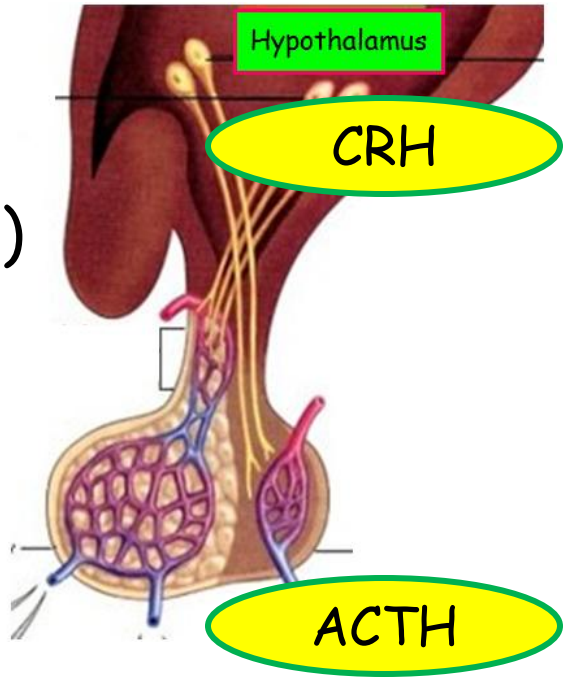
<u>Signs/symptoms of underlying diseases</u>:

- HA, diplopia
- Sepsis, Flank Pain
- Loss/gain of other hormones (FSH/LH, TSH, Prolactin)
- Lung cancer, HIV
- Autoimmune disorders (2)

Response to Hypocortisolism (Hypoadrenalism)

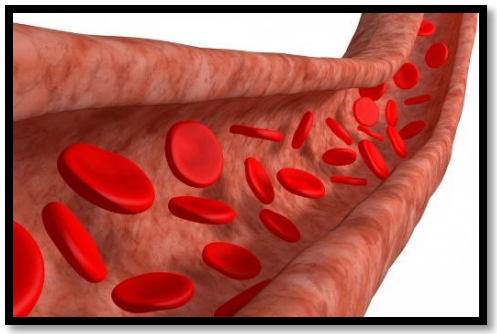
- Acute (adrenal hemorrhage, pituitary apoplexy)
  - Autopsy (too acute but one would predict ↑ CRH/↑ ACTH)
- Hypothalamic Failure, Exogenous Cessation
  - No CRH ∴ no ACTH or cortisol
- Pituitary Failure (any cause)
  - ↑ CRH, ↓ ACTH, cortisol
- Adrenal Failure (e.g. adrenalitis, CAH)
  - ↑ CRH, ACTH, ↓ cortisol





Hypocortisolism: Diagnostics

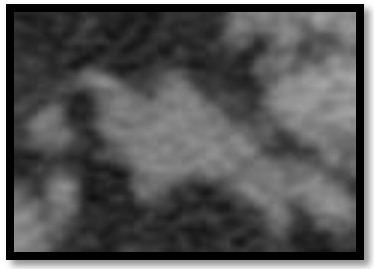
- Clinical Suspicion
  - Hypotension. Low Na, High K, Metabolic Acidosis (NAG), weight loss, [hyperpigmentation, eosinophilia]
- Labs
  - Random AM cortisol: decreased
  - ACTH stimulation test is gold standard
    - Obtain baseline cortisol level
    - Administer ACTH
    - Check cortisol 30, 60 mins later
    - Normal cortisol level should be >20 mcg/dL or double from baseline
  - ACTH level (should be elevated w/ adrenal failure)
    - If low cortisol and ACTH, central etiology suspected.



Normal adrenal

Cortisol ↑↑

Diseased Adrenal
(i.e. end organ failure



Cortisol
No response

ACTH Stimulation Test

Loose Ends: Hypocortisolism

- Exogenous Steroid Cessation
  - Physiologic stress (like going to OR and not getting med)
  - They will describe a patient with a steroid requiring disease such as SLE (they won't tell you the patient is on steroids)
  - They will query you on CRH, ACTH, Cortisol levels
    - May give a CRH stimulation test and ask you the result
  - No pigmentation the HPA axis is suppressed.

- Autoimmune Adrenalitis
  - Associated with other syndromes such as DM1, pernicious anemia, Hashimoto's…just be aware.
  - Atrophy of all 3 layers of the cortex
    - Hypothalamic and Pituitary causes, glomerulosa intact

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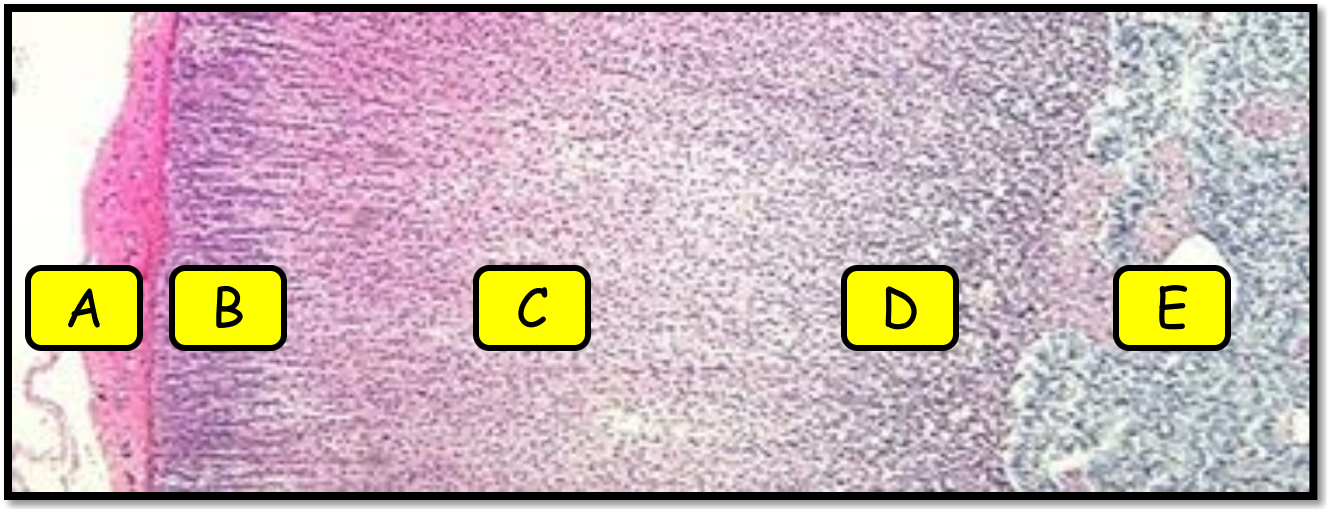
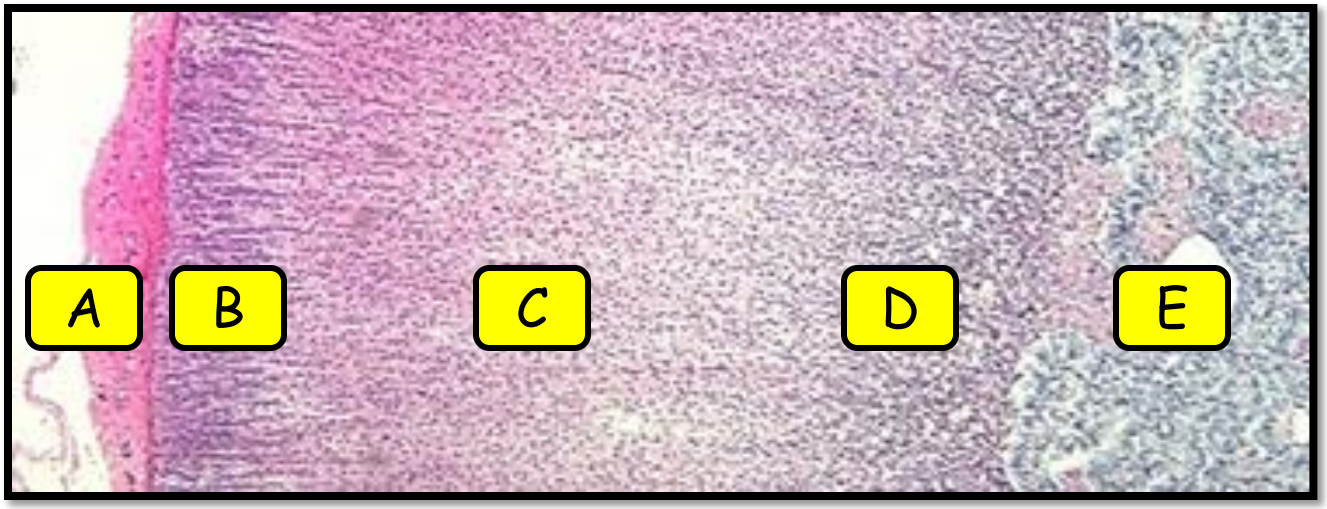
Sample questions for cortisol dysfunction



In the diagram above, choose the appropriate stimulus to hormone release at the region designated by letter E.



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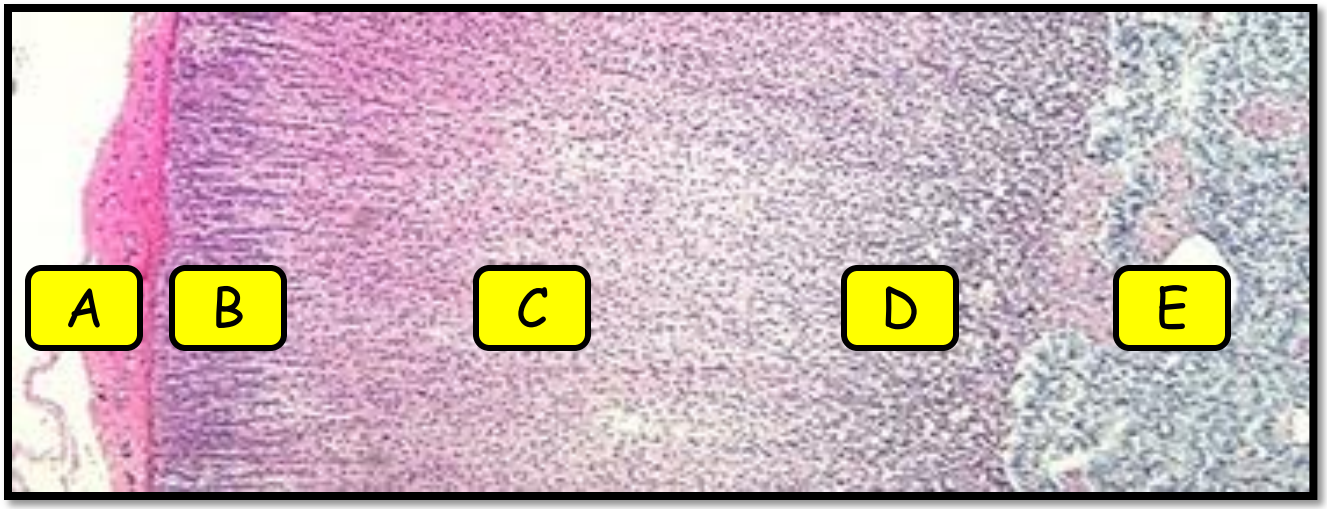
B- Glomerulosa
C – Fasciculata
D – Reticularis
E - Medulla

What type of cells are present in the adrenal medulla?



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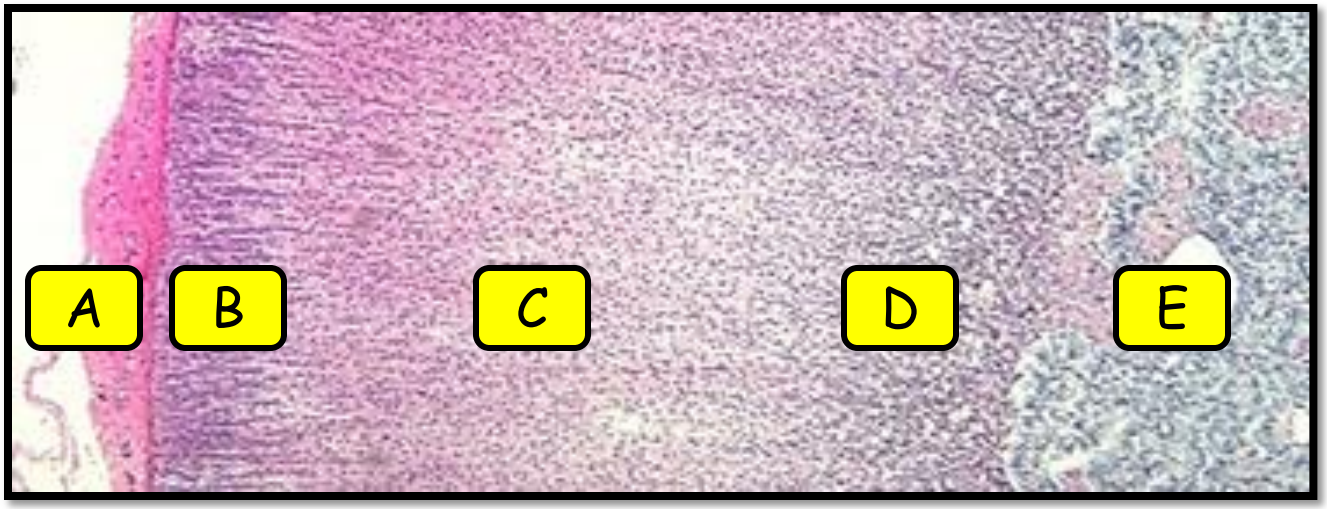
Postganglionic sympathetic neurons.
What stimulates hormonal release?



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A – Capsule
B- Glomerulosa – Renin → ATII → Aldosterone; Hyperkalemia
C – Fasciculata - ACTH
D – Reticularis - ACTH
E – Medulla: Answer - Ach

Patient has SLE using medicine to treat the condition.
Noted with truncal obesity, hirsutism, facial plethora.
She complains of proximal muscle weakness.
Labs reveal an elevated glucose. She dies suddenly.
How does the adrenal appear histologically?

A. Atrophy of three cortical layers
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They continue to push the point that
Aldosterone secretion and the Glomerulosa are ACTH independent

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Describe the levels of hormones at the time of her death.

	CRH	ACTH	Cortisol
A.	Inc	Inc	Dec
B.	Inc	Inc	Inc
C.	Inc	Dec	Dec
D.	Dec	Dec	Dec
E.	Dec	Inc	Inc
F.	Dec	Dec	Inc

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F.	Dec	Dec	Inc

60 yo with difficulty climbing stairs and dyspnea. Wt gain over several months. CXR lung mass. Labs with high cortisol and ACTH. Next diagnostic study?

A. Chest CT scan
B. MRI of Pituitary
C. Dexamethasone suppression test
D. Echocardiography
E. CPK level

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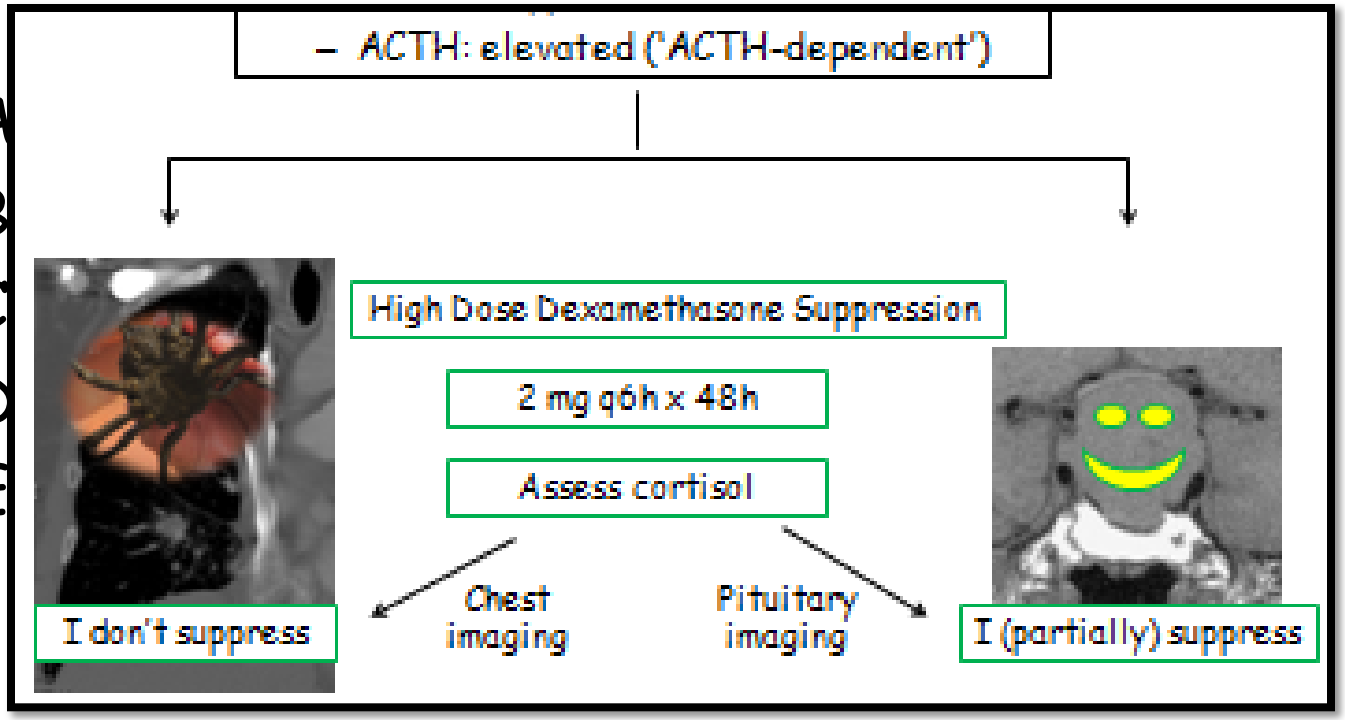

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