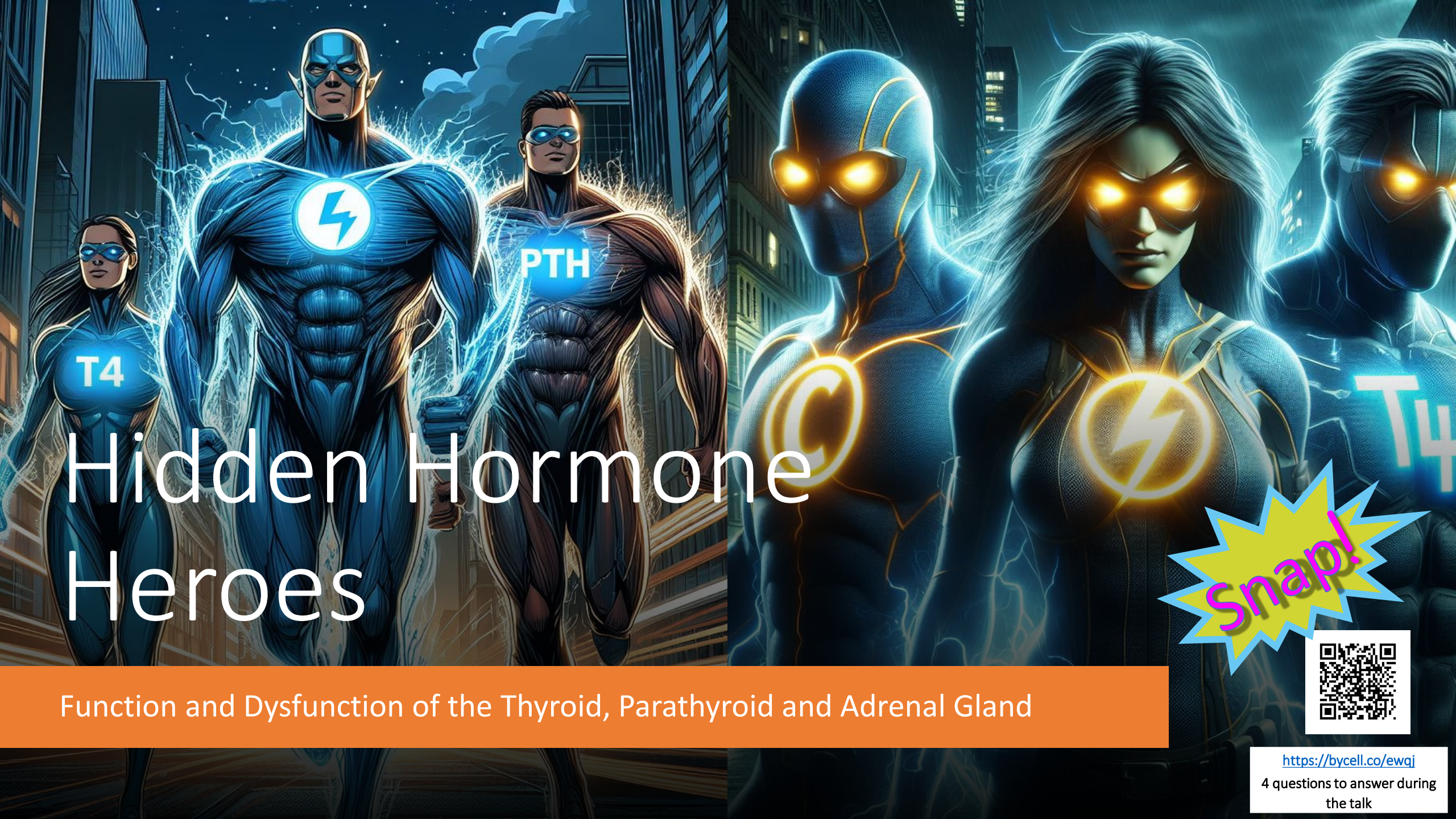


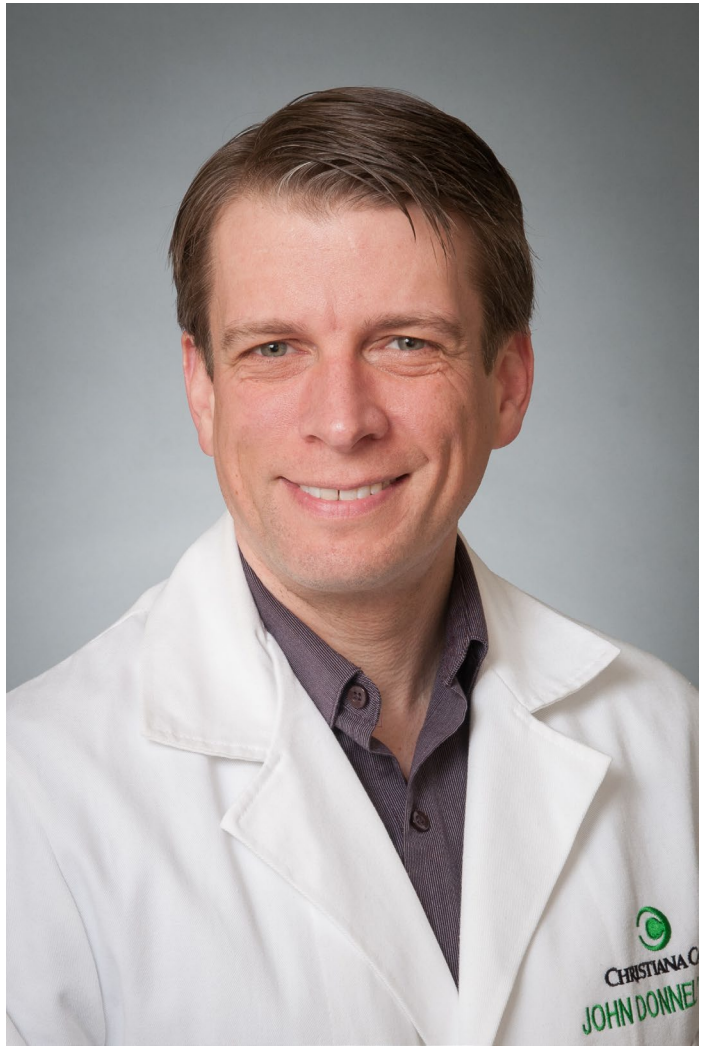
Hidden Hormone Heroes

Function and Dysfunction of the Thyroid, Parathyroid and Adrenal Gland

Snap!

https://bycell.co/ewqj

4 questions to answer during the talk



John Donnelly, MD
Clinical Professor
Sidney Kimmel Medical College at Thomas Jefferson University

Elizabeth Klingensmith, MD
Internal Medicine Resident
ChristianaCare

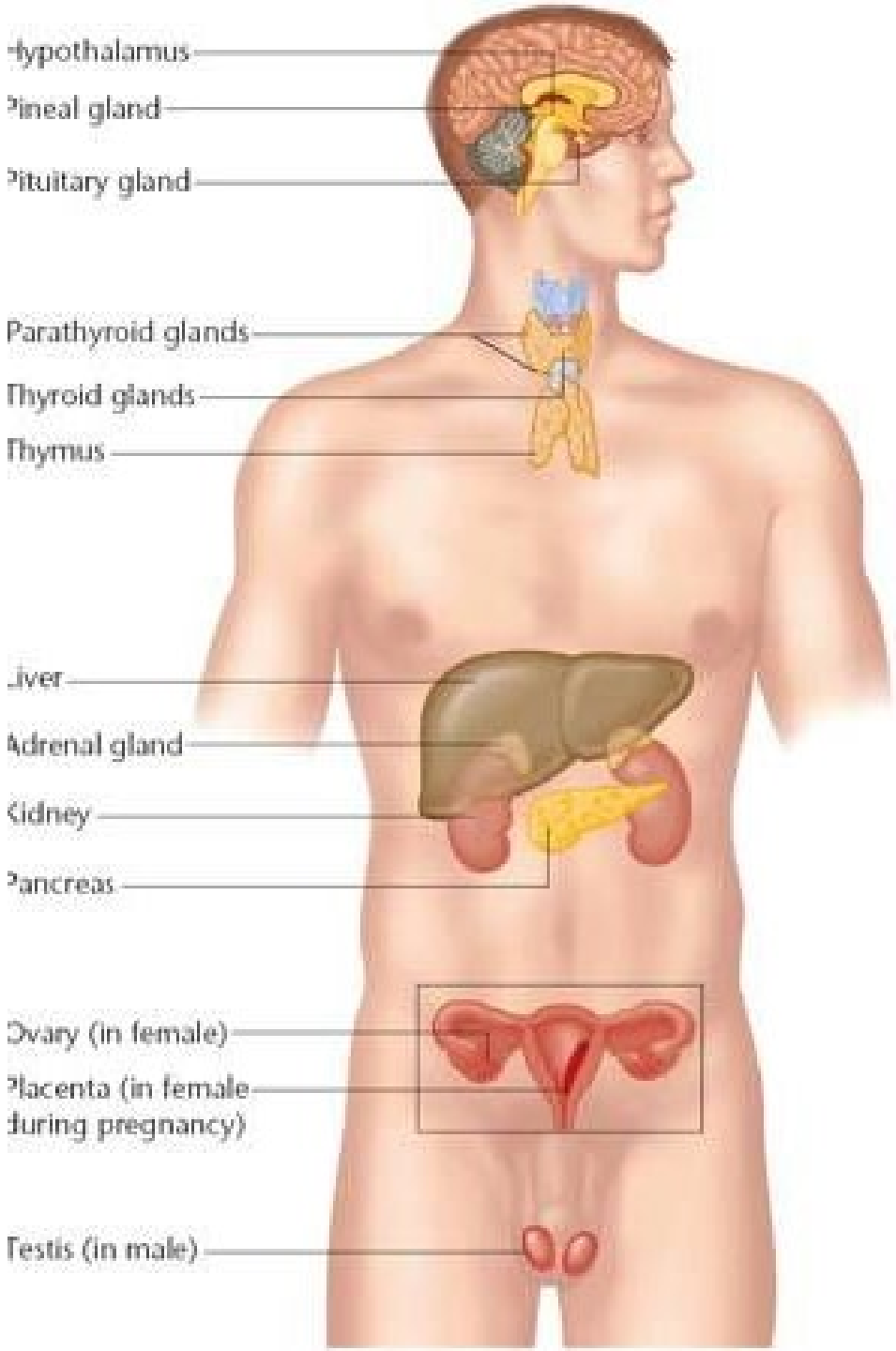
Learning Objectives

1. Learn how the endocrine system uses feedback systems to keep hormones in balance
2. Learn the hormones and the function of the thyroid, parathyroid, and adrenal gland
3. Learn how imbalance in the feedback system can cause disease and dysfunction
4. Learn some of the common ways medicine can treat endocrine diseases by resetting the balance

Quiz Questions:

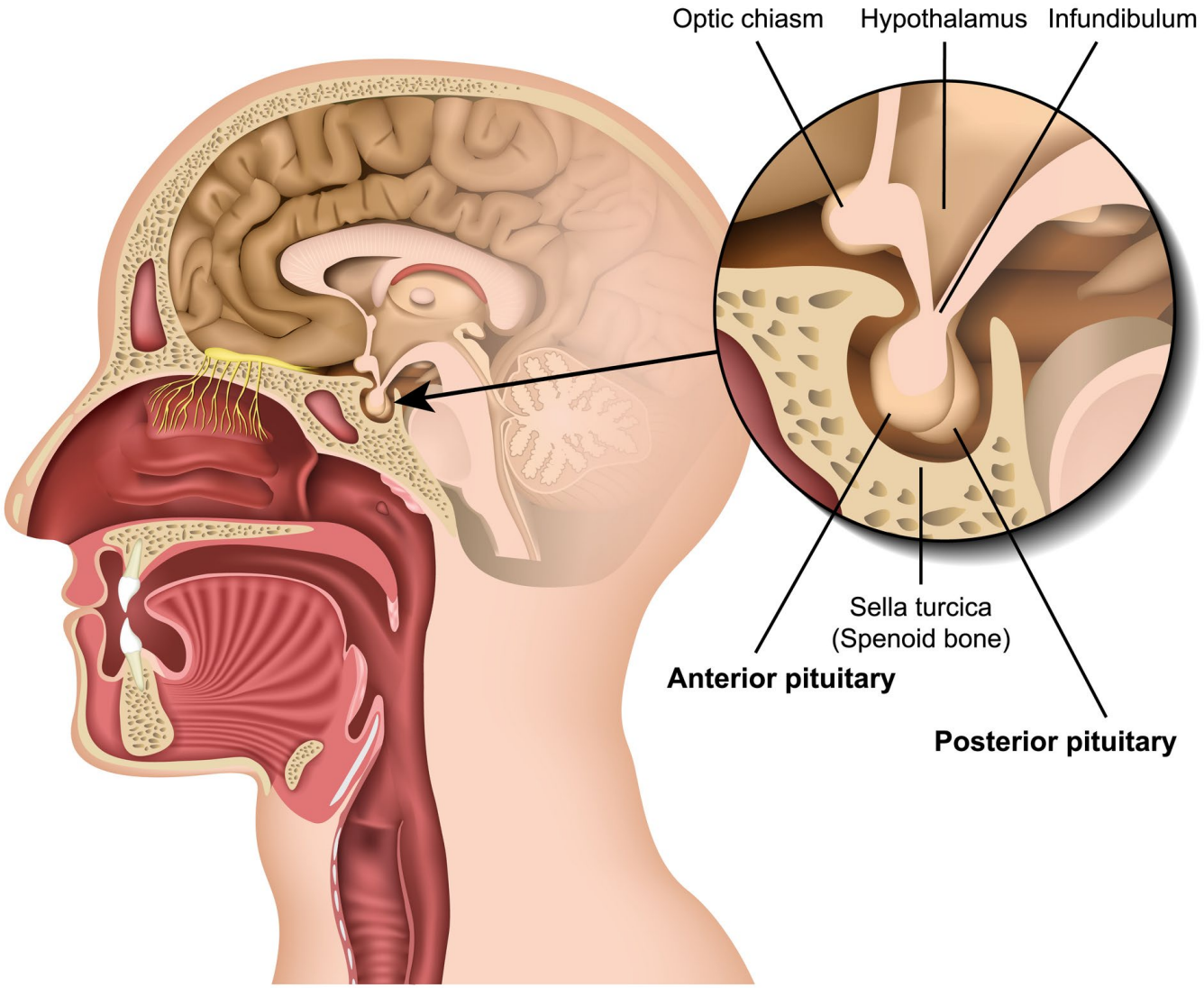
The Endocrine System

The glands and organs that make hormones and release them directly into the blood so they can travel to tissues and organs all over the body.



The command center

- The pituitary gland is the command center for the endocrine system
- With signals from the hypothalamus in the brain, the pituitary creates hormones that signal other glands to produce their hormones.



Hormones

Hormones are messengers created by glands and organs. They give other glands, organs, and tissues messages to increase or slow down cellular functions

Hormones of the Pituitary

- Adrenocorticotrophic Hormone (ACTH)
- Thyroid Stimulating Hormone (TSH)
- Luteinizing Hormone (LH)
- Follicle Stimulating Hormone (FSH)
- Prolactin
- Growth Hormone (GH)
- Melanocyte-stimulating Hormone (MSH)
- Oxytocin
- Antidiuretic Hormone (ADH)

Hormones of the Endocrine System

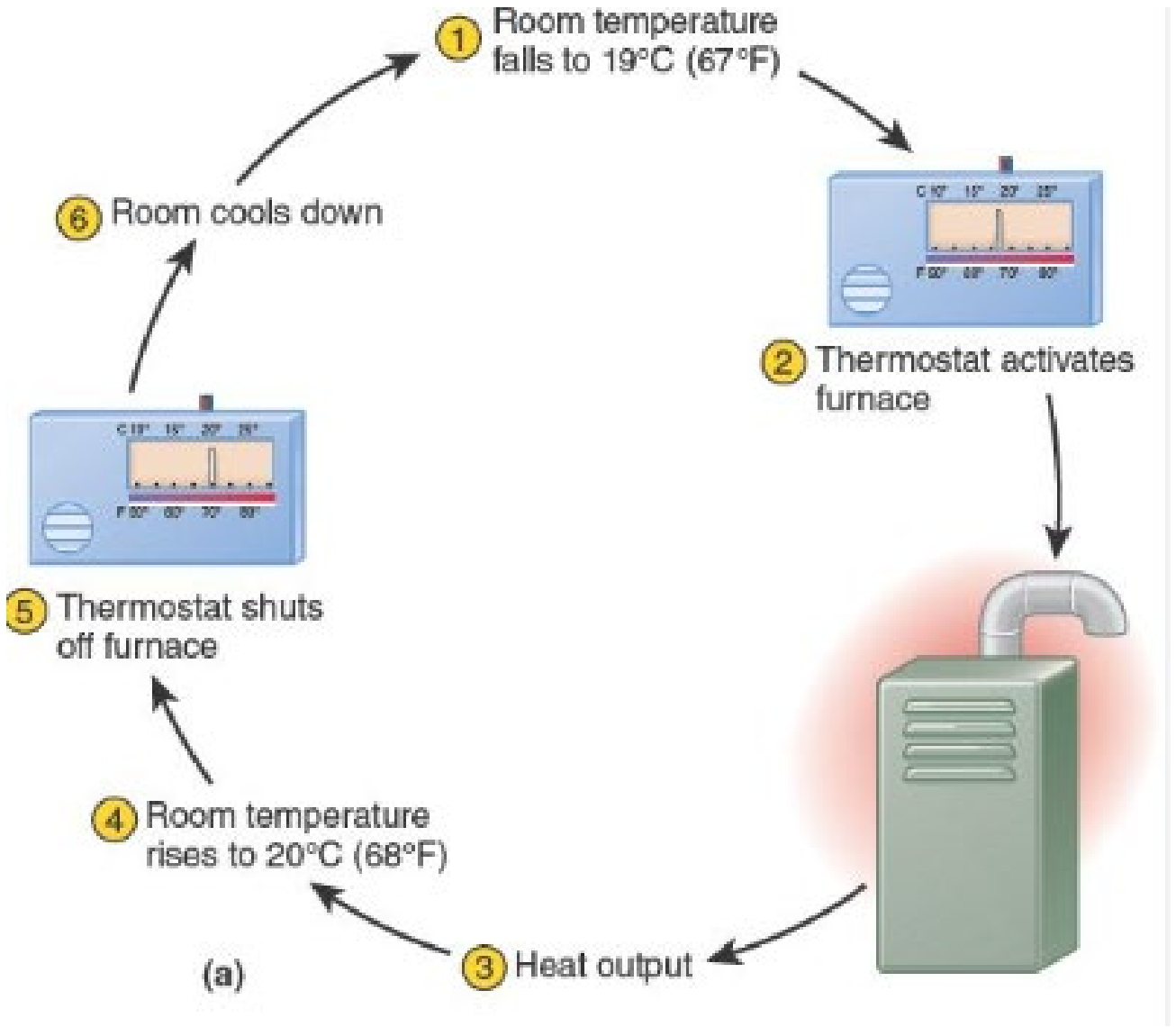
- Thyroid gland
  - Thyroxine (T3 and T4)
  - Calcitonin
- Parathyroid gland
  - Parathyroid hormone
- Testes
  - Testosterone
- Ovaries
  - Estrogen

Hormones of the Endocrine System

- Adrenal Gland
  - Aldosterone
  - Cortisol
  - Dehydroepiandrosterone (DHEA)
  - Epinephrine
- Liver
  - Angiotensinogen
  - Thrombopoietin

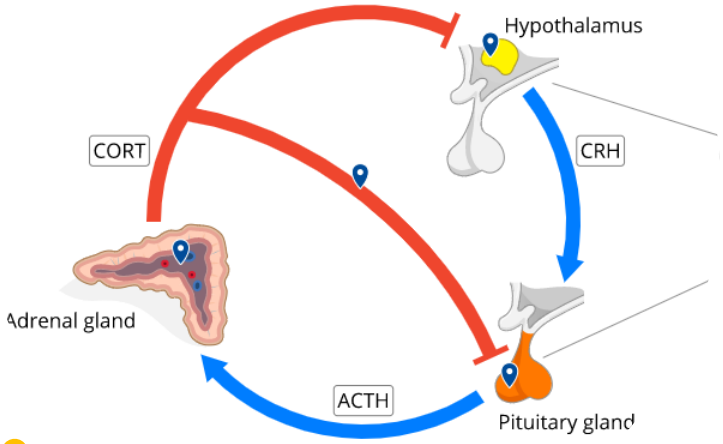
Homeostasis through feedback

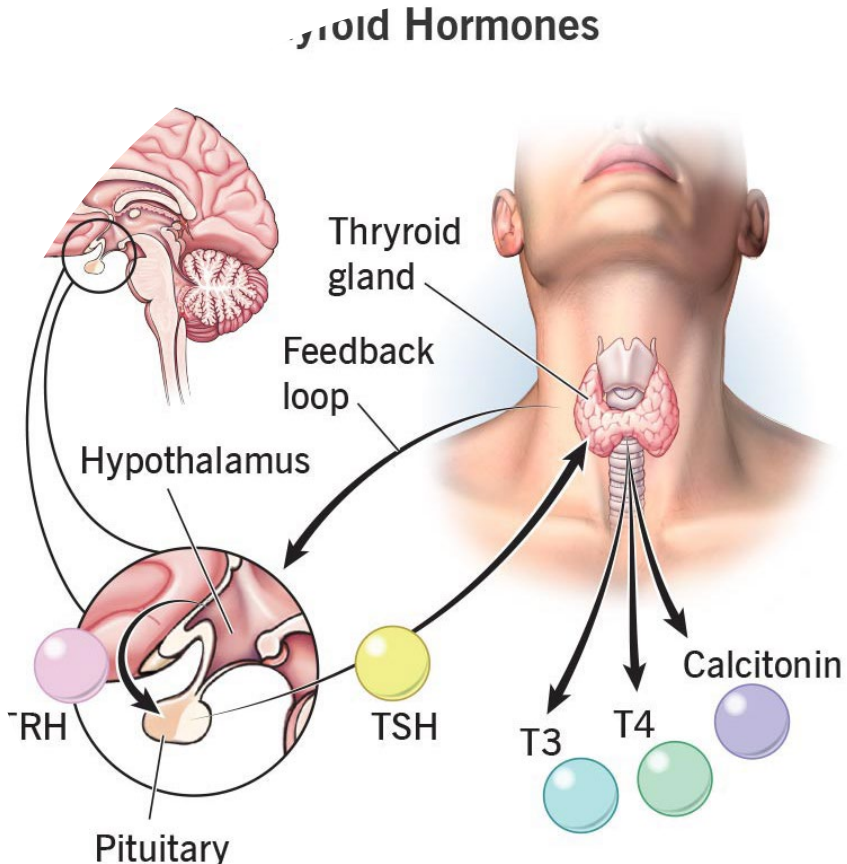
The endocrine system excels at using feedback to create homeostasis. Most of these are negative feedback loops where a gland is stimulated to make a hormone and that hormone then leads to suppression of more hormone creation. Why is this important?



Examples of feeback loops

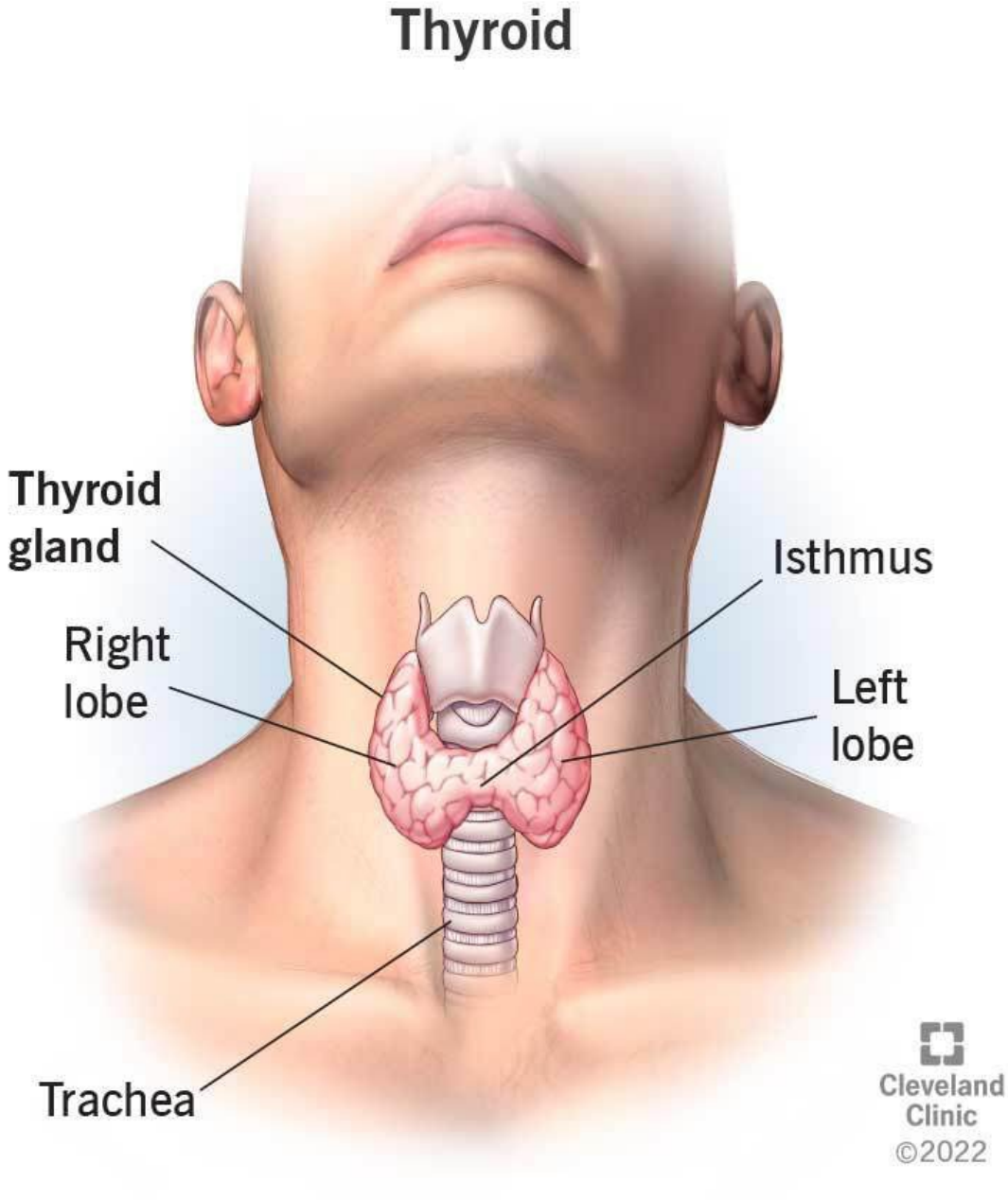
- Pituitary makes TSH that stimulate the thyroid to produce T4. Higher T4 levels suppress the TSH production from the pituitary
- Pituitary makes ACTH that stimulates the adrenal to make cortisol. Higher cortisol levels suppress the ACTH production in the pituitary



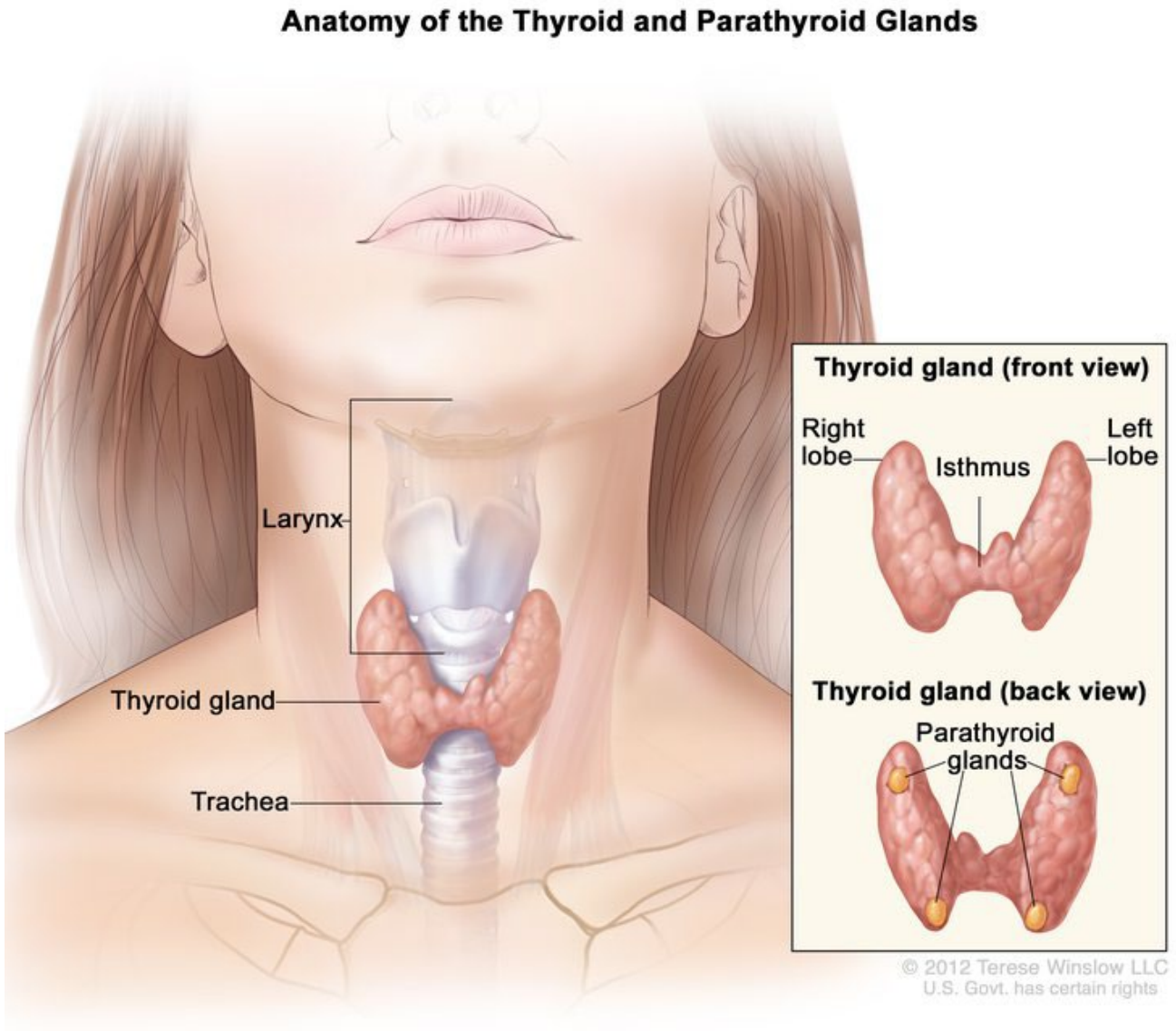


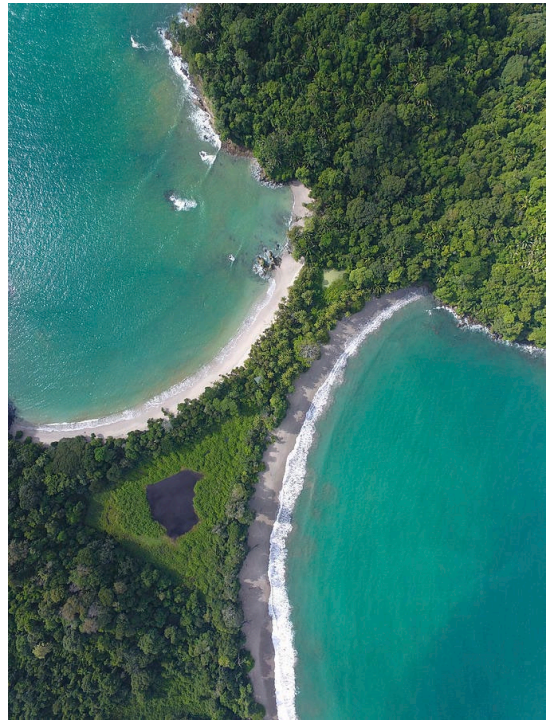
The Thyroid

The thyroid


Thyroid
Thyroid gland
Right lobe
Isthmus
Left lobe
Trachea
Cleveland Clinic
©2022

Anatomy of the thyroid

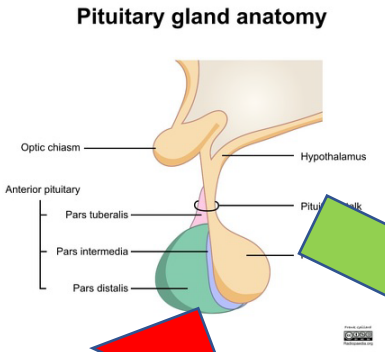




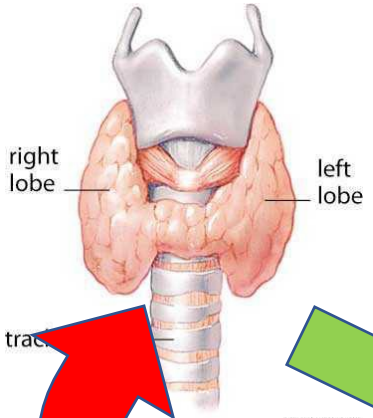
What does the thyroid do?

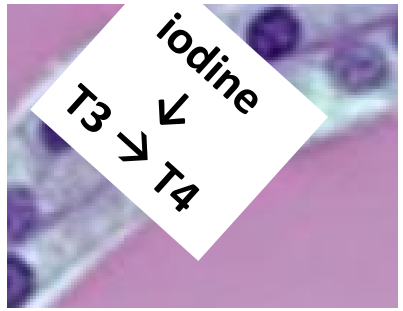
- The thyroid makes 2 hormones, T3 & T4
  - heart rate
  - metabolic rate
  - energy levels
  - weight
  - skin & hair
  - bowels

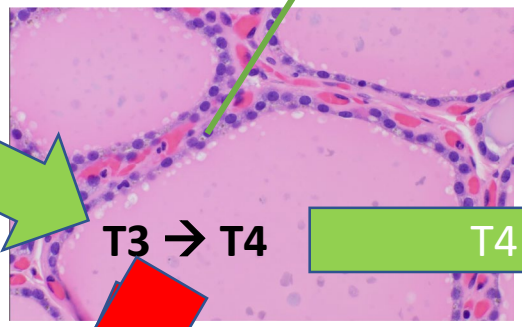
How does the thyroid work?



TSH







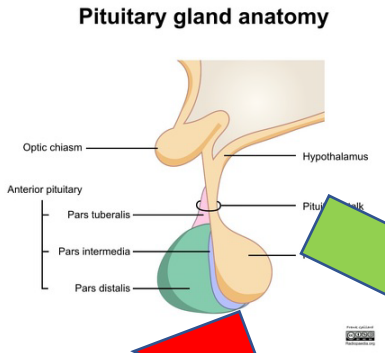
T4

- heart rate
- metabolic rate
- energy levels
- weight
- skin & hair
- bowels

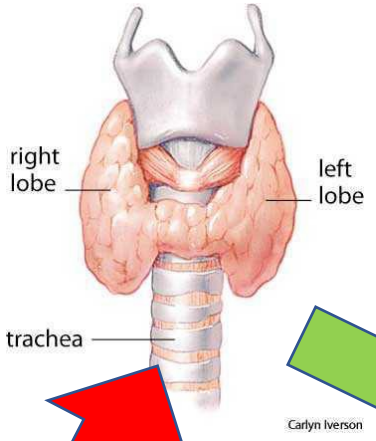
Hypothyroidism

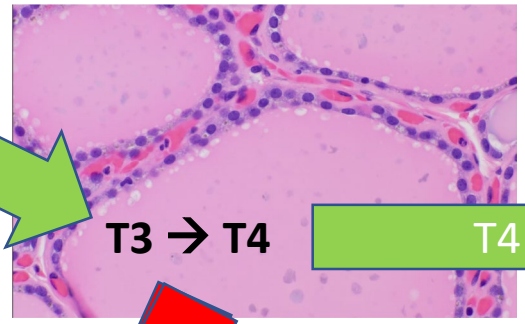
Low thyroid function

What if the thyroid isn't working?



TSH



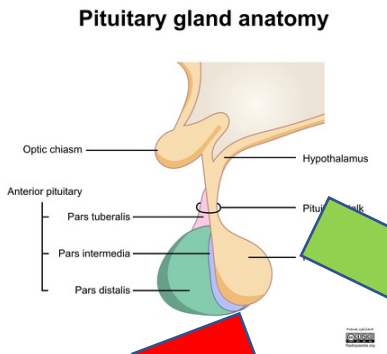


T4

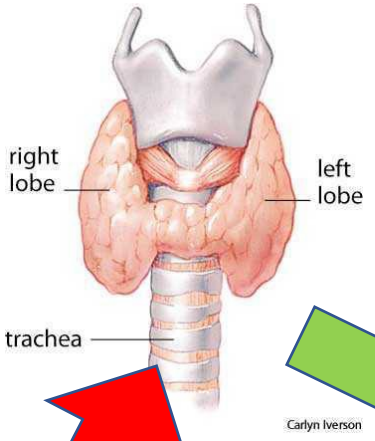
- ↓ heart rate
- ↓ metabolic rate
- ↓ energy levels
- ↑ weight
- skin & hair
- bowels

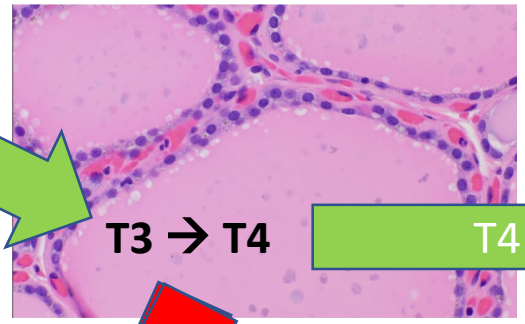
Secondary Hypothyroidism
- ↓ TSH
- ↓ T4

What if the thyroid isn't working?



TSH





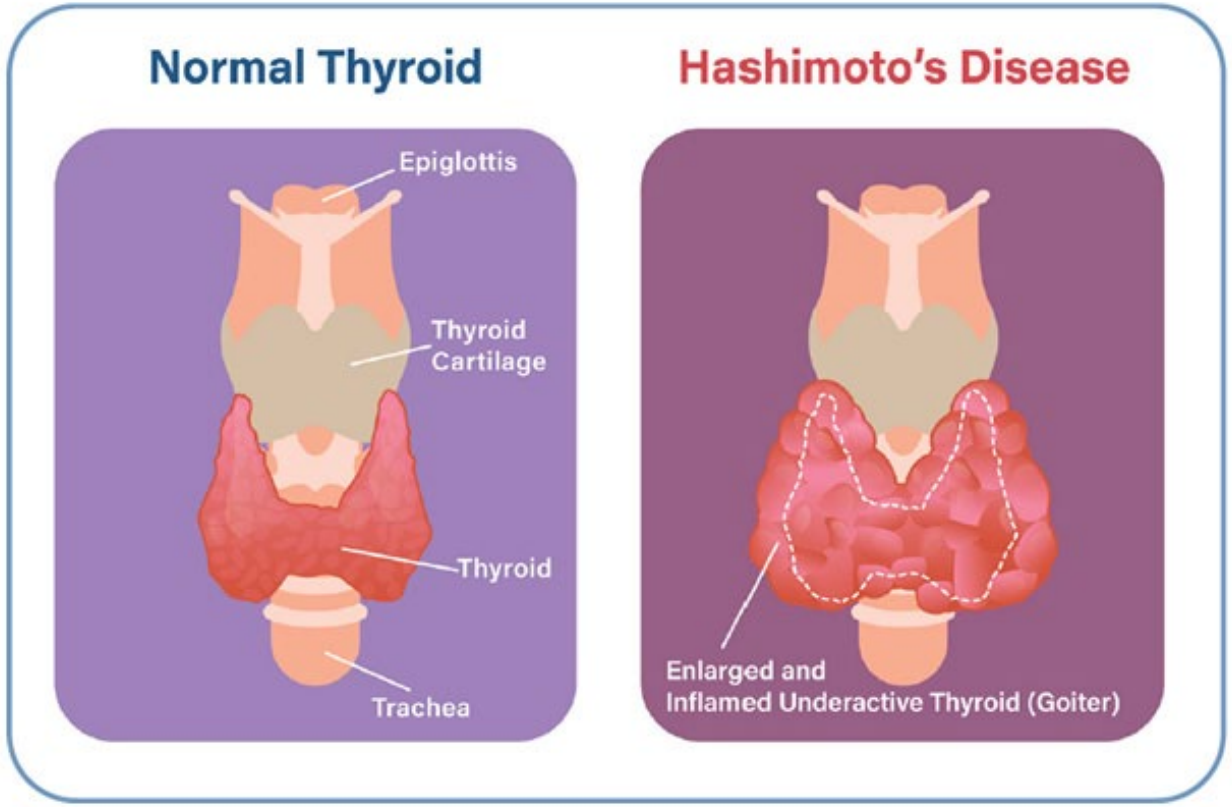
T4

Primary Hypothyroidism
- ↑ TSH
- ↓ T4

- ↓ heart rate
- ↓ metabolic rate
- ↓ energy levels
- ↑ weight
- skin & hair
- bowels

Hashimoto thyroiditis

- Autoimmune disease
- One of the most common causes of hypothyroidism
- Due to antibodies that attack the thyroid & prevent it from working



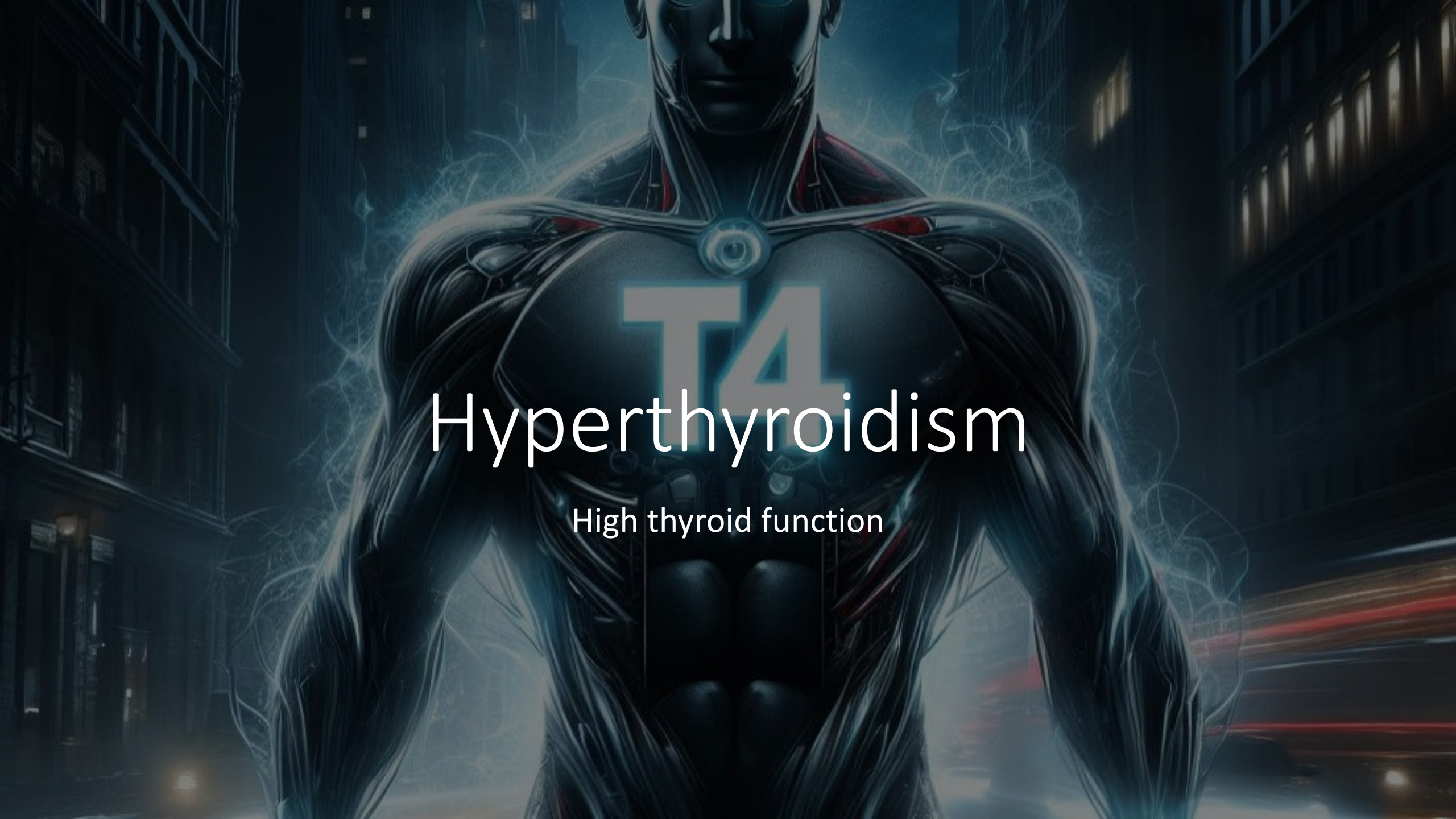
Symptoms of hypothyroidism

- Remember the things the thyroid does…
  - ↑ heart rate → ↓ heart rate
  - ↑ metabolic rate → ↓ metabolic rate
  - ↑ energy levels → ↓ energy levels
  - weight → ↑ weight
  - skin & hair → dry skin & brittle hair
  - Bowels → hypoactive bowels (constipation)
  - Cold intolerance

Treatment of hypothyroidism

- Replace the thyroid hormone!
  - Levothyroxine = T4

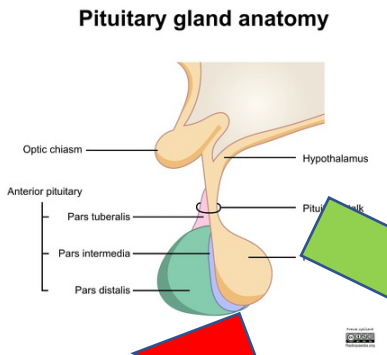
- There are many special instructions for taking levothyroxine
  - Other medications
  - In the morning



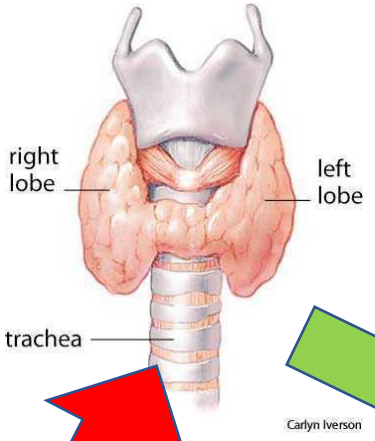
Hyperthyroidism

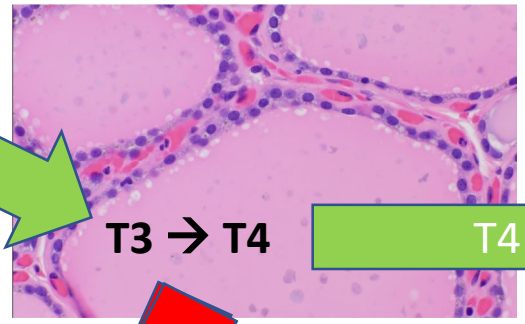
High thyroid function

What if the thyroid isn't working?



TSH





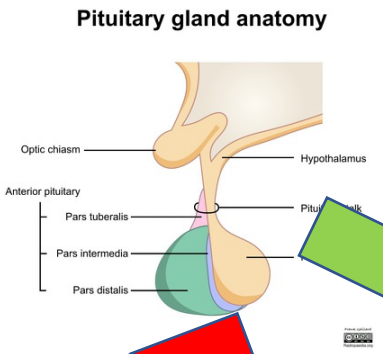
T4

Secondary Hyperthyroidism
(Very rare!)

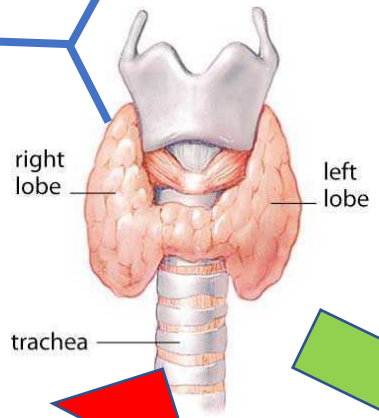
- ↑ TSH
- ↑ T4

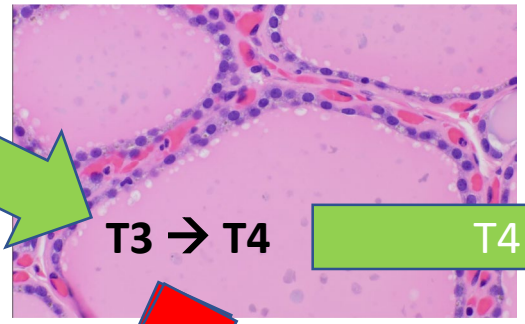
- ↑ heart rate
- ↑ metabolic rate
- ↑ energy levels
- ↓ weight
- skin & hair
- bowels

What if the thyroid isn't working?



TSH





T3 → T4

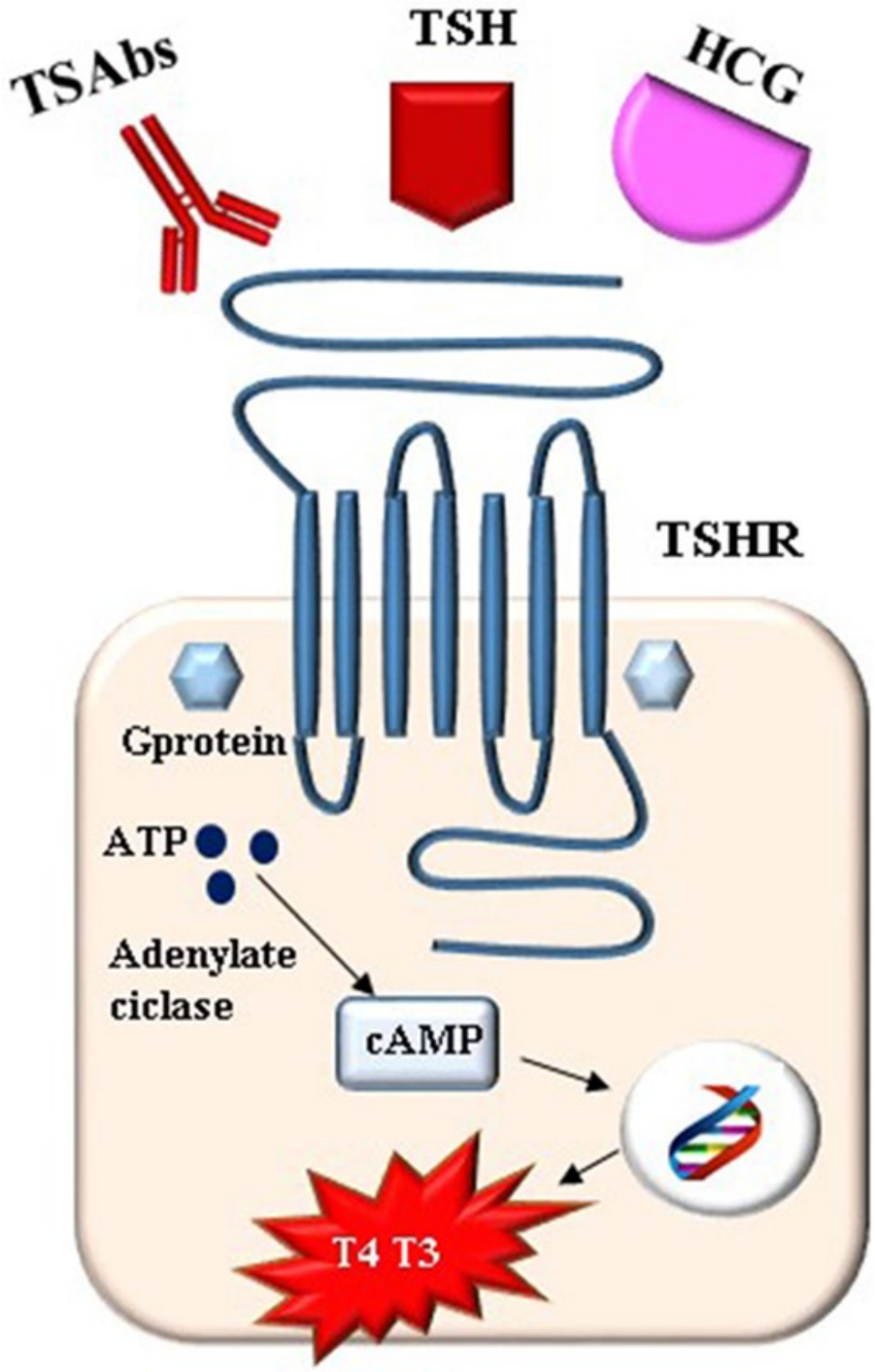
T4

Primary Hyperthyroidism
- ↓ TSH
- ↑ T4

- ↑ heart rate
- ↑ metabolic rate
- ↑ energy levels
- ↓ weight
- skin & hair
- bowels

Graves Disease

- Autoimmune disorder
- Most common cause of hyperthyroidism (60-80% of cases)
- Thyroid stimulating antibodies
- Symptoms of hyperthyroidism

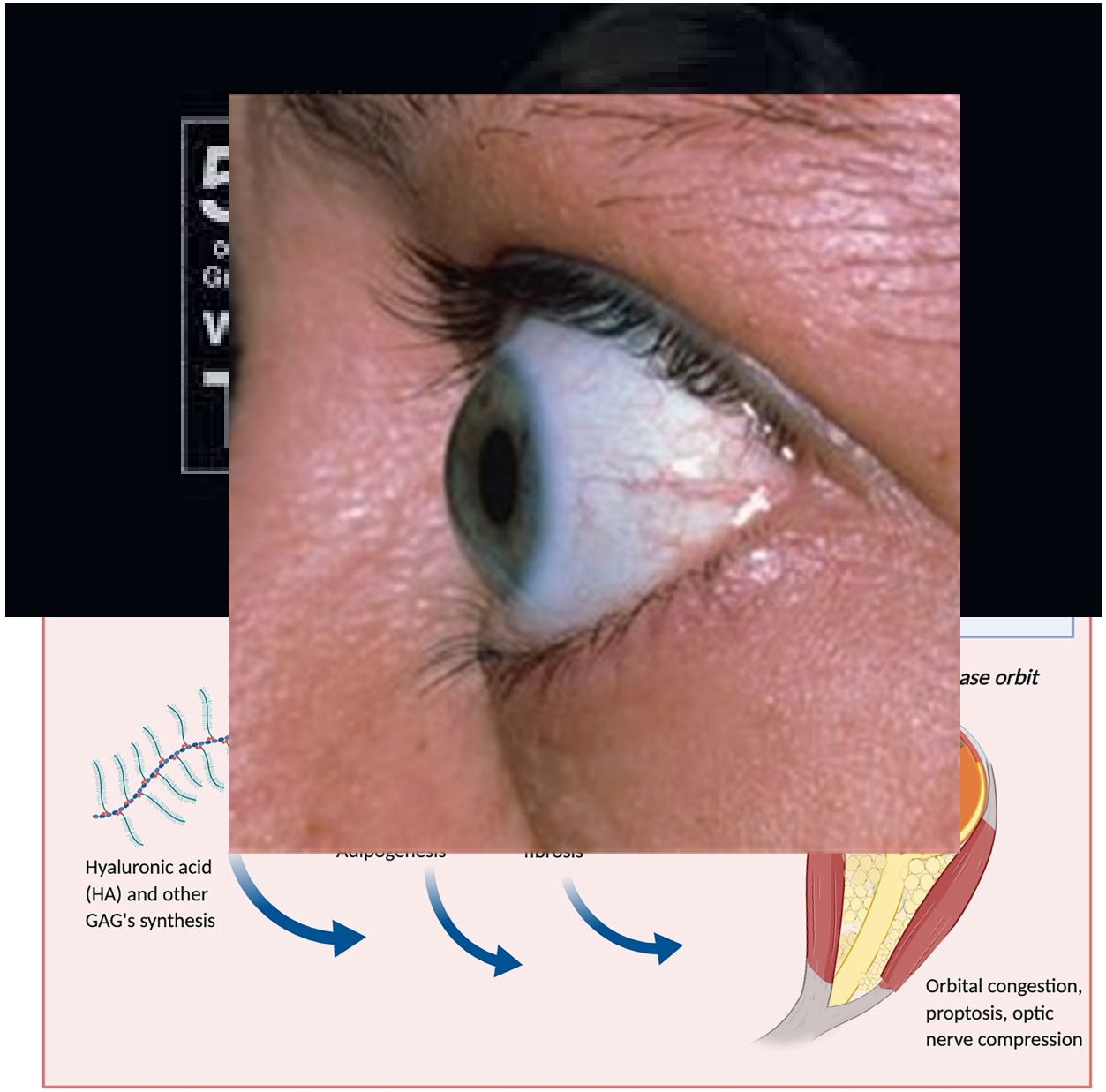


Symptoms of hyperthyroidism

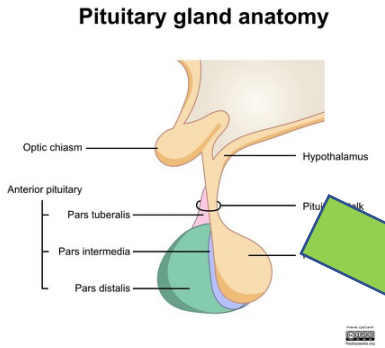
- Remember the things the thyroid does…
  - ↑ heart rate → ↑ ↑ ↑ heart rate
  - ↑ metabolic rate → ↑ ↑ ↑ metabolic rate
  - ↑ energy levels → ↑ ↑ ↑ energy levels
  - weight → ↓ weight
  - skin & hair → sweaty skin
  - Bowels → hyperactive bowels (diarrhea)
  - Heat intolerance

Thyroid eye disease

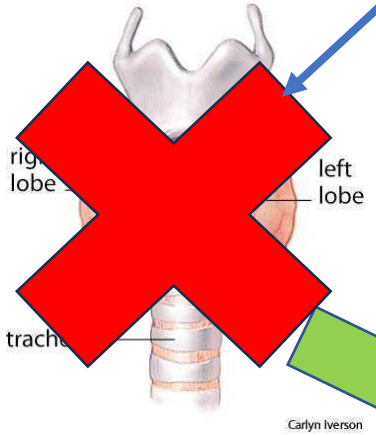
- Unique to Graves disease
- Thyroid stimulating antibodies bind to cells in the orbital fat cells, causing increased growth of those cells
- Symptoms include:
  - Ocular pain
  - Eye redness, dryness
  - Visual changes
  - Proptosis



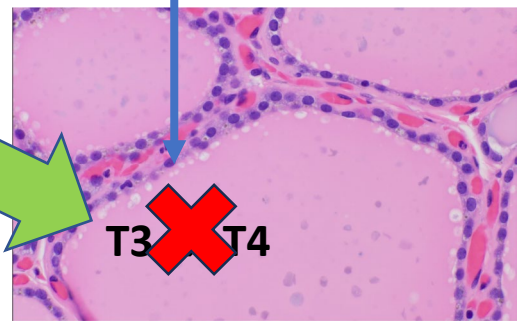
How do we treat hyperthyroidism?



Surgery, radioactive iodine



PTU, methimazole



What about treating thyroid eye disease?

- Utilize other treatments for hyperthyroidism
  - PTU, methimazole, surgery
  - NOT radioactive iodine!
- Medications specific to TED
  - Teprotumumab → an antibody that blocks the effect of thyroid stimulating antibodies in the orbits

Question 1

A patient comes to the office reporting feeling her heart beating faster than usual. On her physical exam, she appears anxious, her skin is sweaty, the thyroid appears enlarged, and her eyes are mildly bulging.

You order blood work for this patient. What do you expect to find?

A. High TSH & high T4
B. Low TSH & high T4
C. Low TSH & low T4
D. High TSH & low T4

Question 1 Answer

A patient comes to the office reporting feeling her heart beating faster than usual. On her physical exam, she appears anxious, her skin is sweaty, the thyroid appears enlarged, and her eyes are mildly bulging.

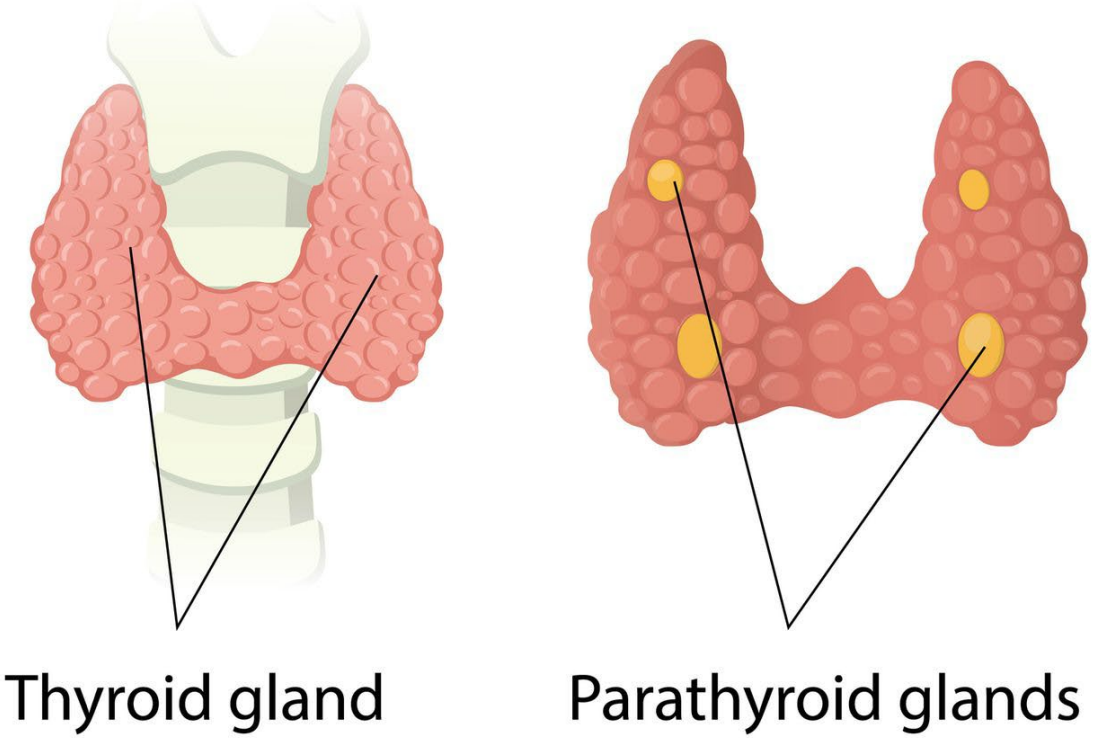
You order blood work for this patient. What do you expect to find?

A. High TSH & high T4
B. Low TSH & high T4
C. Low TSH & low T4
D. High TSH & low T4

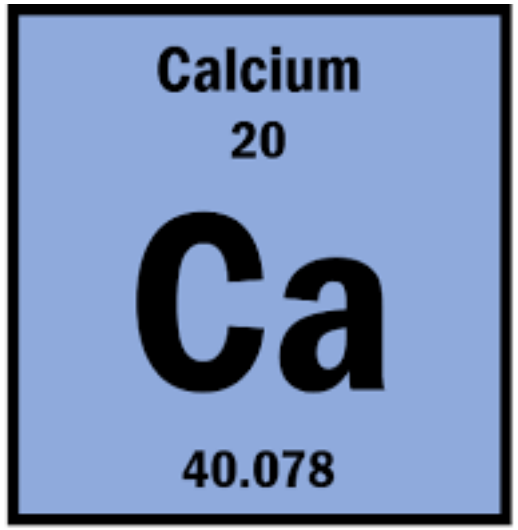
This patient is presenting with symptoms of hyperthyroidism (high heart rate, sweaty skin, enlarged thyroid). She has proptosis (bulging eyes), which would suggest Graves Disease. Since the problem is coming from an overactive thyroid gland, in Graves Disease the TSH is low and T4 is high.


The Parathyroid

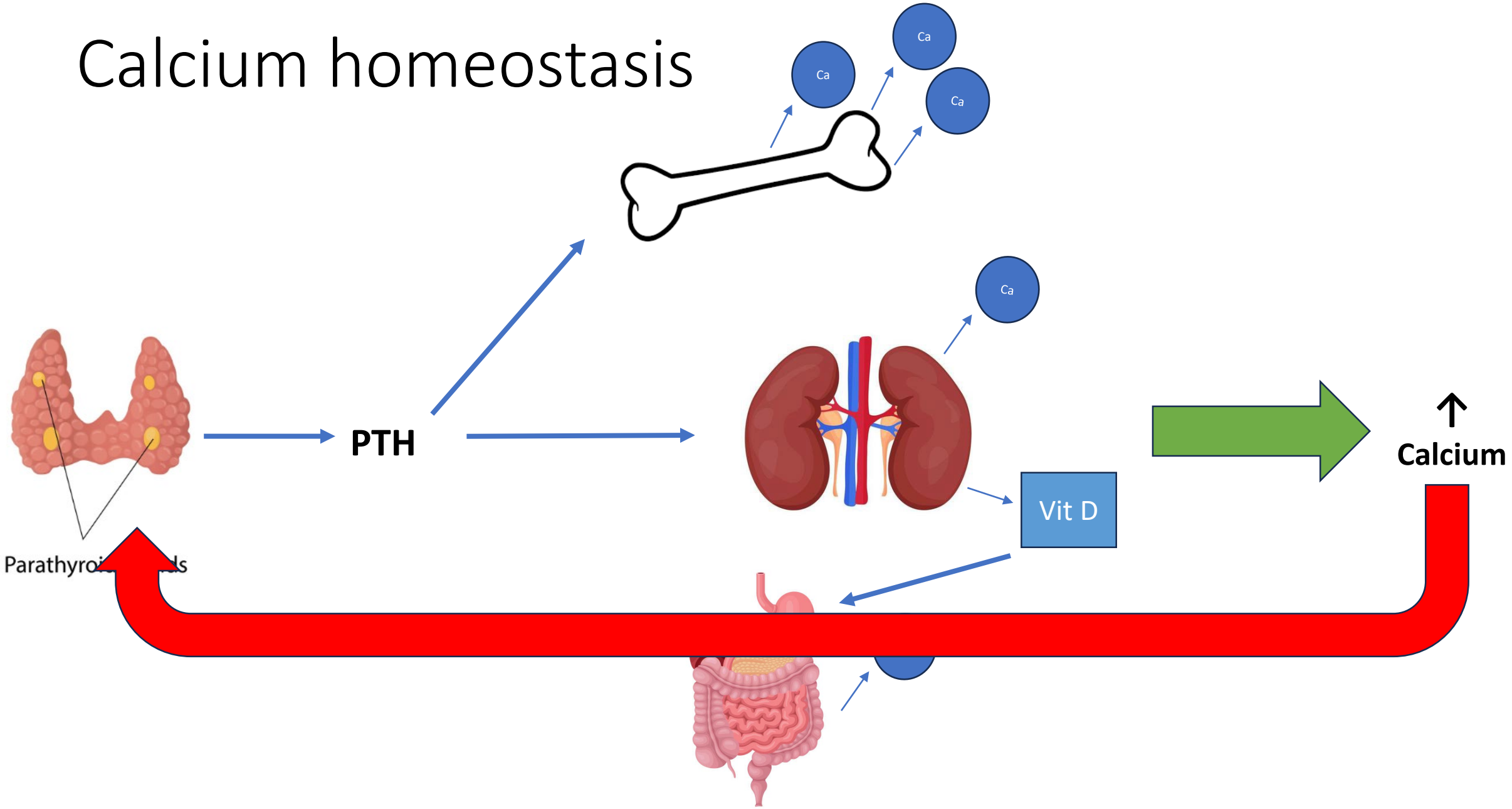
The parathyroid



What do the parathyroids do?

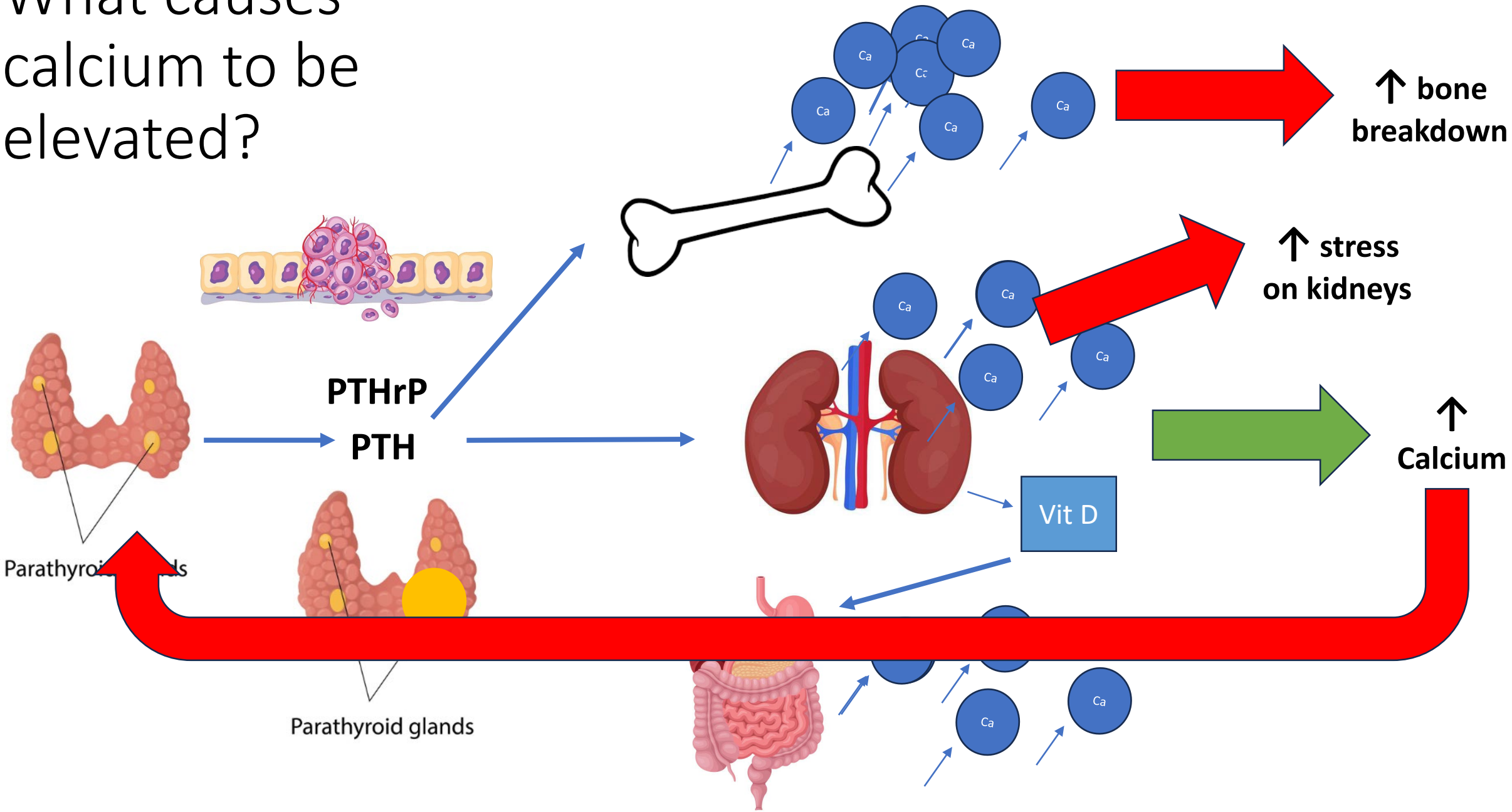


Calcium homeostasis

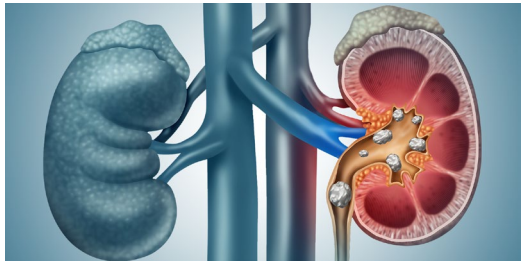


What can go wrong with calcium?

What causes calcium to be elevated?



stones



psychiatric overtones

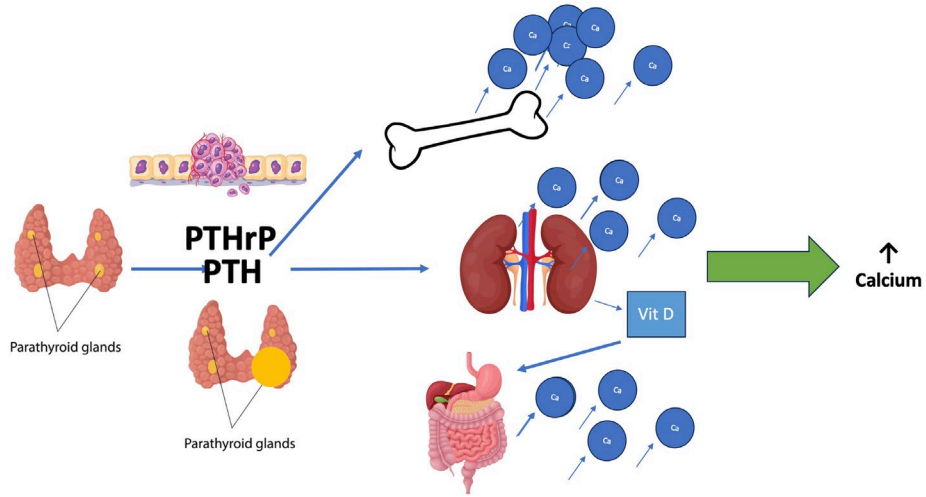
↑ calcium

bones

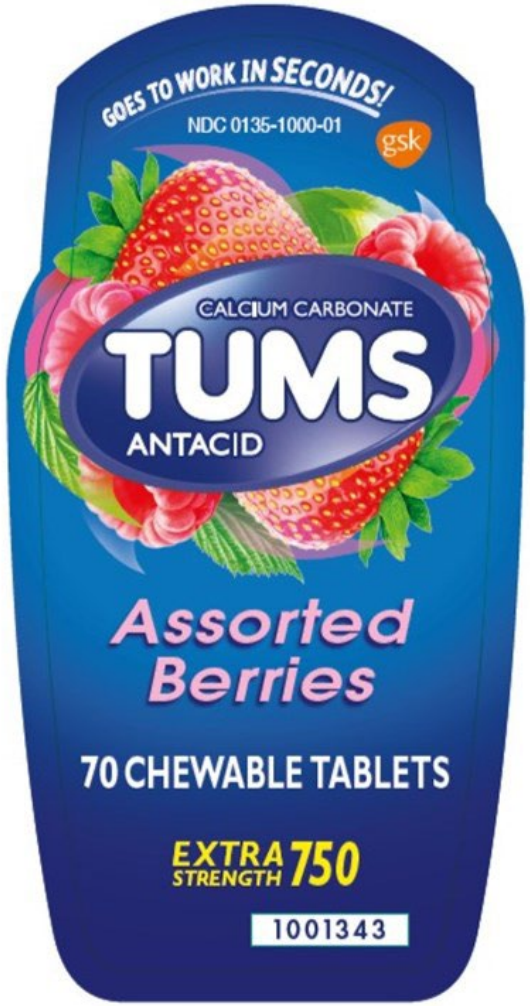
thrones

groans

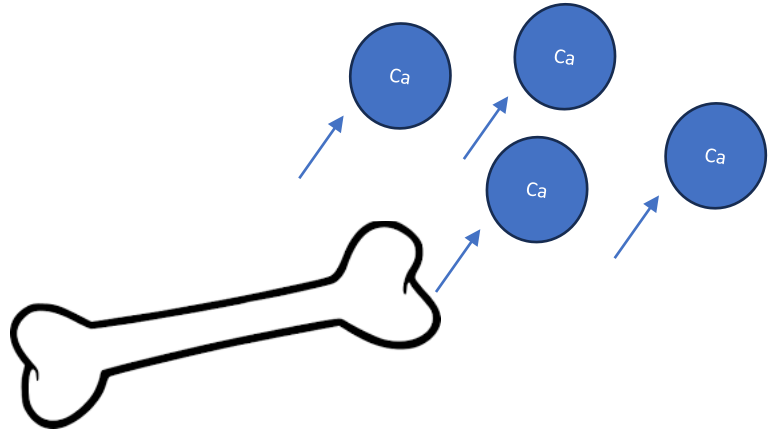
Diagnosing parathyroid disorders



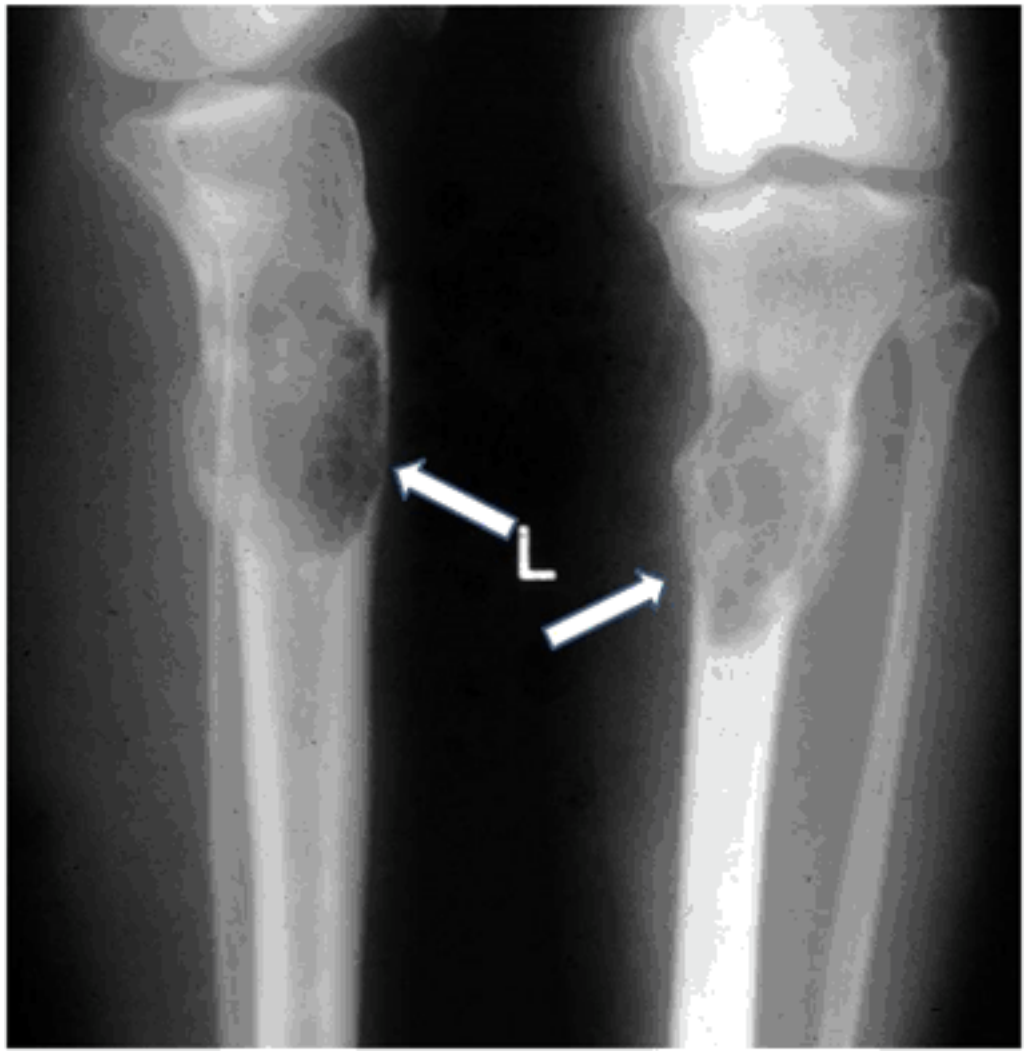
Calcium		Possible causes
↑		Primary hyperparathyroidism → parathyroid adenoma is the most common cause
↑		PTHrP or eating too much calcium
↓		Primary hypoparathyroidism → are the parathyroids there?



Parathyroid bone disease



- Overproduction of PTH causes increase bone breakdown in an attempt to raise blood calcium levels
- Can lead to osteitis fibrosa cystica in severe cases
  - Bone pain
  - Abnormal bone fractures
  - Skeletal deformities
  - Low bone mineral density
- Reversible with treatment of hyperparathyroidism



6 months
post-parathyroidectomy

18 months
post-parathyroidectomy

Question 2

A patient comes to the office for a follow up after recently going to the emergency room for their first kidney stone. They also tell you they've had increased constipation, abdominal pain, pain in their extremities, and some mild confusion. On their labs, calcium and PTH are both elevated.
What is the most likely source of high calcium?

a. Parathyroid adenoma
b. Lung cancer releasing PTHrp
c. Eating too many Tums

Question 2 Answer

A patient comes to the office for a follow up after recently going to the emergency room for their first kidney stone. They also tell you they've had increased constipation, abdominal pain, pain in their extremities, and some mild confusion. On their labs, calcium and PTH are both elevated.
What is the most likely source of high calcium?

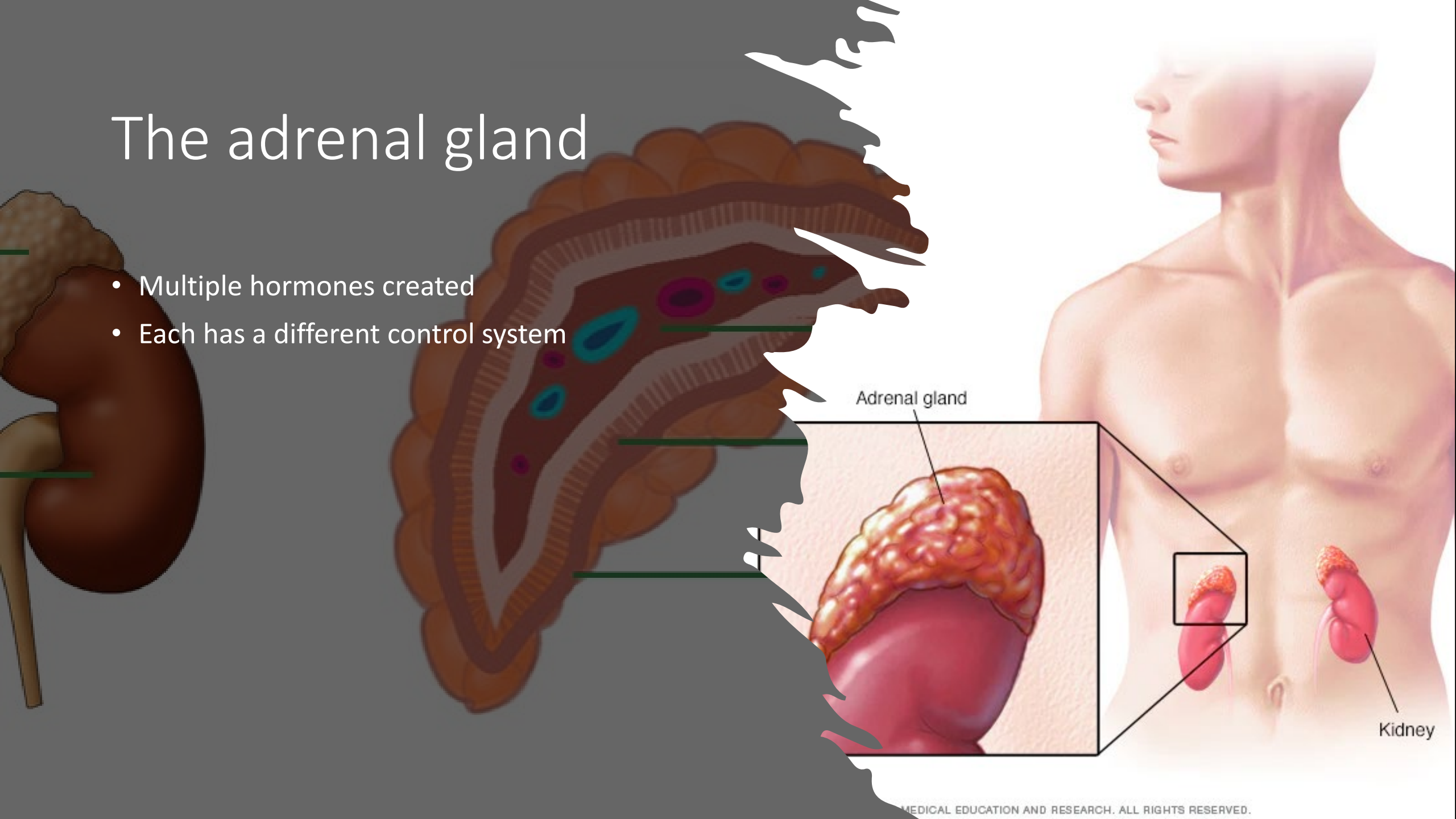
a. Parathyroid adenoma
b. Lung cancer releasing PTHrp
c. Eating too many Tums

This patient has symptoms of hypercalcemia (stones, bones, groans, thrones, and psychiatric overtones). Since their PTH is high, the source of the hypercalcemia is most likely originating in the parathyroid, as a parathyroid adenoma. If it was due to eating too many Tums, PTH would be low due to the feedback loop!

The Adrenal Hormones

The adrenal gland

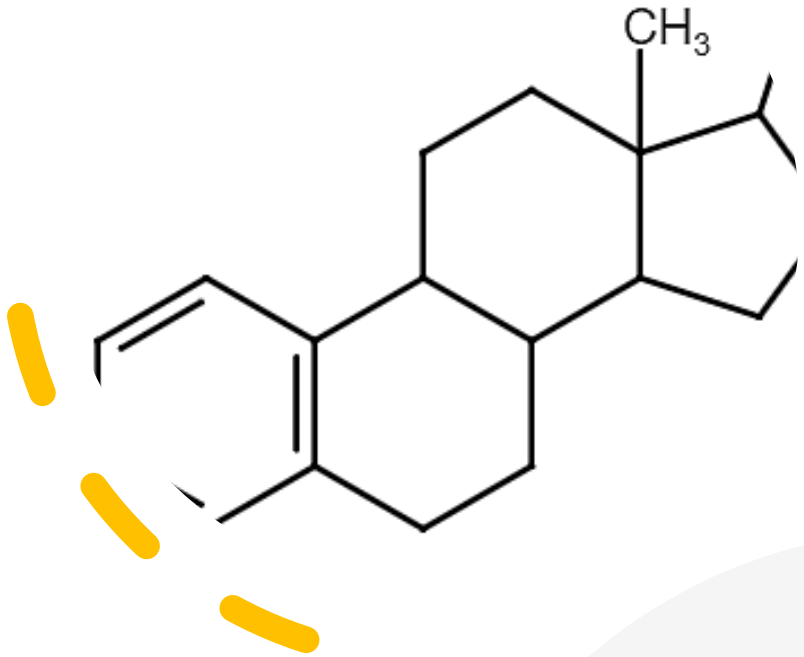
- Multiple hormones created
- Each has a different control system

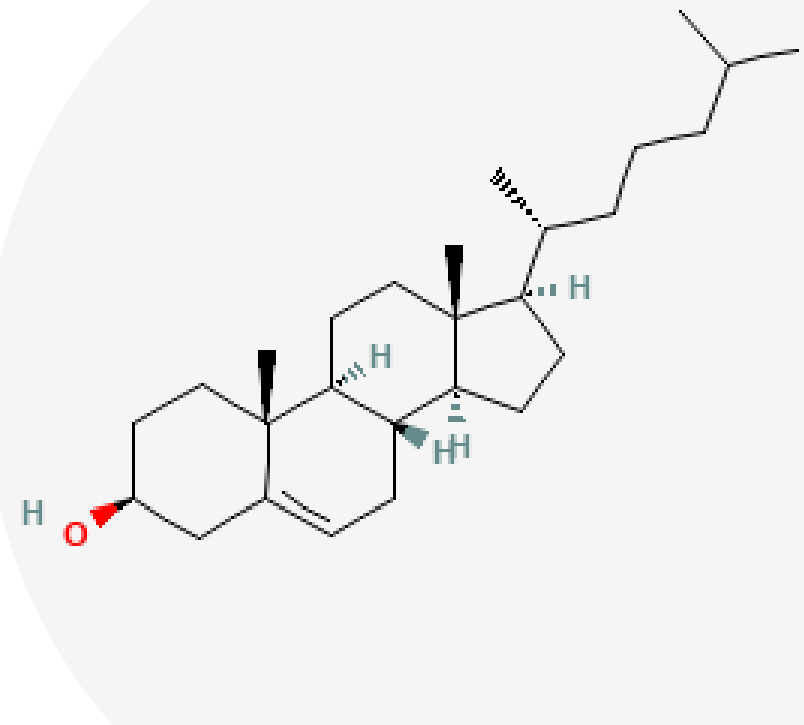



Steroids

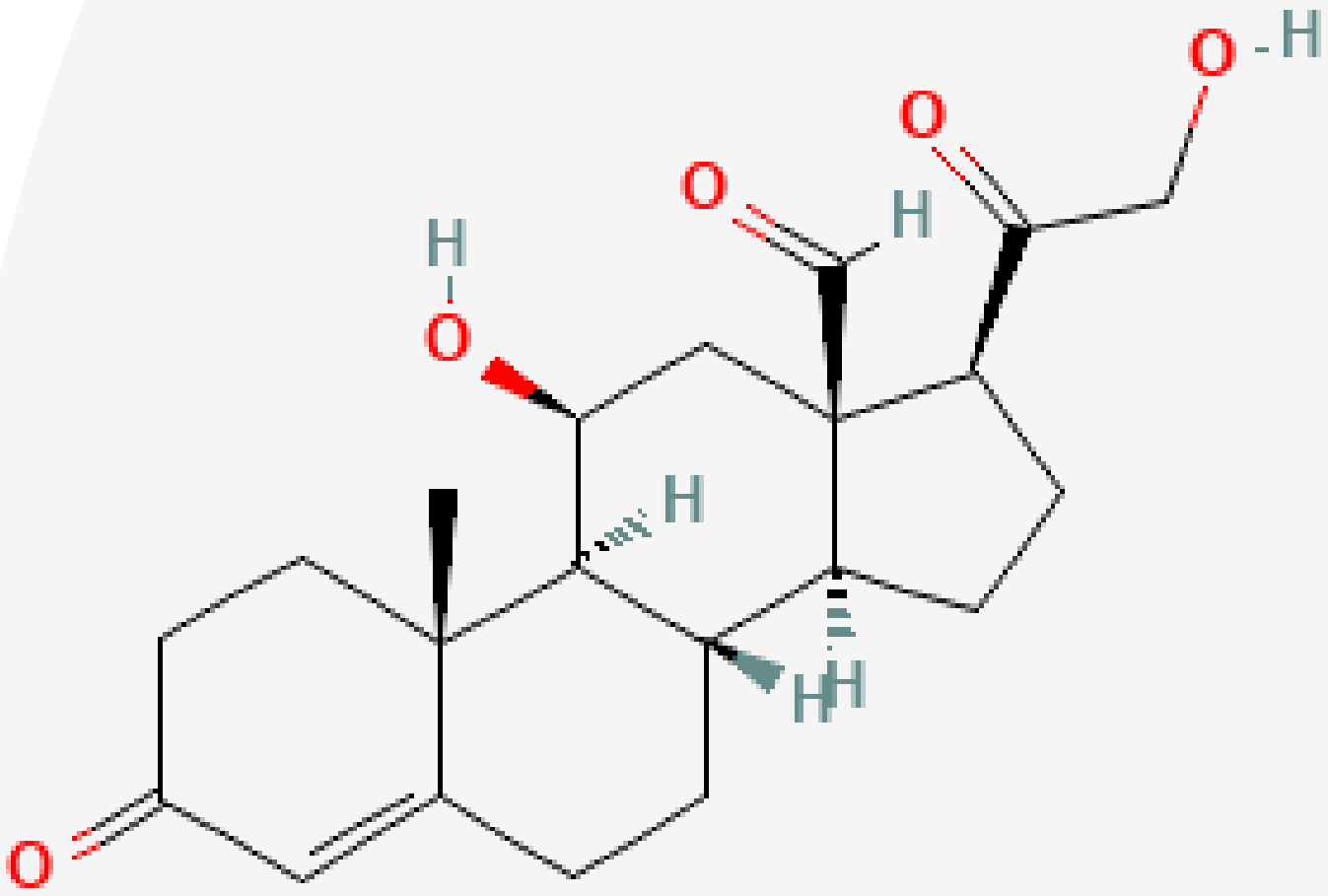
Steroids

- Steroids are fatty hormones with a similar chemical structure
- Cholesterol is an essential building block

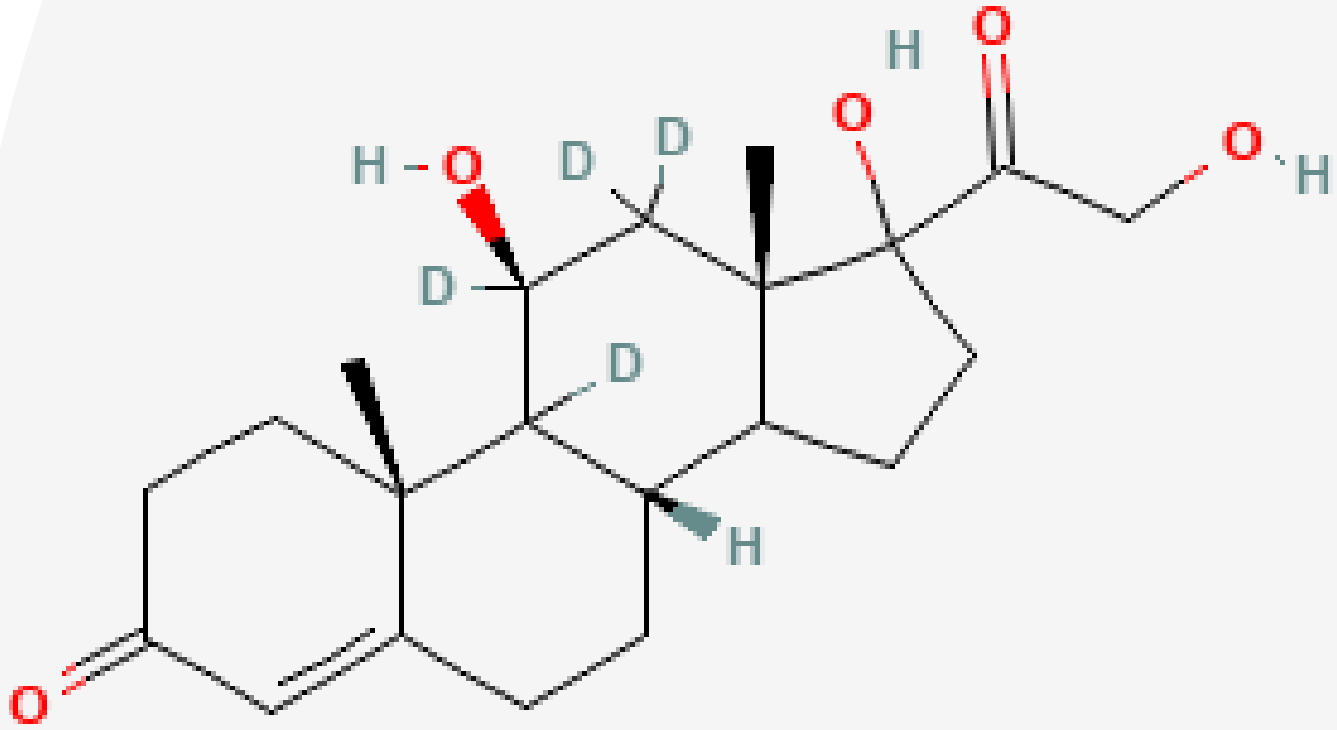




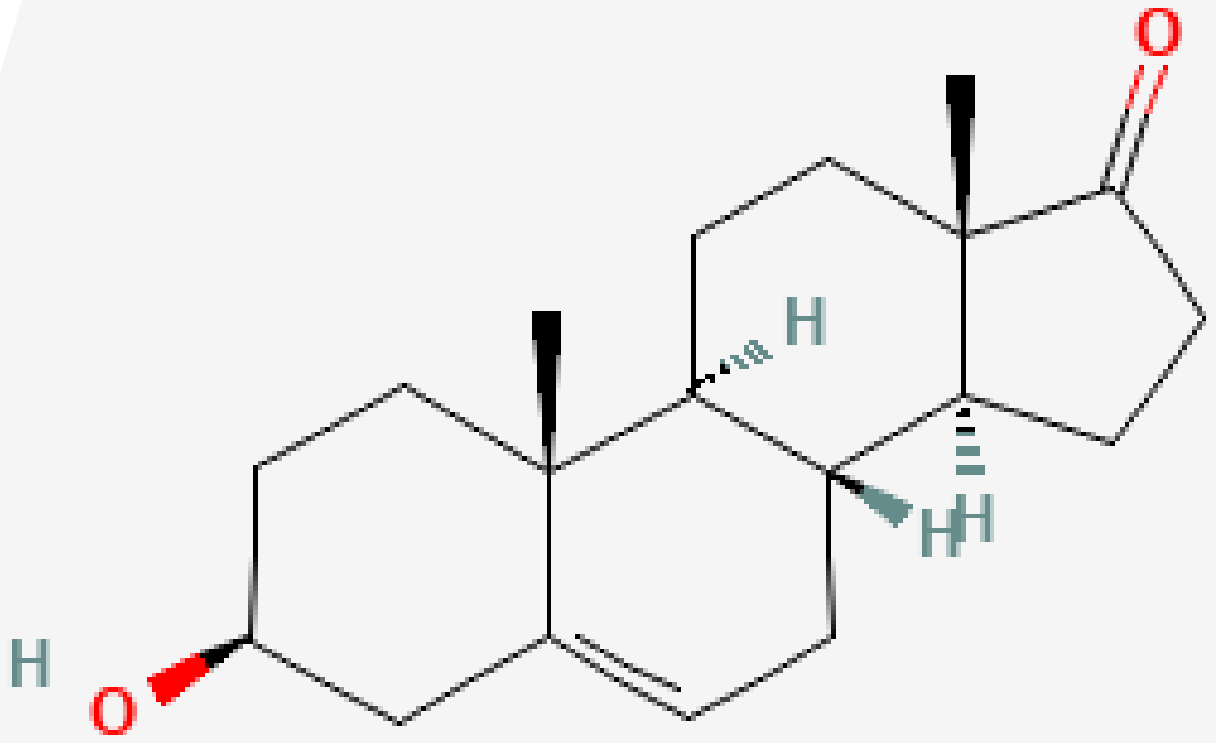
Aldosterone

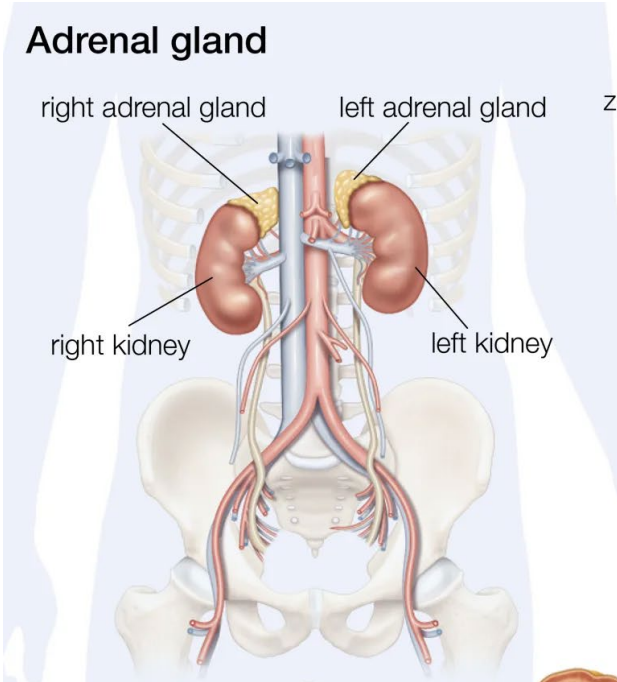


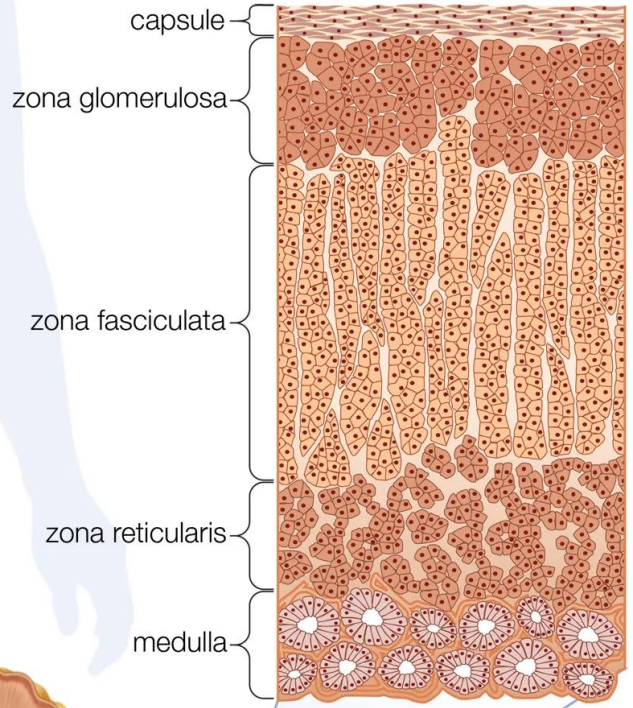
Cortisol



DHEA





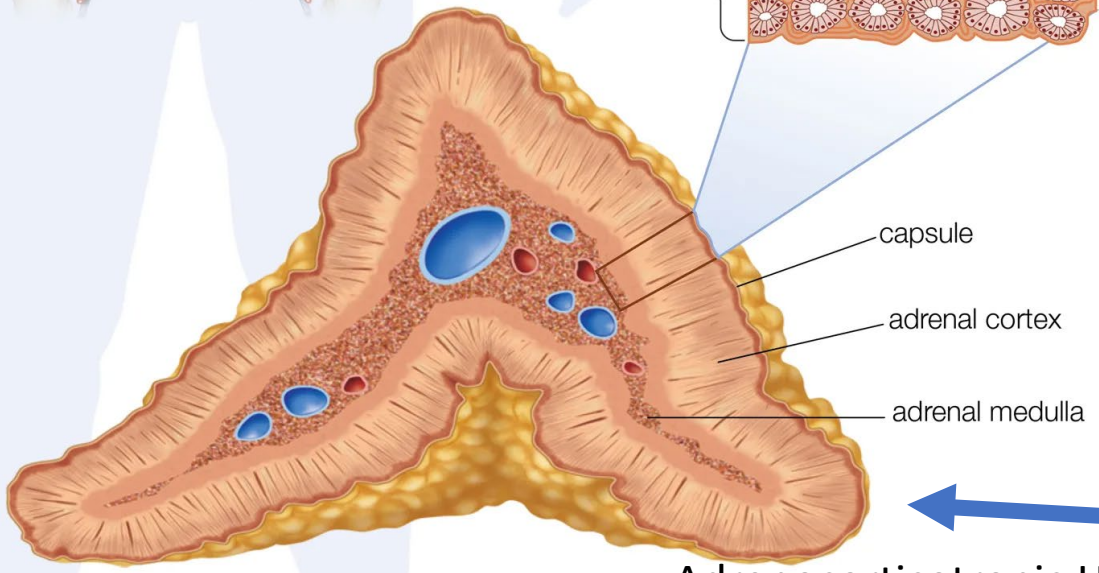


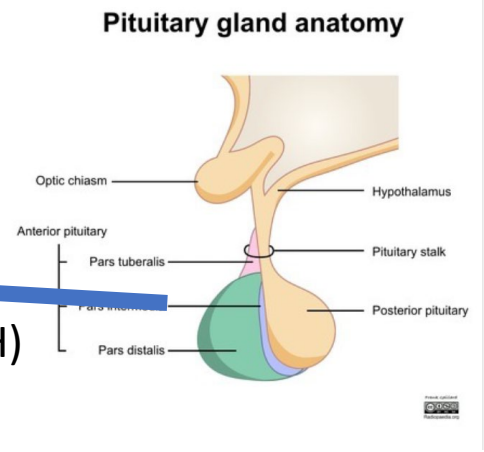
Aldosterone

Cortisol

Dehydroepiandrosterone (DHEA)

Epinephrine
Norepinephrine





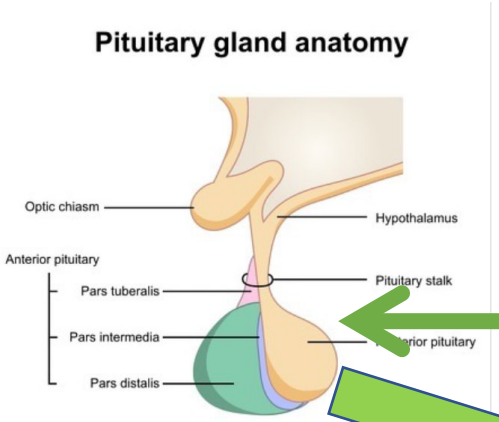
Adrenocorticotropic Hormone (ACTH)

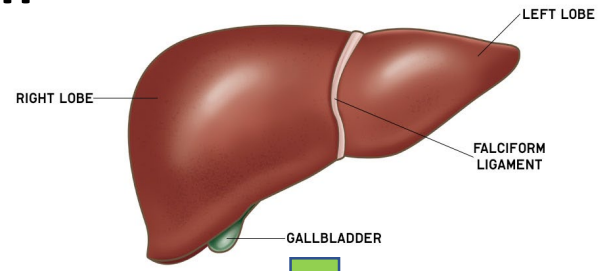
Aldosterone

- **Mineralocorticoid**
- Part of the Renin Angiotensin Aldosterone System
- Primary function is to manage blood pressure
- Functions on the kidney to cause sodium retention and potassium excretion

Renin Angiotensin Aldosterone System

Blood Pressure Control





ADH

Hold onto water

Low Blood Pressure

Raises the Blood Pressure

Sympthetic Nervous

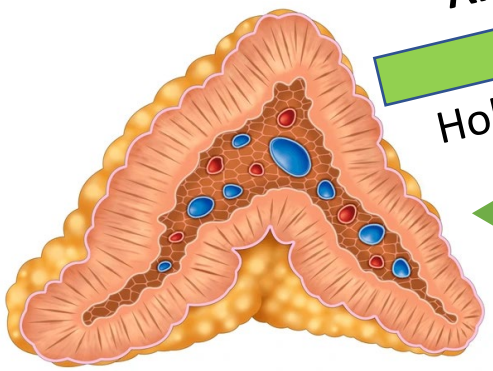
Renin

Angiotensinogen

Angiotensin I

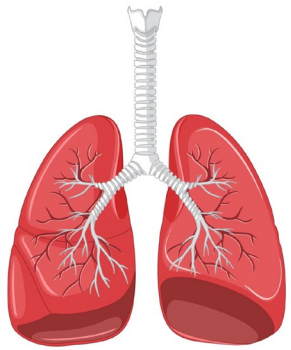
Aldosterone

Hold onto sodium



Adrenal Glomerulosa

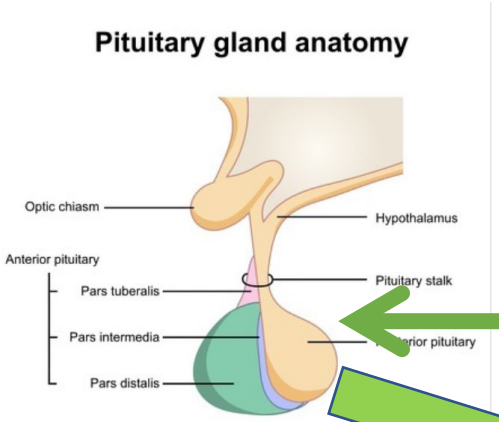
Angiotensin II



Angiotensin Converting Enzyme

Vasoconstriction

Blood Pressure Medicines

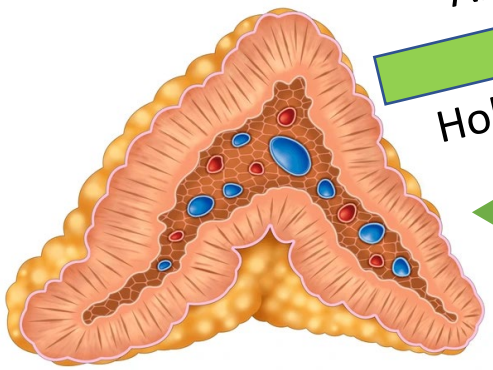


ADH

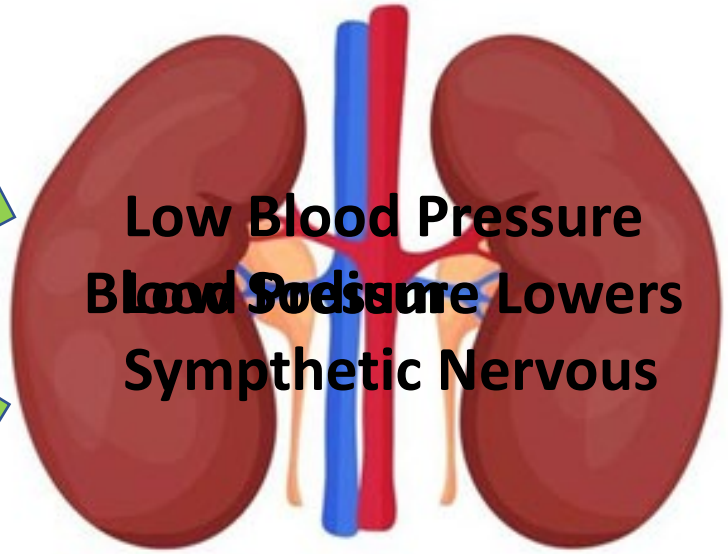
Hold onto water

Aldosterone

Hold onto sodium



Adrenal Glomerulosa



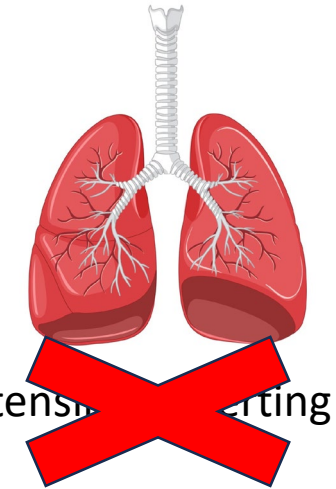
Low Blood Pressure

Blood Pressure Lowers

Sympthetic Nervous

Angiotensin II

Vasoconstriction

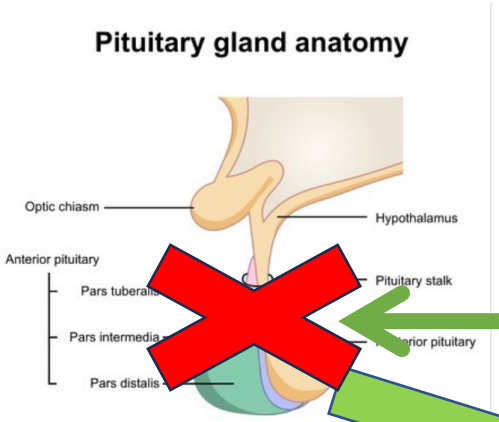


Angiotensin Converting Enzyme

Angiotensin Converting Enzyme Inhibitor

- ACE inhibitors
- Commonly used
  - Lisinopril
  - Enalapril
  - Captopril
  - Benazepril

Blood Pressure Medicines

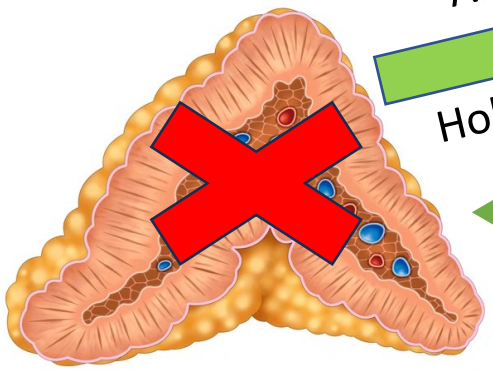


ADH

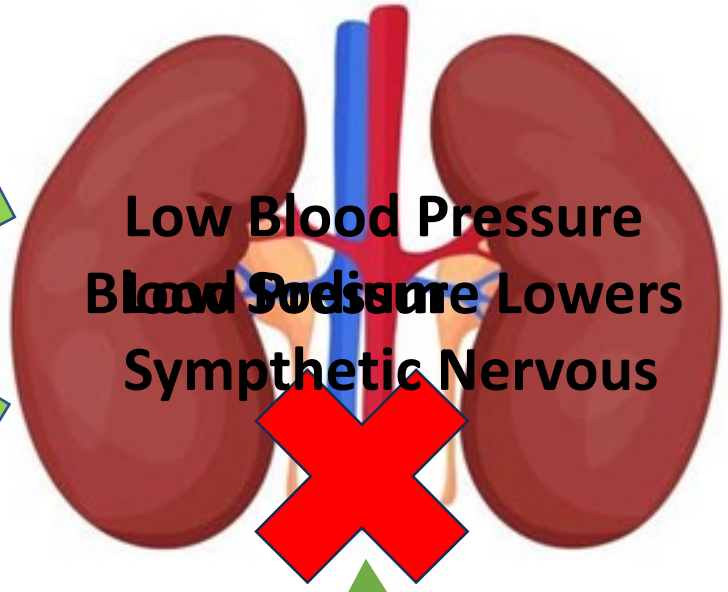
Hold onto water

Aldosterone

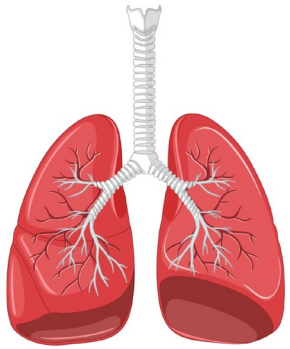
Hold onto sodium



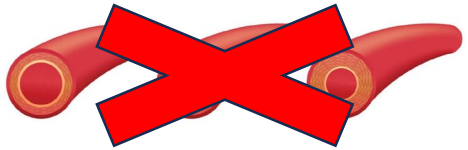
Adrenal Glomerulosa



Angiotensin II



Angiotensin Converting Enzyme

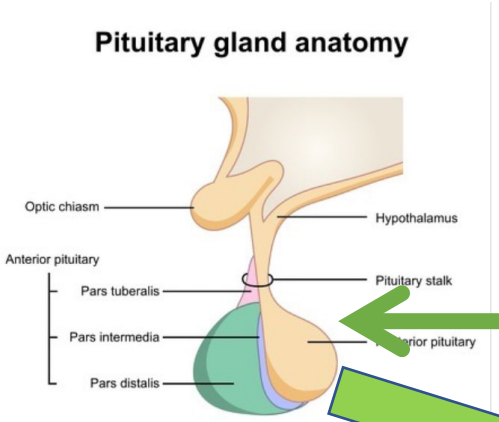


Vasoconstriction

Angiotensin Receptor Blockers

- ARBs
- Commonly used
  - Losartan
  - Valsartan
  - Irbesartan
  - Olmesartan

Blood Pressure Medicines

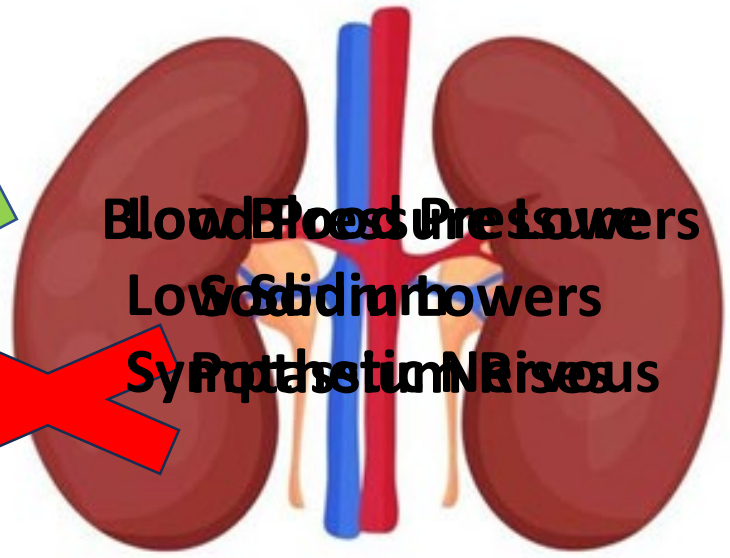


ADH

Hold onto water

Aldosterone

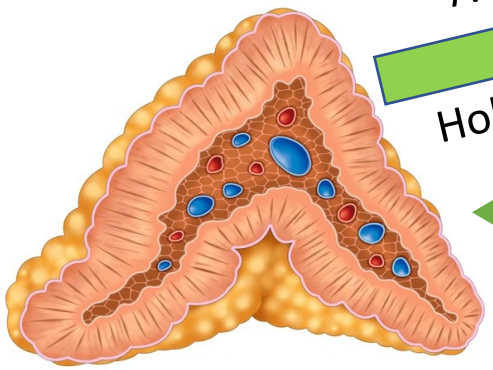
Hold onto sodium



Blood Pressure Lowers

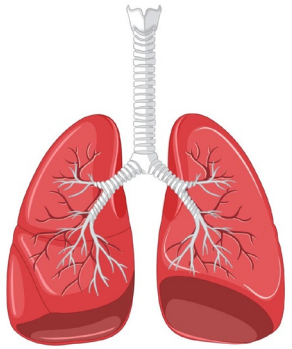
Sodium Lowers

Potassium Rises



Adrenal Glomerulosa

Angiotensin II



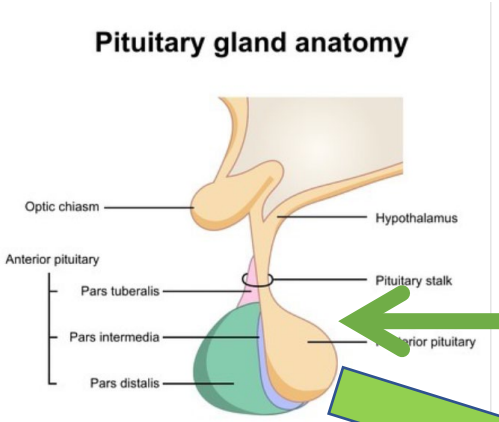
Angiotensin Converting Enzyme

Vasoconstriction

Mineralocorticoid Receptor Antagonist (aldosterone blocker)

- MRAs
- Commonly used
  - Spironolactone
  - Eplerenone

Conn's Syndrome: too much aldosterone



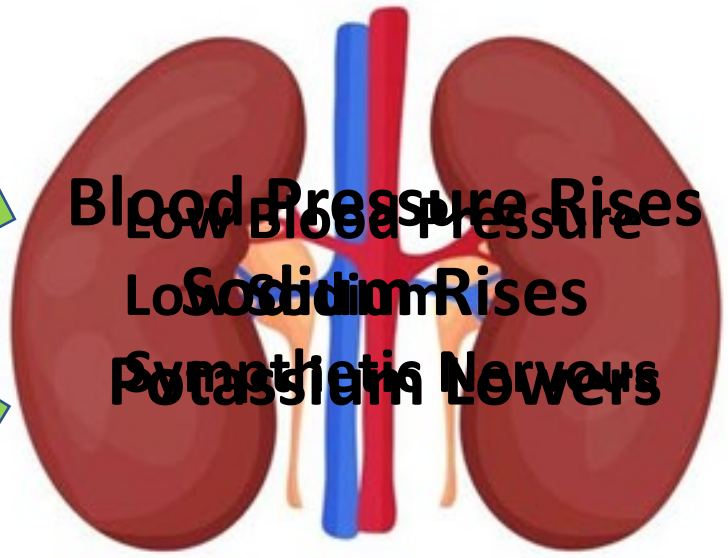
ADH

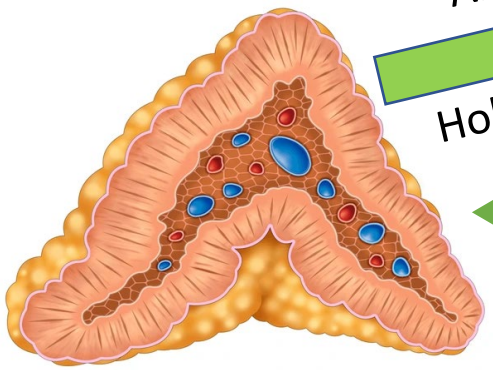
Hold onto water

ACTH

Aldosterone

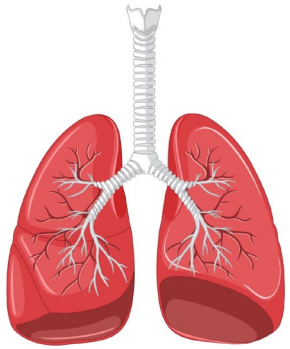
Hold onto sodium





Adrenal Glomerulosa

Angiotensin II



Angiotensin Converting Enzyme

Vasoconstriction

Conn's Syndrome

- High blood pressure
- High sodium
- Low Potassium
- Treated with medicine that blocks aldosterone

Question 3

The RAAS (Renin Angiotensin Aldosterone System) is an essential mechanism for blood pressure control that uses hormones to send signals that can raise blood pressure. Unfortunately for many patients, high blood pressure is now causing more harm than good. When considering the RAAS, what would be a good target for a medication that lowers blood pressure.

A. Block the effect of aldosterone
B. Block the conversion of angiotensin I to angiotensin II
C. Block the receptor for angiotensin II
D. Block the effect of renin
E. All of the above

Question 3 Answer

The RAAS (Renin Angiotensin Aldosterone System) is an essential mechanism for blood pressure control that uses hormones to send signals that can raise blood pressure. Unfortunately for many patients, high blood pressure is now causing more harm than good. When considering the RAAS, what would be a good target for a medication that lowers blood pressure.

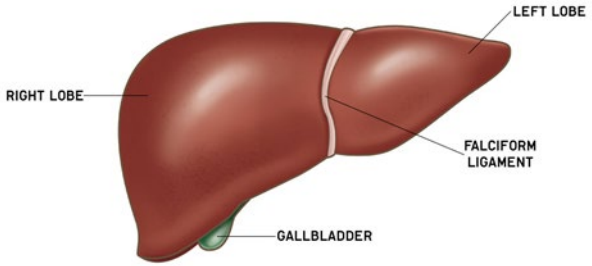
A. Block the effect of aldosterone
B. Block the conversion of angiotensin I to angiotensin II
C. Block the receptor for angiotensin II
D. Block the effect of renin
E. All of the above

Common blood pressure medications include ACE inhibitors, Angiotensin receptor blockers, and mineralocorticoid (aldosterone) receptor antagonists. Although not commonly used, blocking of renin with a Direct Renin Inhibitor can also reduce blood pressure by decreasing the production of angiotensin I.

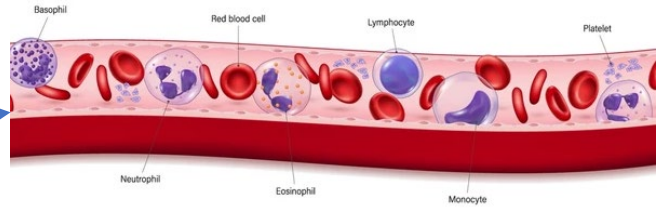
Cortisol

- Corticosteroid
- Regulating stress response
- Helping control of fats, proteins, and carbohydrates
- Suppressing inflammation
- Regulating blood sugar
- Helping control your sleep-wake cycle

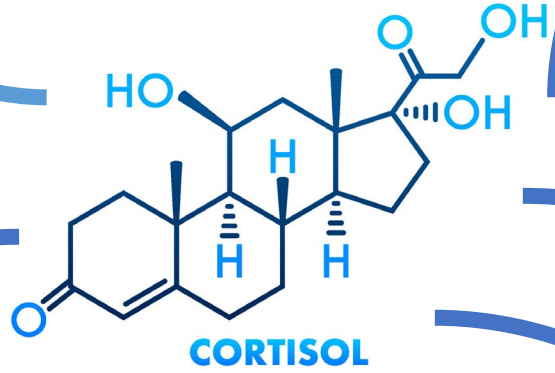
Get Ready For Action

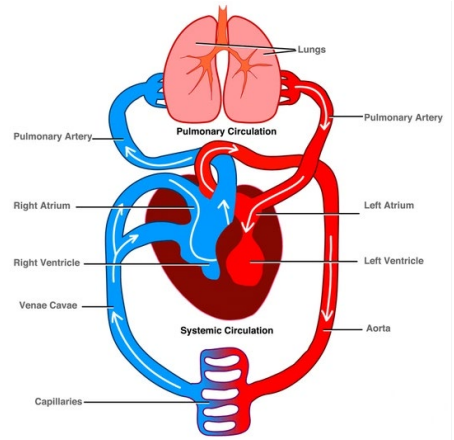


Increase Glucose (gluconeogenesis)

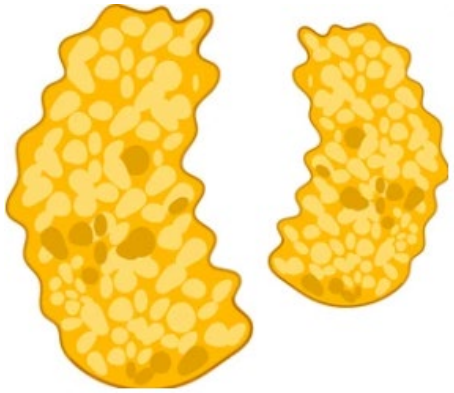


Keeps white blood cells in circulation



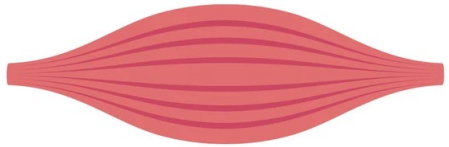


Increases response to sympathetic system

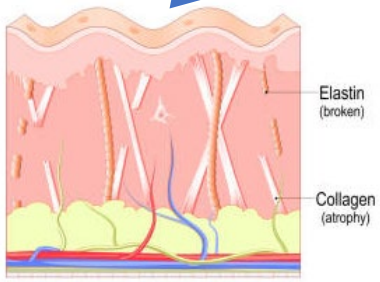


Fat utilization and redistribution

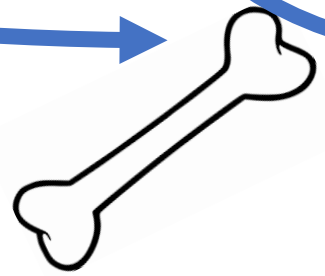
Protein utilization



Muscle breakdown

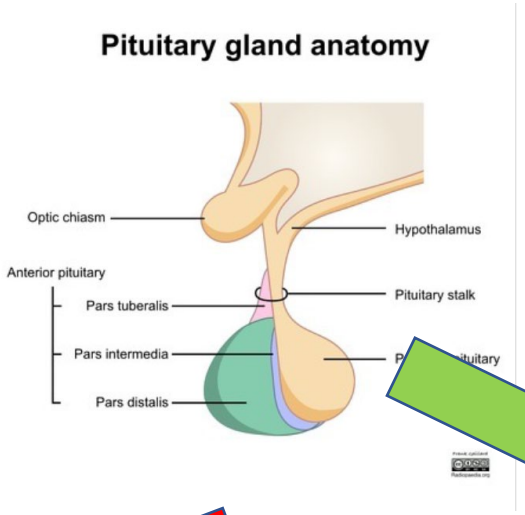


Skin breakdown

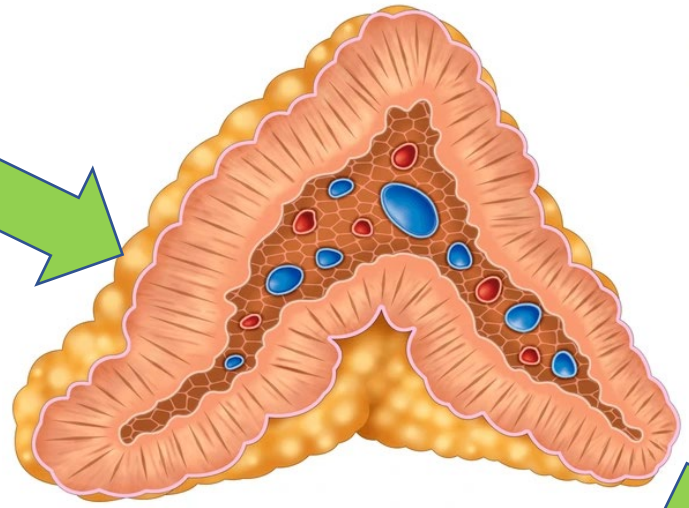


Bone thinning

Stimulation



ACTH

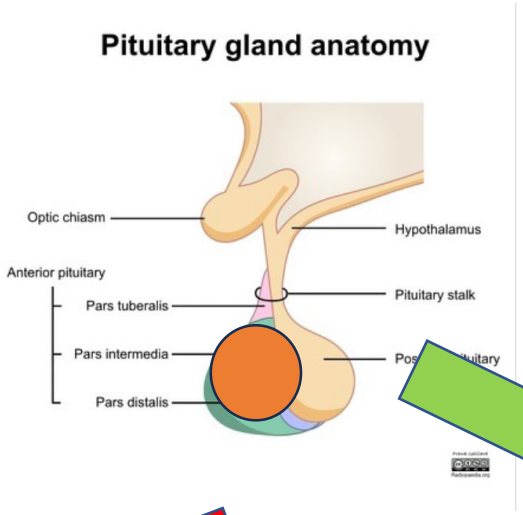


- ↑ blood pressure
- ↑ glucose
- ↑ appetite
- ↑ increase fat stores
- ↑ protein use from muscle
- ↓ immune system

Cortisol

Cushing Syndrome

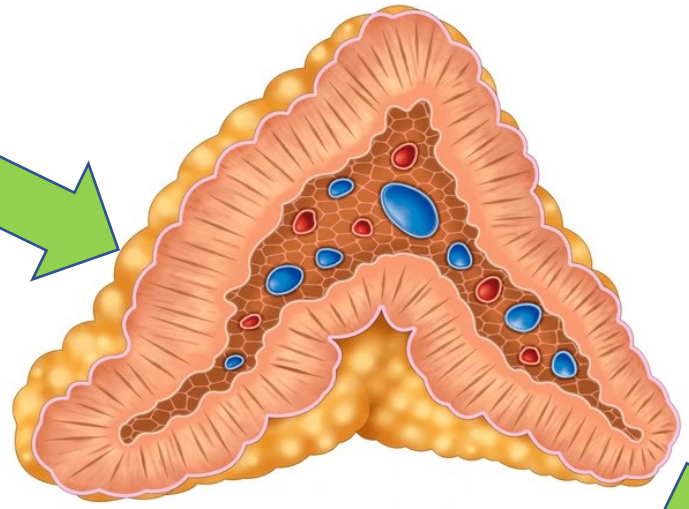
Too much cortisol



Cushing's Syndrome: Too much Cortisol

- ↑ blood pressure
- ↑ glucose
- ↑ Fat deposits in abdomen, face, and between shoulder blades
- ↓ muscle mass
- ↓ bone mass
- ↓ wound healing
- Stretch marks
- Easy bruising
- Acne

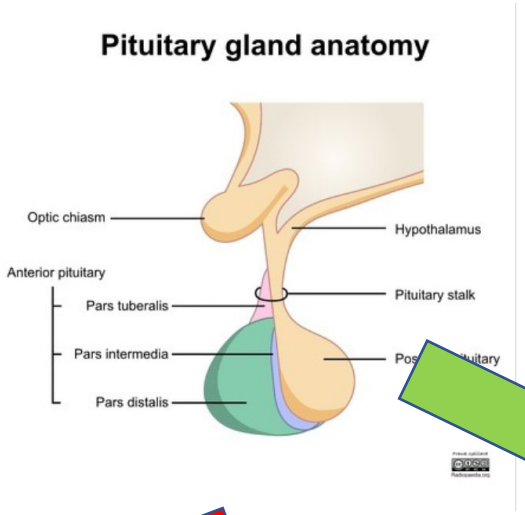
ACTH



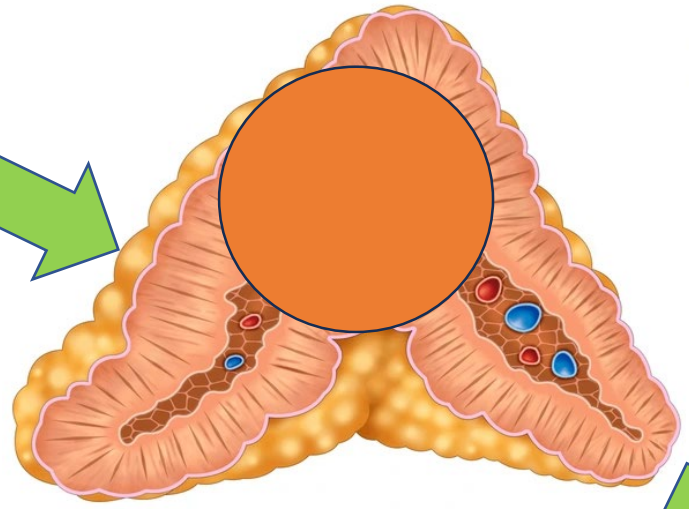
Cortisol
Aldosterone
DHEA

Pituitary Tumor:
High ACTH
High Cortisol

Cushing's Syndrome: Too much Cortisol



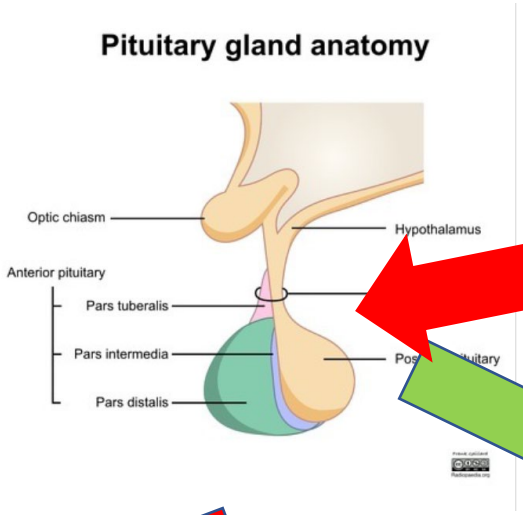
ACTH



- ↑ blood pressure
- ↑ glucose
- ↑ Fat deposits in abdomen, face, and between shoulder blades
- ↓ muscle mass
- ↓ bone mass
- ↓ wound healing
- Stretch marks
- Easy bruising
- Acne

Cortisol

Adrenal Tumor:
Low ACTH
High Cortisol

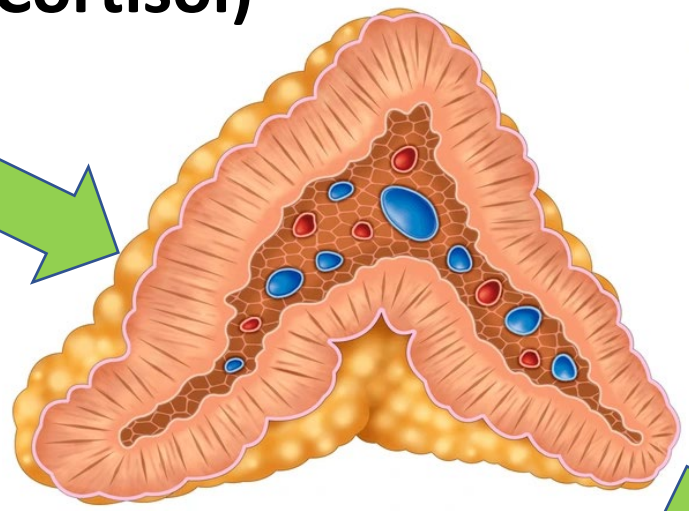


Cushing's Syndrome: Too much Cortisol

Cortisone
(=Cortisol)

- ↑ blood pressure
- ↑ glucose
- ↑ Fat deposits in abdomen, face, and between shoulder blades
- ↓ muscle mass
- ↓ bone mass
- ↓ wound healing
- Stretch marks
- Easy bruising
- Acne

ACTH

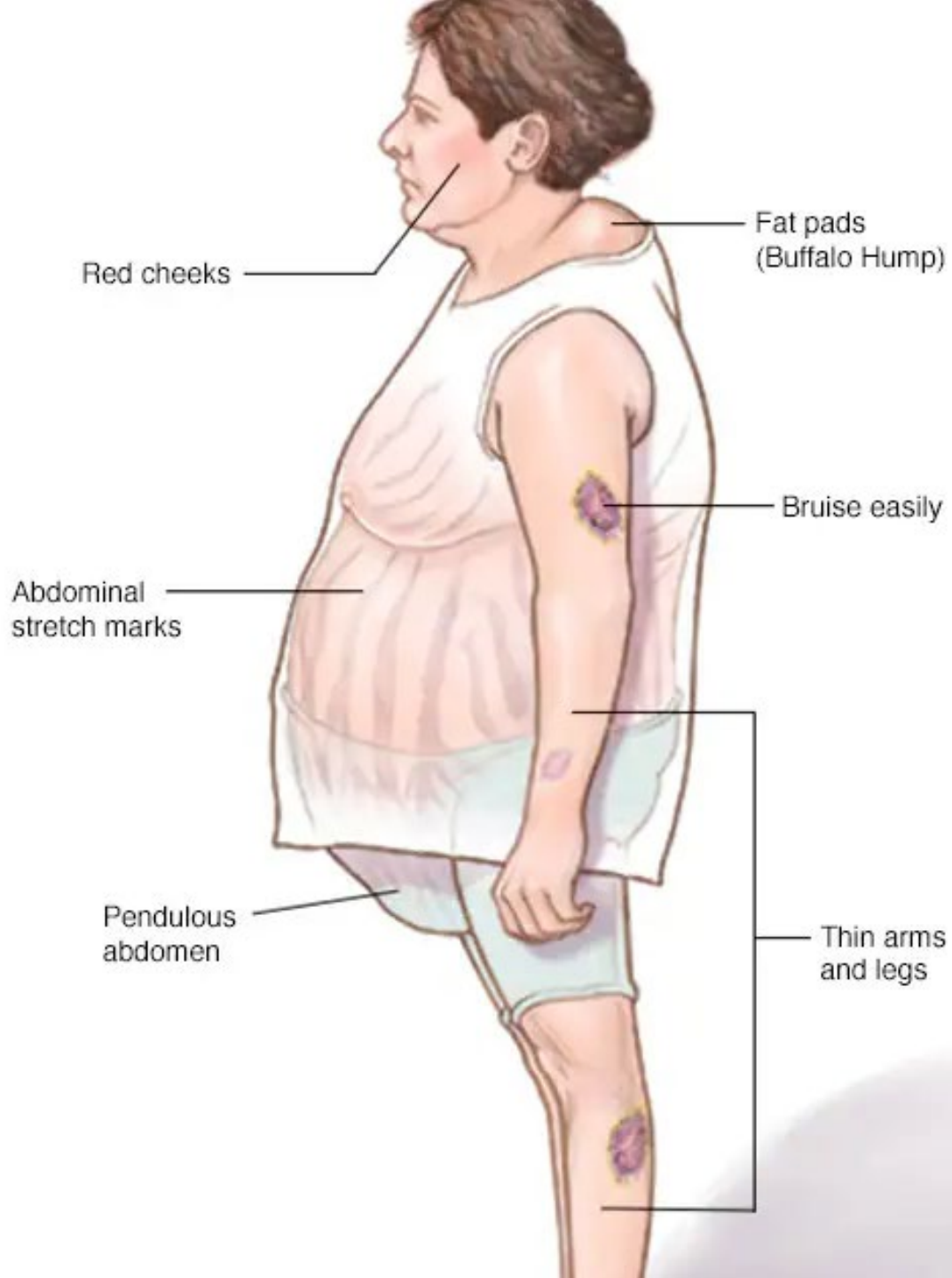


Cortisol

Taking Cortisone Medicine (Exogenous):
Low ACTH
High or Low Cortisol depending on medicine

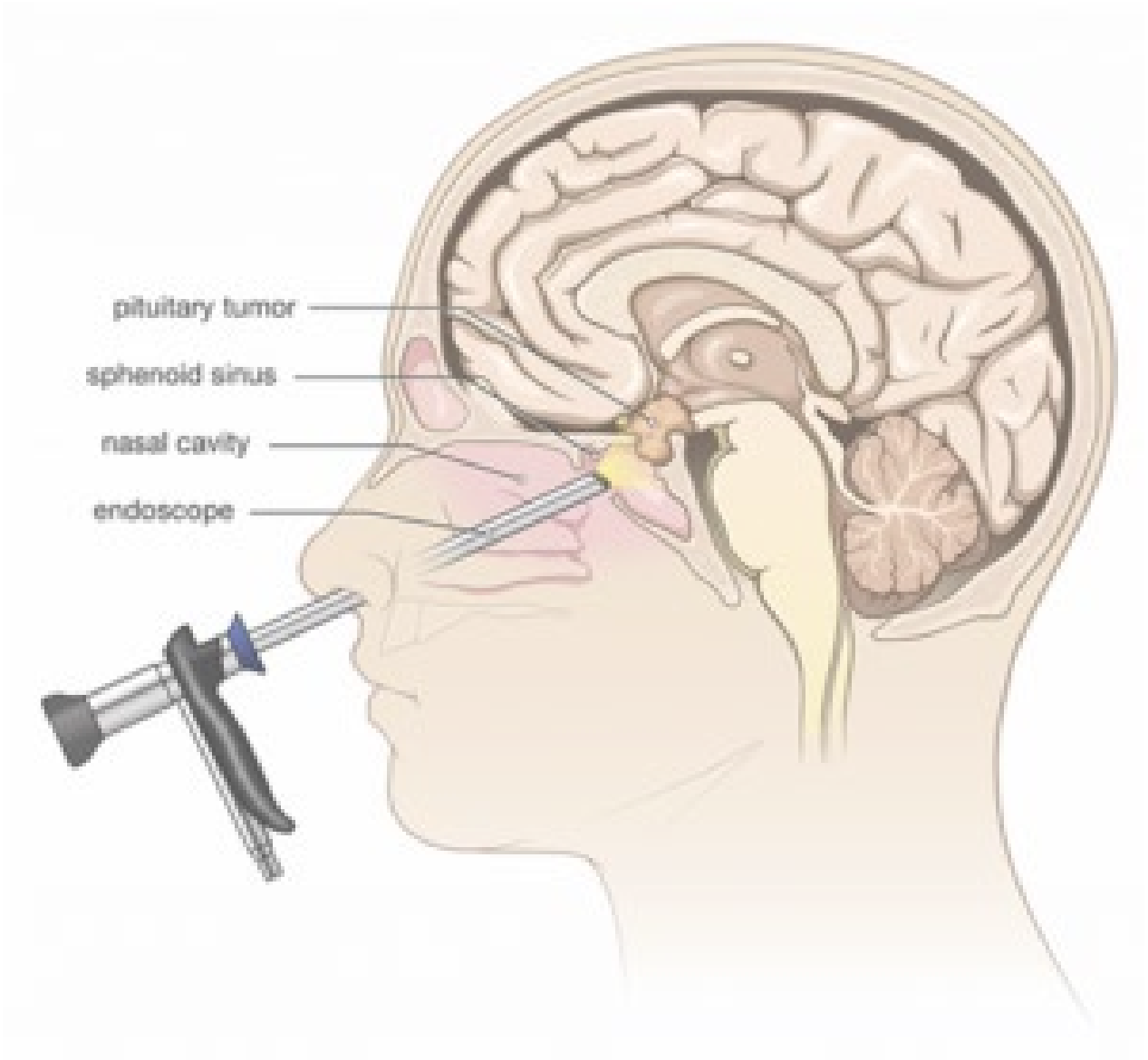
Cushing's Syndrome: Too much cortisol

- ↑ blood pressure
- ↑ glucose
- ↑ Fat deposits in abdomen, face, and between shoulder blades
- ↓ muscle mass
- ↓ bone mass
- ↓ wound healing
- Stretch marks
- Easy bruising
- Acne



Treatment of Cushing's Syndrome

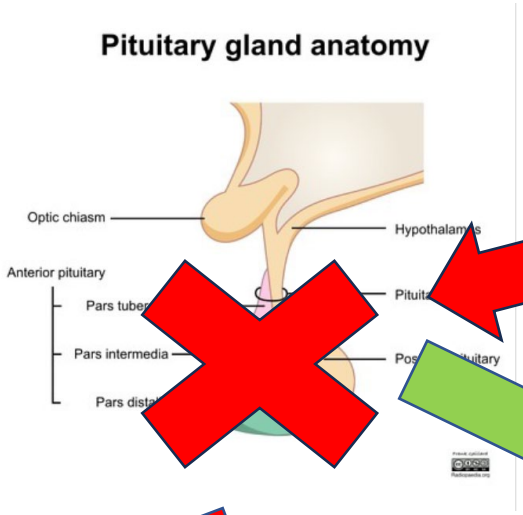
- **Pituitary tumor**
  - **Surgery**
  - **Radiation**
  - **Medication**
    - **Cabergoline reduces ACTH production**
    - **Ketoconazole reduces cortisol production**
    - **Mifepristone blocks effects of cortisol**
- **Adrenal tumor**
  - **Surgery**
- **Too much cortisone medicine**
  - **Slowly reduce medicine**



Adrenal Insufficiency

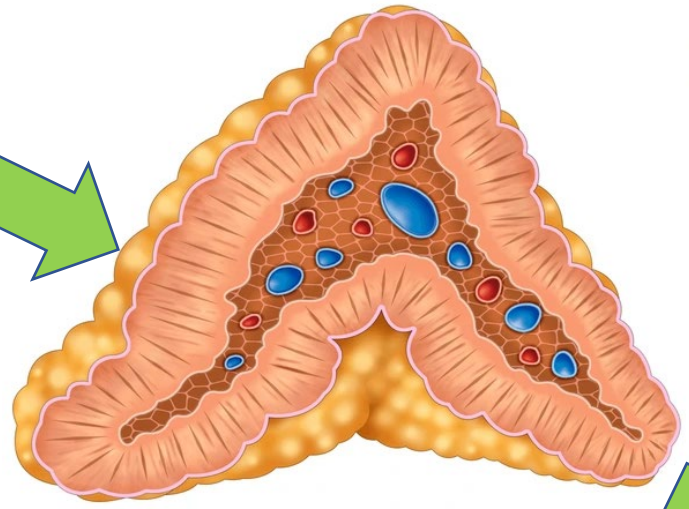
Low cortisol and aldosterone

Adrenal Insufficiency: not enough cortisol



Cortisone

ACTH

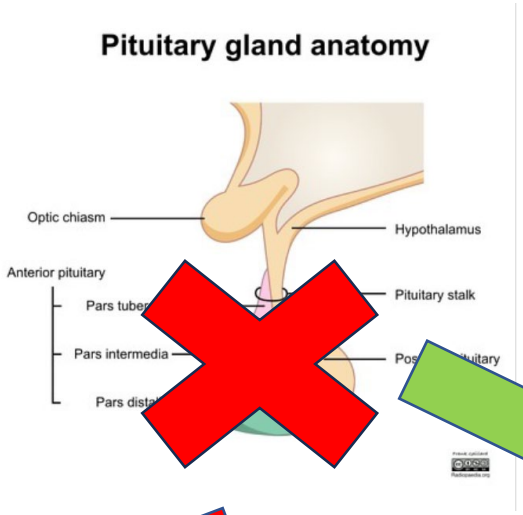


- fatigue
- weakness
- weight loss
- low temperature
- low blood pressure
- low sugar

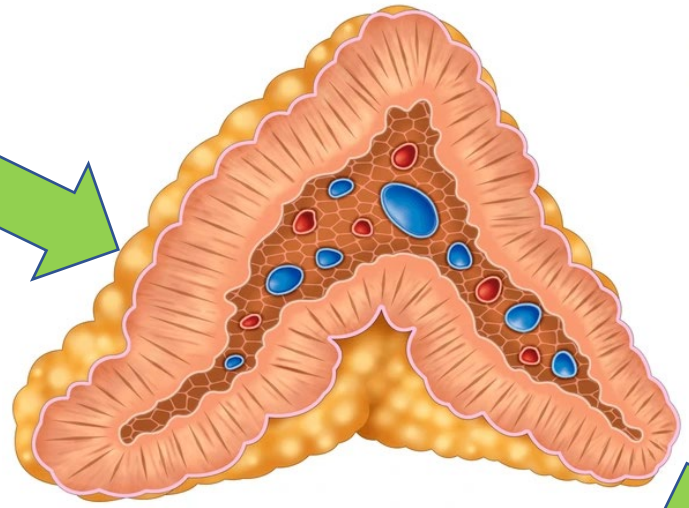
Cortisol

Pituitary Suppression:
Low ACTH
Low Cortisol

Adrenal Insufficiency: not enough cortisol



ACTH

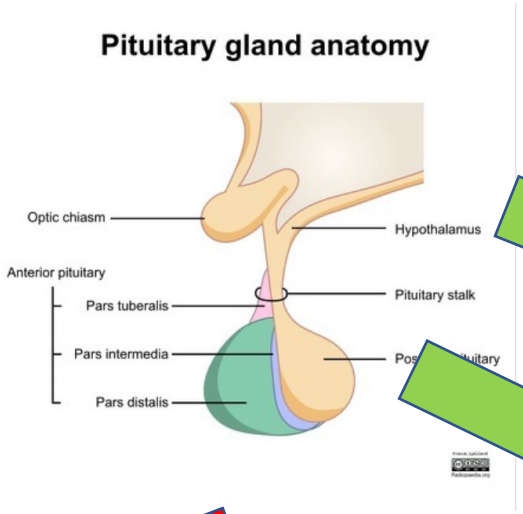


- fatigue
- weakness
- weight loss
- low temperature
- low blood pressure
- Low sugar

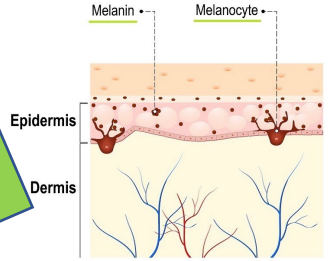
Cortisol

Pituitary failure:
Low ACTH
Low Cortisol

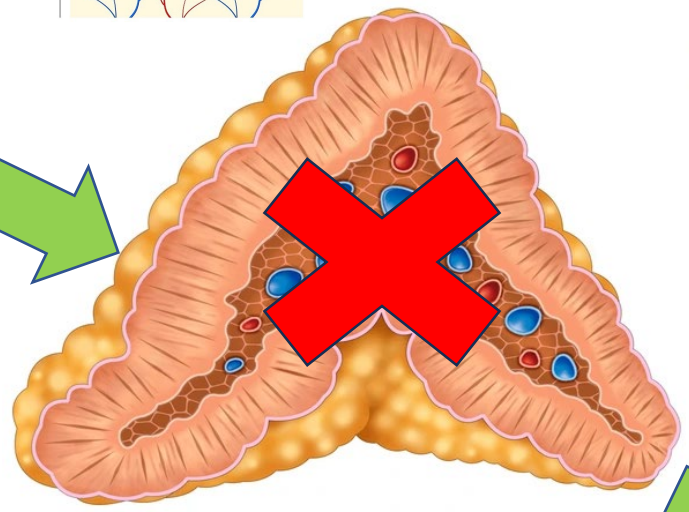
Adrenal Insufficiency: not enough cortisol



MSH



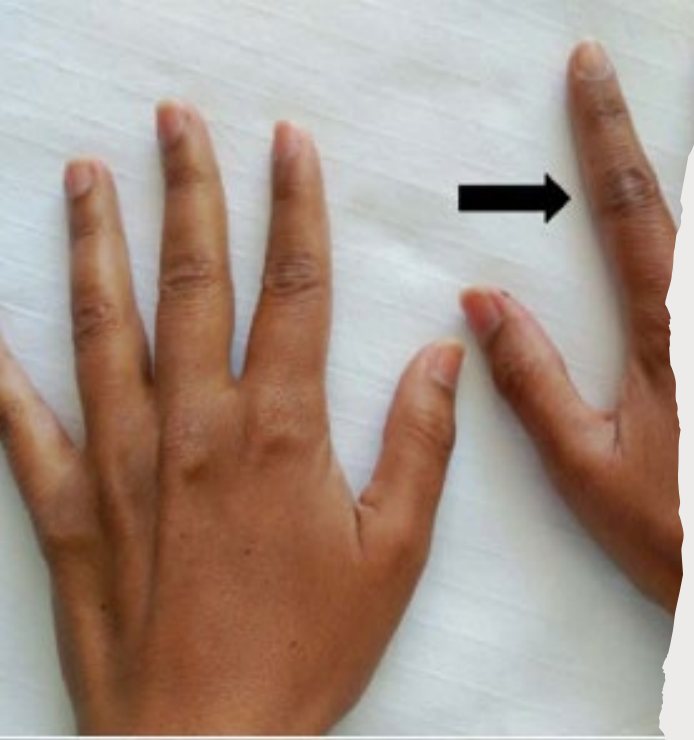
ACTH

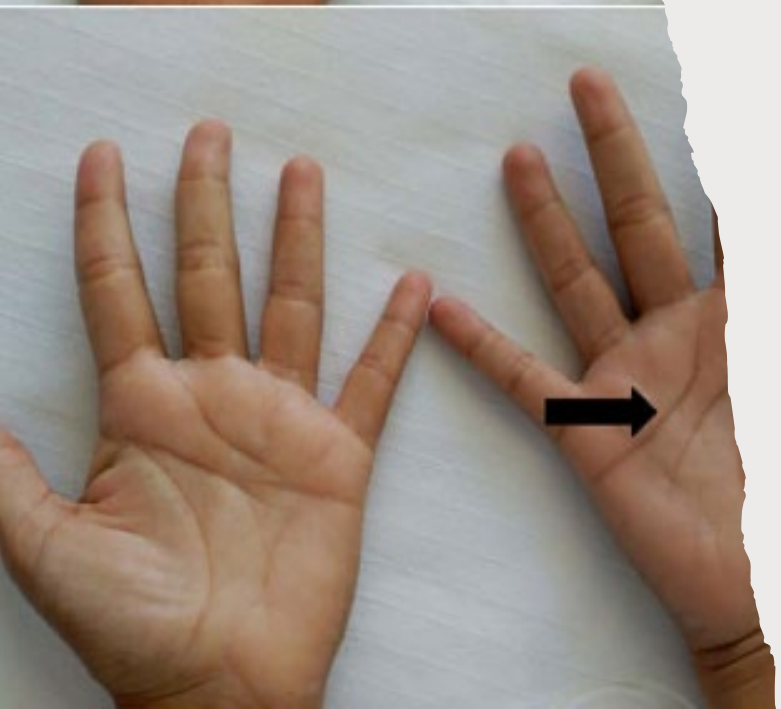


- fatigue
- weakness
- weight loss
- low temperature
- low blood pressure
- low sugar
- low sodium
- high potassium
- tan skin and membranes

Adrenal failure:
High ACTH
Low Cortisol

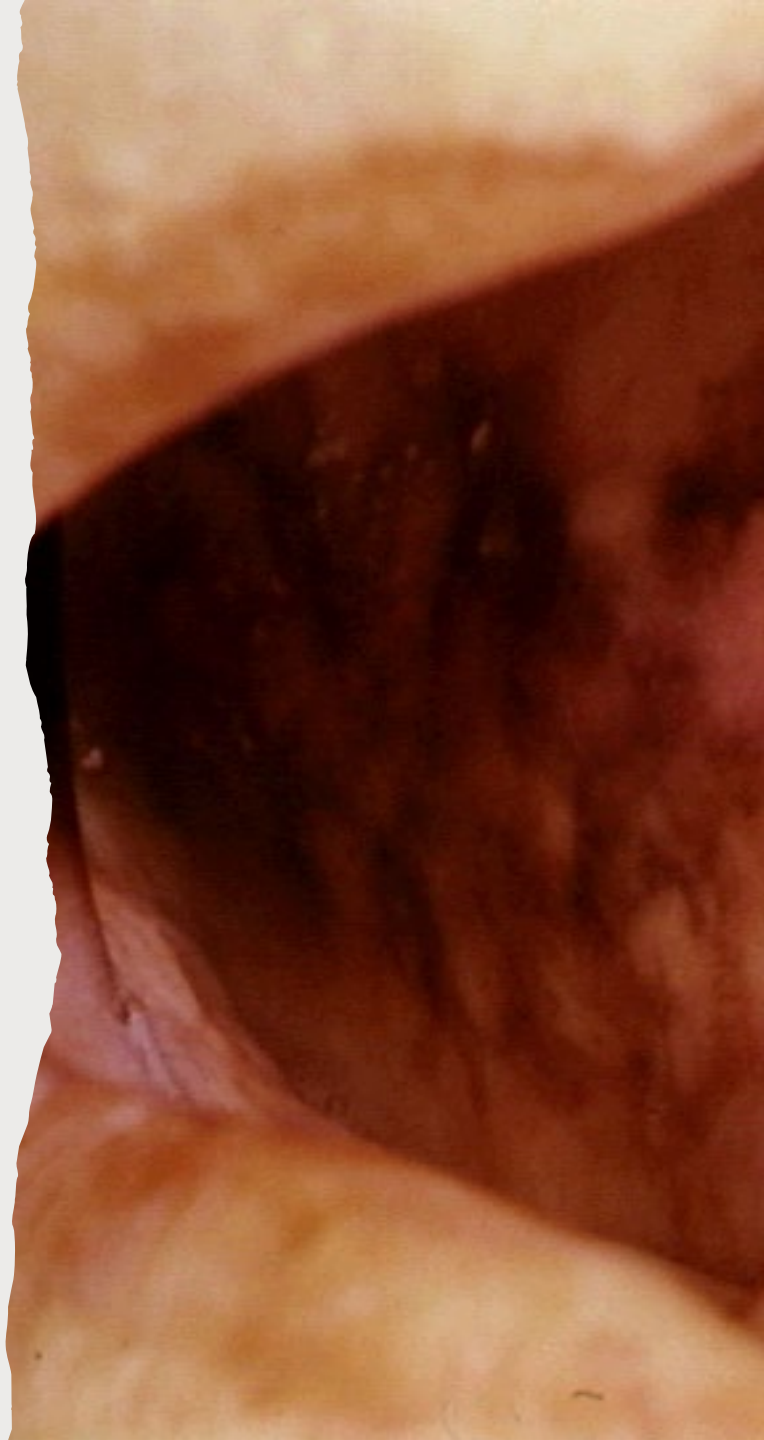
Cortisol
Aldosterone
DHEA





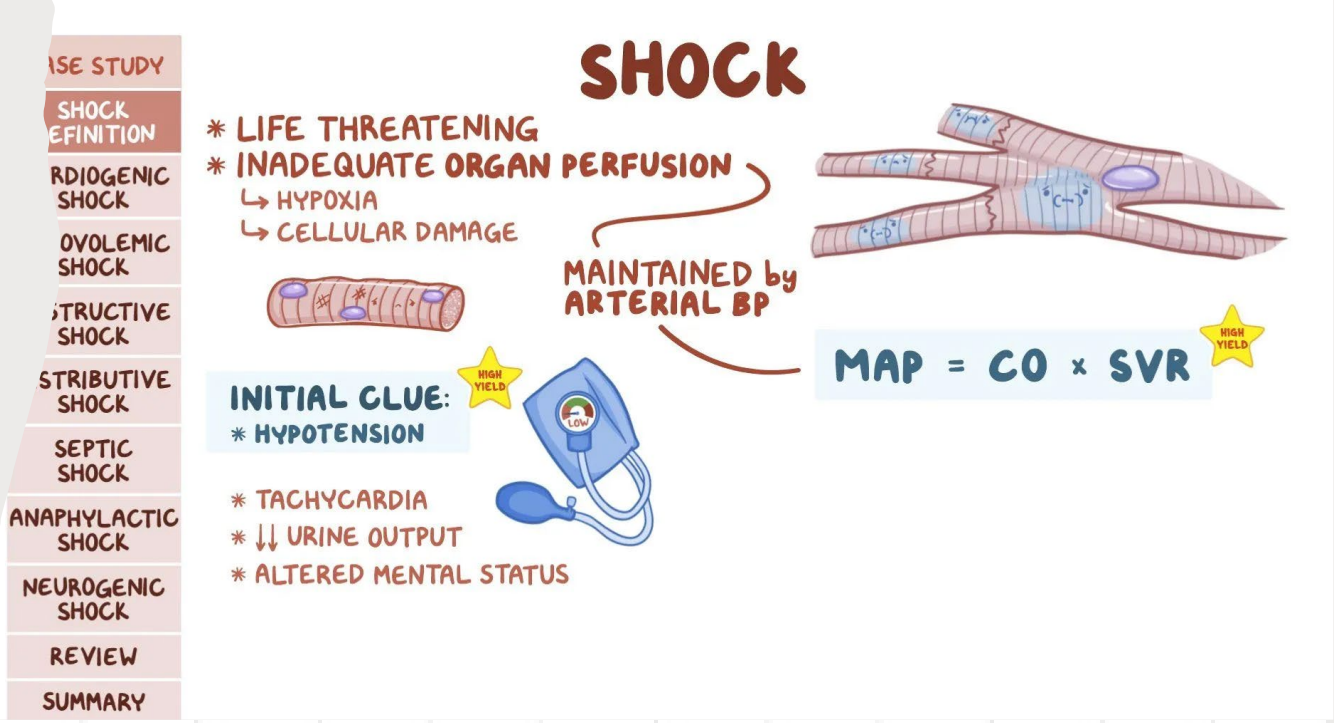
Adrenal Insufficiency

- Addison's disease = Adrenal gland failure
  - Fatigue
  - Muscle weakness
  - Weight loss
  - Low body temperature
  - Low blood pressure
  - Low blood sugar
  - Low sodium
  - High potassium
  - Darkened skin and mucus membranes



Addisonian Crisis

- Life threatening
  - Low blood sugar
  - Low blood pressure
  - High potassium
- Not enough cortisol and aldosterone
  - Triggered by stress
  - Surgery
  - Infection
  - Unable to take medicine for Addison's



Treatment of Adrenal Gland Failure

- **Hydrocortisone – replaces cortisol**
  - **Daily dose – 5-10 mg 3 times per day**
  - **Sick day dosing**
    - **Mild stressor (cold virus, fever, minor surgery)**
      - **2 x normal dose for 2-3 days**
    - **Moderate stressor (general anesthesia)**
      - **2-3 x daily dose on surgery day**
    - **Major stressor (critical illness)**
      - **100-200 mg per day**
- **Fludrocortisone – replaces aldosterone**
- **DHEA – can help energy and sexual function**

Question 4

A patient arrives to the ER with severely low blood pressure. The family reports they had the flu the past 3 days and were unable to take their normal medicines.

Vital signs, Heart rate 100, Temperature 96.5, Respirations 22, blood pressure 72/35

On physical exam the patient is nearly unconscious with cold clammy skin. The skin appears darkened on their hands and there are some darkened areas on their lips.

Lab studies show a low blood sugar, low sodium, and high potassium level.

In addition to iv fluids for volume replacement, the most important next step of treatment is?

A. Starting IV antibiotics
B. Give Levothyroxine 100 mcg
C. Give 20 mg of hydrocortisone
D. Give 200 mg of hydrocortisone
E. Give 50 mg of spironolactone

Question 4 Answer

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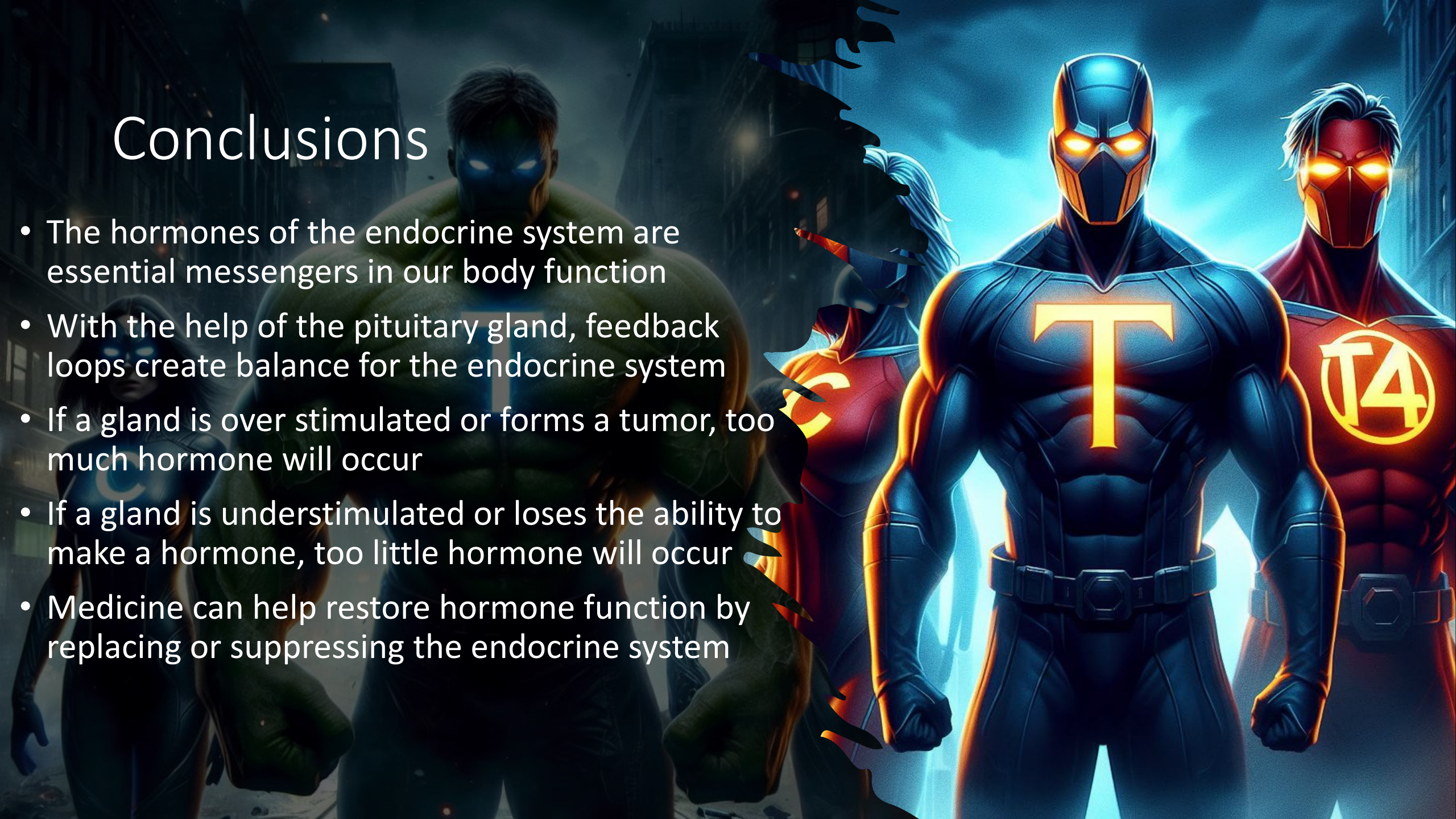
This patient is having symptoms of shock and an adrenal crisis and needs immediate treatment with stress dose hydrocortisone. This patient likely missed their doses of home medication because of illness and then had a serious stressor from the flu. Without replacement of high dose cortisone, the patient could be facing worsening shock, serious irregular, heart rhythm and death.

Conclusions

- The hormones of the endocrine system are essential messengers in our body function
- With the help of the pituitary gland, feedback loops create balance for the endocrine system
- If a gland is over stimulated or forms a tumor, too much hormone will occur
- If a gland is understimulated or loses the ability to make a hormone, too little hormone will occur
- Medicine can help restore hormone function by replacing or suppressing the endocrine system




T4
PTH

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