

# Endocrine Regulation of Blood Pressure

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# Learning Objectives

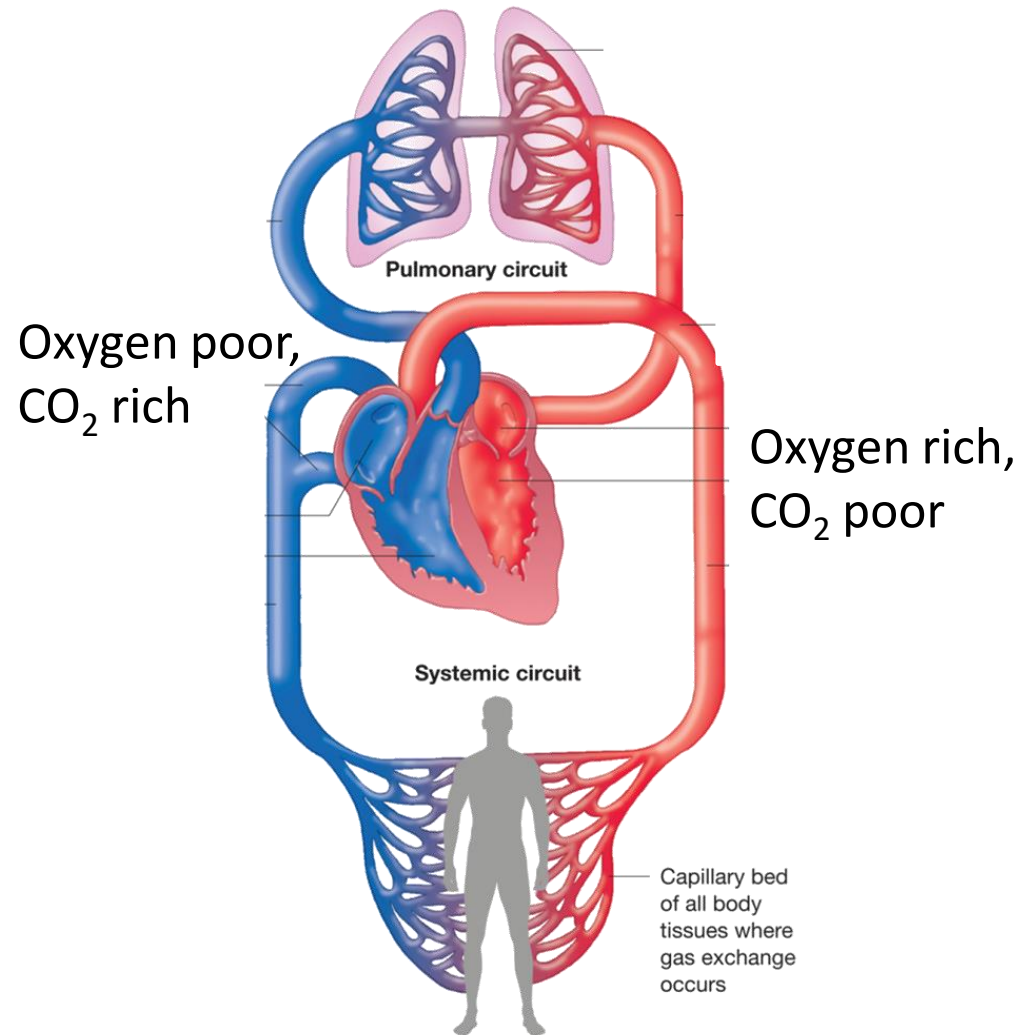
1. List the hormones that regulate blood pressure.
2. Compare the presentation of endocrine diseases that may cause hypertension.
3. Interpret laboratory testing results for primary hyperaldosteronism and diabetes insipidus.

# Outline

- Blood pressure
  - Regulation
- Hypertension
  - Primary hyperaldosteronism
  - Laboratory testing
  - Rare causes of apparent mineralocorticoid excess
- Hypotension
  - Diabetes insipidus
  - Laboratory testing

# Why is appropriate blood pressure important?

- Needed to ensure nutrient and oxygen delivery to tissues
- Too high blood pressure → **hypertension**
- Too low blood pressure → **hypotension**



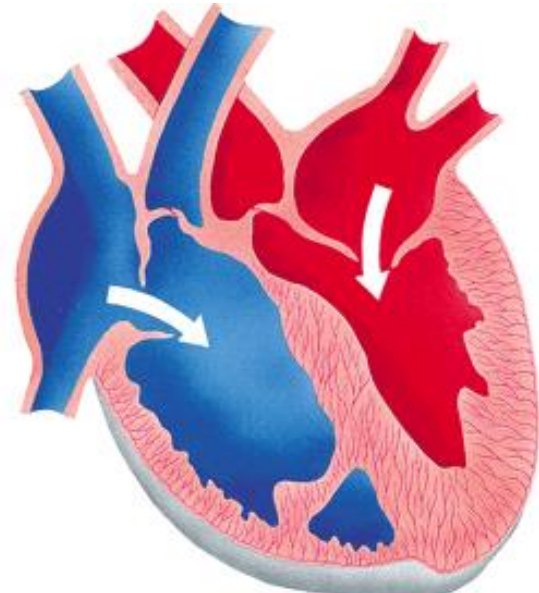
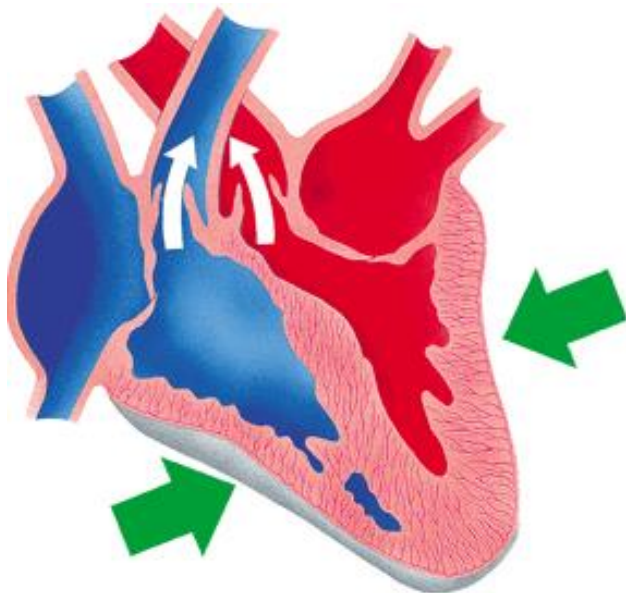
# Blood Pressure Components

$\frac{120}{80}$

Systolic blood pressure (SBP)  
Diastolic blood pressure (DBP)

Systole: contraction

Diastole: relaxation



# What factors change blood pressure?

## 1. Cardiac output

- Depends on blood volume
- Average adult has 5 liters of blood



Larger volume → ↑ pressure



Smaller volume → ↓ pressure

# What factors change blood pressure?

1. Cardiac output

2. Vascular resistance

- Depends on the size of blood vessels
- Range from 5-10  $\mu\text{m}$  to 2-3 cm!



Vasoconstriction

Smaller size  $\rightarrow$   $\uparrow$  pressure



Vasodilation

Larger size  $\rightarrow$   $\downarrow$  pressure

# How is blood pressure controlled?

Increase blood pressure

Increase blood volume

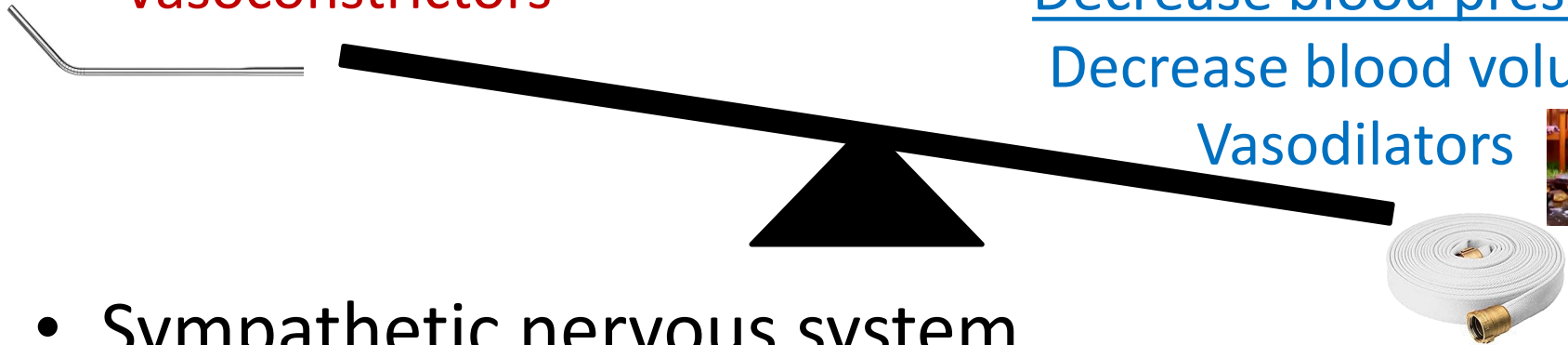
Vasoconstrictors



Decrease blood pressure

Decrease blood volume

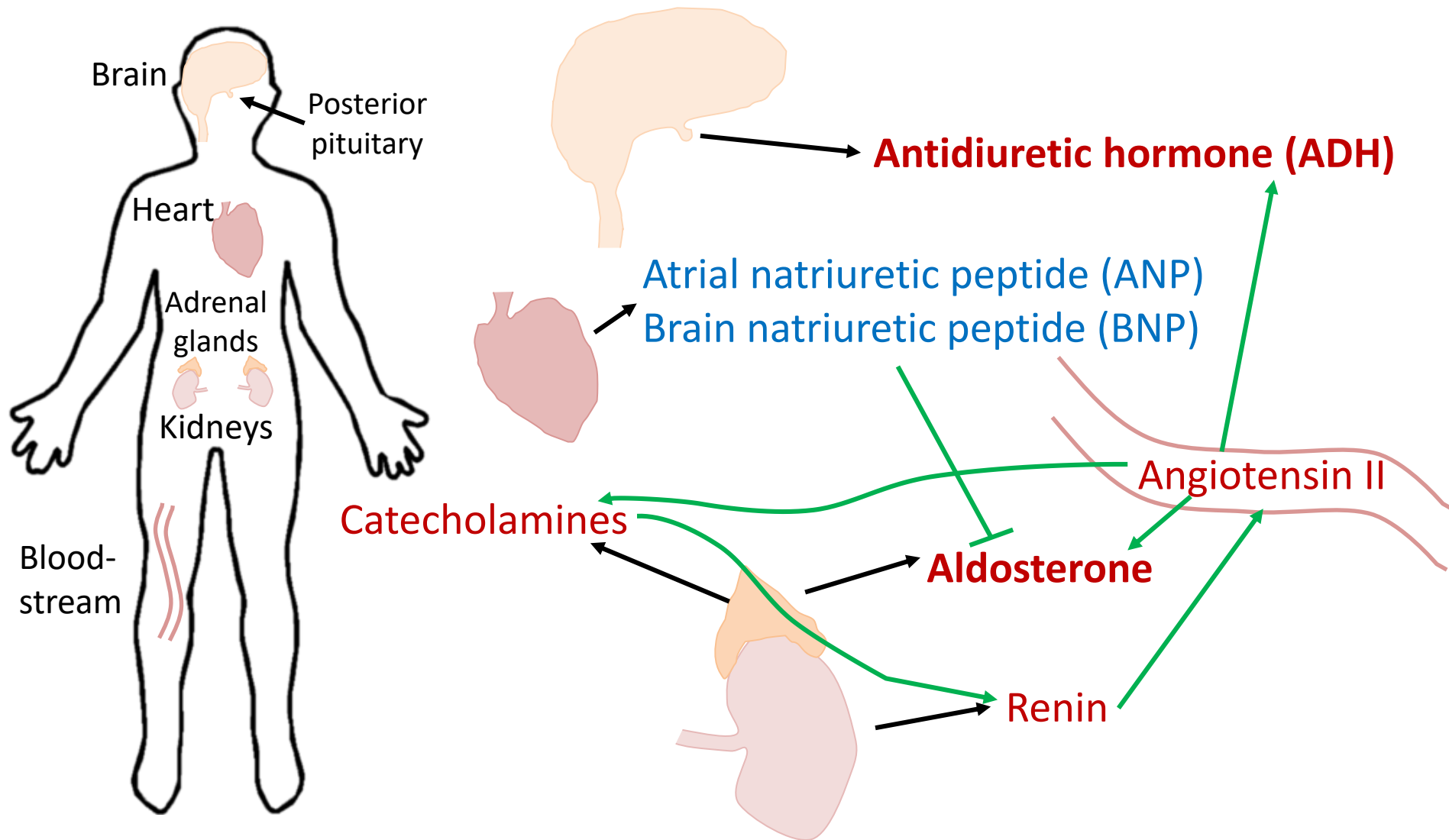
Vasodilators



- Sympathetic nervous system
- Endocrine system
  - Hormones affect blood volume and blood vessel size
- Kidney
  - Produce antihypertensive substances



# Endocrine Interconnection

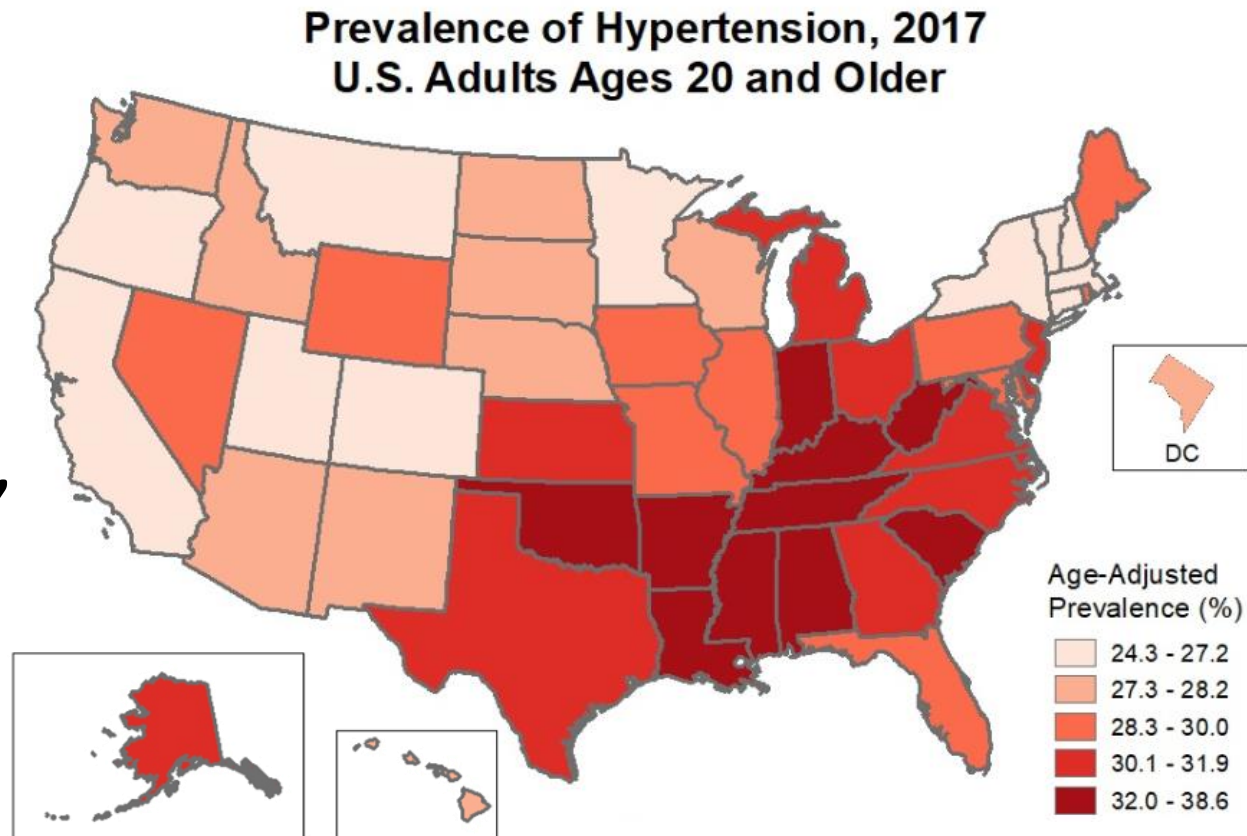


# Outline

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# Hypertension (HTN) is a significant public health concern

- Estimated US prevalence among adults: 46%
- Increases risk of heart attack, heart failure, kidney disease and stroke



\*Based on self-report

# Stages of Hypertension

- Change in 2017 to lower cut-off increased prevalence

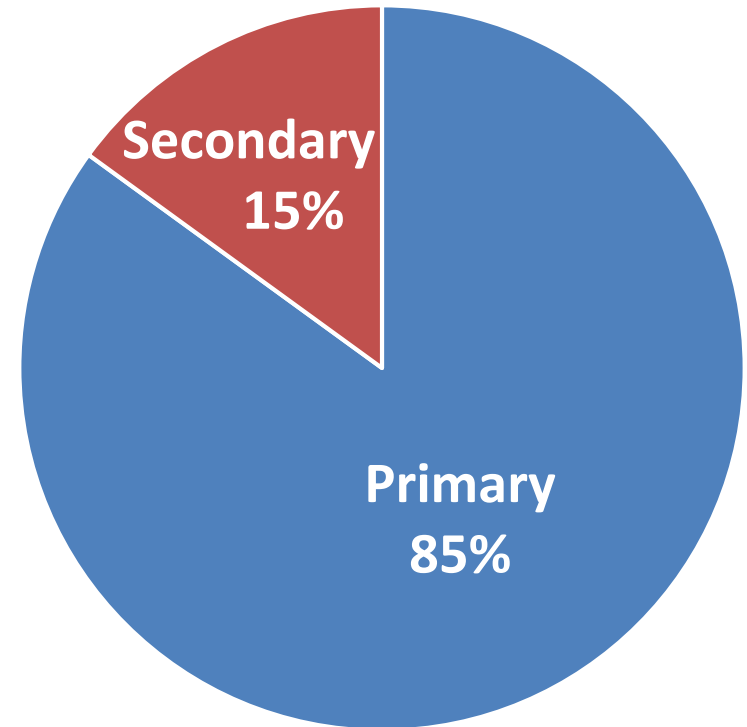
Category	SBP		DBP
Healthy	<120 mmHg	and	<80 mmHg
Elevated	120-129 mmHg	and	<80 mmHg
Stage 1 HTN	130-139 mmHg	or	80-89 mmHg
Stage 2 HTN	≥140 mmHg	or	≥90 mmHg

- No perfect cut-off to eliminate risk
  - Often asymptomatic until severe complications develop



# Classification of Hypertension

- Primary hypertension
  - Contributing factors:
    - Genetics
    - Stress
    - Obesity
    - Smoking
    - Physical inactivity
    - High-salt diet
- Secondary hypertension
  - Renal or endocrine malfunction

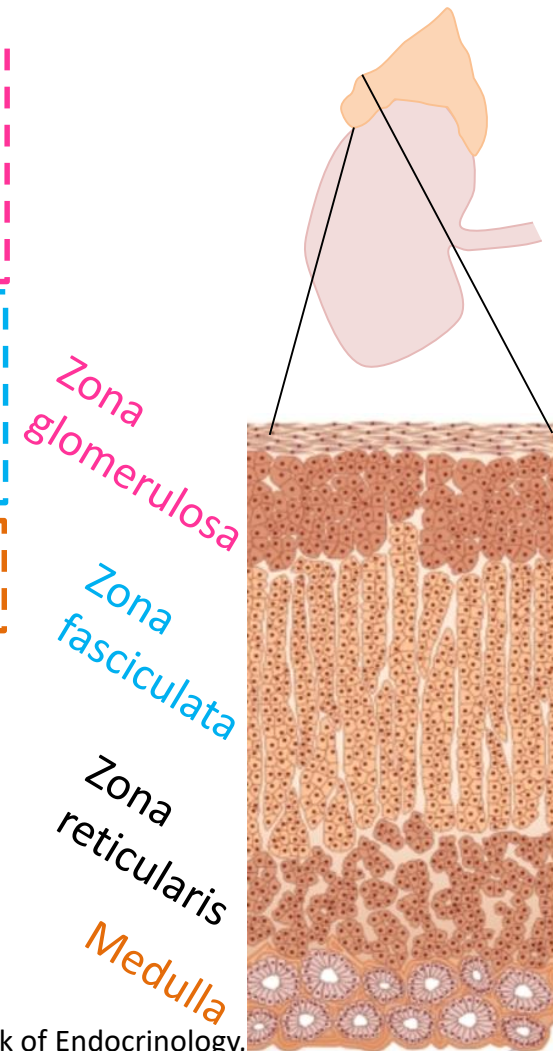


# What endocrine disorders may cause hypertension?

- |                                     |          |
|-------------------------------------|----------|
| • Hyperaldosteronism                | 8-20%    |
| • Congenital adrenal hyperplasia    | Rare     |
| • Cushing syndrome                  | 0.1%     |
| • Apparent mineralocorticoid excess | Rare     |
| • Increased catecholamines          | 0.1-0.6% |
| • Acromegaly                        | Rare     |
| • Hyperthyroidism                   | <1%      |
| • Hypothyroidism                    | <1%      |

# What endocrine disorders may cause hypertension?

- Hyperaldosteronism
- Congenital adrenal hyperplasia
- Cushing syndrome
- Apparent mineralocorticoid excess
- Increased catecholamines
- Acromegaly
- Hyperthyroidism
- Hypothyroidism



"Chapter 11," *Robbins and Cotran Pathological Basis of Disease*, 2010; "Chapter 16," *Williams Textbook of Endocrinology*, hypertension in adults," *Up to Date*, 2019; "Evaluation of secondary hypertension," *Up to Date*, 2019; 2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults; Image adapted from <https://adrenoleukodystrophy.info/treatment-options/the-adrenal-gland>.

# What other symptoms might patients have?

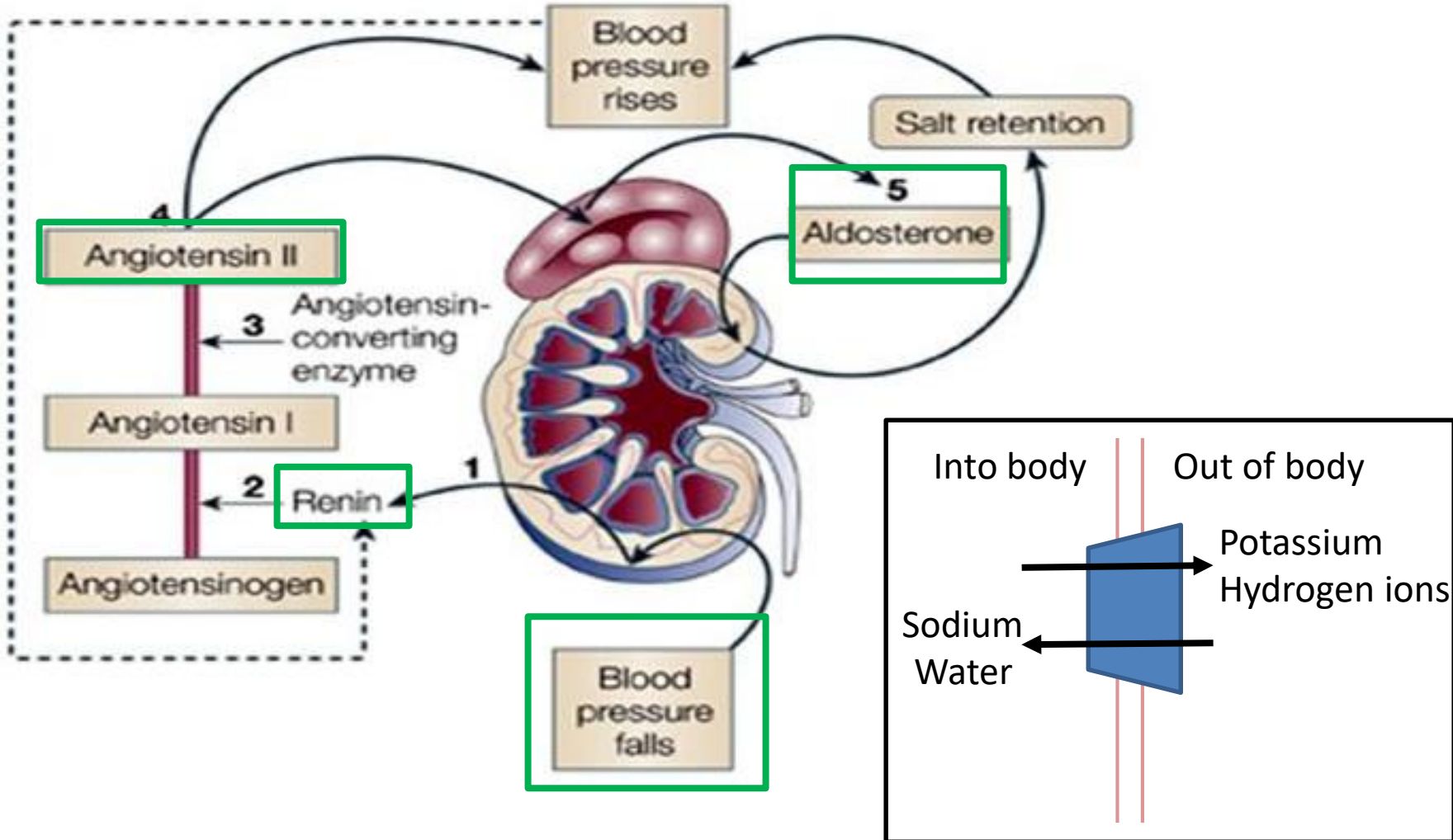
Diagnosis	Signs and Symptoms
Hyperaldosteronism	HTN, hypokalemia, muscle weakness
Cushing syndrome	Central obesity, facial changes, glucose intolerance, purple striae
Acromegaly	Facial changes, increasing size of hands/feet
Hyperthyroidism	Weight loss, warm skin, heat intolerance, nervousness, diarrhea
Hypothyroidism	Weight gain, dry skin, cold intolerance, constipation



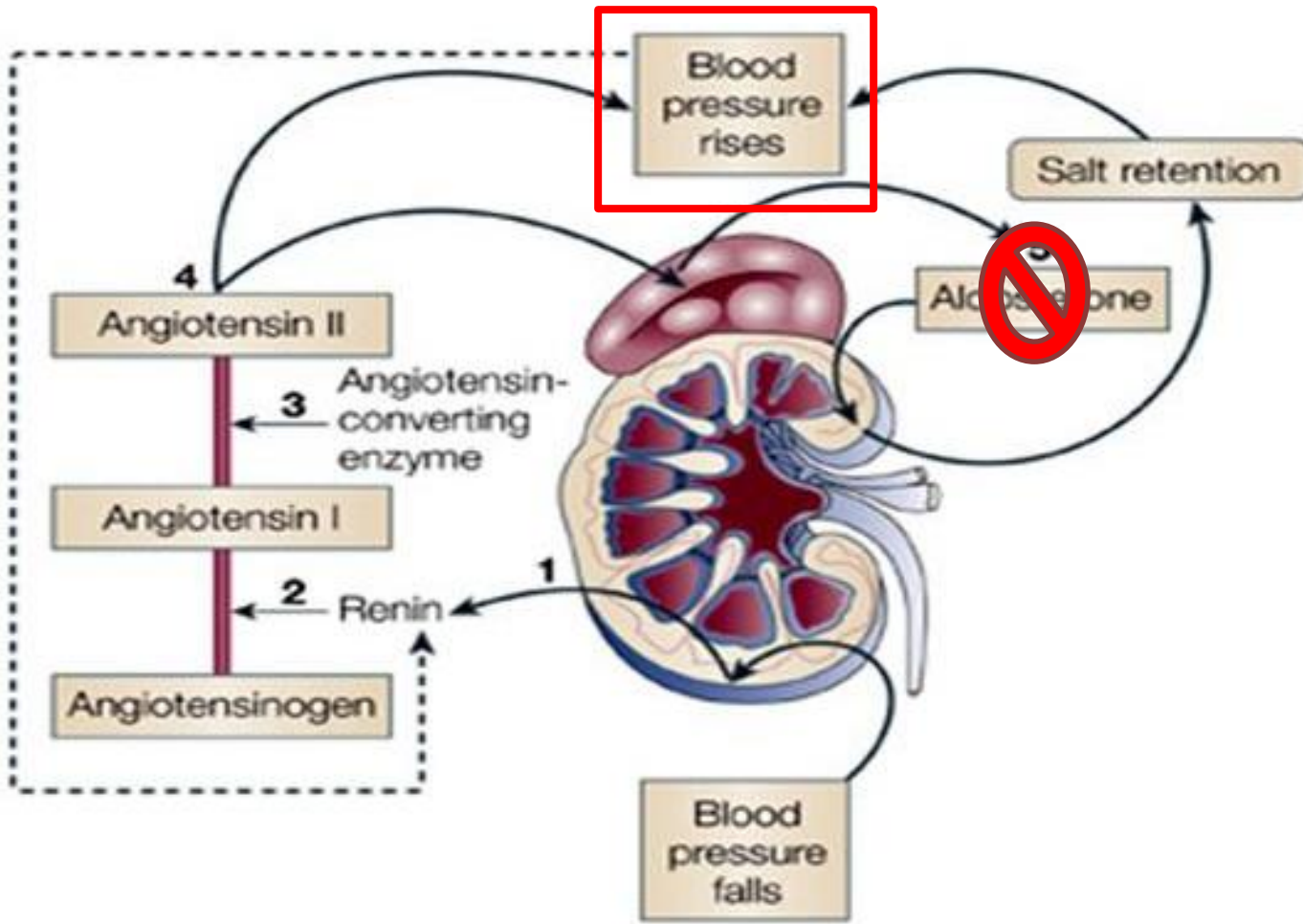
# How do physicians know to consider secondary testing?

- Abrupt onset of HTN
- New onset of HTN at early or late age
- Initial presentation with stage 2 HTN
- Clinical clue(s) suggesting specific cause
- Drug resistant HTN
  - Occurs when goal BP is not obtained with 3 different classes of medications, or is obtained with  $\geq 4$  medications
  - Up to 14.8% of treated hypertensive patients

# Renin-Aldosterone System



# Renin-Aldosterone System



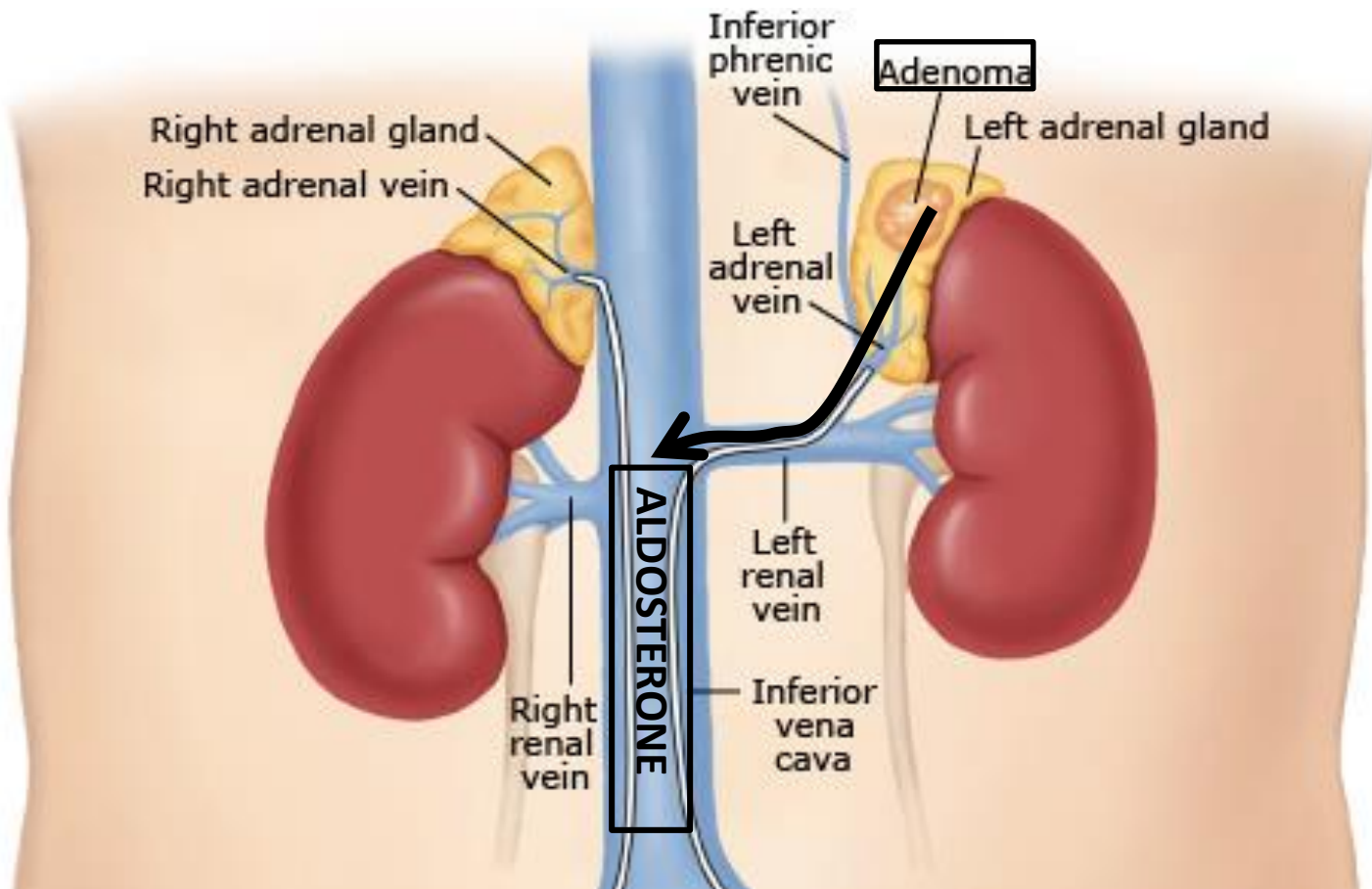
# What is primary hyperaldosteronism?

- High blood pressure due to uncontrolled excretion of aldosterone
  - Most common:
    - Aldosterone-producing adenoma
    - Bilateral idiopathic hyperaldosteronism
  - Relatively rare:
    - Familial hyperaldosteronism
    - Unilateral adrenal hyperplasia
    - Adrenal carcinoma
    - Ectopic aldosterone-producing tumor
- Increased risk for cardiovascular complications

One or both  
adrenal glands?

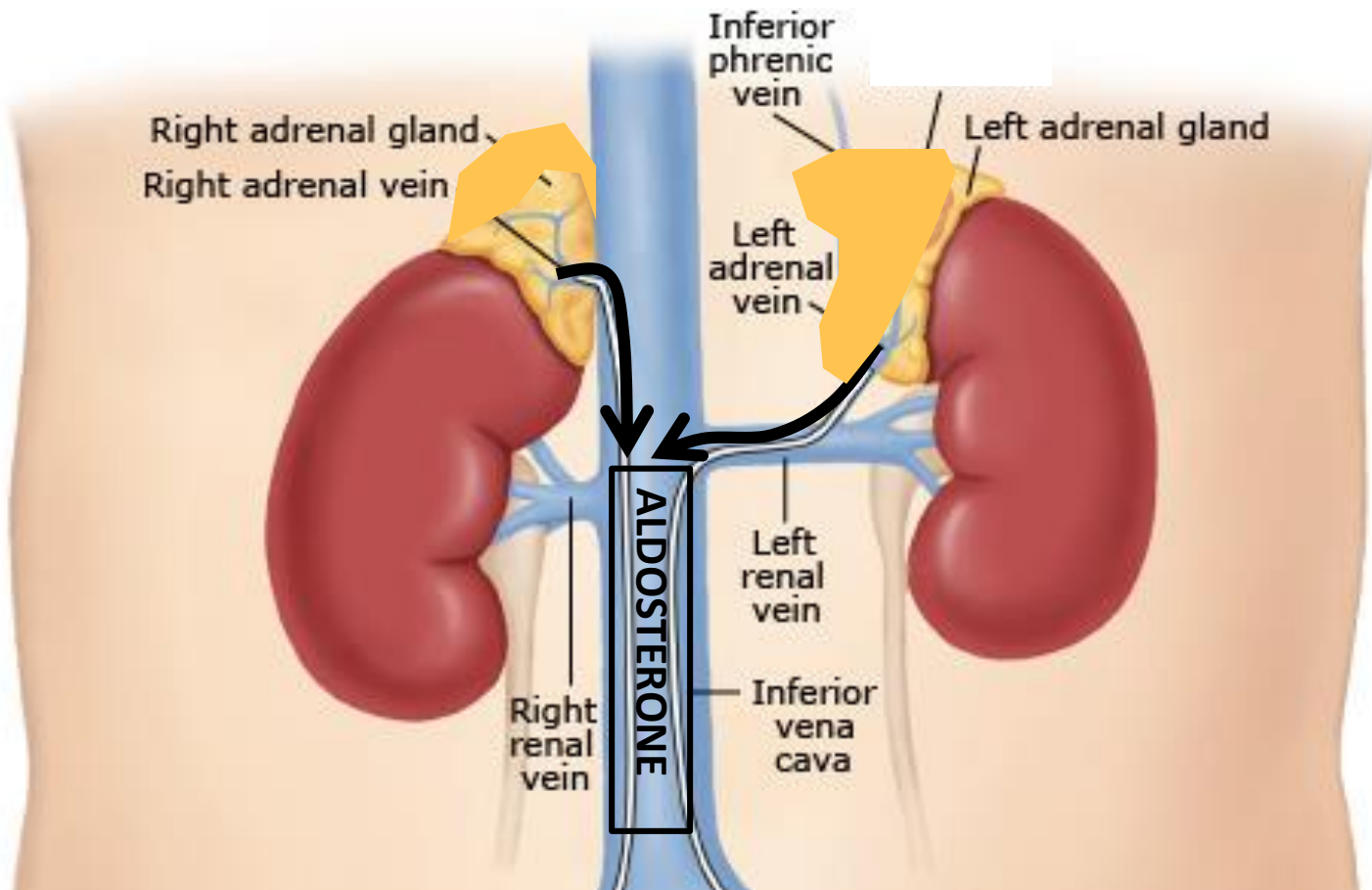
# What is primary hyperaldosteronism?

- One adrenal gland affected → aldosterone producing adenoma (~30% of cases)



# What is primary hyperaldosteronism?

- Both adrenal glands affected → bilateral adrenal hyperplasia (~60% of cases)



# Testing for primary hyperaldosteronism

- Screening hypertensive patients
- Confirming primary hyperaldosteronism
- Classifying disease as unilateral or bilateral

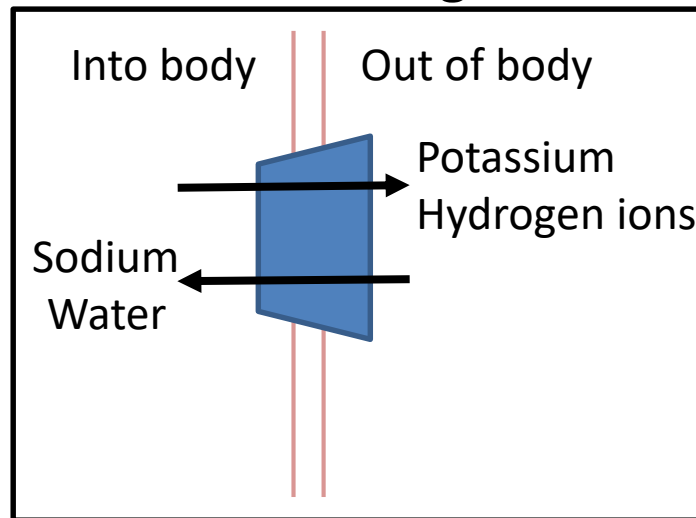
# Testing for primary hyperaldosteronism

- Screening hypertensive patients
  - Prevalence may be up to 5-10% of hypertensive patients
  - Plasma aldosterone: renin ratio
  - Expect: high aldosterone, low renin → elevated ratio
    - Normal ratio is between 4 and 10
    - Abnormal ratio can be > 30-50



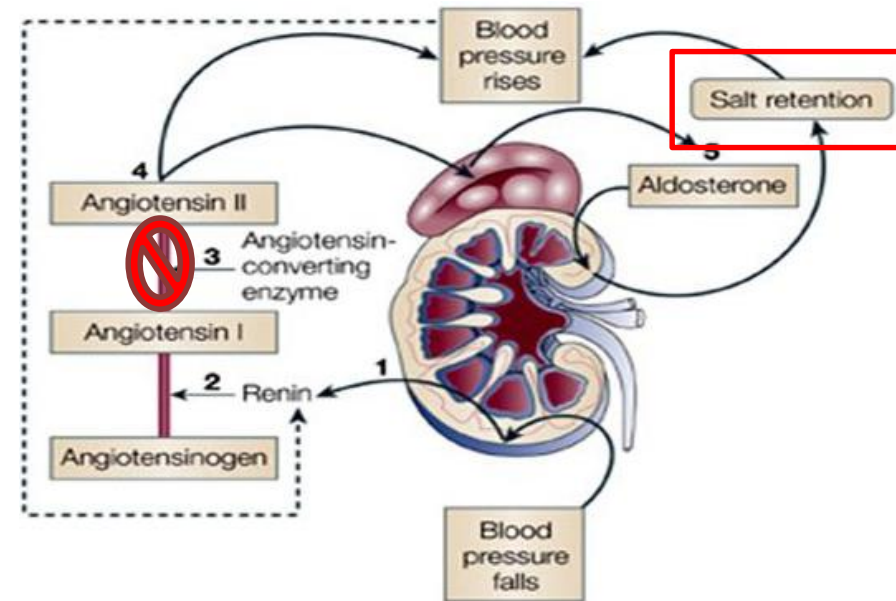
# Testing for primary hyperaldosteronism

- Screening hypertensive patients
  - Pre-analytical concerns:
    - Unrestricted salt intake
    - Normal potassium
    - No mineralocorticoid antagonists within 4 weeks



# Testing for primary hyperaldosteronism

- Screening hypertensive patients
- Confirming primary hyperaldosteronism
  - Sodium loading to test aldosterone suppression
  - Urine or plasma aldosterone

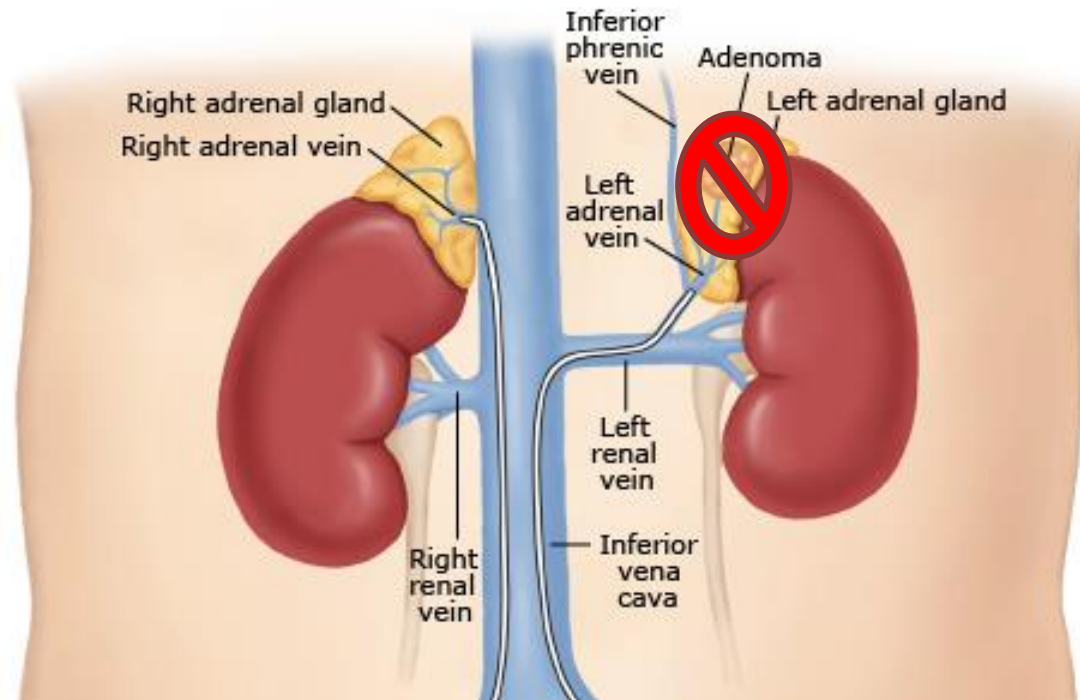


# Testing for primary hyperaldosteronism

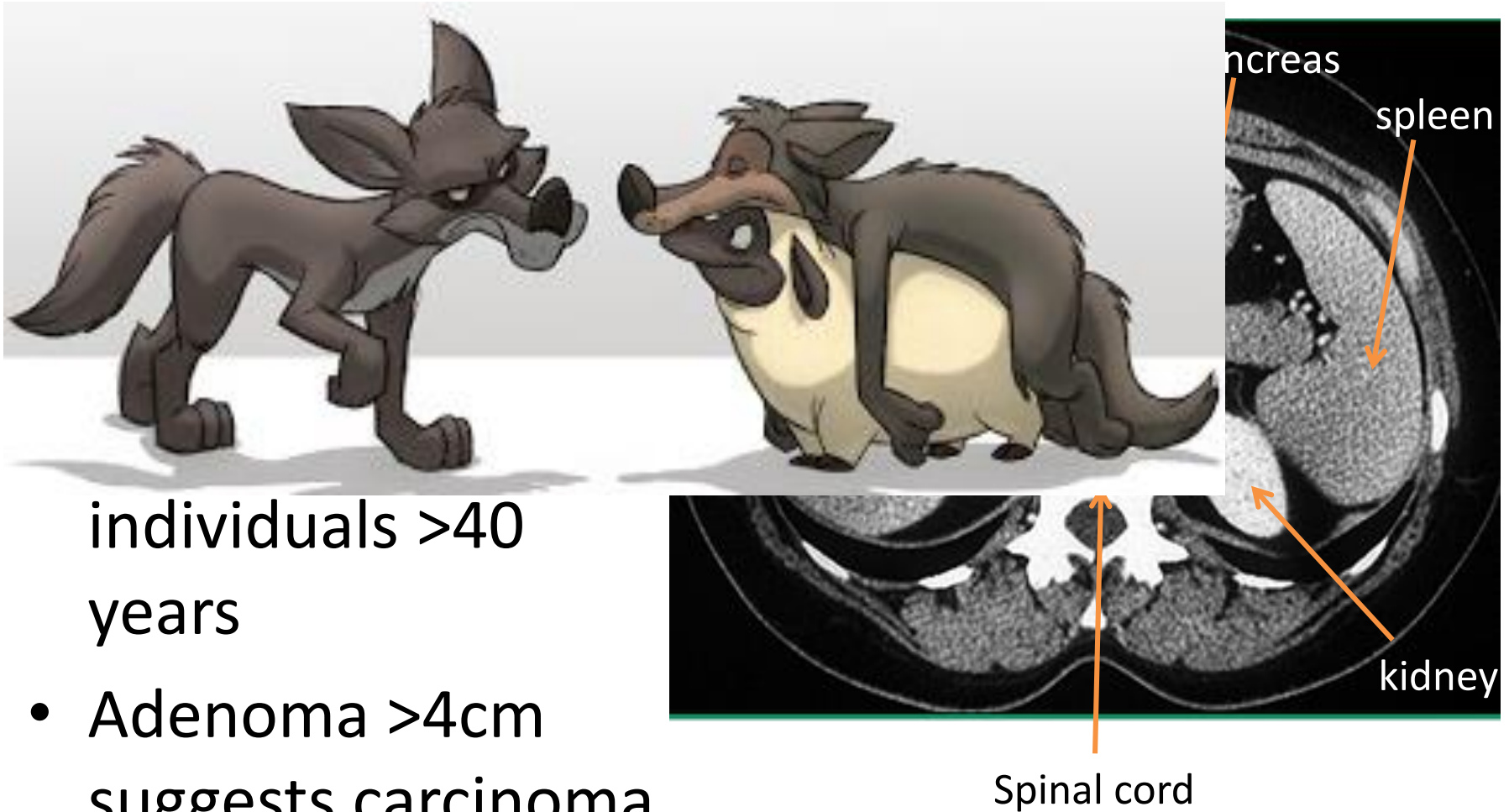
- Screening hypertensive patients
- Confirming primary hyperaldosteronism
- Classifying disease as unilateral or bilateral
  - CT (computed tomography) imaging and/or adrenal venous sampling
  - Critical for making treatment decisions

# Why is classification so important?

- Treatment depends on classification:
  - One adrenal affected → surgery to remove it
  - Both adrenals affected → treat with drugs

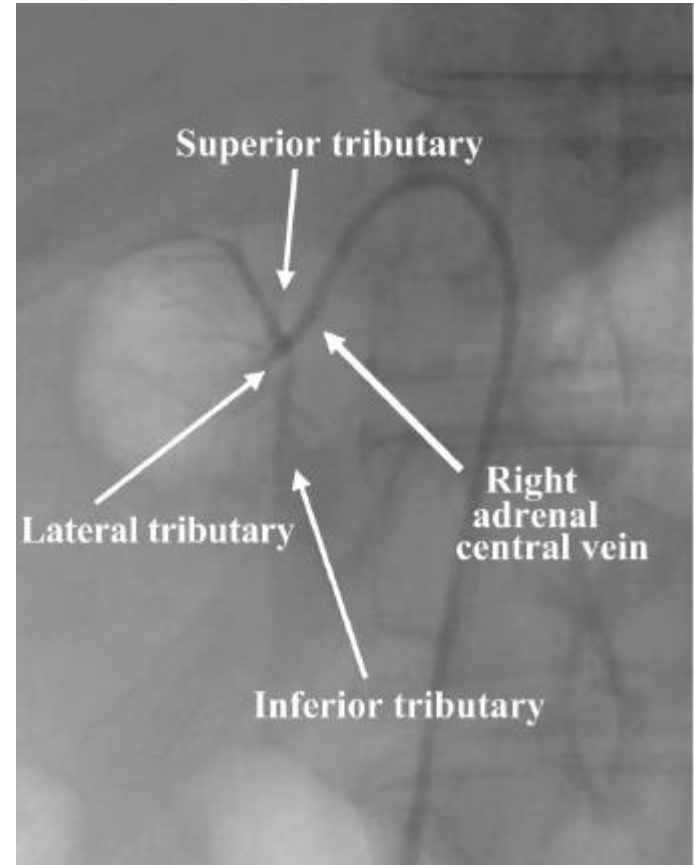


# Why can't we just look at it?



# How does adrenal venous sampling (AVS) work?

- Is more aldosterone produced from one adrenal gland or another?
- May use cosyntropin stimulation
  - Minimize stress-induced changes
  - Maximize aldosterone and cortisol production
- Use fluoroscopy to help image catheter

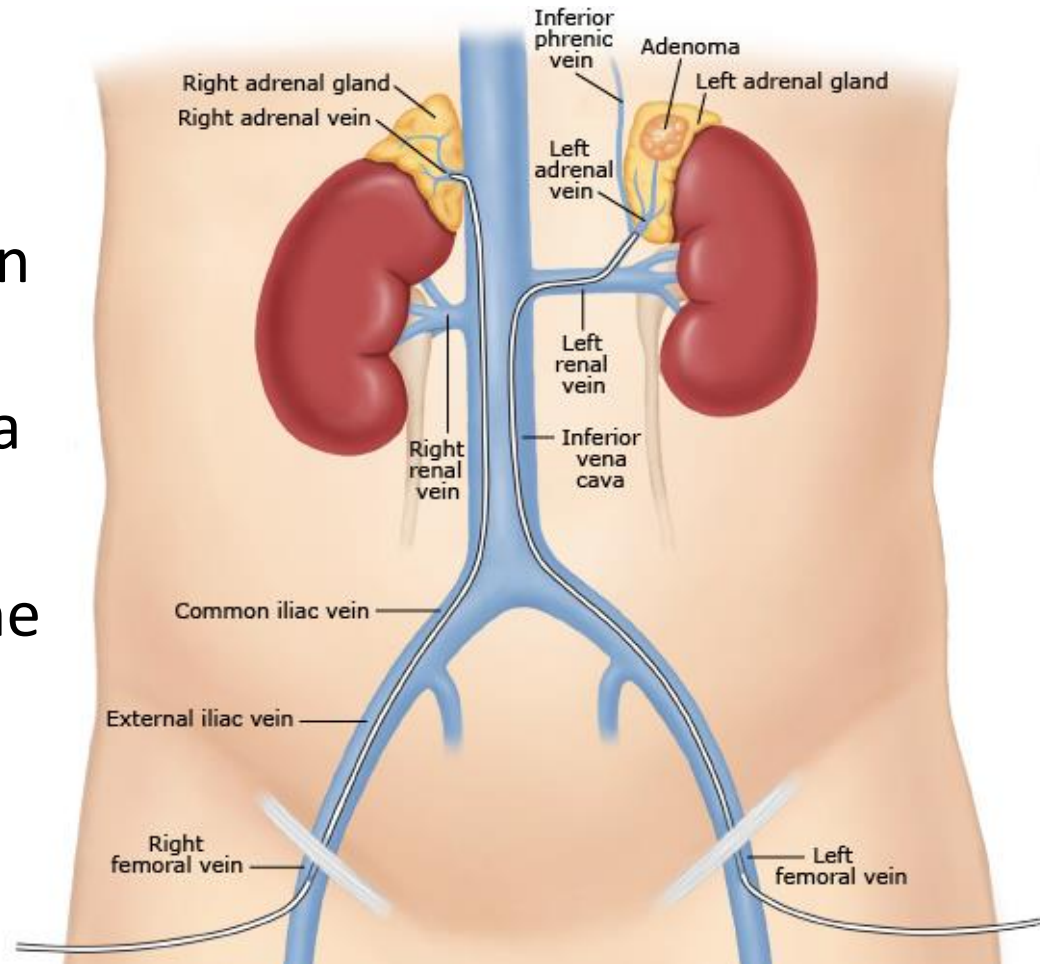


# AVS Procedure Overview

## Goals

1. Right adrenal vein
2. Left adrenal vein
3. Inferior vena cava

Measure aldosterone  
and cortisol



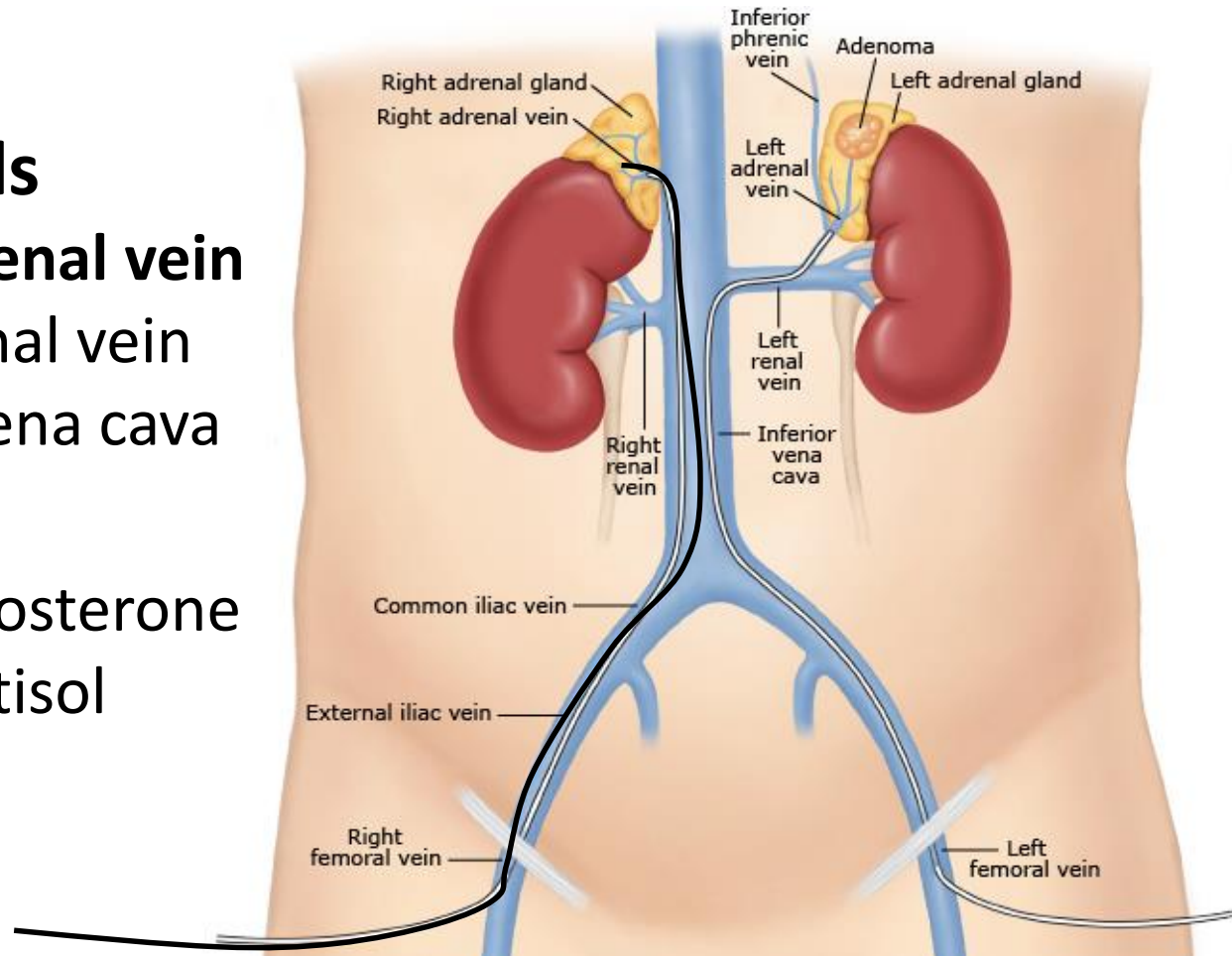


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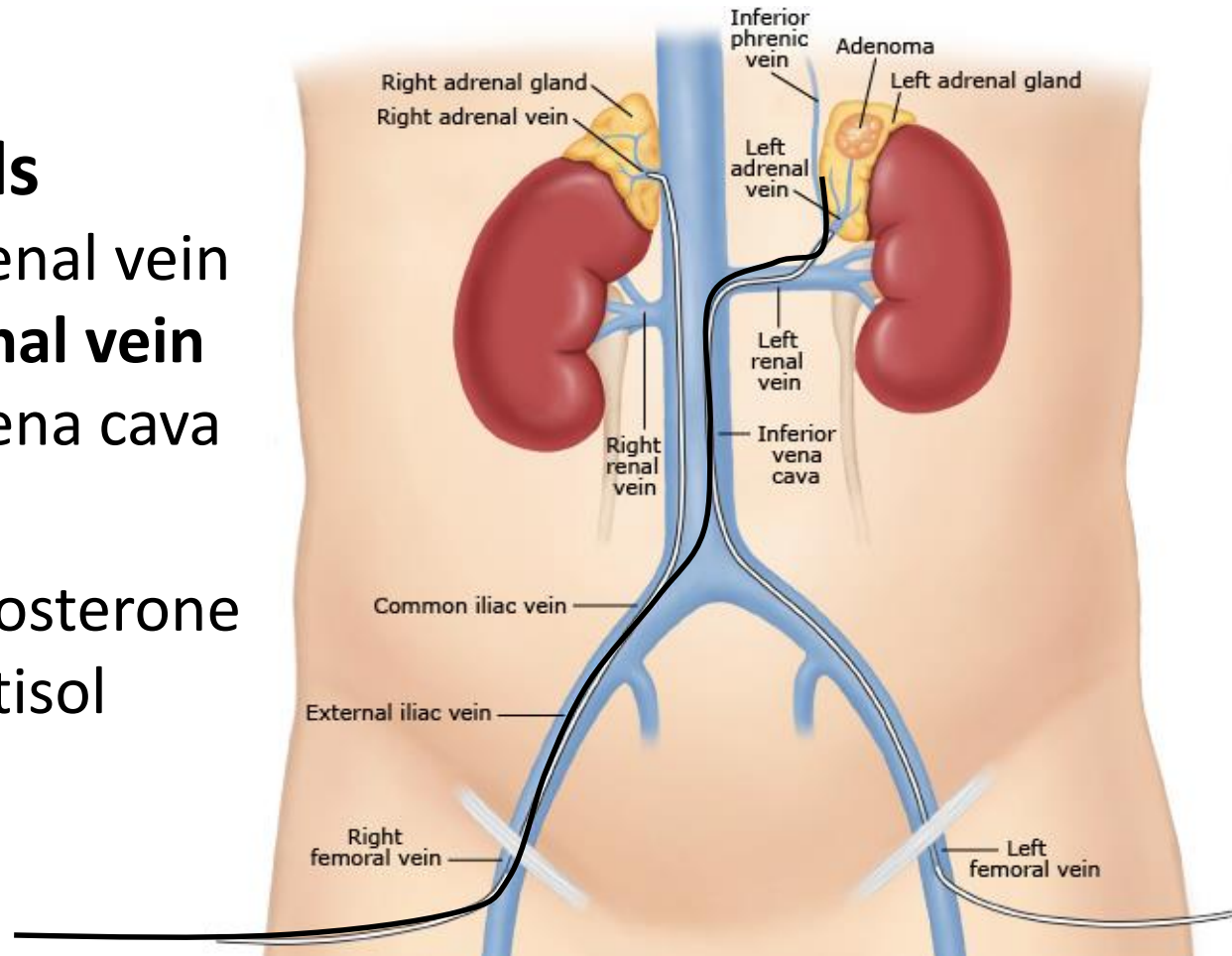


# AVS Procedure Overview

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2. **Left adrenal vein**
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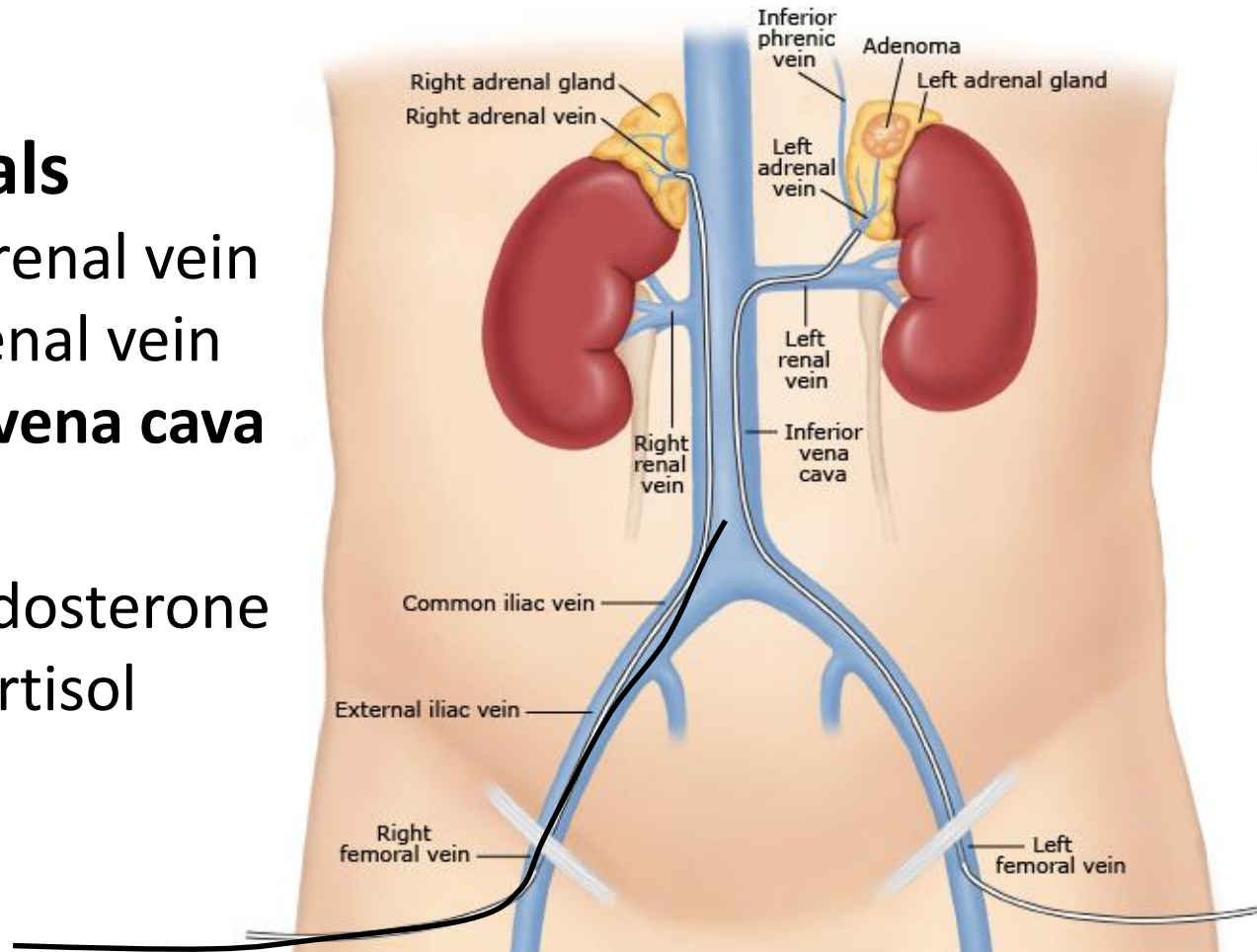


# AVS Procedure Overview

## Goals

1. Right adrenal vein
2. Left adrenal vein
3. **Inferior vena cava**

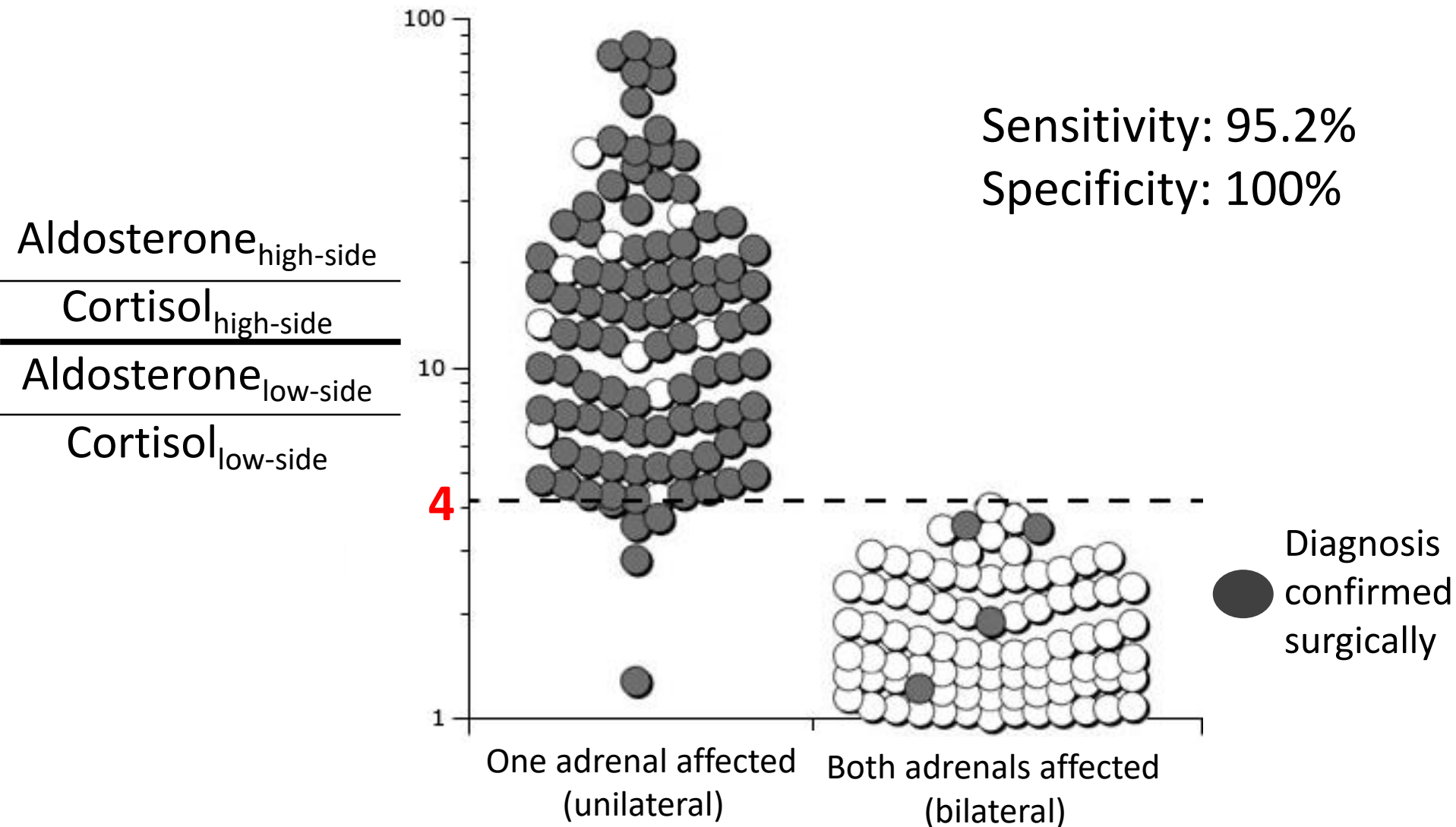
Measure aldosterone  
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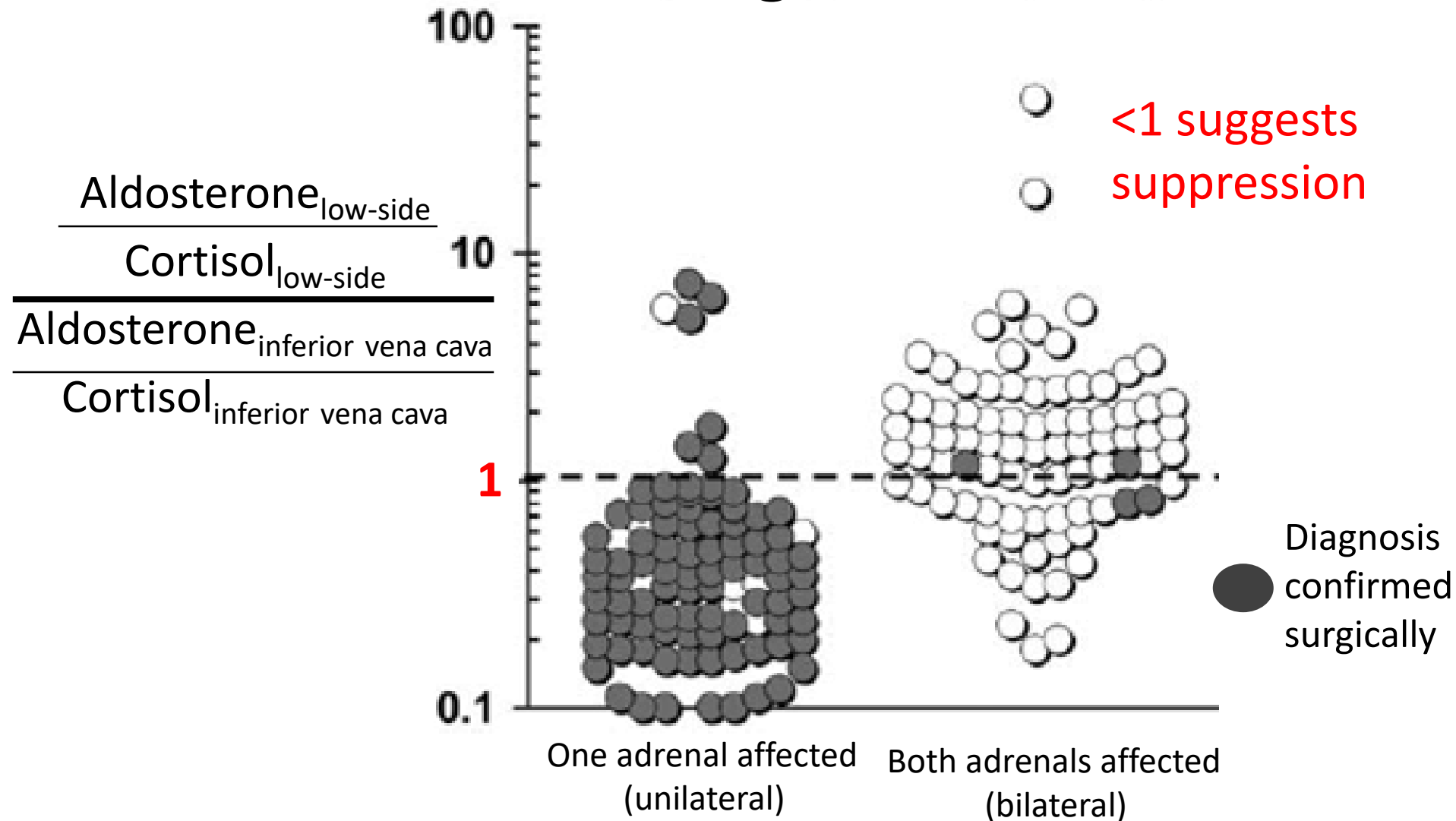
# How are the results interpreted?

- Did the sample come from the correct spot?
- Are one or both adrenals secreting too much aldosterone?
- If only one is affected, does the other adrenal have suppressed aldosterone secretion levels?
- Aldosterone: cortisol ratios employed

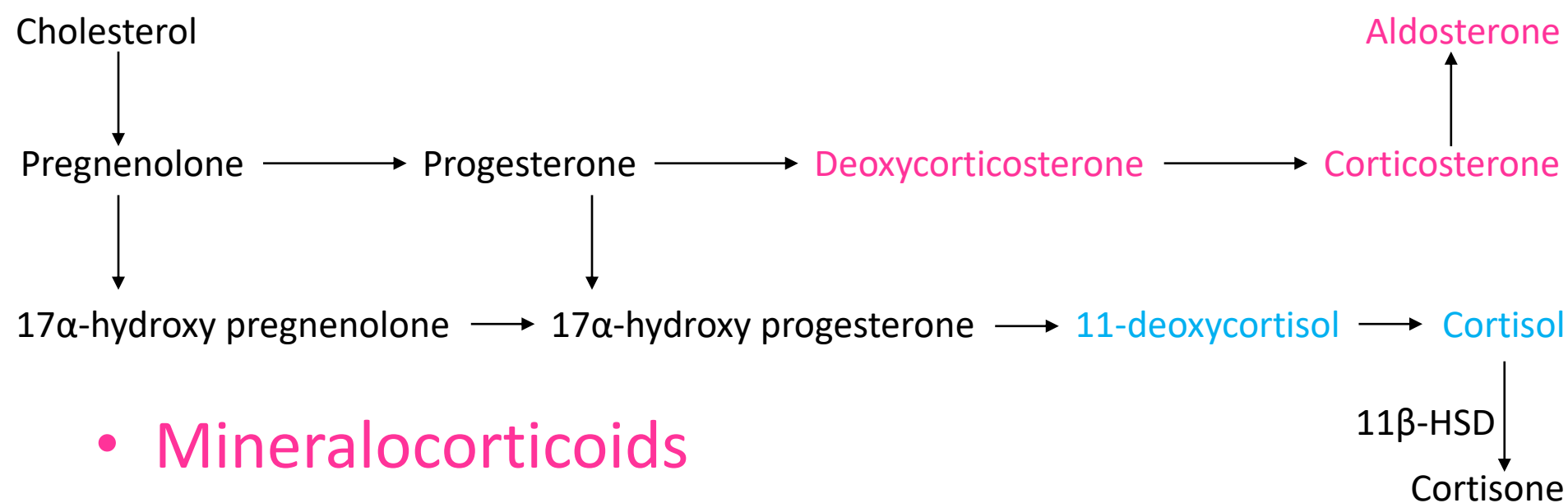
# Identifying unilateral or bilateral disease



# Is there suppression of the unaffected adrenal gland?



# Why might elevated cortisol cause HTN?

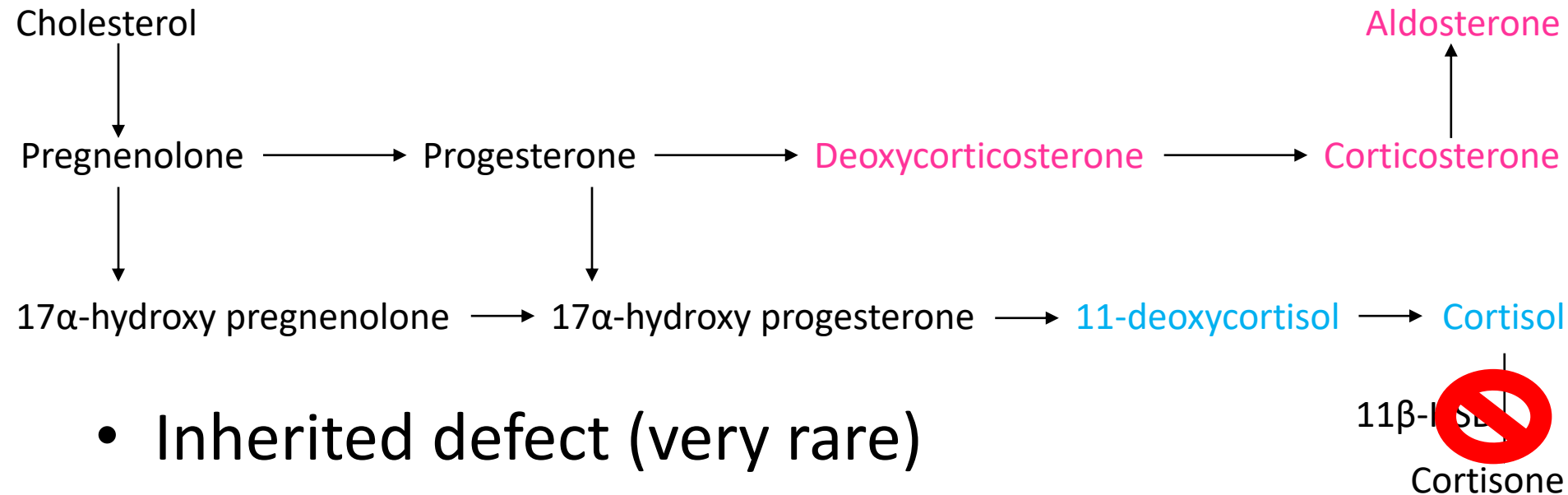


- Mineralocorticoids

- Glucocorticoids

- Also able to bind the mineralocorticoid receptor
- Usually inactivated by 11 $\beta$ -HSD

# Apparent mineralocorticoid excess



- Inherited defect (very rare)
- Inhibition by glycyrrhizic acid metabolites

**Eating too much black licorice can be dangerous. Should you be worried this Halloween?**

**N'dea Yancey-Bragg** USA TODAY

Published 5:28 a.m. ET Oct. 31, 2019 | Updated 12:30 p.m. ET Oct. 31, 2019



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# Hypotension

- Absolute hypotension
  - SBP <90 mmHg
- Relative hypotension
  - SBP drop >20-40 mmHg
- Causes inadequate tissue perfusion
- May manifest with fainting
- When severe, will cause shock

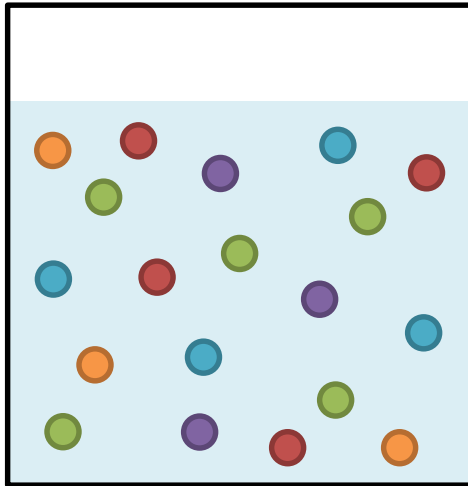


"Chapter 11," *Robbins and Cotran Pathological Basis of Disease*, 2010; "Evaluation of and initial approach to the adult patient with undifferentiated hypotension and shock," *Up to Date*, 2020; "Syncope in adults: Risk assessment and additional diagnostic evaluation," *Up to Date*, 2020; "The Studio" by Sophie Anderson (<https://fineartamerica.com/featured/the-studio-sophie-anderson.html?product=framed-print>)

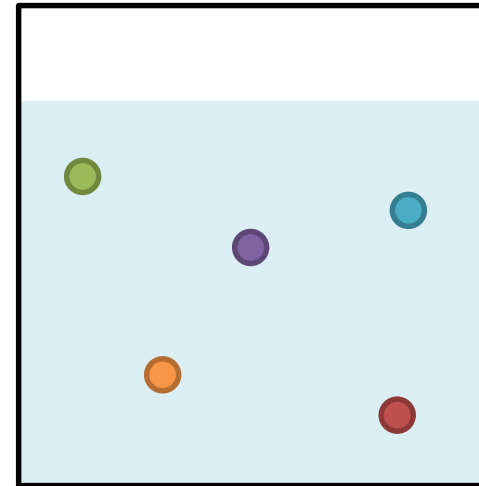
# What is osmolality?

- Concentration of dissolved particles in blood

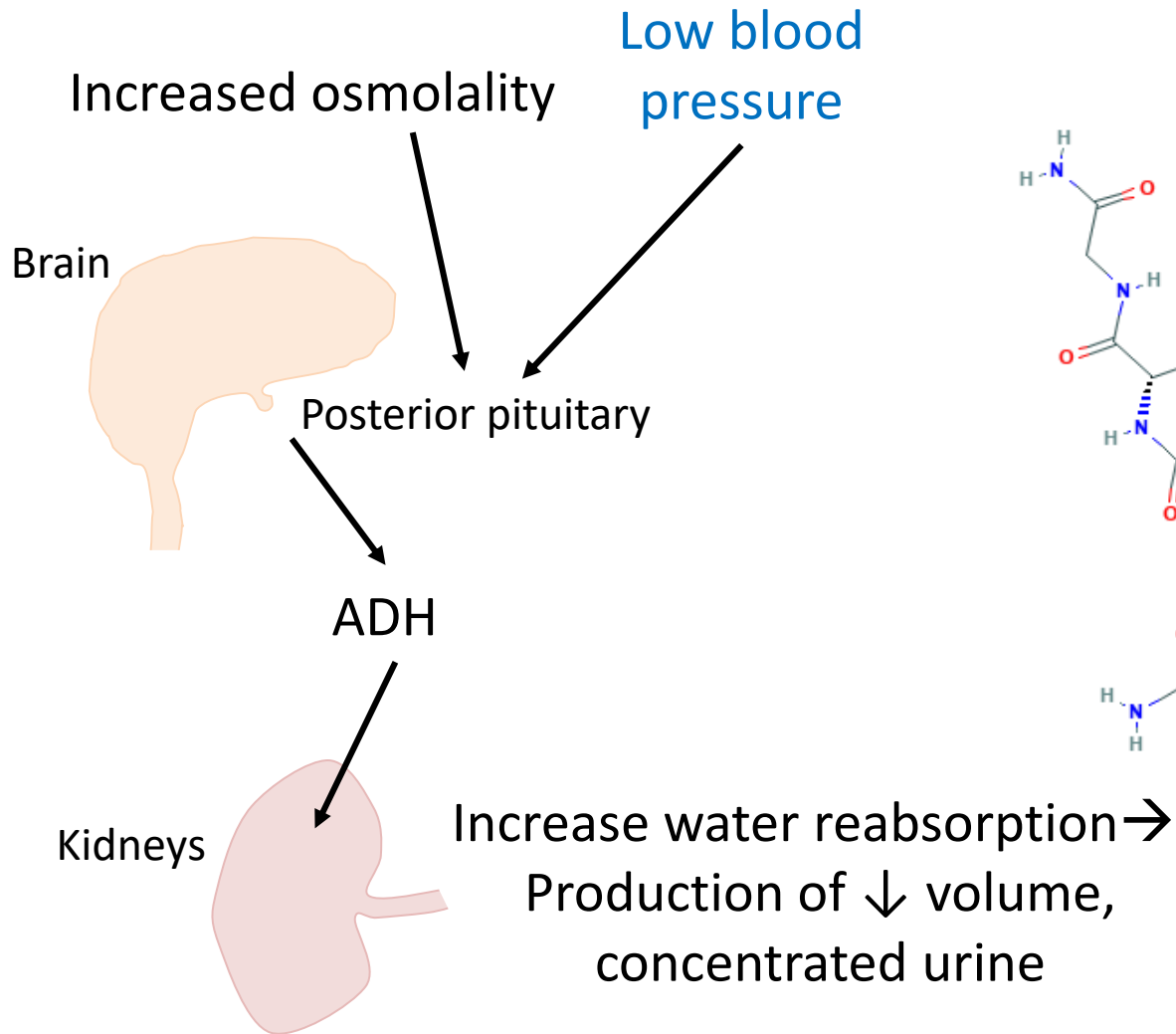
High osmolality = concentrated



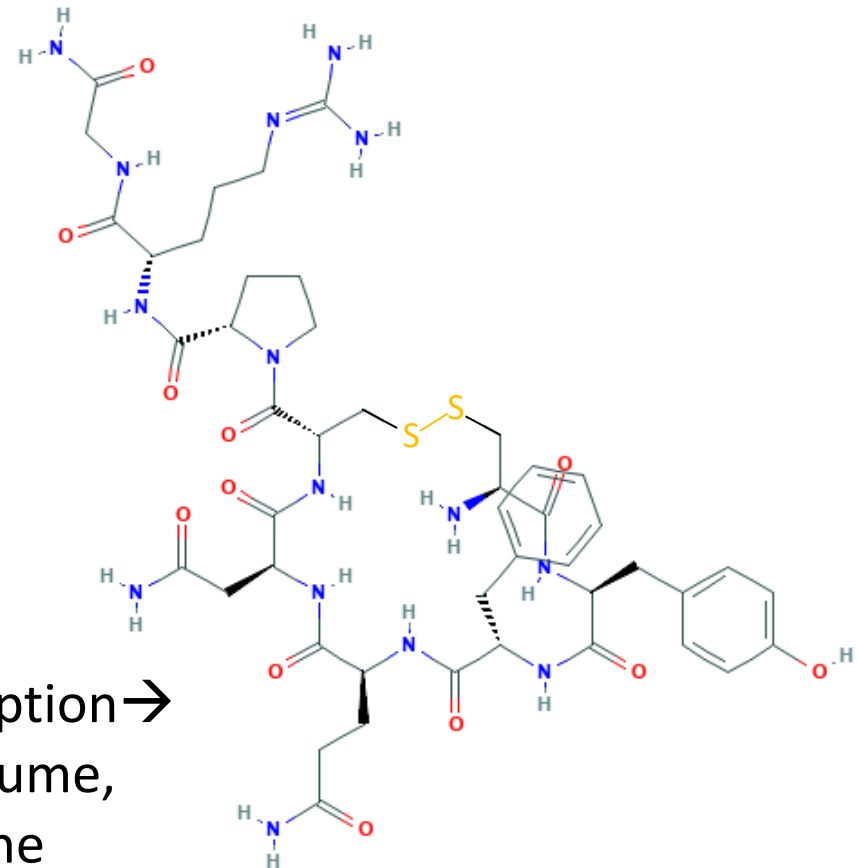
Low osmolality = dilute



# Antidiuretic hormone (ADH)/Vasopressin

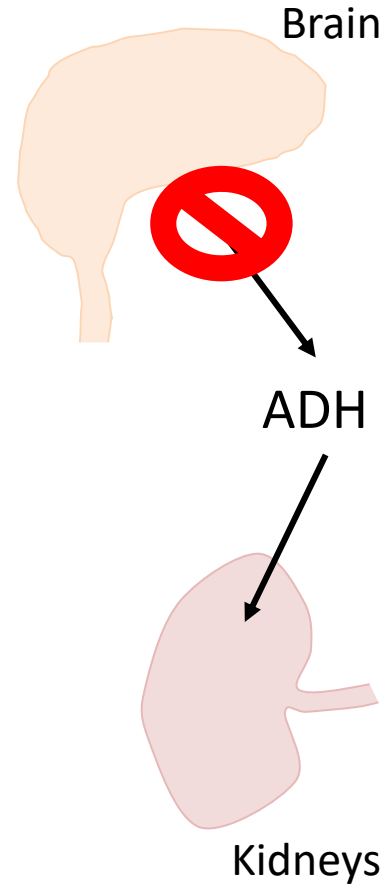


Diuretic: substance that increases urine production



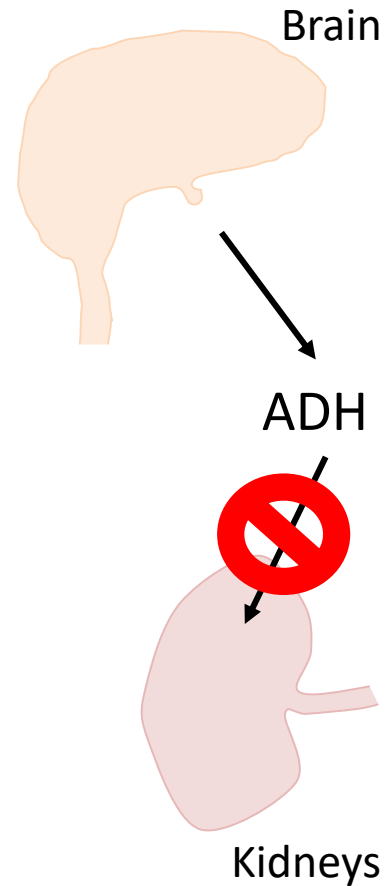
# What is diabetes insipidus?

- Symptoms: polyuria and polydipsia
  - Lab testing often shows hypernatremia
  - Without water intake → dehydration, **hypotension**
- Central diabetes insipidus: ADH deficiency
  - Hypothalamic lesion



# What is diabetes insipidus?

- Symptoms: polyuria and polydipsia
  - Lab testing often shows hypernatremia
  - Without water intake → dehydration, hypotension
- Central diabetes insipidus: ADH deficiency
  - Hypothalamic lesion
- Nephrogenic diabetes insipidus: problem with ADH action
  - Congenital mutations
  - Kidney disease or drug-induced kidney damage



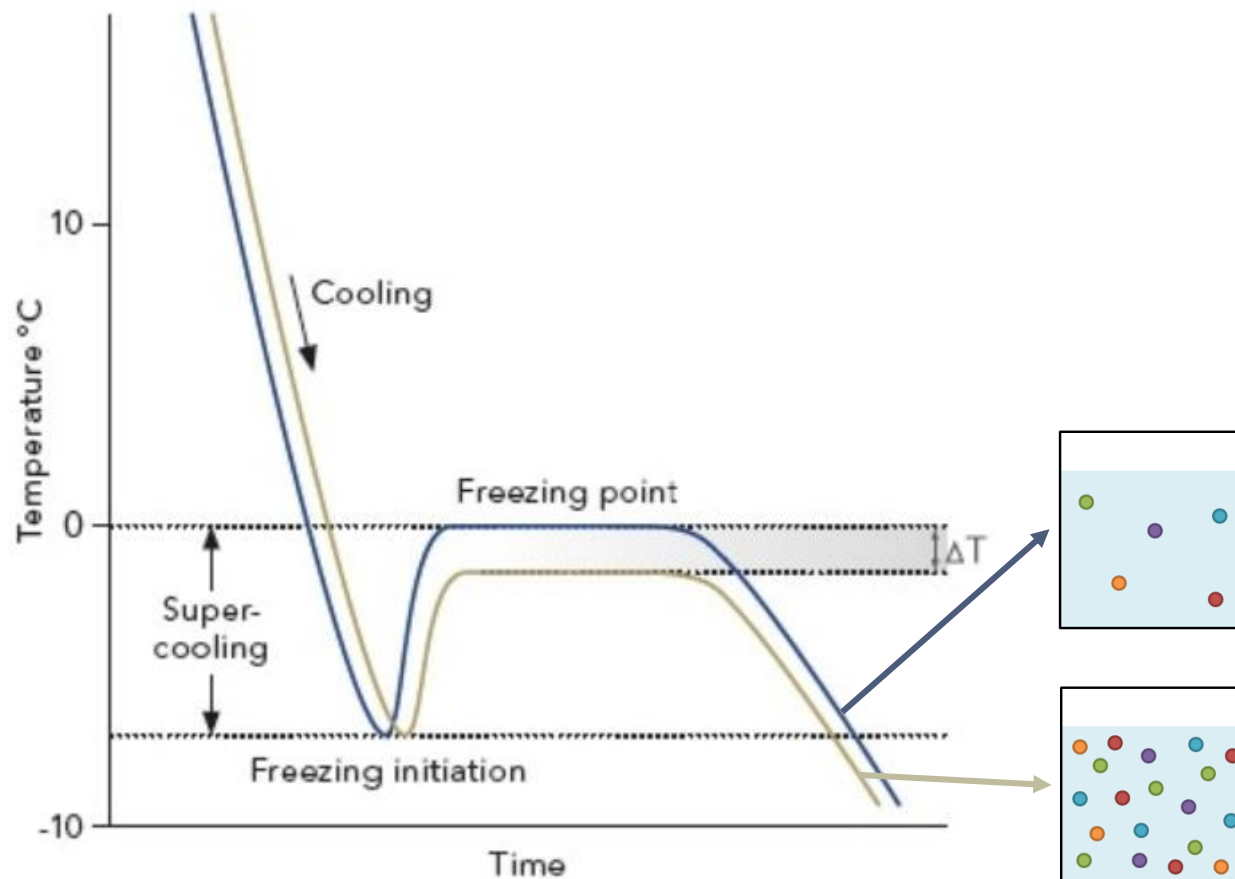
# What testing is performed for diabetes insipidus?

- ADH testing not usually required

Assay	Expected result in diabetes insipidus
Urine volume	>2.5 L/day
Urine osmolality	↓
Serum osmolality	↑ or ≈

# How is osmolality measured?

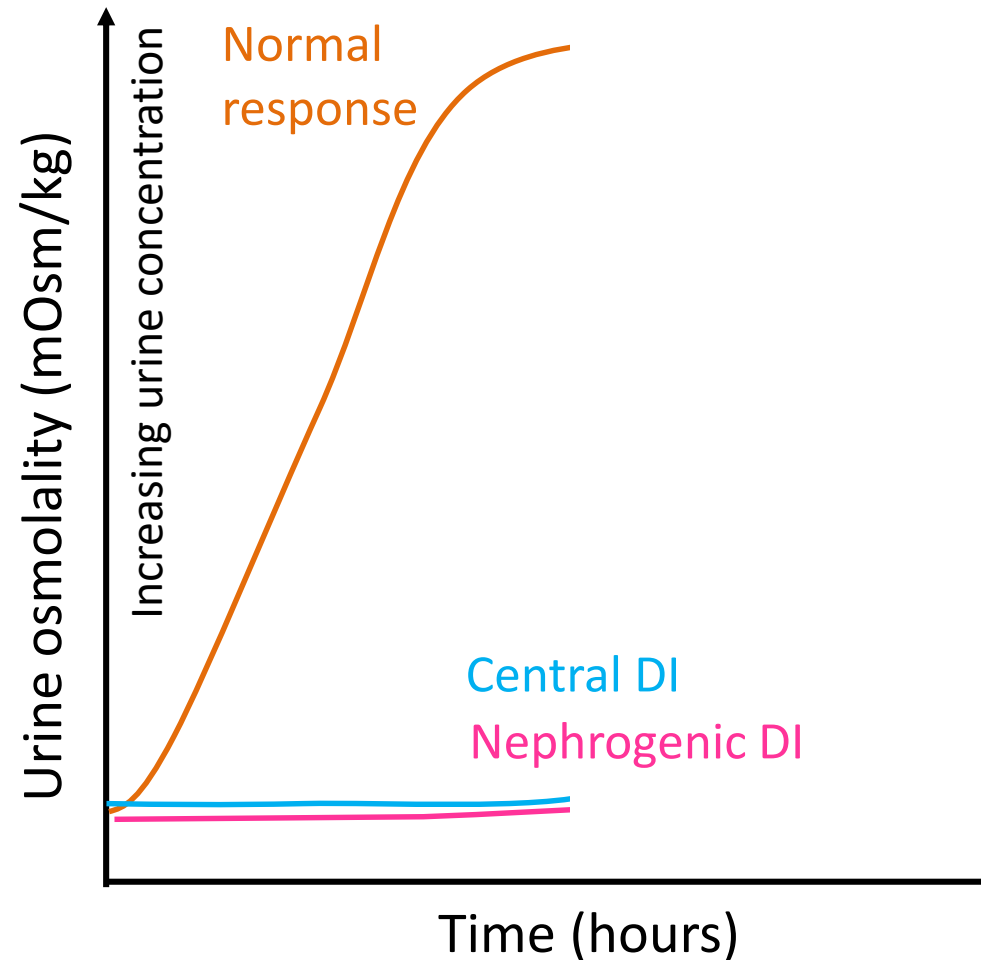
- Performed by freezing point depression



# What dynamic lab testing may be done?

- Water deprivation test
- Monitor urine output, serum osmolality and urine osmolality

*Central*: deficiency of ADH  
*Nephrogenic*: ADH not able to act on kidneys

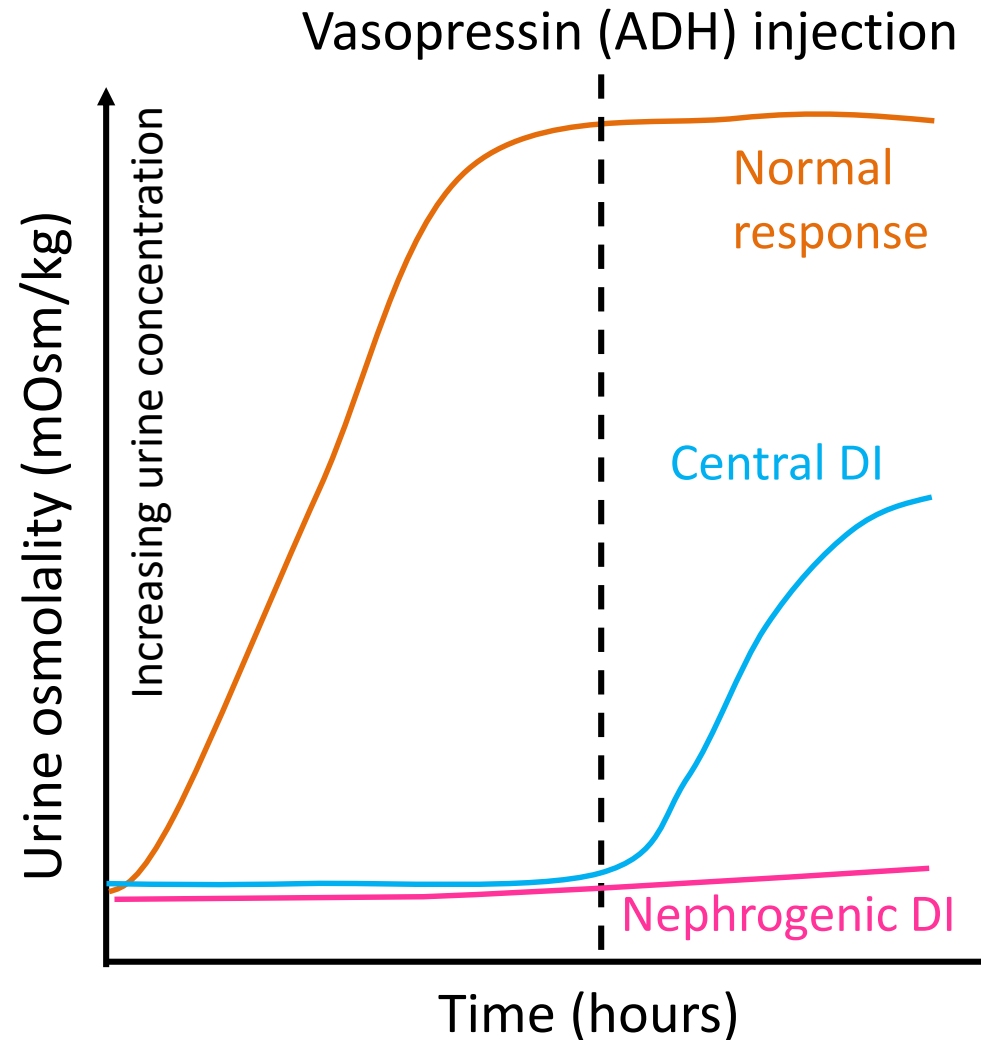




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*Central:* deficiency of ADH  
*Nephrogenic:* ADH not able to act on kidneys



# Summary

- Blood pressure regulation is complex
- Critical to investigate secondary endocrine causes of HTN
  - Most common endocrine cause is primary hyperaldosteronism
- Diabetes insipidus may cause hypotension

# Acknowledgements

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