Adrenal Venous Sampling

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Learning Objectives

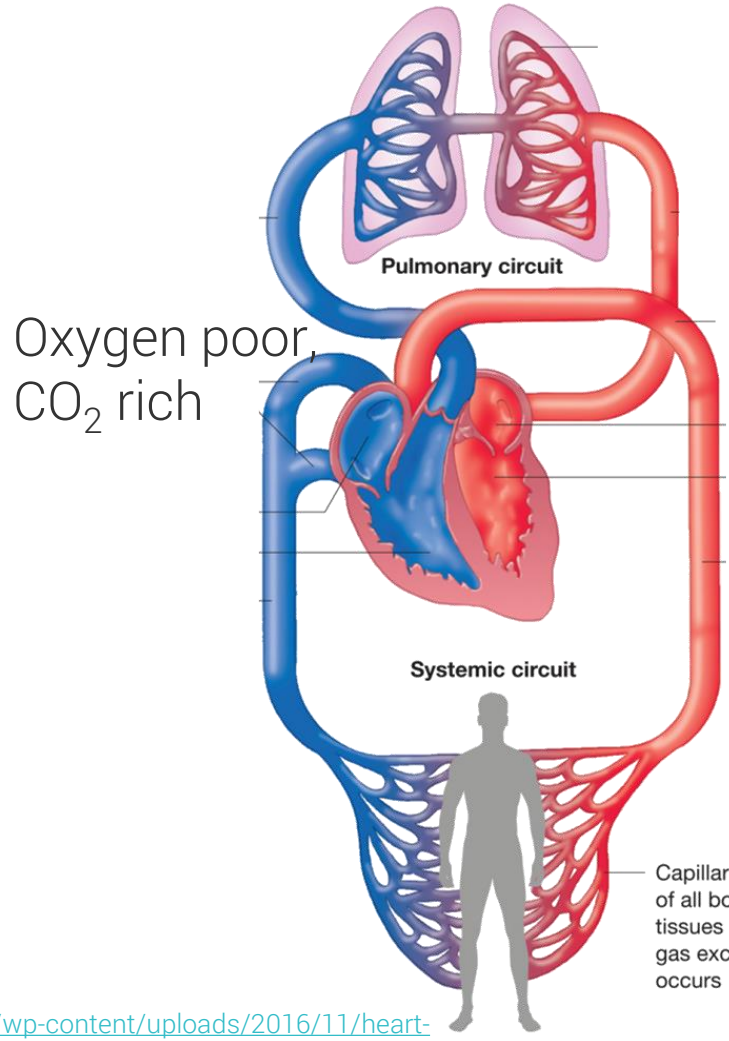
1. Describe how the renin-aldosterone system controls blood pressure.
2. List the tests important in screening for, confirming, and classifying primary hyperaldosteronism.
3. Explain the benefits of adrenal venous sampling in classifying primary hyperaldosteronism.

Outline

- Blood pressure
- Renin-aldosterone system
- Diagnosis of primary hyperaldosteronism
- AVS
  - » Procedure
  - » Interpretation

Importance of blood pressure

- Pressure needed to ensure nutrient and oxygen delivery to tissues
- Hypertension and hypotension→ both problematic
- Hypertension = significant medical condition



"Overview of hypertension in adults," Up to Date, 2019; Image adapted from http://humananatomyclass.com/wp-content/uploads/2016/11/heart-and-lungs-blood-circulation-images-of-diagram-of-blood-flow-through-the-heart-and-lungs-diagrams.jpg.

How is blood pressure controlled?

- Cardiac output and vascular resistance determine blood pressure
- Cardiac output depends on blood volume

- Vascular resistance mediated by the size of blood vessels

Robbins and Cotran. "Chapter 11," *Pathological Basis of Disease*, 2010; Images from https://commons.wikimedia.org/wiki/File:Canadian_Horseshoe_Falls_with_city_of_Niagara_Falls,_Ontario_in_background.jpg; https://blog.gardenloversclub.com/diy/add-a-small-waterfall/; https://www.amazon.com/North-American-Fire-Hose-Polyurethane/dp/B06XDJ2BNF; https://www.amazon.com/VEHHE-Straws-Stainless-Drinking-Reusable/dp/B07CZW9V7W/ref=sr_1_8?dchild=1&keywords=reusable+straws&qid=1586189250&s=home-garden&sr=1-8

Renin-Aldosterone System

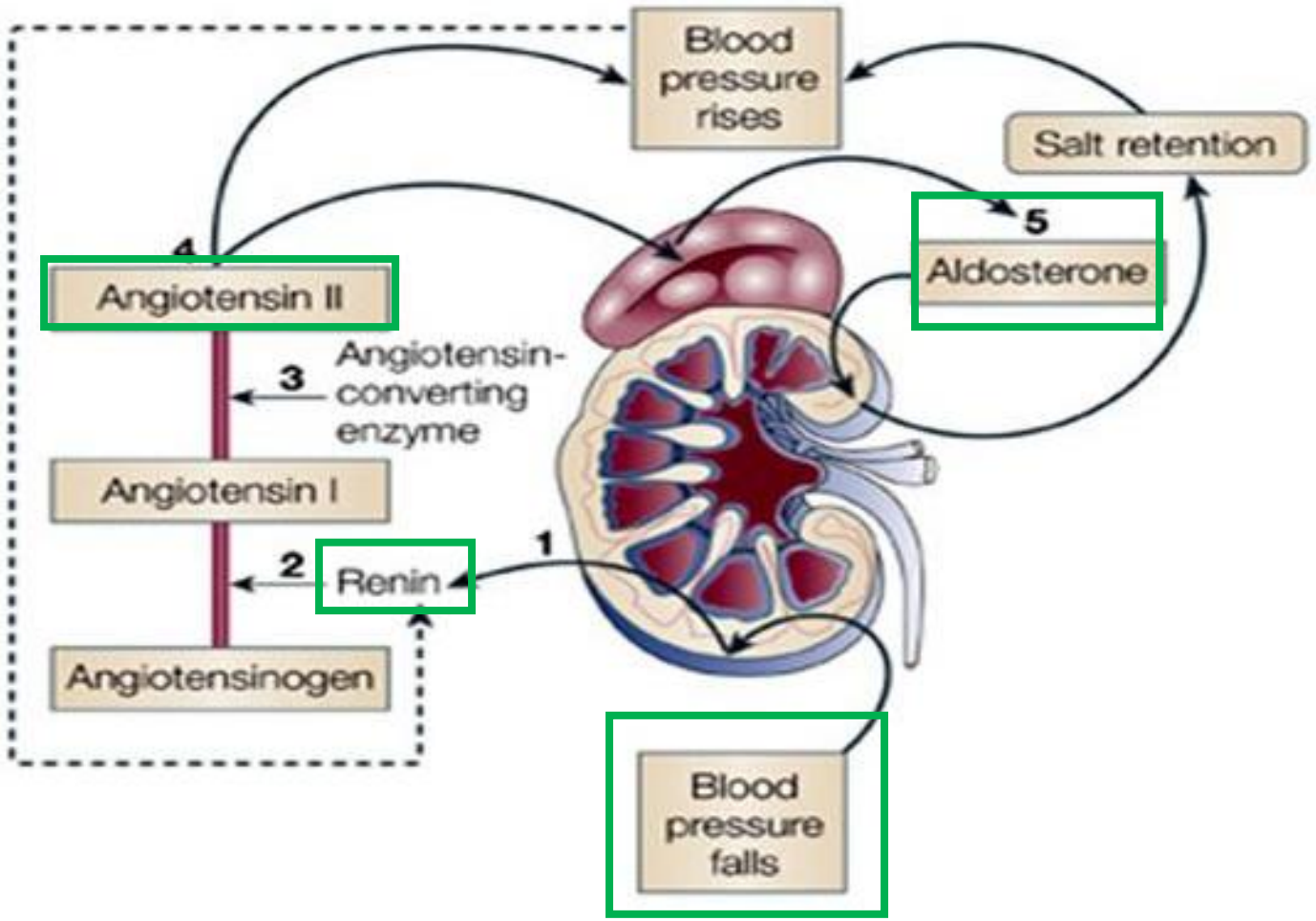


Image from Chemistry Class Slides, Horbachevsky Ternopil State Medical University, Ukraine.

Renin-Aldosterone System

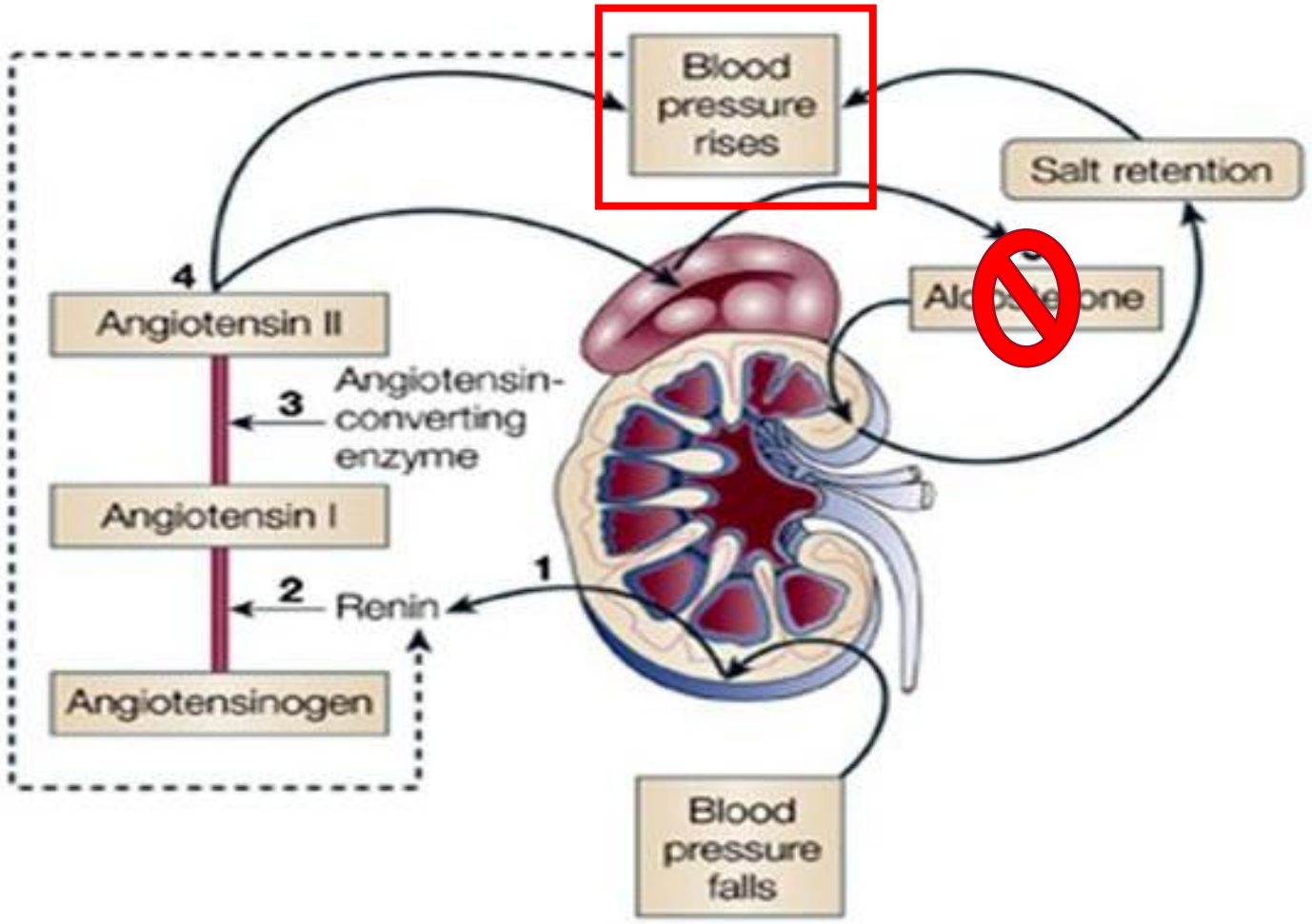


Image from Chemistry Class Slides, Horbachevsky Ternopil State Medical University, Ukraine.

What is primary hyperaldosteronism?

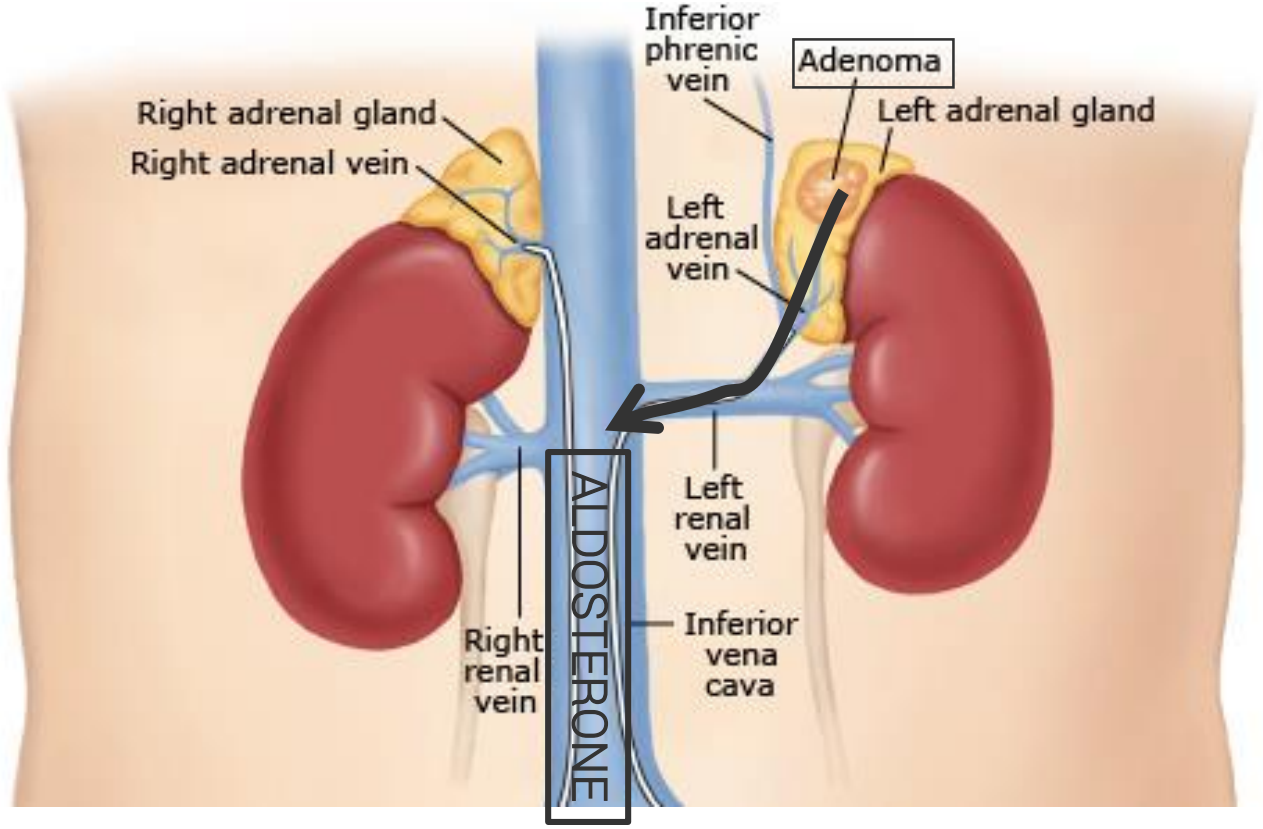
- High blood pressure due to uncontrolled excretion of aldosterone
  - » Most common:
    - Aldosterone-producing adenoma (APA)
    - Bilateral idiopathic hyperaldosteronism
  - » Relatively rare:
    - Familial hyperaldosteronism
    - Unilateral adrenal hyperplasia
    - Adrenal carcinoma
    - Ectopic aldosterone-producing tumor
- Patients with primary hyperaldosteronism are more at risk for cardiovascular complications

Are both adrenal glands bad or is just one going rogue?

Diagnosis of primary aldosteronism, *Up To Date*, July 2018; Young *et al.* "Role of AVS in primary hyperaldosteronism," *Surgery*, 2004; Funder *et al.* Endocrine Society Guidelines, 2016.

What is primary hyperaldosteronism?

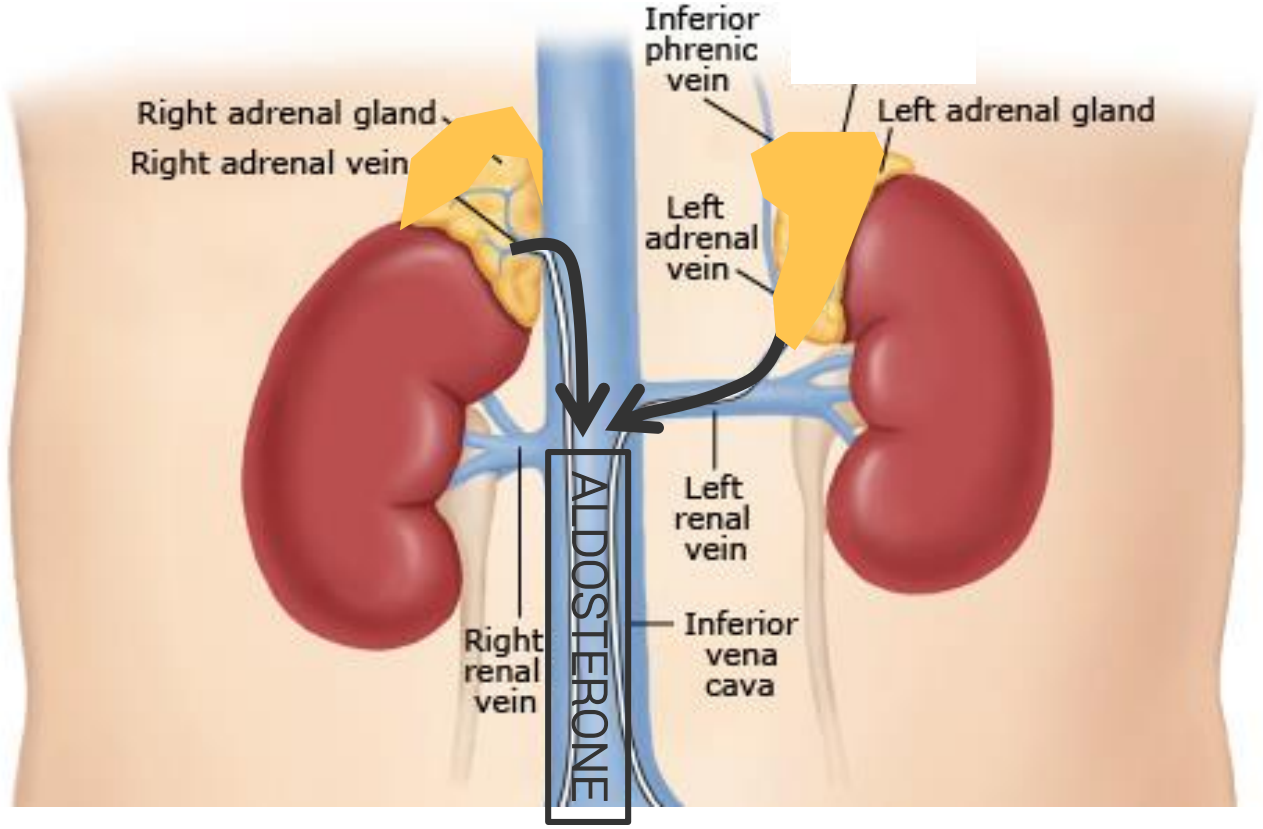
- Aldosterone producing adenoma (~30% of cases)



Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

What is primary hyperaldosteronism?

- Bilateral adrenal hyperplasia (~60% of cases)



Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

Testing for primary hyperaldosteronism

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

Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

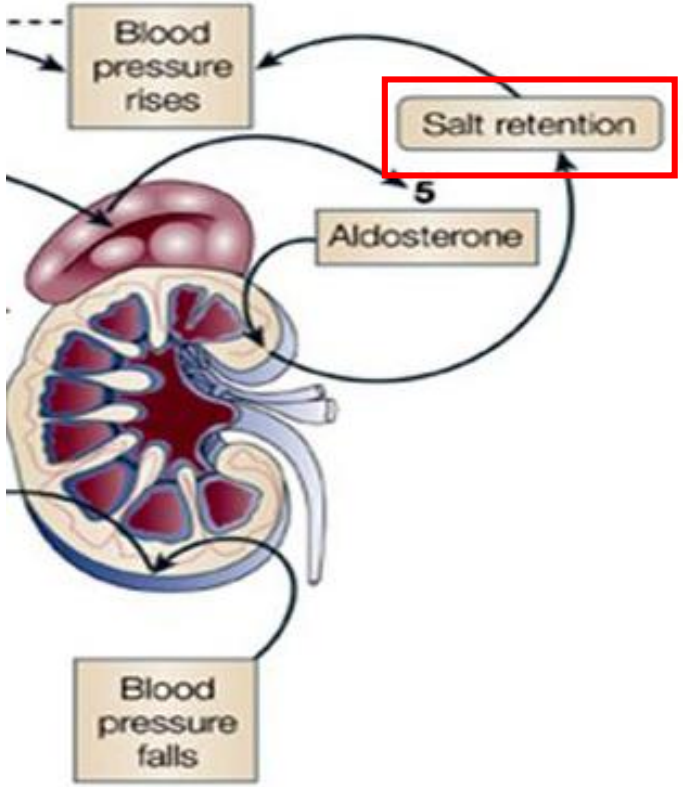
Testing for primary hyperaldosteronism

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

Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

Testing for primary hyperaldosteronism

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



Diagnosis of primary aldosteronism, *Up To Date*, July 2018; Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention and Treatment of Hypertensions in Adults and Children, *Can. J. Cardiol.* 2018.

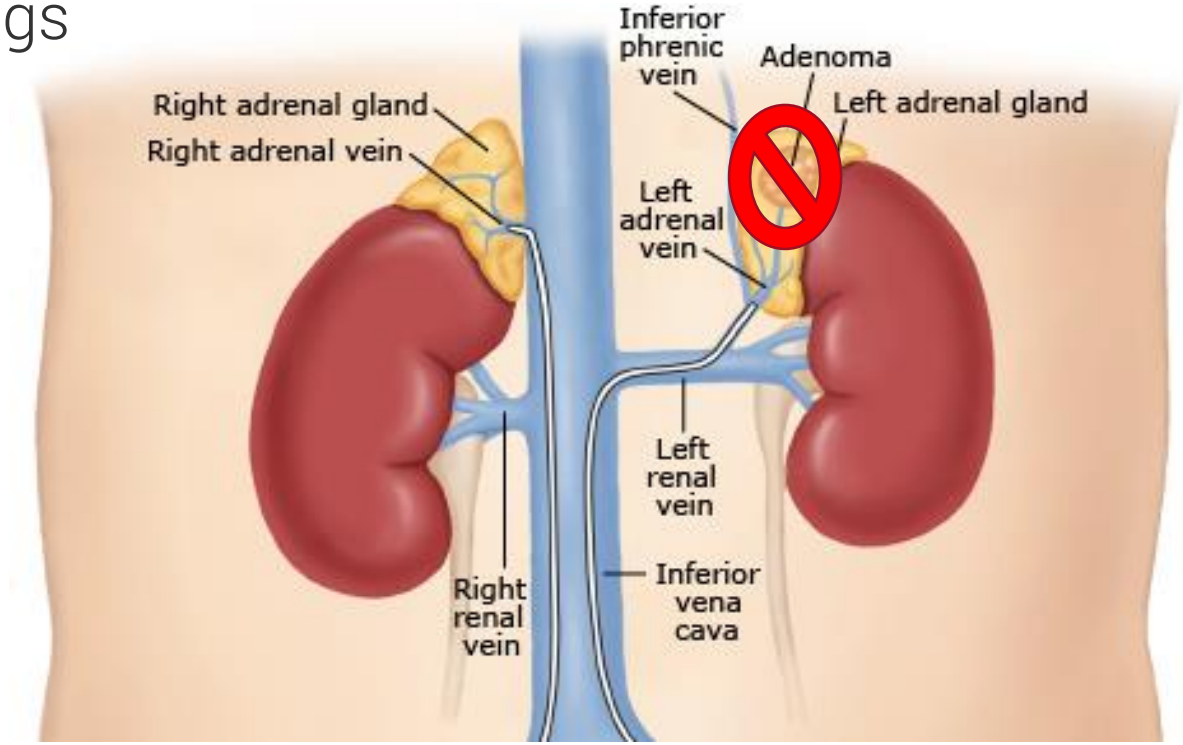
Testing for primary hyperaldosteronism

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

Diagnosis of primary aldosteronism, *Up To Date*, July 2018; Hypertension Canada's 2018 Guidelines for Diagnosis, Risk Assessment, Prevention and Treatment of Hypertensions in Adults and Children, *Can. J. Cardiol.* 2018.

Why is classification so important?

- Treatment depends on classification:
  - » One bad adrenal → surgery to remove it
  - » Two bad adrenals → treat with drugs

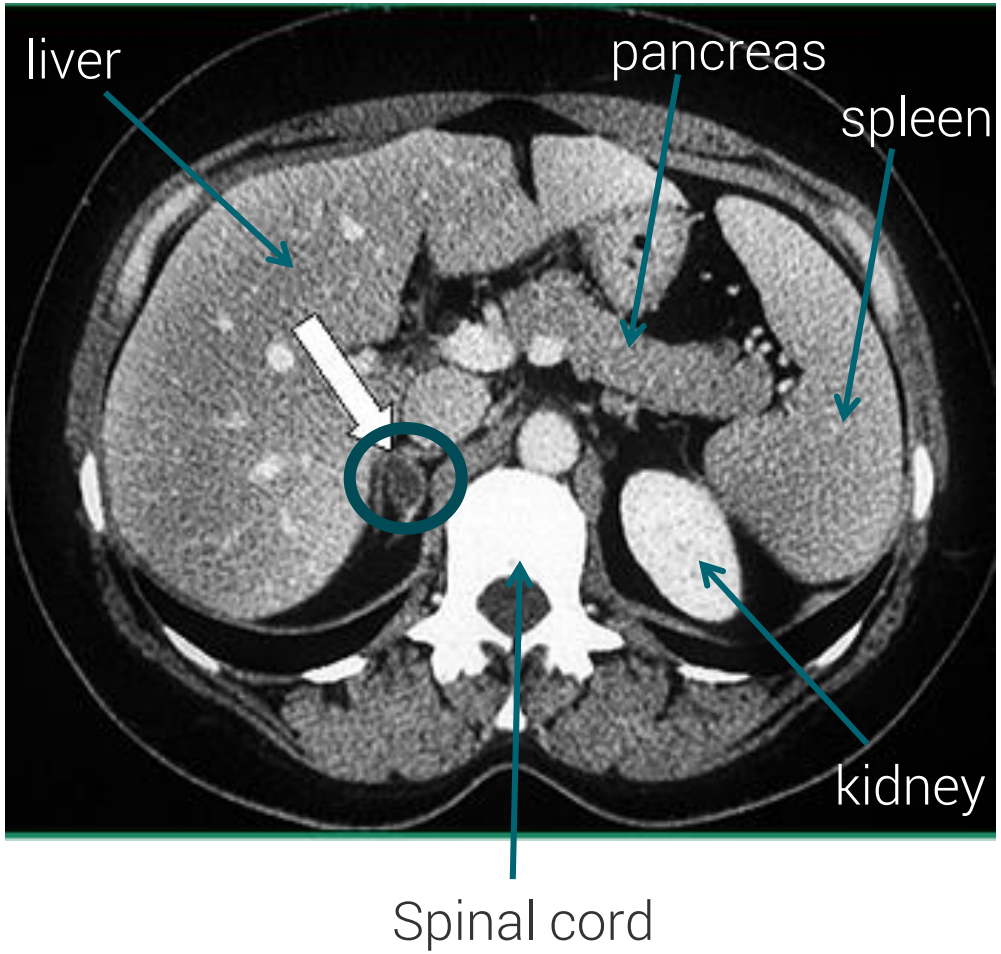


Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

Why can't we just look at it?

- CT imaging not always accurate or sensitive enough

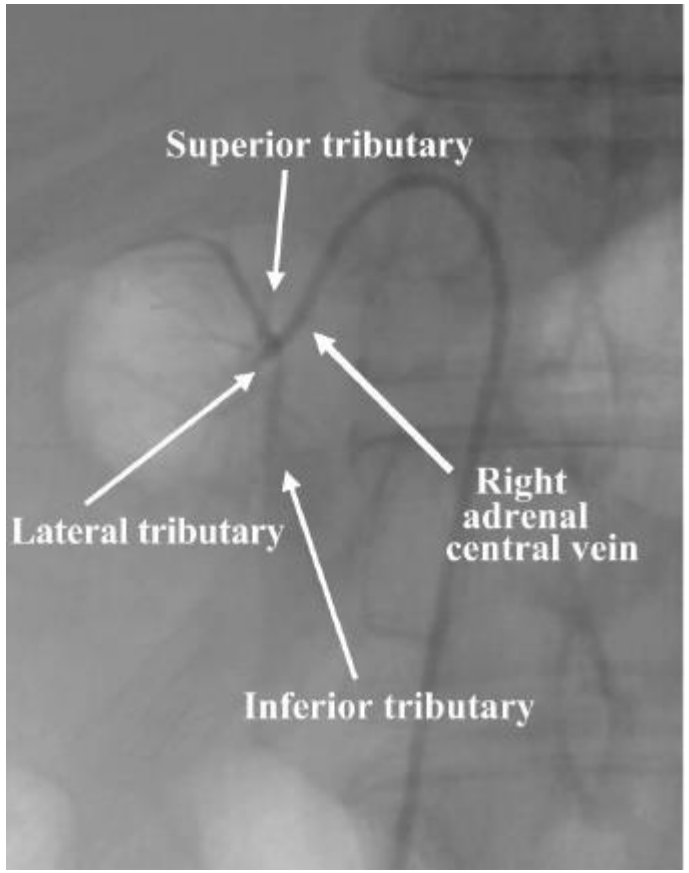
- Older patients can have incidentalomas



Diagnosis of primary aldosteronism, *Up To Date*, July 2018; Image from http://stlewis.blogspot.com/2007/08/sheep-in-wolfs-clothing.html.

How does AVS work?

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

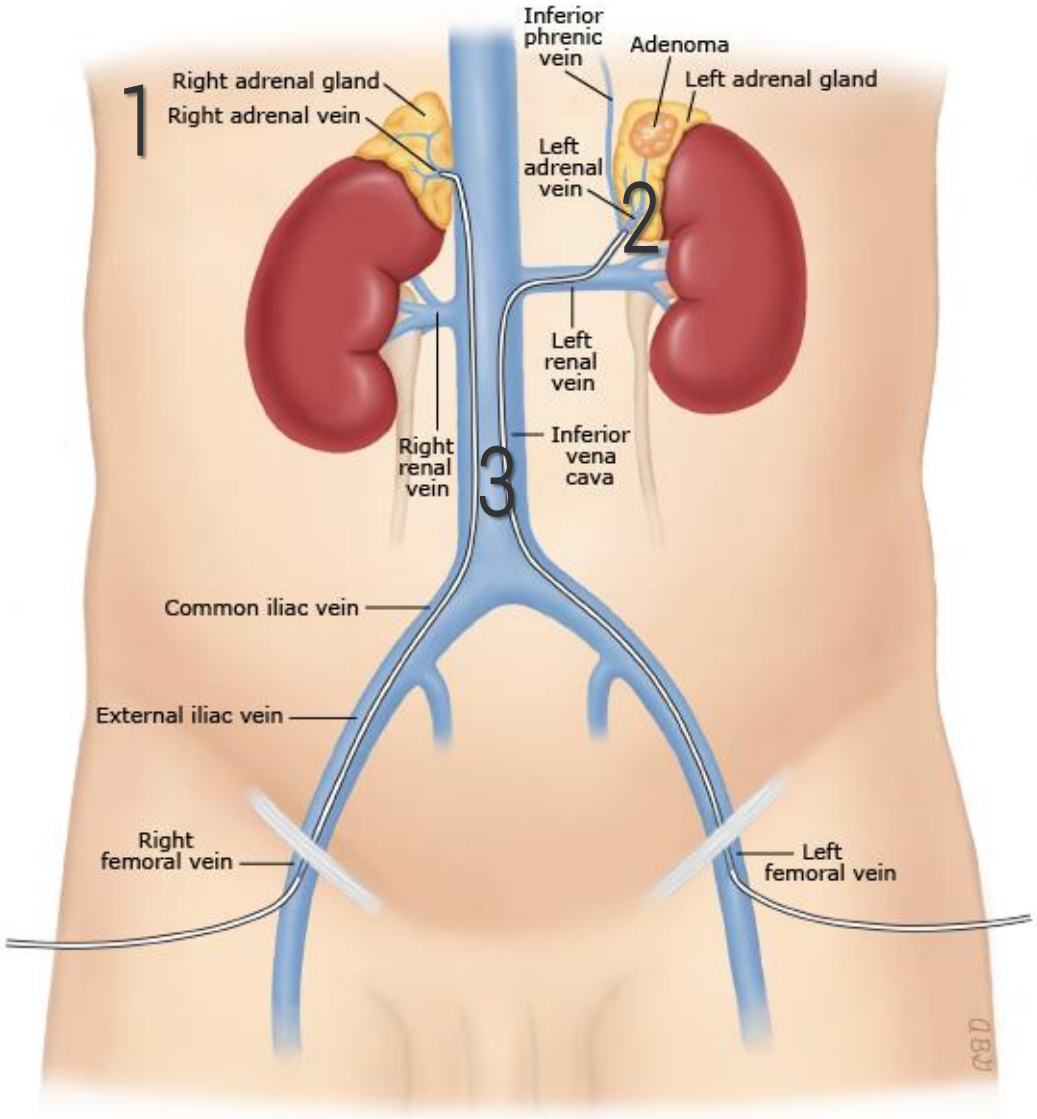


Rossi *et al*. "Expert Consensus Statement on Use of AVS for primary aldosteronism subtyping." *Hypertension* 2014; Daunt, N. "AVS: How to Make it Quick, Easy and Successful," *RadioGraphics,* 2005; Nishikawa *et al. Endocrine Journal*, 2011.

AVS Procedure Overview

GOALS

1. RAV
2. LAV
3. IVC

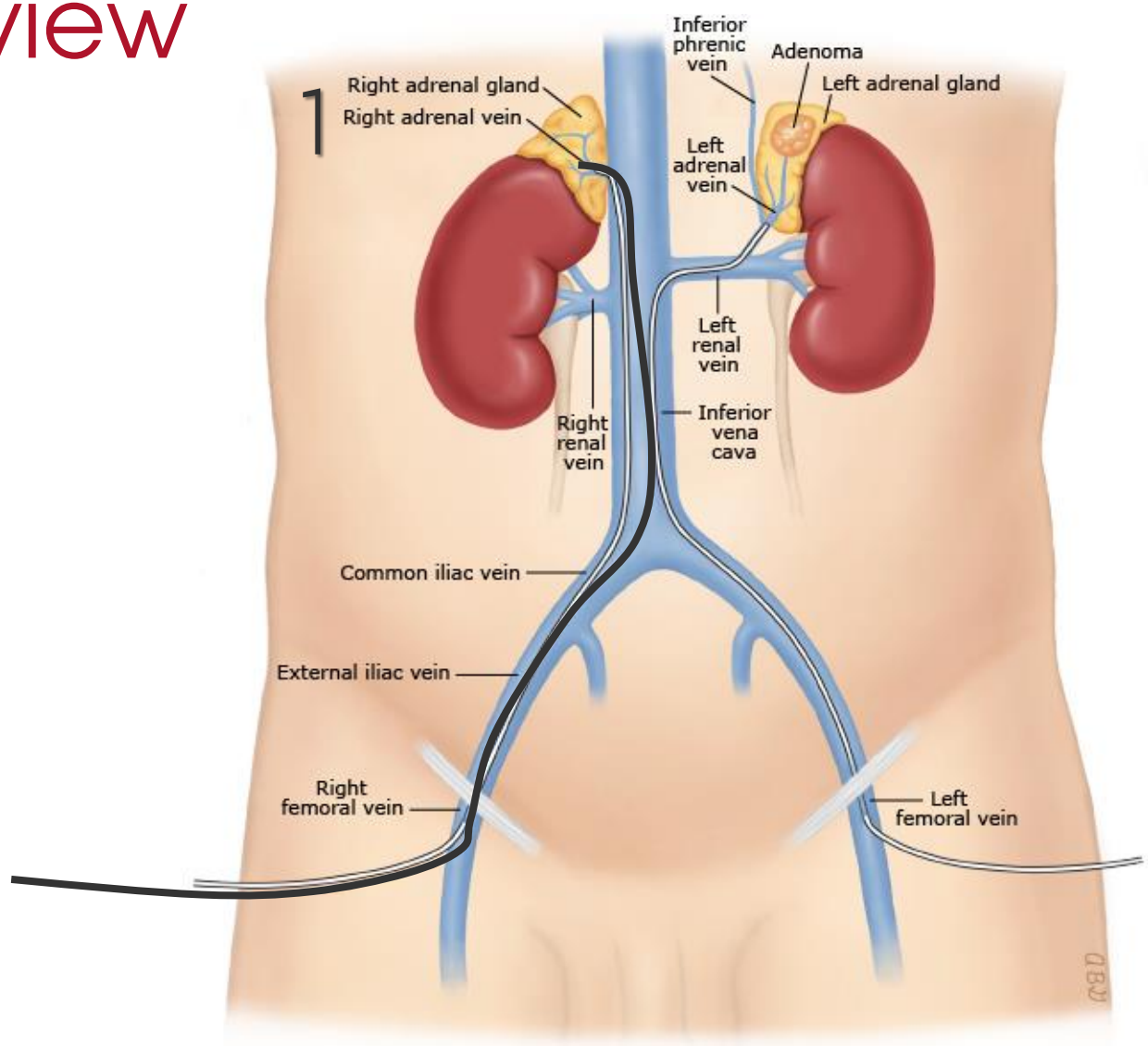


Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

AVS Procedure Overview

GOALS

1. RAV



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AVS Procedure Overview

GOALS

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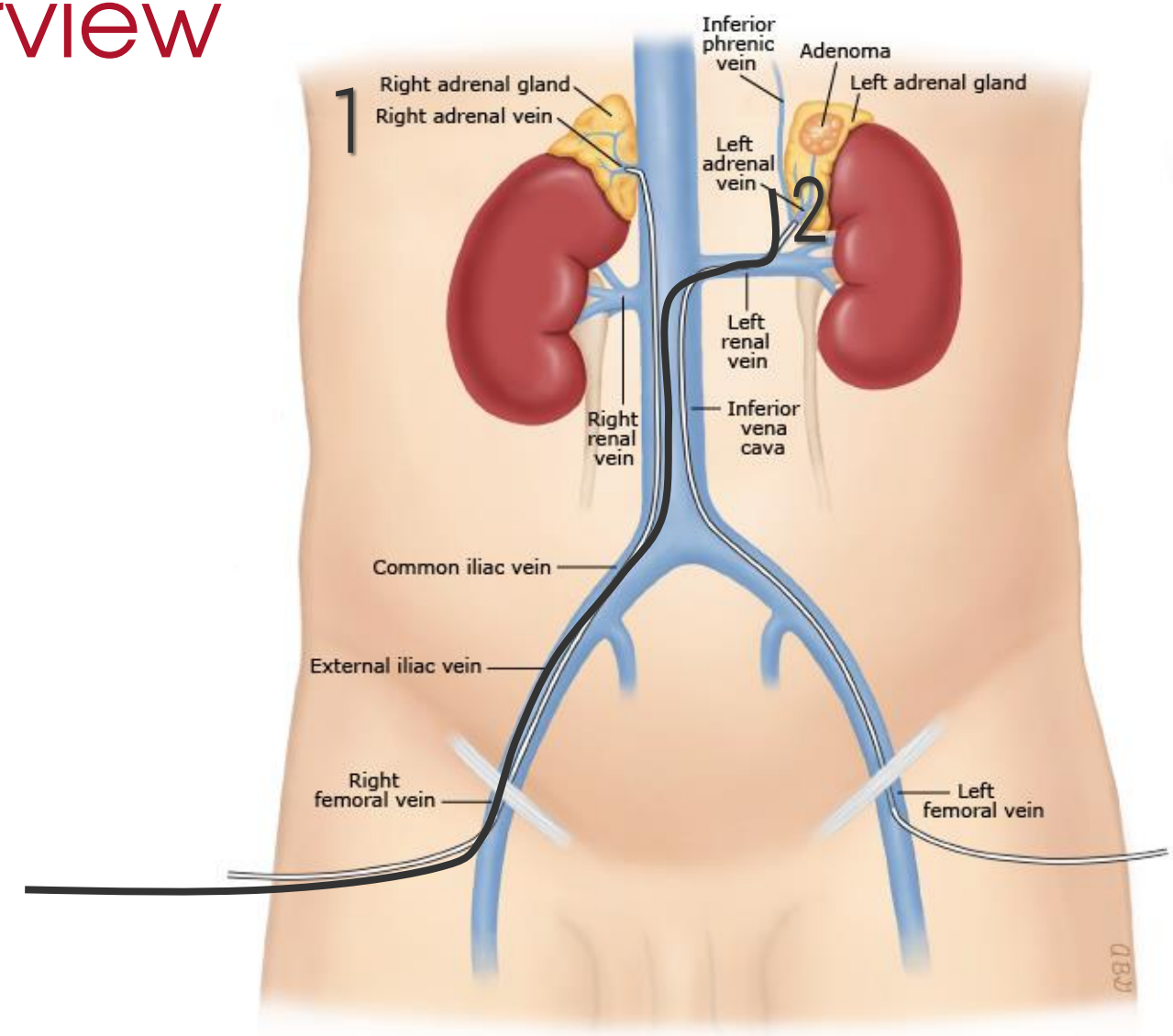
2. LAV



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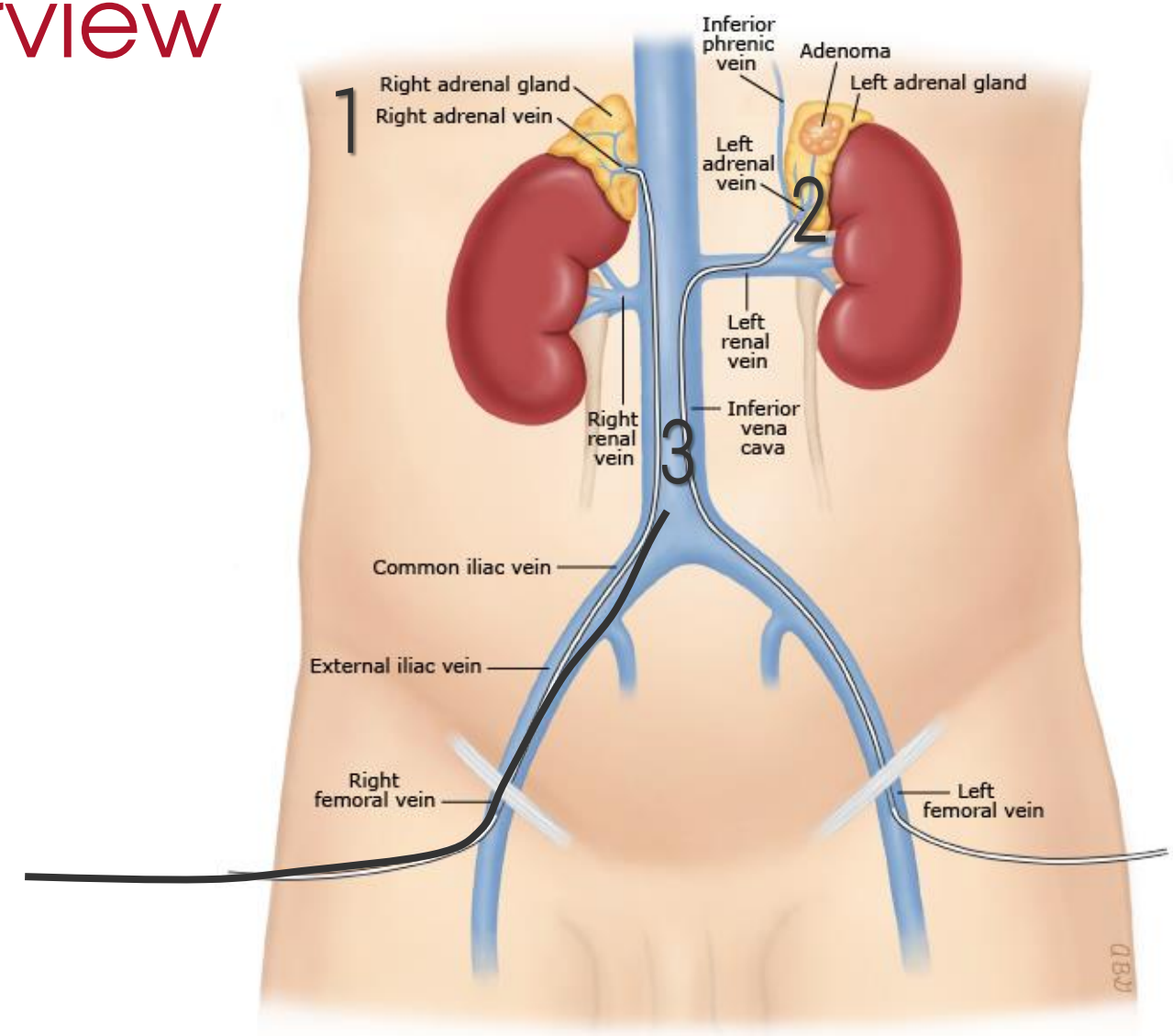


Diagnosis of primary aldosteronism, *Up To Date*, July 2018.

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 ‘bad’, does the other adrenal have suppressed aldosterone secretion levels?

- Always considering aldosterone:cortisol ratios

Sample Results- Case 1

	Aldosterone		Cortisol
RAV	5000	÷	500
LAV	500	÷	500
IVC	100	÷	50

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Sample Results- Case 1

	Aldosterone		Cortisol		A:C ratio
RAV	5000	÷	500	=	10
LAV	500	÷	500	=	1
IVC	100	÷	50	=	2

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Sample Results- Case 1

	Aldosterone	Cortisol	A:C ratio	Location?
RAV	5000	500	10	
LAV	500	500	1	
IVC	100	50	2	

500 ÷ 50

500 ÷ 50

Correct spot? $Cortisol_{adrenal\ vein}/Cortisol_{IVC}$ >3 desired

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Sample Results- Case 1

	Aldosterone	Cortisol	A:C ratio	Location?
RAV	5000	500	10	10
LAV	500	500	1	10
IVC	100	50	2	--

500 ÷ 50

500 ÷ 50

Correct spot? $Cortisol_{adrenal\ vein}/Cortisol_{IVC}$ >3 desired

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Sample Results- Case 1

	Aldosterone	Cortisol	A:C ratio	Location?	Side?
RAV	5000	500	10	10	
LAV	500	500	1	10	
IVC	100	50	2	--	

10 ÷ 1

Correct spot? $Cortisol_{adrenal\ vein}/Cortisol_{IVC}$ >3 desired

Which side is worse? $A:C\ ratio_{high\text{-}side}/\ A:C\ ratio_{low\text{-}side}$

>4 suggests surgery is good option for patient

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Sample Results- Case 1

	Aldosterone	Cortisol	A:C ratio	Location?	Side?
RAV	5000	500	10	10	10
LAV	500	500	1	10	--
IVC	100	50	2	--	--

Correct spot? $\text{Cortisol}_{\text{adrenal vein}}/\text{Cortisol}_{\text{IVC}}$ >3 desired

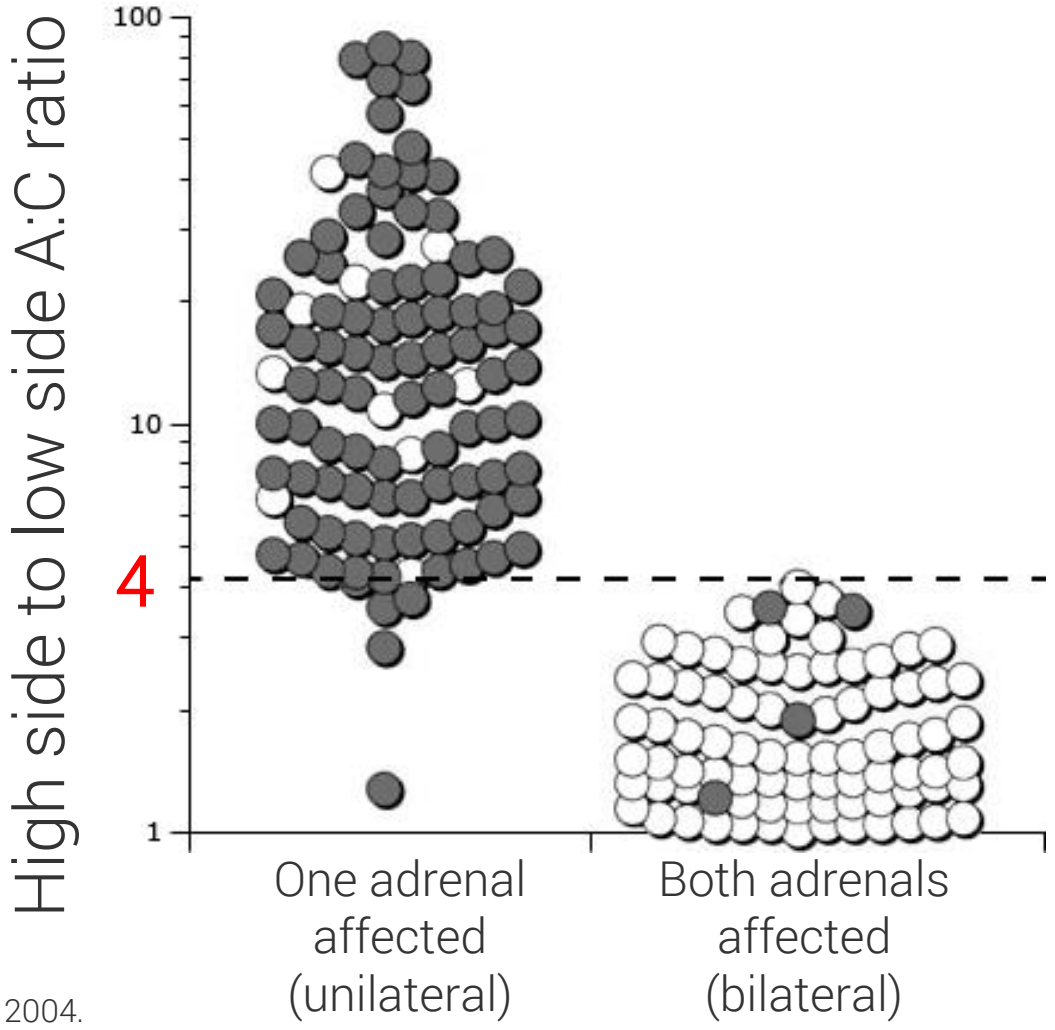
→ Successful AVS, showing unilateral adenoma

Which side is worse? $\text{A:C ratio}_{\text{high-side}}/\ \text{A:C ratio}_{\text{low-side}}$

>4 suggests surgery is good option for patient

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Comparison of ratios



Sensitivity: 95.2%
Specificity: 100%

Diagnosis confirmed surgically

Image modified from Young *et al. Surgery*, December 2004.

Sample Results- Case 1

	Aldosterone	Cortisol	A:C ratio	Location?	Side?
RAV	5000	500	10	10	10
LAV	500	500	1	10	--
IVC	100	50	2	--	--

Correct spot? $Cortisol_{adrenal\ vein}/Cortisol_{IVC}$ >3 desired

→ Successful AVS, showing unilateral adenoma

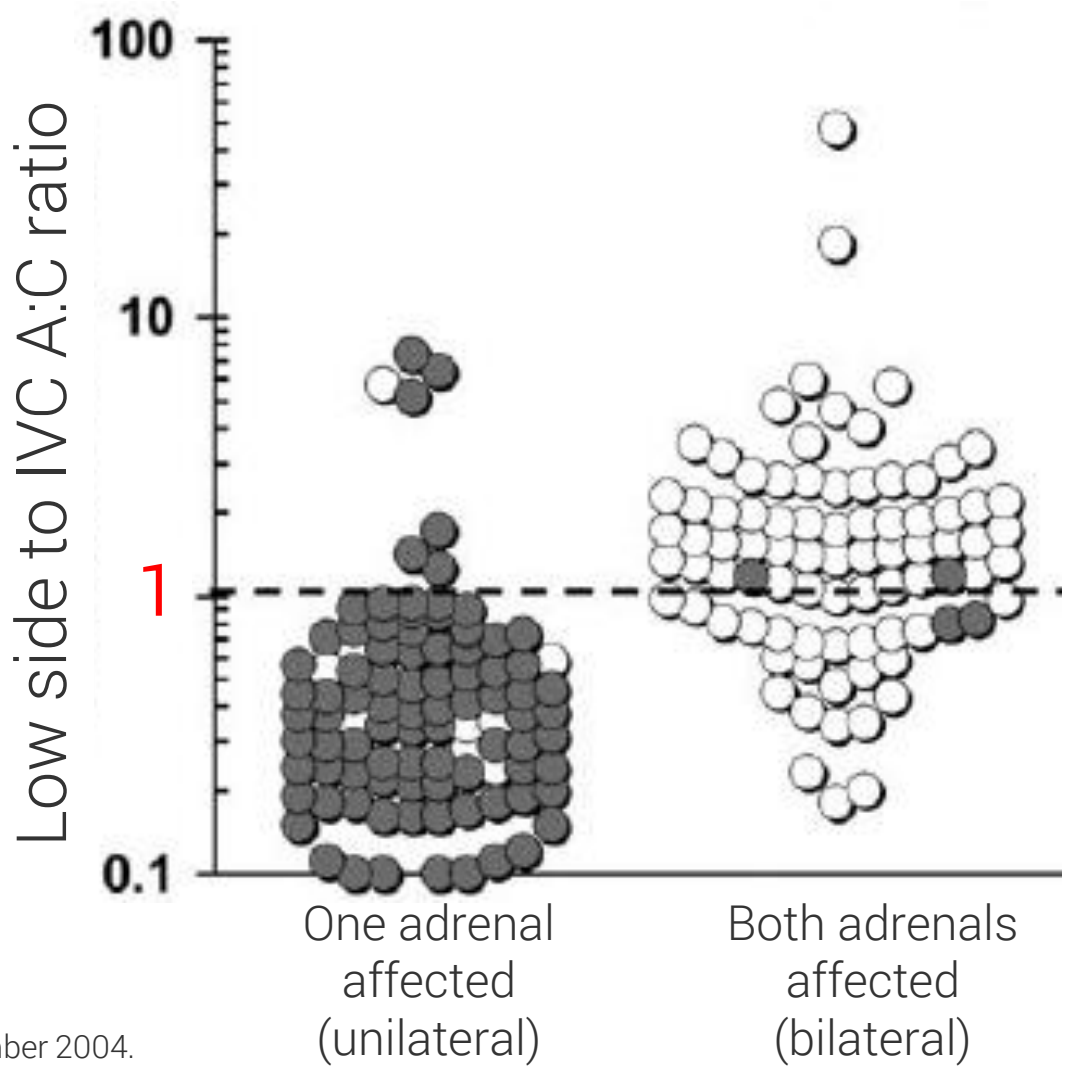
Which side is worse? $A:C\ ratio_{high\text{-}side}/\ A:C\ ratio_{low\text{-}side}$

>4 suggests surgery is good option for patient

Is the other side suppressed? $A:C\ ratio_{low\text{-}side}/\ A:C\ ratio_{IVC}$ $1 \div 2 = 0.5$

University of Pennsylvania, AVS YouTube video (https://www.youtube.com/watch?v=te5pvrOQWXs)

Comparison of ratios



Diagnosis confirmed surgically

<1 suggests suppression

Image modified from Young *et al. Surgery*, December 2004.

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 2

- 52 yo male, left adrenal adenoma on CT
- AVS results:

	Aldosterone		Cortisol		A:C ratio
RAV	2000	÷	400	=	
LAV	4000	÷	400	=	
IVC	100	÷	50	=	

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 2

- 52 yo male, left adrenal adenoma on CT
- AVS results:

	Aldosterone		Cortisol		A:C ratio
RAV	2000	÷	400	=	5
LAV	4000	÷	400	=	10
IVC	100	÷	50	=	2

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 2

- 52 yo male, left adrenal adenoma on CT
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?
RAV	2000	400	5	
LAV	4000	400	10	
IVC	100	50	2	

400 ÷ 50

400 ÷ 50

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 2

- 52 yo male, left adrenal adenoma on CT
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?	
RAV	2000	400	5	8	400 ÷ 50
LAV	4000	400	10	8	400 ÷ 50
IVC	100	50	2	--	

Good sampling location

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 2

- 52 yo male, left adrenal adenoma on CT
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?	Side?
RAV	2000	400	5	8	
LAV	4000	400	10	8	10 ÷ 5
IVC	100	50	2	--	

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 2

- 52 yo male, left adrenal adenoma on CT
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?	Side?
RAV	2000	400	5	8	--
LAV	4000	400	10	8	2
IVC	100	50	2	--	--

- High side to low side A:C ratio < 4 indicates bilateral disease (i.e. both adrenals are affected)

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 3

- Nothing obvious on CT imaging
- AVS results:

	Aldosterone		Cortisol		A:C ratio
RAV	160	÷	80	=	
LAV	400	÷	500	=	
IVC	100	÷	50	=	

Rossi *et al.* "Expert Consensus Statement on Use of AVS for primary aldosteronism subtyping." *Hypertension* 2014.

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 3

- Nothing obvious on CT imaging
- AVS results:

	Aldosterone		Cortisol		A:C ratio
RAV	160	÷	80	=	2
LAV	400	÷	500	=	0.8
IVC	100	÷	50	=	2

Rossi *et al.* "Expert Consensus Statement on Use of AVS for primary aldosteronism subtyping." *Hypertension* 2014.

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 3

- Nothing obvious on CT imaging
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?
RAV	160	80	2	
LAV	400	500	0.8	
IVC	100	50	2	

80 ÷ 50

500 ÷ 50

Rossi *et al.* "Expert Consensus Statement on Use of AVS for primary aldosteronism subtyping." *Hypertension* 2014.

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 3

- Nothing obvious on CT imaging
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?
RAV	160	80	2	1.6
LAV	400	500	0.8	10
IVC	100	50	2	--

- $Cortisol_{RAV}$:$Cortisol_{IVC}$ < 3 → didn't sample from the correct spot

Rossi *et al.* "Expert Consensus Statement on Use of AVS for primary aldosteronism subtyping." *Hypertension* 2014.

Correct spot?	Ratio > 3
One-sided?	Ratio > 4
Suppression?	Ratio < 1

Sample Results- Case 3

- Nothing obvious on CT imaging
- AVS results:

	Aldosterone	Cortisol	A:C ratio	Location?	Side?
RAV	160	80	2	1.6	--
LAV	400	500	0.8	10	--
IVC	100	50	2	--	--

- $Cortisol_{RAV}$:$Cortisol_{IVC}$ < 3 → didn't sample from the correct spot
- However, A:C $ratio_{LAV}$ /A:C $ratio_{IVC}$ = 0.4 0.8 ÷ 2 = 0.4

Rossi *et al.* "Expert Consensus Statement on Use of AVS for primary aldosteronism subtyping." *Hypertension* 2014.

Summary

- Renin-aldosterone system disruption can cause hypertension
- Treatment is dependent on correct disease classification (unilateral or bilateral)
- AVS is the gold standard for determining classification
- Laboratory plays crucial role in optimizing patient care

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