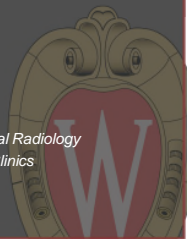


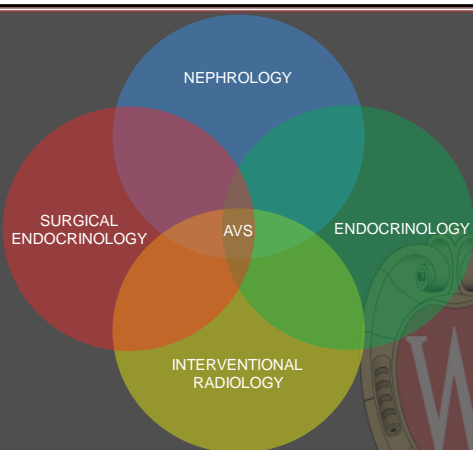
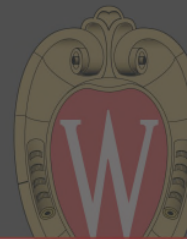
## Adrenal Vein Sampling: A Critical Tool for Subtyping Primary Aldosteronism

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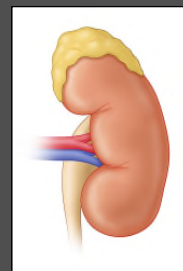
## Disclosures

- No conflicts of interest relevant to this presentation



## Outline

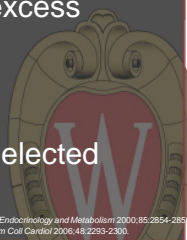
- Definitions
- Patient selection and preparation
- Technique
- Controversies
- Assessment of successful catheterization
- Interpretation of results and assessment of successful lateralization



## Primary Aldosteronism

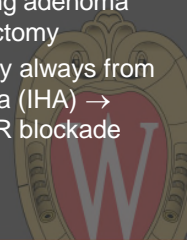
- Most common adrenal hypersecretory disease, characterized by excess aldosterone secretion
- Physiology of aldosterone excess
  - Hypertension
  - Hypokalemia
  - Metabolic alkalosis
- Prevalence of 5-10% in unselected hypertensive patients<sup>1,2</sup>

1. Loh K, et al. Journal of Clinical Endocrinology and Metabolism 2000;85:2854-2859  
2. Rossi GP, Bertini G, et al. J Am Coll Cardiol 2006;48:2293-2300.

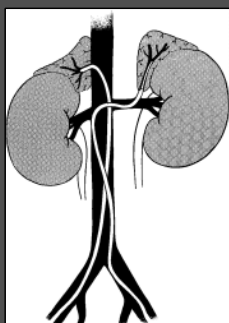


## Sampling for Lateralization

- Is over-secretion unilateral or bilateral?
  - Unilateral hypersecretion nearly always from an aldosterone-producing adenoma (APA) → Unilateral adrenalectomy
  - Bilateral hypersecretion nearly always from bilateral idiopathic hyperplasia (IHA) → Medical management with MR blockade



## AVS is Underutilized!



- Technically challenging, risky, invasive
- Lack of accepted standards for performance of AVS
- Lack of established criteria for interpretation of results
- Failure rates are unacceptably high!

## Evaluation of the German Conn's Registry

Vonend O, et al. Hypertension 2011; 57:990-995.

- Retrospective Data Analysis
  - 230 of 569 patients with PA underwent AVS in 5 participating centers between 1990-2007
  - Selectivity index  $\geq 2.0$  denoted successful adrenal vein catheterization
    - 61/200 patients (30.5%) successfully catheterized on both sides
    - In 42.5%, AVS selective only on the left
    - 33/200 patients (16.5%), AVS unsuccessful on BOTH sides

## German Conn's Registry

Vonend O, et al. Hypertension 2011; 57:990-995.

**Table. Center-Specific AVS Procedure Performance**

Center	A	B	C	D	E
Retrospective study (n=200)					
Patients received AVS/all registered patients (%)	19/53 (36)	67/75 (89)	13/79 (16)	61/204 (21)	40/68 (59)
Bilateral selective	2 (10)	21 (31)	1 (8)	18 (30)	19 (48)
Only left selective	10 (53)	30 (45)	3 (23)	28 (46)	14 (35)
Only right selective	3 (16)	4 (6)	2 (15)	8 (13)	4 (10)
Bilateral nonselective	4 (21)	12 (18)	7 (54)	7 (11)	3 (7)
Prospective study (n=196)					
Patients received AVS/all registered patients (%)	31/57 (54)	23/26 (88)	7/14 (50)	26/30 (87)	19/29 (66)
Bilateral selective	16 (52)	17 (74)	2 (29)	19 (73)	11 (58)
Only left selective	9 (29)	4 (17)	3 (43)	5 (19)	6 (32)
Only right selective	4 (13)	1 (4)	1 (14)	0 (0)	2 (11)
Bilateral nonselective	2 (6)	1 (4)	1 (14)	2 (8)	0 (0)
Change in success rate bilateral selective from retrospective to prospective, %	+42%	+43%	+21%	+42%	+10%
Measures to improve success rate	1 to 4	1 to 5	1, 2, 4	1 to 4	1 to 2

Evaluation of patients who received AVS in 5 different centers (A through E). The individual quote of selective catheterization is given for each center. Data based on AVS using a selectivity index of  $\geq 2.0$ . Measures introduced to improve success rate are as follows: (1) pre-AVS guiding CT; (2) defined standard operation procedure protocol for AVS including preselected test tubes; (3) rapid cortisol assay during AVS; (4) focusing procedure to 1 to 2 interventional staff members; (5) interdisciplinary procedure (endocrinologist or nephrologist attending AVS). Selectivity index = cortisol in adrenal vein/cortisol in inferior vena cava. C indicates cortisol; A, aldosterone; AV, adrenal vein; IV, inferior vena cava. AVS indicates adrenal vein sampling; CT, computed tomography.

## Patient Selection for AVS

- Laboratory analysis
  - Plasma Aldosterone Concentration to Plasma Renin ratio (PAC/PRA)
    - Normal PAC/PRA is 4-10
    - In primary aldosteronism PAC/PRA is  $\sim 30-50$
    - PAC/PRA  $> 32$  (sensitivity 100%, specificity 61% for APA)<sup>1</sup>
  - APAs associated with more severe hypokalemia ( $\leq 3.0$  mEq/L) and higher plasma levels of aldosterone ( $\geq 25$  ng/dL) compared to IHA

1. Hirschara D, et al. J Clin Endocrinol Metab 2001;86:4292-4298.

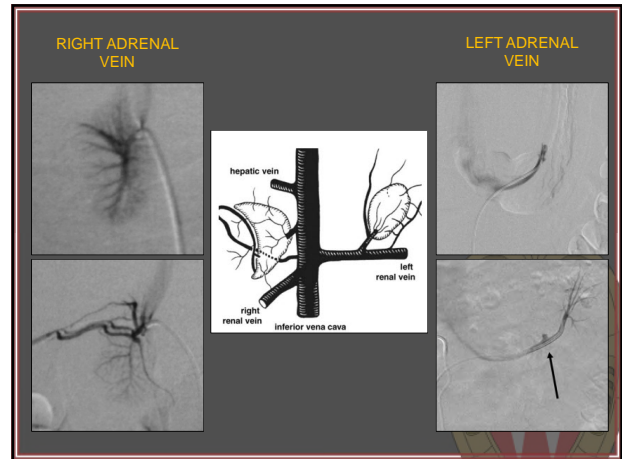
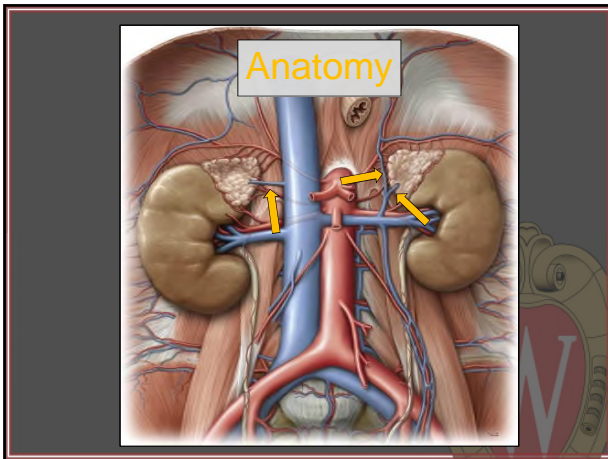
AVS influences the management in as many as 35.7% of patients who would otherwise have been treated incorrectly based on results of CT or other modalities<sup>1</sup>



1. White ML, et al. Surgery 2008;144:926-933.

## Patient Preparation

- Optimally performed in the morning
- Supine position for 1 hour prior to AVS
- Correct hypokalemia, if present
- Careful adjustment of antihypertensive agents before and during AVS
- MR antagonists or amiloride stopped for at least 4 weeks before AVS
- Pre-AVS contrast-enhanced CT

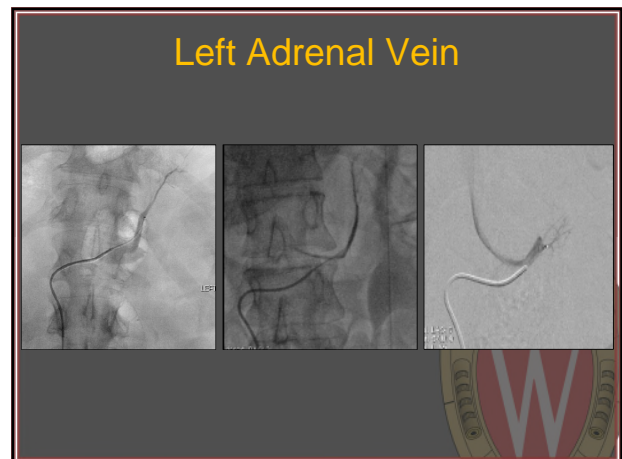
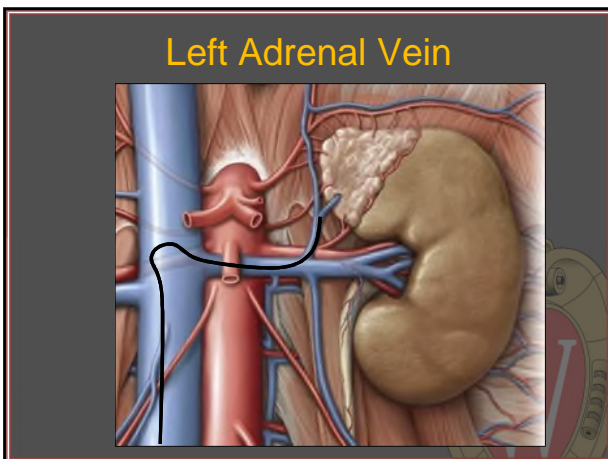


### AVS Technique

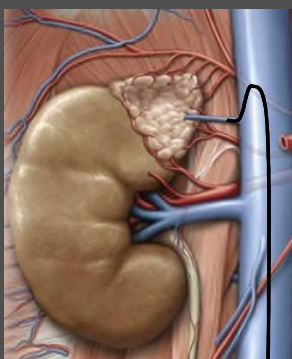
- Transfemoral access
- Single femoral vein access → *sequential* AVS
- Dual femoral vein access → *simultaneous* AVS
- Sampling order: 1) Right adrenal vein 2) Left adrenal vein 3) Infrarenal IVC
  - Minimize time between sample collection

### AVS: Technique

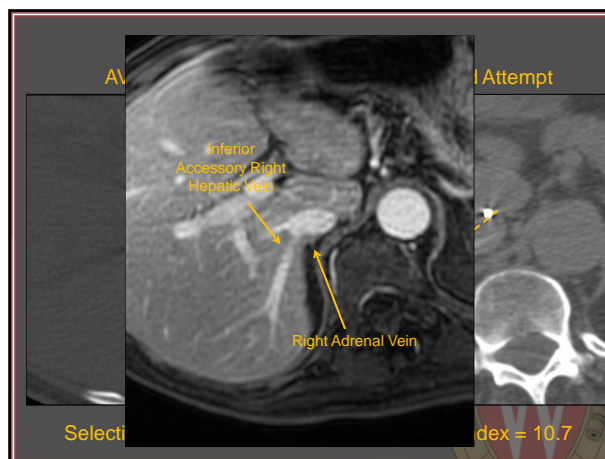
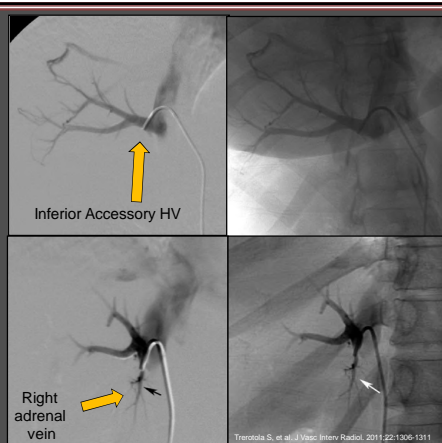
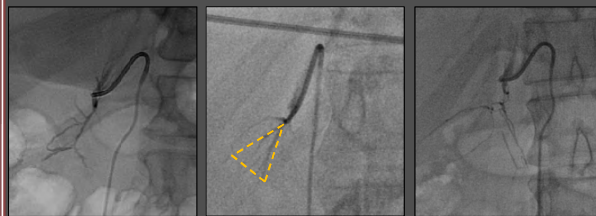
- ± Heparin bolus prior to adrenal vein selection (70-100 U/kg)
- Catheter selection
  - Right adrenal vein → Cobra 2, Mikaelsson, Simmons-1, RDC
  - Left adrenal vein → Simmons-2, Simmons-3
  - Extra sidehole on catheter to permit blood aspiration without adrenal vein collapse\*



## Right Adrenal Vein



## Right Adrenal Vein



## Sample Processing

- 8 mL aliquots of blood are aspirated sequentially from each adrenal vein and the infrarenal IVC
  - Right side sampled first as it is technically most challenging to cannulate
- Each 8 mL sample is divided between sampling vials (i.e. 4 mL in each vial) and sent for **rapid** cortisol assay and aldosterone
- If each selectivity index (SI)  $\geq 3$ , AVS successful

## AVS: Results Interpretation

- Selectivity Index (SI) = Adrenal vein:peripheral vein cortisol ratio
- Successful catheterization of the adrenal vein is reflected in a selectivity index  $\geq 3^*$
- Lateralization Index (LI) = Ipsilateral A/C: Contralateral A/C ratio
- LI  $\geq 4.0$  denotes unilateral APA
- LI  $\leq 2.0$  denotes IHA
- LI 2.0-4.0 borderline

*\*When cosyntropin is used; SI  $\geq 2$  reflects consensus threshold when cosyntropin is not used*



## 5