



THE UNIVERSITY OF  
**CHICAGO**  
MEDICINE &  
BIOLOGICAL  
SCIENCES

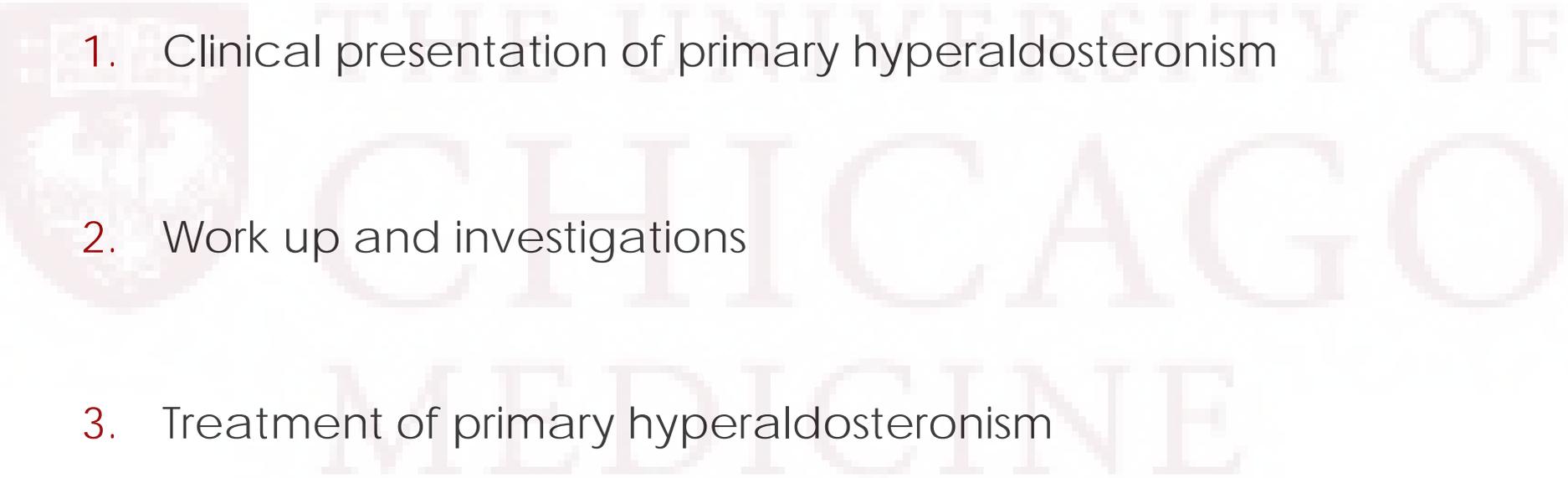
# “Spectrum of Hypertension & Hypokalemia”

Farheen K. Dojki, PGY-6  
Hypertension Fellow, ASH Hypertension Center

Dr. Dojki does not have any relevant financial relationships with any commercial interests.



# OBJECTIVES:

1. Clinical presentation of primary hyperaldosteronism
  2. Work up and investigations
  3. Treatment of primary hyperaldosteronism
  4. Outcomes
- 

# Case # 1

- \* 44 y/o female self referred in 06/2016 for BP management.
- \* PMHx: Hx of pre-eclampsia in 2003, 2005 and 2009.
- \* Did not require meds between pregnancies, however after last delivery needed anti-hypertensives (amlodipine 5mg).
- \* MRA Abdomen negative for Renal Artery Stenosis (2006)
- \* Normal thyroid function
- \* No evidence of Cushing's or pheochromocytoma
- \* History of hypokalemia and needed supplements
- \* Family Hx of hypertension – father in 60s.
- \* Started on Edarby-clor 40/12.5mg – unable to tolerate due to SE → switched to lisinopril 40mg, amlodipine 10mg and HCTZ 25mg.

# Labs 06/29/2016

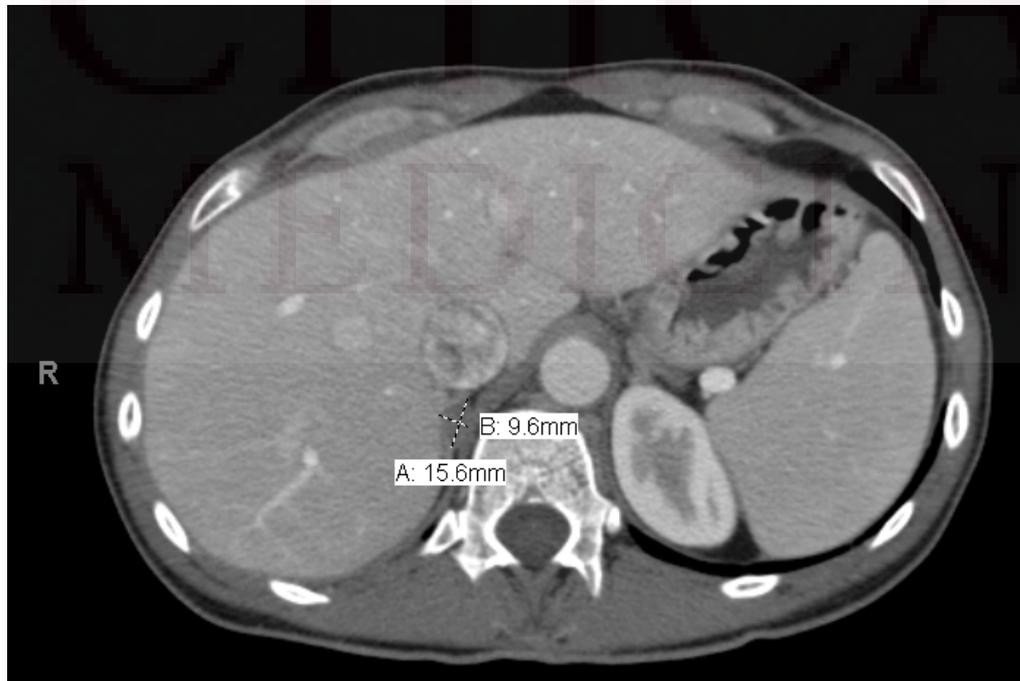
BLOOD	Normal range	Patient
Potassium	3.5 – 5.0	3.5
Aldosterone	< 21 ng/dL	26
Renin	0.6 – 3.0	<0.6

URINE	Normal range	Patient
24 hr aldosterone	< 12 mcg/24hr	19.5 mcg/24hr
24 hr sodium	52 – 380 mmol/24hr	186 mmol/24hr
24 hr creatinine	0.63 – 2.50 g/24hr	1.47 g/24hr

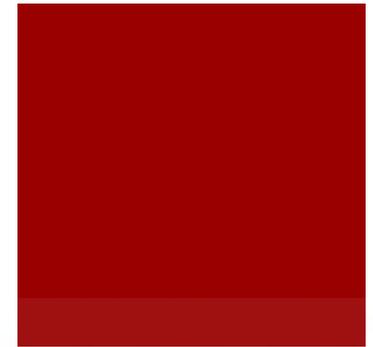
# Radiology

\* CT Abdomen w/ and w/o contrast 07/14/16:

- Right adrenal gland lesion measuring 1.6 x 1.0 cm. Measures – 10HU on unenhanced CT and is compatible with adenoma.



# AVS 08/29/2016



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Attending: George Bakris  
 Pager: 6350  
 Radiologist: Funaki/Lorenz

Sample	Draw Time	Accession #	Location	MEASURED VALUES		CALCULATED VALUES				
				Aldosterone (ng/dL)	Cortisol (ug/dl)	Aldosterone (pmol/L)	Cortisol (nmol/L)	Adrnl/Fem Cortisol Ratio	Aldo/Cortisol Ratio	Aldo/Cortisol Ratio (Highest side/Lowest side)
1R	11:57:00	M50207	Right Adrenal Vein	758	108	20997	2981	2.6	7.0	<b>45.6</b>
1L	12:11:00	M50222	Left Adrenal Vein	81	526	2244	14520	12.6	0.2	
1F	12:15	M50226	Femoral Vein	65	42	1801	1154			
2R	12:04:00	M50229	Right Adrenal Vein	1800	140	49860	3856	3.3	12.9	<b>83.7</b>
1L	12:11:00	M50222	Left Adrenal Vein	81	526	2244	14520	12.6	0.2	
1F	12:15	M50226	Femoral Vein	65	42	1801	1154			

# Outcome:

- Right robotic adrenalectomy 11/10/2016
- Pathology: benign adrenal adenoma
- Able to come off lisinopril and HCTZ. Still on Amlodipine 5mg. BP controlled.
- Off potassium supplements
- Potassium 10 days post op 4.7

# Case # 2

- 30 y/o female referred by PCP as had Hx of hypertension since age 22 and currently 6 weeks pregnant.
- Meds switched to labetalol.
- Delivered without complication at term without pre-eclampsia
- Switched to amlodipine 5mg after delivery. Had to be switched to diltiazem.
- Evaluation for primary hyperaldosteronism started as Hx of hypokalemia on and off
- PMHx: Hypertension, Anxiety.
- PSHx: none.
- Exam: non-contributory

# Labs

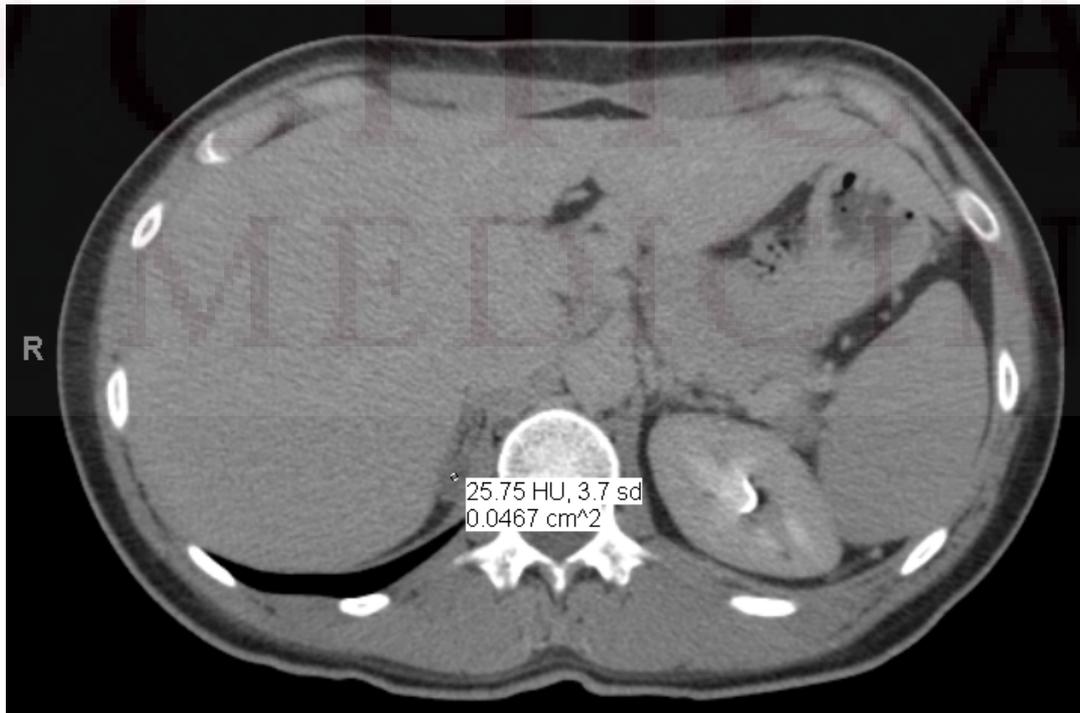
BLOOD	Normal range	Patient
Potassium	3.5 – 5.0	3.8 (on replacement) as low as 2.8 previously
Aldosterone	< 21 ng/dL	33
Renin	0.6 – 3.0	<0.6

URINE	Normal range	Patient
24 hr aldosterone	< 12 mcg/24hr	49 mcg/24hr
24 hr sodium	40 – 220 mmol/24hr	153 mmol/24hr
24 hr creatinine	800 - 1800 mg/24hr	1482 mg/24hr

# Radiology

- \* CT Abdomen w/ and w/o contrast 09/14/2015:
  - Right adrenal gland lesion measuring 1.3 x 0.6 cm. Measures 28HU pre-contrast, 10 minute delay 33HU and is compatible with lipid poor adrenal adenoma.



# AVS 10/03/2016



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Page: 0000  
Radiologist: Funaki, Brian

Sample	Draw Time	Accession #	Location	MEASURED VALUES		CALCULATED VALUES				
				Aldosterone (ng/dL)	Cortisol (ug/dl)	Aldosterone (pmol/L)	Cortisol (nmol/L)	Adrn/Fem Cortisol Ratio	Aldo/Cortisol Ratio	Aldo/Cortisol Ratio (Highest side/Lowest side)
1R	11:05:00	M22029	Right Adrenal Vein	7030	634	194731	17498	16.9	11.1	<b>39.7</b>
1L	11:22:00	M22035	Left Adrenal Vein	84	301	2327	8308	8.0	0.3	
1F	11:25:00	M22038	Femoral Vein	59	38	1634	1038			
2R	11:15:00	M22039	Right Adrenal Vein	16600	1000	459820	27600	26.6	16.7	<b>59.5</b>
1L	11:22:00	M22035	Left Adrenal Vein	84	301	2327	8308	8.0	0.3	
1F	11:25:00	M22038	Femoral Vein	59	38	1634	1038			

# Outcome:

- Right robotic adrenalectomy 11/10/2016
- Pathology: benign adrenal adenoma
- Able to come off diltiazem and BP controlled off meds
- Off potassium supplements

# Hypertension

- Hypertension: **About 70 million** American adults (29%) have high blood pressure—that's **1 of every 3** adults (1)
- Only **about half (52%)** of people with high blood pressure have their condition under control (1)
- Nearly **1 of 3 American adults** have pre-hypertension (1)
- 90-95% essential or primary hypertension
- 5-10% secondary hypertension.
- PA: Consists of 9-13% of cases of secondary hypertension.

# Primary Hyperaldosteronism ~ Conn's syndrome

- Hypertension, Hypokalemia, suppressed plasma renin activity (PRA), and increased aldosterone excretion characterize the syndrome of primary aldosteronism, which was first described in 1955 at the University of Michigan.



*JW Conn*

- Dr. Jerome Conn, was an endocrinologist whose major work during World War II in the 1940s was focused on the regulation of salt loss in the sweat of subjects exposed to elevated heat and humidity, as was of military concern in the South Pacific at the time.

# First case:

- In 1955, Dr. Conn described a case of a 34 year old female patient who had been complaining of seven years of episodic muscle weakness, muscle spasms and cramping of her hands.
- Dr. Conn hypothesized that endogenous corticoids might have also played a role in this patients pathophysiology, and so was able to demonstrate that the patient had elevated mineralocorticoid levels compared to normotensive controls.
- The patients condition greatly improved after removal of a 4cm unilateral adrenal tumor

- Group of disorders in which aldosterone production is **inappropriately high**, relatively autonomous from the renin-angiotensin system, and **nonsuppressible by sodium loading**.
- Such inappropriate production of aldosterone causes cardiovascular damage, suppression of plasma renin, hypertension, sodium retention, and potassium excretion that if prolonged and severe may lead to hypokalemia.
- PA is commonly caused by an adrenal adenoma, by unilateral or bilateral adrenal hyperplasia, or in rare cases by the inherited condition of GRA.
- In recent studies, only a minority of patients with PA (9– 37%) had hypokalemia (1)
- Thus, normokalemic hypertension constitutes the most common presentation of the disease, with hypokalemia probably present in only the more severe cases.

1. Mulatero P, Stowasser M, Loh KC, Fardella CE, Gordon RD, Mosso L, Gomez-Sanchez CE, Veglio F, Young Jr WF 2004 Increased diagnosis of primary aldosteronism, including surgically correctable forms, in centers from five continents. J Clin Endocrinol Metab



### Types of primary aldosteronism

Type	Approximate prevalence (%)
Aldosterone-producing adenoma	30
Idiopathic hyperaldosteronism	65
Primary adrenal hyperplasia	<2
Aldosterone-producing adrenocortical carcinoma	1
Aldosterone-producing ovarian tumor	<1
Familial hyperaldosteronism	
Type I (glucocorticoid-remediable aldosteronism)	<2
Type II (aldosterone-producing adenoma or idiopathic hyperaldosteronism)	<2

**Role for adrenal venous sampling in primary aldosteronism.** [William F. Young Jr., MD](#), [Anthony W. Stanson, MD](#), [Geoffrey B. Thompson, MD](#), [Clive S. Grant, MD](#), [David R. Farley, MD](#), [Jon A. van Heerden, MB](#), ChBAmerican Association of Endocrine Surgeon. [Volume 136, Issue 6](#), December 2004, Pages 1227–1235.



Who to evaluate for Primary  
Hyperaldosteronism??

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# Who to evaluate for PA:

- According to the Endocrine society guidelines (2016), screen:
  1. patients with sustained BP above 150/100 mm Hg on each of three measurements obtained on different days;
  2. hypertension (BP140/90 mm Hg) resistant to three conventional antihypertensive drugs (including a diuretic), or
  3. controlled BP (140/90 mm Hg) on four or more antihypertensive drugs;
  4. hypertension and spontaneous or diuretic-induced hypokalemia;
  5. hypertension and adrenal incidentaloma;
  6. hypertension and sleep apnea;
  7. hypertension and a family history of early onset hypertension or cerebrovascular accident at a young age (40 years); and
  8. all hypertensive first-degree relatives of patients with PA.

# Work-up:

## When to Consider Screening for Primary Aldosteronism:

- Hypertension and Hypokalemia
- Resistant Hypertension
- Adrenal Incidentaloma and Hypertension
- Whenever Considering Secondary Hypertension

Morning blood sample in seated ambulant patient:

- Plasma renin activity (PRA)
- Plasma aldosterone concentration (PAC)

↓ PRA  
↑ PAC

PAC/PRA ratio  $\geq 20$  ng/dL per ng/mL/hr  
( $\geq 555$  pmol/L per ng/mL per hr)

and

PAC  $\geq 15$  ng/dL ( $\geq 416$  pmol/L)

↓  
**Investigate for  
Primary Aldosteronism**

FIG. 1. In patients with suspected primary aldosteronism, screening can be accomplished by measuring a morning (preferably 0800 h) ambulatory paired random PAC and PRA. This test may be performed while the patient is taking antihypertensive medications and without posture stimulation. Spironolactone is the only medication that will absolutely interfere with interpretation of the ratio.

# Confirmation testing:

## 1. ORAL SALT LOADING:

- Patients increase their sodium intake to 200 mmol/d ( ~ 6 g/d) for 3 d, verified by 24-h urine sodium content.
- Adequate potassium supplementation to maintain plasma potassium in the normal range.
- 24 hr Urinary aldosterone, sodium and creatinine measured.
- **urine aldosterone >12ug/24hr with urine Na >200mmol/24hr**

## 2. SALINE SUPPRESSION TEST:

- Patient stays in the recumbent position for at least 1 h before and during the infusion of 2 liters of 0.9% saline iv over 4 h, starting at 0800 – 0930 h.
- Blood samples for renin, aldosterone, cortisol, and plasma potassium are drawn at time zero and after 4 h, with blood pressure and heart rate monitored throughout the test.
- **Post-infusion plasma aldosterone levels >10ng/ dl suggestive of PA;** <5 ng/dl makes the diagnosis unlikely, and values between 5 and 10 ng/dl are indeterminate.

### 3. FLUDROCORTISONE SUPPRESSION:

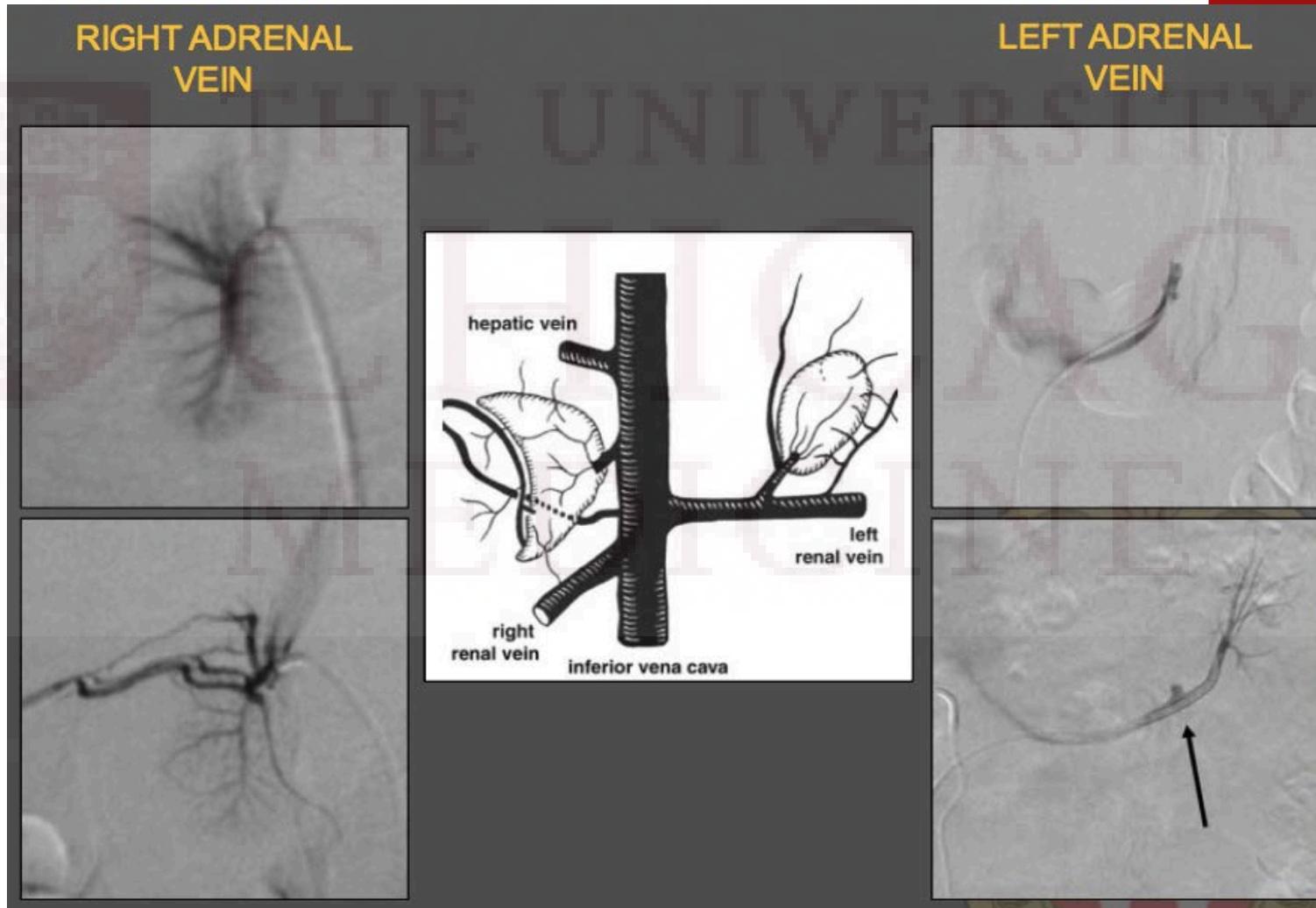
- 0.1 mg oral fludrocortisone every 6 h for 4 d,
- potassium supplements (every 6 h) keep K=4.0 mmol/L
- NaCl supplements and sufficient dietary salt to maintain a urinary sodium excretion rate of at least 3 mmol/kg body wt.
- On day 4, plasma aldosterone and PRA are measured at 1000 h with the patient in the seated posture, and plasma cortisol is measured at 0700 and 1000 h.
- Upright plasma aldosterone > 6 ng/dl on day 4 at 1000 h confirms PA, provided PRA is < 1 ng/ml h and plasma cortisol concentration is lower than the value obtained at 0700 h (to exclude a confounding ACTH effect)

### 4. CAPTOPRIL CHALLENGE TEST:

- 25–50 mg captopril orally after sitting or standing for at least 1 h.
- Blood samples are drawn for measurement of PRA, PAC & cortisol at time 0, 1 and 2 hr after challenge, with the patient remaining seated during this period.
- Plasma aldosterone is normally suppressed by captopril ( 30%).
- In patients with PA, it remains elevated and PRA remains suppressed.

# AVS

In 1967, selective adrenal venous sampling (AVS) for aldosterone was first proposed as a test to distinguish between APA and IHA.



# How to interpret AVS:

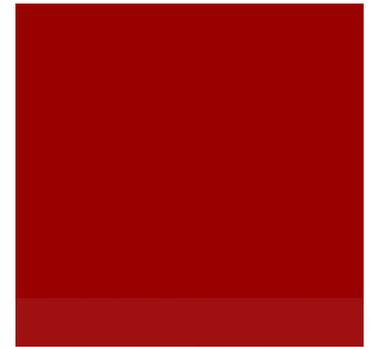
**Step 1: Selectivity Index (SI):** Adrenal vein : femoral vein cortisol ratio.

- Successful catheterization of the adrenal vein is reflected in a  $SI \geq 3:1$  with co-syntropin [5:1 at U of C]
- $SI \geq 2:1$  without co-syntropin. [3:1 at U of C]

**Step 2: Lateralization index (LI):** Highest side adrenal:cortisol ratio of adrenal vein : lowest side adrenal:cortisol ratio.

- $LI \geq 4:1$  denotes a unilateral adenoma
- $LI \leq 3:1$  denotes bilateral adrenal hyperplasia
- $LI 3 - 4$ : grey area.

# 1

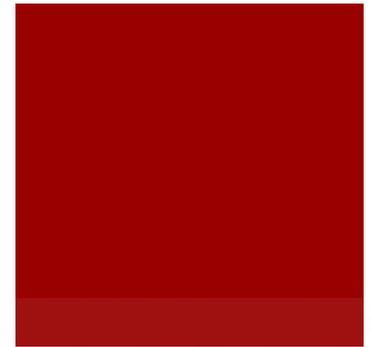


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Page: 0000  
Radiologist: Funaki, Brian

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1F	11:25:00	M22038	Femoral Vein	59	38	1634	1038			

#2:



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 Radiologist: Lorenz, Jonathan M.

Sample	Draw Time	Accession #	Location	MEASURED VALUES		CALCULATED VALUES				
				Aldosterone (ng/dL)	Cortisol (ug/dl)	Aldosterone (pmol/L)	Cortisol (nmol/L)	Adrm/Fem Cortisol Ratio	Aldo/Cortisol Ratio	(Highest side/Lowest side)
1R	10:19:00	H42273	Right Adrenal Vein	2080	624.5	57616	17236	20.0	3.3	1.5
1L	10:33:00	H42292	Left Adrenal Vein	888	399.1	24598	11015	12.8	2.2	
1F	10:35:00	H42311	Femoral Vein	35	31.3	970	864			

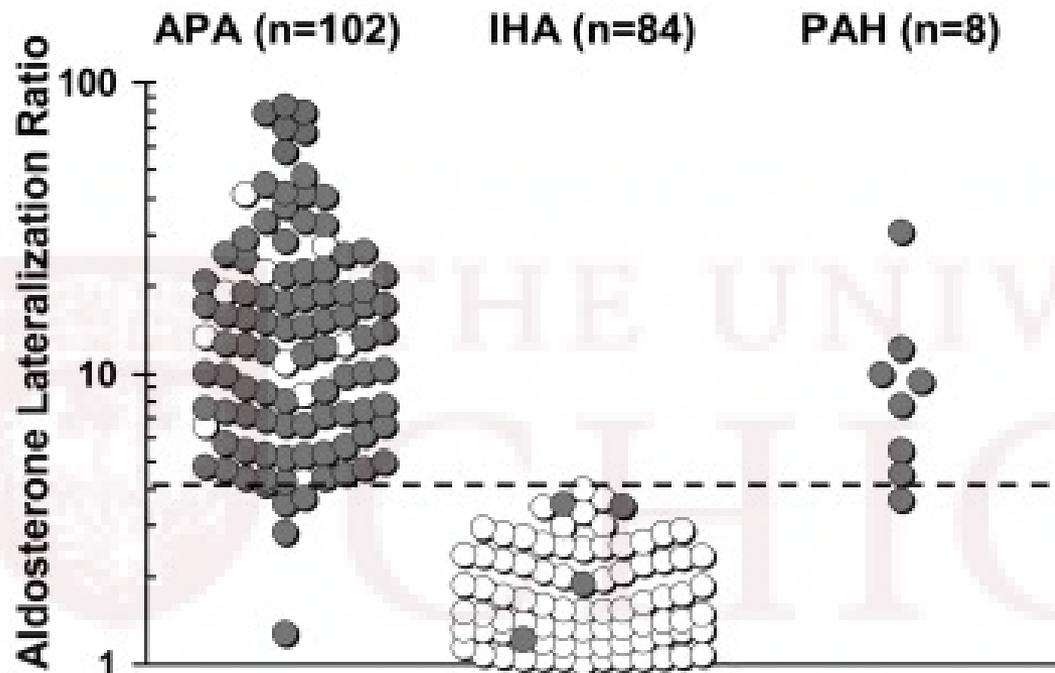
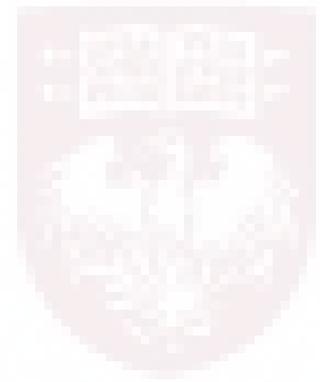
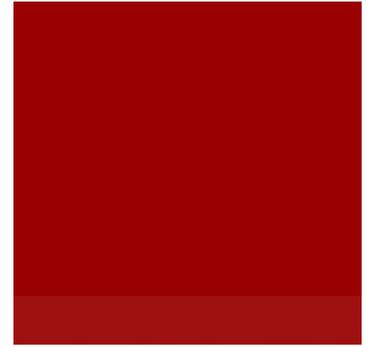


Fig 2. Adrenal vein aldosterone ratios for patients with unilateral APA, PAH, and bilateral IHA. The sensitivity and specificity of the cortisol-corrected PAC lateralization ratio  $>4.0$  for unilateral disease are 95.2% and 100%, respectively. *Shaded symbols* indicate the diagnosis was confirmed surgically.

PAH: Primary Adrenal Hyperplasia      APA: Aldosterone producing adenoma      IHA: idiopathic hyperaldosteronism  
 Role for adrenal venous sampling in primary aldosteronism. [William F. Young Jr.](#), MD, [Anthony W. Stanson](#), MD, [Geoffrey B. Thompson](#), MD, [Clive S. Grant](#), MD, [David R. Farley](#), MD, [Jon A. van Heerden](#), MB, ChBAmerican Association of Endocrine Surgeon.  
[Volume 136, Issue 6](#), December 2004, Pages 1227–1235.

Who does not need AVS  
prior to surgery?



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## No need for AVS if:

- Younger patients (age less than 35 years) with spontaneous hypokalemia, marked aldosterone excess and unilateral adrenal lesions with radiological features consistent with a cortical adenoma on adrenal CT scan may not need AVS before proceeding to unilateral adrenalectomy.
- Patients not interested in pursuing surgery.

# Accuracy of Adrenal Imaging and Adrenal Venous Sampling in Predicting Surgical Cure of Primary Aldosteronism

Vivien Lim, Qinghua Guo, Clive S. Grant, Geoffrey B. Thompson, Melanie L. Richards, David R. Farley, and William F. Young Jr

Divisions of Endocrinology, Diabetes, Metabolism, Nutrition, and Internal Medicine (V.L., W.F.Y.) and the Division of Gastroenterologic and General Surgery (C.S.G., G.B.T., D.R.F., M.L.R.), Mayo Clinic, Rochester, Minnesota 55905; and the Division of Endocrinology (Q.G.), Chinese PLA General Hospital, Beijing, People's Republic of China 100853

J Clin Endocrinol Metab 99: 2712–2719, 2014)

- Retrospective observational study at the Mayo Clinic.
- 263 pts over 19 yrs (1993 – 2011) who underwent unilateral adrenalectomy for treatment of PA. Long term post op f/u in 143 patients (54.45%).
- Overall effective cure rate was 95.5% (resolution of autonomous aldosterone secretion).
- Hypertension was cured in 41.7% and improved in 46.5% (BP<140/90 without meds)
- 4.2% patients not cured
- Adrenal imaging and AVS were concordant to the surgically documented side in **58.6%** and **97.1%** respectively.

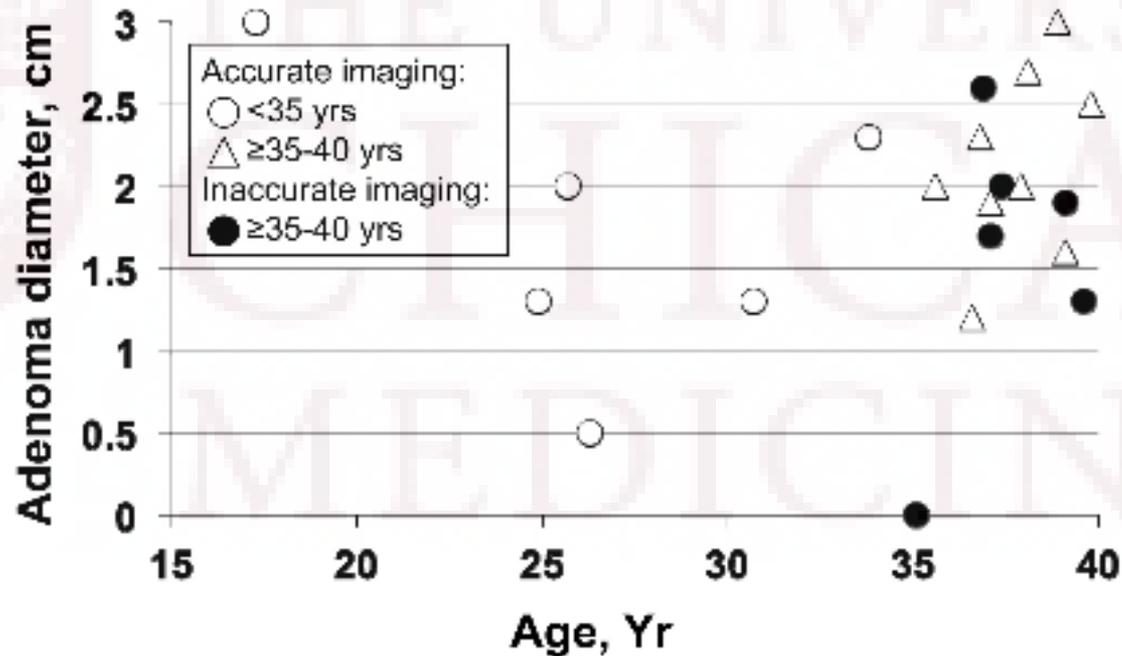
**Table 2.** Preoperative and Postoperative Data in Those Patients With Known Surgical Outcomes<sup>a</sup>

	PA Cured	PA Not Cured
Preoperative data		
n	127	6
Sex	Male: 74 (58.3%)	Male:6 (100%)
Age at surgery, y	50.9 ± 10.7	54.7 ± 6.9
BMI, kg/m <sup>2</sup>	30.0 ± 5.6	30.9 ± 5.6
BP systolic, mm Hg	147 ± 23	158 ± 11
BP diastolic, mm Hg	88 ± 13	92 ± 9
Number of BP medications	2.9 ± 1.3	3.7 ± 1.4
Number on potassium supplements, %	90 (70.9%)	4 (66.7%)
Serum potassium, mmol/L	3.7 ± 0.5	4.1 ± 0.3 <sup>b</sup>
Potassium dosage, mEq/d	40 (0, 80)	25 (0, 60)
Plasma aldosterone, ng/dL	30 (19, 43)	23 (11, 58)
Plasma renin activity, ng/ml/h	0.6 ± 0.1	0.7 ± 0.1
ARR	50.0 (31.4, 74.2)	30.0 (18.9, 92.9)
24-hour urine aldosterone, μg per 24 h	32 (25, 49)	41 (30, 81)
CT or MRI scan with unilateral adrenal abnormality	79 (62.2%)	5 (83.3%)
Number who had AVS, %	102 (80.3%)	5 (83.3%)
AVS cortisol-corrected ALR	14.8 (7.4, 26.3)	5.5 (3.2, 7.4) <sup>c</sup>
Contralateral adrenal-IVC cortisol-corrected lateralization ratio	0.3 (0.2, 0.5)	0.8 (0.5, 0.8) <sup>b</sup>
Adrenal vein aldosterone from presumptive affected adrenal, ng/dL	7245 (3740, 11819)	10682 (2688, 11000)
Postoperative follow-up		
Postoperative plasma aldosterone, ng/dL	2 (1, 4)	20 (10, 29)
Duration of follow-up of BP, y	6.8 ± 4.9	7.2 ± 3.3
BP systolic, mm Hg	125 ± 15	132 ± 19
BP diastolic, mm Hg	77 ± 9	79 ± 4
Number of BP drugs	1 (0, 2)	3 (2.8, 3.5) <sup>d</sup>
Change in number of BP drugs	1.7 ± 1.4	0.5 ± 1.4
Number of patients with BP cure, %	53 (41.7%)	0 (0%)
Duration of follow-up of serum potassium, y	6.6 (2.6, 11.1)	7.7 (3.9, 10.1)
Serum potassium, mmol/L	4.5 ± 0.5	4.4 ± 0.4
Number of patients on potassium supplements, %	4 (3.1%)	2 (33.3%) <sup>b</sup>
Duration of follow-up of plasma aldosterone, y	3.9 (0.8, 10.3)	5.3 (1.6, 8.9)
Plasma aldosterone, ng/dL	7 (4, 11) (n = 16)	24 (12, 36) (n = 2)

<sup>a</sup> Unless noted otherwise, data are shown as mean ± SD or median (interquartile range) or as number (percentage of cohort).

<sup>b</sup> P = .03.

<sup>c</sup> P = .02.



**Figure 2.** Relationship between size of the adenoma and age of the patients younger than 40 years.



Predictors of improved  
clinical outcomes after  
surgery???

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# Predictors of improved clinical outcomes after surgery:

1. 2 or fewer antihypertensive medications,
2. body mass index  $\leq$  25 kg/m<sup>2</sup>,
3. duration of hypertension  $\leq$  6 years, and
4. female sex.

Based on the resulting 4-item aldosteronoma resolution score (ARS), 3 likelihood levels for complete resolution were identified:

low (0-1)	27% resolution
medium (2-3)	46% resolution
high (4)	75% resolution

# Characteristics predicting clinical improvement and cure following laparoscopic adrenalectomy for primary aldosteronism in a large cohort

Patrick J. Worth, M.D.<sup>a</sup>, Nicholas R. Kunio, M.D.<sup>b</sup>, Issac Siegfried, B.S.<sup>a</sup>, Brett C. Sheppard, M.D.<sup>a</sup>, Erin W. Gilbert, M.D., M.C.R.<sup>a</sup>  

<sup>a</sup> Department of Surgery, Division of Gastrointestinal and General Surgery, Oregon Health & Science University, 3181 SW Sam Jackson Pk. Rd., L223A Portland, OR 97239, USA

<sup>b</sup> Division of General & Vascular Surgery, Department of Surgery, Advocate Medical Group, Elgin, IL, USA

Received 18 February 2015, Revised 2 May 2015, Available online 17 August 2015

1. BMI < 30 had improved outcomes Vs BMI >30 (27.4 Vs 32.7) [p=0.02]
2. Duration of Hypertension (9.1yrs Vs 14.9 yrs) [p=0.02]
3. No. of pre-op anti-hypertensives (2.1 Vs 3.7) [p=0.002]
4. Serum creatinine (0.94 Vs 1.32mg/dL) [p=0.016]
5. Pre-op systolic BP (147.5 Vs 159.7) [p=0.47]



Review article

## Primary aldosteronism and pregnancy

Adam Morton ✓

- Primary hyper-aldosteronism is under diagnosed in pregnancy
- Review from 1960-2015 only reported 47 cases of PA in pregnancy
- Associated with significant fetal mortality and maternal morbidity and mortality
- Complications: 5 IUFD; 2 neonatal deaths, 8 IUGR; 6 placental abruptions; 10 cases of pre-eclampsia and 3 cases of HELLP syndrome.
- Elevated progesterone levels acts as antagonist at mineralocorticoid receptors, hence aldosterone levels rise in parallel with changes in progesterone. Plasma Aldosterone increases by 3-8 fold during gestation, plateau in 3<sup>rd</sup> trimester.
- Estrogen stimulates renin secretion, PRA increases by 4 fold at 8wks, 7 fold at term.
- Fall in ARR during gestation, giving false negatives. **An elevated ARR together with PRA less than 4 ng/ml/h make the diagnosis of PA likely.**



- Best time to check for PA is pre pregnancy or 3 months post partum.
- From above cases: 9 subjects underwent laparoscopic adrenalectomy between 14-24 weeks (second trimester).
- Spironolactone not recommended in pregnancy due to anti-androgenic effect on male fetus.
- Prior to 1980 spiro was used in Tx of HTN, pre-eclampsia, liver disease in pregnancy.
- 1975: No evidence of anti-androgenic effect in male rats whose mothers were exposed to 400mg of spironolactone from Day 14 of pregnancy to delivery. (1)
- 1980: study reported de-masculinization of external genitalia of exposed rats (1)
- Spironolactone used in 6 pregnancies in women with PA: 2 used from prior to conception till first trimester – one male neonate showing no evidence of virilization (3)
- Spironolactone used in Bartter & Gitelman syndrome with no adverse effect in 6 male and 6 female newborns when used in first trimester (3)

(1) L.I. Rose, Q. Regestein, J.M. Reckler Lack of effect of spironolactone on male genital development. Invest. Urol., 13 (1975), pp. 95-96

(2) A. Hecker, S.H. Hasan, F. Neumann Disturbances in sexual differentiation of rat fetuses following spironolactone treatment. Acta Endocrinol. (Copenh), 95 (1980), pp. 540-545

(3) Primary aldosteronism and pregnancy: Adam Morton. Pregnancy Hypertension, an international journal of women's cardiovascular health. [Volume 5, Issue 4](#), October 2015, Pages 259-262

- 
- Amiloride used in 17 pregnancies with severe hypertension, Liddle, Bartter and Gitelman syndromes without adverse effects.
  - Eplerenone used from conception to delivery in 3 pregnancies with Gitelman syndrome with no adverse events.
  - Spironolactone is safe for use during breastfeeding.

When to get pregnant after  
adrenalectomy for APA??



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- No data
- Recommended to avoid pregnancy for 6 months after surgery. No literature to support it.

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# Familial Hyperaldosteronism

## Type I (GRA):

- Autosomal dominant, responsible for 1% of cases of PA.
- The mutation in patients with GRA is fusion of the promoter region of the gene for CYP11B1 and the coding sequences of CYP11B2, resulting in a CYP11B1/ CYP11B2 chimeric gene.
- GRA is a form of hyperaldosteronism in which the hypersecretion of aldosterone is dependent upon endogenous ACTH secretion, which activates aldosterone synthesis.
- Presentation is highly variable, with some patients presenting with normal BP and some characterized by aldosterone excess, suppressed PRA, and hypertension of early onset that is usually severe and refractory to conventional antihypertensive therapies.
- Genetic testing by either Southern blot or long PCR techniques for the underlying hybrid CYP11B1/ CYP11B2 mutation is sensitive and specific.
- Genetic testing for GRA should be considered for PA patients with a family history of PA or of strokes at a young age, or with onset at a young age (eg, 20 years).

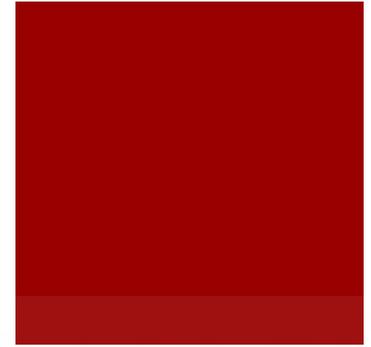
- Tx: low dose dexamethasone

Clinical Practice Guidelines - The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. John W. Funder, Robert M. Carey, Franco Mantero, M. Hassan Murad, Martin Reincke, Hirotaka Shibata, Michael Stowasser, and William F. Young, Jr

# Familial Hyperaldosteronism Type II:

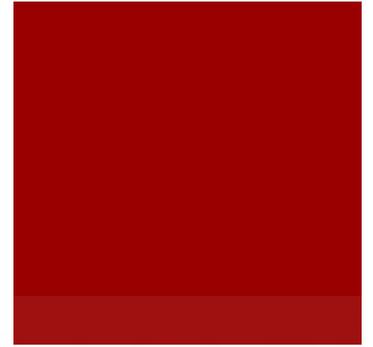
- Autosomal dominant disorder.
- Unlike FH-I, the hyper-aldosteronism in FH-II does not suppress with dexamethasone, and GRA mutation testing is negative.
- FH-II families may have APA, IAH, or both and are clinically indistinguishable from patients with apparent nonfamilial PA. Although FH-II is more common than FH-I, accounting for at least 7% of patients with PA in one series, its true prevalence is unknown.
- The molecular basis for FH-II is unclear, although several linkage analyses have shown an association with chromosomal region 7p22.
- Few families of European decent.

# Familial Hyperaldosteronism Type III:



- FH-III was first described in a family characterized by severe hypertension in early childhood associated with hyperaldosteronism, hypokalemia, and resistance to antihypertensives requiring bilateral adrenalectomy.
- The cause of FH-III is a mutation in the KCNJ5 gene encoding the potassium channel Kir 3.4 (potassium inwardly rectifying channel, subfamily 1, member 5). Mutations occur near the selectivity filter for potassium, resulting in increased sodium conductance and cell depolarization. This opens voltage-activated calcium channels leading to increased calcium signaling, followed by increased aldosterone production and cell proliferation.
- Typically a milder phenotype than other causes.

Thank you!



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