

Adrenal Disorders

Anand Vaidya, MD MMSc

Director, Center for Adrenal Disorders

Chief (Interim), Division of Endocrinology, Diabetes, & Hypertension

Brigham and Women's Hospital

Associate Professor of Medicine, Harvard Medical School

anandvaidya@bwh.harvard.edu

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Training

- Harvard Medical School
- Internal Medicine Residency @BWH
- Clinical Endocrinology Fellowship @BWH
- Cardiovascular Endocrinology Research Post-Doc @BWH

Positions

- Director, Center for Adrenal Disorders @BWH
- Chief (Interim), Division of Endocrinology, Diabetes, and Hypertension @BWH
- Associate Professor of Medicine @HMS
- Director, e-Learning Initiative @BWH/@NEJM
- Former Director, Homeostasis II Curriculum @HMS

Learning Objectives

1. To provide a updates and pragmatic approaches to **primary aldosteronism and hypertension**
2. To provide a pragmatic approach to evaluation of **adrenal insufficiency**
3. To provide a pragmatic approach to the assessment of incidentally discovered **adrenal masses**

Primary Aldosteronism

Case

36-year old woman presents for hypertension management

Age 27: 1st pregnancy, preeclampsia => Persistent HTN => nifedipine

Age 28 (CCB)

PAC (LC-MS/MS): 8.3 ng/dL
(230 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 4.1 mEq/L

Age 32 (no meds)

PAC (LC-MS/MS): 6.6 ng/dL
(183 pmol/L)

PRA <0.6 ng/mL/h

ARR >11

K 4.4 mEq/L

Age 33 (CCB, **ACEi**)

K **3.3 mEq/L**

Age 36 (CCB, **ACEi**)

PAC (LC-MS/MS): 8.1 ng/dL
(225 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 4.3 mEq/L

Does this patient have primary aldosteronism?

Is further testing needed to make the diagnosis?

Case

**Low-Renin HTN
Renin-Independent
Aldosteronism**

36-y

Age

Age 28 (CCB)

PAC (LC-MS/MS): 8.3 ng/dL
(230 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 4.1 mEq/L

**Low-Renin HTN
Renin-Independent
Aldosteronism**

Age 32 (no meds)

PAC (LC-MS/MS): 6.6 ng/dL
(183 pmol/L)

PRA <0.6 ng/mL/h

Negative Confirmatory Test PA

(expert opinion)

Oral Sodium Suppression Test:

24h UNa of 190 mEq

24h UAldo 9.7 mcg (>12)

**Hypokalemia
on ACEi?**

Age 33 (CCB, **ACEi**)

PAC (LC-MS/MS): 8.1 ng/dL
(225 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K **3.3 mEq/L**

**Renin low on ACEi
ALDO not suppressed
on ACEi**

Age 36 (CCB, **ACEi**)

PAC (LC-MS/MS): 8.1 ng/dL
(225 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 4.3 mEq/L

Case

36-year old woman presents for hypertension management

Age 27: 1st pregnancy, preeclampsia => Persistent HTN => nifedipine

Age 28 (CCB)

PAC (LC-MS/MS): 8.3 ng/dL
(230 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 4.1 mEq/L

Age 32 (no meds)

PAC (LC-MS/MS): 6.6 ng/dL
(183 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 4.4 mEq/L

Age 33 (CCB)

PAC (LC-MS/MS): 3.3 ng/dL
(90 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

K 3.3 mEq/L

Age 36 (CCB, **ACEi**)

PAC (LC-MS/MS): 8.1 ng/dL
(225 pmol/L)

PRA <0.6 ng/mL/h

ARR >14

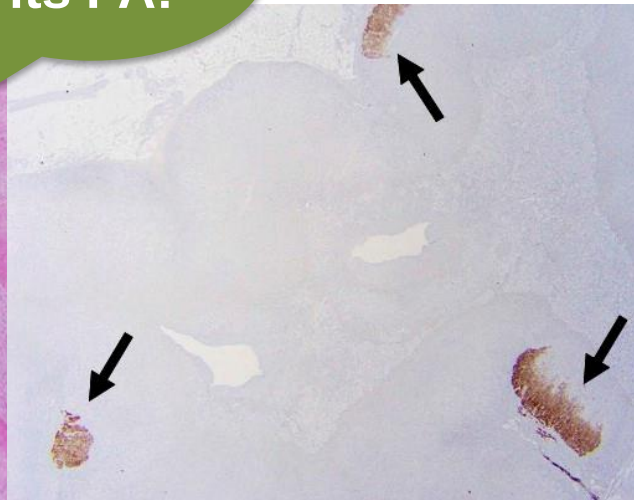
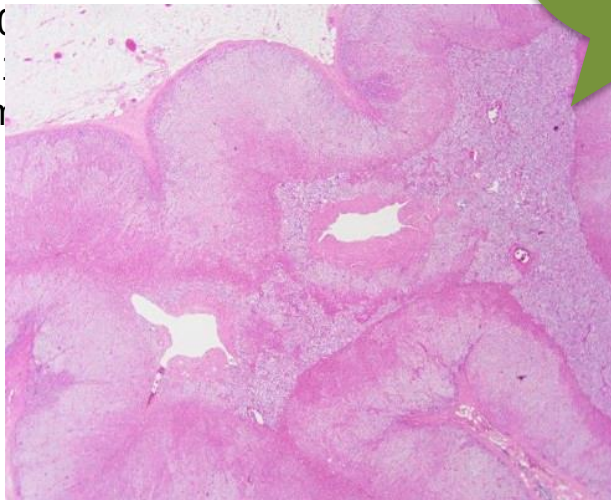
K 3.3 mEq/L

Of course
its PA!

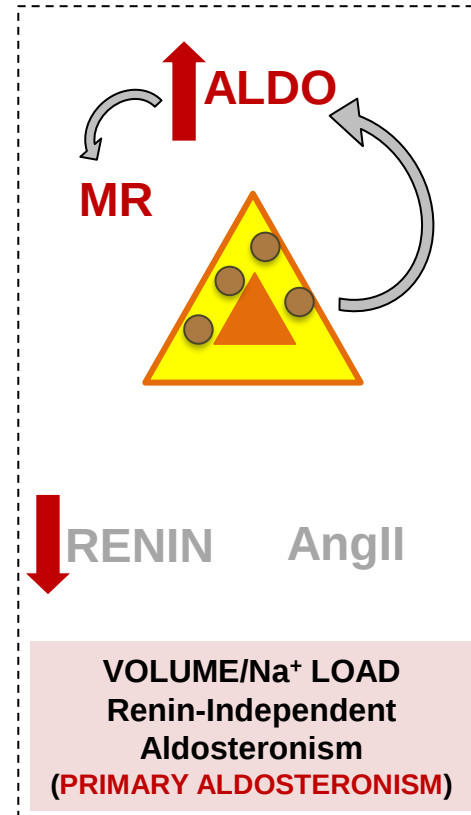
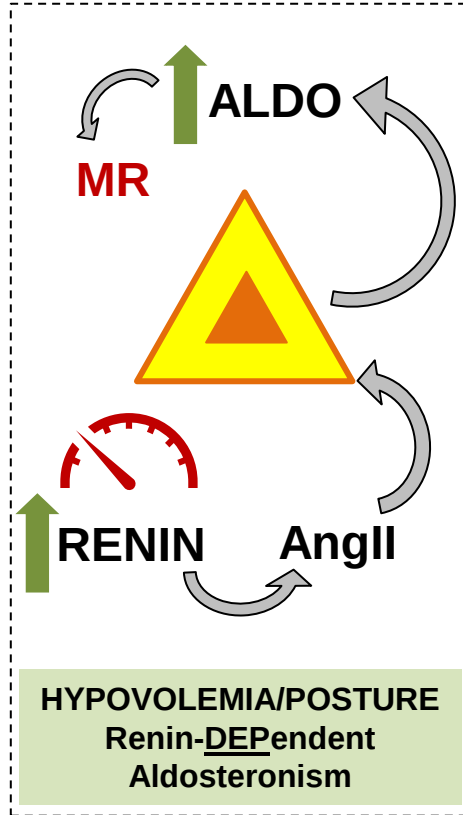
Oral Sodium Suppression Test:

24h UNa of 190 mEq

24h UAldo 9.7 mcg (>12)



Primary Aldosteronism



What is Primary Aldosteronism?

PATHOPHYSIOLOGIC SYNDROME:

- Inappropriate aldosterone production: **renin-independent aldosterone production, relatively non-suppressible**
- Excessive activation of the MR, vicious cycle of volume expansion, hypertension, CV and Kidney disease *independent of BP*

Clinical Manifestations:

Most patients with PA **do not have** hypokalemia or Resistant HTN

Hallmark Biochemical Diagnostics:

Suppression of Renin

Inappropriate/Dysregulated Production of Aldosterone

Why should you care?

Part I: Preventable Cardiovascular Risk

Part II: Under-recognition

Part III: High Prevalence

Risk for Incident Composite Cardiovascular Events

	Overt Primary Aldosteronism (No Targeted Therapy)	Matched Idiopathic Hypertension
CAD	~2x	-
Heart failure	~2x	-
Stroke	~2.5x	-
Afib	~3.5x	-
LVH	~2.3x	-

↑CVD independent of BP

Risk for Incident Composite Cardiovascular Events

Why should you care?

Part I: Preventable Cardiovascular Risk

**Primary Aldosteronism increases the risk for
CVD, CKD, and death...**

**...we have targeted therapies that can
mitigate this risk**

Why should you care?

Part I: Preventable Cardiovascular Risk

Part II: Under-recognition

Part III: High Prevalence

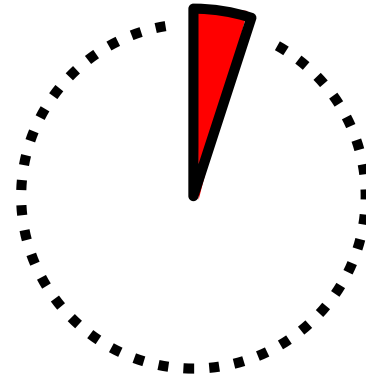
Failure to Screen for Primary Aldosteronism

Recommended Indications to Screen

Resistant HTN

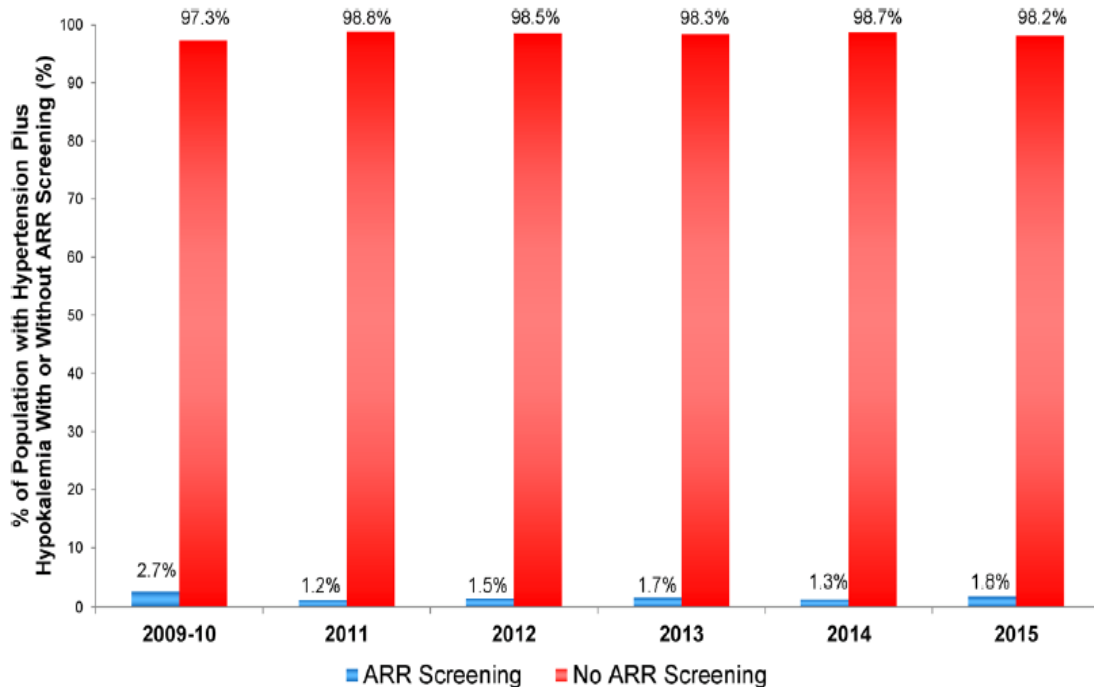
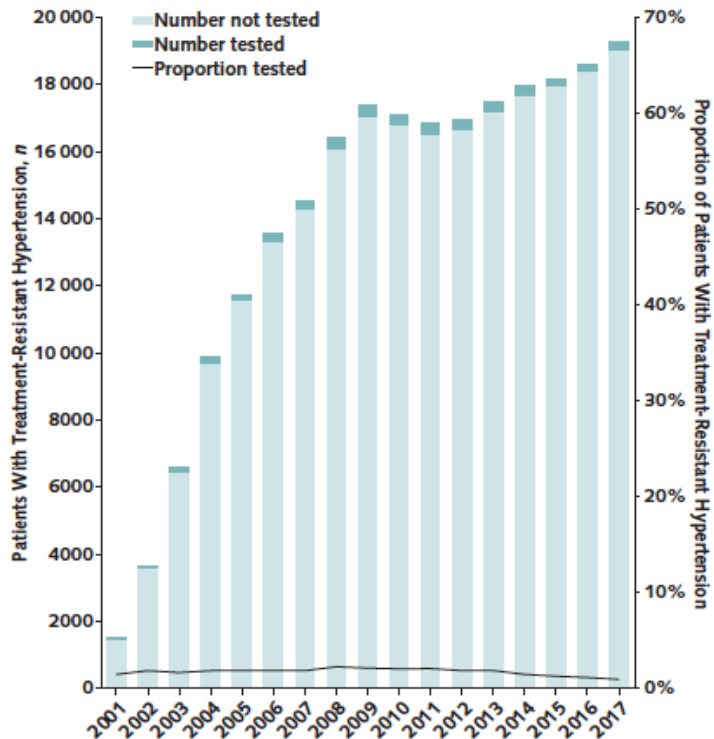
HTN + HypoK

Reality

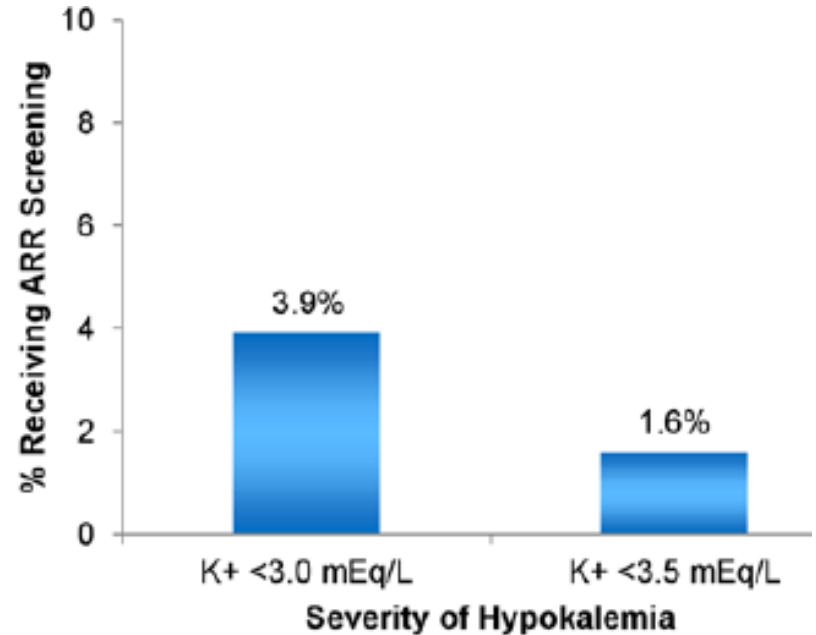
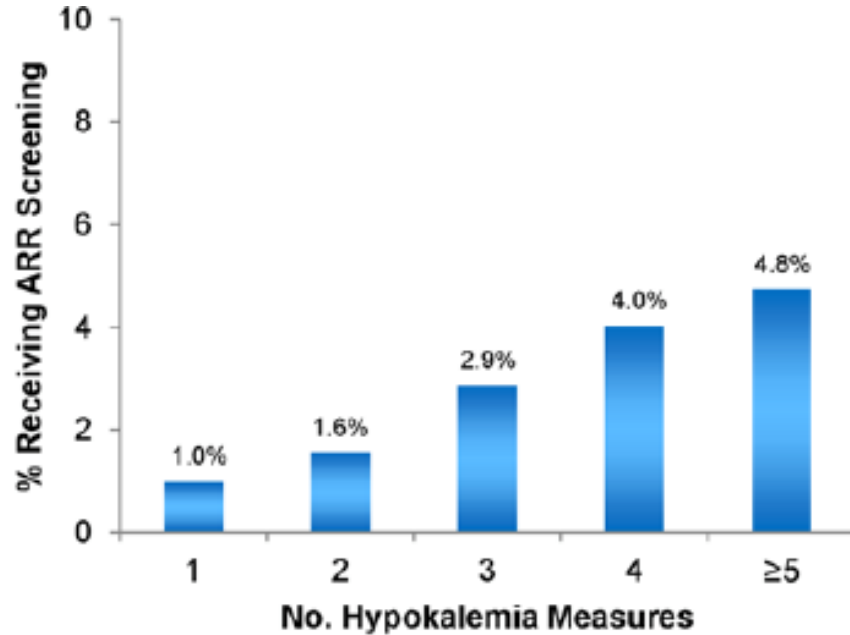


<1-2% !!

Failure to Screen for Primary Aldosteronism



Failure to Screen for Primary Aldosteronism



Failure to Screen for Primary Aldosteronism

Reasons Why PA is Under-Diagnosed

- 1) We don't look for it!
- 2) *When we do look for it, we often misinterpret or ignore the results*

Why should you care?

Part I: Preventable Cardiovascular Risk

Part II: Under-recognition

Part III: High Prevalence

Conservative Prevalence Estimates

Resistant Hypertension	>25-30%
HTN + Hypokalemia	>30%
Stage I-II Hypertension	>15-20%
Pre-HTN/Normal BP	~10%

Diagnostic Testing Complexity

Key Point: The landscape of PA testing is dominated by *relatively arbitrary* and *unnecessarily complex* practices that rely on *unvalidated* diagnostic thresholds

Diagnostic Testing

*There is no reference/gold-standard diagnostic
Diagnostic thresholds are relatively arbitrary and not rigorously validated*

ARR



Relatively Arbitrary Thresholds
30, 25, 20, etc.

Aldosterone



Relatively Arbitrary Thresholds
20, 15, 10 ng/dL, etc.

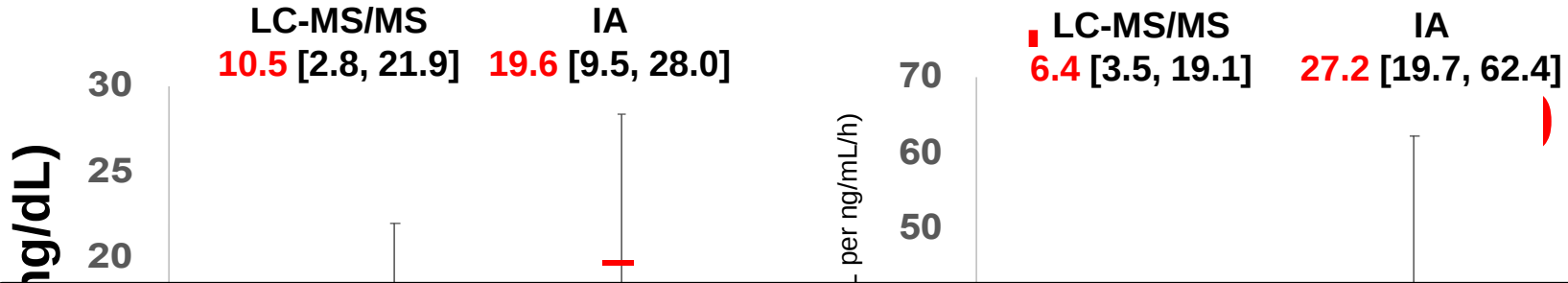
**Aldosterone
Suppression Tests**



Multiple Protocols
Arbitrary Thresholds

Aldosterone Assays

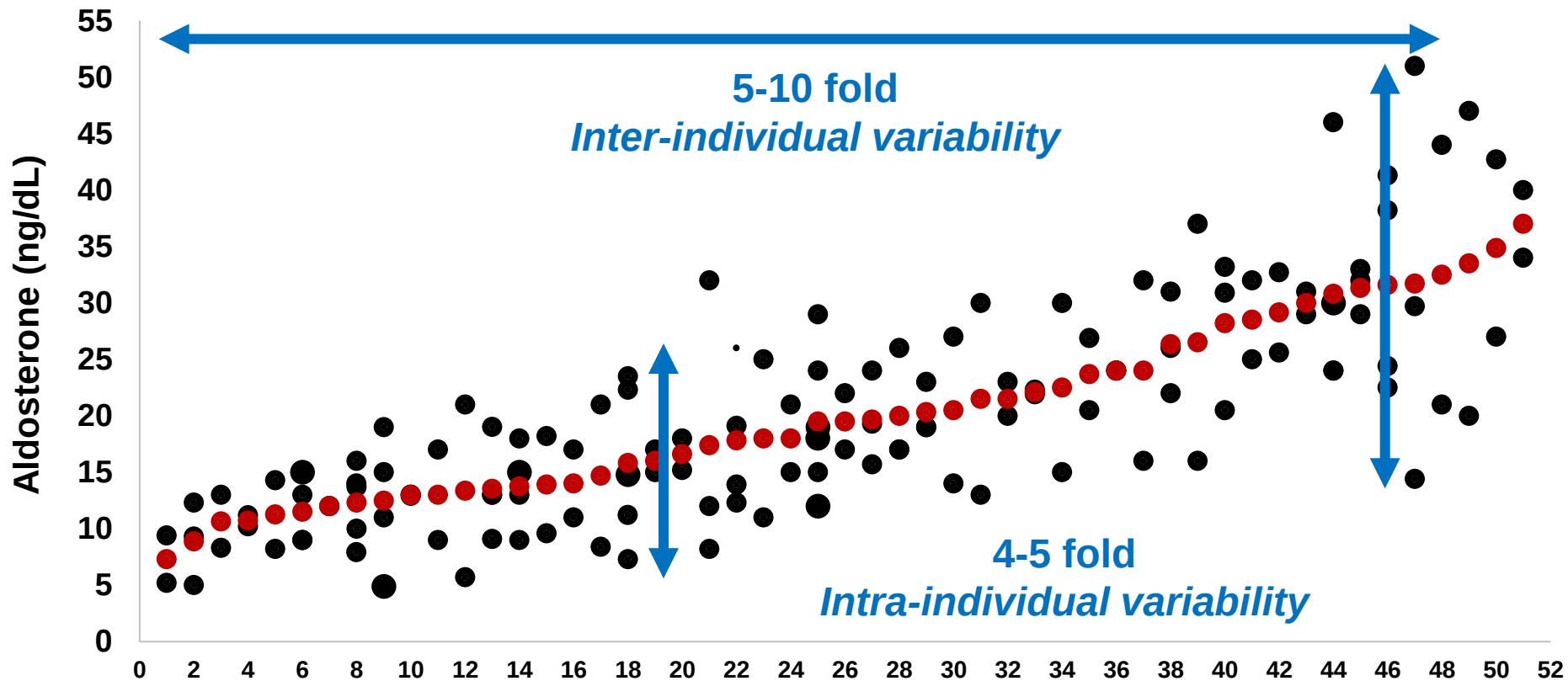
Immunoassay → LC-MS/MS



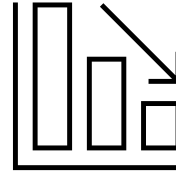
LC-MS/MS aldosterone assays require you to re-calibrate your expectations and interpretations

Variability of Aldosterone Production

Variability of Aldosterone Production



Variability of Aldosterone Production



ALDO Thresholds

< 15 ng/dL: **49%**

< 10 ng/dL: **29%**

A single aldosterone measurement should not be used to confidently *exclude* the possibility of PA when the pre-test probability is high

Continuum of Primary Aldosteronism

Arbitrary/conventional diagnostic thresholds aside



How common is “*inappropriate, non-suppressible, renin-independent aldosterone production*”
(aka *Primary Aldosteronism Pathophysiology*)?

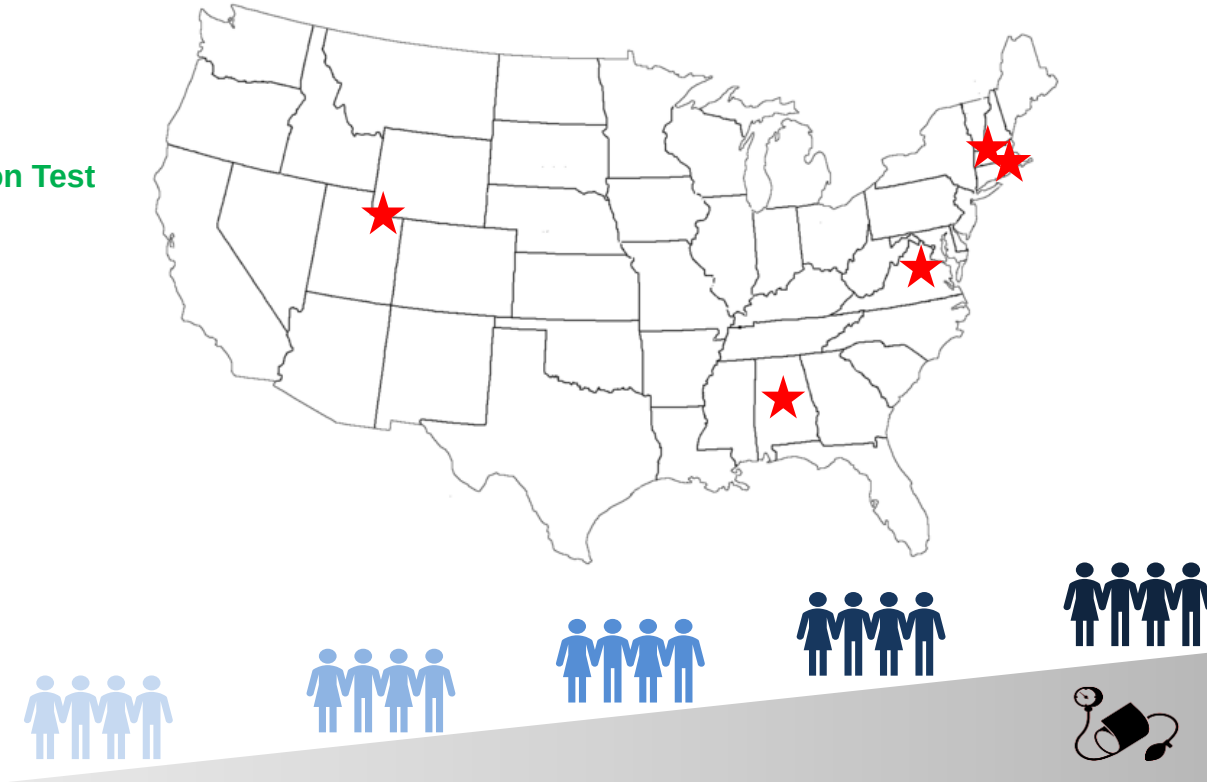
**Aldosterone
Suppression Test**



Visualize the spectrum of PA
(*agnostic of conventional thresholds*)

Continuum of Primary Aldosteronism

Oral Sodium Suppression Test

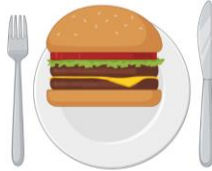


Continuum of Primary Aldosteronism

Oral Sodium Suppression Test

Supplemental Na⁺ Intake

~2-4 g/d x 3-4 days



+



Mean U.S. Dietary Na⁺ Intake

~3.5 g/d

Net Summary

~4-6 g/d Na⁺ x 3-4d

~1.5 L/d H₂O/NS x 3-4d

Physiologic Expectations

ECV/IVV Expansion

↓Renin

↓AngII

↓**Aldosterone**

Continuum of Primary Aldosteronism

CONTINUUM: severity spectrum of non-suppressible, renin/AngII-independent aldosterone production

This is
pathophysiologic
(aka overt PA)

This is
physiologic

When does physiology end?
When does pathophysiology begin?

Number of Participants with Suppressed Renin/AngII

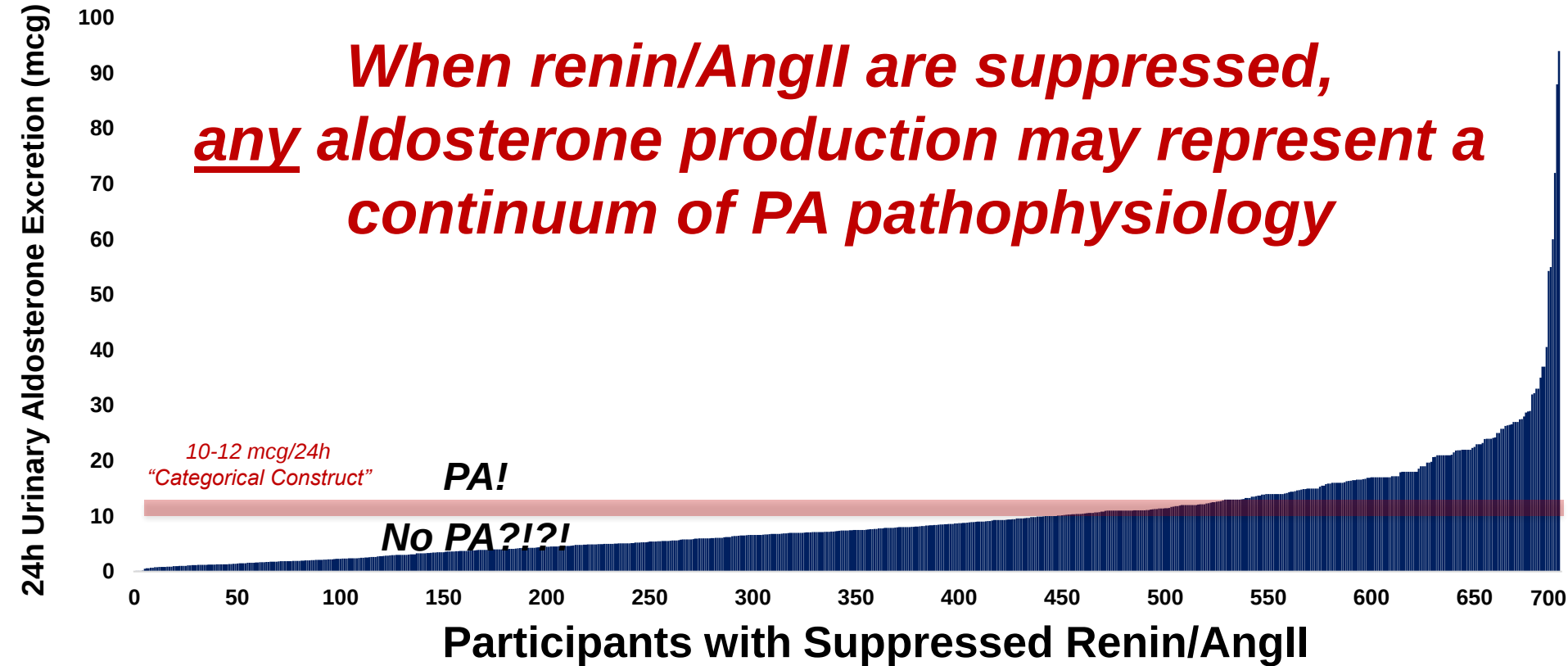
24h Urinary Aldosterone Excretion (mcg)

Magnitude of Primary Aldosteronism

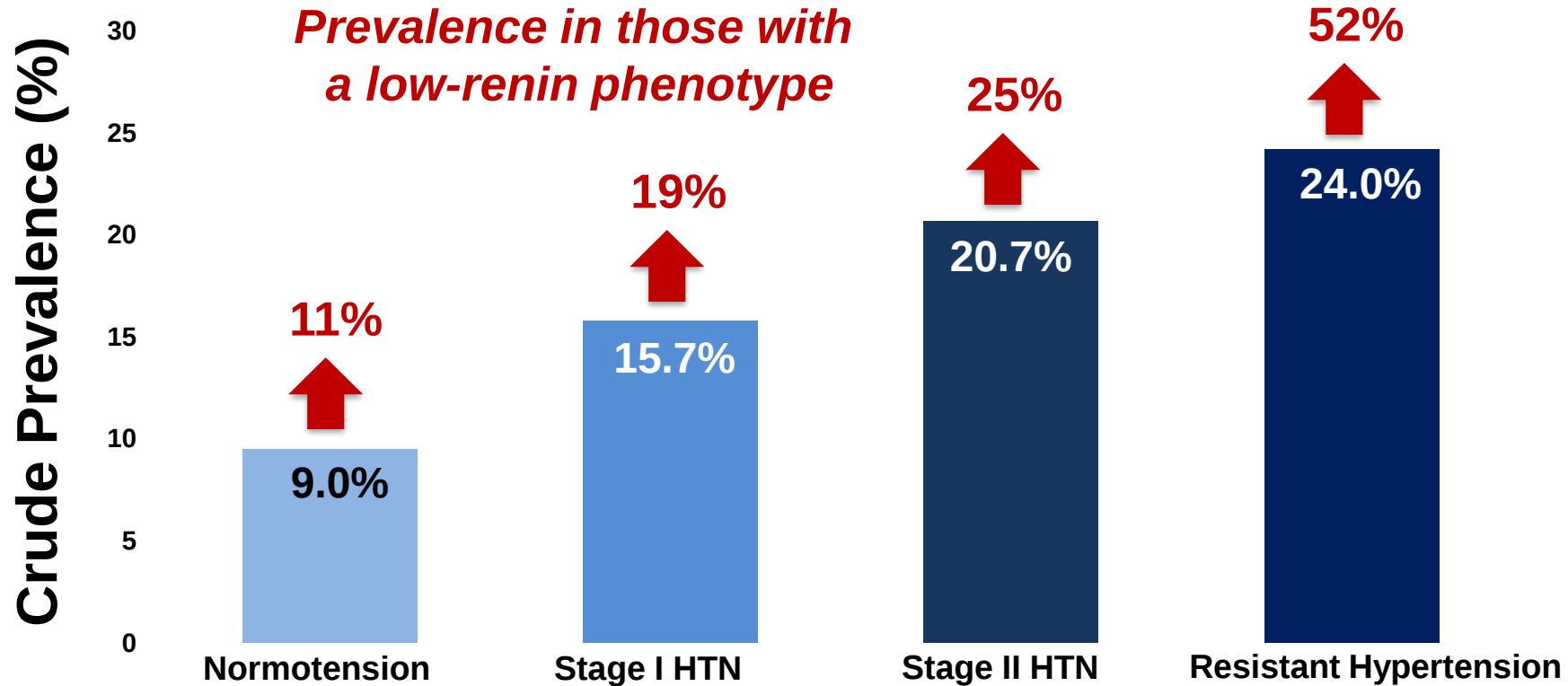


Continuum of Primary Aldosteronism

When renin/AngII are suppressed, any aldosterone production may represent a continuum of PA pathophysiology



The Prevalence of Primary Aldosteronism



***Is the continuum of Primary Aldosteronism
Pathophysiology clinically relevant?***

Clinical Trials

PATHWAY-2 trial : What is the best 4th drug for treat Resistant Hypertension?

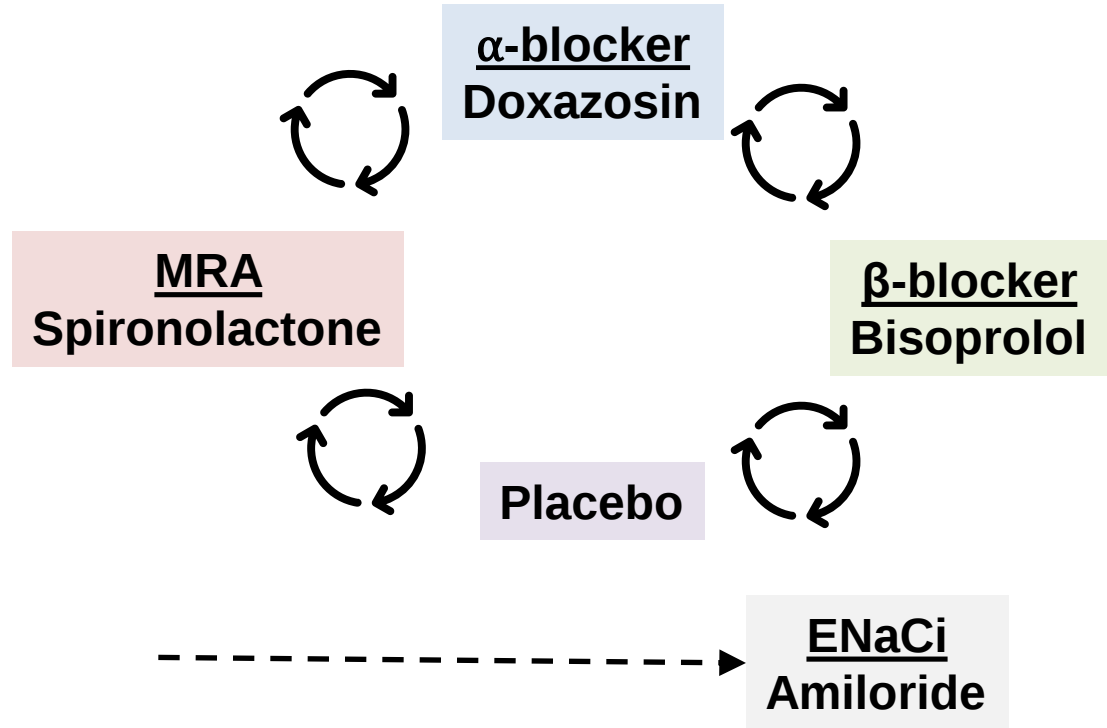
Patients with R-HTN

(RAASi, diuretic, CCB)



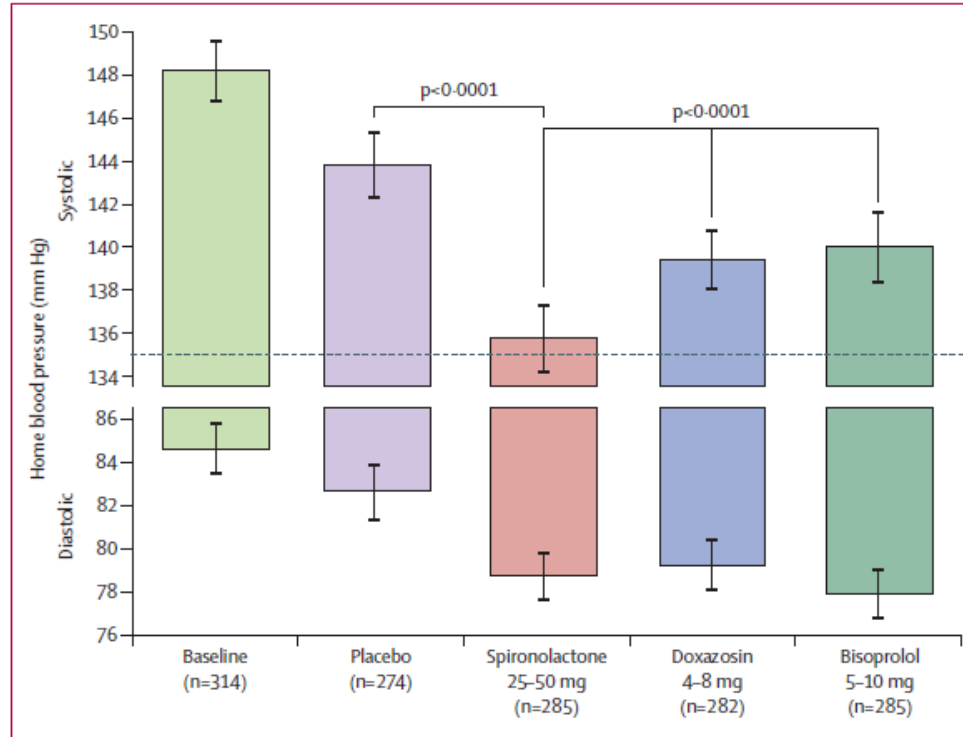
“Secondary HTN excluded”

Primary Aldosteronism
[presumptively] excluded -
Aldo/ARR not “high enough”



Clinical Trials

Best 4th Drug: MR Antagonist (& ENaCi)



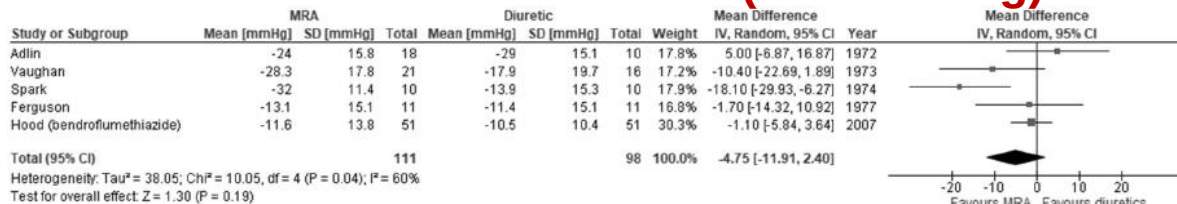
Clinical Trials

This IS Primary Aldosteronism!

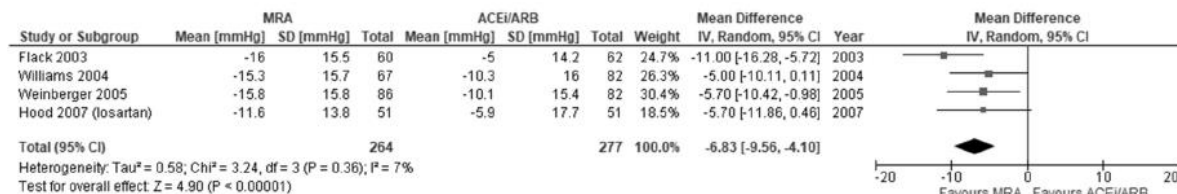
A substantial proportion of patients thought to have idiopathic resistant HTN have a form of renin-independent aldosteronism that is also MR-mediated and responsive to MRAs; however, the “traditional” approach to diagnosing primary aldosteronism misclassified this phenomenon

Meta-Analysis of RCTs in LRH

MRA vs Thiazides (- 4.8 mmHg)



MRA vs ACEi/ARB (- 6.8 mmHg)



MRA vs β -blocker (- 4.5 mmHg)
MRA vs α -blocker (- 4.0 mmHg)

Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial

ESC European Heart Journal - Cardiovascular Pharmacotherapy 2018; 18(1): 1-10 ORIGINAL ARTICLE
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Spironolactone effect on the blood pressure of patients at risk of developing heart failure: an analysis from the HOMAGE trial

João Pedro Ferreira ^{1,2}, Timothy Collier ³, Andrew L. Clark ⁴, Mamas A. Mamas ⁵, Hans-Peter Brunner-La Rocca ⁶, Stéphane Heymans ⁷, Arantxa González ⁸, Felix Z. Agha ⁹, Johannes Peitschberger ¹⁰, Blazina Mujajic ¹¹, Joe Culbert ¹², Philippe Rouet ¹³, Pierpaolo Pellicori ¹⁴, Beatrice Mariottoni ¹⁵, Franco Cosmi ¹⁶, Frank Edelmann ¹⁷, Lugardo Tsigi ¹⁸, Jan A. Smeets ¹⁹, Mark Haedbrook ²⁰, Job Vervaeke ²¹, Patrick Rougier ²², Nicolas Girard ²³, John G. Cleland ²⁴, and Falek Zaman ²⁵

KEY CONCEPT

Greater aldosterone production in the context of a low-renin phenotype is associated with progressive risk for CV and kidney disease and responds preferentially to MRA therapy

PA is a syndrome of pathophysiology characterized by *any* aldosterone production when renin is low; there is no lower limit of aldosterone that confidently excludes PA Pathophysiology

Re-Calibrating the Diagnostic Approach

Adopting a new mindset...

***“It’s Primary Aldosteronism
Until Proven Otherwise”***

100
↑
with
Mc

High-Risk Populations

Severe/Resistant Hypertension
HTN with hypokalemia
HTN with adrenal mass

*Coming soon: all patients with
hypertension*

TEST

SUPPRESSED?

Majority PA pts have ↓renin

PRA < 1.0 ng/mL/h

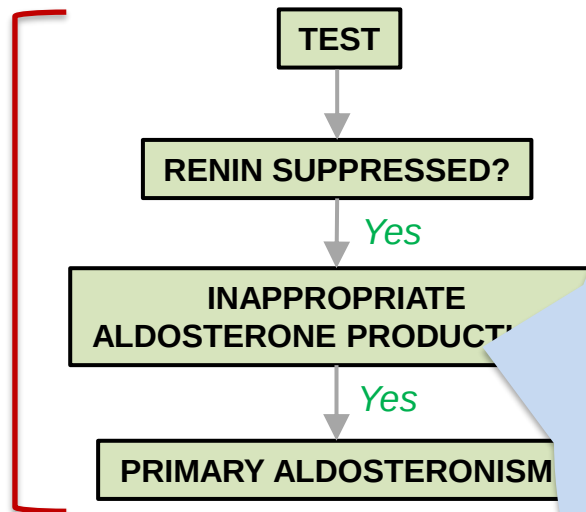
PRC < 10 mU/L

~90%

*if ↓renin despite
MRA or ENaCi or RAASi or Diuretic
(>80% of HTNive pts):*

“PA until proven otherwise”

CENTRAL DOGMA



Diagnostic
Pre-Test Probability

>25%

Continuum: any aldosterone production when $\downarrow$ renin represents PA pathophysiology amenable to targeted therapy

Categorical: > XX ng/dL

If on ACEi/ARB (75-80%):
“PA until proven otherwise”

1. Liberally test high-risk group
2. Low or persistently suppressed renin highly indicative
3. Any inappropriate aldosterone production when renin is suppressed

“Confirmatory”/Suppression Tests:

Are not validated or calibrated...

Are labor and resource intensive...

Add little to PPV, but contribute to false-negative case detection...

Are NOT necessary in the vast majority of scenarios

certainty

REPEAT TESTING or
MED(s) WASHOUT or
SUPPRESSION TEST or
REFER/ASK A FRIEND or

~90%

100%

ALWAYS

right answer!!

Mild Primary Aldosteronism
or

tension

Younger patients & those
with more severe PA

REFER TO SPECIALIST

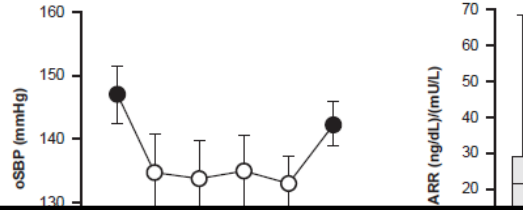
ADRENALECTOMY

Yes

ad

MRA THERAPY

Aldosterone Synthase Inhibitors



ASIs appear to be a new anti-HTN class, highly effective at lowering aldosterone, and BP in R-HTN, uncontrolled HTN, and PA

They affirm that a large proportion of essential/idiopathic HTN is aldosterone-mediated

Adrenal Insufficiency

Case

- 28yoF presents to ER 6 weeks after having a baby
- Cannot breastfeed well
- Presents with progressive fatigue, dizziness, orthostasis, salt craving, hyperpigmentation, anorexia, and weight loss
- BP=60/40 mmHg
- IV saline (8L) and BP improves

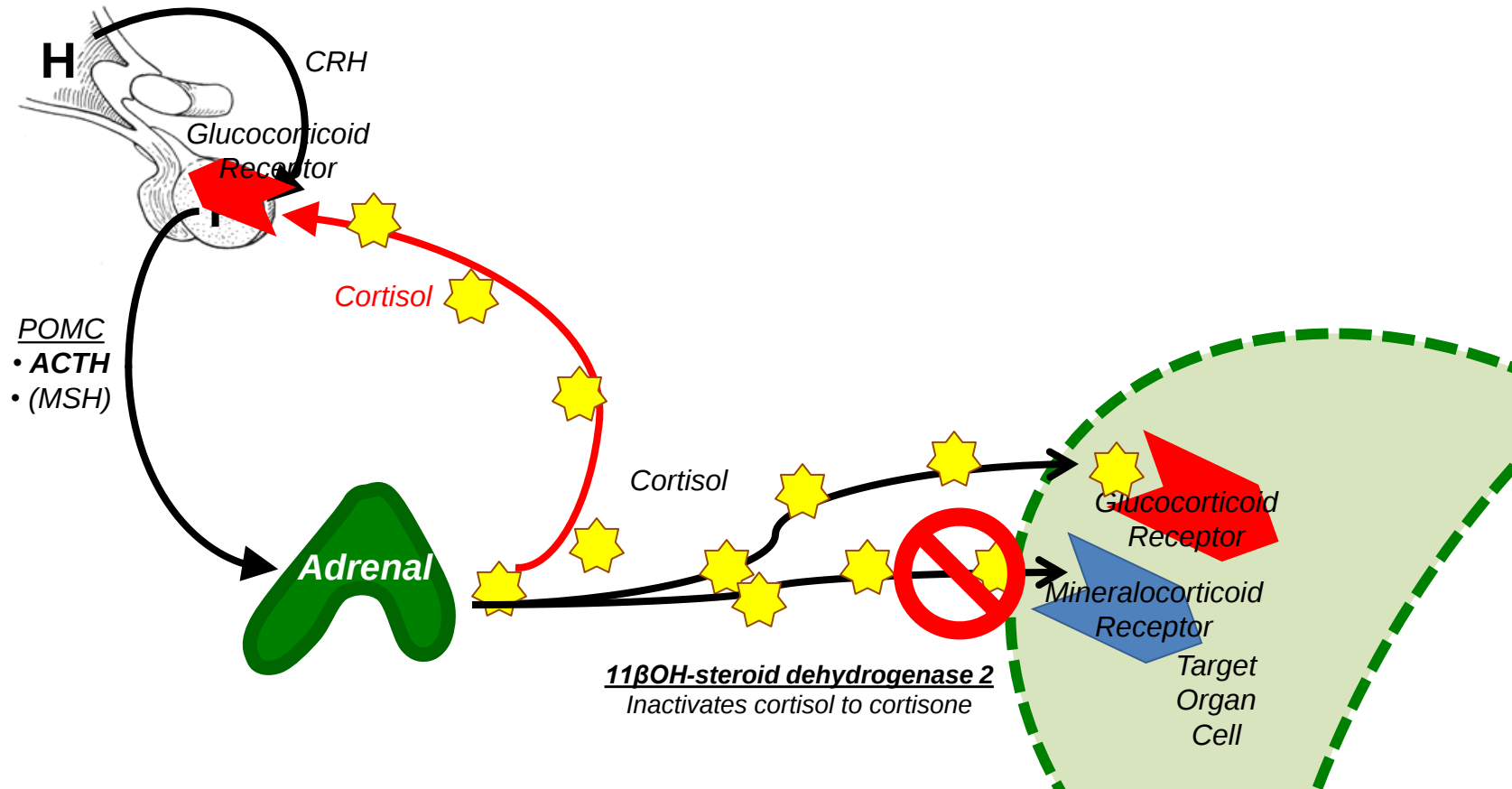
- Cortisol 0.80 mcg/dL (3-21)
- ACTH>1000pg/mL (15-75)
- (60mins after 250 mcg cosyntropin)= 1.0 mcg/dL

Question

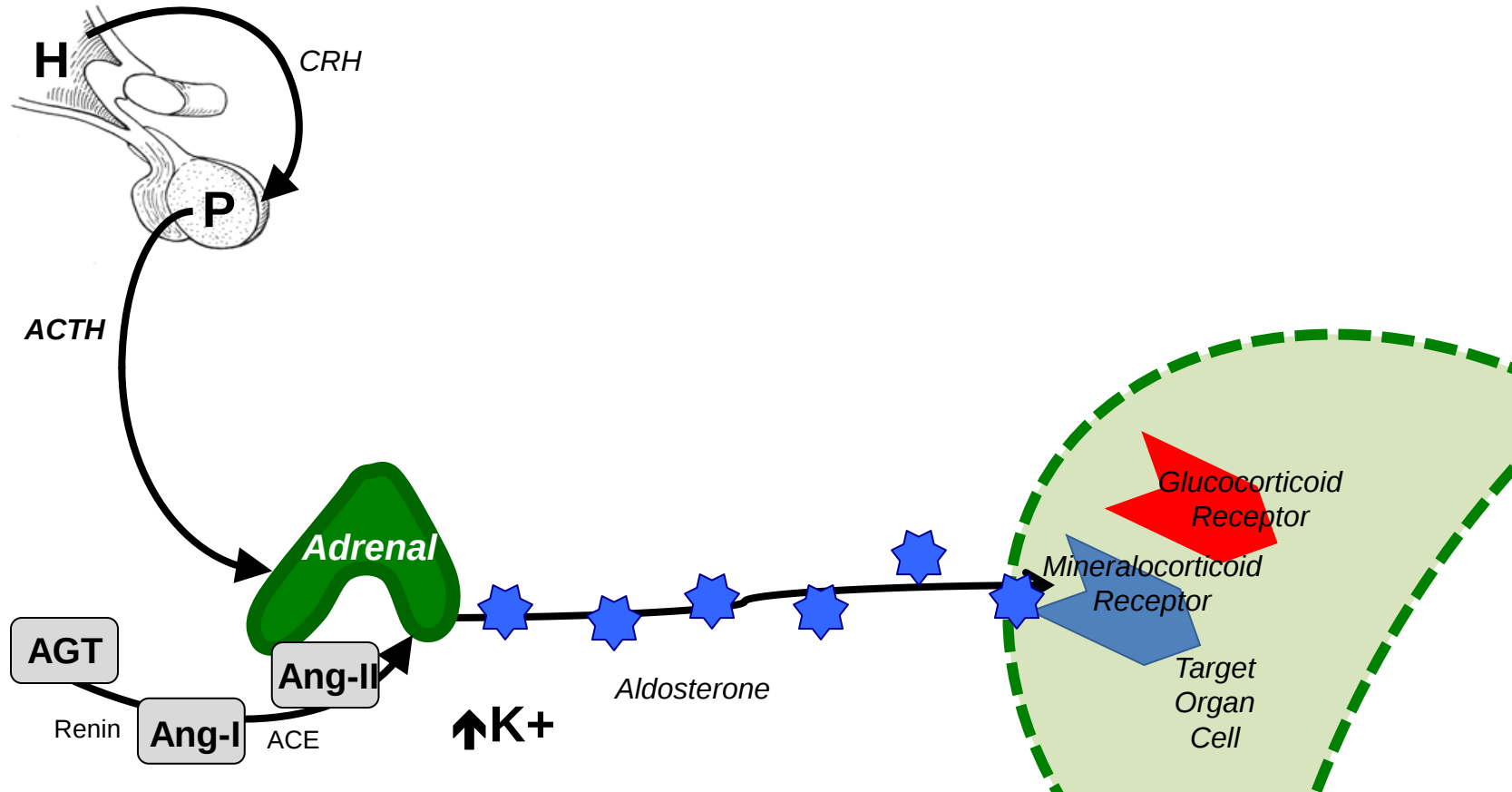
The most likely diagnosis is:

- A) **Primary adrenal insufficiency**
- B) Acute secondary adrenal insufficiency
- C) Chronic secondary adrenal insufficiency
- D) Ectopic ACTH syndrome
- E) Cushing's disease

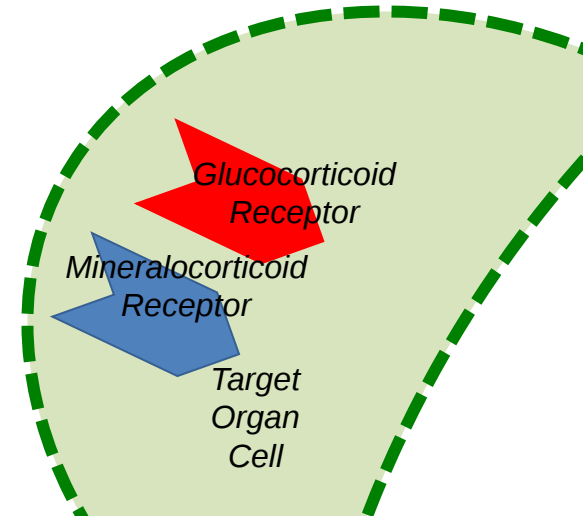
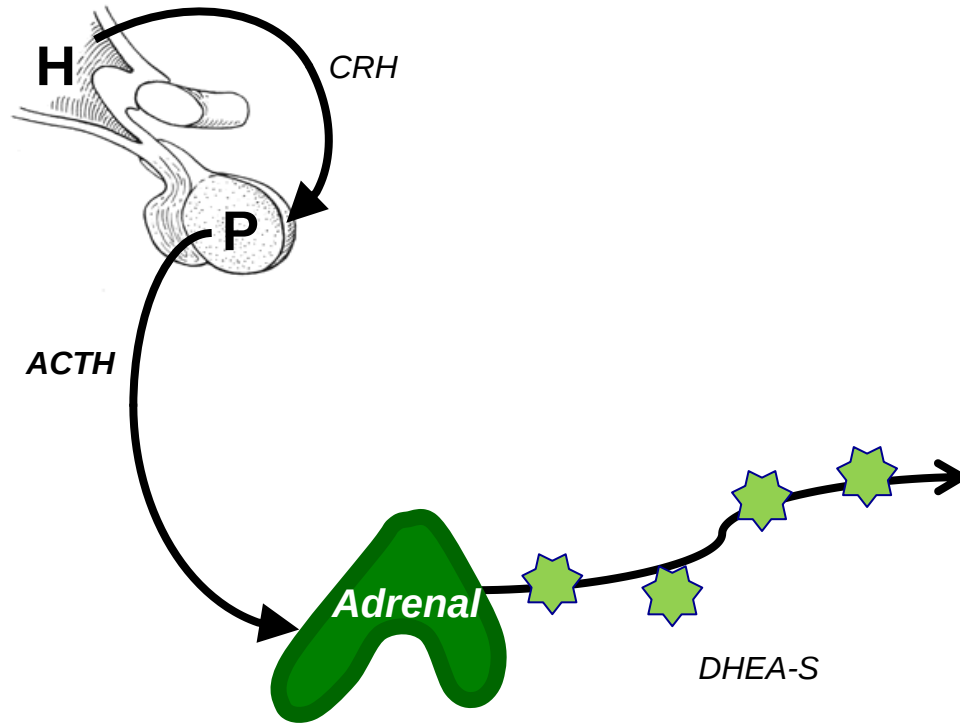
Hypothalamic-Pituitary-Adrenal Physiology



Hypothalamic-Pituitary-Adrenal Physiology



Hypothalamic-Pituitary-Adrenal Physiology



Hypothalamic-Pituitary-Adrenal Physiology

- 1) Cortisol and DHEA production are entirely dependent on ACTH; they are low in every form of adrenal insufficiency**

DHEA-S is the sulfated, stable, long-acting metabolite of DHEA

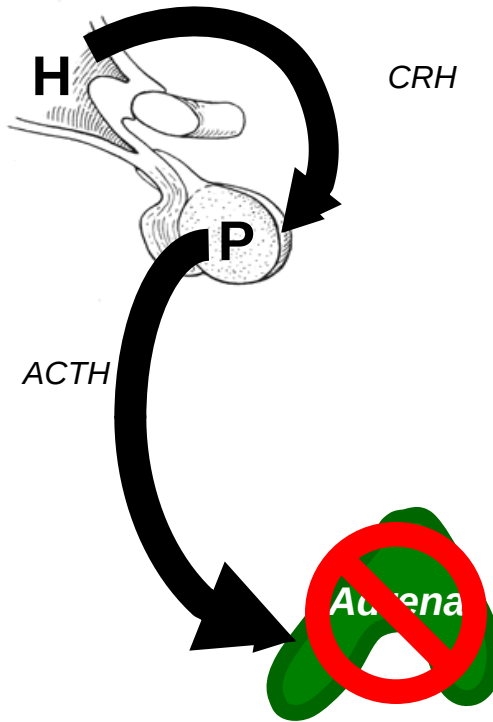
- 2) Aldosterone is not dependent on ACTH. It is regulated in part by:**

- Angiotensin II (Renin-angiotensin system)
- K⁺ balance
- ACTH

- 3) HPA axis responds to:**

- Diurnal variation/clock
- “stress”: ACTH & cortisol secretion is augmented “relative” to the degree of stress

Primary Adrenal Insufficiency (Addison's Disease)



Manifestations/Characteristics:

Labs:

- low cortisol & DHEAS
- high ACTH
- low aldosterone
 - hyperkalemia, hyponatremia, hypovolemia

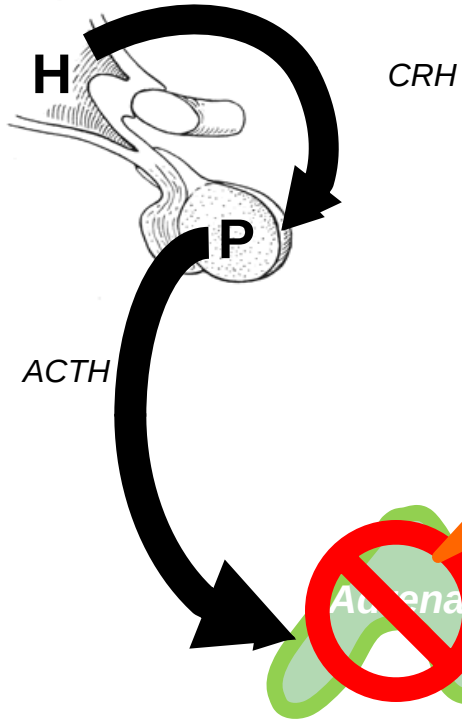
Physical Exam:

- fatigue/lethargy/anorexia
- hypotension/orthostasis/salt craving
- weight loss
- hyperpigmentation
- abdominal pain
- many many more

corticoid
receptor
id

et
organ
Cell

Primary Adrenal Insufficiency (Addison's Disease)

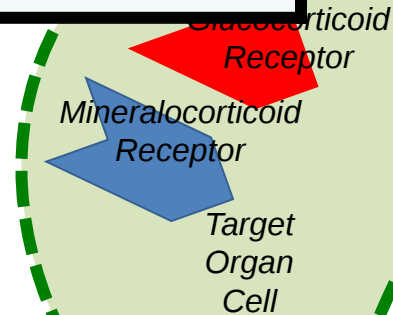


Response to Cosyntropin:

- sub-optimal

EXAMPLE:

	Morning	60 mins following 250 µg cosyntropin
Cortisol (µg/dL)	1.8 ↓	2.1
ACTH (pg/mL)	1100 ↑	
DHEAS (mcg/mL)	33 ↓	



Primary Adrenal Insufficiency (Addison's)

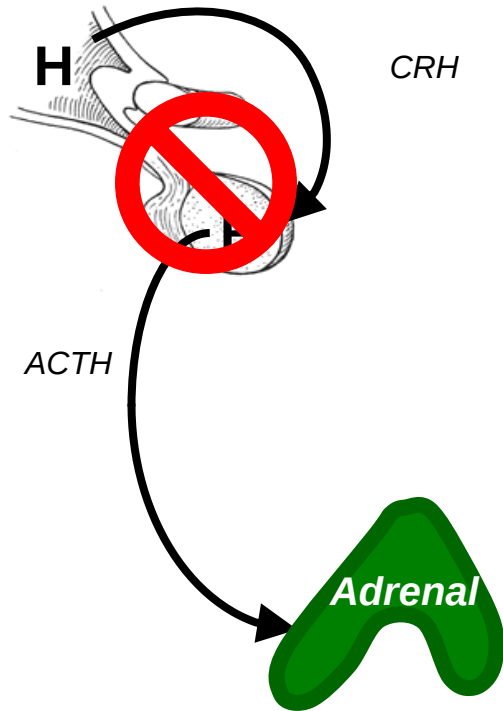
Causes:

- Autoimmune
- Infiltrative infections (TB, fungal)
- Hemorrhage
- Infiltrative malignancy
- Congenital adrenal hyperplasia
- adrenoleukodystrophy

Medications:

- Anti-fungal medications
- Immunotherapies
- Heparin
- Etomidate

ACUTE Secondary Adrenal Insufficiency



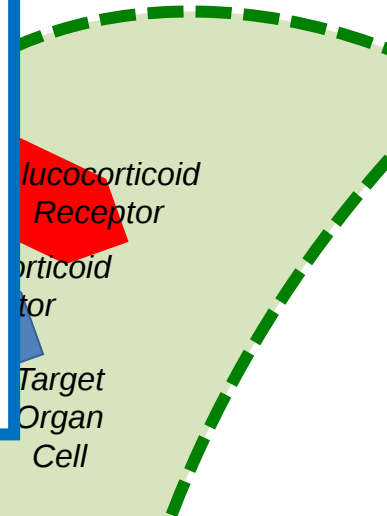
Manifestations/Characteristics:

Labs:

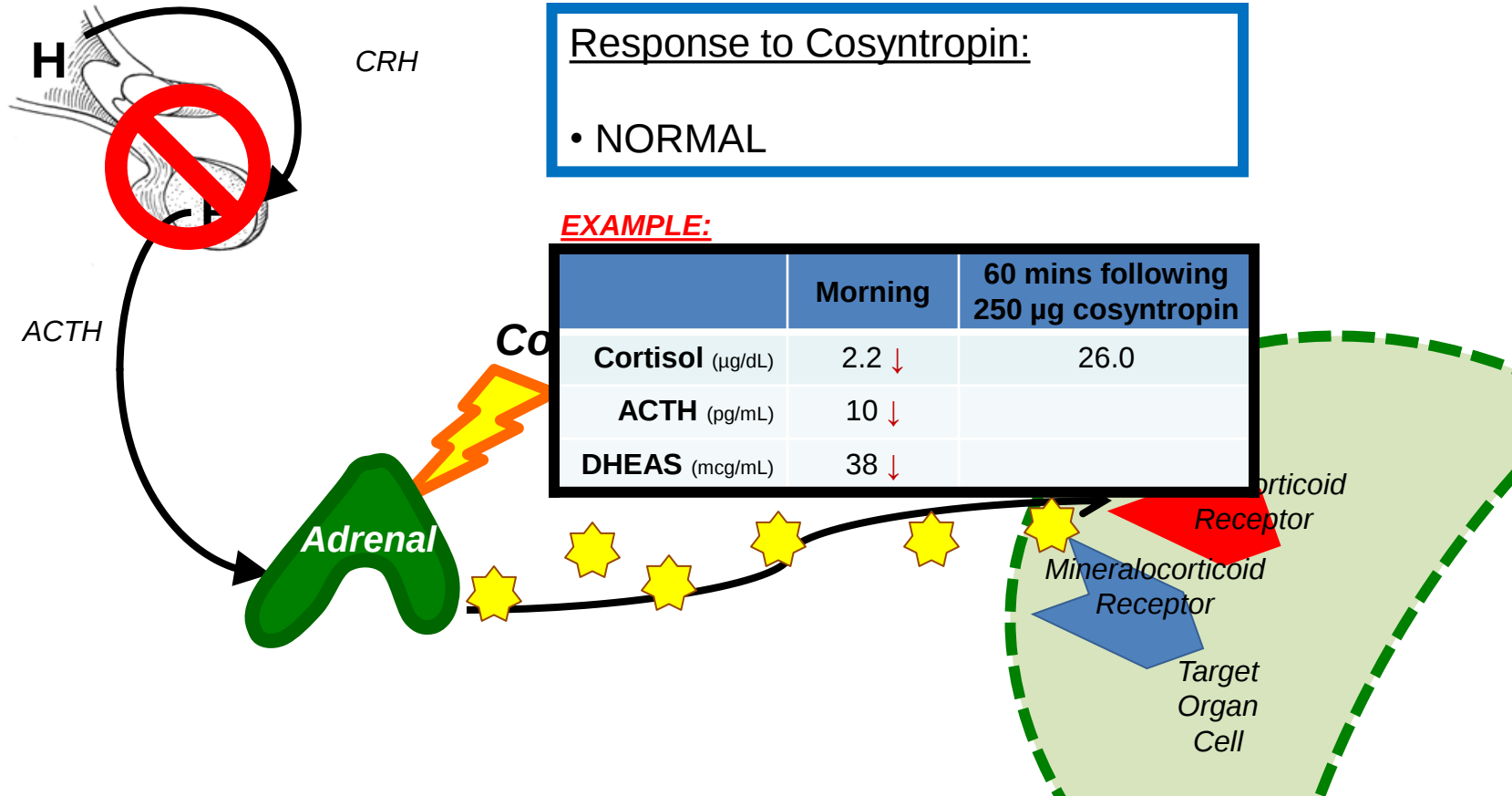
- low basal cortisol & DHEAS
- inappropriately low ACTH
- $\pm$ hyponatremia
- Normal K and aldosterone regulation

Physical:

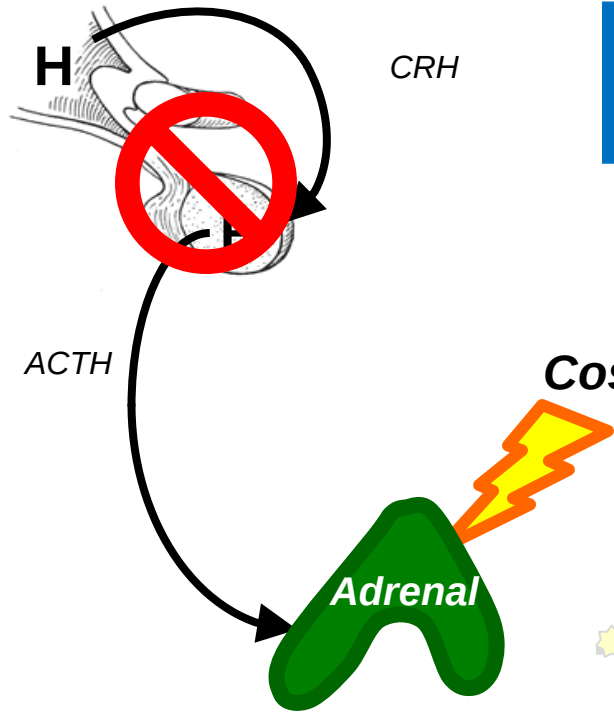
- completely normal
- mild, progressive, fatigue at baseline
- severe fatigue, orthostasis, hypotension, in situations of stress



ACUTE Secondary Adrenal Insufficiency



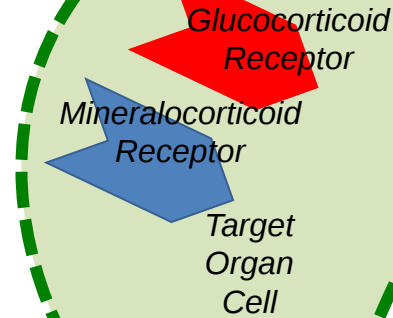
CHRONIC Secondary Adrenal Insufficiency



With chronic ACTH deficiency, **adrenal cortex (ZF) will atrophy**, and will progressively respond less to cosyntropin stimulation

EXAMPLE:

	Morning	60 mins following 250 µg cosyntropin
Cortisol (µg/dL)	2.2 ↓	4.5
ACTH (pg/mL)	10 ↓	
DHEAS (mcg/mL)	38 ↓	



Secondary Adrenal Insufficiency

Causes:

- Pituitary mass: adenoma or metastatic lesion
- Pituitary infection
- Pituitary infiltration (granulomatous disease, iron)
- Pituitary trauma

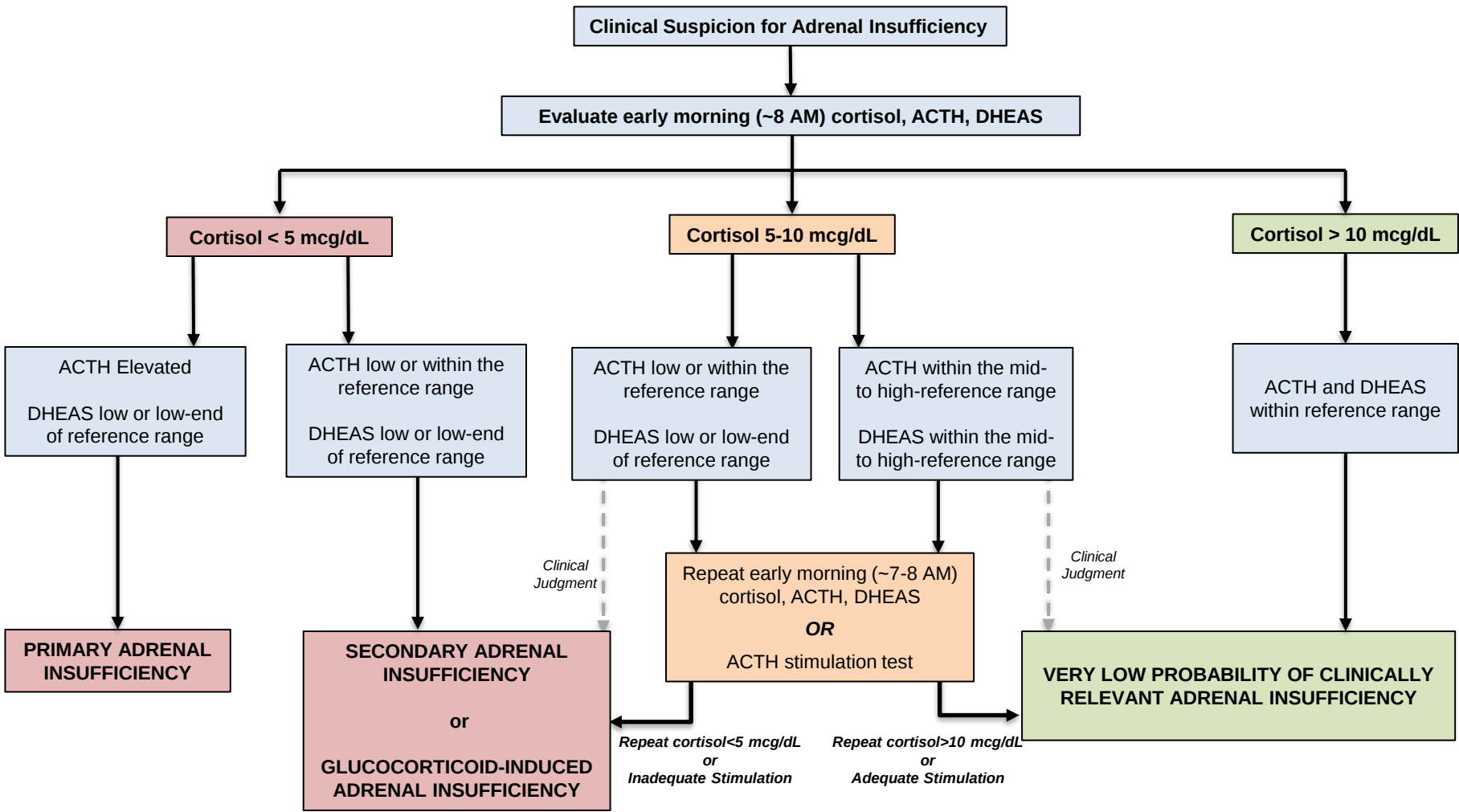
Medications:

- **Glucocorticoids (oral, inhaled, nasal, intra-articular)**

Glucocorticoid-induced adrenal insufficiency (iatrogenic) is common

Glucocorticoid-Induced Adrenal Insufficiency

- **Common** (1-3% of adults are prescribed glucocorticoids at some point in their life)
- Supra-physiologic dosing for >3 weeks can induce GAI (e.g. prednisone >5mg per day for >3 weeks)
- Can be induced by non-oral formulations (inhaled, intranasal, intraarticular, topical)
- Can be reversed with gradual tapering of glucocorticoids to demonstrate normal cortisol and HPA axis function



Adrenal Crisis

Hemodynamic instability or shock due to cortisol deficiency

All patients with AI should be educated on the risk of adrenal crisis during periods of illness (fevers, vomiting, etc), trauma, or surgical procedures

Additional oral glucocorticoid therapy should be prescribed to match the insult; if oral therapy cannot be taken, IM or IV therapy is required

All patients should be prescribed and taught to administer IM glucocorticoid for emergencies

Adrenal Crisis

<https://doi.org/10.1093/ejendo/lvae029>

Table 8: Suggested glucocorticoid regimens in patients at risk of or with diagnosed glucocorticoid-induced adrenal insufficiency during exposure to stress

	General considerations	Examples	Suggested regimen
Minor stress	If the patient is already taking hydrocortisone ≥40 mg daily, prednisone ≥10 mg daily, or dexamethasone ≥1 mg daily, there is typically no need to increase the dose unless there are signs of hemodynamic instability.	- Illness requiring bed rest - Illness with fever (out of hospital) - Illness requiring treatment with antibiotics (out of hospital) - Significant emotional stress (e.g., bereavement)	If not on daily glucocorticoid give hydrocortisone 40 mg total daily dose, to be given in three divided doses (e.g., 20 mg on rising, 10 mg 12 midday, 10 mg 5pm). Continue for 2-5 days until well (or for the duration of antibiotic treatment). If on hydrocortisone <40 mg total daily dose; increase to 40 mg total daily dose, to be given in three divided doses (e.g., 20 mg on rising, 10 mg 12 midday, 10 mg 5pm). Continue for 2-5 days until well (or for the duration of antibiotic treatment). If on prednisone <10 mg total daily dose; increase to 10 mg total daily dose, to be given in one or two divided doses. Continue for 2-5 days until well (or for the duration of antibiotic treatment). If on dexamethasone <1 mg total daily dose; increase to 1 mg once daily. Continue for 2-5 days until well.
		Minor surgery including any procedure requiring local anesthesia	If not on daily glucocorticoid give oral hydrocortisone 40 mg total daily dose, to be given in three divided doses (e.g., 20 mg one hour prior to the procedure, 10 mg six hours after the procedure, 10 mg after a further six hours). Continue glucocorticoids in patients who remain unwell after the procedure until clinically stable. If on hydrocortisone <40 mg total daily dose; increase to 40 mg total daily dose, to be given in three divided doses (e.g., 20 mg one hour prior to the procedure, 10 mg six hours after the procedure, 10 mg after a further six hours). Continue increased dose in patients who remain unwell after the procedure until clinically stable. If on prednisone <10 mg total daily dose; increase to 10 mg total daily dose, to be given one hour prior to the procedure. Continue increased dose in patients who remain unwell after the procedure until clinically stable. If on dexamethasone <1 mg total daily dose; increase to 1 mg total daily dose, to be given one hour prior to the procedure. Continue increased dose in patients who remain unwell after the procedure until clinically stable.
		Bowel procedures not carried out under general anesthesia	If not on daily glucocorticoid give hydrocortisone 20 mg total daily dose, to be given in three divided doses (e.g., 10 mg one hour prior to the procedure, 5 mg six hours after the procedure, 5 mg after a further six hours). If on daily glucocorticoid continue normal glucocorticoid dose. Give an equivalent I.V. dose if prolonged nil by mouth.
Moderate and major stress	If the patient is already taking hydrocortisone ≥200 mg daily, prednisone ≥50 mg daily, or dexamethasone ≥6-8 mg daily, there is typically no need to increase the dose. In patients with suspected reduced absorption (persistent vomiting or diarrhoea), nil by mouth, or unable to take	Severe intercurrent illness, for example: - Persistent vomiting or diarrhoea from gastro-intestinal illness. - Infection requiring hospital admission or I.V. antibiotics (e.g., sepsis).	For patients with persistent vomiting or diarrhoea who are well enough to remain out of hospital: Hydrocortisone 100 mg I.M. injection immediately, which can be repeated after 6 hours if needed. If symptoms do not resolve or hemodynamic instability develops, admit to hospital for I.V. urgent



Incidentally Discovered Adrenal Masses

Adrenal Tumors

Adrenal tumors are incidentally discovered in 1-10% of adults who are scanned.

A minority represent malignant entities (primary adrenal malignancy or extra-adrenal metastasis)

In contrast, ~10-25% of adrenal tumors autonomously secrete adrenal hormones. These “functional” tumors are associated with an increased risk for cardiometabolic outcomes, such as CV disease, diabetes, and osteoporosis/fracture.

Therefore, all incidentally discovered adrenal tumors should be carefully evaluated to determine whether they are: 1) **malignant** and/or 2) **functional**.

Differential Diagnosis of Adrenal Mass

	NON-FUNCTIONAL (85-95%)	FUNCTIONAL (5-15%)
BENIGN (~90-95%)	Adrenocortical Adenoma Cyst Ganglioneuroma Hemangioma Hemorrhage Infections and granulomatous disease (tuberculosis, fungi, sarcoidosis) Lymphangioma Myelolipoma Pheochromocytoma Schwannoma	Adrenocortical Adenoma <i>Aldosterone producing</i> <i>Cortisol producing</i> Micro- or Macro-nodular Disease <i>Aldosterone producing</i> <i>Cortisol producing</i> Pheochromocytoma Myelolipoma* Ganglioneuroma*
MALIGNANT (~5%)	Adrenocortical carcinoma Metastatic cancer from a non-adrenal primary Neuroblastoma	Adrenocortical carcinoma Pheochromocytoma

Radiographic Characteristics

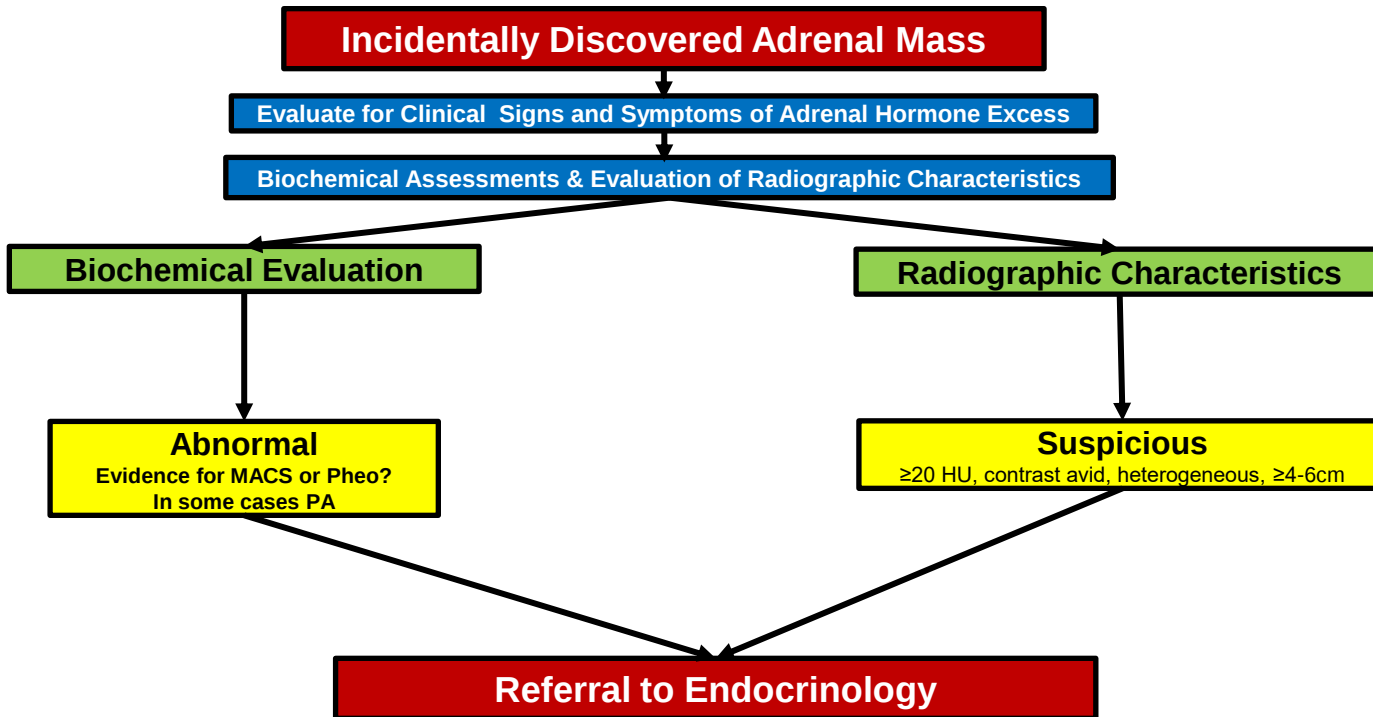
Characteristics	Likely Benign	Potentially Malignant
Irregular Shape	No	Yes
Heterogeneous content	No	Yes
Necrosis or Calcifications	No	Yes
Rate of Growth	< 1cm/y	≥1cm/y
Attenuation on unenhanced CT	<10 HU	≥ 20 HU
Contrast washout on CT protocol at 15 minutes	Absolute>60% Relative>40%	Absolute ≤60% Relative ≤40%
MRI chemical shift suggestive of lipid-rich content	Yes	No
FDG avidity on PET	No	Yes
Size	< 4 cm	≥ 4-6 cm

Biochemical Testing

Suggested **screening biochemical evaluation** for adrenal masses:

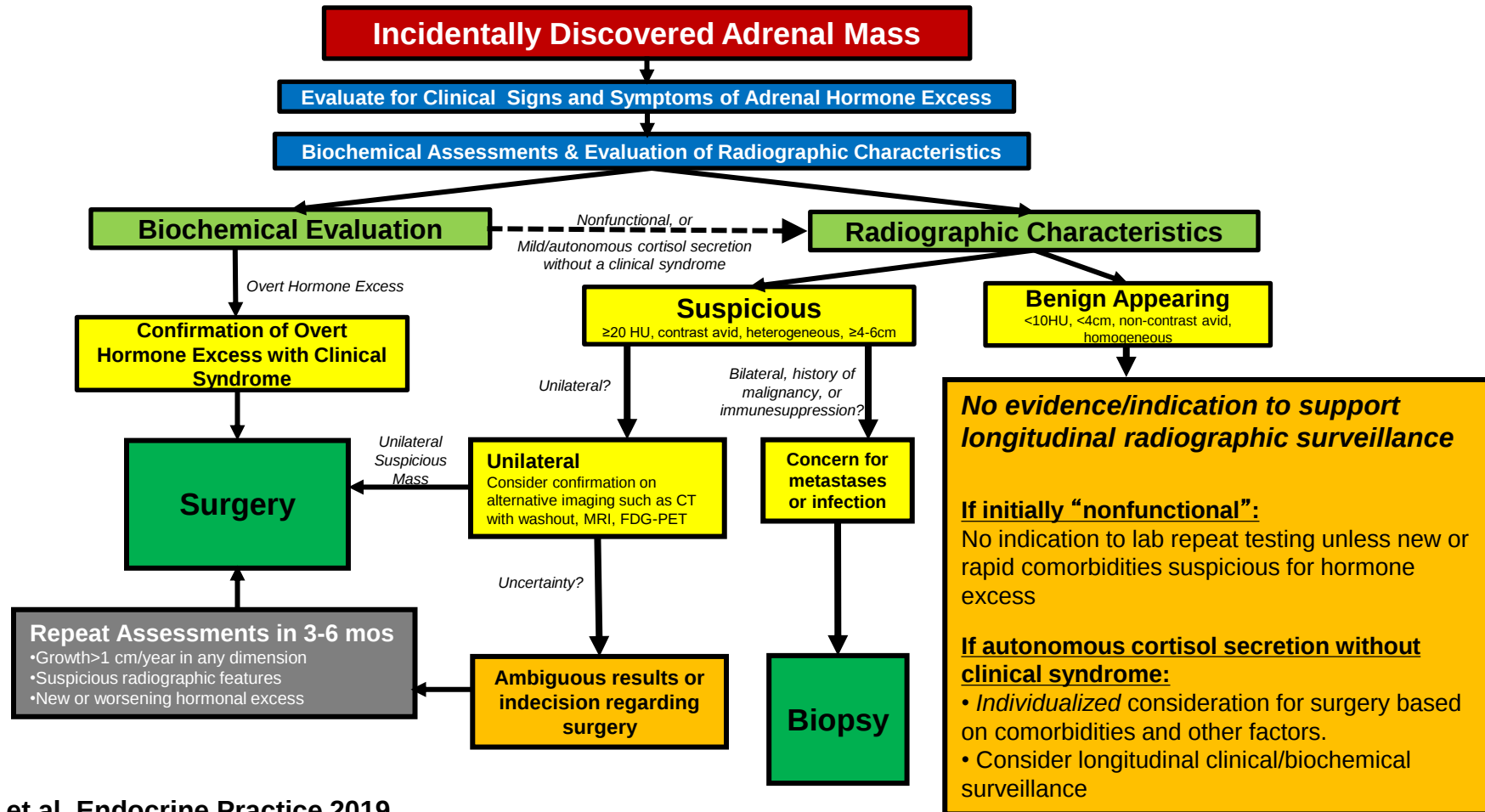
Condition	Patients	Test	Abnormal Value
Hypercortisolism	ALL	1 mg Dexamethasone Suppression Test	None: ≤ 1.8 mcg/dL MACS: 1.9-5.0 mcg/dL ACS: > 5.0 mcg/dL
Primary Aldosteronism	HTN and/or hypokalemia	Serum aldosterone to plasma renin activity	MACS is autonomous cortisol secretion without overt Cushing syndrome Mild Autonomous Cortisol Secretion (MACS) is <u>common</u> MACS contributes to cardiometabolic disease
Pheochromocytoma	Lipid poor, contrast avid, heterogeneous adrenal masses	Plasma free metanephrins	(Anxiety/stress/pain, Anti-depressants)
Adrenal androgen excess	Hirsutism or virilization	DHEAS Total Testosterone	Higher than ULN

SIMPLIFIED Approach to the Incidentally Discovered Adrenal Mass



If a lipid-rich adenoma and no evidence of hormone excess: no need for referral, no need for repeated imaging, no need for repeated biochemical testing, unless dramatic/unexpected changes in clinical status

Comprehensive Approach to the Incidentally Discovered Adrenal Mass



Summary

Primary aldosteronism is a highly prevalent, but largely unrecognized, syndrome. All patients with hypertension (but at minimum those with resistant hypertension and/or hypokalemia) should be screened at least once using a liberalized diagnostic approach

Understanding the pathophysiology of adrenal insufficiency can guide the approach to diagnosis and treatment; a morning cortisol, ACTH, DHEAS is the most pragmatic approach to diagnosis

Incidentally discovered adrenal masses are common. All adrenal masses should be evaluated for malignancy and adrenal hormone excess.

Adrenal Disorders

Anand Vaidya, MD MMSc

Director, Center for Adrenal Disorders

Chief (Interim), Division of Endocrinology, Diabetes, & Hypertension

Brigham and Women's Hospital

Associate Professor of Medicine, Harvard Medical School

anandvaidya@bwh.harvard.edu