Update in hypertension

Jasmine Tan

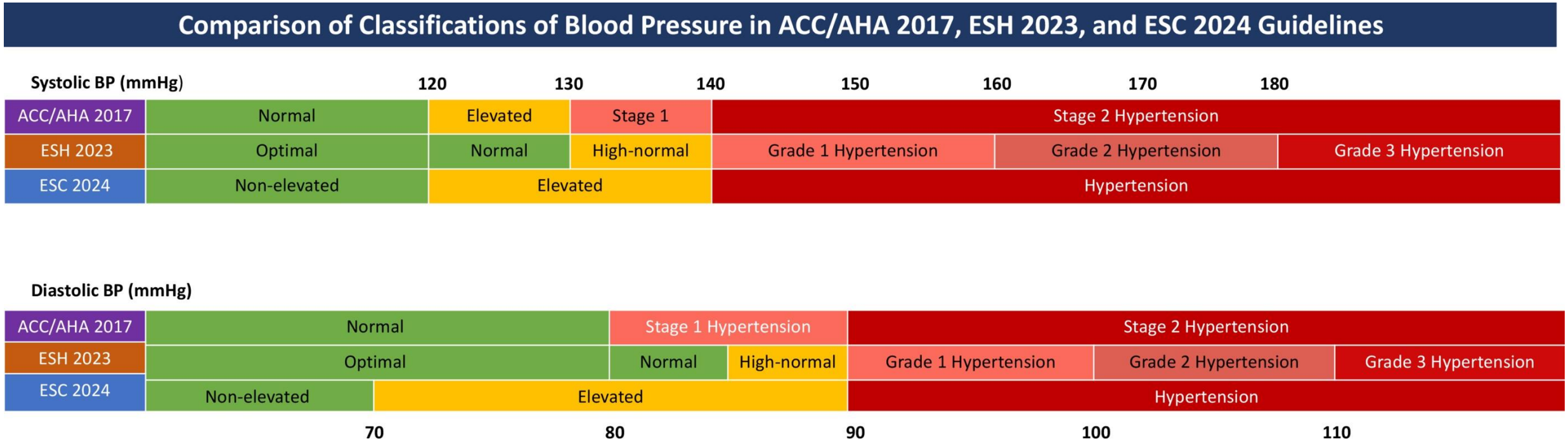
29th April 2026

Greenlane
Medical Specialists

Overview

- Identifying Primary Aldosteronism in hypertension
  - Work up of Primary aldosteronism
  - 2025 guidelines on PA
- Case discussions

Reclassification 2024



	AHA/ACC (2025 update)	ESC/ESH (2023/24)
Hypertension threshold	≥130/80	≥140/90
BP treatment target	<130/80 (possibly <120 SBP)	SBP 120 – 129 if tolerated (cf <135/85 mmHg)

Hypertension

2025 AHA/ACC, 2024 ESC guidelines

COMMENTARY

Expanding the Search for Primary Aldosteronism in Clinical Settings

John M. Flack, Michael G. Buhnerkempe, Garry L.R. Jennings

Volume

Broadening Primary Aldosterc
Across Contemporary Guideli

Lily Owei, MD[1], Heather Wachtel, MD, MTR

[1]Department of Surgery, Perelman School of
PA

ESC
European Society of Cardiology

Menu

Primary hyperaldosteronism in hypertension

4 Nov, 2025

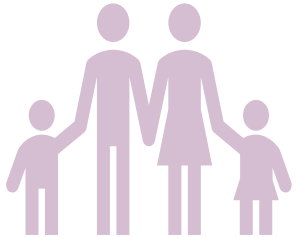
Scientific | Hypertension

The Journal of Clinical Endocrinology & Metabolism, 2025, **110**, 2453–2495
https://doi.org/10.1210/clinem/dgaf284
Advance access publication 14 July 2025
Clinical Practice Guideline

Primary Aldosteronism: An Endocrine Society Clinical Practice Guideline

Gail K. Adler,[1] Michael Stowasser,[2] Ricardo R. Correa,[3] Nadia Khan,[4] Gregory Kline,[5] Michael J. McGowan,[6] Paolo Mulatero,[7] M. Hassan Murad,[8] Rhian M. Touyz,[9] Anand Vaidya,[1] Tracy A. Williams,[10] Jun Yang,[11,12] William F. Young,[8] Maria-Christina Zennaro,[13,14] and Juan P. Brito[8,15]

Who should be evaluated?



Resistant hypertension	Early onset	Rapid onset Or Acute exacerbation	Family history of PA in first degree relatives	Hypertension with OSA	Diabetes

Broader, earlier and more practical screening for PA

Primary aldosteronism (PA)

- PA accounts for 5 – 10% of patients with hypertension; 20 – 30 % of resistant hypertension

Table 3. Prevalence of primary aldosteronism in different subgroups

Setting	Prevalence
Hypertension in Primary Care	5.9% (range, 3.2-14.0)
Hypertension in referral centers	7.2% (range, 0.7-21.9)
Hypertension in young adults (ages 18-40 years)	16.2%
[a]Grade 1 hypertension	3.9%-15.7%
[a]Grade 2 hypertension	9.7%-21.6%
[a]Grade 3 hypertension	11.9%-19%
Resistant hypertension	11.3%-29.1%
Hypertension and hypokalemia	28.1%
Hypertension and adrenal incidentaloma	4.4% (range, 0.4-24.6%)
Hypertension and atrial fibrillation[b]	42.5%
Hypertension and type 2 diabetes mellitus	11.3%-19.1%

[a]Grades 1,2 and 3 hypertension refer to the classification of the 2023 European Society of Hypertension guideline

Primary aldosteronism (PA)

- Refers to the inappropriate and non-suppressible aldosterone production
- Initial screening in the context of normokalaemia (K ≥ 3.5 mmol/L) & 1 hr post breakfast:

Elevated aldosterone: renin ratio (ARR) at > 55 in the context of normokalaemia

+

Low renin (Renin <8.2 mU/L)
AND
High aldosterone (≥277 pmol/L)

Meets criteria

- Potassium to be measured alongside aldosterone and renin to aid accurate interpretation of aldosterone level (low serum potassium can lead to falsely low aldosterone)

J Clin Endo Metab. 2020; 105(12): 1–13.
Hypertension. 2018; 72(5): e53–e90.

Spectrum of PA phenotypes

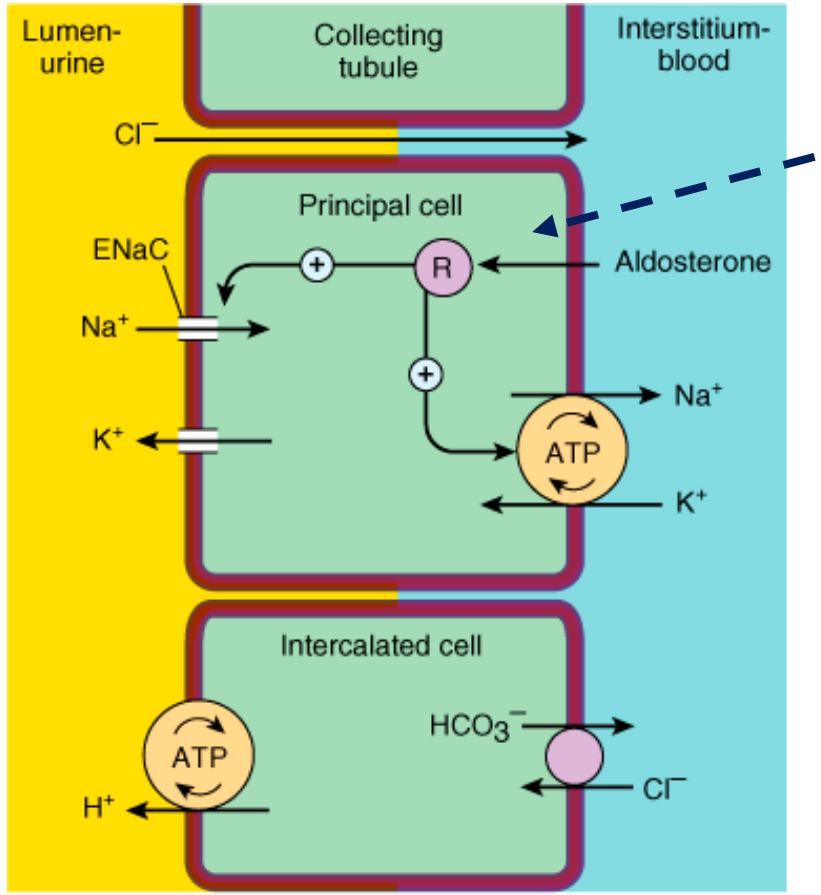
68% higher 5-yr risk of incident hypertension in normotensive with suppressed renin vs normal renin

Common subtypes include bilateral hyperplasia and aldosterone-producing adenoma

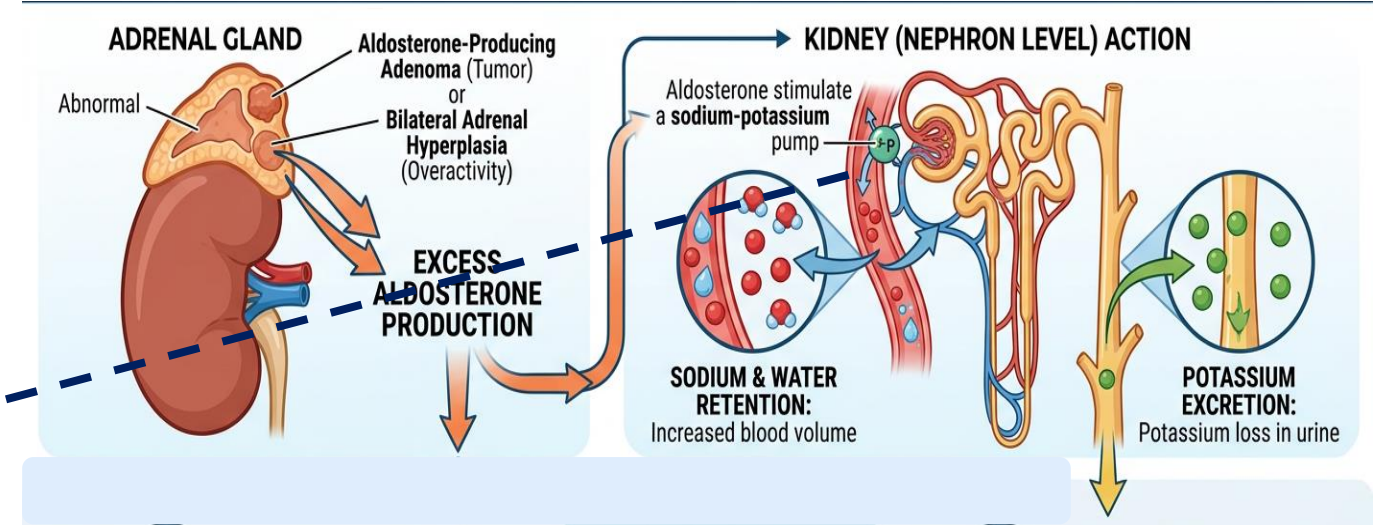
Positive association between OSA severity and PA

Subtypes	Frequency
Idiopathic hyperplasia, bilateral (IHA)	60 – 65%
Aldosterone-producing adenoma (APA)	30 – 35%
Primary adrenal hyperplasia, unilateral	2 – 3%
Glucocorticoid-remediable aldosteronism (GRA)/ familial hyperaldosteronism FH type 1	<1%
Familial hyperaldosteronism type 2	<1%
Familial hyperaldosteronism type 3	<1%
Aldosterone-producing adenoma or carcinoma or ectopic lesion	<1%

Ann Med 2013;45:375
J Clin Endo Metab. 2020; 105(12): 1–13.
Hypertension. 2018; 72(5): e53–e90.

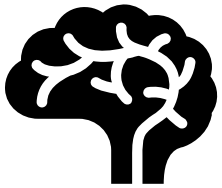


Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition*: http://www.accessmedicine.com

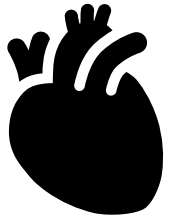


- Hypertension
  - Sodium absorption
  - Volume expansion
  - Metabolic alkalosis
  - SNS expansion
- Hypokalaemia (9 – 37%)
  - Provoked or spontaneous

Consequences of untreated PA



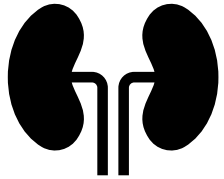
Stroke
OR 2.58
(95%CI 1.93 – 3.45)



CAD
OR 1.77
(95%CI 1.10 – 2.83)

AF
OR 3.52
(95%CI 2.26 – 5.99)

HF
OR 2.05
(95%CI 1.11 – 3.78)



Proteinuria
OR 2.68
(95%CI 1.89 – 3.79)

Compared with patients with essential hypertension

J Hypertens. 2020;38(1):3-12
Lancet Diab Endocrinol. 2018;6(1):41-50.

Residual risk in medically treated PA

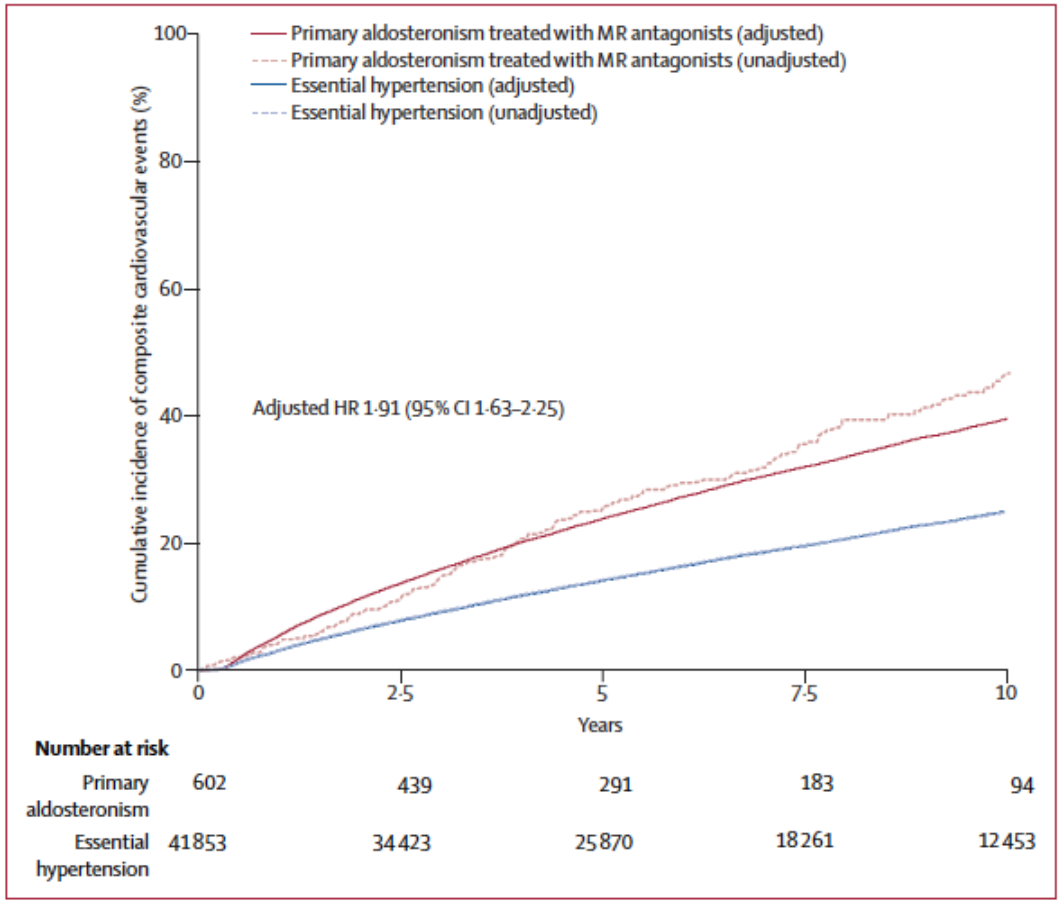


Figure 2: **Standardised cumulative incidence curve of composite cardiovascular events**

Adjusted to CV profiles and BP

602 medically treated PA
41,853 age-matched patients with EH

CV events higher in PA patients on MR antagonist
HR = 1·91 [1·63–2·25]
(14.1 excess events/100 people over 10 years)

Mortality higher in PA patients on MR antagonist
HR = 1·34 [1·06–1·71]

Atrial fibrillation
HR 1·93 [1·54–2·42]

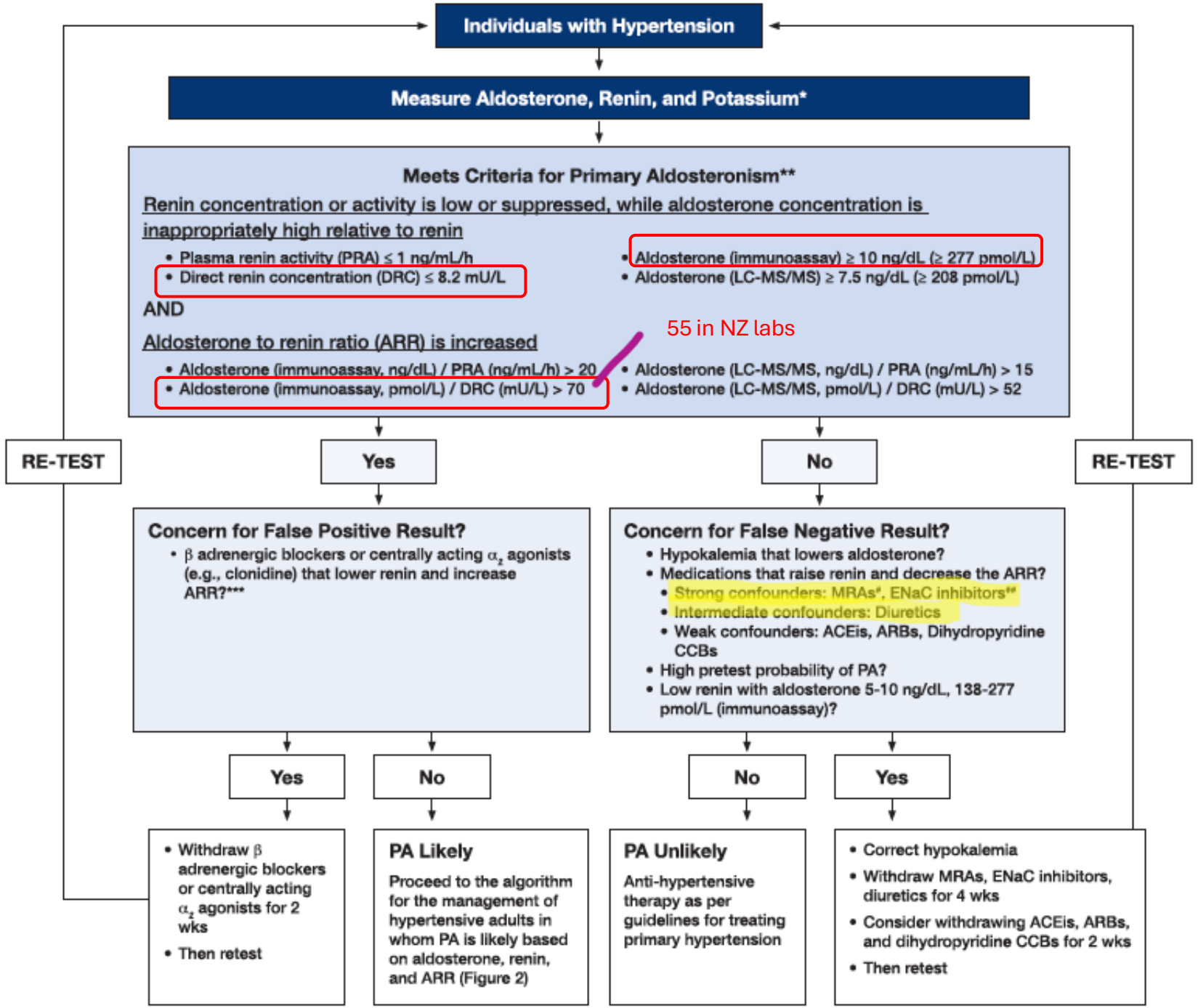
Lancet Diab Endocrinol 2018; 6: 51–59.

Influence on aldosterone/renin ratio

In situations when BP cannot be appropriately controlled without interfering antihypertensive agents:

- Beta-blockers should be discontinued when possible to reduce risk of false-positive results.
- Withdrawal of beta-blockers unlikely to have significant compromise on BP

Conditions	Effect on aldosterone concentration	Effect on renin concentration	Effect on ARR calculation	
Potassium/ sodium				
Hypokalaemia	↓	→↑	↓ FN	
Potassium loading	↑	→↓	↑ FP	
Sodium restriction (natriuresis<100 mmol/24h)	↑	↑↑	↓ FN	
Sodium loading (natriuresis>200mmol/24h)	↓	↓↓	↑ FP	
Anti-hypertensive drugs				**Withdrawal duration**
Dihydropyridine calcium channel blockers	→↓	→	↓ FN	2 weeks
ACE inhibitors	↓	↑↑	↓ FN	2 weeks
ARB	↓	↑↑	↓ FN	2 weeks
Potassium-sparing diuretics (MRA and amiloride)	↑	↑↑	↓ FN	4 weeks
Potassium-wasting diuretics (loop and thiazide diuretics)	→↑	↑↑	↓ FN	4 weeks
Beta-adrenergic blockers	↓	↓↓	↑ FP	2 weeks
Alpha-2 adrenergic agonists (clonidine, methyldopa)	↓	↓↓	↑ FP	2 weeks
Other drugs				
SGLT2 inhibitors	→	↑	↓ FN	2 weeks
Steroids	↓	→↓	↑ FP	4 weeks
NSAID	↓	↓↓	↑ FP	2 weeks
Oestrogen-containing contraceptive agents and drospirenone	↑	↑	↑ FP	6 weeks


Individuals with Hypertension
Measure Aldosterone, Renin, and Potassium*
Meets Criteria for Primary Aldosteronism**
Renin concentration or activity is low or suppressed, while aldosterone concentration is inappropriately high relative to renin
• Plasma renin activity (PRA) ≤ 1 ng/mL/h
• Direct renin concentration (DRC) ≤ 8.2 mU/L
• Aldosterone (immunoassay) ≥ 10 ng/dL (≥ 277 pmol/L)
• Aldosterone (LC-MS/MS) ≥ 7.5 ng/dL (≥ 208 pmol/L)
AND
Aldosterone to renin ratio (ARR) is increased
• Aldosterone (immunoassay, ng/dL) / PRA (ng/mL/h) > 20
• Aldosterone (immunoassay, pmol/L) / DRC (mU/L) > 70
• Aldosterone (LC-MS/MS, ng/dL) / PRA (ng/mL/h) > 15
• Aldosterone (LC-MS/MS, pmol/L) / DRC (mU/L) > 52
55 in NZ labs
RE-TEST
Yes
No
RE-TEST
Concern for False Positive Result?
• β adrenergic blockers or centrally acting α2 agonists (e.g., clonidine) that lower renin and increase ARR?***
Concern for False Negative Result?
• Hypokalemia that lowers aldosterone?
• Medications that raise renin and decrease the ARR?
• Strong confounders: MRAs#, ENaC inhibitors##
• Intermediate confounders: Diuretics
• Weak confounders: ACEis, ARBs, Dihydropyridine CCBs
• High pretest probability of PA?
• Low renin with aldosterone 5-10 ng/dL, 138-277 pmol/L (immunoassay)?
Yes
No
No
Yes
• Withdraw β adrenergic blockers or centrally acting α2 agonists for 2 wks
• Then retest
PA Likely
Proceed to the algorithm for the management of hypertensive adults in whom PA is likely based on aldosterone, renin, and ARR (Figure 2)
PA Unlikely
Anti-hypertensive therapy as per guidelines for treating primary hypertension
• Correct hypokalemia
• Withdraw MRAs, ENaC inhibitors, diuretics for 4 wks
• Consider withdrawing ACEis, ARBs, and dihydropyridine CCBs for 2 wks
• Then retest

Confirmatory testing in positive screening

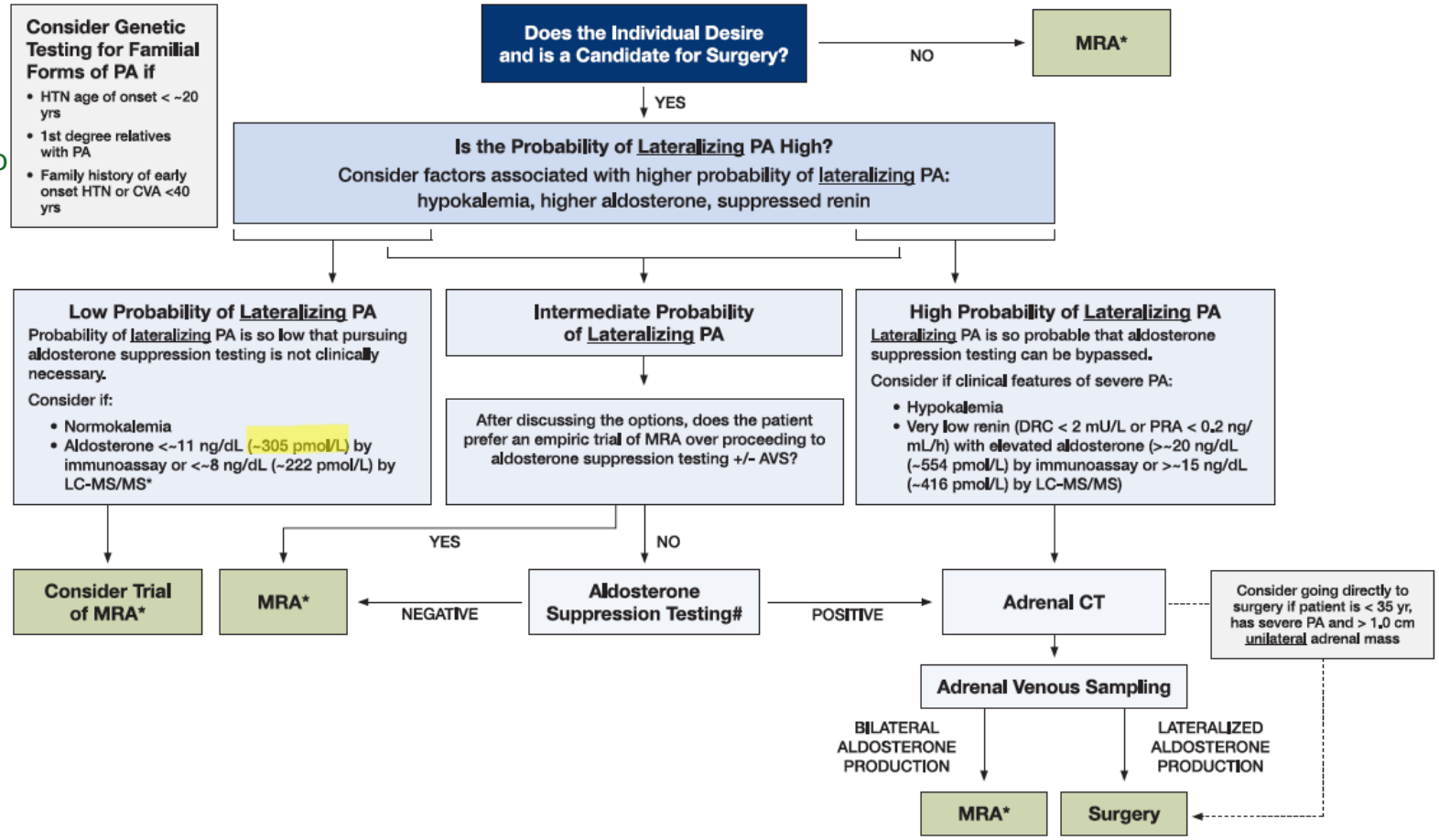
Pretest probability

- Aldo suppression testing required in:
  - Those with intermediate probability of having lateralizing PA, who are willing and able to undergo surgical adrenalectomy
- Not required:
  - Resistant hypertension
  - Hypertension with hypokalemia

  AND
  - Overt biochemical evidence of renin-independent aldosterone production

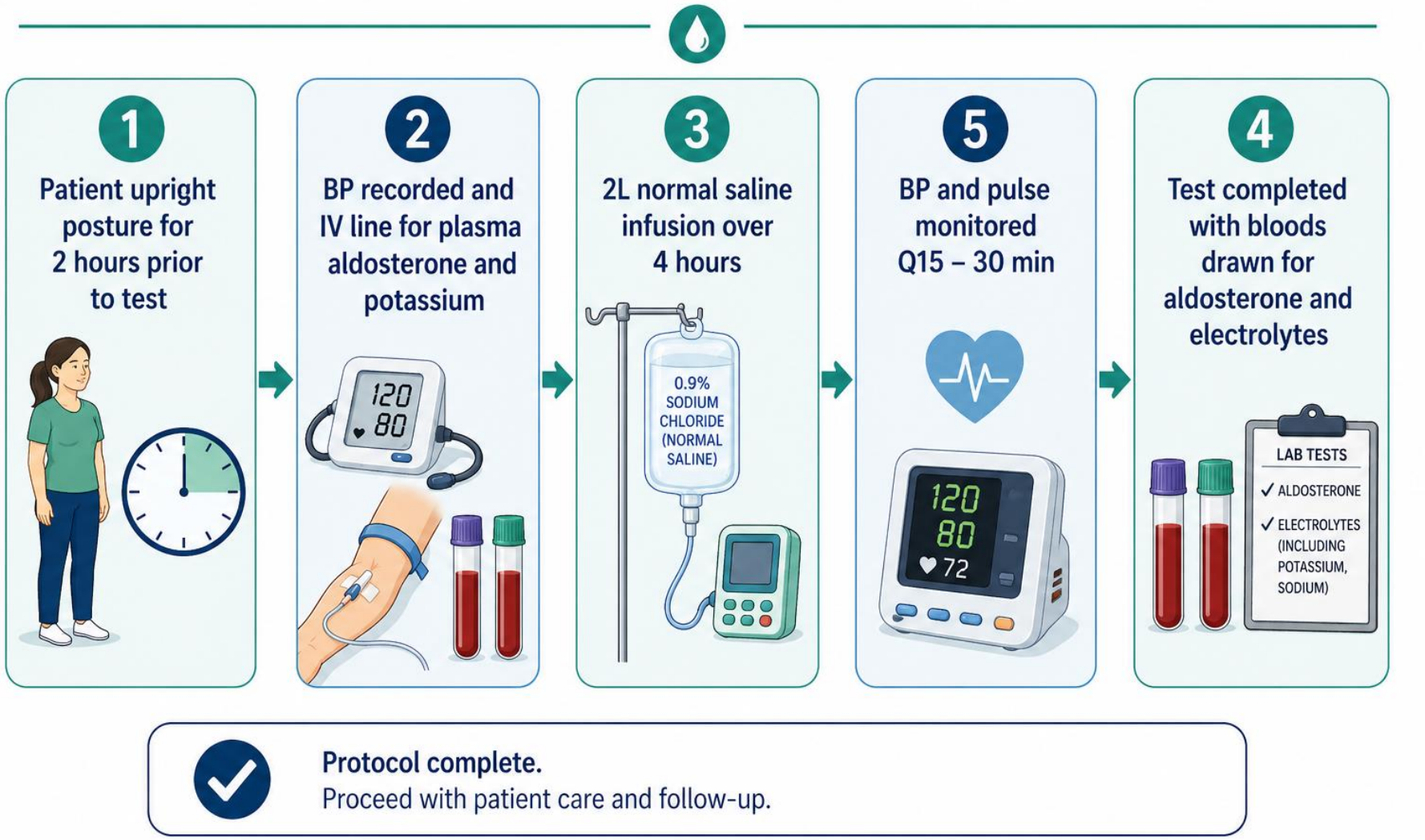
    (Renin <2 mU/L & Aldo >554 pmol/L)

- Those who are not proceeding with Sx
- Germline mutations
- Low likelihood of lateralizing PA:
  - Normal plasma K
  - Aldosterone <305 pmol/L



In patients with adrenal adenoma, dex suppression test (DST) recommended

Aldosterone suppression test



Likely PA

Aldosterone = 217 pmol/L and above

Adrenal vein sampling

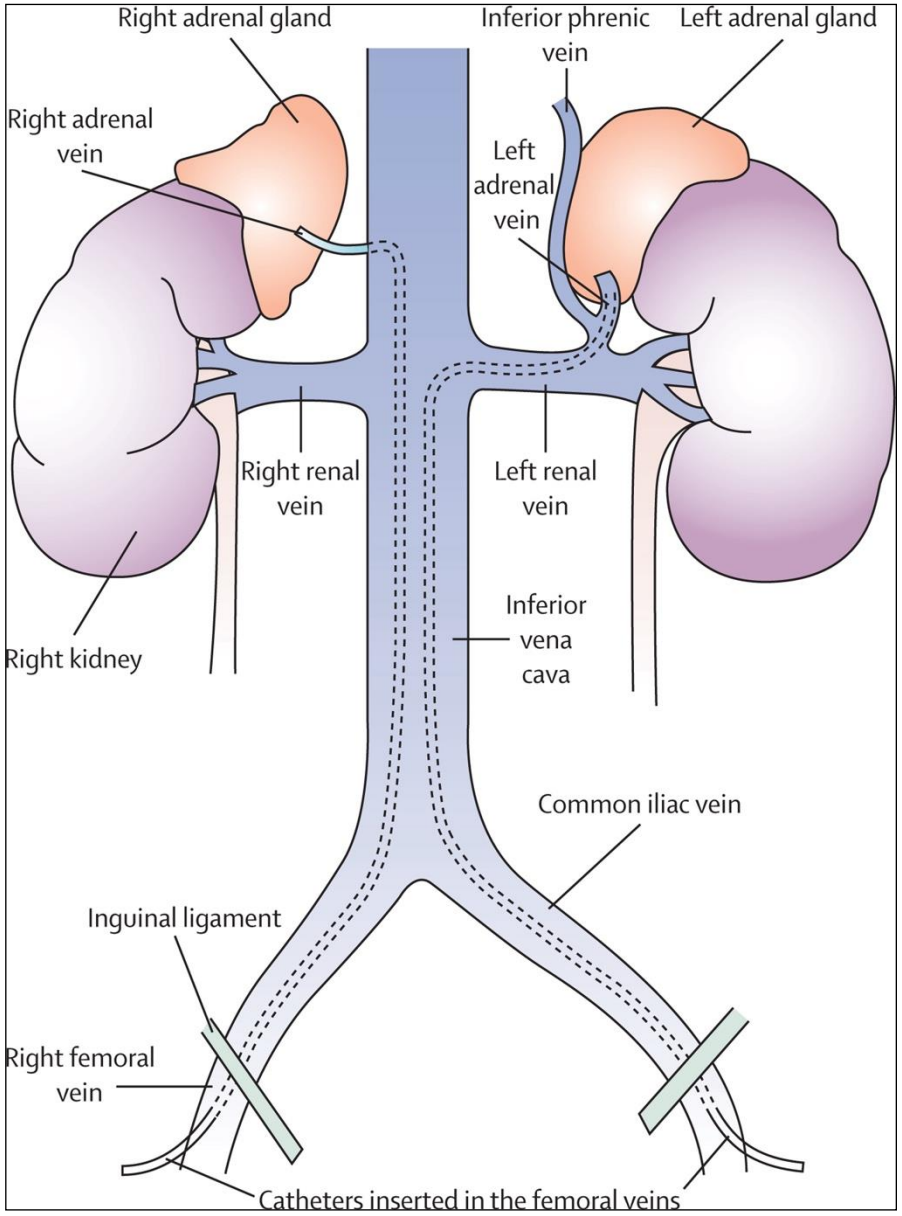
Co-syntropin stimulated

- Exclude < 35 years old with marked PA and adrenal adenoma on CT

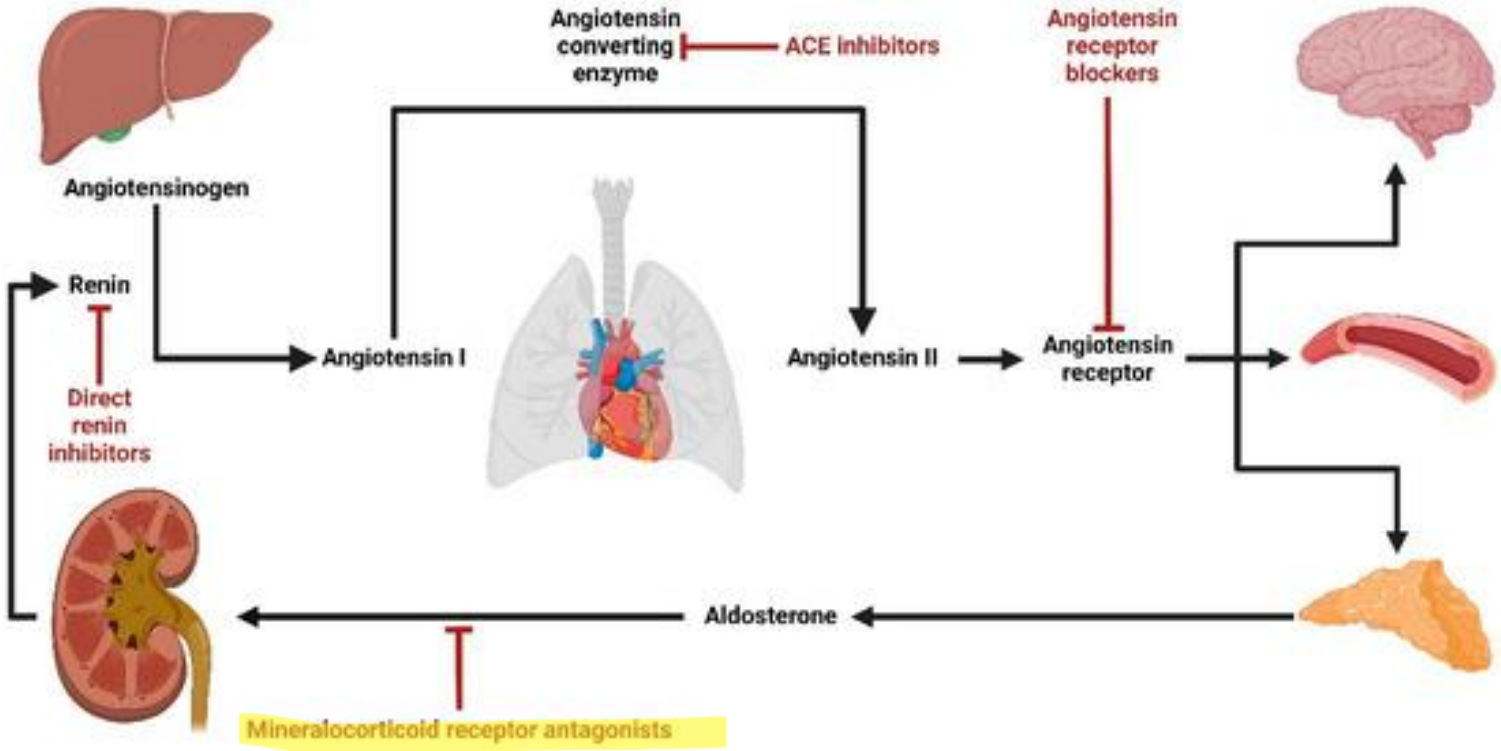
  0.28% adrenal incidentalomas in this group

- Surgical candidates
- Irrespective of side of adrenal adenoma on CT

- Selectivity index > 3 – 5
- Lateralization index ≥4
- Contralateral suppression < 1



Lifelong medical therapy



<u>Therapeutic goals:</u>

1. Reverse/ mitigate adverse effects of excess aldosterone
2. Normalize serum potassium
3. Normalize renin levels*

* Unclear benefit on raising renin when BP is controlled

In summary

- Broader, earlier screening of PA allows for early intervention and reduction in CV and renal risks
- Medication adjustments after screening tests if pretest probability remains high
- Aldosterone suppression testing indicated for intermediate likelihood of PA AND patient keen and suitable for adrenalectomy
- Appears to support a lower threshold for the use or empiric use of Spironolactone in hypertension and with low renin alone *without medication interferences*

Cases

Ms SJ

62 female

T2D for 6 years

Hypertension 10 years, well controlled

- Recent exacerbation of hypertension, with elevated home BP and today's average clinic BP 180/110 mmHg.
- She has been increasing exercise and been drinking a herbal tea to help with weight loss and remission of diabetes
- Her examination was non-contributory.

Medications

Galvumet 1 BD

Losartan 100 mg

Frusemide 40 mg

Verapamil 120 mg

Vitamin E

Vitamin C

Labwork post clinic

Na 144 | K 2.6 |Bicarb 35 (22 – 31)| Cl 95 (95 – 110)

Renin <2 mU/L | aldosterone <70 pmol/L

3 months ago:

Na 138| K 4.5 |Bicarb 26 |Cl 101 mmol/L

What is her diagnosis?

A. Cushing's disease

B. Primary Aldosteronism

C. Apparent mineralocorticoid excess

D. Additional diuretic effect with herbal preparation

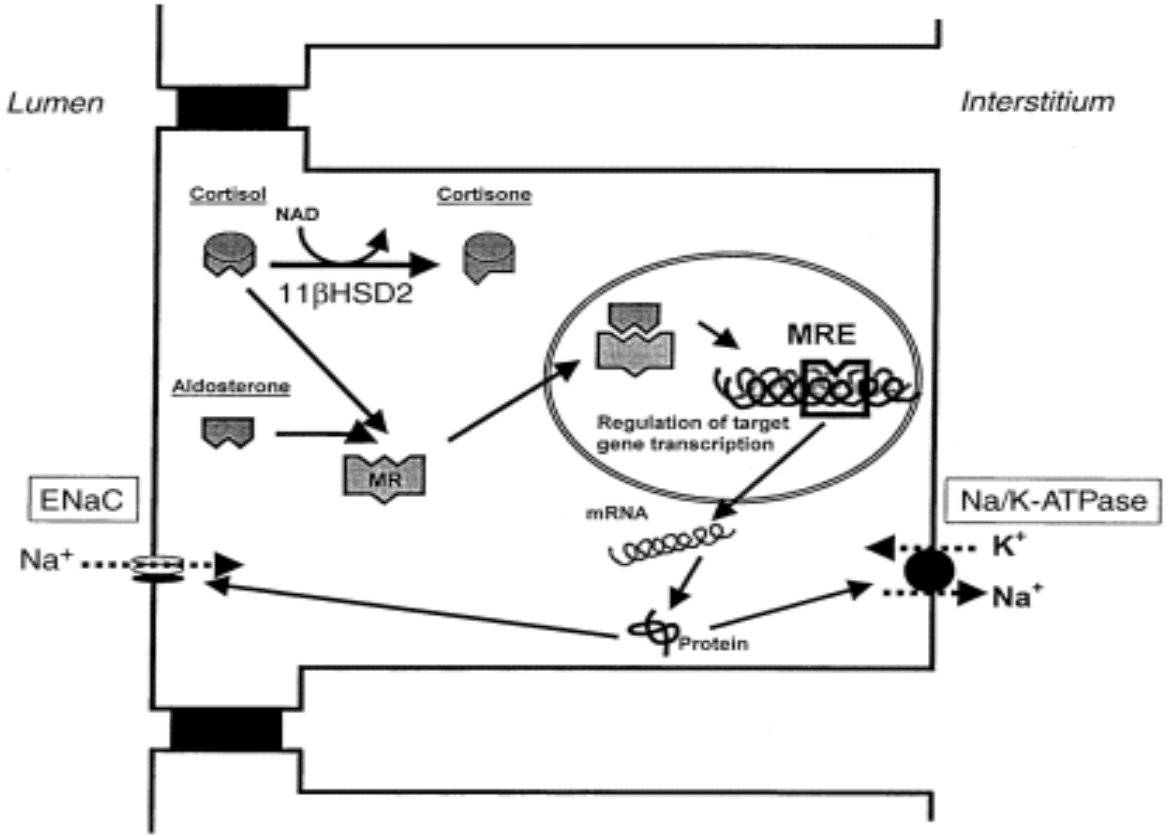
Acquired apparent mineralocorticoid excess

Glycyrrhizic Acid (Licorice)

Inactivates 11BHSD 2

Increases cortisol binding to MR receptor → sodium retention + potassium loss

Low renin, low aldosterone, metabolic alkalosis



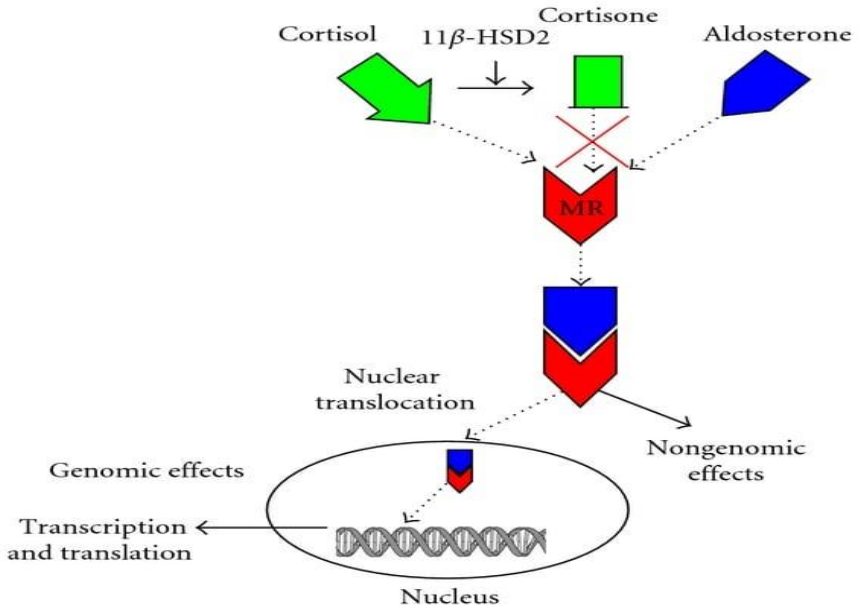
What is her diagnosis?

A. Cushing's disease

B. Primary Aldosteronism – *expect low renin, high aldo*

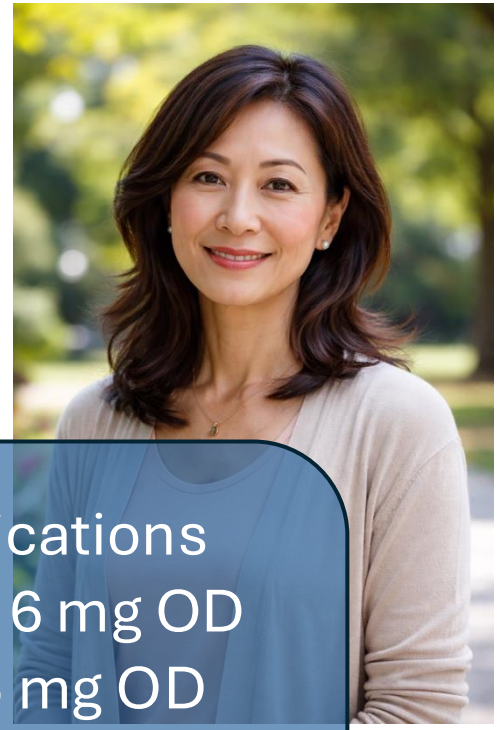
C. Apparent mineralocorticoid excess

D. Additional diuretic effect with herbal preparation – *expect high renin, (N) aldo*



Essick, Eric & Sam, Flora. IJH 2011 (7): 346985.

Mrs YM



52 Chinese female with clinic BP 170/105 mmHg

BMI 25 kg/m^2

Non smoker

CKD 3a

CABG X 4 following NSTEMI July 2014

Recent L) MCA infarct with good recovery

Current medications
Candesartan 16 mg OD
Amlodipine 5 mg OD
Metoprolol CR 95 mg OD
Atorvastatin 40 mg OD
Aspirin 100 mg OD

Previously developed hypokalaemia after starting Bendrofluazide

Examination findings non-contributory, apart from mild retinopathy. HR 58 bpm

Labwork:

Aldo 483 pmol/L | renin 3 mU/L | ARR 161(<55)

Na 140 | K 3.6 | Cr 120 umol/L

Urine ACR 6.7

Thyroid function tests and serum metanephrines – normal

CT : bilateral prominent adrenal glands with 21 mm left adrenal nodule (HU 8)

What is the next step?

A. Add Chlorthalidone 12.5mg daily

B. Stop Metoprolol, replace with Frusemide 40mg daily and recheck aldosterone renin ratio (ARR) after 2 weeks

C. Stop Metoprolol, replace with Doxazosin and recheck aldosterone renin ratio (ARR) after 2 weeks

D. Refer to surgeons for removal of left adrenal lesion

- Repeated ARR 88; renin 4 mU/L; aldosterone 350 pmol/L
- Seated saline suppression, aldosterone 250 pmol/L (<217)
- 1 mg dexamethasone suppression test = negative

What’s your next step?

A. Start on Spironolactone and titrate to potassium and BP control
B. Start on Spironolactone and refer for adrenal vein sampling
C. Refer for adrenal vein sampling
D. Start on Spironolactone and refer to surgeons for resection of left adrenal adenoma

Case study 1

32yrs female referred by GP with resistant hypertension

Background: Asthma, normal echocardiogram 2008, family history of hypertension, BMI 30 kg/m2

Medications at referral:

- Amlodipine 5mg nocte
- Bendroflumethiazide 2.5mg mane

Blood pressure 140/95mmHg (1); 144/94 mmHg (2)

ARR 136, K 3.7 mmol/L (03/2018)

Investigations

- SST Aldosterone 354 pmol/L; Renin 2 mU/L
- CT adrenals: Normal
- Adrenal vein sampling did not demonstrate lateralization

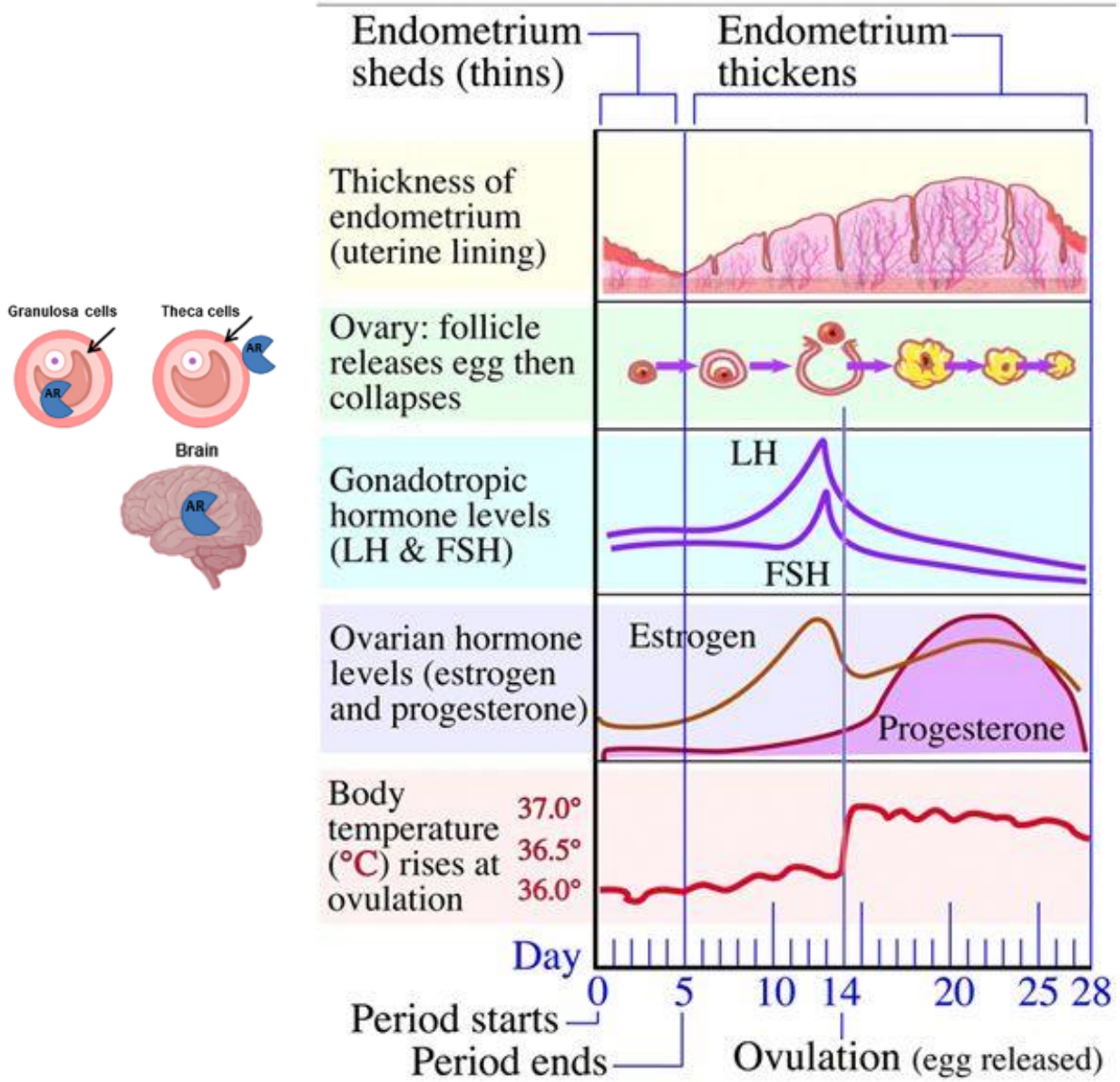
- Commenced on Spironolactone 12.5mg daily with progressive increase 100mg mane and 50 mg nocte over 11 months
- 24 hour ABPM on 75 mg Spironolactone daily
  - Average overall blood pressure: 141/97mmHg
  - Average awake blood pressure: 145/101mmHg
  - Average asleep blood pressure: 129/86mmHg

Amenorrhoea

- Secondary amenorrhoea for 6 months, since Spironolactone dose increased > 100mg daily
- FSH 3 U/L (4 - 25); LH 7 U/L (10 – 75); oestradiol 95 pmol/L (150 – 1450); prolactin 250 mU/L(100 – 500)

Progress

- Reduced spironolactone to 25mg
- Started on Amlodipine 5mg daily and clinic BP 133/87mmHg
- Periods returned after 2-3 months

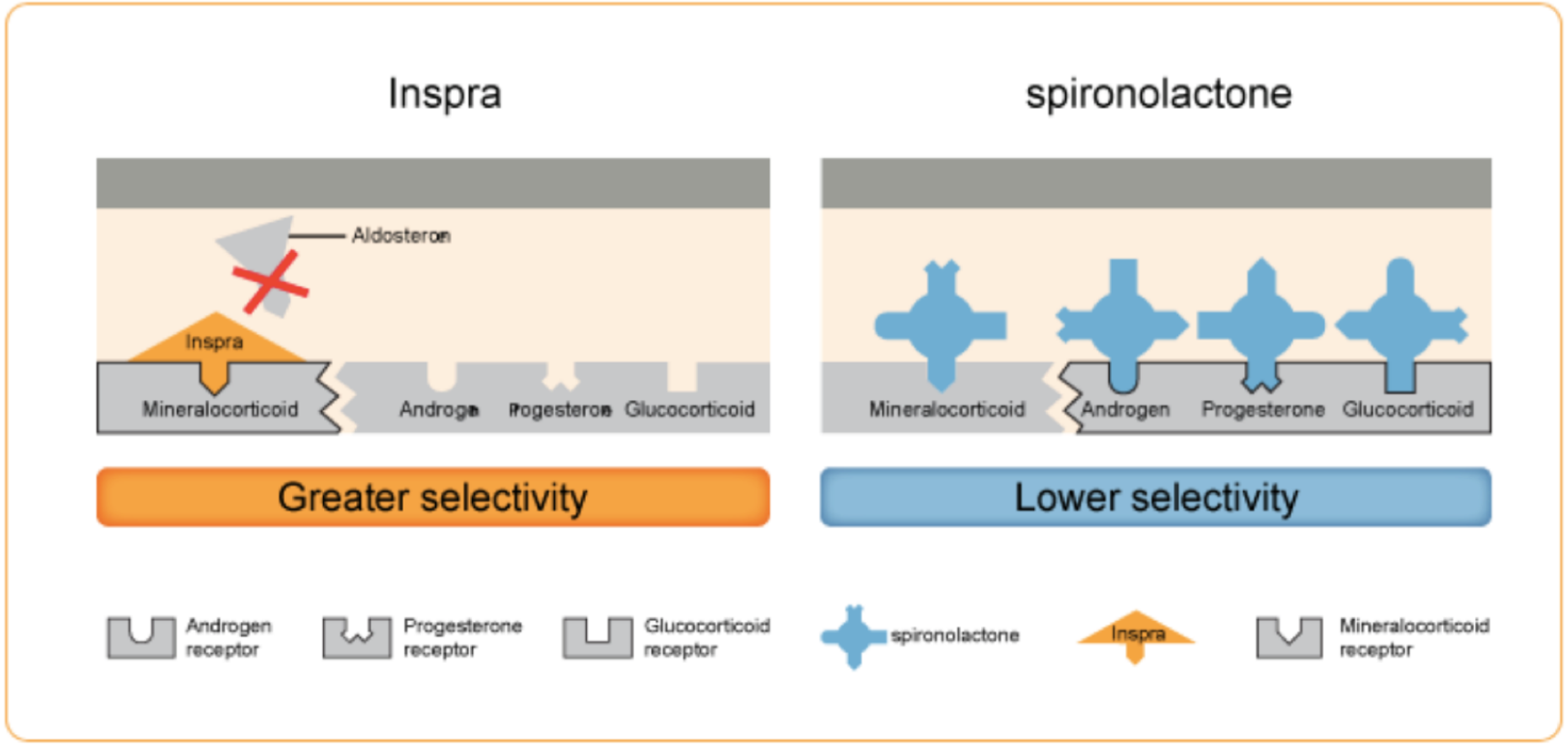


ARKO mice:

1. Defective follicular development and poorer follicle health
2. Reduced FSH at all estrous cycle and LH, affecting late stages of follicle development.

J Endocrinology 2019; 242, R23–R50

Mechanism of sex steroid adverse effects of Spironolactone



https://medium.com/minimalist-pharmacist/aldosterone-antagonists-entresto-corlanor-ed3a572b4a2b

- Menstrual irregularities include metrorrhagia, amenorrhoea and menorrhagia
  - 20% with Spironolactone 50 – 100 mg/day
  - 70% with Spironolactone 200mg/day
- Return of normal menstrual cycle usually occurs within 2 months of Spironolactone discontinuation.

J Clin Aesthet Dermatol. 2012; 5 (3): 37–50.

Case study 2

87 female

Resistant hypertension (2024) with negative secondary screen

Background: AF, myelofibrosis, anxiety, CKD G3aA3, chronic hyponatraemia on 1-1.2L/day FR

Medications

- Losartan 50 mg twice daily
- Amlodipine 10 mg nocte
- Doxazosin 4 mg mane, 2 mg nocte
- Spironolactone 12.5 mg daily
- Bendrofluazide 1.25 mg daily
- Metoprolol CR 23.75 mg daily
- Dabigatran 110 mg twice daily
- Colecalciferol 1.25 mg monthly

Medication intolerance

Chlorthalidone hyponatraemia (in the context gastro)

Bisoprolol fatigue

Bendrofluazide moderate hyponatraemia

- 19/2/26: Symptomatic tachybrady syndrome, HR 34 bpm
  - PPM inserted 25/2/26
  - Metoprolol increased 47.5 mg daily
  - Bendrofluazide stopped
  - Fluid restriction lifted

- 8/3/26: Hospitalized for moderate hyponatraemia
  - 9am Cortisol 473 nmol/L
  - TSH = 3.0 mU/L (0.4 – 4.0 mU/L)
  - Urine sodium 79 mmol/L (normal <40) and osmolality 444 (normal <100)

Date	23/10/25	9/1/26	19/2/26	23/2/26	26/2/26	8/3/25	11/3/26	16/3/26	17/4/26
Na	132	133	129	126	125	126	127	131	137

- Bendrofluazide 1.25 mg stopped
- Metoprolol increased
- FR removed

Readmission with symptomatic hyponatraemia

FR restarted

Metoprolol reduced to 23.75 mg daily

Continued on spiro

Betablocker hyponatraemia

- Rare, usually occurring on initiation of betablockers
- Usually modest
- Increased risk in those on concurrent diuretics
- Mechanism uncertain, but associated with inhibition of renin secretion and reduced tubular Na reabsorption