PERCORSO DIAGNOSTICO TERAPEUTICO DELLE LESIONI SURRENALICHE NELLA PROVINCIA DI FERRARA

Inquadramento clinico e laboratoristico

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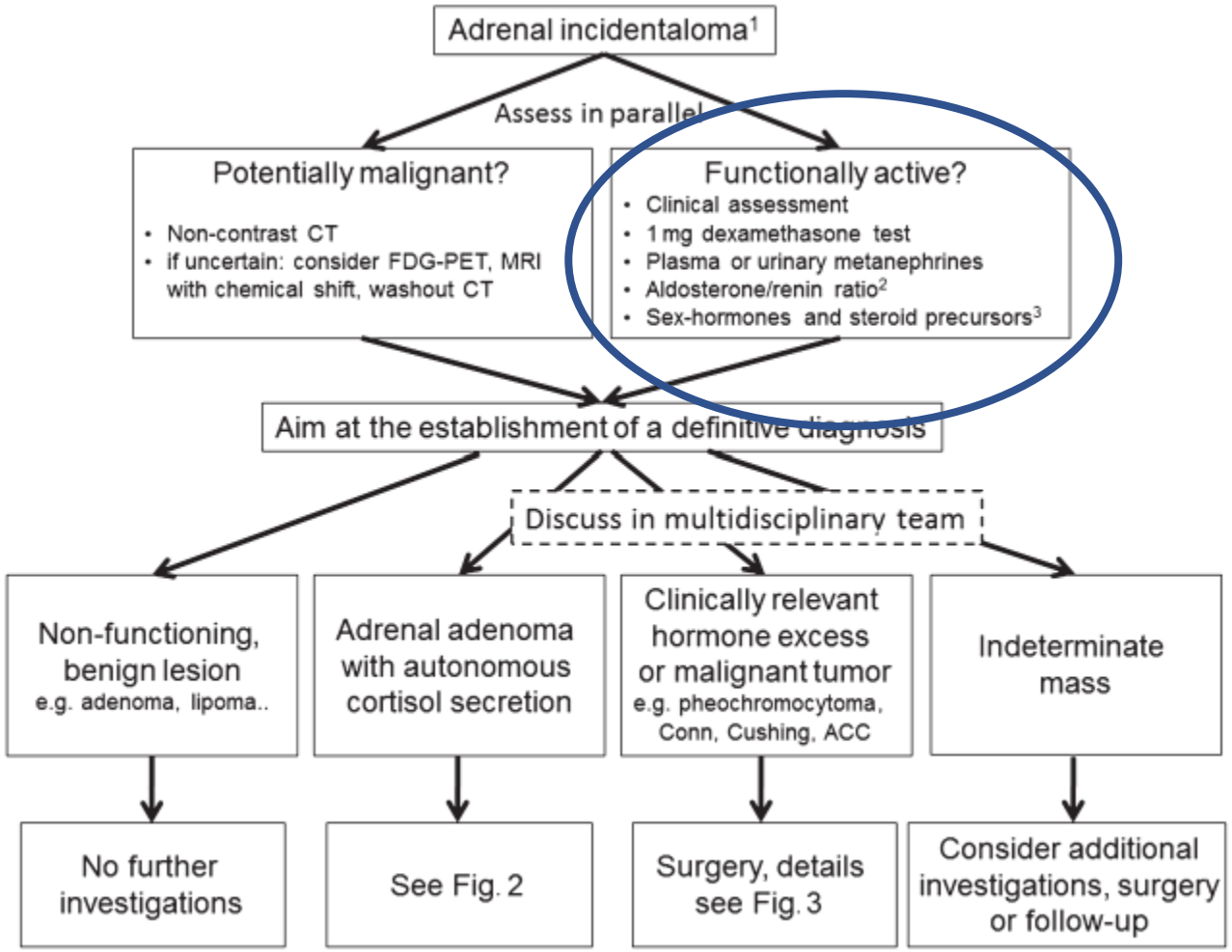
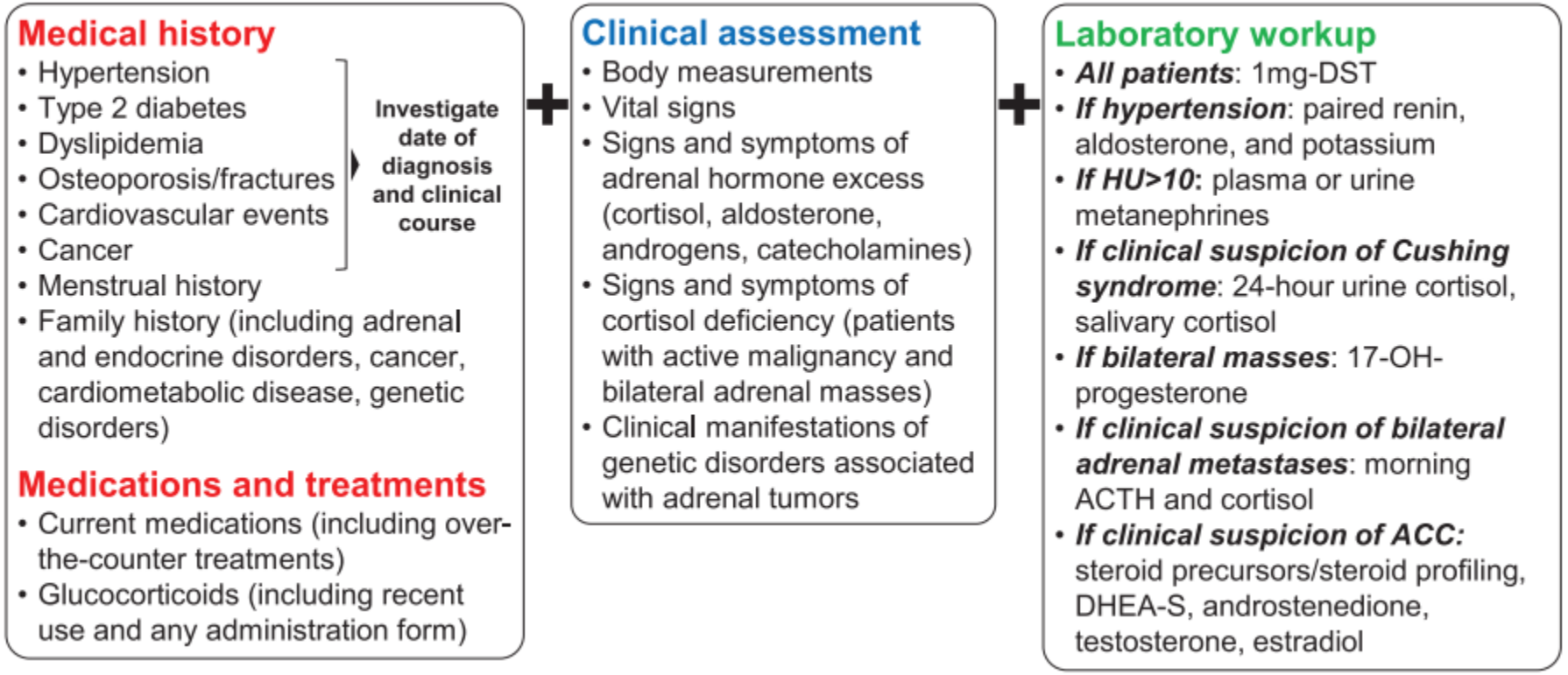
Adrenal Incidentaloma



Fassnacht et al. Management of adrenal incidentalomas: European Society of Endocrinology Clinical Practice Guideline in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol. 2016

Adrenal Incidentaloma



Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Pheochromocytoma

Hormone excess

Catecholamine excess

General considerations

- Pheochromocytomas are increasingly diagnosed incidentally (60%).
- Most patients do not have the classic "spell" symptoms.
- Germline pathogenic variants are common (up to 40%-50%). Syndromic associations can be a clue to the diagnosis (Table 4).

Clinical Manifestations

- Hypertension in up to 90% cases (paroxysmal in 50%).
- Classic triad ("spell"): headaches, sweating, palpitations.
- Pallor, nausea, tremor, anxiety.
- Postural hypotension
- Supraventricular tachycardia.
- Myocardial ischemia/ infarction.
- Cardiomyopathy and heart failure (takotsubo syndrome).
- Hypertensive crisis triggered by stressors (e.g., surgery, colonoscopy, some medications).

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Pheochromocytoma

Adrenal Hormone abnormality	Indication for testing	First-line testing	Second-line/confirmatory testing	Others considerations and remarks
Catecholamine excess	Anyone with indeterminate adrenal mass (HU ≥ 10), with or without symptoms	Plasma or 24-h urine metanephrines. *Abnormal result:* usually >2× upper limit of normal. *Possible causes of false-positive results:* • Collection of plasma metanephrines under not controlled conditions. • Medications: tricyclic antidepressants; psychoactive agents; prochlorperazine; L-dopa; adrenergic receptor agonists; phenoxybenzamine. • Physical stress or illness: significant illness requiring hospitalization; congestive heart failure; panic attacks; subarachnoid bleeding; obstructive sleep apnea. • Withdrawal from alcohol, clonidine, and other drugs. *Possible causes of false-negative results:* small pheochromocytomas (especially with maximum diameter < 2 cm).[c]	• Usually not needed unless false-positive results are suspected.[d] • Urinary or plasma dopamine or plasma methoxy tyramine is a possible add-on test to detect tumors with dopamine hypersecretion (increased risk of malignancy).	• 24-h urine fractionated metanephrines have excellent sensitivity and specificity. • Plasma fractionated metanephrines have excellent sensitivity but suboptimal specificity if not collected appropriately. Fasting collection after 30 min in the supine position and the use of age-adjusted upper limits of normal increase specificity. • In patients with suspected pheochromocytoma, extra-adrenal disease and associated genetic predisposition need to be considered (Table 4).

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Cortisol excess

Hormone excess		General considerations	Clinical Manifestations
Cortisol excess	MACS	• Diagnosed in up to 50% of patients with incidentalomas. • Absence of stigmata of overt cortisol excess (Cushing syndrome). • Associated with frailty and an increased cardiometabolic morbidities.	• Metabolic syndrome: hyperglycemia; hypertension; dyslipidemia; obesity. • Cardiovascular events. • Atrial fibrillation and other arrhythmias. • Osteoporosis and fragility fractures (high prevalence of asymptomatic vertebral fractures). • Anxiety/depression. • Chronic kidney disease. • Frailty
	Cushing syndrome	• Rare (3%-5% of patients with adrenal adenomas). • Up to 50% are diagnosed during adrenal incidentaloma work up. • Requires prompt recognition and work up to confirm the diagnosis and offer treatment. • If untreated, it is associated with high morbidity and mortality. • Concomitant adrenal androgen excess indicates adrenocortical carcinoma.	• Stigmata of cortisol excess: facial plethora; dorsocervical fat pad; supraclavicular fat pads; muscle loss, proximal myopathy, and muscle weakness; easy bruising; red stretchmarks. • Increased mortality risk, mainly driven by cardiovascular and thromboembolic events. • Metabolic syndrome: hyperglycemia; hypertension; dyslipidemia; obesity. • Osteoporosis and fragility fractures. • Immunosuppression and susceptibility to infections. • Depression and other psychiatric disorders, insomnia, memory loss, irritability, panic attacks. • Amenorrhea and reduced fertility. • Heart failure.

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Cortisol excess

Adrenal Hormone abnormality	Indication for testing	First-line testing	Second-line/confirmatory testing	Others considerations and remarks
Cortisol excess	Anyone with adrenal mass, regardless of symptoms	1-mg DST. *Abnormal result:* serum cortisol >1.8 mcg/dL. The ESE-ENSAT guidelines on adrenal incidentalomas define MACS as "possible" when 1-mg DST serum cortisol is 1.8-5.0 mcg/dL and "confirmed" when 1-mg DST serum cortisol is >5.0 mcg/dL. *Possible causes of false-positive results:* • Oral estrogens (e.g., OCP) • CYP3A4 inducers. • Exogenous glucocorticoids (assay interference). • Uncontrolled hyperglycemia. • Alcoholism. • Psychiatric disorders. • Morbid obesity. • Pregnancy. • Chronic active hepatitis. • Kidney failure • Older age • Dementia	• ACTH. • DHEAS. • 24-h urine free cortisol (if Cushing syndrome is suspected). • Salivary cortisol (if Cushing syndrome is suspected). • In selected cases: repeat 1-mg DST; perform 8-mg DST; 2-day, low-dose DST (Liddle test); CRH test.	• ACTH-independent cortisol excess must be confirmed before considering adrenal surgery. • Patients with adrenal hypercortisolism have abnormal DST, low ACTH, and DHEA-S. • 24h urine free cortisol is usually normal in MACS. • The accuracy of salivary cortisol in MACS is low.

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

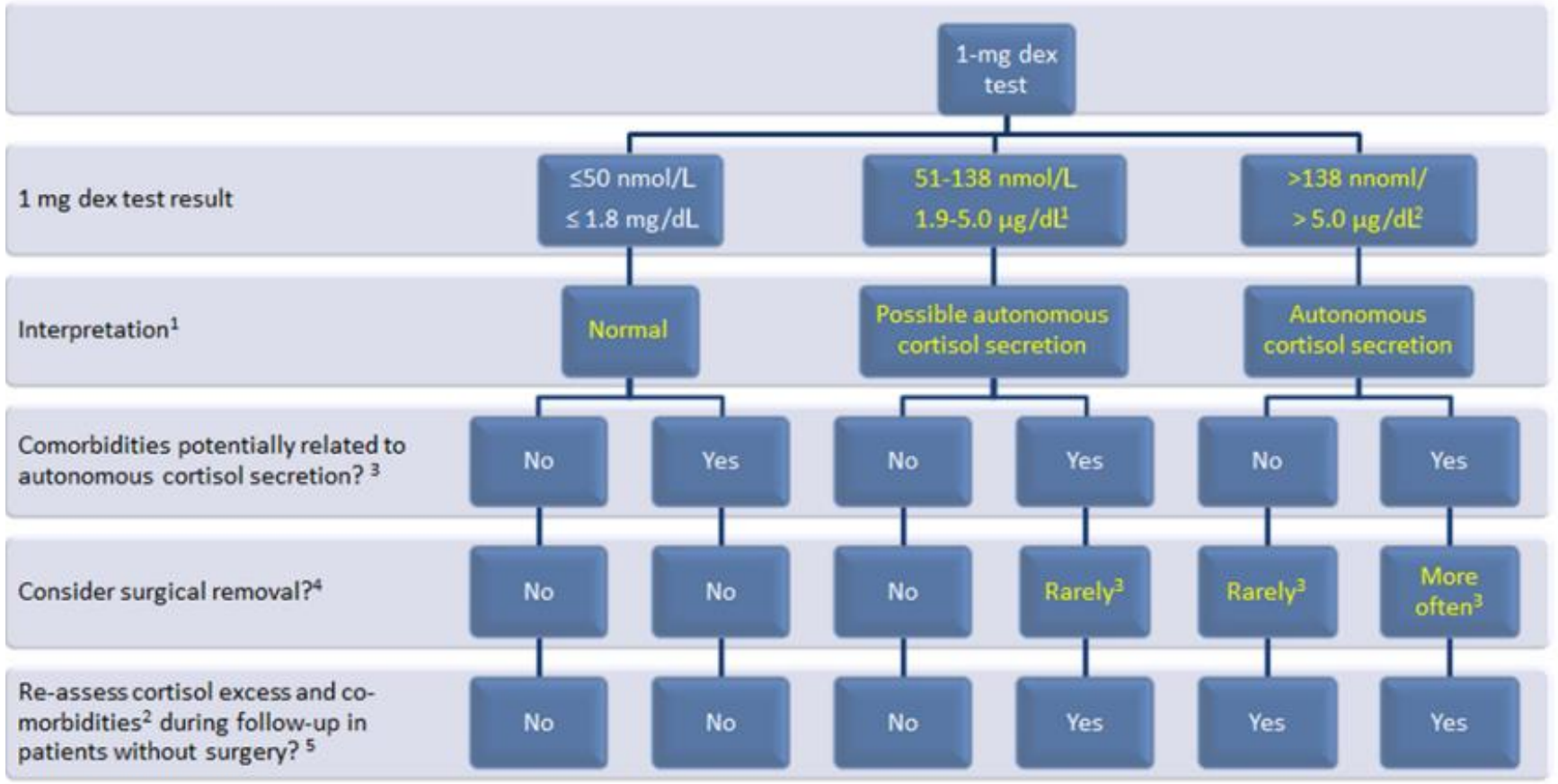
Autonomous Cortisol Secretion

R 3.2. We recommend that all patients with adrenal incidentalomas undergo a 1 mg overnight dexamethasone suppression test to exclude cortisol excess (⊕⊕OO).

R 3.3. We suggest interpretation of the results of the 1 mg overnight dexamethasone test as a continuous rather than categorical (yes/no) variable (⊕OOO). However, we recommend using serum cortisol levels post dexamethasone ≤50 nmol/l (≤1.8 µg/dL) as a diagnostic criterion for the exclusion of autonomous cortisol secretion (⊕⊕OO).

R 3.4. We suggest that post-dexamethasone serum cortisol levels between 51 and 138 nmol/L (1.9–5.0 µg/dL) should be considered as evidence of 'possible autonomous cortisol secretion' and cortisol levels post dexamethasone >138 nmol/L (>5.0 µg/dL) should be taken as evidence of 'autonomous cortisol secretion'. Additional biochemical tests to confirm cortisol secretory autonomy and assess the degree of cortisol secretion might be required (Fig. 2). However, for the clinical management, the presence of potentially cortisol-related comorbidities (Table 2, Fig. 2) and age of the patient are of major importance.

R 3.5. We recommend against considering 'autonomous cortisol secretion' as a condition with a high risk for the development of overt Cushing's syndrome (⊕⊕OO).



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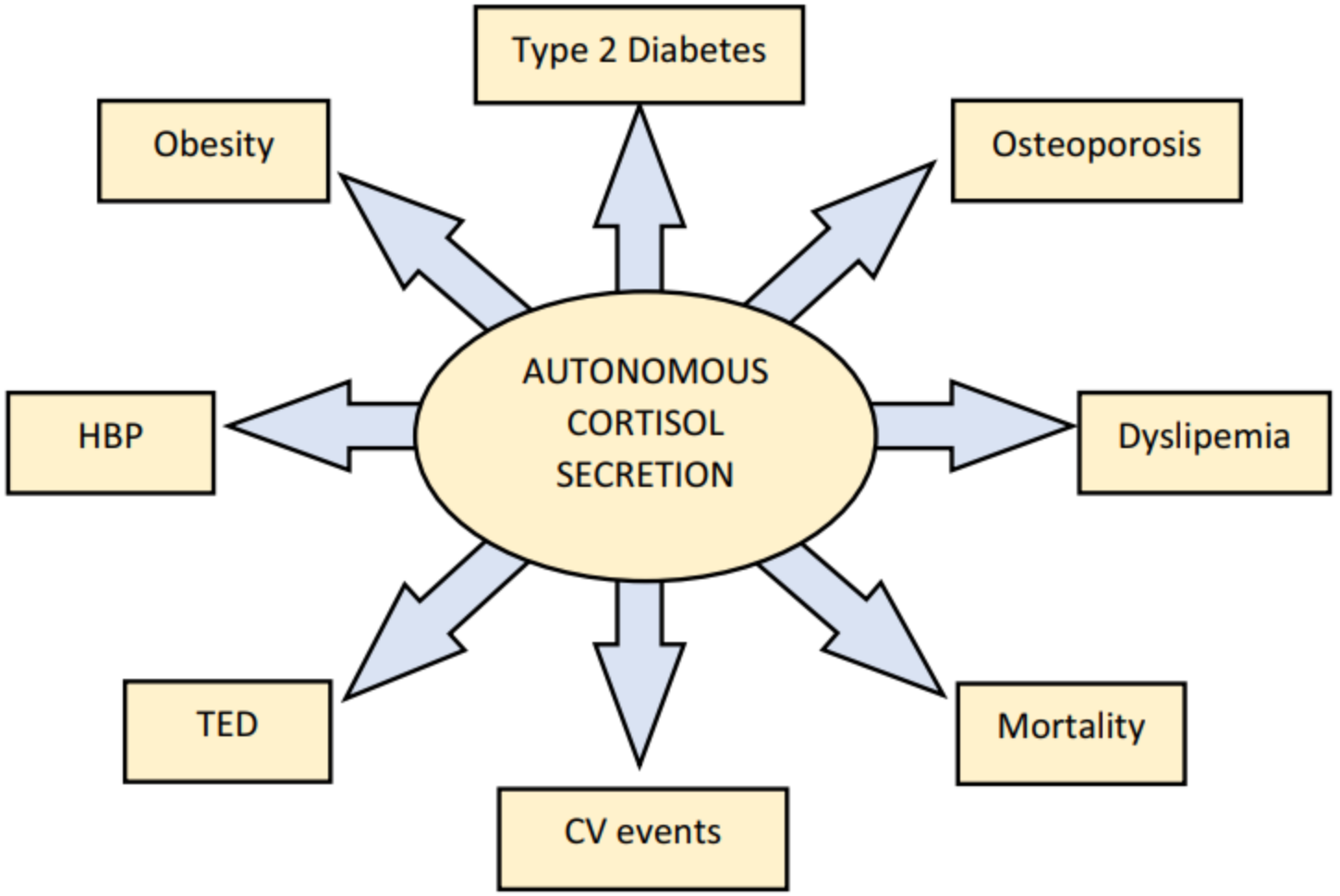
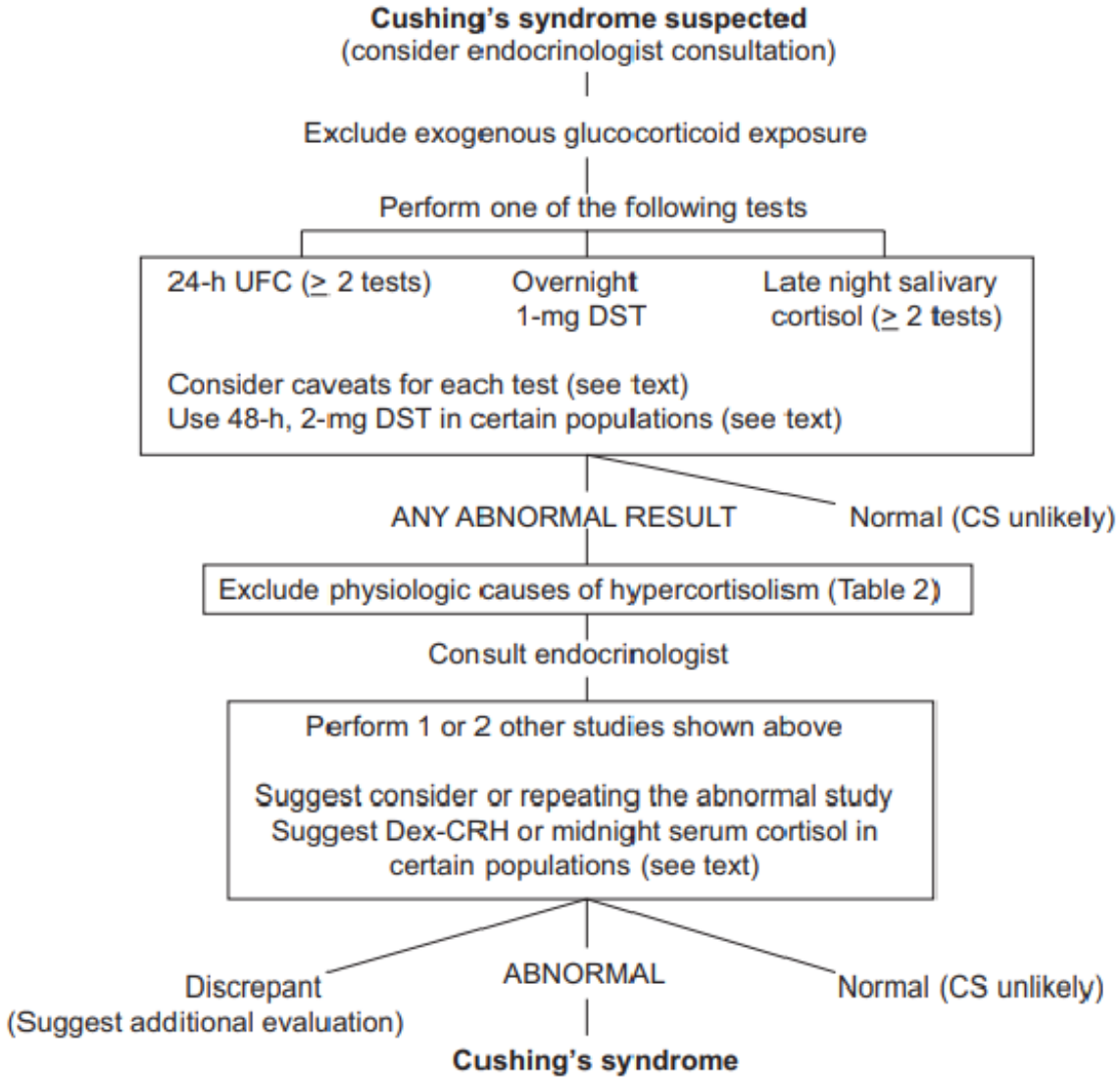
Autonomous Cortisol Secretion



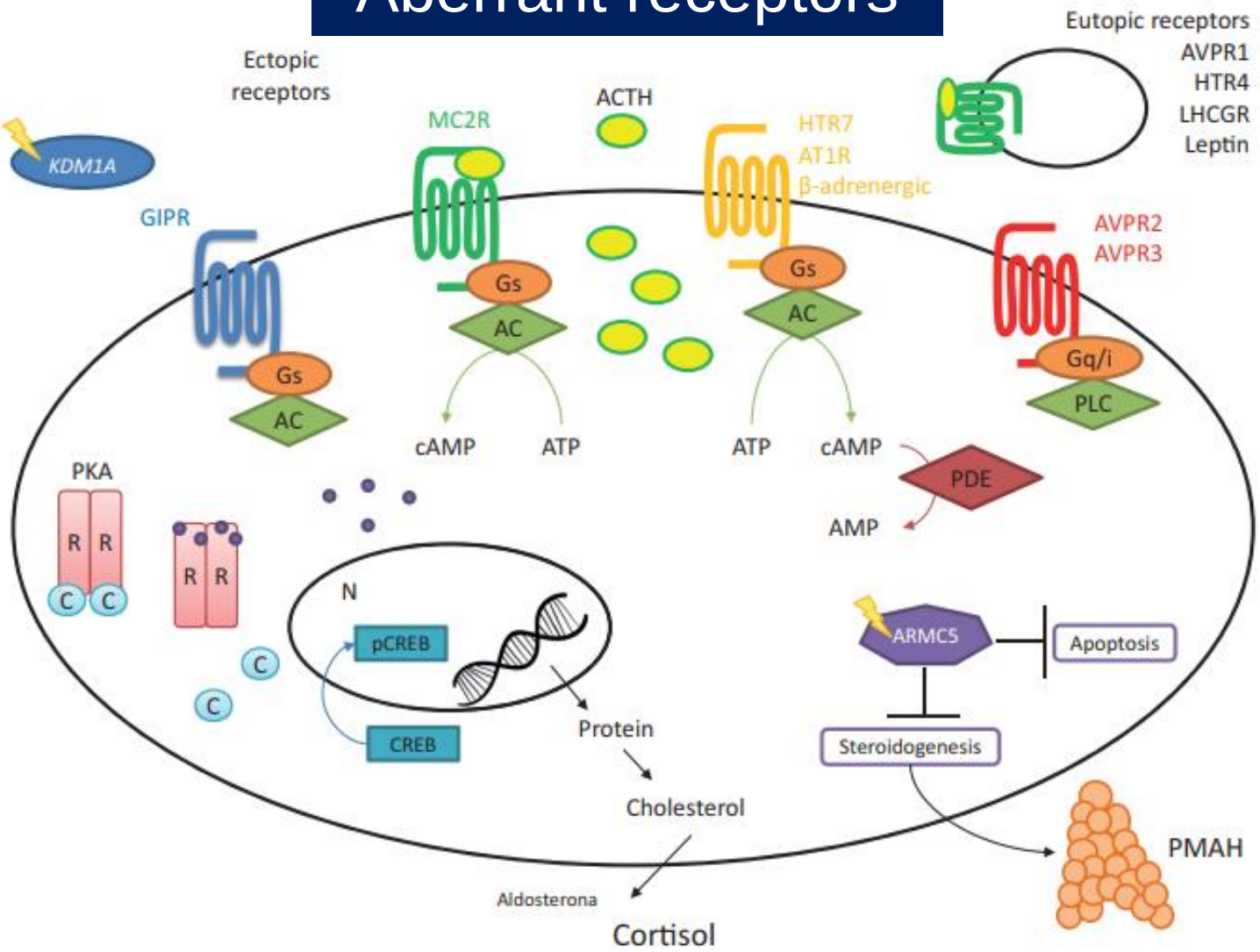
Araujo-Castro M, Sampedro Núñez MA, Marazuela M. Autonomous cortisol secretion in adrenal incidentalomas. Endocrine. 2019

Cushing's syndrome



Nieman et al. The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2008

Aberrant receptors



Charchar HLS, Fragoso MCBV. An Overview of the Heterogeneous Causes of Cushing Syndrome Resulting From Primary Macronodular Adrenal Hyperplasia (PMAH). J Endocr Soc. 2022

Aberrant receptors

Aberrant receptor	Phenotype	*In vivo* screening protocol	Co-expression	Targeted medical therapy
GIP receptor (ectopic) (37, 38, 39, 45, 52, 54, 55, 57)	Food-induced hypercortisolism	Mixed meal Oral glucose	LH/hCG R 5-HT_4 R	Octreotide, pasireotide GIPR antagonist
Vasopressin receptor V_1 (eutopic) (32, 45, 49, 50, 53, 78, 79, 84, 105, 144) V_2, V_3 (ectopic) (32, 79)	Upright posture-related hypercortisolism	Upright posture AVP/desmopressin	β-AR 5-HT_4 R	Specific AVP receptors antagonist
β-adrenergic receptor (ectopic) (45, 78, 117)	Upright posture Insulin-induced hypoglycemia exercise/ stress test hypercortisolism	Upright posture Isoproterenol (β1-agonist) Salbutamol (β2-agonist)	V_1 5-HT_4 R	β-blockers
AT-1 receptor (ectopic) (55, 145)	Posture-dependent hypercortisolism	Upright posture Angiotensin II		AT-1 receptor antagonist
LH/hCG receptor (eutopic) (50, 52, 54, 55, 64, 121)	Pregnancy (transient) Postmenopausal (persistent)-dependent hypercortisolism	GnRH hCG, Recombinant LH	5-HT_4 R GIPR	Long-acting GnRH agonist (leuprolide acetate)
5-HT_4 receptor (eutopic) (64, 79, 85) 5-HT_7 receptor (ectopic) (71, 87)	Serotonin-dependent hypercortisolism	5-HT4 receptor agonists (metoclopramide, cisapride)	LH/hCG R GIPR β-AR	5-HT_4 receptor antagonist (GR113808) 5-HT_7 receptor antagonist
Glucagon receptor (ectopic) (47, 72, 73, 74, 75)	Hypoglycemia ?	Intravenous glucagon	5-HT_4 R LH/hCG R	Octreotide

El Ghorayeb N, Bourdeau I, Lacroix A. Multiple aberrant hormone receptors in Cushing's syndrome. Eur J Endocrinol. 2015

Aberrant receptors

In-vivo screening protocol to detect the presence of aberrant adrenal hormone receptors in adrenal Cushing's syndrome.

Time (min)	Day 1	Day 2	Day 3
−60	Fasting supine	Fasting supine	Fasting supine
−15	[a]	[a]	[a]
0	Upright[a]	GnRH 100 μg i.v.[a]	Glucagon 1 mg i.v.[a]
+30	Upright[a]	[a]	[a]
+60	Upright[a]	[a]	[a]
+90	Upright[a]	[a]	[a]
+120	Upright[a]	[a]	[a]
+150	Supine[a]	(meal)	
+180	Mixed meal[a]		Vasopressin 10 IU i.m.
+210	[a]		[a]
+240	[a]		[a]
+270	[a]	[a]	[a]
+300	[a]	TRH 200 μg i.v.[a]	[a]
+330		[a]	
+360	ACTH 1–24 250 μg i.v.[a]	[a]	Metoclopramide 10 mg orally[a]
+390	[a]	[a]	[a]
+420	[a]	[a]	[a]
+450	[a]		[a]
+480	[a]		[a]

ACTH, adrenocorticotropic hormone; GnRH, gonadotrophin-releasing hormone; TRH, thyrotropin releasing hormone.
Modified from Lacroix et al (1999, *The Endocrinologist* **9:** 9–15) with permission.

[a] Blood samples for determination of cortisol, other hormones, and vital signs.

Lacroix A. ACTH-independent macronodular adrenal hyperplasia. Best Pract Res Clin Endocrinol Metab. 2009

Primary Aldosteronism

Hormone excess	General considerations	Clinical Manifestations
Aldosterone excess	• Incidentalomas causing primary aldosteronism are almost invariably benign. • Hypokalemia is not required to make the diagnosis. • Associated with increased cardiometabolic risk. • Concomitant cortisol excess (usually MACS) is common.	• Hypertension. • Hypokalemia (10%-40% of cases). • Symptoms and complications related to hypokalemia: polyuria and nocturia; fatigue and weakness; muscle cramps; constipation. • Cardiovascular and cerebrovascular events. • Chronic kidney disease. • Heart failure and atrial fibrillation. • Left ventricular hypertrophy. • Metabolic syndrome: hyperglycemia; obesity. • Osteoporosis. • Depression. • The spectrum of biochemically proven primary aldosteronism includes also subjects with normal blood pressure. Primary aldosteronism should be suspected in young normotensive subjects with unexplained hypokalemia.

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Primary Aldosteronism

Adrenal Hormone abnormality	Indication for testing	First-line testing	Second-line/confirmatory testing	Others considerations and remarks
Aldosterone excess	Anyone with hypertension, with or without spontaneous hypokalemia	Morning aldosterone + renin (DRCorPRA). *Abnormal result:* aldosterone >10 ng/dL and suppressed renin (DRC or PRA). *Possible causes of false-positive results:*[a] • Beta-blockers. • α-methyldopa • NSAIDs. • Oral estrogens (renin measured as DRC). • Testing during the luteal phase (women of reproductive age). • Impaired renal function with hyperkalemia. *Possible causes of false-negative results:*[a] • Mineralocorticoid receptor antagonists. • Diuretics. • Dihydropyridine calcium channel blockers. • Inhibitors. • Angiotensin II receptor blockers. • SSRIs. • SGLT2-inhibitors.	Unnecessary if positive first-line test and spontaneous hypokalemia. Otherwise: salt loading test, saline infusion test, captopril challenge, or fludrocortisone test.	• Patients with confirmed primary aldosteronism will need subtype evaluation with imaging and adrenal vein sampling. • Imaging finding of adrenal mass is accurate only in 60% of cases in subtype determination. • Cortisol co-secretion is highly prevalent in primary aldosteronism (abnormal 1-mg DST is found in up to 22% of patients).[b]

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Primary Aldosteronism

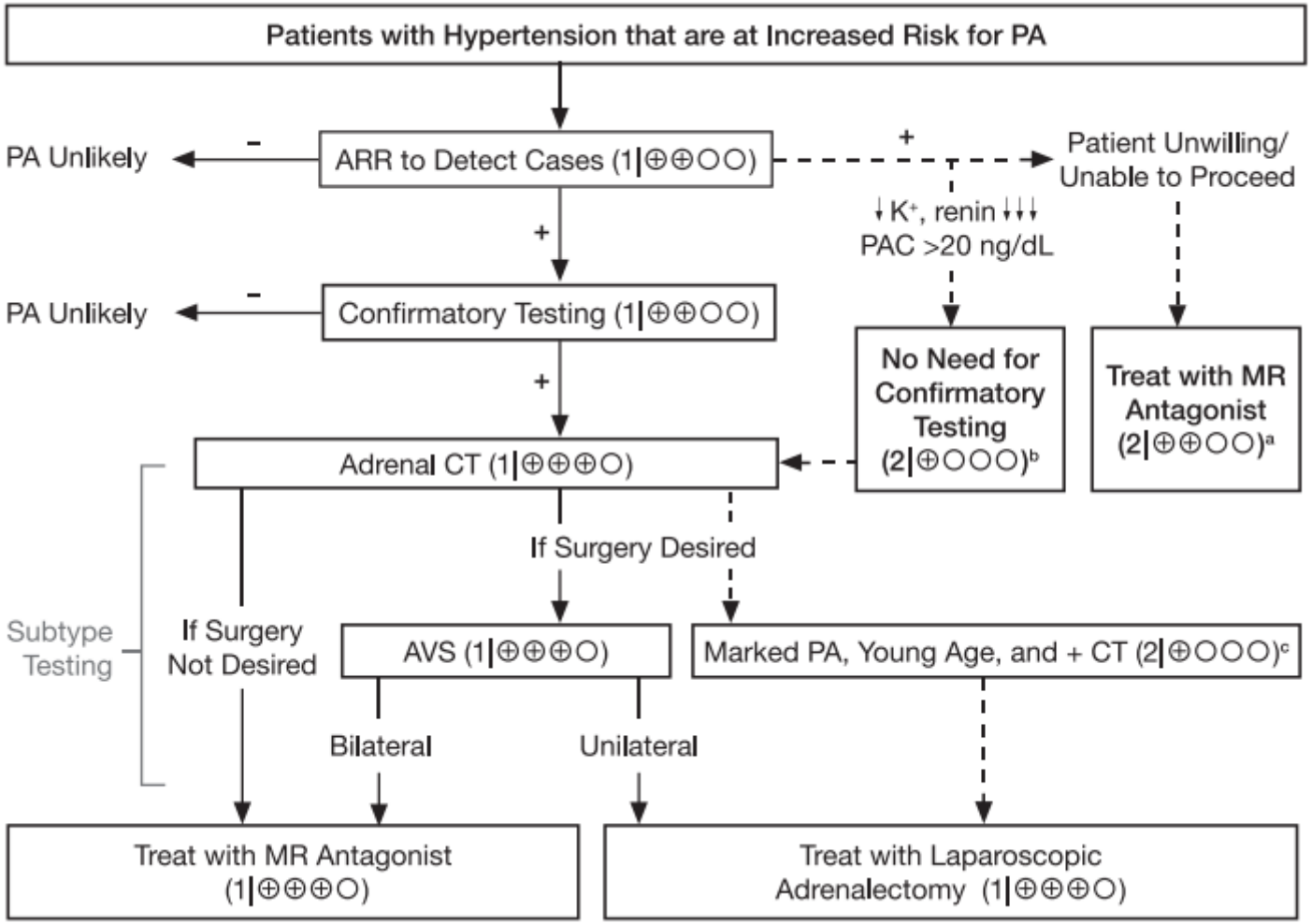


Table 6. ARR Cutoff Values, Depending on Assay and Based on Whether PAC, PRA, and DRC Are Measured in Conventional or Système International (SI) Units

	PRA, ng/mL/h	PRA, pmol/L/min	DRC, mU/L[a]	DRC, ng/L[a]
PAC (as ng/dL)	20	1.6	2.4	3.8
	30[b]	2.5	3.7	5.7
	40	3.1	4.9	7.7
PAC (as pmol/L)	750[b]	60	91	144
	1000	80	122	192

Funder et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016

Primary Aldosteronism

Table 4. Measurement of ARR: A Suggested Approach

A. Preparation: agenda

1. Attempt to correct hypokalemia. Measure plasma potassium in blood collected slowly with a syringe and needle [preferably not a Vacutainer to minimize the risk of spuriously raising potassium]. During collection, avoid fist clenching, wait at least 5 seconds after tourniquet release (if used) to achieve insertion of needle, and ensure separation of plasma from cells within 30 minutes of collection. A plasma [K^+] of 4.0 mmol/L is the aim of supplementation.
2. Encourage patient to liberalize (rather than restrict) sodium intake.
3. Withdraw agents that markedly affect the ARR (219) for at least 4 weeks:
   a. Spironolactone, eplerenone, amiloride, and triamterene
   b. Potassium-wasting diuretics
   c. Products derived from licorice root (eg, confectionary licorice, chewing tobacco)
4. If the results of ARR after discontinuation of the above agents are not diagnostic, and if hypertension can be controlled with relatively noninterfering medications (see Table 5), withdraw other medications that may affect the ARR (219) for at least 2 weeks, such as:
   a. β-Adrenergic blockers, central α-2 agonists (eg, clonidine, α-methyldopa), and nonsteroidal anti-inflammatory drugs
   b. Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, renin inhibitors, and dihydropyridine calcium channel antagonists
5. If necessary to maintain hypertension control, commence other antihypertensive medications that have lesser effects on the ARR (*e.g.* verapamil slow-release, hydralazine [with verapamil slow-release, to avoid reflex tachycardia], prazosin, doxazosin, terazosin; see Table 5).
6. Establish OC and HRT status because estrogen-containing medications may lower DRC and cause false-positive ARR when DRC (rather than PRA) is measured (220). Do not withdraw OC unless confident of alternative effective contraception.

Funder et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016

Primary Aldosteronism

Table 5. Medications With Minimal Effects on Plasma Aldosterone Levels That Can Control Hypertension During Case Finding and Confirmatory Testing for PA

Drug	Class	Usual Dose	Comments
Verapamil slow-release	Non-dihydropyridine slow-release antagonist calcium channel	90–120 mg twice daily	Use singly or in combination with the other agents listed in this table
Hydralazine	Vasodilator	10–12.5 mg twice daily, increasing as required	Commence verapamil slow-release first to prevent reflex tachycardia. Commencement at low doses reduces risk of side effects (including headaches, flushing, and palpitations)
Prazosin hydrochloride	α-Adrenergic blocker	0.5–1 mg two or three times daily, increasing as required	Monitor for postural hypotension
Doxazosin mesylate	α-Adrenergic blocker	1–2 mg once daily, increasing as required	Monitor for postural hypotension
Terazosin hydrochloride	α-Adrenergic blocker	1–2 mg once daily, increasing as required	Monitor for postural hypotension

Funder et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016

Primary Aldosteronism

Table 7. PA Confirmatory Tests

Test and Procedure	Interpretation	Concerns
Oral sodium loading test Patients should increase their sodium intake to >200 mmol (~6 g)/d for 3 d, verified by 24-h urine sodium content. Patients should receive adequate slow-release potassium chloride supplementation to maintain plasma potassium in the normal range. Urinary aldosterone is measured in the 24-h urine collection from the morning of day 3 to the morning of day 4.	PA is unlikely if urinary aldosterone is <10 μg/24 h (28 nmol/d) in the absence of renal disease where PA may coexist with lower measured urinary aldosterone levels. Elevated urinary aldosterone excretion (>12 μg/24 h [>33 nmol/d] at the Mayo Clinic; >14 μg/24 h [39 nmol/d] at the Cleveland Clinic) makes PA highly likely.	This test should not be performed in patients with severe uncontrolled hypertension, renal insufficiency, cardiac arrhythmia, or severe hypokalemia. 24-h urine collection may be inconvenient. Laboratory-specific poor performance of the RIA for urinary aldosterone (aldosterone 18-oxo-glucuronide or acid labile metabolite) may blunt diagnostic accuracy—a problem obviated by the currently available HPLC-tandem mass spectrometry methodology (223). Aldosterone 18-oxo-glucuronide is a renal metabolite, and its excretion may not rise in patients with renal disease.
SIT Patients stay in the recumbent position for at least 1 h before and during the infusion of 2 L of 0.9% saline iv over 4 h, starting at 8–9.30 AM. Blood samples for renin, aldosterone, cortisol, and plasma potassium are drawn at time zero and after 4 h, with BP and heart rate monitored throughout the test. In a modified approach, which appears (in preliminary studies) to have much higher sensitivity for diagnosing PA, patients remain in a seated position for at least 30 min and during the infusion (73).	Postinfusion plasma aldosterone levels <5 ng/dL (140 pmol/L) make the diagnosis of PA unlikely, whereas levels >10 ng/dL (280 nmol/L) are a sign of very probable PA. Values between 5 and 10 ng/dL are indeterminate, although a cutoff of 6.8 ng/dL (190 pmol/L) has been found to offer the best trade-off between sensitivity and specificity (57, 58, 224, 225). For the seated SIT, a postinfusion plasma aldosterone of >6 ng/dL (170 pmol/L) confirms PA, provided plasma cortisol concentration is lower than the value obtained basally (to exclude a confounding ACTH effect) (73).	This test should not be performed in patients with severe uncontrolled hypertension, renal insufficiency, cardiac arrhythmia, or severe hypokalemia.

Funder et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016

Primary Aldosteronism

FST Patients receive 0.1 mg oral fludrocortisone every 6 h for 4 d, together with slow-release KCl supplements (every 6 h at doses sufficient to keep plasma K^+, measured four times a day, close to 4.0 mmol/L), slow-release NaCl supplements (30 mmol three times daily with meals) and sufficient dietary salt to maintain a urinary sodium excretion rate of at least 3 mmol/kg body weight. On day 4, plasma aldosterone and PRA are measured at 10 AM with the patient in the seated posture, and plasma cortisol is measured at 7 and 10 AM.	Upright plasma aldosterone >6 ng/dL (170 nmol/L) on day 4 at 10 AM confirms PA, provided PRA is <1 ng/mL/h and plasma cortisol concentration is lower than the value obtained at 7 AM (to exclude a confounding ACTH effect) (39, 52, 53, 112, 226).	Although some centers (23, 27) conduct this test in the outpatient setting (provided that patients are able to attend frequently to monitor their potassium), in other centers several days of hospitalization are customary. Most of the data available come from the Brisbane group (39, 52, 53, 89, 112, 226) who have established, on the basis of a very large series of patients, a cutoff of a PAC of 6 ng/dL (170 nmol/L) at 10 AM in an ambulatory patient on day 4. Proponents of the FST argue that: a) it is the most sensitive for confirming PA; b) it is a less intrusive method of sodium loading than SIT and therefore less likely to provoke non-renin-dependent alterations of aldosterone levels; c) it allows for the potentially confounding effects of potassium to be controlled, and for ACTH (via cortisol) to be monitored and detected; and d) it is safe when performed by experienced hands.
Captopril challenge test Patients receive 25–50 mg of captopril orally after sitting or standing for at least 1 h. Blood samples are drawn for measurement of PRA, plasma aldosterone, and cortisol at time zero and at 1 or 2 h 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 (58, 60, 163, 227). Differences may be seen between patients with APA and those with IAH, in that some decrease of aldosterone levels is occasionally seen in IAH (228).	There are reports of a substantial number of false-negative or equivocal results (59, 229).

Funder et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016

Androgen excess

Hormone excess

Androgen excess

General considerations

- Adrenal androgen excess typically indicates adrenocortical carcinoma. Androgen-producing adenomas are extremely rare.
- Androgen and cortisol co-secretion (both MACS and Cushing syndrome) are common in adrenocortical carcinoma.

Clinical Manifestations

Women can present with:

- Hirsutism.
- Oily skin and acne.
- Hair loss.
- Changes in libido.
- Menstrual irregularities.
- Metabolic syndrome (chronic androgen excess).

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Androgen excess

Adrenal Hormone abnormality	Indication for testing	First-line testing	Second-line/confirmatory testing	Others considerations and remarks
Suspected steroid precursor, androgen, or estrogen excess	Anyone suspected to have adrenocortical carcinoma, with or without symptoms	DHEA-S, progesterone, 17-OH-progesterone, 17-OH-pregnenolone, 11-deoxycortisol, androstenedione, testosterone (women), estradiol (men, postmenopausal women). If available, consider urine multisteroid profiling.		• Avoid adrenal biopsy. • Open adrenalectomy is usually recommended. • Experienced adrenal surgeon is key!
	Anyone with bilateral adenomas or myelolipomas should be evaluated for congenital adrenal hyperplasia	Early-morning 17-OH-progesterone (to be collected during the early follicular phase in menstruating females).	ACTH stimulation test for cortisol and 17-OH-progesterone.	Consider genetic testing.

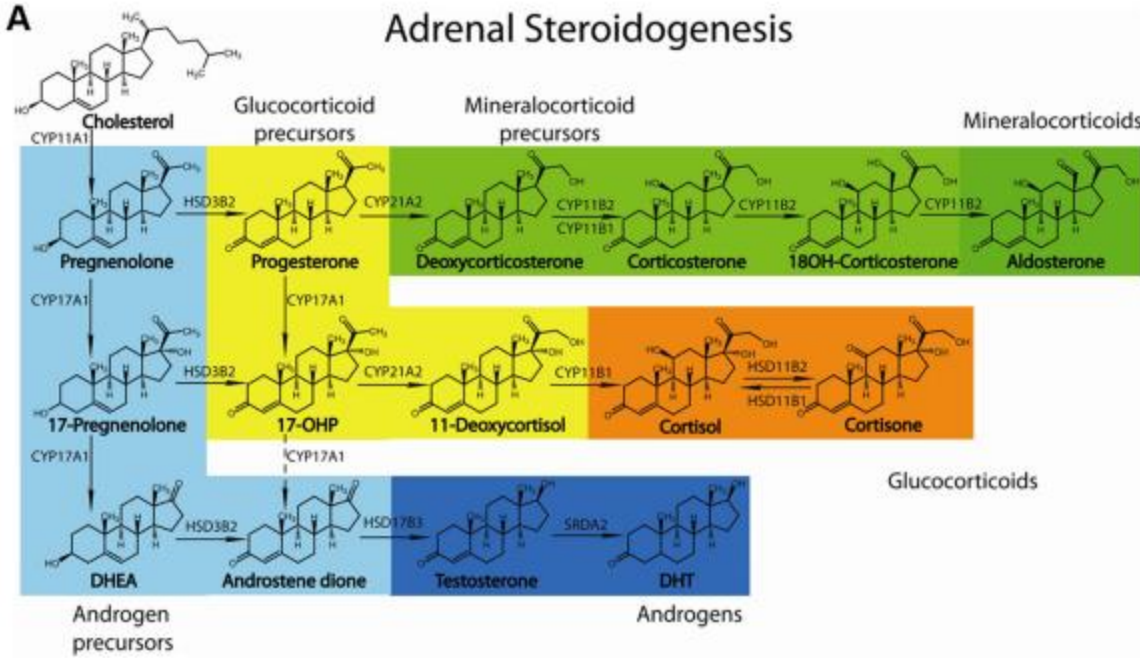
Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

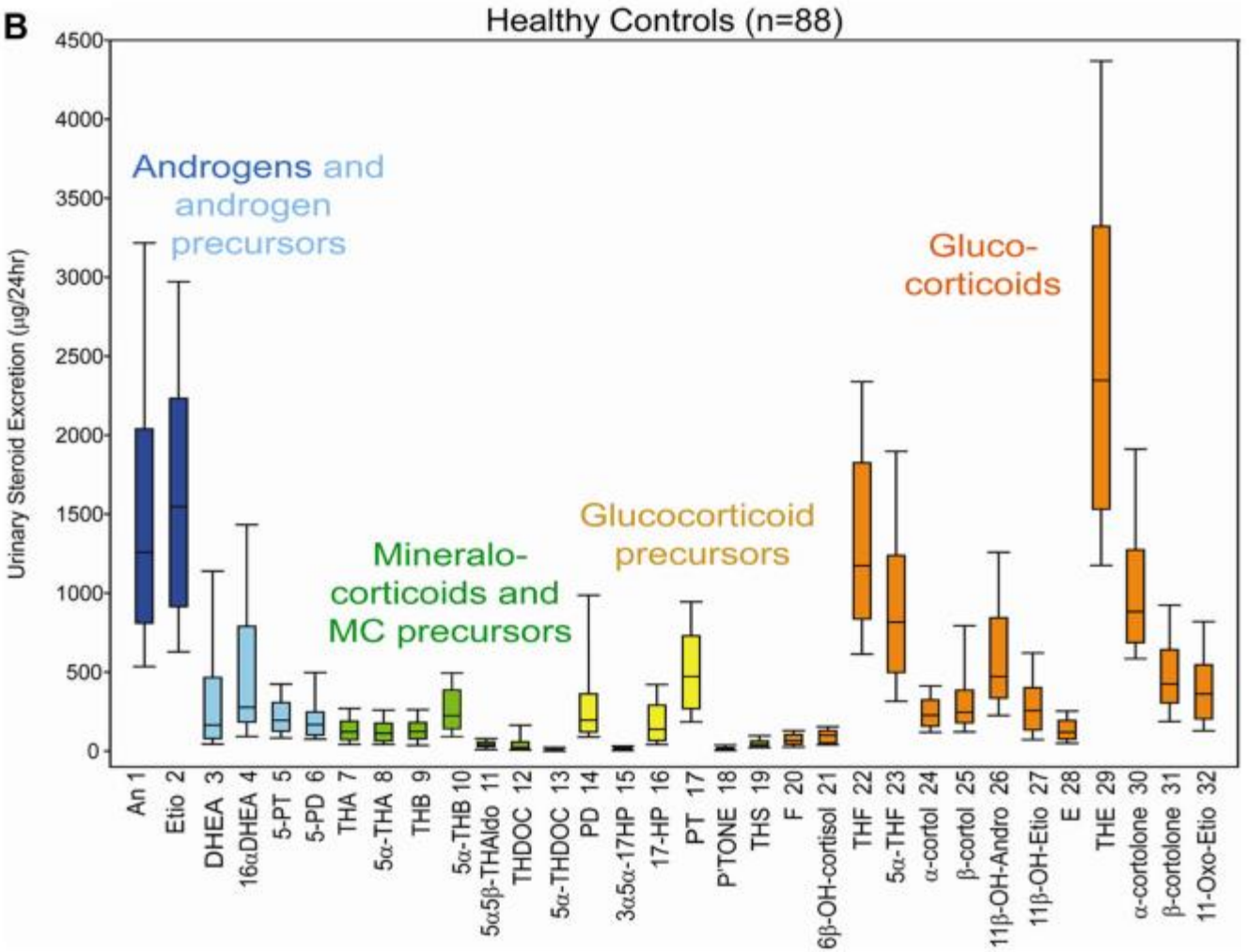
Adrenal Insufficiency

Adrenal Hormone abnormality	Indication for testing	First-line testing	Second-line/confirmatory testing
Adrenal insufficiency	Anyone with indeterminate bilateral masses likely to be adrenal metastases or bilateral infiltration of other causes	Morning ACTH and cortisol. If electrolyte abnormalities, test for aldosterone deficiency (paired aldosterone and renin).	Potential need for additional dynamic testing such as ACTH stimulation.

Bancos I, Prete A. Approach to the Patient With Adrenal Incidentaloma. J Clin Endocrinol Metab. 2021

Steroid Metabolomics





Arlt et al. Urine steroid metabolomics as a biomarker tool for detecting malignancy in adrenal tumors. J Clin Endocrinol Metab. 2011

Steroid Metabolomics

KEY POINTS

- Novel advancement in the field of mass spectrometry is improving the measurement selectivity and implementing the steroidomic profiling.
- Steroid profiling in primary aldosteronism has shown implication for patients' subtyping (unilateral versus bilateral forms) with potential future application in the diagnosis of the disease.
- The measurement of a single serum steroid panel in Cushing's syndrome may provide good power in disease subtyping and potentially simplify the diagnostic workup of hypercortisolism.
- Patients with adrenocortical cancer have a specific steroid fingerprint, even though a large interindividual heterogeneity is frequently observed. Future studies are needed to address the potential implication of serum steroid profiling for diagnosis and tailored follow-up of the patients.

Fanelli F, Di Dalmazi G. Serum steroid profiling by mass spectrometry in adrenocortical tumors: diagnostic implications. Curr Opin Endocrinol Diabetes Obes. 2019

Grazie per l’attenzione!