Adrenal Mass

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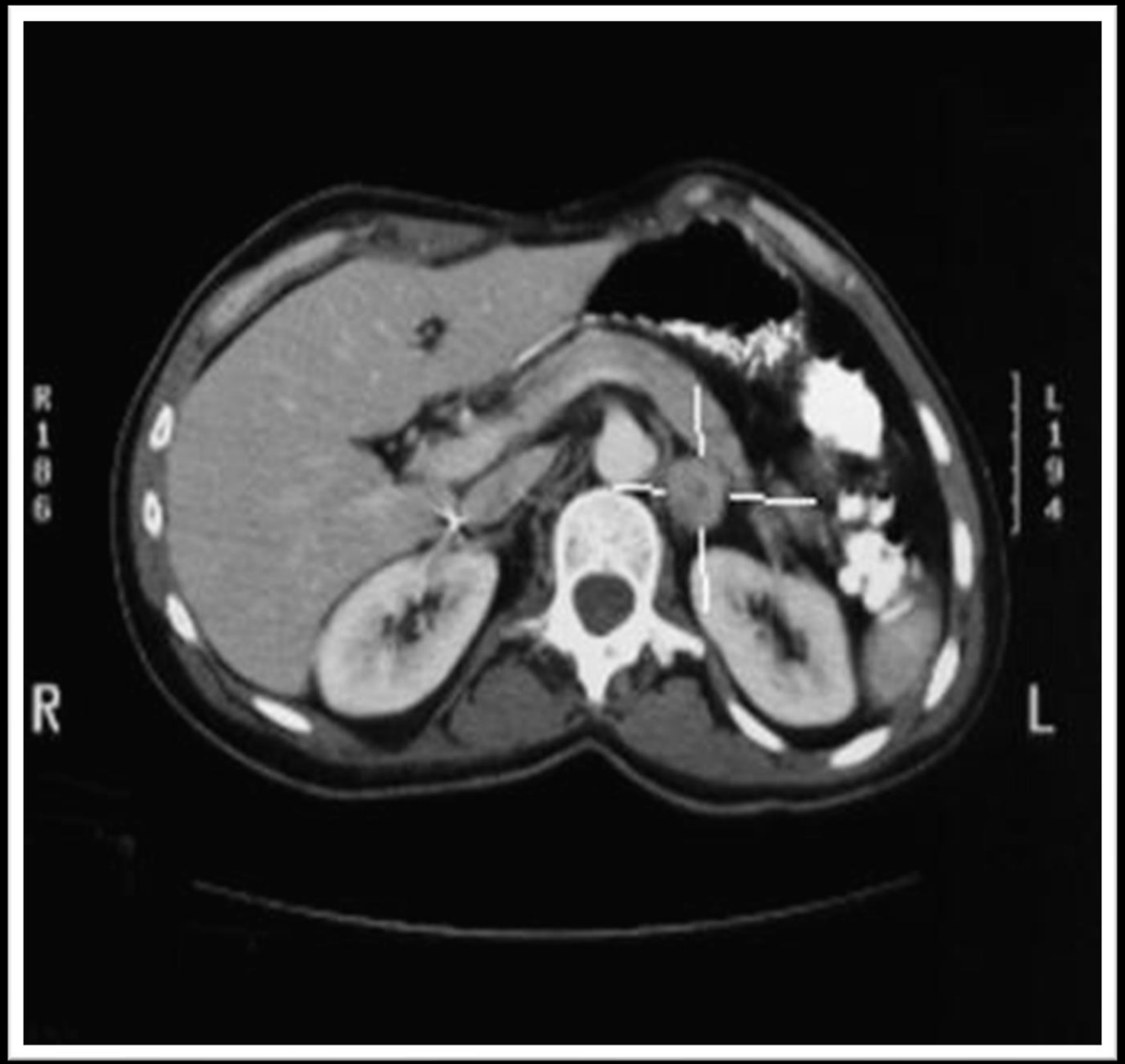
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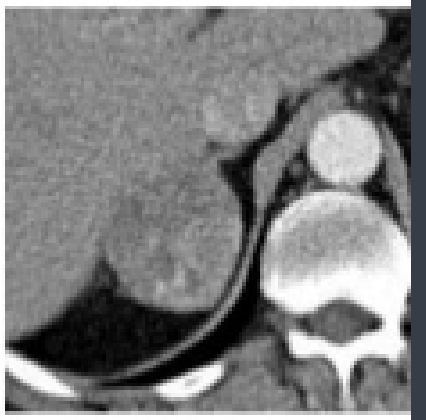
Adrenal Mass

incidental adrenal mass is detected on cross-sectional imaging (rarely on ultrasound)



✓ No known neoplasm (CT is performed for other reasons e.g. vascular, trauma)

➔ **Incidentaloma**

Imaging can not distinguish between functioning and nonfunctioning adrenal mass

Incidentally discovered adrenal masses, commonly termed adrenal “incidentalomas,” are common, with a prevalence of at least 2% in the general population as documented in CT and autopsy series. The prevalence increases with age, with 1% of 40-year-olds and 7% of 70-year-olds harboring an adrenal mass.

Most adrenal nodules are endocrine-inactive adrenocortical adenomas. However, larger series suggest that up to 25% of adrenal nodules are hormonally active, due to a cortisol- or aldosterone-producing adrenocortical adenoma or a pheochromocytoma associated with catecholamine excess. Adrenocortical carcinoma is rare but is the cause of an adrenal mass in 5% of patients. However, the most common cause of a malignant adrenal mass is metastasis originating from another solid tissue tumor

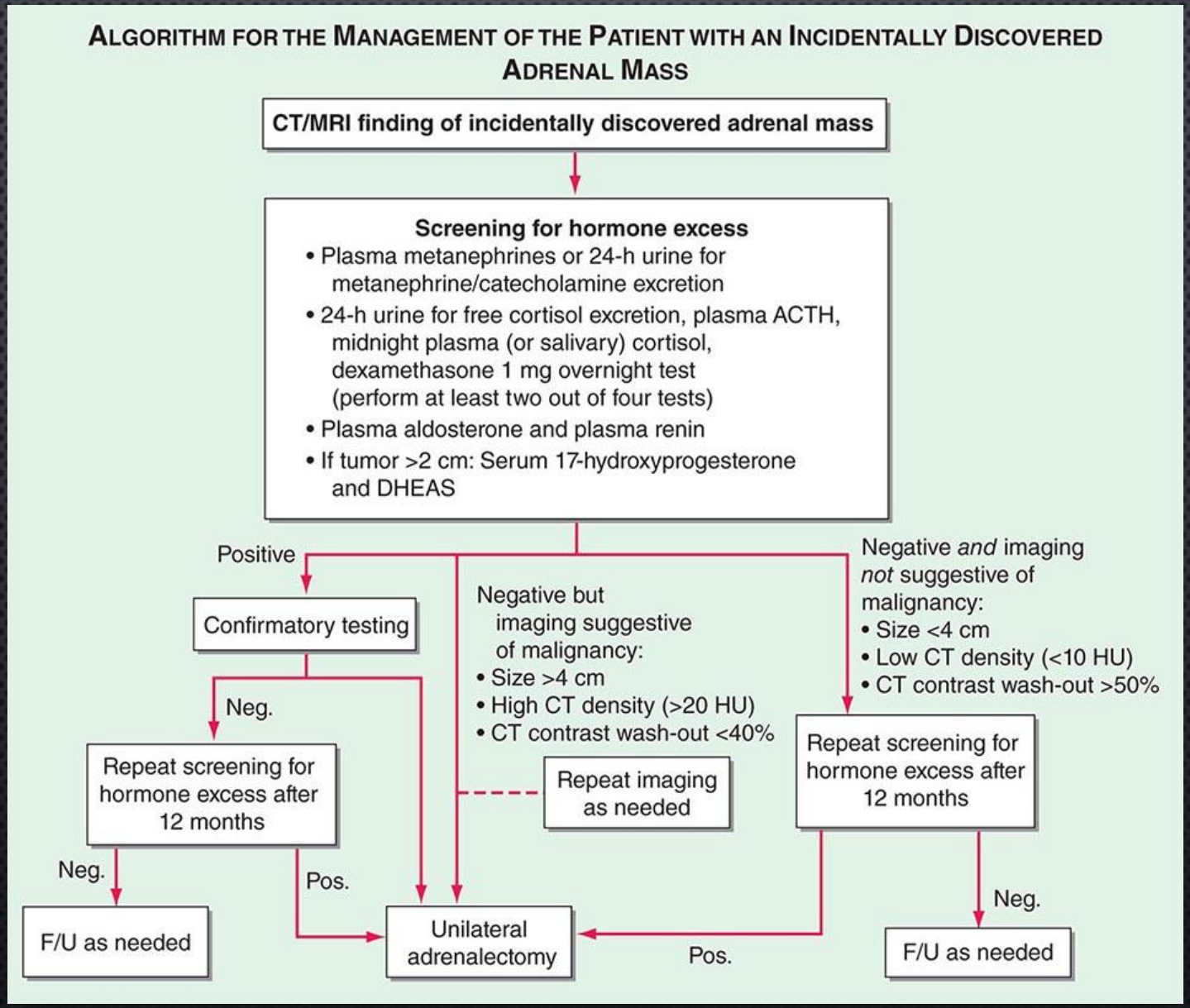
Classification of unilateral adrenal masses

Mass	Approximate Prevalence (%)
Benign	
Adrenocortical adenoma	
Endocrine-inactive	60–85
Cortisol-producing	5–10
Aldosterone-producing	2–5
Pheochromocytoma	5–10
Adrenal myelolipoma	<1
Adrenal ganglioneuroma	<0.1
Adrenal hemangioma	<0.1
Adrenal cyst	<1
Adrenal hematoma/hemorrhagic infarction	<1
Indeterminate	
Adrenocortical oncocytoma	<1
Malignant	
Adrenocortical carcinoma	2–5
Malignant pheochromocytoma	<1
Adrenal neuroblastoma	<0.1
Lymphomas (including primary adrenal lymphoma)	<1
Metastases (most frequent: breast, lung)	15

Note: Bilateral adrenal enlargement/masses may be caused by congenital adrenal hyperplasia, bilateral macronodular hyperplasia, bilateral hemorrhage (due to antiphospholipid syndrome or sepsis-associated Waterhouse-Friderichsen syndrome), granuloma, amyloidosis, or infiltrative disease including tuberculosis.

Differential Diagnosis and Treatment Patients with an adrenal mass >1 cm require a diagnostic evaluation. Two key questions need to be addressed: (1) Does the tumor autonomously secrete hormones that could have a detrimental effect on health? (2) Is the adrenal mass benign or malignant?

Hormone secretion by an adrenal mass occurs along a continuum, with a gradual increase in clinical manifestations in parallel with hormone levels. Exclusion of catecholamine excess from a pheochromocytoma arising from the adrenal medulla is a mandatory part of the diagnostic workup. Furthermore, autonomous cortisol and aldosterone secretion resulting in Cushing's syndrome or primary aldosteronism, respectively, require exclusion. Adrenal incidentalomas can be associated with lower levels of autonomous cortisol secretion, and patients may lack overt clinical features of Cushing's syndrome. Nonetheless, they may exhibit one or more components of the metabolic syndrome (e.g., obesity, type 2 diabetes, or hypertension). There is ongoing debate about the optimal treatment for these patients with mild or subclinical Cushing's syndrome. Overproduction of adrenal androgen precursors, DHEA and its sulfate, is rare and most frequently seen in the context of adrenocortical carcinoma, as are increased levels of steroid precursors such as 17-hydroxyprogesterone.


ALGORITHM FOR THE MANAGEMENT OF THE PATIENT WITH AN INCIDENTALLY DISCOVERED ADRENAL MASS
CT/MRI finding of incidentally discovered adrenal mass
Screening for hormone excess
• Plasma metanephrines or 24-h urine for metanephrine/catecholamine excretion
• 24-h urine for free cortisol excretion, plasma ACTH, midnight plasma (or salivary) cortisol, dexamethasone 1 mg overnight test (perform at least two out of four tests)
• Plasma aldosterone and plasma renin
• If tumor >2 cm: Serum 17-hydroxyprogesterone and DHEAS
Positive
Confirmatory testing
Neg.
Repeat screening for hormone excess after 12 months
Neg.
F/U as needed
Pos.
Negative but imaging suggestive of malignancy:
• Size >4 cm
• High CT density (>20 HU)
• CT contrast wash-out <40%
Repeat imaging as needed
Negative and imaging not suggestive of malignancy:
• Size <4 cm
• Low CT density (<10 HU)
• CT contrast wash-out >50%
Repeat screening for hormone excess after 12 months
Neg.
F/U as needed
Pos.
Unilateral adrenalectomy

For the differentiation of benign from malignant adrenal masses, imaging is relatively sensitive, although specificity is suboptimal. CT is the procedure of choice for imaging the adrenal glands. The risk of adrenocortical carcinoma, pheochromocytoma, and benign adrenal myelolipoma increases with the diameter of the adrenal mass. However, size alone is of poor predictive value, with only 80% sensitivity and 60% specificity for the differentiation of benign from malignant masses when using a 4-cm cut-off. Metastases are found with similar frequency in adrenal masses of all sizes. Tumor density on unenhanced CT is of additional diagnostic value, with most adrenocortical adenomas being lipid rich and thus presenting with low attenuation values (i.e., densities of <10 HU). By contrast, adrenocortical carcinomas, but also pheochromocytomas, usually have high attenuation values (i.e., densities >20 HU on pre-contrast scans). Generally, benign lesions are rounded and homogenous, whereas most malignant lesions appear lobulated and inhomogeneous. Pheochromocytoma and adrenomyelolipoma may also exhibit lobulated and inhomogeneous features. Additional information can be obtained from CT by assessment of contrast wash-out after 15 min, which is >50% in benign lesions but <40% in malignant lesions, which usually have a more extensive vascularization. MRI also allows for the visualization of the adrenal glands with somewhat lower resolution than CT

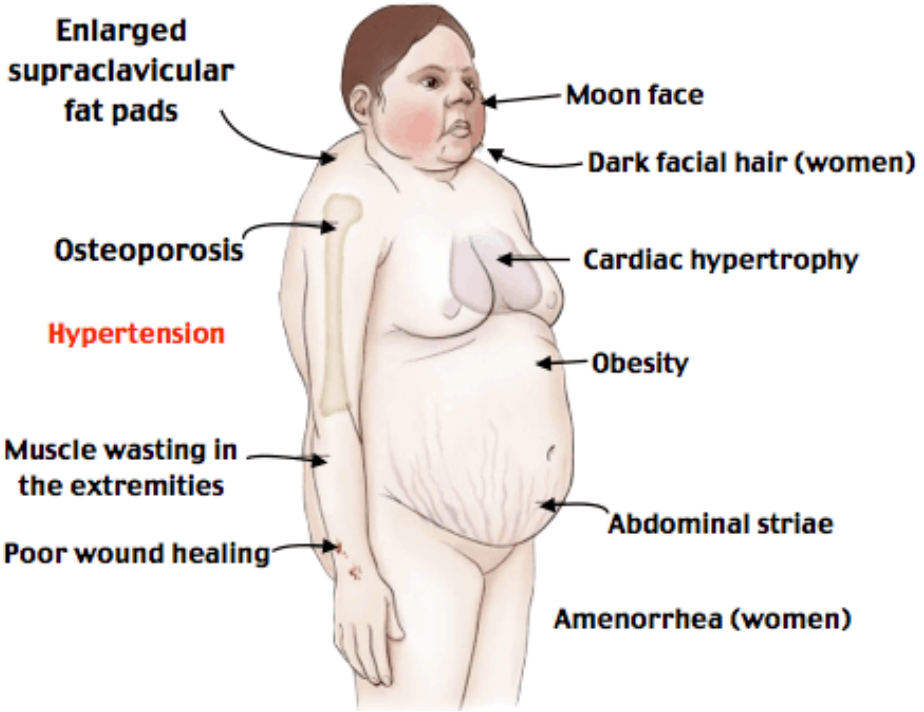
Fine-needle aspiration (FNA) or CT-guided biopsy of an adrenal mass is almost never indicated.

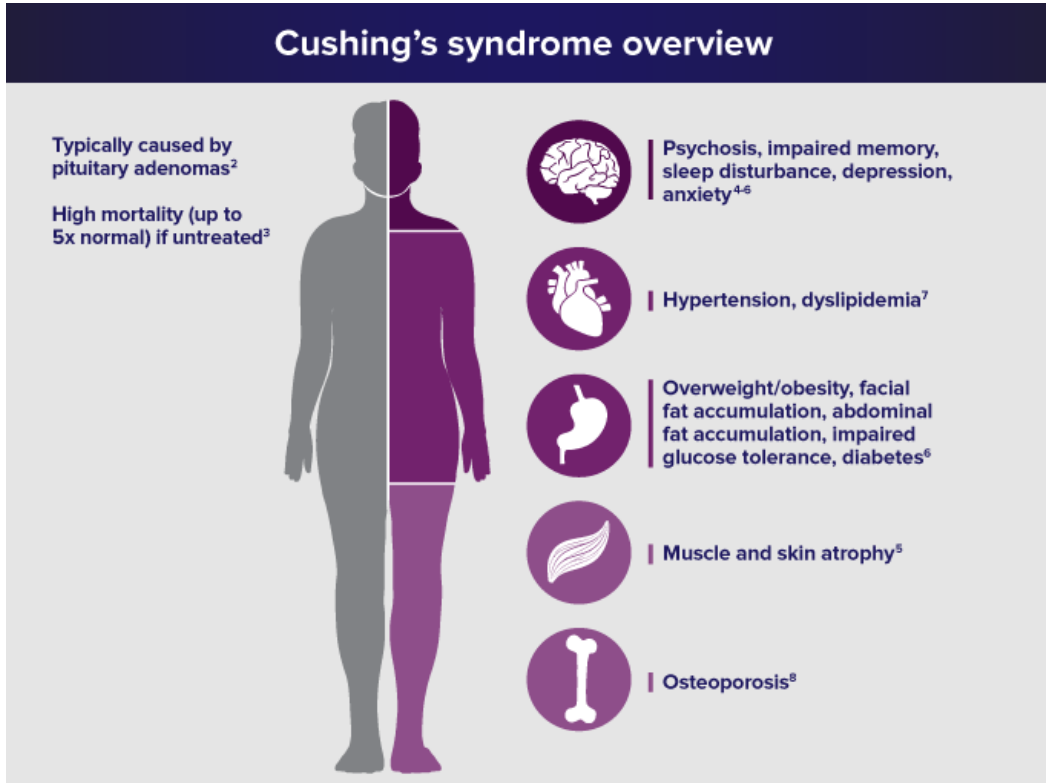
FNA of a pheochromocytoma can cause a life-threatening hypertensive crisis. FNA of an adrenocortical carcinoma violates the tumor capsule and can cause needle track metastasis. FNA should only be considered in a patient with a history of nonadrenal malignancy and a newly detected adrenal mass, after careful exclusion of pheochromocytoma, and if the outcome will influence therapeutic management. It is important to recognize that in 25% of patients with a previous history of nonadrenal malignancy, a newly detected mass on CT is not a metastasis.

Cushing's syndrome

Due to **excess cortisol-like medication** (prednisone) or **tumor** that produces or results in production of **excessive cortisol**

[Cases due to a pituitary adenoma = Cushing's disease]



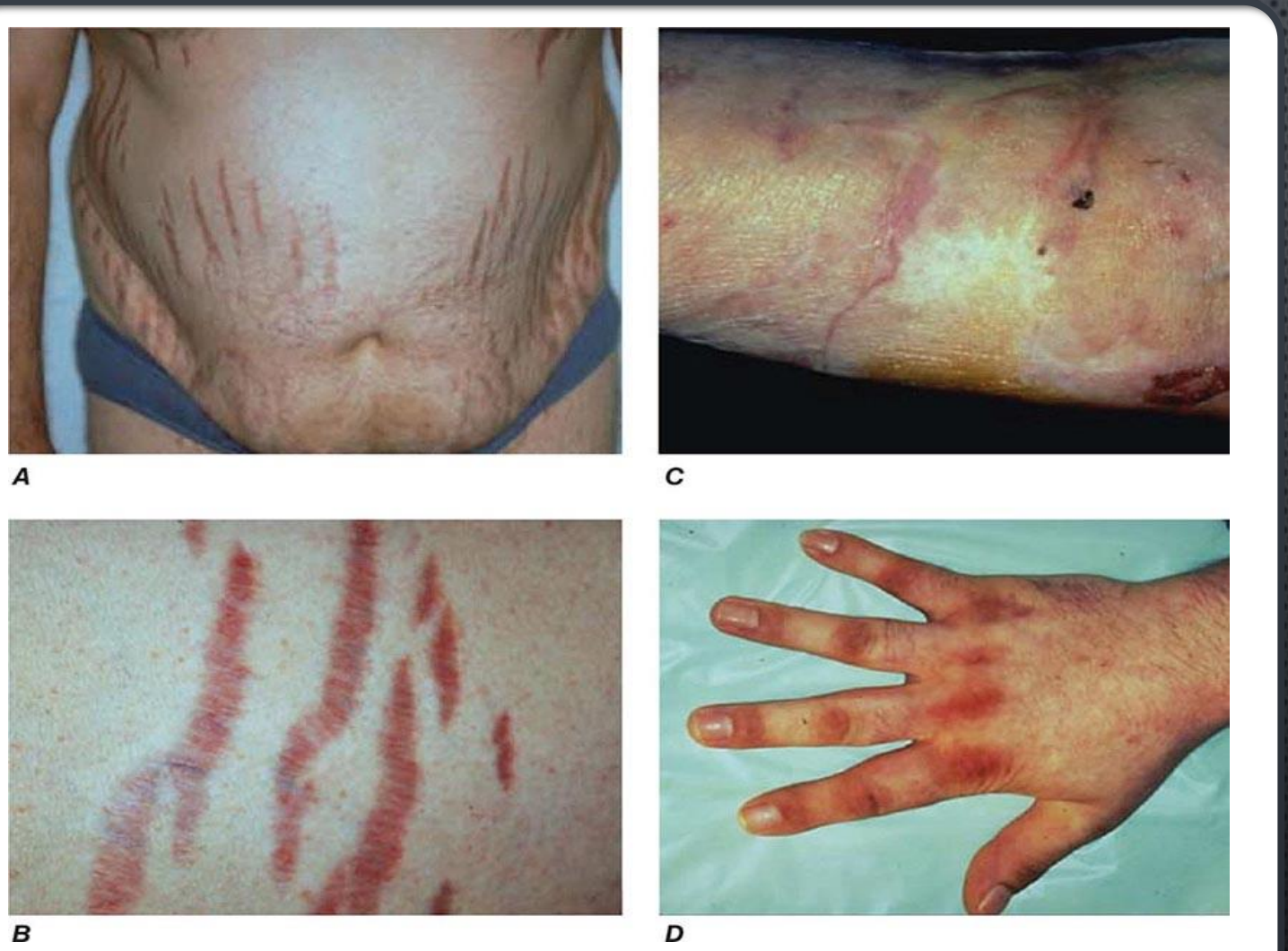


Body Compartment/ System	Signs and Symptoms
Body fat	Weight gain, central obesity, rounded face, fat pad on back of neck ("buffalo hump")
Skin	Facial plethora, thin and brittle skin, easy bruising, broad and purple stretch marks, acne, hirsutism
Bone	Osteopenia, osteoporosis (vertebral fractures), decreased linear growth in children
Muscle	Weakness, proximal myopathy (prominent atrophy of gluteal and upper leg muscles with difficulty climbing stairs or getting up from a chair)
Cardiovascular system	Hypertension, hypokalemia, edema, atherosclerosis
Metabolism	Glucose intolerance/diabetes, dyslipidemia
Reproductive system	Decreased libido, in women amenorrhea (due to cortisol-mediated inhibition of gonadotropin release)
Central nervous system	Irritability, emotional lability, depression, sometimes cognitive defects; in severe cases, paranoid psychosis
Blood and immune system	Increased susceptibility to infections, increased white blood cell count, eosinopenia, hypercoagulation with increased risk of deep vein thrombosis and pulmonary embolism

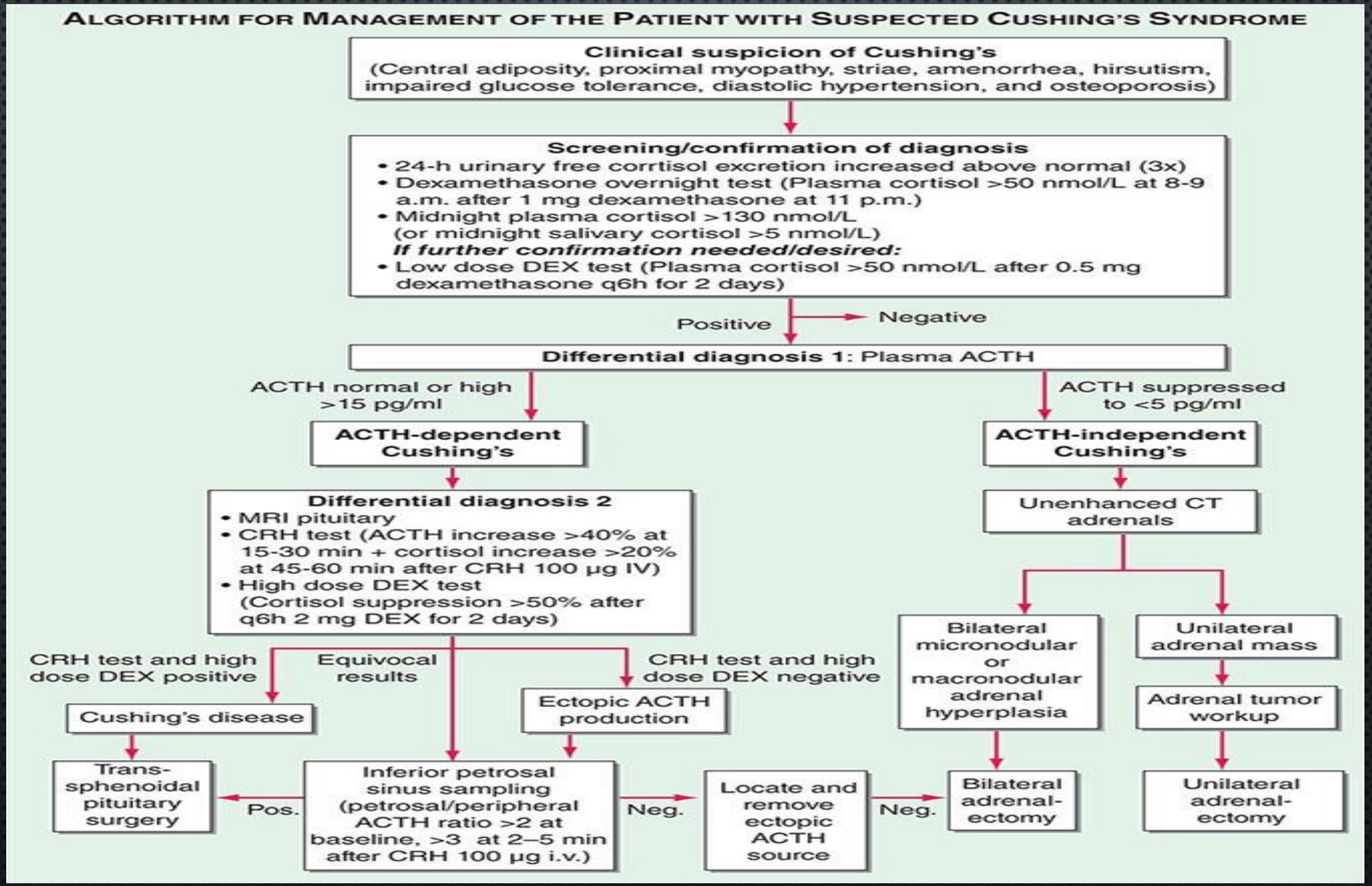
Clinical Manifestations Glucocorticoids affect almost all cells of the body, and thus signs of cortisol excess impact multiple physiologic systems, with upregulation of gluconeogenesis, lipolysis, and protein catabolism causing the most prominent features. In addition, excess glucocorticoid secretion overcomes the ability of 11β-HSD2 to rapidly inactivate cortisol to cortisone in the kidney, thereby exerting mineralocorticoid actions, manifest as diastolic hypertension, hypokalemia, and edema. Excess glucocorticoids also interfere with central regulatory systems, leading to suppression of gonadotropins with subsequent hypogonadism and amenorrhea, and suppression of the hypothalamic-pituitary-thyroid axis, resulting in decreased thyroid-stimulating hormone (TSH) secretion.

Most clinical signs and symptoms observed in Cushing’s syndrome are relatively nonspecific and include features such as obesity, diabetes, diastolic hypertension, hirsutism, and depression that are commonly found in patients who do not have Cushing’s. Therefore, careful clinical assessment is an important aspect of evaluating suspected cases. A diagnosis of Cushing’s should be considered when several clinical features are found in the same patient, when more specific features are found. These include fragility of the skin, with easy bruising and broad (>1 cm), purplish striae**)**, and signs of proximal myopathy, which becomes most obvious when trying to stand up from a chair without the use of hands or when climbing stairs. Clinical manifestations of Cushing’s do not differ substantially among the different causes of Cushing’s. In ectopic ACTH syndrome, hyperpigmentation of the knuckles, scars, or skin areas exposed to increased friction can be observed and is caused by stimulatory effects of excess ACTH and other POMC cleavage products on melanocyte pigment production. Furthermore, patients with ectopic ACTH syndrome, and some with adrenocortical carcinoma as the cause of Cushing’s, may have a brisker onset and rapid progression of clinical signs and symptoms.

Patients with Cushing’s syndrome can be acutely endangered by deep vein thrombosis, with subsequent pulmonary embolism due to a hypercoagulable state associated with Cushing’s. Most patients also experience psychiatric symptoms, mostly in the form of anxiety or depression, but acute paranoid or depressive psychosis may also occur. Even after cure, long-term health may be affected by persistently impaired health-related quality of life and increased risk of cardiovascular disease and osteoporosis with vertebral fractures, depending on the duration and degree of exposure to significant cortisol excess.



Clinical features of Cushing's syndrome. ***A***. central obesity and broad, purple stretch marks (***B.*** close-up). ***C.*** Thin and brittle skin in an elderly patient with Cushing's syndrome. ***D***. Hyperpigmentation of the knuckles in a patient with ectopic adrenocorticotropic hormone (ACTH) excess.


ALGORITHM FOR MANAGEMENT OF THE PATIENT WITH SUSPECTED CUSHING'S SYNDROME
Clinical suspicion of Cushing's
(Central adiposity, proximal myopathy, striae, amenorrhea, hirsutism, impaired glucose tolerance, diastolic hypertension, and osteoporosis)
Screening/confirmation of diagnosis
• 24-h urinary free corrtisol excretion increased above normal (3x)
• Dexamethasone overnight test (Plasma cortisol >50 nmol/L at 8-9 a.m. after 1 mg dexamethasone at 11 p.m.)
• Midnight plasma cortisol >130 nmol/L (or midnight salivary cortisol >5 nmol/L)
If further confirmation needed/desired:
• Low dose DEX test (Plasma cortisol >50 nmol/L after 0.5 mg dexamethasone q6h for 2 days)
Positive
Negative
Differential diagnosis 1: Plasma ACTH
ACTH normal or high >15 pg/ml
ACTH suppressed to <5 pg/ml
ACTH-dependent Cushing's
ACTH-independent Cushing's
Differential diagnosis 2
• MRI pituitary
• CRH test (ACTH increase >40% at 15-30 min + cortisol increase >20% at 45-60 min after CRH 100 µg IV)
• High dose DEX test (Cortisol suppression >50% after q6h 2 mg DEX for 2 days)
Unenhanced CT adrenals
CRH test and high dose DEX positive
Equivocal results
CRH test and high dose DEX negative
Bilateral micronodular or macronodular adrenal hyperplasia
Unilateral adrenal mass
Cushing's disease
Ectopic ACTH production
Adrenal tumor workup
Trans-sphenoidal pituitary surgery
Pos.
Inferior petrosal sinus sampling (petrosal/peripheral ACTH ratio >2 at baseline, >3 at 2–5 min after CRH 100 µg i.v.)
Neg.
Locate and remove ectopic ACTH source
Neg.
Bilateral adrenal-ectomy
Unilateral adrenal-ectomy

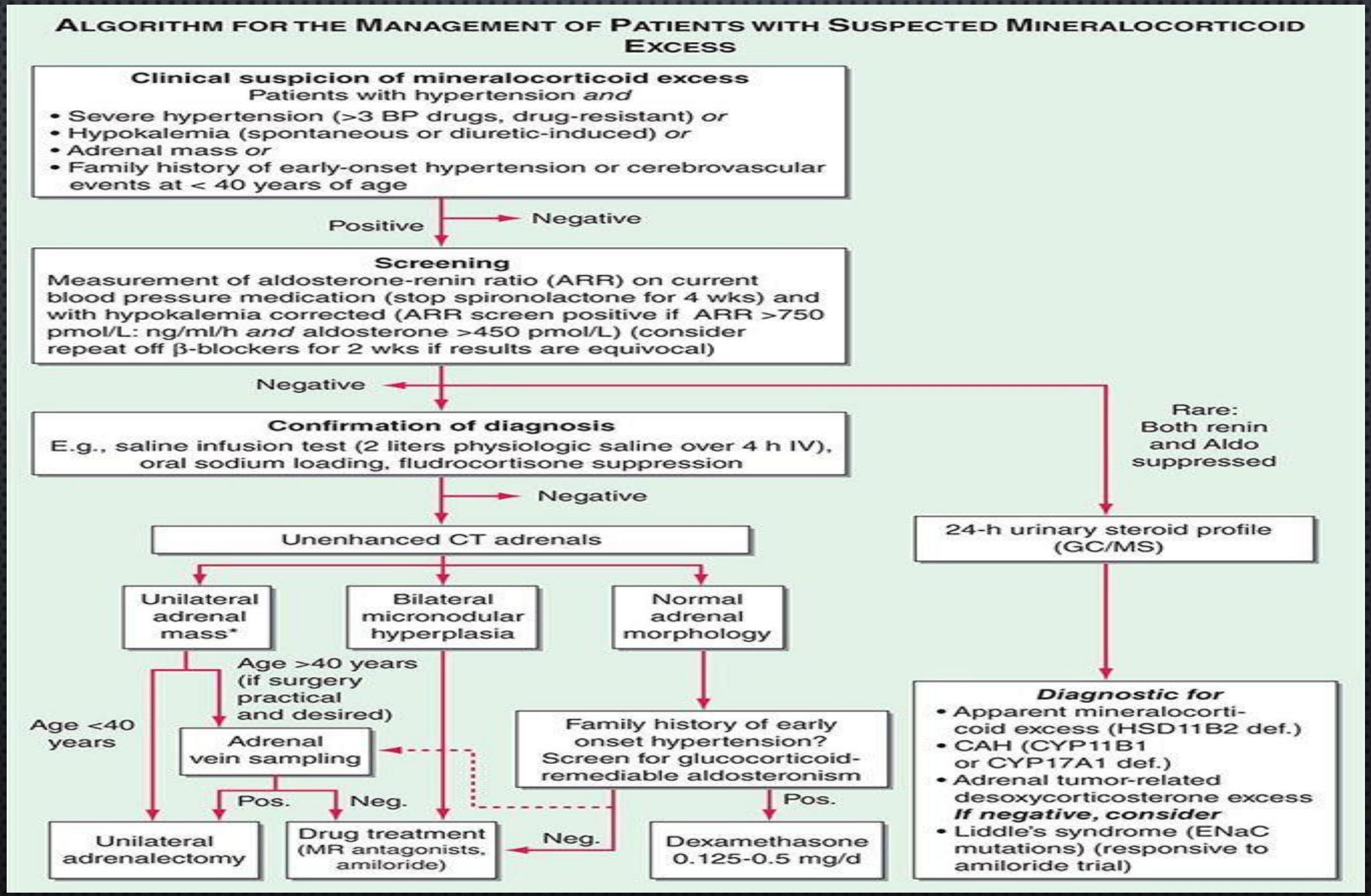
CONN'S SYNDROME

The most common cause of mineralocorticoid excess is primary aldosteronism, reflecting excess production of aldosterone by the adrenal zona glomerulosa. Bilateral micronodular hyperplasia is somewhat more common than unilateral adrenal adenomas.

Clinical Manifestations Excess activation of the mineralocorticoid receptor leads to potassium depletion and increased sodium retention, with the latter causing an expansion of extracellular and plasma volume.

The clinical hallmark of mineralocorticoid excess is hypokalemic hypertension; serum sodium tends to be normal due to the concurrent fluid retention, which in some cases can lead to peripheral edema. Hypokalemia can be exacerbated by thiazide drug treatment, which leads to increased delivery of sodium to the distal renal tubule, thereby driving potassium excretion. Severe hypokalemia can be associated with muscle weakness, overt proximal myopathy, or even hypokalemic paralysis. Severe alkalosis contributes to muscle cramps and, in severe cases, can cause tetany.

Algorithm for the Management of Patients with Suspected Mineralocorticoid Excess



Thank You