

ADRENAL: Fear Not, You Can Do This!

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Disclosures

- Avvio Medical: Primary Investigator and Consultant
- Novo Nordisk: Scientific Advisor
- Canadian Urological Association Adrenal Guidelines: Reviewer

Learning Objectives

(what I want you to be able to do after this lecture)

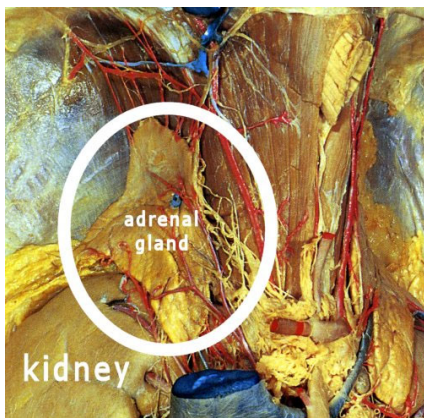
- Define adrenal anatomy, histology, & function
- Identify clinical manifestations of adrenal pathophysiology
- Distinguish radiographic characteristics of adrenal masses
- Execute and interpret metabolic and hormonal evaluations
- Discuss the medical and surgical treatments for adrenal pathology
- Crush adrenal questions on the in-service and your boards



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Embryology



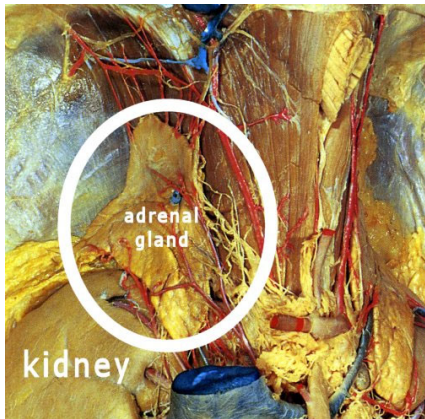
- Cortex: derived from mesoderm in 5th week
- Medulla: ??



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Embryology

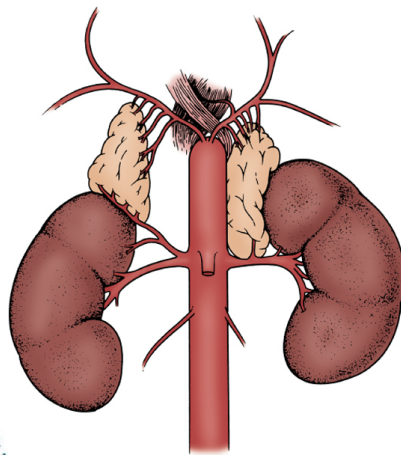


- Cortex: derived from mesoderm in 5th week
- Medulla: derived from neural crest cells
 - Chromaffin cells innervated by sympathetic fibers
 - Controls secretion of catecholamines

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Adrenal Arterial Supply



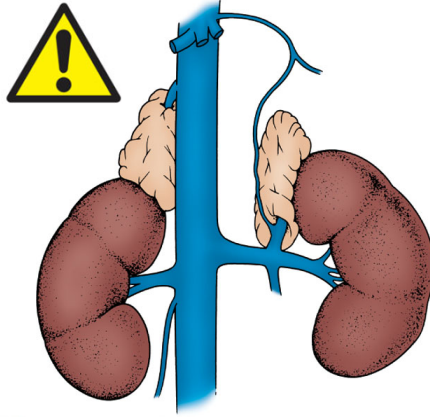
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- Main supply is the Inferior Phrenic
- Other branches
 - Aorta
 - Renal artery

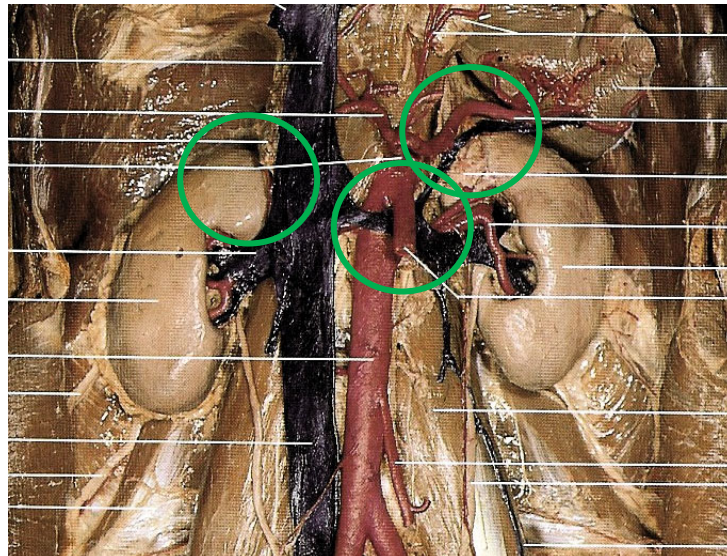
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Adrenal Venous Drainage

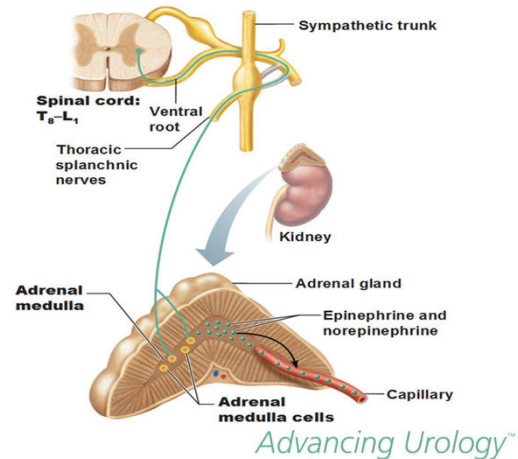


- Left: renal vein & inferior phrenic vein
- Right: posterio-lateral IVC
 - Short and fragile!
 - More cephalad than you think
- Can be accessories on either side!



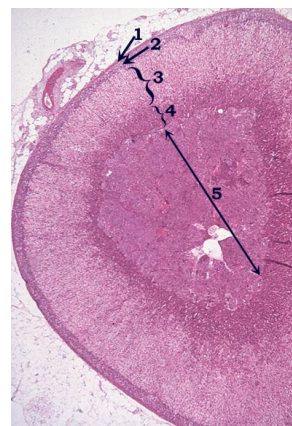
Nerve Supply

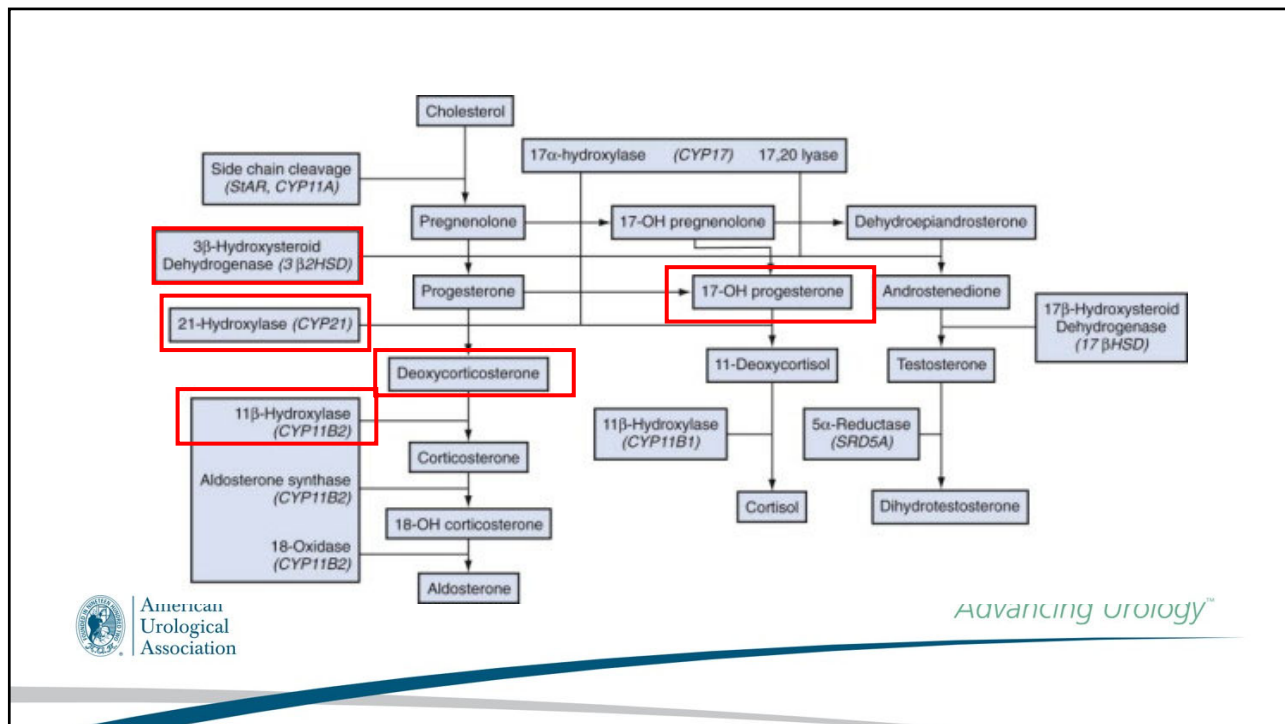
- Cortex = none!
- Medulla (think sympathetic ganglion)
 - T8 – L1 sympathetic fibers
 - Triggers **Epi** and Norepi release



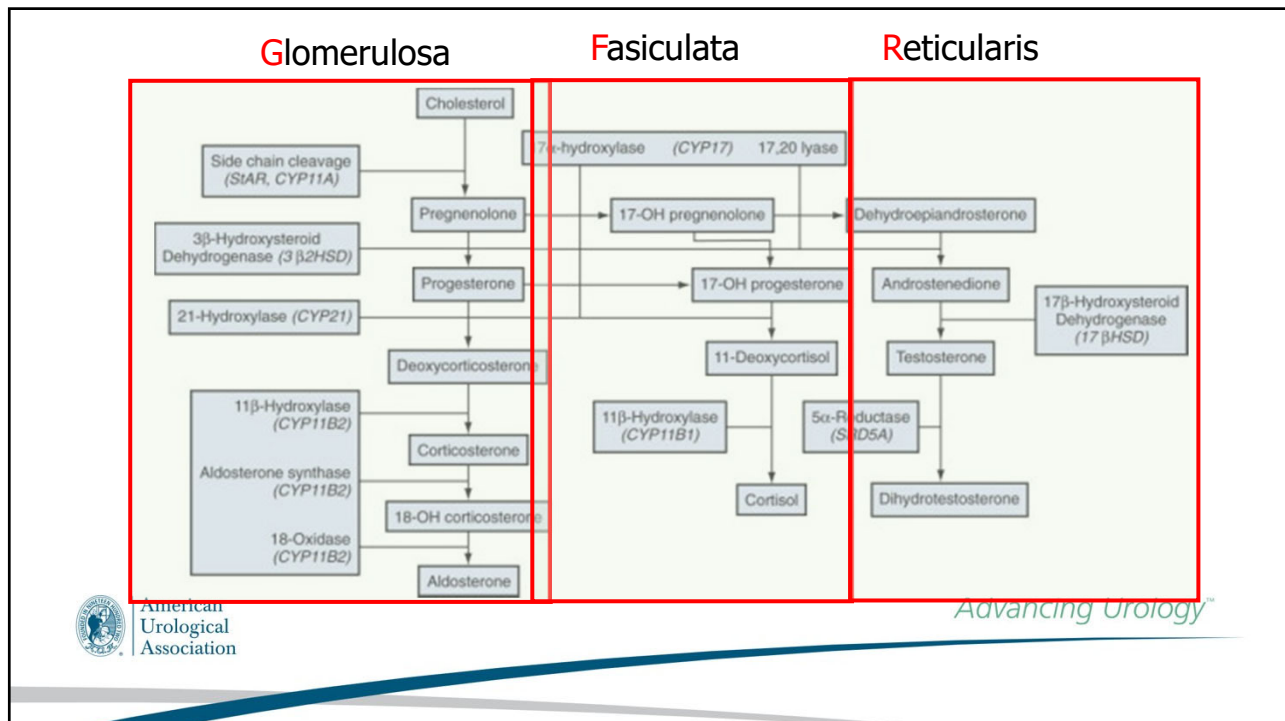
Histology

1. Capsule
2. **G**lomerulosa: Aldosterone
3. **F**asciculata: Cortisol
4. **R**eticularis: Sex steroids
5. Medulla: **Epi** and Norepi (Chromaffin Cells)



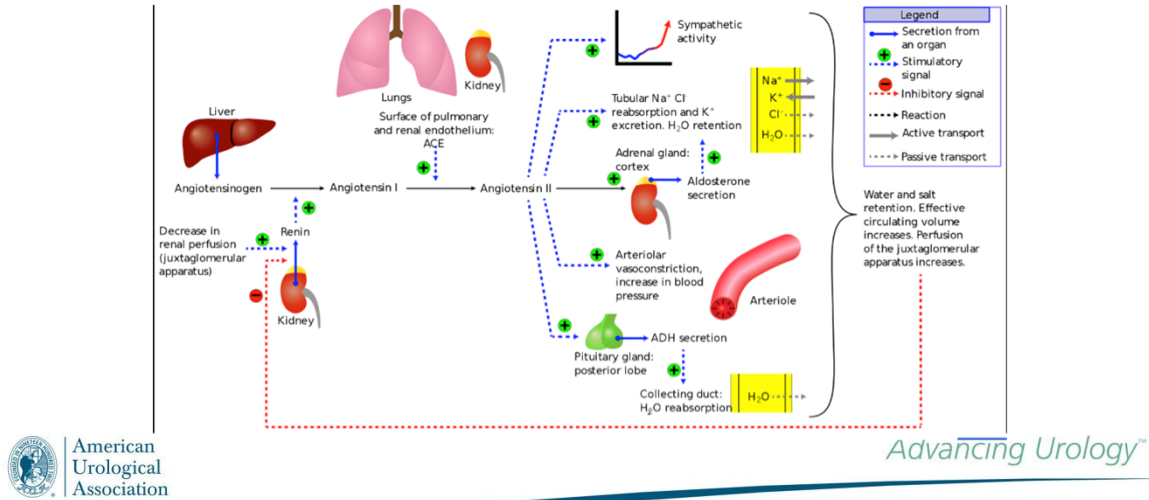


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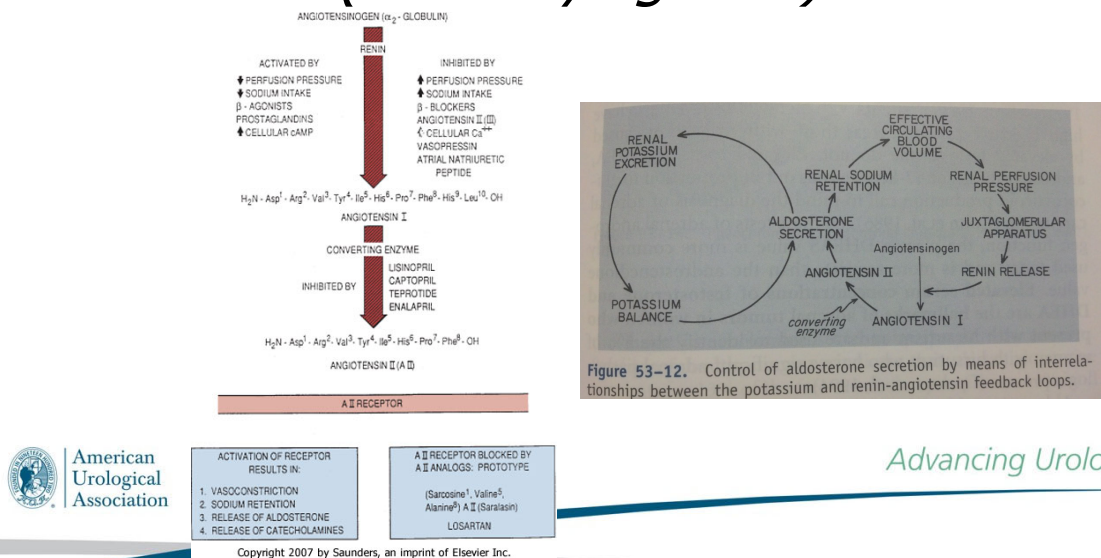
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Renin-Angiotensin-Aldosterone System (for studying later)



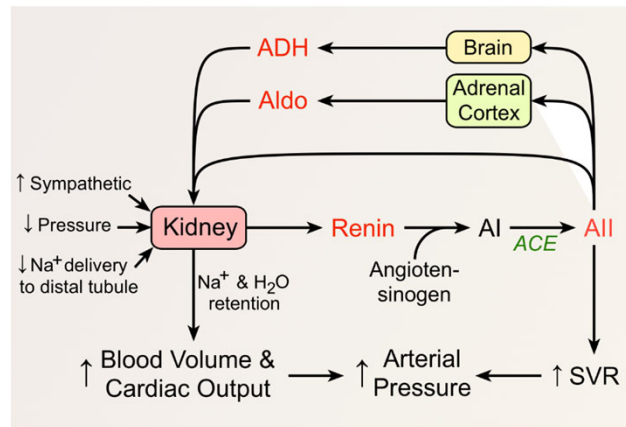
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Renin-Angiotensin-Aldosterone System (for studying later)



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Renin-Angiotensin-Aldosterone System (for studying later)



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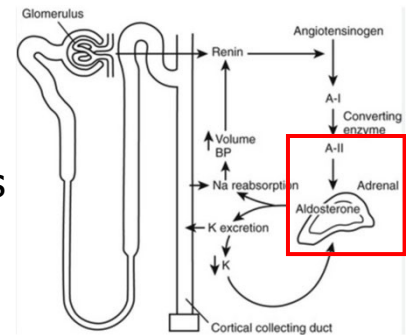
Aldosterone

- The primary human mineralocorticoid
- Acts on the late distal tubule and collecting duct
- Reabsorbs Na^+ and Cl^- , while secreting H^+ and K^+
 - Concentration of Na^+ does not change bc water is reabsorbed
- Primarily affects total body volume

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Aldosterone – High Yield

- Primarily regulated by Angiotensin II
- Also directly regulated by \uparrow K and \downarrow Na
- ACTH is a secondary less important stimulus
- ANP is the main inhibitory factor

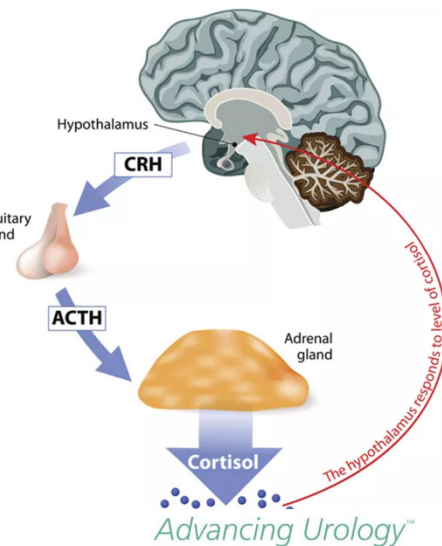
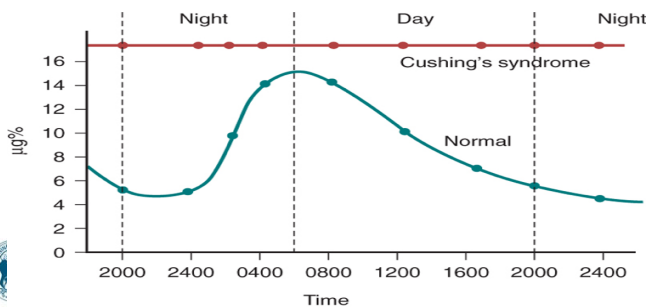


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Cortisol

- Primary glucocorticoid in humans
- Tightly controlled by ACTH
- Glycogen storage & gluconeogenesis



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Cortisol (for studying later)

EFFECTS	CLINICAL IMPLICATIONS
Enhance skeletal & cardiac muscle contraction	Absence results in weakness
Cause protein catabolism	Excess results in muscle wasting and weakness
Inhibit bone formation	Excess decreases bone density
Inhibit collagen synthesis	Excess causes thin skin and fragile capillaries
Increase vascular contractility and decrease permeability	Absence makes it difficult to maintain blood pressure
Have anti-inflammatory activity	Exogenous steroids treat inflammatory diseases
Have anti-immune system activity	Exogenous steroids useful in promoting transplant tolerance and treating autoimmune disorders
Maintain normal glomerular filtration (GFR)	Absence reduces glomerular filtration rate

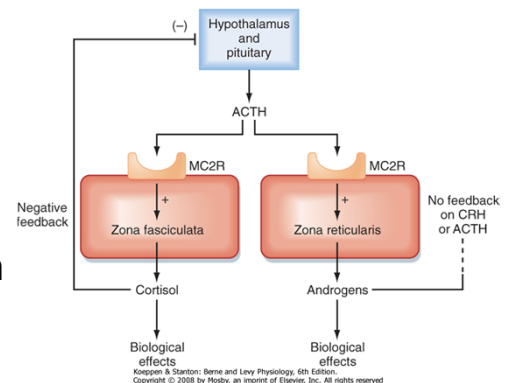


Table 57-2 -- Primary Effects of Glucocorticoids
From Howard's SS, Carey RM. The adrenals. In: Gillenwater JY, Grayhack JT, Howards SS, Duckett JW, editors. Adult and pediatric urology. 2nd ed. Chicago: Year Book; 1991.

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Sex Steroids

- Stimulated by ACTH
- DHEA, DHEA-S, and androstenedione
- Congenital Adrenal Hyperplasia: aberrations in production
- Target for pharmacologic manipulation for advanced CaP



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Adrenal Medulla

- Part of autonomic nervous system

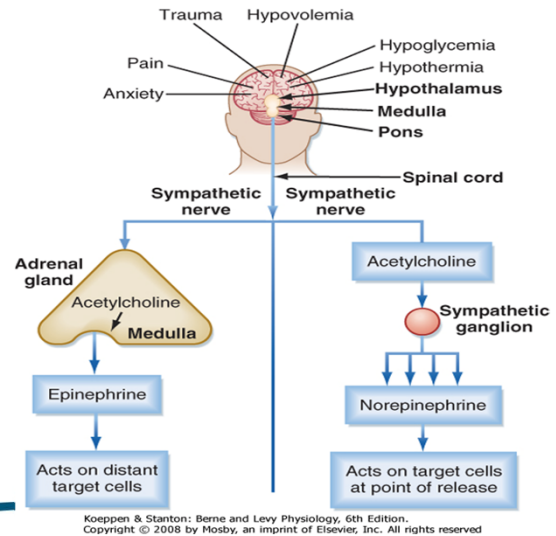
- Tyrosine → catecholamines

- PNMT (phenylethanolamine N-methyltransferase): Norepi → Epi

➤ Medulla

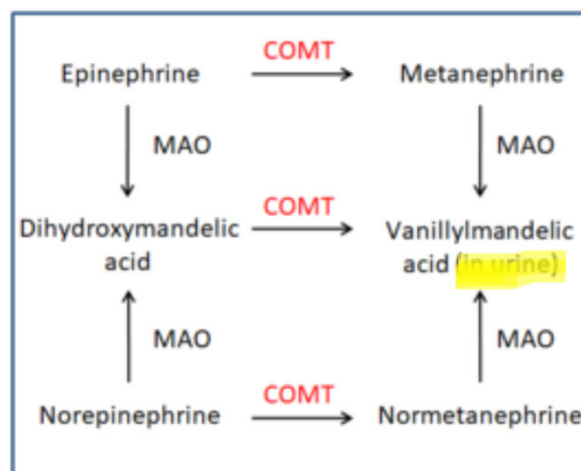
➤ Organ of Zuckermandl

➤ Brain



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Catecholamine Metabolism



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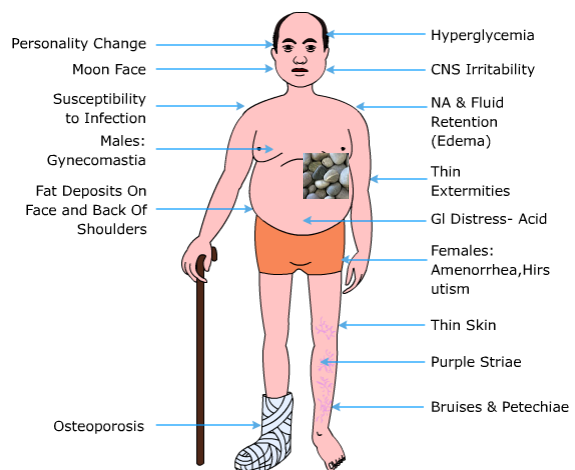


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Cushing's Syndrome

- Excess circulating glucocorticoids
- Includes:
 - Cushing's Disease (pituitary)
 - Functional adrenal adenomas & ACCs
 - Ectopic secretion of ACTH or CRH
- Divided into:
 - Exogenous
 - ACTH-dependent
 - ACTH-independent



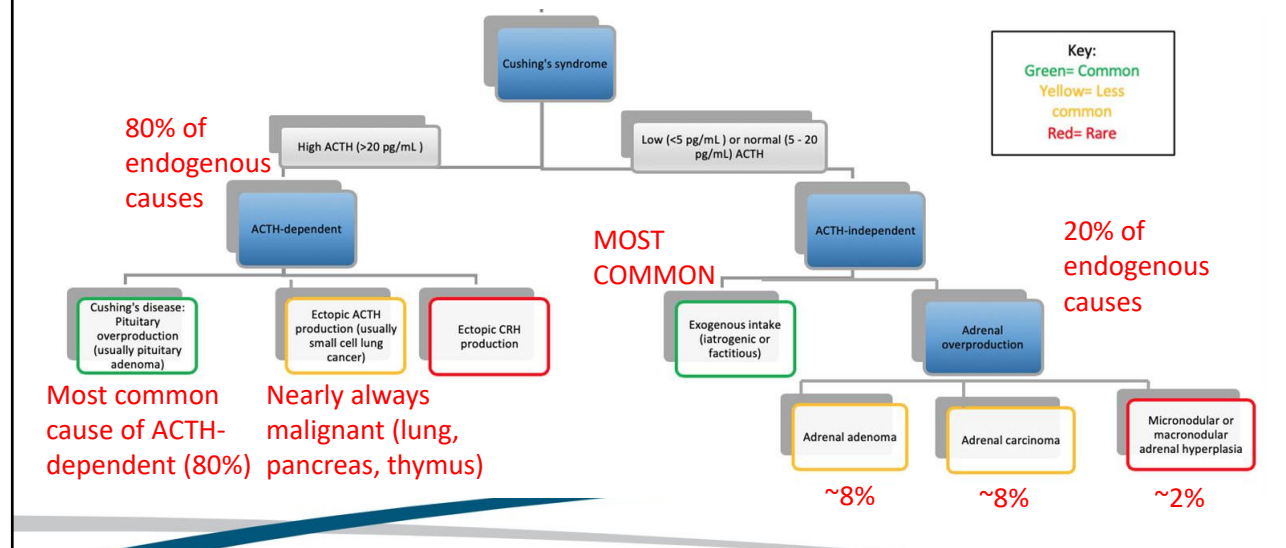
24

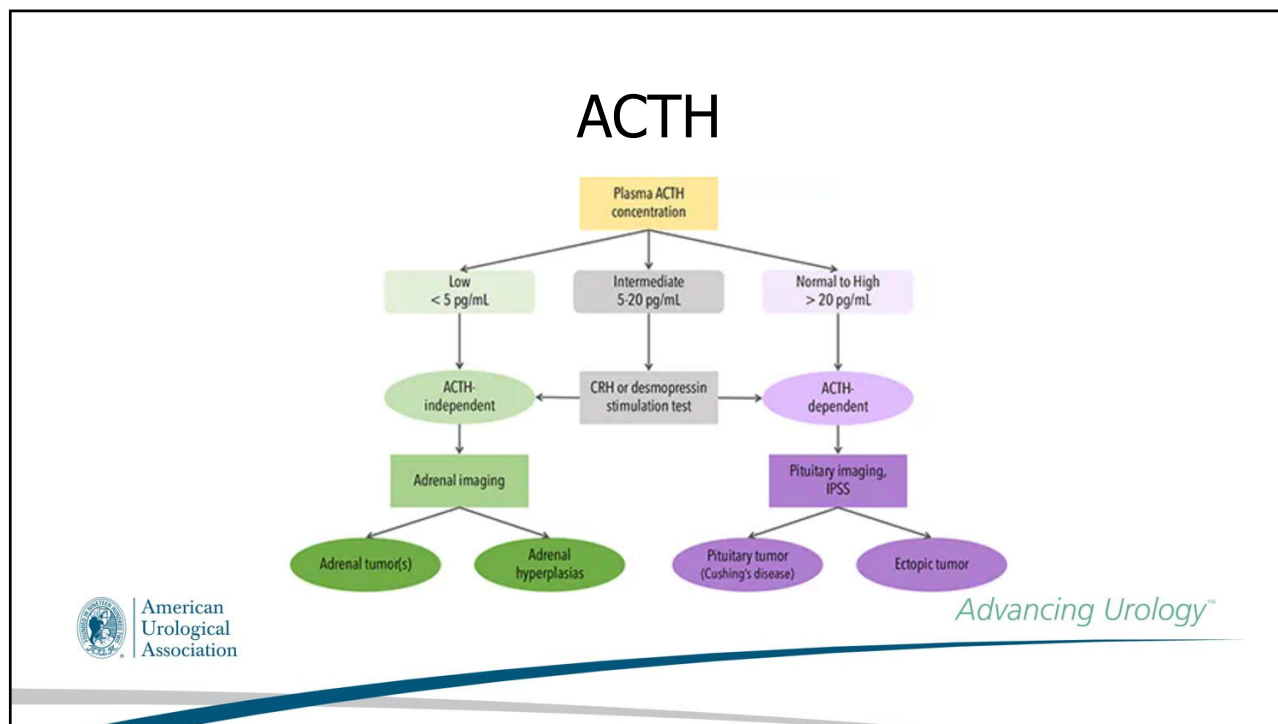
Cushing's Syndrome: Tests

- 24-hour urine free cortisol
 - Sensitive for diagnosis of subclinical Cushing's
- Low-dose dexamethasone suppression test
 - 1 mg at 11pm and obtain an 8am morning level
 - > 1.8 is diagnostic for autonomous cortisol secretion
- Late-night salivary cortisol
- Midnight plasma cortisol level

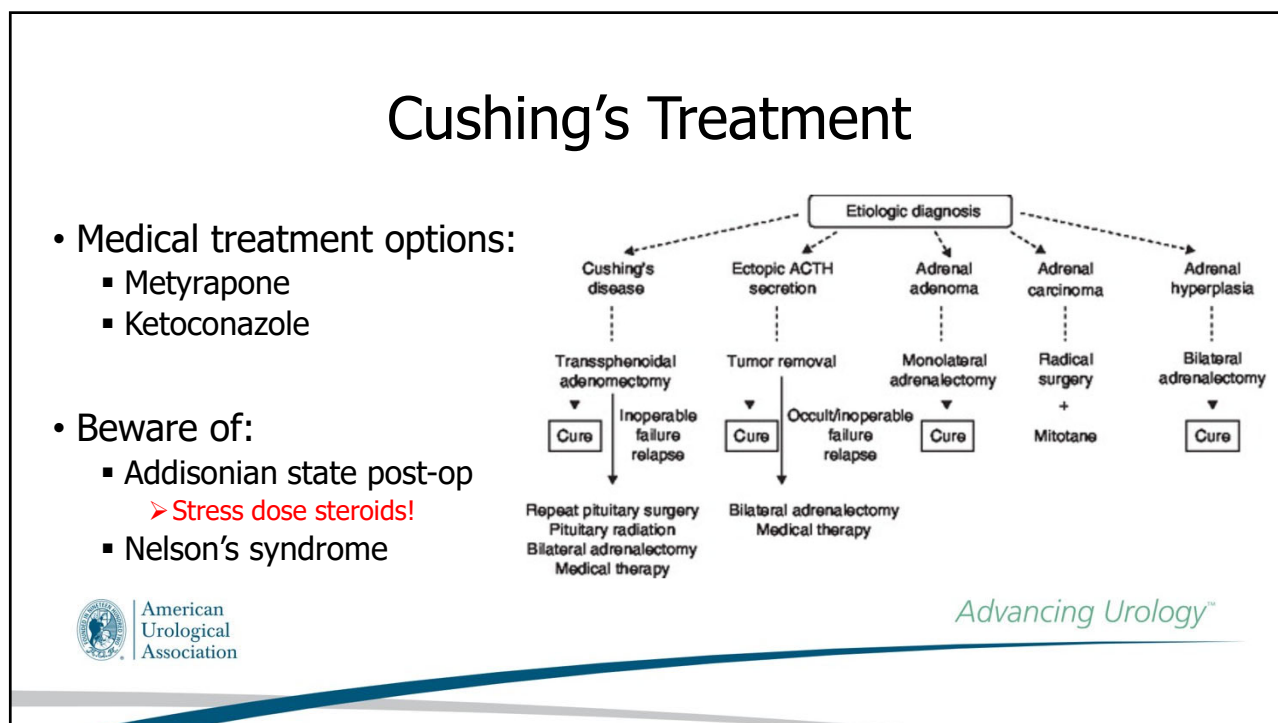


Cushing's Syndrome





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“Subclinical” Cushing’s (Mild Autonomous Cortisol Secretion)

- Elevated cortisol levels without obvious clinical signs
- Associated with:
 - Pregnancy
 - Depression
 - Alcohol dependence
 - Morbid obesity
 - Poorly controlled DM
- Treatment controversial, trials ongoing; probably Adrenalectomy



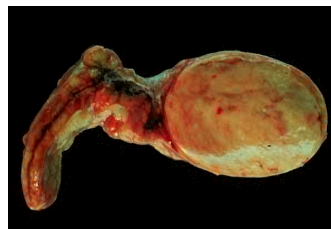
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Fassnacht et al. Management of adrenal incidentalomas: European Society of Endocrinology clinical practice guideline. Eur J Endocrin. 2016;175:G1–34.

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Primary Hyperaldosteronism (PHA)

- 5-13% prevalence in contemporary HTN series
- ~3% of patients with adrenal masses
 - ~65% aldosteronoma
 - ~35% hyperplasia
- Clinical features:
 - Moderate to severe HTN
 - CV and renal damage
 - ↓ K (~40-60%)



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PHA Screening

Hypertension with hypokalemia
Resistant hypertension (three or more oral agents with poor control)
Adrenal incidentaloma with hypertension
Early-onset hypertension (<20) or stroke (<50 years)
Severe hypertension ($\geq 160/\geq 110$)
Whenever considering secondary causes of hypertension
Unexplained hypokalemia
Organ damage disproportionate to degree of hypertension



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PHA: Work-up

- Correct potassium and stop certain meds
 - 3 days: Calcium & Beta blockers, ACEI/ARBs, Diuretics
 - 4 weeks: mineralocorticoid antagonists
- Obtain morning aldosterone and plasma renin activity
 - Aldo-to-renin ratio (ARR): $\geq 20-30$ **and**
 - Aldosterone $> 15 - 20$ ng/dL
- Confirmatory test needed due to ~30% false positives
 - Oral sodium or IV saline load test, look for lack of aldo suppression



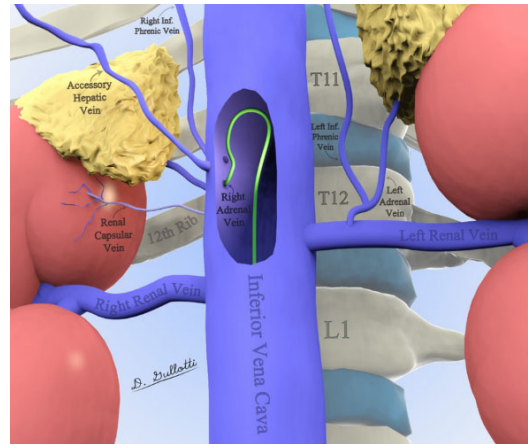
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Check out [Adrenalmass.org](https://adrenalmass.org) for patient friendly instructions

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Adrenal Vein Sampling

- Deciding on treatment by CT alone:
 - 22% incorrectly excluded from adrenalectomy
 - 25% receive inappropriate adrenalectomy
- Perform if > 40 years old or bilateral findings on CT



Young et al, 2004. Young WF, Stanson AW, Thompson GB, et al: [Role for adrenal venous sampling in primary aldosteronism](#). Surg 2004; 136(6):1227-1235.

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PHA Treatment

- Adrenalectomy for unilateral adenoma with AVS localization
 - 33-77% no longer require HTN meds post-op
 - > 90% have resolution or improvement of HTN
 - Post-op:
 - Maintain high sodium diet
 - Watch for hyperkalemia and repeat ARR
- Medical therapy with spironolactone or eplerenone if bilateral or not a surgical candidate



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Pheochromocytoma

- Catecholamine-producing tumor
- Accounts for 0.5% in HTN series and 5% of adrenal masses
- Extra-adrenal (paragangliomas): arise from neural crest
 - Parallels the SNS and PSN
- 10% present without HTN and 20% are asymptomatic



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Pheochromocytoma

	FREQUENCY
Headache	60%-90%
Palpitations (tachycardia)	50%-70%
Sweating	55%-75%
Pallor	40%-45%
Nausea	20%-40%
Flushing	10%-20%
Weight loss	20%-40%
Tiredness	25%-40%
Psychologic symptoms (anxiety, panic)	20%-40%
Sustained hypertension	50%-60%
Paroxysmal hypertension	30%
Orthostatic hypotension	10%-50%
Hyperglycemia	40%



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Table 57-10 -- Clinical Manifestations of Pheochromocytoma
Adapted from Lenders JW et al. *Phaeochromocytoma*. *Lancet* 2005;366(9486):665-75.

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Pheochromocytoma: Work-Up

Biochemical Test	Sensitivity	Specificity	Sensitivity at 100% Specificity
Plasma metanephrine level	99	89	82
Plasma catecholamine level	85	80	38
Urinary catecholamine level	83	88	64
Urinary metanephrine level	76	94	53
Urinary vanillylmandelic acid level	63	94	43



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Pheochromocytoma: Work-Up

- Not concerning until $> 2-3x$ upper limit of normal
- Stop tobacco and licorice x 5-7 days
- No caffeine for 24 hours
- Stop certain medications:
 - Acetaminophen, levodopa, MOAI, BZ, tetracycline
 - Careful with stopping clonidine!

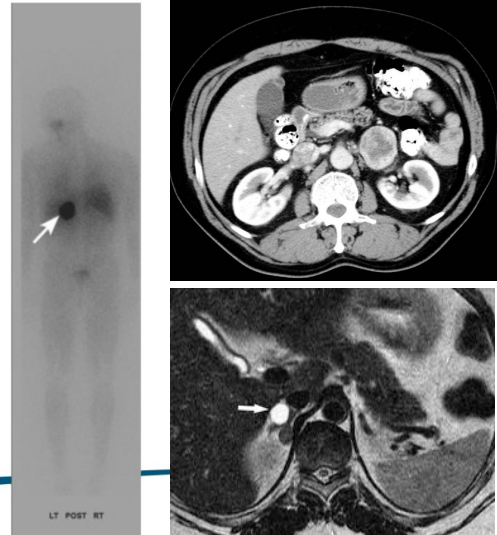


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Pheochromocytoma: Imaging

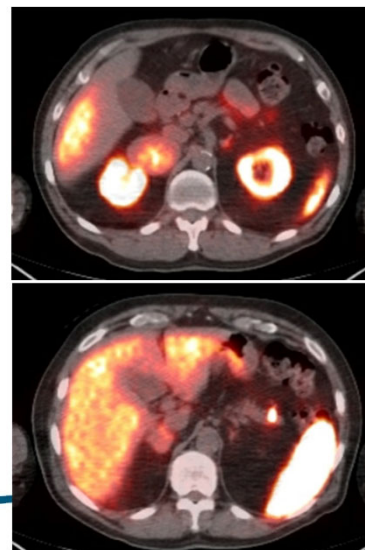
- CT:
 - > 25 HUs on NCCT, round, clear margins
 - Heterogeneous enhancement
- MRI
 - Bright on T2 ("light bulb sign")
 - No signal dropout on out-of-phase images
- MIBG Scan
 - > 95% specificity, > 83% sensitive
 - Integral part of w/u for extra-adrenal pheos, mets, recurrence



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Pheochromocytoma: Imaging

- GA-68-Dotatate PET CT
 - Lower specificity than MIBG
 - Better for paragangliomas and mets



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Pheochromocytoma: Rule of 10s??

- 10% are bilateral and 10% are pediatric BUT . . .
- Up to 30% are familial
- Up to 25% are extra-adrenal
- ~5% are malignant
 - Diagnosed clinically, not based on pathologic appearance
 - Much more common in extra-adrenal disease



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Pheochromocytoma: Genetic Associations

Syndrome	Frequency of Pheo (%)	Gene	Chromosome location	Clinical Findings
MEN type II	30-50	RET oncogene	10q11	2A: Medullary thyroid Ca (MTC), HPT 2B: MTC, neuromas, marfanoid
VHL disease	15-20	VHL tumor suppressor gene	3p25	RCC, cysts, angiomas and hemangioblastomas, epididymal cystadenomas, endolymphatic cysts
NF type 1	1-5	Neurofibromatosis type 1	17q11	Neurofibromas Café-au-lait spots
Familial carotid body tumors		Paraganglioma	11q21-23	



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https://www.researchgate.net/figure/Hereditary-Forms-of-Pheochromocytoma_tbl2_41893857 [accessed 7 Apr 2025]

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Pheochromocytoma: Medical Management

- Consults: Cardiology, Anesthesia, Endocrinology
- Blood Pressure Control: aim for orthostasis
 - Phenoxybenzamine is irreversible
 - Prazosin / terazosin are reversible
 - Calcium channel blockers if mild symptoms / HTN
- Beta-1 blockade for arrhythmias (only after alpha blockade)
- Catecholamine synthesis blockade (metryosine)
- Expand intravascular volume: liberal salt and fluid intake



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Pheochromocytoma: Intra- and Post-Op

- Intraoperatively
 - Good communication with anesthesia
 - Take vein early, minimal tumor manipulation
- Postoperatively
 - ICU overnight if any concerns at all
 - Watch for rebound hypoglycemia
- Follow-up
 - Recurrence in 16% so need annual screening
 - Consider genetic testing

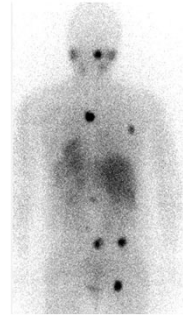


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Malignant Pheochromocytoma

- Clinical diagnosis
 - Invasion into adjacent structure
 - Metastatic spread
- Cytoreductive surgery and metastasectomy preferred
- Chemotherapy CVD: cyclophosphamide, vincristine, dacarbazine
- Radioactive ¹³¹I-MIBG



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Adrenal Cortical Carcinoma (ACC)

- Rare and bimodal with peaks in 1st and 4th – 5th decades
 - 1-2 cases per million / 300-500 cases per year in the UA
 - Pediatric ACC present with lower-stage tumors
- Syndromes: Li-Fraumeni, BWS, MEN Type 1
- Adrenal metastases are much more common
 - If previous malignancy, 50% chance a new adrenal lesion is a met
 - Most common are lung and melanoma



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ACC: Presentation

- Advanced disease
- Symptoms: hormonal production (70-80%) and local disease
- Mixed hormonal production
 - Most common is cortisol (ACTH-independent!)
 - More virilizing than adenomas (DHEA and 17-ketosteroids)

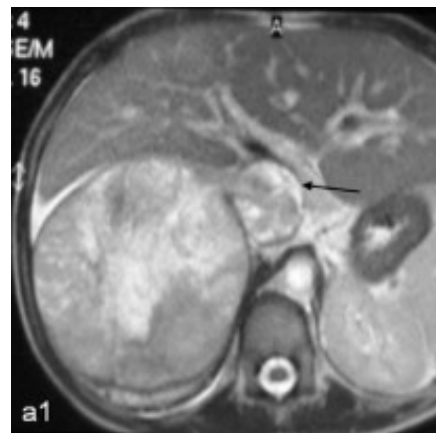


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ACC: Imaging

- Large
 - Average size > 10cm
 - 90% > 5 cm
- Irregular
 - Nondescript borders, necrosis, calcification
- Locally advanced
 - Involves local structures
 - Vascular involvement (IVC)



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ACC: Management

- Surgical en-bloc excision is essential
 - Regional LND important
- Cytoreductive debulking if 90% can be removed
- Multimodal approach (60-80% recur)
 - Radiation for bone and CNS metastases
 - **Mitotane for palliation**
 - Response rates 14-36%
 - Little survival benefit



STAGE	2004 UICC/WHO	AT DIAGNOSIS	5-YEAR SURVIVAL
1	T1N0M0	3%-4%	33%-66%
2	T2N0M0	29%-46%	20%-58%
3	T1-2N1M0 T3N0M0	11%-19%	18%-24%
4	T1-4N0-1M1 T3N1M0 T4N0-1M0	39%-49%	<5%

T1 = <5 cm; T2 = >5 cm;
T3 = infiltration of surrounding adipose tissue;
T4 = invasion into adjacent organs

Kapoor A et al. Can Urol Assoc J 2011: 241-7; CUA Guideline for the management of the incidentally discovered adrenal mass
Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2016.
Kutikov A, Mehrazin R, Uzzo R. Assessment and management of an Adrenal Mass in Urological Practice. AUA Update, 2014.

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Incidental Adrenal Mass

- >1 cm lesion from the medulla or cortex
- Advances in imaging → ↑ prevalence
 - 1985 – 1990: incidentalomas found in 0.4%
 - Contemporary numbers from 2% to 10% (increases with age)



Incidental ≠ Insignificant

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Young WF, Kebebew E. The Adrenal Incidentaloma. Uptodate.com.

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Adrenal Masses

Tumor entity	Median (%)	Range (%)
Series including all patients with an adrenal mass*		
Adenoma	80	33–96
Nonfunctioning	75	71–84
Autonomously cortisol-secreting	12	1.0–29
Aldosterone-secreting	2.5	1.6–3.3
Pheochromocytoma	7.0	1.5–14
Adrenocortical carcinoma	8.0	1.2–11
Metastasis	5.0	0–18
Surgical series**		
Adenoma	55	49–69
Nonfunctioning	69	52–75
Cortisol-secreting	10	1.0–15
Aldosterone-secreting	6.0	2.0–7.0
Pheochromocytoma	10	11–23
Adrenocortical carcinoma	11	1.2–12
Myelolipoma	8.0	7.0–15
Cyst	5.0	4.0–22
Ganglioneuroma	4.0	0–8.0
Metastasis	7.0	0–21



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Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2016.

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Three Important Questions

- Are there imaging characteristics suggestive of a malignancy?
- Does the patient have a history of malignancy?
- Is the mass hormonally active?



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Radiographic Evaluation

- Distinguish between:

- Adenoma
- Adrenal carcinoma
- Pheochromocytoma
- Myelolipoma
- Metastasis

Method	Criteria
Noncontrast CT	≤10 HU
MRI – chemical shift ^b	Loss of signal intensity on out-phase imaging consistent with lipid-rich adenoma
CT with delayed contrast media washout ^{b,c}	Absolute washout >60% Relative washout >40%
18F-FDG-PET ^b	Absence of FDG uptake or uptake less than the liver ^d



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Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2016.

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Size and Risk of Malignancy

- Chances of malignancy are linked to tumor size

- ~33% of tumors > 6 cm prove to be malignant
- However, ACC is rare

- Traditional size cut-off: > 4 - 6 cm

- Sensitivity is 93% HOWEVER specificity is 42%

- Growth Kinetics

- 9% of adrenal incidentalomas grow > 1 cm in follow-up
- ESE recommends trigger of >20% with an absolute increase of >5 mm



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Kapoor A et al. Can Urol Assoc J 2011; 5(4): 241-7, CUA Guideline for the management of the incidentally discovered adrenal mass.

Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2016.

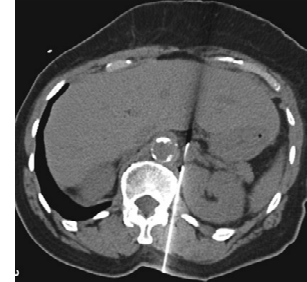
Kutikov A, Mehrazin R, Uzzo R. Assessment and management of an Adrenal Mass in Urological Practice. AUA Update, 2014.

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What about Adrenal Mass Biopsy / PET?

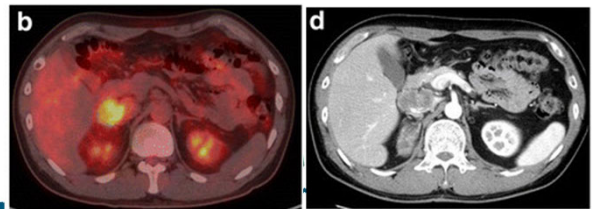
- Biopsy:

- If **hormonally inactive**, indeterminate, and affects management (h/o extra-adrenal malignancy)
- **Avoid if you suspect ACC**
- Non-Dx 8.7%, sensitivity 70-87%, specificity 98-100%
- Risks 2.5%



- ¹⁸F-FDG-PET

- Same indications as above OR
- HUs > 20, heterogeneous, & > 4 cm



Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2023.
Zeiger MA et al. AACE and AAES Medical Guidelines for the management of Adrenal incidentalomas. Endocrine Practice. 2009

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Functional or Not?

- ~80% of adrenal masses are adenomas
 - Of these, ~25% are functional
- **All adrenal masses > 1 cm should be evaluated for at least autonomous cortisol secretion (CUA, AACE, ESE)**
- Most patients (80%) do not receive an evaluation



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Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2023.
Yip L et al. American Association of Endocrine Surgeons Guidelines for Adrenalectomy. Jama Surgery, 2022; 157(10): 870
Kutikov A, Mehrazin R, Uzzo R. Assessment and management of an Adrenal Mass in Urological Practice. AUA Update, 2014.

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History and Physical is Important!

- Cushing's Syndrome
 - Obesity, DM, virilization, STONES, weakness, osteoporosis, easy bruising
- Primary Hyperaldosteronism
 - Hypertension, fluid retention
- Pheochromocytoma
 - Hypertension, headaches, palpitations, sweating, anxiety
- Adrenal Cortical Carcinoma
 - Any of the above but also virilization



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Functional or Not?

- Autonomous Cortisol Secretion (All patients)
 - Low dose dexamethasone suppression test
- Mineralocorticoid Excess (if HTN and/or hypokalemia)
 - Ratio of aldosterone-to-plasma renin activity (ARR) and BMP
- Catecholamine Excess (if NCCT HUs >10 or S/Sxs)
 - Plasma-free metanephrines OR
 - 24-hour urinary metanephrines and catecholamine levels



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Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2023.
Kutikov A, Matrozin R, Uzzo R. Assessment and management of an Adrenal Mass in Urological Practice. AUA Update, 2014.
Zeiger MA et al. AACE and AAES Medical Guidelines for the management of Adrenal Incidentalomas. Endocrine Practice. 2009
Yip L et al. American Association of Endocrine Surgeons Guidelines for Adrenalectomy. Jama Surgery, 2022; 157(10): 870
Rowe et al. Canadian Urological Association Guideline. Can Urol Assoc J, 2023; 17(2): 12

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Follow-Up: Adenoma

- Cost-effective follow-up strategy is unknown
- Low risk of “events” during follow-up (more likely if >3 cm):
 - malignancy (0.1%)
 - subclinical hyperfunction (1.2%)
 - overt disease (0.9%)
- Others report higher rates of conversion to hormonal activity (9.5 – 47%) and mass growth (6 – 29%) over 5 years



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Baltzer P et al. European Urology Focus 1. Work-up of the Incidental Adrenal Mass 2016.
Zeiger MA et al. AACE and AAES Medical Guidelines for the management of Adrenal incidentalomas. Endocrine Practice 2009
Kapoor A et al. Can Urol Assoc J 2011 5(4): 241-7; CUA Guideline for the management of the incidentally discovered adrenal mass

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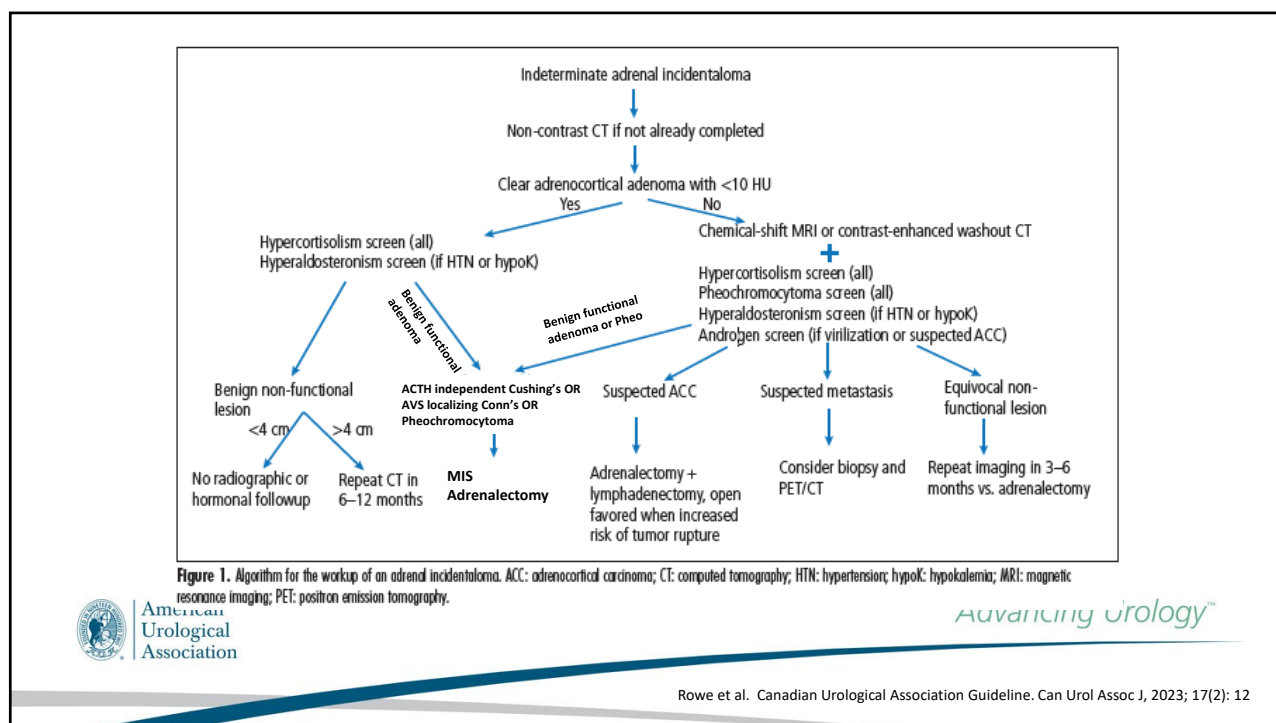
Follow-Up Recommendations

- AUA Update 2014
 - Annual hormonal evaluation for 3-4 years; repeat imaging at 6, 12, and 24 months
- CUA
 - No further follow up for benign nonfunctioning adenomas <4 cm or myelolipomas
 - Follow-up imaging in 6-12 months if >4 cm; stop if <3 mm/year growth
- ESE
 - No repeated hormonal work-up if initially normal; no comment on imaging
- AACE
 - No routine follow-up for benign-appearing nonfunctional masses <4 cm
 - If indeterminate imaging, need at least 1 repeated imaging at 6-12 months
 - Can re-evaluate for ACS at 2- to 5-year intervals



Fassnacht et al. European Society of Endocrinology Clinical Practice Guideline. 2023.
Kutikov A, Mehrazin R, Uzzo R. Assessment and management of an Adrenal Mass in Urological Practice. AUA Update, 2014.
Yip L et al. American Association of Endocrine Surgeons Guidelines for Adrenalectomy. Jama Surgery, 2022; 157(10): 870
Rowe et al. Canadian Urological Association Guideline. Can Urol Assoc J, 2023; 17(2): 12

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AUA 2024

MAY 3-6
San Antonio

Comprehensive scoring system predicts evidence- based management of adrenal incidentalomas

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Results

Question	Points/Factor
What is the Hounsfield units?	
<10 HU	0 points
≥10 HU	10 points
Is it functional?	
No	0 points
Indeterminate	T
Yes	80 points + T
What is the size?	
<4cm	0 points
≥4cm	10 points
Second-line Imaging - Contrast-enhanced washout CT	
Relative washout >40% with absolute washout >60% (Benign)	0 points
Relative washout ≤40% with absolute washout ≤60% (Suggestive of other)	20 points
Relative washout ≤40% with absolute washout ≤60% (Suggestive of metastasis with history of cancer)	50 points
Relative washout ≤40% with absolute washout ≤60% (Suggestive of ACC)	80 points
Second-line Imaging - Chemical shift MRI	
Microscopic fat with homogenous signal intensity drop (Benign)	0 points
Heterogenous signal intensity dropout (Suggestive of other)	20 points
Heterogenous signal intensity dropout (Suggestive of metastasis with history of cancer)	50 points
Heterogenous signal intensity dropout (Suggestive of ACC)	80 points

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Results

Sum of points/Factor	Outcomes
0 points	No follow up
10 points	Repeat CT in 6-12 months
20 – 40 points	Repeat imaging in 3-6 months vs. consider adrenalectomy
50 – 70 points	Consider biopsy or PET/CT
80+ points	Adrenalectomy
T factor	Ancillary T tests recommended

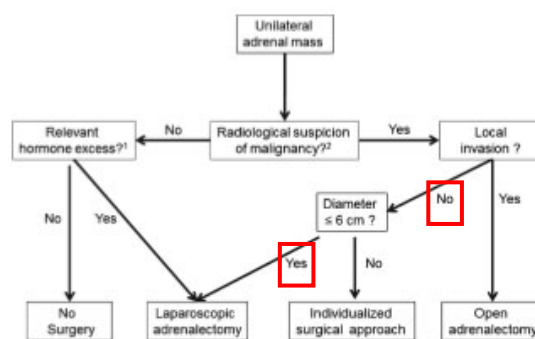
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Surgical Management

- Laparoscopic Adrenalectomy is SOC for most masses (ESE, CUA)
 - Equal efficacy to open
 - Shorter hospital stay, less pain, less EBL
 - Quicker recovery
- AACE Guideline 2009: "Open adrenalectomy should be performed if ACC is suspected"



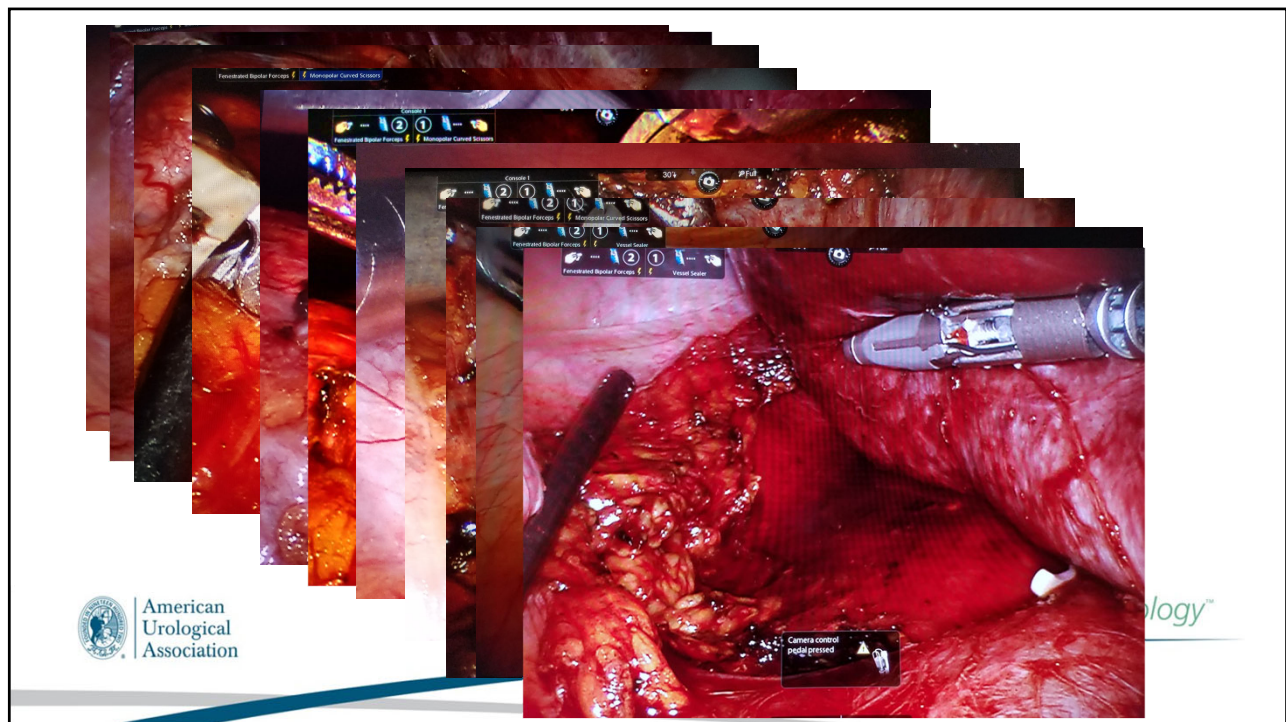
¹'Autonomous cortisol secretion' is not automatically judged as clinically relevant (see Section 5.3 for details).

²In tumors with benign radiological features and a tumor size >4 cm, surgery might also be individually considered (see text).

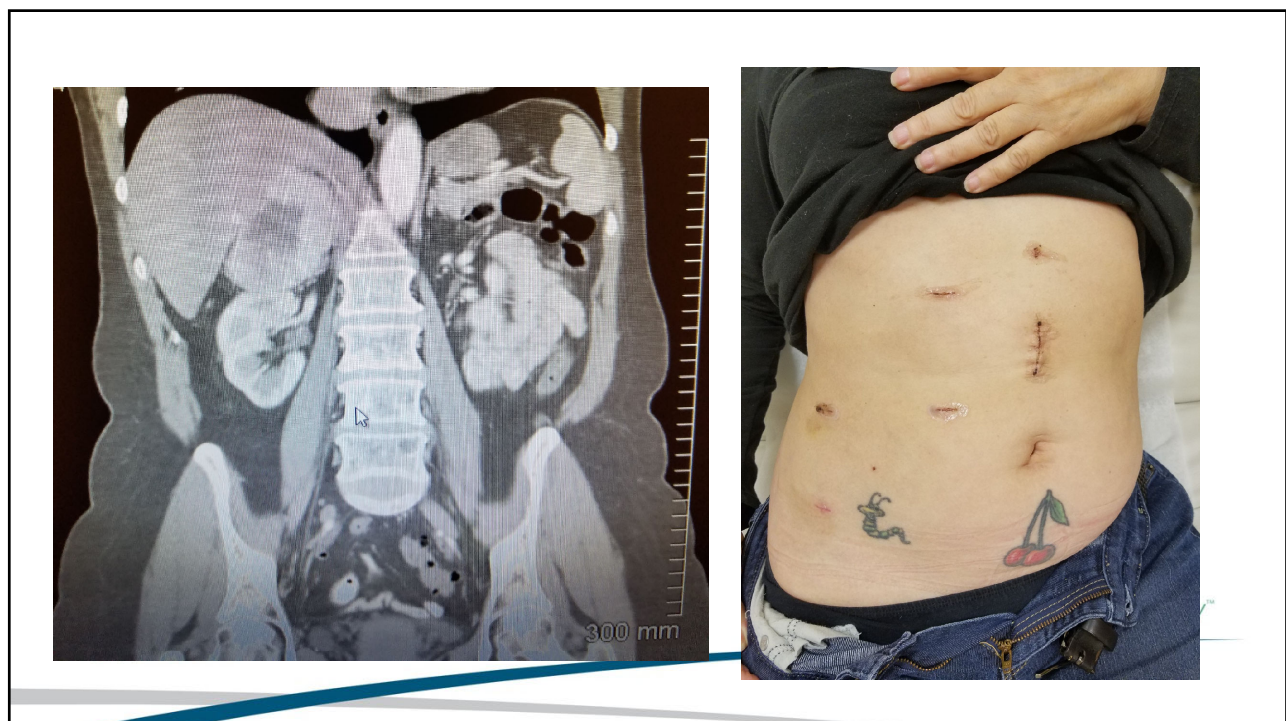


Young WF and Kebebew E. The Adrenal Incidentaloma. Uptodate. 2017
 Easseyent et al. European Society of Endocrinology Clinical Practice Guideline. 2016.
 Zeiger MA et al. AACE and AAES Medical Guidelines for the management of Adrenal incidentalomas. Endocrine Practice. 2009
 Kapoor A et al. Can Urol Assoc J 2011 5(4): 241-7; CUA Guideline for the management of the incidentally discovered adrenal mass

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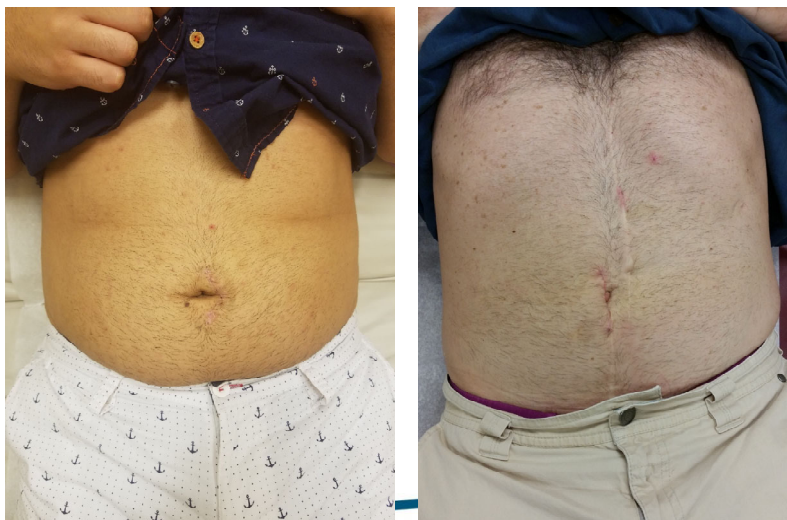


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LESS Adrenalectomy



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Adrenalectomy During Nephrectomy?

- Adrenal involvement
 - Occult involvement
 - Adrenalectomy
 - Consider
- otherwise
- up imaging
d features



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Adrenalectomy During Nephrectomy?



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Essential Contributors



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AR 1: What is the embryologic origin of the Adrenal medulla?

- a. Endoderm
- b. Mesoderm
- c. Ectoderm
- d. Neural crest cells
- e. None of the above



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AR 2: In renal agenesis, malrotation, or malascient, adrenal gland development:

- a. is absent ipsilaterally and normal contralaterally
- b. is found along the path of the gonadal vessels
- c. proceeds normally
- d. Proceeds as an ectopic adrenal rest



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AR 3: Which of the following is not a recommended test for establishing a diagnosis of Cushing's Syndrome?

- a. 24-hour urinary free cortisol
- b. Morning cortisol level
- c. Low-dose dexamethasone suppression test
- d. Late-night salivary cortisol
- e. Midnight plasma cortisol level



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AR 4: What is the ideal way to determine whether a patient has ACTH-dependant or ACTH-independent Cushing's?

- a. 24-hour cortisol excretion assay
- b. Concurrent measurement of ACTH and cortisol
- c. Measurement of diurnal variation of cortisol
- d. Low-dose dexamethasone test
- e. High dose dexamethasone test



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AR 5: What is the most common site for extra-adrenal pheochromocytomas?

- a. Bladder
- b. Carotid body
- c. Mediastinum
- d. Organ of Zuckerkandl
- e. Brain



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AR 6: Which of the following genetic conditions has a known association with pheochromocytoma?

- a. Neurofibromatosis-1
- b. Polycystic Kidney Disease
- c. Tuberous Sclerosis
- d. Multiple Endocrine Neoplasia - 1
- e. Birt-Hogg-Dube



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