# Incidental Adrenal Mass:
## Approach for the primary care provider

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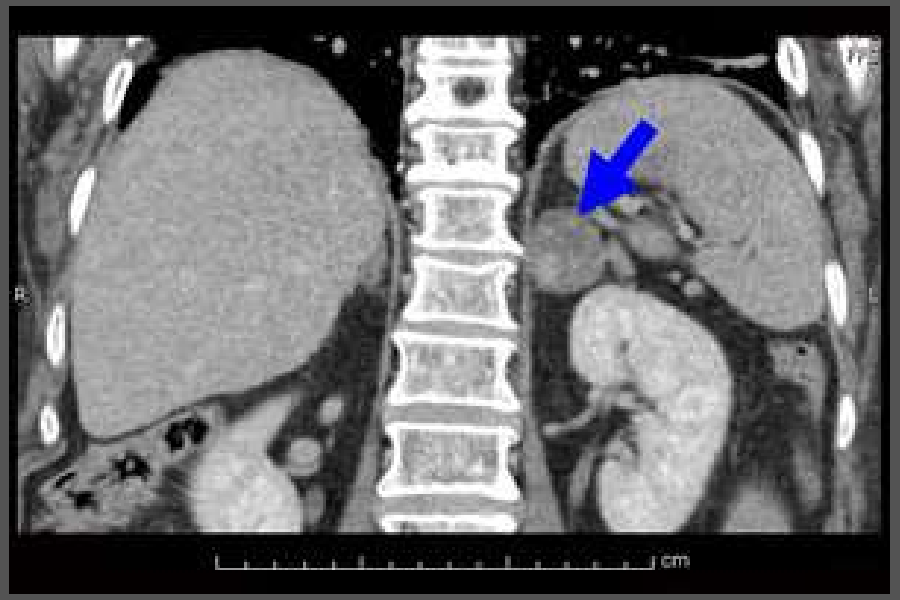
Minimally Invasive Urologic Surgery

# Learning Objectives

- Understand the pathologies of adrenal tumors
- Understand the basics of adrenal imaging and laboratory testing
- Be able to evaluate incidental adrenal mass and determine if urology/endocrine referral is needed

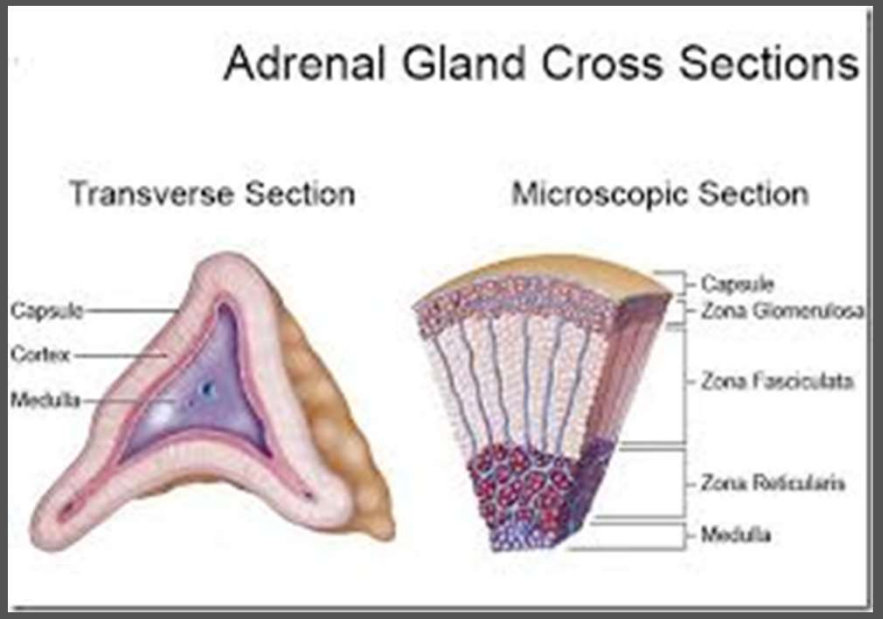
# What is adrenal incidentaloma and what is the significance?

- Definition: adrenal mass > 1 cm
- Only 15% are clinically relevant



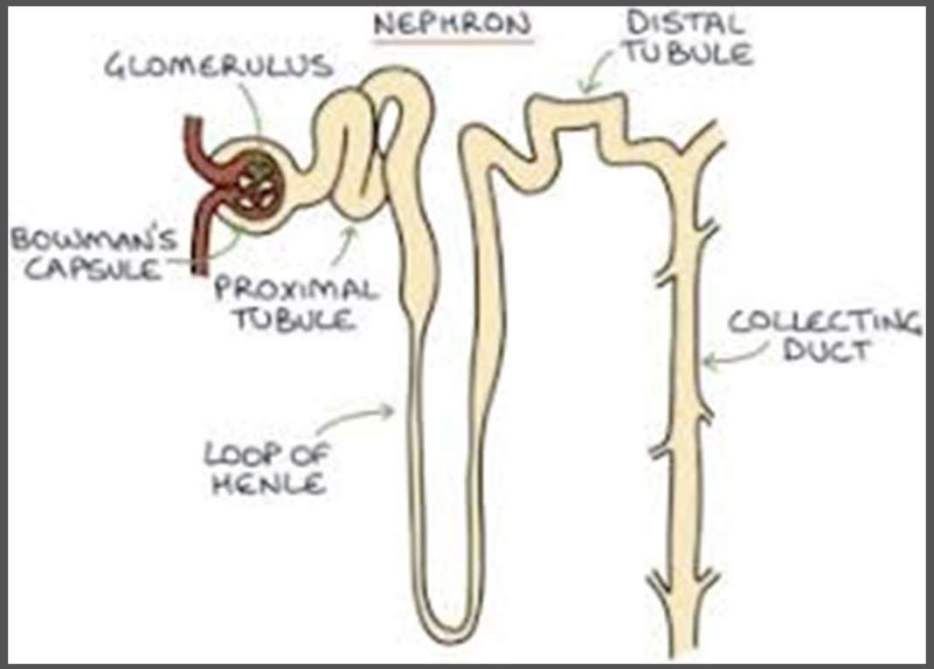
# Adrenal anatomy/function review

- Cortex
  - 3 zones:
    - Glomerulosa (Aldosterone)
    - Fasiculata (Cortisol)
    - Reticularis (Sex steroids)
- Medulla
  - Catecholamines
    - Epinephrine
    - Norepinephrine
    - Dopamine



# What does aldosterone do?

- Acts on distal tubule.
- Sodium up
- Potassium down



# What does cortisol do?

- Body's main stress hormone
- Manages metabolism
- Regulates inflammatory responses
- Regulates blood pressure
- Increases blood sugar
- Plays a role in sleep/wake cycle
- Boosts energy

# What are catecholamines?

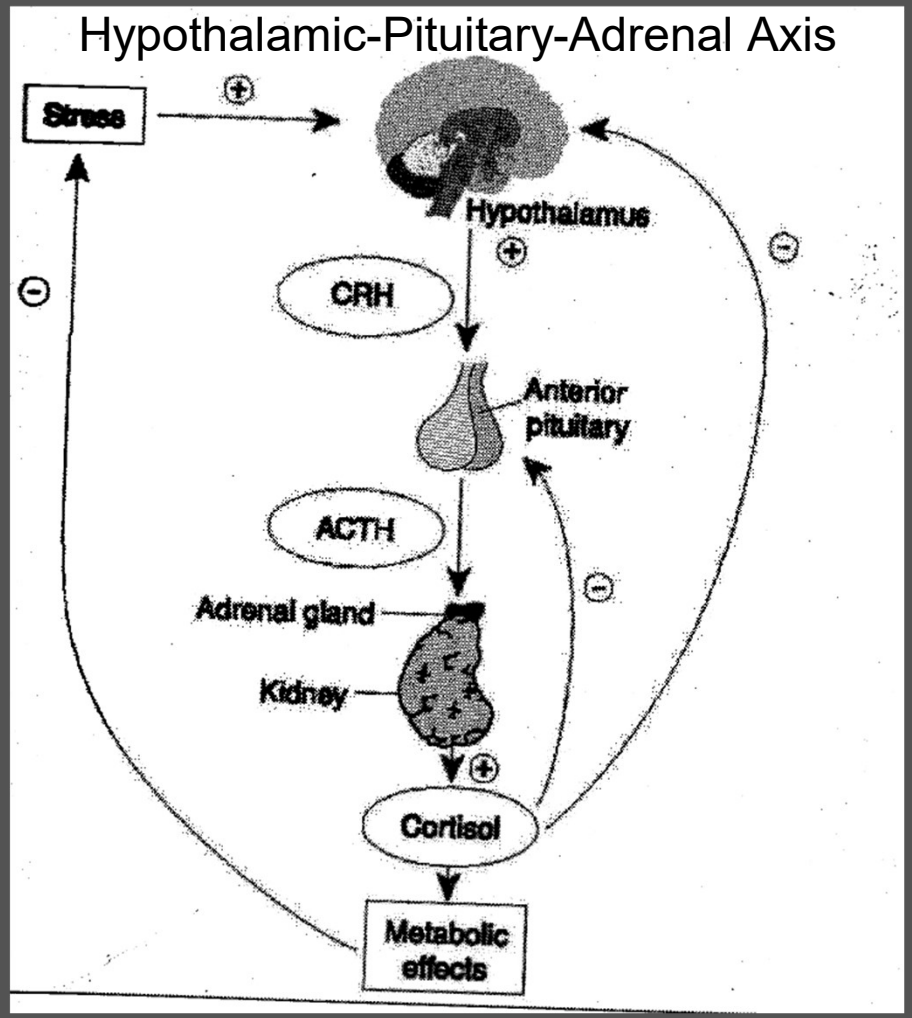
- Epinephrine (adrenaline), norepinephrine (noradrenaline), dopamine
- Activate the body's "fight or flight" responses
  - Increase heart rate and blood flow to muscles, heart, lungs
  - Affect mood

# What pathologies are we looking for in AI workup?

- Too much cortisol (Cushing's syndrome, subclinical Cushing's "mild autonomous cortisol secretion (MACS)
- Too much aldosterone (primary hyperaldosteronism; Conn's syndrome)
- Too much catecholamines (pheochromocytoma)
- Too much sex steroids (very rare and not routinely screen tested unless overt signs/symptoms)
- Cancer

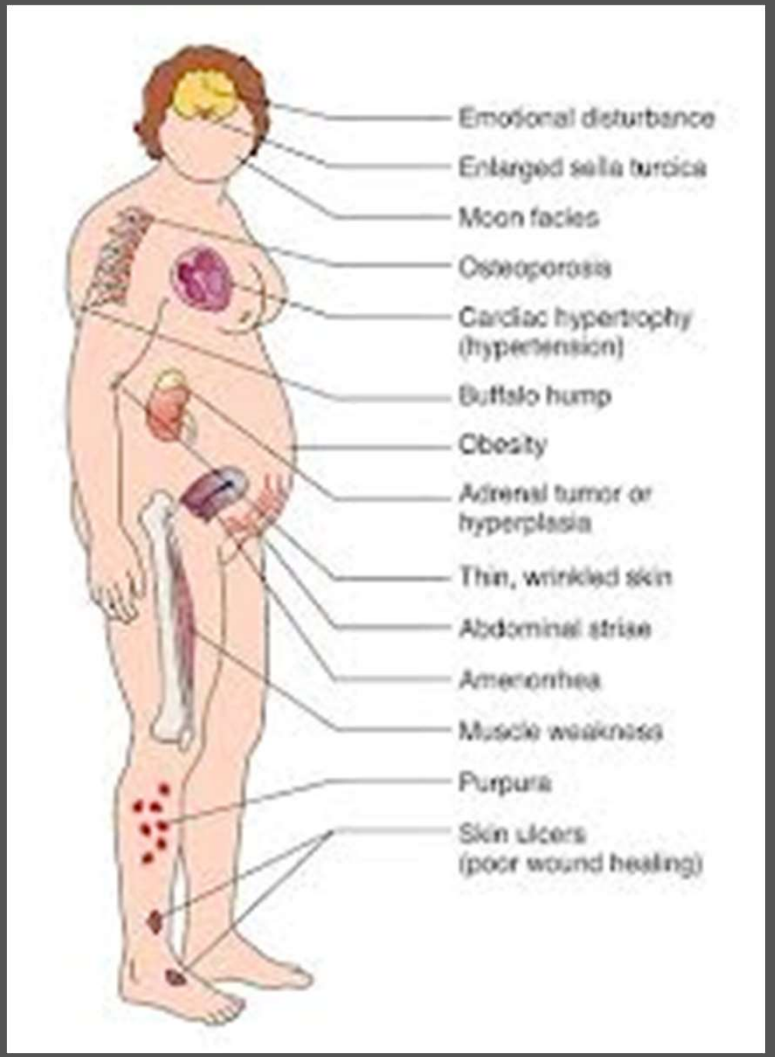
# Cushing's Syndrome (~5% of AI)

- Glucocorticoid excess
- Among endogenous causes:
  - Most commonly ACTH-dependent (82%)
    - Cushing's disease: 70%
    - Ectopic ACTH: 12%
      - Lung Carcinoma: 52%
      - Pancreatic CA: 11%
      - Thymoma: 11%
  - Less commonly ACTH-independent (18%)
    - Adrenal adenoma: 8%
    - Adrenal carcinoma: 6%
    - Bilateral adrenal hyperplasia: 4%



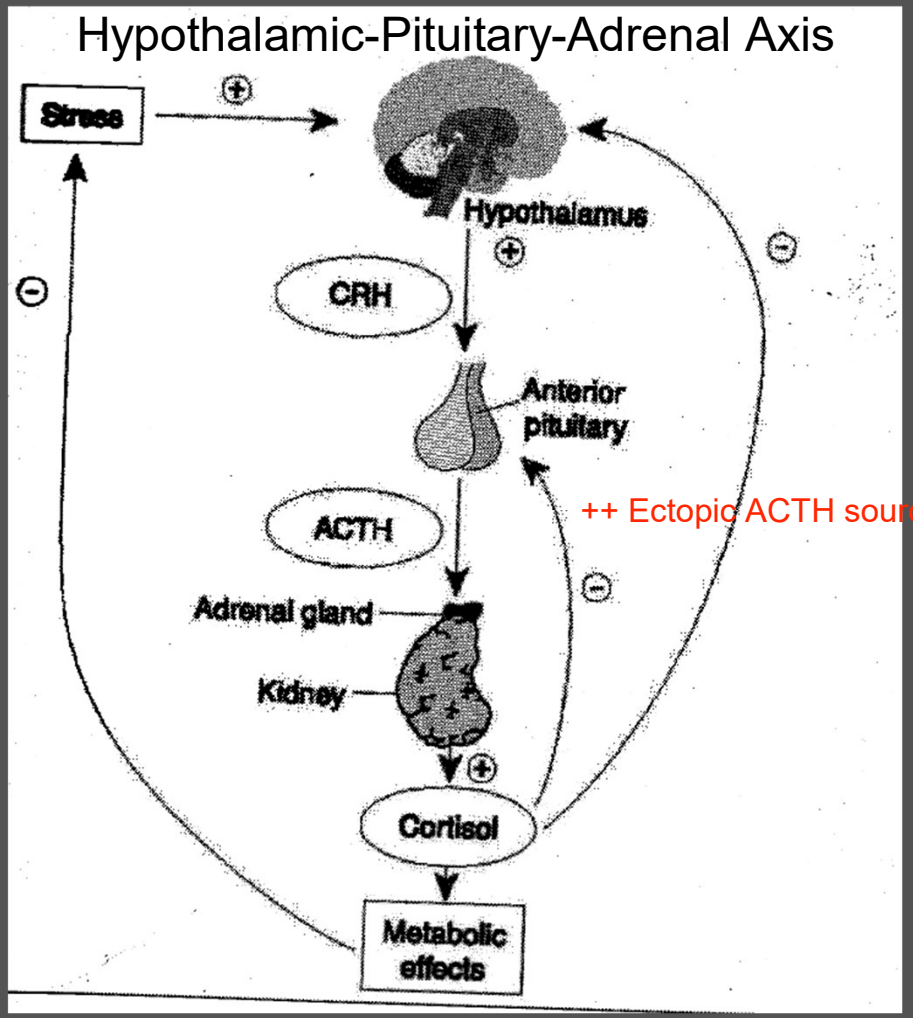
# Cushing's Syndrome

- Clinical signs/symptoms
  - Obesity (90%)
  - HTN (80%)
  - Diabetes (80%)
  - Weakness (80%)
  - Muscle atrophy (70%)
  - Hirsutism (70%)
  - Skin striae (70%)
  - Moon facies (60%)
  - Easy bruising (50%)
  - Acne (50%)
  - Psychological changes (50%)



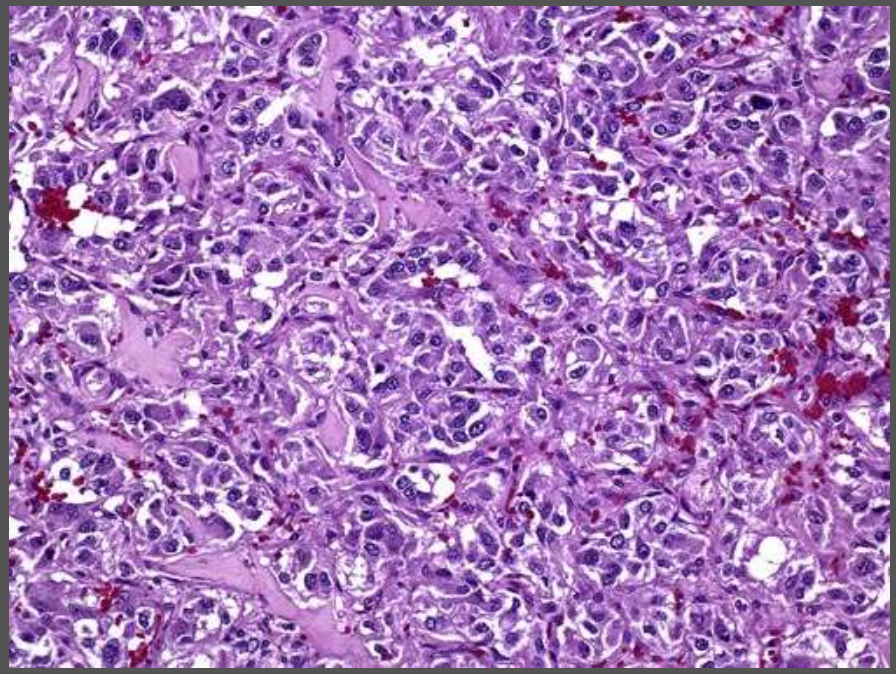
# Diagnostic tests

- Screening
  - Low dose dexamethasone suppression test (1mg at 11pm; am cortisol < 1.8 mcg/dL is normal)
  - Late night salivary cortisol
  - 24 hour urine cortisol
- Confirmatory
  - 24 hour urine cortisol: >100mg/24hrs
  - High dose dexamethasone (8mg) suppression test
  - Cortisol hi/normal and ACTH suppressed in adrenal Cushing's



# Pheochromocytoma (~5% of AI)

- Excess catecholamine secretion
- Classic clinical triad:
  - Headache
  - Tachycardia
  - Diaphoresis
- Hypertension in 90% (paroxysmal, sustained, or both)



# Pheochromocytoma – signs/symptoms

- Tachycardia
- HTN
- Orthostatic hypotension
- Palpitations
- Anxiety/panic attacks
- Excessive sweating
- Head ache
- Weight loss

# Pheochromocytoma – Diagnostic tests

- Plasma free metanephrines (99% sens.) — 3x upper limit of normal
- 24-hour urinary catecholamines (2x normal is diagnostic)
- 24-hour urinary metanephrines: total metanephrines, VMA (vanillyl mandellic acid)

# Primary Hyperaldosteronism (Conn's Syndrome) (~1% of AI)

- Clinical presentation (variable)
  - Hypertension (~100%)
  - Hypokalemia (K<3.0 mmol/L)
  - Often asymptomatic
    - If severe hypoK: muscle weakness/cramps, tetany, headache, polydipsia, paresthesias

# Primary Hyperaldosteronism (Conn's Syndrome)

- Screening tests:
  - Random serum K <3.0 mmol/L
  - Plasma aldosterone >15 ng/dL
  - Aldosterone:renin > 20:1

- Confirmatory testing:
  - Salt load and then measure aldosterone
  - Adrenal Vein Sampling

# Cancer: primary (<<1% of AI)

- Adrenal Cortical Carcinoma
  - Incidence: about 300 cases per year in USA
  - Usually >6cm at presentation.
  - Presentation:
    - Constitutional symptoms
      - Weight loss, malaise, fever
    - 80% are functional; secrete multiple hormones

# Cancer: metastatic

- With known primary cancer and an adrenal mass
  - 50-75% likelihood of metastasis
- Common primaries: melanoma, breast, lung, kidney, colon

# So how do we evaluate AI?

- Imaging
- Labs

# So how do we evaluate AI? IMAGING

- CT
  - Noncontrast: <10HU (“lipid rich”) = benign adenoma (high lipid content)
  - Noncontrast: macroscopic fat (< -20 HU) = myelolipoma (benign, usually no treatment unless “very large”)
  - “Adrenal protocol” — to assess lipid poor lesions (HU>10)
    - Noncontrast followed by contrast (60 seconds) followed by 15 minute delayed
      - No enhancement: benign
      - Enhances with > 60% absolute washout: benign
      - Enhances with < 40% absolute washout: concerning

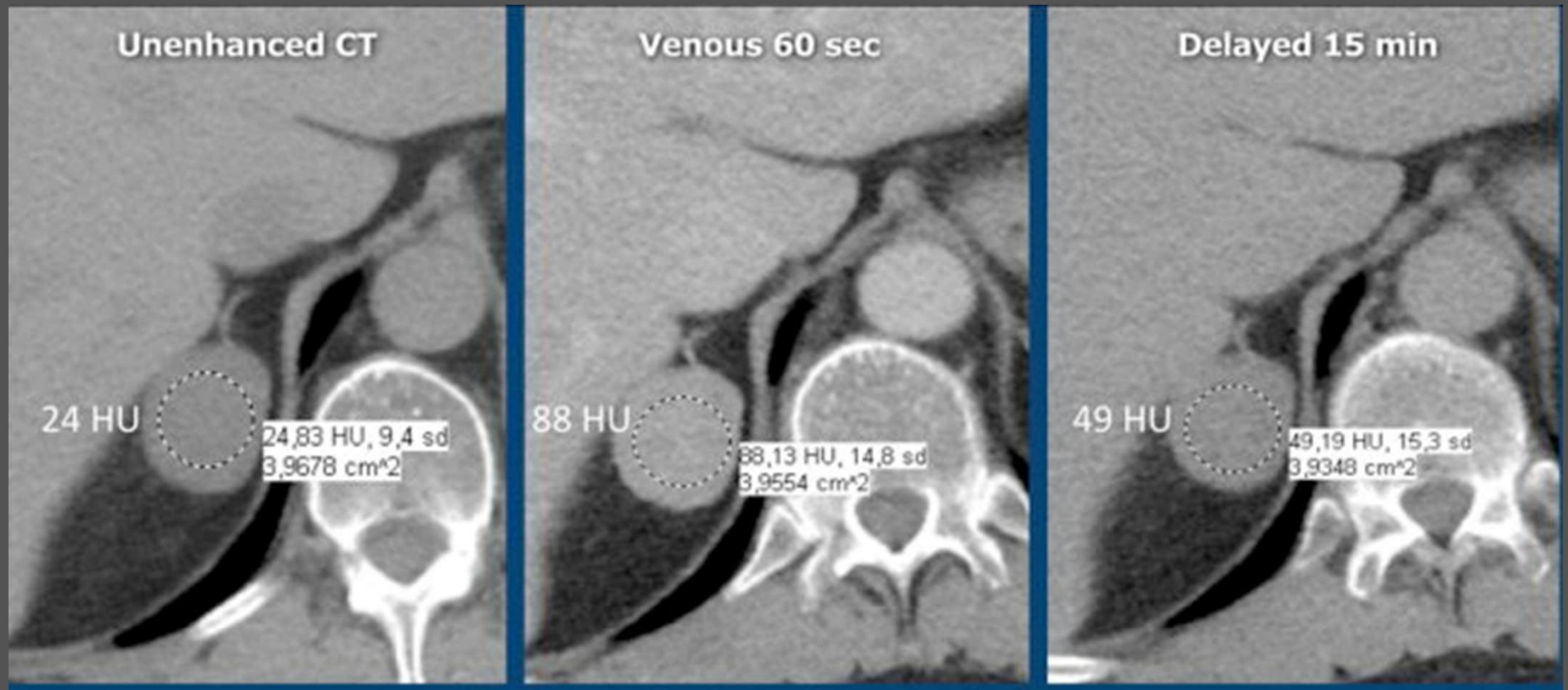
# So how do we evaluate AI? IMAGING

- MRI
  - Chemical shift imaging
    - Low signal on T1 and T2 = adenoma
    - Signal drop out on opposed phase T1 = adenoma
    - Low T1, high T2 = pheo/cyst
    - High T1, low T2 = myelolipoma
  - Contrast enhancement
    - Homogenous enhancement = adenoma
    - Heterogenous enhancement = concerning

# So how do we evaluate AI? IMAGING

- Size and shape
  - 4 cm and smaller = benign
  - > 4 cm = concerning (unless it is an adrenal cyst or macroscopic fat is seen = myelolipoma)
  - Well defined borders = benign
  - Irregular borders = concerning

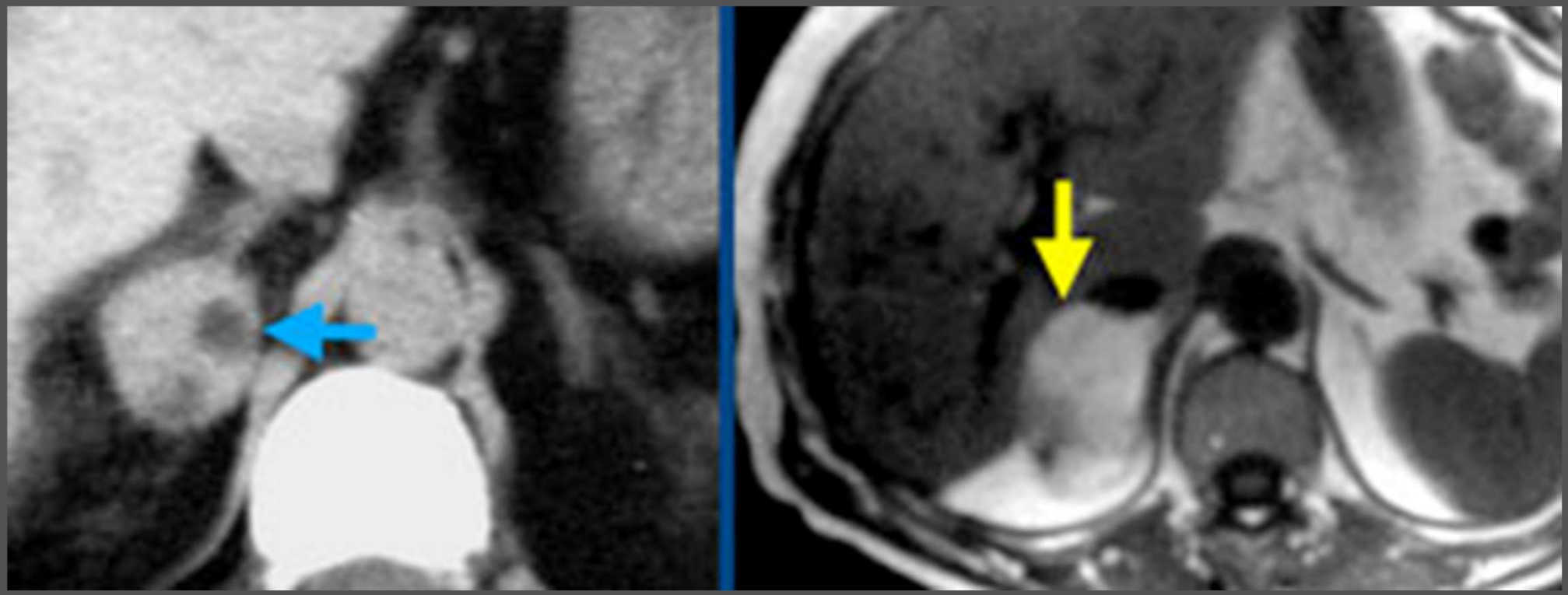
# CT adrenal protocol



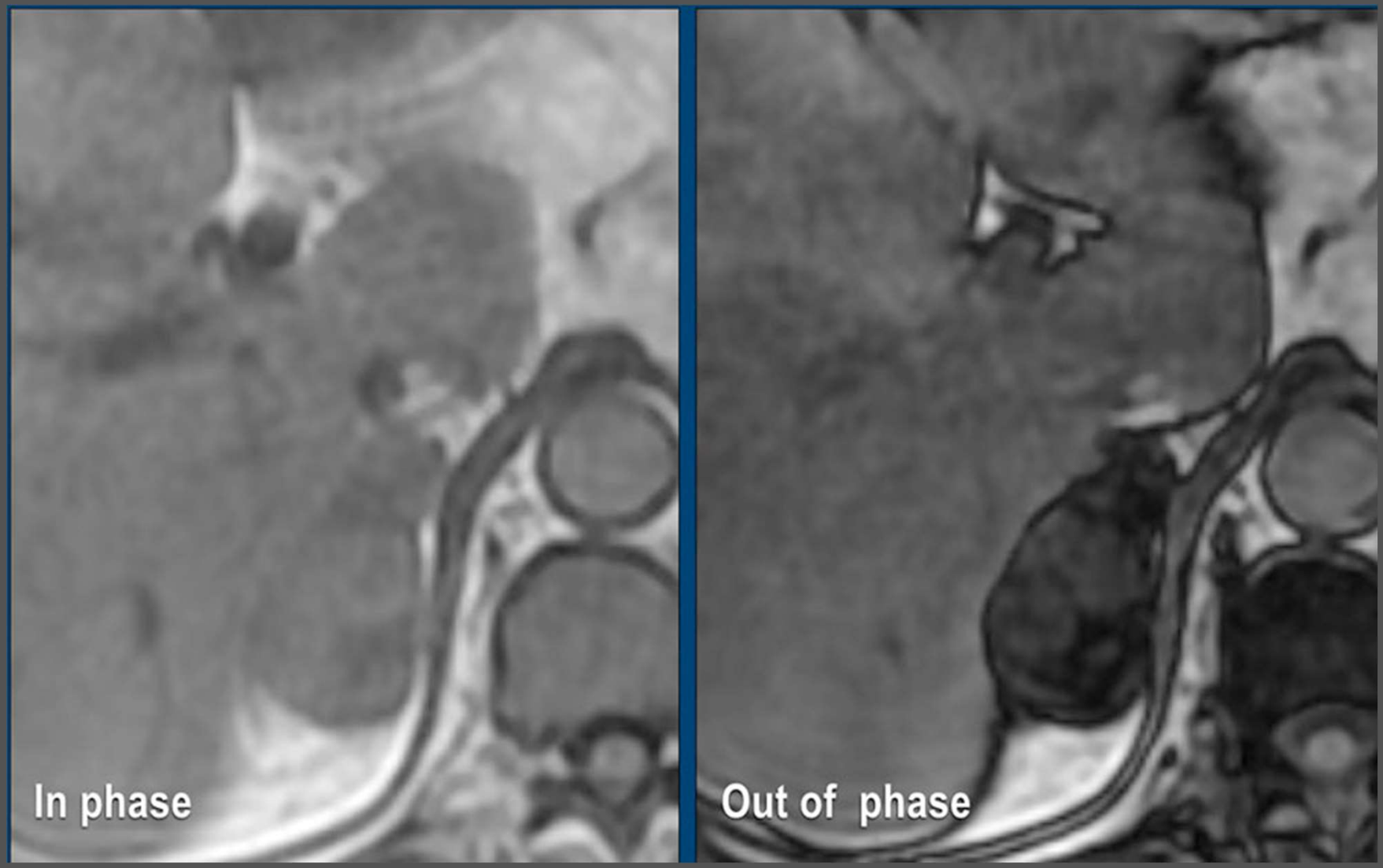

$$\text{Absolute wash out} = \frac{\text{Enhanced CT (HU)} - \text{Delayed CT (HU)}}{\text{Enhanced CT (HU)} - \text{Unenhanced CT (HU)}} \times 100\% = \frac{88 - 49}{88 - 25} = 62\%$$

$$\text{Relative wash out} = \frac{\text{Enhanced CT (HU)} - \text{Delayed CT (HU)}}{\text{Enhanced CT (HU)}} \times 100\% = \frac{88 - 49}{88} = 44\%$$

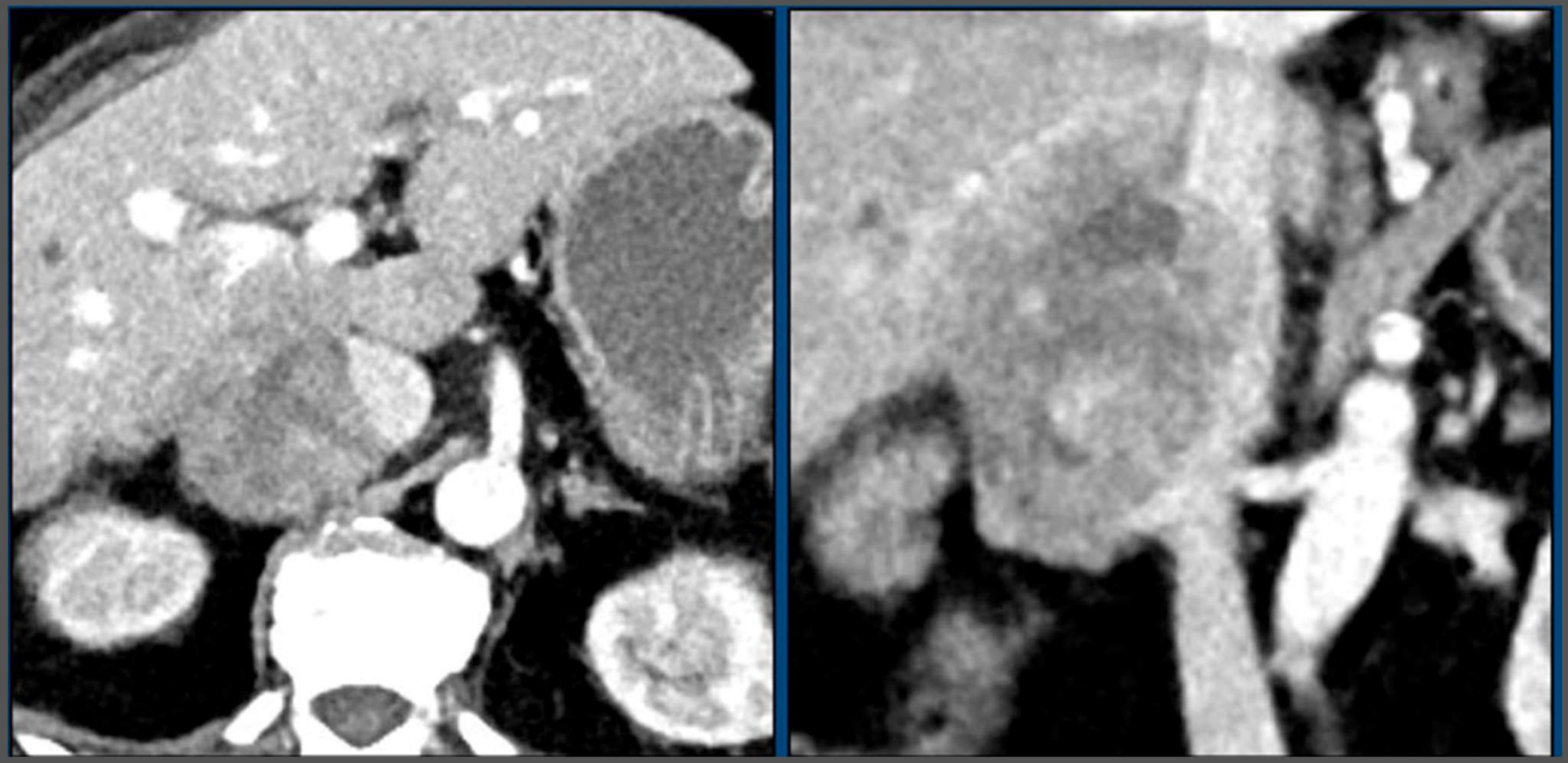
# CT and MRI - myelolipoma



# MRI - adenoma (T1 opposed phase imaging)



# CT - adrenal cortical carcinoma



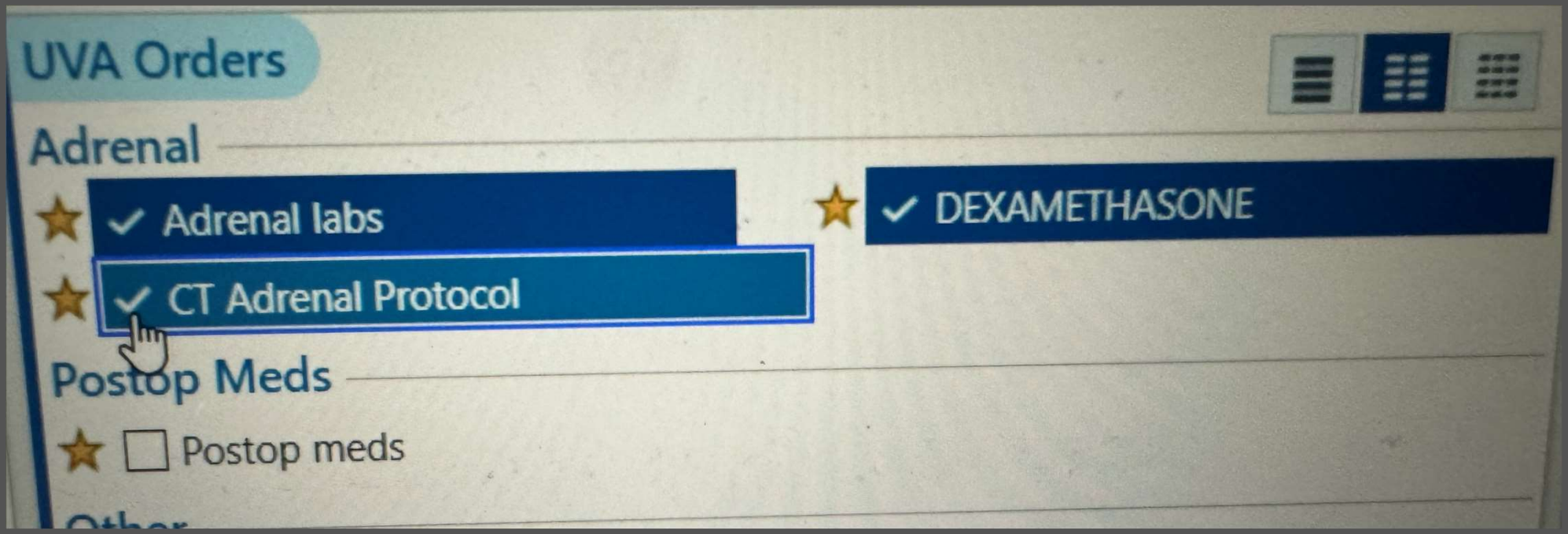
# So how do we evaluate AI? IMAGING

- You don’t need to be a radiologist.  Just read the report and know how to order the correct study for further evaluation.
  - Usually it is a CT adrenal protocol.  If patient can’t get iodinated contrast, then order MRI and w/wo.

# So how do we evaluate AI? LABS

- Primary screening targets:
  - Hypercortisolism
  - Hyperaldosteronism
  - Pheochromocytoma
- Simplest screening lab set:
  - Low dose dexamethasone suppression test:
    - 1 mg dexamethasone at 11 pm. Cortisol the next morning at 8 or 9 am.
  - Aldosterone and renin
  - Plasma metanephrines

# Summary: AI Evaluation



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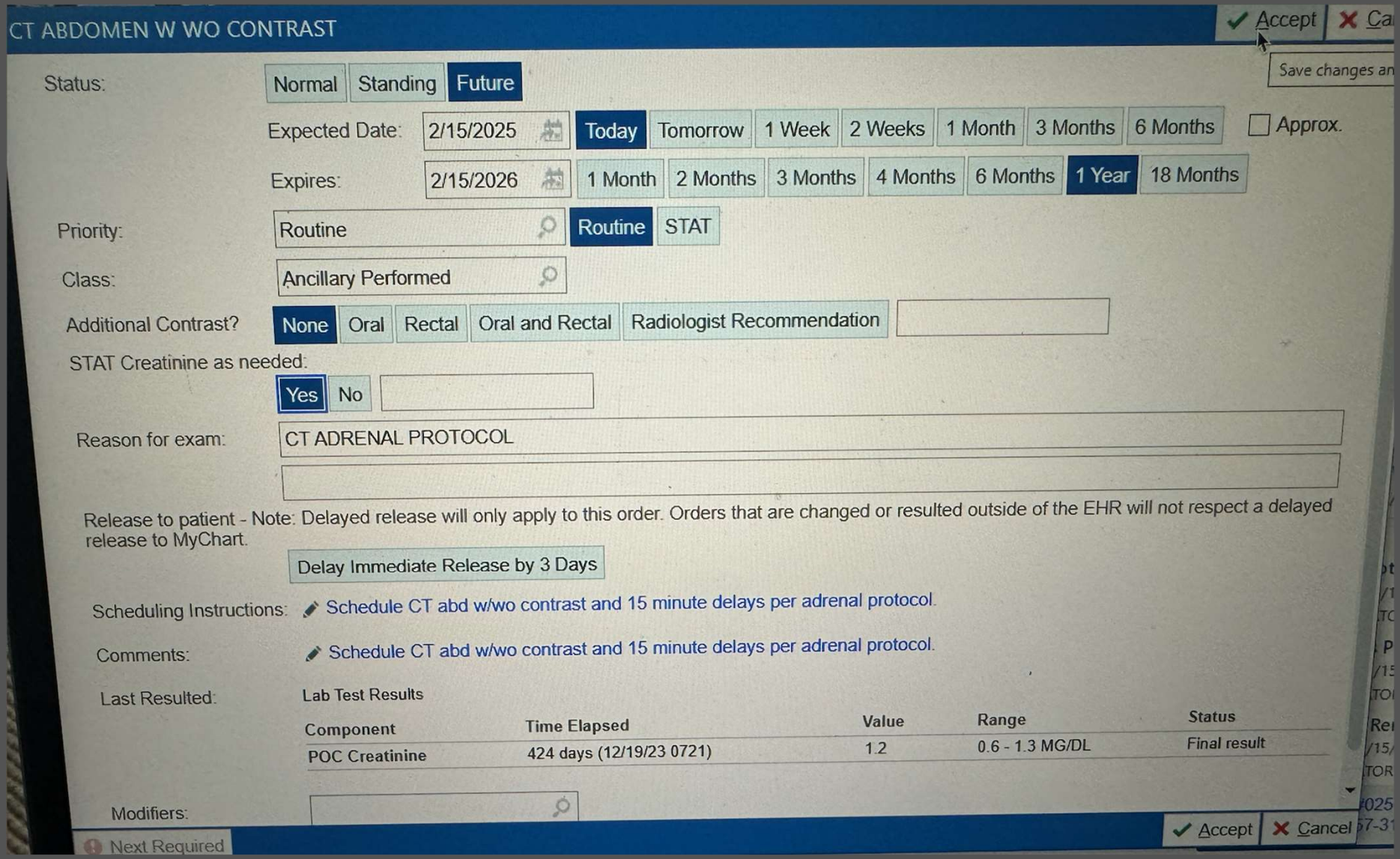

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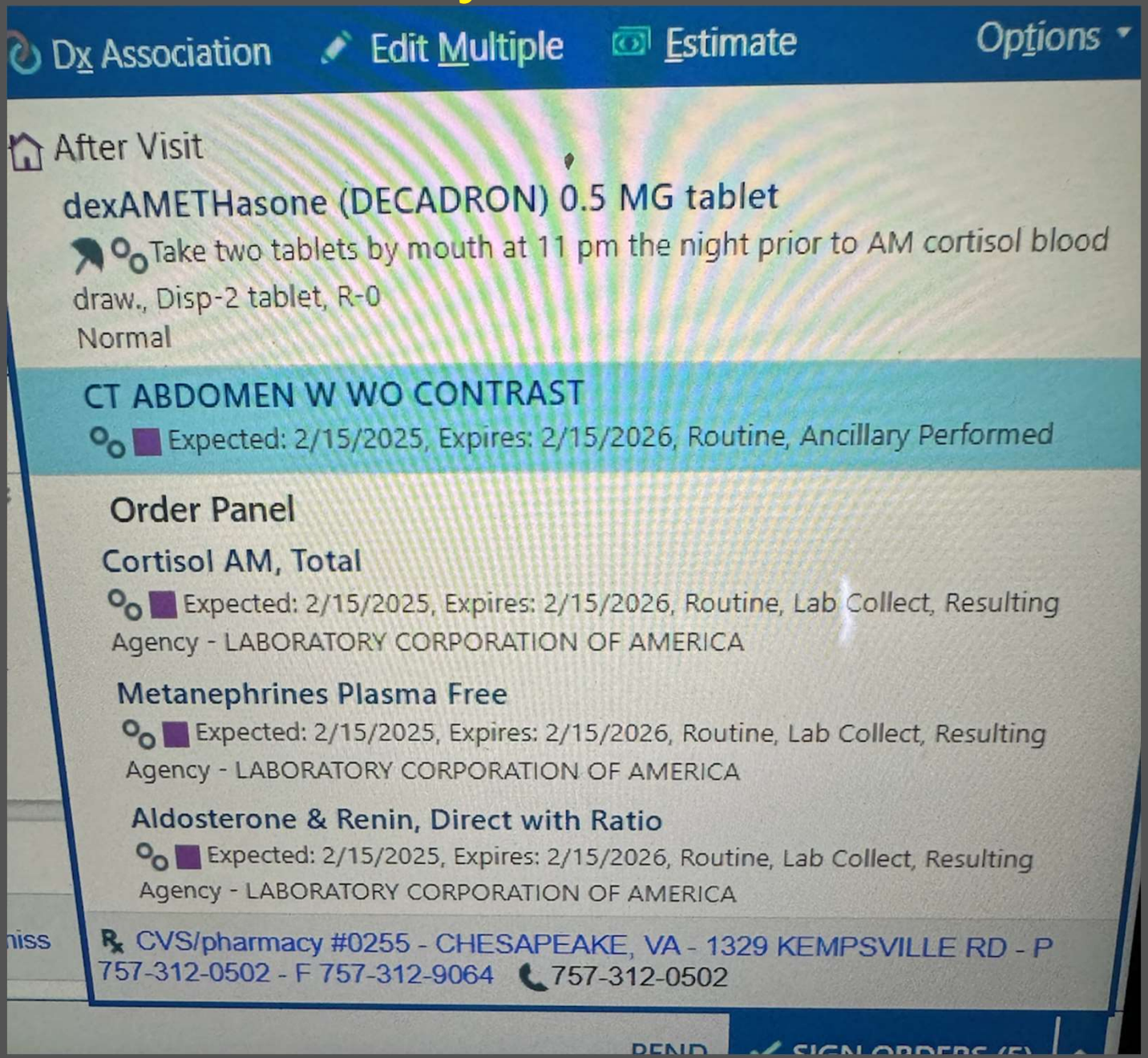

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# Instructions for Adrenal Hormonal Testing

You have been diagnosed with a growth in your adrenal gland.

Usually these are not harmful in any way, but sometimes they can make hormones which can have unwanted effects on your body.

We can test for these with a simple blood draw, but it is very important that you are properly prepared for the day of the blood draw

## Steps

1. Pick up the medication that your doctor prescribed (dexamethasone 1mg) -- it is just one pill!
2. Your doctor may also prescribe a potassium supplement, which you should start taking as soon as you pick it up
3. **4 weeks before** the blood draw: stop taking the following medications
    a. Spironolactone, eplerenone
    b. Amiloride, triamterene
4. **1 week before** the blood draw
    a. If you are on a low-salt diet, return to a normal salt intake
    b. Do not use chewing tobacco or eat licorice
    c. Stop the following medications
        i. Tylenol
        ii. Amitriptyline, doxepin, imipramine, nortriptyline or other "tricyclic" antidepressants -- talk to the doctor who prescribes these to ensure you can stop these safely. If stopping these medications will be unsafe or harmful, alternative forms of testing may need to be considered
        iii. Phenoxybenzamine – ensure your endocrinologist is aware of and approves of this plan
        iv. Oral contraceptive pills (OCPs)- if you are taking these, ask your doctor if you should stop taking them. If you do stop taking these, you should make sure you have a plan for alternative contraception until you can take them again long enough for them to be effective.
5. **The day before** the blood draw
    a. Do not drink caffeine
    b. At 11pm take the dexamethasone pill
6. **The day of** the blood draw
    a. Do not eat or drink anything after midnight
    b. Try to arrive early to your appointment and relax in a seated or lying down position for at least 20 minutes before your blood is drawn
    c. Ensure your blood is drawn before 9:30am

# Interpreting Lab Results

- LDDST: should be less than 1.8 mcg/dL
  - If higher, consider 24 hour urinary cortisol measurement or just refer to urology/endocrine
  - Other tests: HDDST, ACTH
- Aldosterone/renin
  - Aldo > 15 ng/dL and aldo/renin ration > 20:1 is a positive screen
    - Refer to endocrine/urology
    - Confirmatory tests and adrenal vein sampling
- Plasma metanephrines: >2x normal is concerning. Refer to endocrine/urology. Mild elevation is common, esp NE.
    - Confirmatory tests, heart eval for CHF, alpha then beta block and fluid expansion and then surgery

# How does urologist manage?

- Hormonally active --> robotic adrenalectomy (2 hour surgery, 1 night hospital stay, 2 weeks to recovery)
- Hormonally inactive -->
  - Remove if > 4 cm and not a cyst or myelolipoma
  - Remove if imaging o/w concerning for malignancy
  - Otherwise observe
    - Reimage and repeat functional screen at 12 mos (no consensus on timing/duration of follow up but age dependent)

Thank you