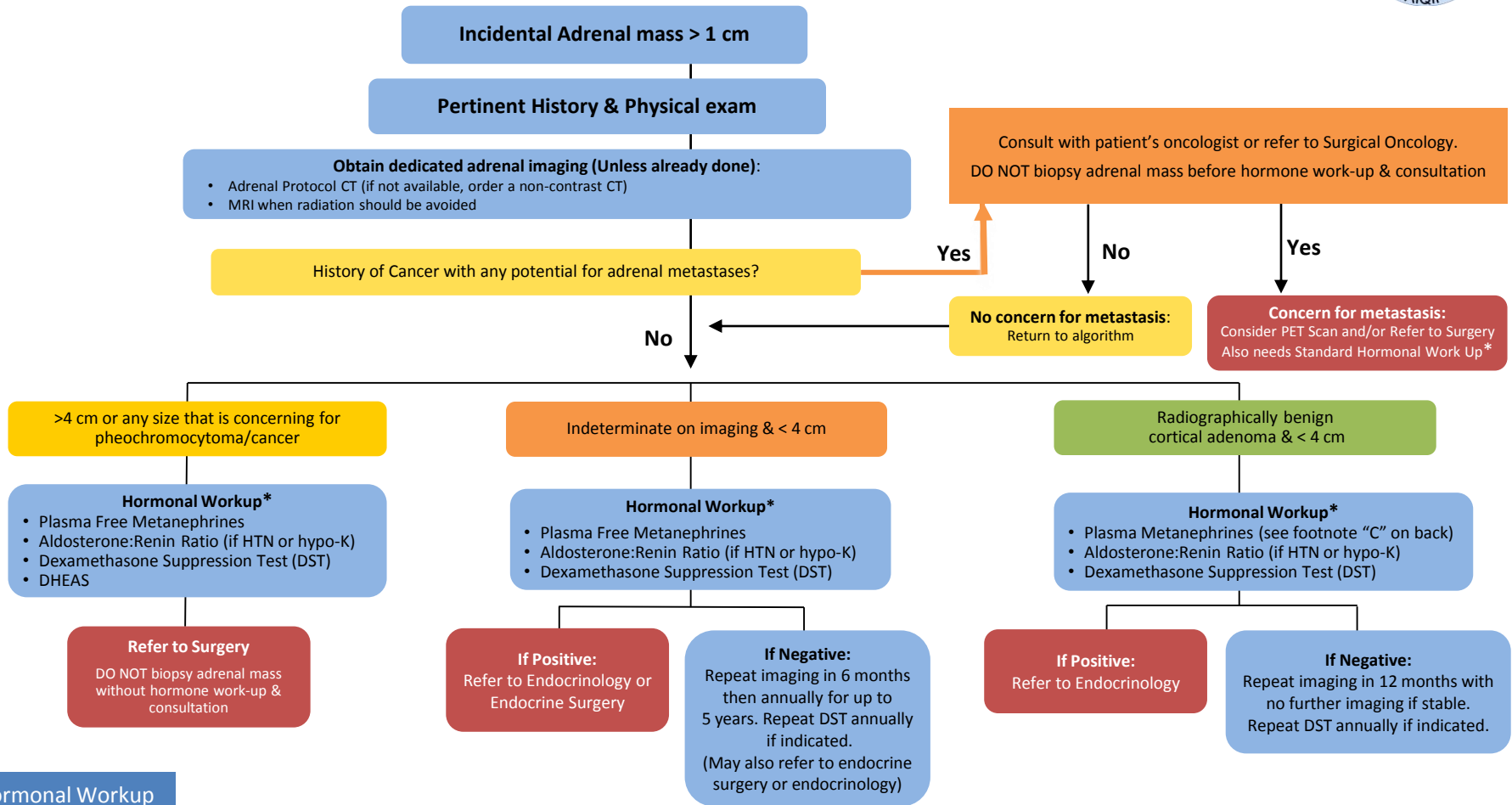


This algorithm is for adrenal masses 1 cm or greater. If a sub-centimeter adrenal mass is noted to be concerning for malignancy or pheochromocytoma, refer for subspecialty evaluation.



***Hormonal Workup**

1. **Plasma free metanephrines** (screen for pheochromocytoma)
 • Considered positive if elevated more than two-fold the upper limit of normal [ULN]. Elevations less than that may be false positives (see other side), and should be considered equivocal.
 • For elevations < twice ULN and no classic signs of pheochromocytoma, confirm with 24-hour urine metanephrines, which are less likely to be falsely positive.
 • For positive results (either plasma free metanephrines or 24 hr urine), refer to Endocrinology or Endocrine Surgery
 • For equivocal results, you may also consider referral.

2. **Aldosterone level and a plasma renin activity (PRA)** *If patient has HTN or a history of hypokalemia.* These must be drawn at the same time. They should not be done with the DST. Divide the aldosterone level by the PRA to calculate the **Aldo:Renin Ratio (ARR)**. If the ARR is > 30 AND the Aldo is > 8, refer to Endocrinology.

3. **Dexamethasone suppression test (DST):** Prescribe 1 mg of oral dexamethasone to be taken at 11 PM. The next morning at 8 AM, a cortisol and dexamethasone level are drawn.
 • If the 8 AM cortisol is less than 1.8 mcg/dL, cortisol excess is ruled out.
 • Cortisol between 1.8 and 5.0 mcg/dL may represent mild cortisol excess:
 • Repeat DST annually for 5 years.
 • If the patient has uncontrolled diabetes, HTN, or early osteoporosis, you may initiate treatment or refer to Endocrinology.
 • Failure to suppress below 5.0 mcg/dL raises concern for cortisol excess. Management will vary depending on the patient. Order a 24-hour urinary cortisol and refer to Endocrinology or Endocrine Surgery.

Incidental adrenal masses are common but require assessment to achieve two main goals:

- 1) Rule out malignancy
- 2) Rule out hormone excess



STANDARDIZED APPROACH TO CLINICAL ENCOUNTER

www.incidentaloma.net

HISTORY

HPI and REVIEW OF SYSTEMS:

- Pertinent to cortisol excess (also known as Cushing's Syndrome): sudden or unexplained weight gain, proximal muscle weakness, easy bruising, history of hard-to-control diabetes or hypertension, early onset or severe osteoporosis or a history of easy fractures.
- Pertinent to aldosterone excess: history of hypertension and/or hypokalemia.
- Pertinent to pheochromocytoma: episodes or "spells" of unexplained anxiety, heart palpitations, tremors, headache, sweating or feeling hot, episodic or severe high blood pressure.
- Pertinent to androgen hormones in women: new onset hirsutism, acne, deepening voice.

PAST MEDICAL HISTORY: In addition to the above, any previous history of cancer

FAMILY HISTORY: Does anyone in the family have a history of adrenal disease, severe hypertension, or unexplained signs/symptoms similar to what was assessed in the HPI/ROS. Is there a history of thyroid cancer (specifically medullary cancer) or of primary hyperparathyroidism or hypercalcemia?

PHYSICAL EXAM

The exam should focus on obtaining vital signs and evaluating for signs of Cushing's such as central obesity with thin extremities, prominent supraclavicular or dorsocervical fat pads (i.e. "buffalo hump"), thick purple striae on abdomen, easy bruising, proximal muscle weakness.

- Aldosterone excess (Conn's Syndrome): difficult to control HTN or low K+
- Androgen excess: Hirsutism, acne, deep voice
- Cortisol excess (Cushing's Syndrome): weight gain, proximal muscle weakness, bruising, HTN
- Pheochromocytoma: anxiety, heart palpitations, tremors, severe headaches, severe HTN

LABORATORY TESTING

See Hormonal Workup (front) to evaluate for cortisol excess, aldosterone excess, pheochromocytoma, and androgen excess. DHEAS only needs to be checked in setting of potential androgen excess or potential adrenocortical cancer. Benign adrenal adenomas can autonomously produce cortisol resulting in Cushing's syndrome or they can autonomously produce aldosterone resulting in primary aldosteronism and hypertension and/or hypokalemia. Non-adenomas, indeterminate lesions and adrenal cancer can produce these same hormones as well as adrenal androgens. Masses that produce more than one kind of hormone should raise suspicion for cancer. Pheochromocytomas hyper-produce catecholamines, and their breakdown products are metanephrines, which can be measured by blood and urine tests.^C

IMAGING

Non-contrast CT provides the best discrimination between malignant lesions and benign adenomas which have low CT attenuation (< 10 HU). Adrenal Protocol CT starts with a non-contrast CT and if the mass is > 10 HU, a specific IV contrast washout procedure is done. The standard CT scan with IV contrast, cannot discriminate benign from malignant lesions. If radiation should be avoided (as in children or young women) then MRI can be used. Adrenal lesions that are NOT adenomas or are classified as indeterminate include pheochromocytomas, primary adrenal carcinoma, metastases from other primary malignancies, and other, less-concerning lesions (for example, myelipoma).

NEXT STEPS

[See flowchart on other side]

1. If a patient has a history of previous cancer, consider a PET scan, but DO NOT biopsy a mass until discussed with an adrenal surgeon or the patient's oncology provider. After discussion with oncology provider, if concerned for metastasis, perform hormonal work-up and consider referral to Endocrine Surgery.^A
2. If the lesion is a benign adenoma radiographically (< 10 HFU), is < 4 cm, is hormonally inactive, and has not changed significantly from any previous scans (if there are any), the work-up is complete. Repeat imaging/labs in 12 months and for no more than 5 years if no changes over time.^B
3. If the history or exam are concerning for adrenal disease, or if the laboratory work-up reveals abnormal findings, refer to Endocrinology or Endocrine Surgery.
4. Small (<4 cm), radiographically indeterminate adrenal masses that are not hormonally active may be referred to Endocrinology or Endocrine Surgery. You may also choose to follow these yourself. They should have follow-up imaging at 6 months, 12 months, and then yearly for 5 years. **For growth of more than 20%, referral to Endocrinology or Endocrine Surgery is advised.**
5. For a lesion > 4 cm (unless there is past imaging to suggest several years of stable size/appearance), perform standard hormonal workup and also refer to Endocrine Surgery.

The information contained herein is not intended to be a substitute for your medical judgment. This is one standardized approach based on best available evidence, but it may need to be altered for mitigating clinical circumstances. We encourage you to reach out to BMC Endocrine Surgery or Endocrinology if you feel that subspecialty evaluation is necessary.

Footnotes

- A. Biopsy is almost never necessary for management of an adrenal mass. Biopsy cannot distinguish between a benign adrenal adenoma and an adrenal carcinoma and the biopsy tract may be seeded with cancerous cells if adrenal carcinoma is inadvertently biopsied. Inadvertent biopsy of a pheochromocytoma could cause a life threatening hypertensive crisis. In general, a decision to biopsy should be made jointly between the adrenal surgeon and oncology provider and ONLY after pheochromocytoma has been ruled out.
- B. Previous guidelines called for labs/imaging annually for 5 years. Newer guidelines call for no further surveillance if the lesion meets radiographic criteria for a benign adenoma AND there is no excess hormonal activity. In our practice, one follow-up study is generally pursued. If clinical signs/symptoms develop, the workup should be repeated.
- C. Tests for pheochromocytoma including 24 hour urine metanephrines and plasma metanephrines may generate false positive results. Certain medications are likely to cause slightly elevated metanephrines including: **tricyclic antidepressants** and derivatives such as trazadone and flexeril; **serotonin reuptake inhibitors** such as venlafaxine, and **sympathomimetics** including cocaine, phentermine, amphetamines, Sudafed and albuterol. Please note that a lesion with imaging characteristics of benign adenoma is unlikely to be a pheochromocytoma.