a. Perform Bilateral Inferior Petrosal Sinus Sampling (IPSS) with concurrent blood sampling for ACTH in the Right and Left inferior petrosal sinus and peripheral vein.

b. An increased central/ peripheral plasma ACTH ratio \( >2 \) at baseline and \( >3 \) at 2-5 minutes after CRH is INDICATIVE of Cushing’s disease--- very high sensitivity and specificity.

*** IPSS cannot be reliably used for lateralization (prediction of location of the tumor within the pituitary) --- Because there is broad interindividual variability in the venous drainage of the pituitary region.

*** IMPORTANT: NO CORTISOL-LOWERING AGENTS should be used prior to IPSS.

- If the differential diagnostic testing indicates ECTOPIC ACTH SYNDROME:
  a. Further imaging should include high-resolution, fine-out CT scanning of the chest and abdomen for evaluating the lung, thymus and pancreas
  b. If NO LESIONS IDENTIFIED:
     1. MRI of the chest can be considered because carcinoid tumors usually show high signal intensity on T2-weighted images
     2. Octreotide scintigraphy can be helpful—Ectopic ACTH-producing tumors express somatostatin receptors

- In ACTH-independent disease:
  a. Treatment consists of surgical removal of the adrenal tumor
     1. Smaller tumors: minimally invasive approach
     2. Large tumors and suspected of malignancy: open approach

- In cushing’s disease
  a. Treatment of choice: selective removal of the pituitary corticotrope tumor--- via an endoscopic transphenoidal approach--- cure rate of 70-80%
  b. Long term follow up is important: may recur late.
  c. If recurs:
     1. 2nd surgery
     2. Radiotherapy
     3. Stereotactic radiosurgery
     4. Bilateral adrenalectomy

- Patients with very severe overt Cushing’s (Difficult to control hypokalemic Hypertension or acute psychosis):
  a. Introduce medical treatment to rapidly control the cortisol excess during the period leading up to surgery

- Patients with metastasized, glucocorticoid- producing carcinomas:

- Ectopic ACTH-syndrome (tumor cannot be located):
  c. Undergo blood sampling for fasting gut hormones, chromogranin A, calcitonin, biochemical exclusion of pheochromocytoma

TREATMENT: