MKSAP 17 Endocrine

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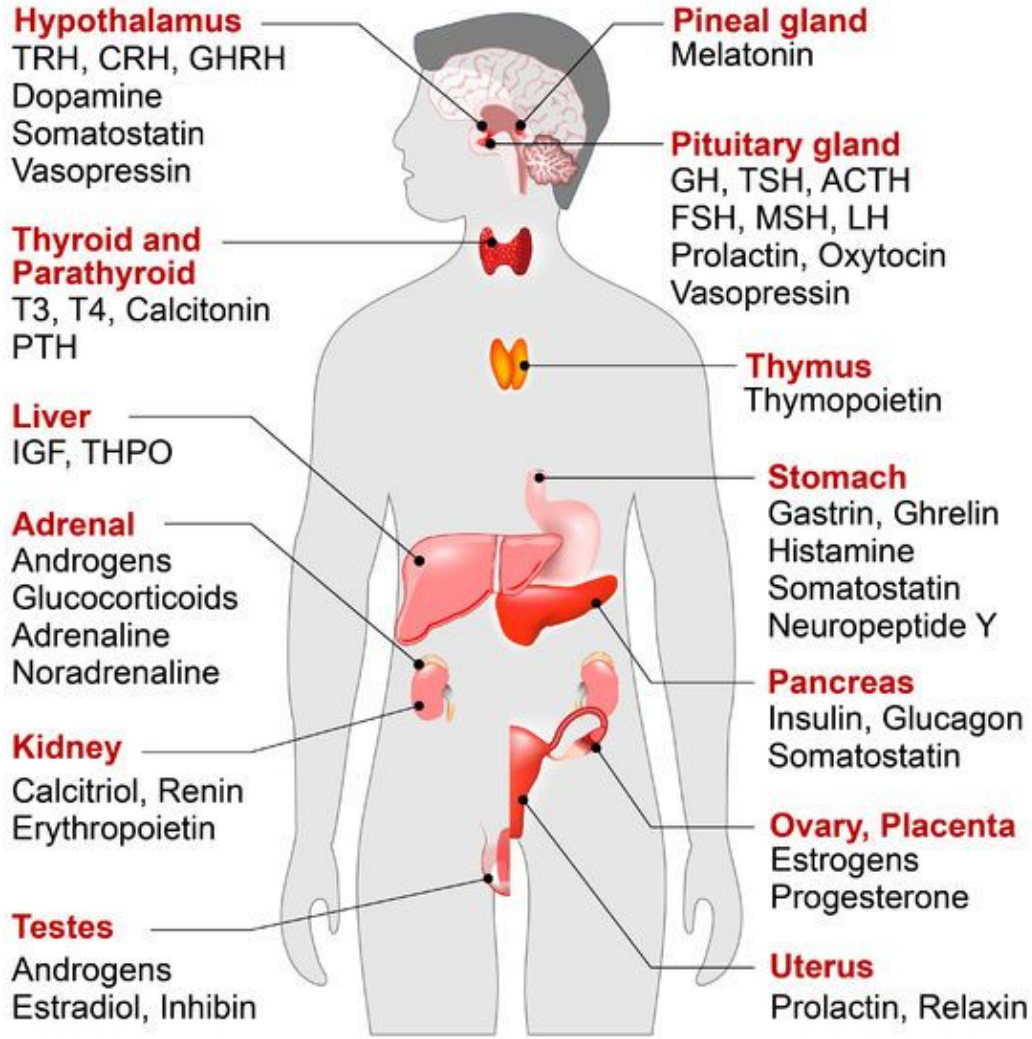
HORMONES



Q#2 Answer C

Diagnose the multiple endocrine neoplasia type 2 (MEN2) syndrome

<u>MEN2A</u>

1. Medullary thyroid cancer
2. Pheochromocytoma
   - usually benign and intra-adrenal in location, but can be multiple or bilateral
3. Primary hyperparathyroidism (due to multiple gland ***hyperplasia***)
   - Sx: polydipsia, polyuria, and constipation 2/2 hyperCa (or nephrolithiasis)

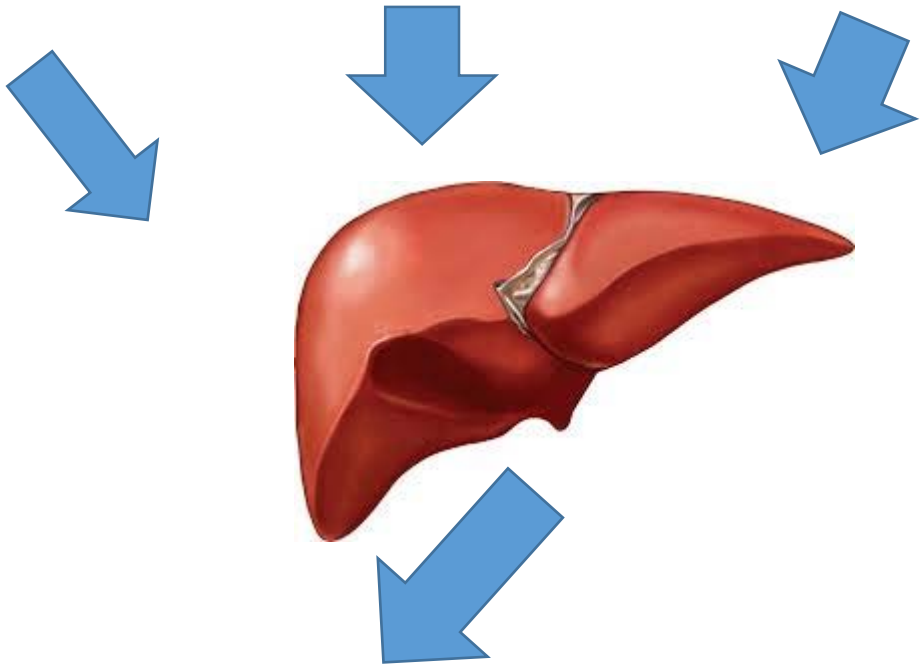
- MEN1: Insulinoma, prolactinoma, primary hyperparathyroidism (due to one or more parathyroid ***adenomas)***

MEN2A	MEN1	MEN2B	Neurofibromatosis type 1
Medullary thyroid cancer Pheochromocytoma Primary Hyperparathyroidism (hyperplasia)	Insulinoma Prolactinoma Primary Hyperparathyroidism (adenomas)	Medullary thyroid cancer Pheochromocytoma Mucosal neuromas and intestinal ganglioneuromas Often Marfanoid Skeletal abnormalities	Neurofibromas Café-au-lait spots Pheochromocytoma

Q#4 Answer D
Manage overnight hypoglycemia

- Somogyi effect (rebound hyperglycemia)
  - 2/2 release of compensatory hormones in response to prolonged nocturnal hypoglycemia from overtreatment or physical exertion
  - Not accepted by all physicians 2/2 questionable clinical significance
- Dawn phenomenon
  - Hyperglycemia not covered by insulin
- Don’t change meds until you know what’s happening

Catecholamines Cortisol Growth hormone



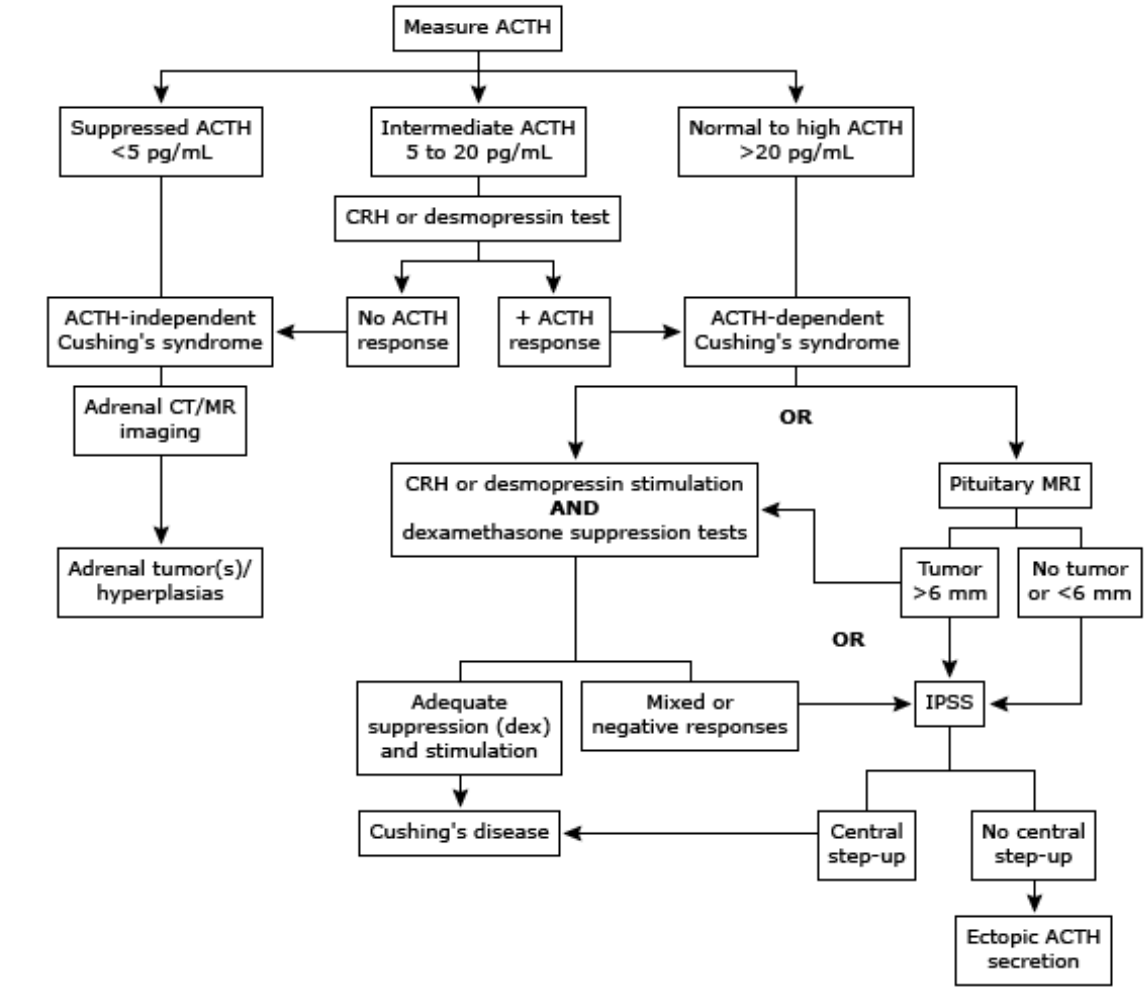
Gluconeogenesis

Q#5 Answer A
Evaluate the cause of Cushing syndrome

- Two abnormal screening tests for CS
  - Low-dose dexamethasone suppression test (LDST) (both standard and overnight)
  - Late night salivary cortisol
  - 24-hour urine free cortisol (UFC)
    - Confirm repeat collection

- Measure ACTH
  - If >20, usually ACTH-dependent
  - If low, ACTH-independent

Testing to establish the cause of Cushing's syndrome*



ACTH: corticotropin; CRH: corticotropin-releasing hormone; CT: computed tomography; MR: magnetic resonance; MRI: magnetic resonance imaging; dex: dexamethasone; IPSS: inferior petrosal sinus sampling.

* Testing can only be interpreted in the context of sustained hypercortisolism and may be inaccurate with cyclic hypercortisolism.

Q#6 Answer D
Manage ketosis-prone type 2 diabetes mellitus

- Ketosis-prone type 2 diabetes
  - Do not have classic autoimmune Type 1 phenotype; require insulin initially
  - Older, overweight/obese, Black or Latino
  - +/-autoantibodies, +/-pancreatic beta cell function

- Fasting C-peptide, glucose checks pancreatic beta-cell function
  - Measure 7 -14 days after acidosis correction (effects of prolonged hyperglycemia are toxic), Can also do glucagon-stimulated C-peptide
  - If repeat greater than or equal to 1.0 ng/mL (0.33 nmol/L) or glucagon-stimulated C-peptide value is greater than or equal to 1.5 ng/mL (0.5 nmol/L), beta cell function is preserved

- SSI without basal causes wide swings
- Switch to metformin only if he has preserved beta cell function and monitor closely
- Antibodies tell you if he is likely to become insulin dependent in future but don’t need to retest

Q#16 Answer A
Treat subclinical hypothyroidism

- +FAM Hx hypothyroidism and anti-TPO increase likelihood of progression to overt thyroid failure
- OK to start levothyroxine rx if TSH mildly elevated (Up to10 µU/mL), **if symptoms**
- RAIU: Hyperthyroid
  - Graves = high
  - Thyroiditis or exposure to exogenous thyroid hormone= low (<5%)
  - If unavailable/contraindicated (pregnancy and breastfeeding), measure thyroid-stimulating immunoglobulins (TSIs) (Graves)

- Up to 30% abnormal TSH will normalize on retest. This patient has persistent elevation of TSH and symptoms, so waiting 12 months not appropriate.

Q#21 Answer A
Evaluate triiodothyronine (T_3) hyperthyroidism

- T3
  - measure in all pts with suspected thyrotoxicosis
    - High T_3 , normal free T_4
  - Don't measure in **hypo**thyroidism (T_3 conserved and may remain normal, even with significant hypothyroidism)
- Determining **TPO** antibodies = Hashimoto's thyroiditis. Check if mildly elevated TSH (**hypo**thyroid)
- Repeating TFTs in 6 weeks may be appropriate if the total or free T_3 level is normal. If T_3 normal= subclinical hyperthyroidism
- Neck US if nodule (this patient diffusely enlarged thyroid) In addition, even if the physical examination were suggestive of nodular disease, the first step would be evaluation of the functional thyroid status

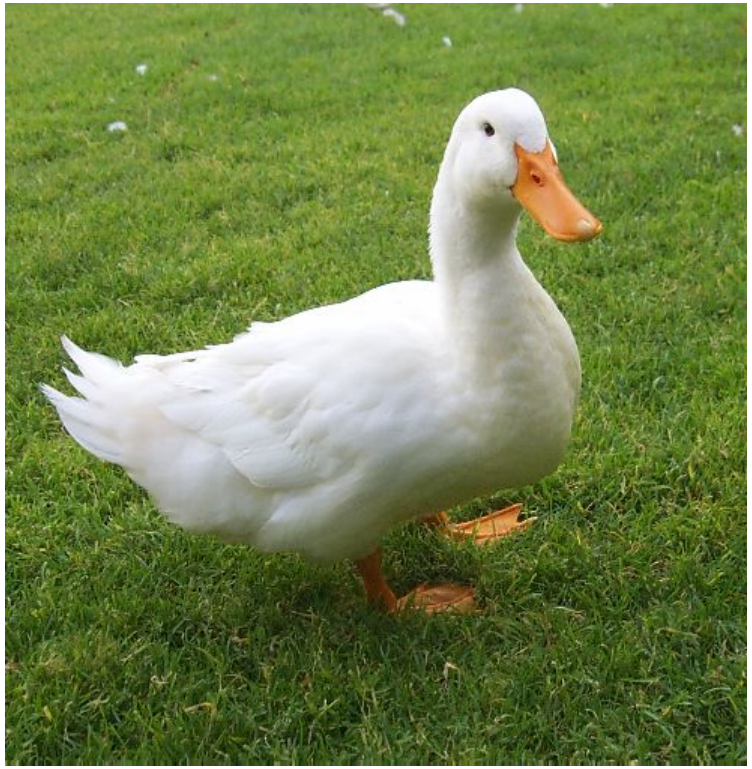
Q#23 Answer D
Diagnose Cushing syndrome from exogenous glucocorticoids

- Cushing syndrome
  - pituitary adenoma (Cushing disease)
  - adrenal tumor cortisol production
  - ectopic ACTH excessive use of glucocorticoids

  - Exogenous glucocorticoid use as a cause of Cushing syndrome is common, whereas the other causes are rare

If it looks like a duck and walks like a duck and quacks like a duck….

Then it’s probably a duck!



Q#30 Answer C
Identify hemochromatosis as a cause of hypogonadotropic hypogonadism

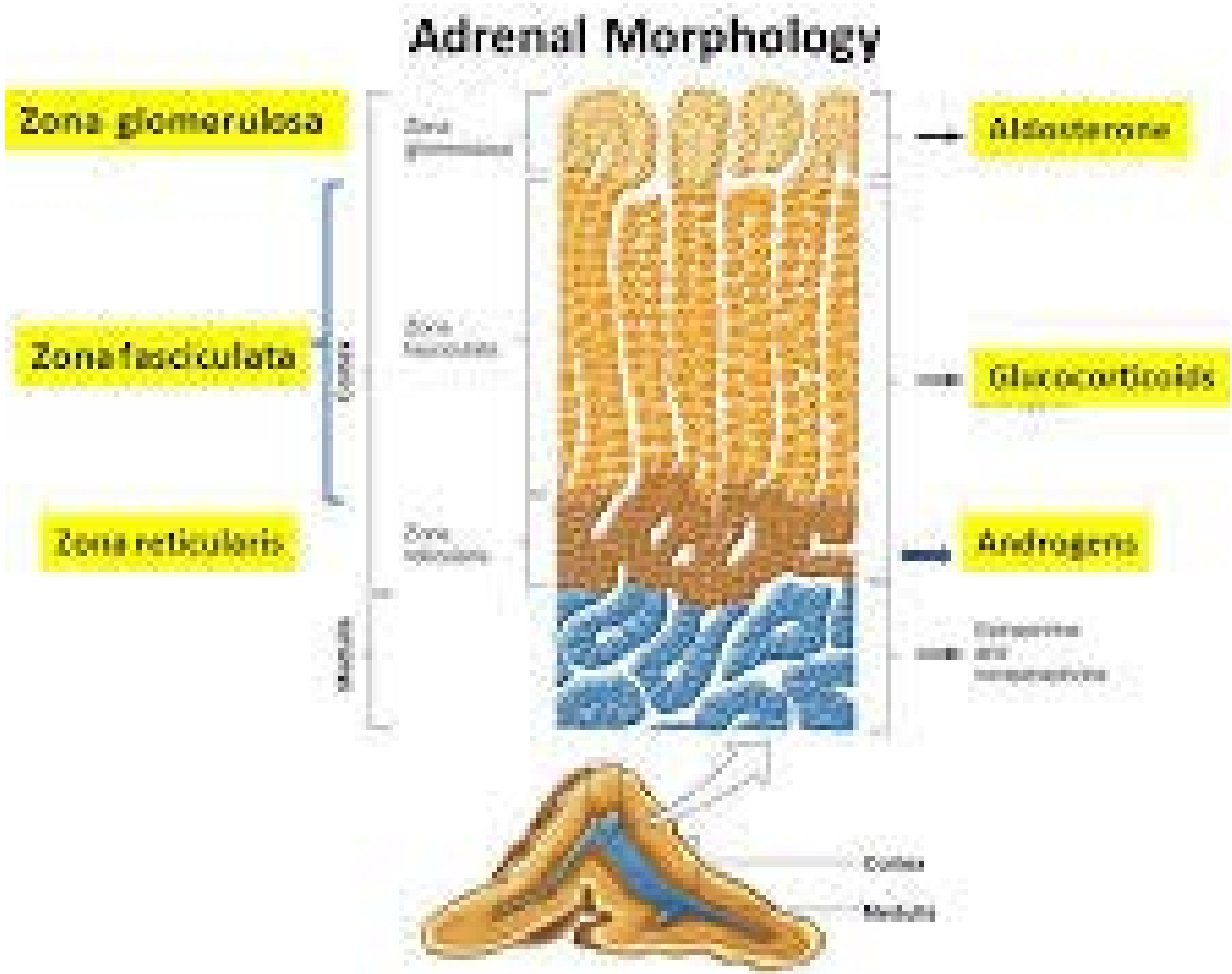
- Check transferrin saturation and ferritin levels for hemochromatosis (arthralgia, hepatomegaly)
  - decreased libido, erectile dysfunction, and low AM testosterone= hypogonadism
  - Low LH and FSH= **hypogonadotropic (hypothalamus or pituitary)** etiology .
    Causes: infiltrative (hemochromatosis, sarcoidosis, cancer metastatic to the pituitary, lymphoma, other large pituitary tumors)
  - Don't start testosterone until you figure out bigger picture
  - Klinefelter syndrome (47,XXY) may cause hypogonadism, patients with this syndrome have **hyper**gonadotropic hypogonadism (High LH and FSH)
- Testicular US – for **primary** testicular failure

Q#44 Answer D
Manage primary adrenal failure

- Primary adrenal failure= all hormones of adrenal cortex =need both glucocorticoid (GC) and mineralocorticoid (MC) replacement
- Prednisone 5 mg = physiologic GC replacement dose
- Fludrocortisone 0.05 to 2 mg = almost pure MC replacement
- Hydrocortisone has both GC and MC (**mostly** GC at physiologic replacement dose)
  - 12.5 to 25 mg in two to three divided doses daily
  - Not enough MC until above 50 mg daily Don't forget additional glucocorticoid at times of physiologic stress!

- Need SDS (stress dose)
  - **minor** (URI, fever, minor surgery under local) 2-3 times the basal dose of hydrocortisone (or equivalent)
  - **moderate** (minor or moderate surgery with general) usually 45 to 75 mg/day
  - **major** (major surgery, trauma, critical illness, or childbirth) up to 150 to 200 mg/day with gradual taper

Adrenal Morphology



Q#45 Answer C
Diagnose primary thyroid lymphoma

- Elderly women with long-standing Hashimoto's
- **Rapid onset (weeks)** of enlarging goiter, weight loss, night sweats
- Order CT scan neck, not US, 2/2 compressive symptoms and positional breathing issues (assess patency of the trachea)
- New-onset **Graves unlikely** (age, long-standing hypothyroidism, no bruit or clinical signs of Grave's, and thyromegaly is not acute onset in Grave's)
- **Papillary thyroid cancer-** very slow growing, typically not diffusely enlarged (distinct nodule +/- cervical lymphadenopathy)
- **Subacute (de Quervain) thyroiditis** = acute onset anterior neck pain.
  - following a viral illness in the preceding months
  - patchy infiltrate with minimal LAN on CT

Q#49 Answer A
Treat an obese patient with type 2 diabetes mellitus with bariatric surgery

- BMI 35-40 *and* complications associated with obesity
- This pt: advanced microvascular disease, hypertension, hyperlipidemia, OSA, GERD, and OA. Diet and exercise attempts unsuccessful
- Increasing insulin could increase hypoglycemia (and he's unaware) and weight gain
- Metformin contraindicated in men with a serum creatinine level above 1.5 mg/dL
- Pramlintide slows gastric emptying, which can decrease appetite
  - Modest weight loss, may not be sufficient, and can worsen hypoglycemia

Q#52 Answer A
Diagnose an androgen-producing adrenal tumor

- 50% benign adenomas, 50% malignant
- Men may have NO symptoms, Women:**rapidly progressive** androgen excess (acne, hirsutism, and virilization- deepening of the voice, clitoromegaly, and male-pattern hair loss), irregular menses.
- Check labs before imaging: testosterone and DHEA-S
  - Ovarian tumor= high testosterone (more than 150-200 mg/dL)
  - Adrenal tumor=high DHEAS (testosterone may be increased d/t conversion) DHEAS above 8 µg/mL are diagnostic

- No Low-dose DST or pituitary MRI- Cushing syndrome unlikely (normal 24-hour urine free cortisol and no signs on PE)
- Pelvic US not appropriate initial imaging test (PCOS only mild elevation of DHEAS)

Q#55 Answer C
Manage a patient with pheochromocytoma

- Preoperative α-blockade (phenoxybenzamine) for BP control and decrease CV complications related to excessive catecholamine release during intraoperative manipulation of the tumor (so rx even if normotensive)
- Rx for 1 to 2 weeks before surgery, target BP <130/80 mm Hg seated and systolic >90 standing, HR 60-80.
- Phenoxybenzamine SE: orthostasis, nasal stuffiness, fatigue, and retrograde ejaculation OK to use short-acting (prazosin, doxazosin, or terazosin)
- If tachycardia, β-blockers **after** α-blockade
  - Labetalol (combined α- and β-blocking) esp if tachyarrhythmias. or preoperative pharmacologic management of the patient's pheochromocytoma with α-blockade.
  - **No** propranolol prior to α-blockade! Unopposed α-adrenoceptor stimulation could precipitate hypertensive crisis
- Avoid contrast-enhanced adrenal CT scan if possible until **after** an α-adrenoceptor antagonist has been initiated. (Iodine contrast could incite a hypertensive crisis).

Q#56 Answer C
Manage hormone replacement therapy in a patient with panhypopituitarism

- Do NOT use TSH, use free thyroxine (T_4) level
  - TSH will be low/low normal
- Desmopressin dose adequate (normal serum Na, no excessive urination)
- Hydrocortisone dose is physiologic- don't adjust based on lab (ACTH and cortisol levels will remain low on adequate therapy), adjust based on symptoms
- Testosterone is normal, and he has normal morning erections
- Growth hormone (GH) replacement can improve lean mass distribution and QOL
  - Discontinuing GH will likely worsen fatigue

Q#58 Answer A
Diagnose Klinefelter syndrome (47XXY)

- **Hyper**gonadotropic hypogonadism (Increased LH, FSH, low T)
- Common cause of hypergonadotropic hypogonadism and azoospermia
- Tall stature, sexual dysfunction, fatigue
- Supplement androgens
- MRI pituitary: **hypo**gonadotropic hypogonadism
- Scrotal US would not identify cause
- Klinefelter syndrome is characterized by primary hypogonadism with normal prolactin levels

Q#60 Answer B
Evaluate an incidentally noted adrenal mass

- Low dose DST –initial screen for autonomous secretion of cortisol, high sens.
- 10-15% of adrenal incidentalomas are functional (although most have no overt clinical manifestations) catecholamines, cortisol (most), or aldosterone
- Long-standing subclinical CS: type 2 DM and osteoporosis, obesity, hypertension
- Check 24-hour urine fractionated metanephrines and catecholamines for pheo
- Adrenal vein sampling (AVS) to evaluate for a bilateral versus unilateral adrenal cause of primary hyperaldosteronism
- Measurement of plasma renin activity and aldosterone concentration is not indicated in patients **without hypertension**
- **No further testing is also inappropriate**! Even if imaging characteristics benign
  - Labs and subsequent radiographic surveillance (first at 3-6 months and then annually for 1-2 years)

Q#61 Answer E
Treat acromegaly with transsphenoidal pituitary surgery

- Transsphenoidal resection of the pituitary adenoma is the **initial treatment of choice**
  - only treatment that is *potentially curative*
  - can debulk (many invade) and preserve vision and decrease GH (measured by IGF-1 levels)
- Pegvisomant (GH receptor blocker/antagonist) works in peripheral tissues but does not decrease production by the tumor.
- Somatostatin analogues (octreotide, lanreotide), inhibit GH secretion
  - unresectable tumors without significant mass effect or contraindication to surgery
- **Radiation therapy** (stereotactic surgery = gamma knife) added to help increase remission or cure
  - not usually initial treatment 2/2 possible damage to surrounding tissues
- Small number can co-secrete prolactin
  - Rx bromocriptine (dopamine agonist)

Q#64 Answer A
Treat infertility related to polycystic ovary syndrome

- Selective estrogen receptor modulators (SERMs) (such as clomiphene) are the established first-line treatment for ovulation induction in anovulatory patients with infertility from polycystic ovary syndrome (PCOS). ?maybe aromatase inhibitors..not yet FDA approved
- IVF only after several failed cycles of ovulation induction with clomiphene
- If clomiphene resistance, gonadotropin therapy appropriate
  - Caution! higher-order multiple gestation may result
- 2012 Cochrane review of the effect of insulin-sensitizing drugs (most involved metformin) in women with infertility and PCOS improved rates of pregnancy
  - metformin compared with placebo
  - metformin plus clomiphene compared with clomiphene alone
  - but **not** metformin compared to clomiphene alone

Q#65 Answer C
Treat a microprolactinoma in a postmenopausal woman

- Postmenopausal (so already hypogonadic)
  - LH/FSH normally high 2/2 ovarian failure; (her levels lower than expected because elevated prolactin is providing negative feedback)
- Found incidentally, no concerning features on MRI, asx (minimal menopausal sx), other pituitary hormones normal
- Retest in 6 -12 months to make sure tumor does not grow
- Dopamine agonists (cabergoline) used to treat *symptomatic* prolactinomas and are first line therapy ahead of surgery
- Radiosurgery for tumors not amenable to standard trans-sphenoidal surgery

Q#71 Answer B
Diagnose primary hyperaldosteronism as a cause of secondary hypertension

- Resistant hypertension: "BP that remains above goal despite concurrent use of three antihypertensive agents of different classes, one of which is a diuretic."
- Up to 10% of patients w HTN
- HypoK+ (persistent despite rx ACE inhibitor and K+ supplement) raises the possibility of primary hyperaldosteronism
  - Measure plasma aldosterone-plasma renin activity ratio
  - If positive, confirm with IV salt loading, fludrocortisone suppression testing, or captopril testing
  - If confirmed, adrenal imaging to determine bilateral or unilateral cause
  - Spironolactone for bilateral, surgery for unilateral

- DST checks for glucocorticoid excess (nothing on hx or PE to suggest)
- Plasma metanephrines and catecholamines checks for pheochromocytoma (nothing to suggest), also doesn't explain hypoK+
- Renal artery Doppler flow studies for renovascular hypertension
  - Most over 50 yo, and associated with ASCVD or functional impairment of the kidney