CHAPTER 9
Endocrinology

DIABETES

What is the pathophysiology of type 1 diabetes?
Insulin deficiency due to autoinflammatory destruction of pancreatic B cells

What is the pathophysiology of type 2 diabetes?
Insulin resistance and relative insulin deficiency

What is the age of onset of type 1 and type 2 diabetes?
Type 1 usually begins in childhood/adolescence and type 2 usually begins in adulthood.

Which of the two types of diabetes has a stronger genetic factor?
Type 2 diabetes (seems counterintuitive)

What are the early symptoms of diabetes?
"The three polys": polyuria, polydipsia, and polyphagia; **and** weight loss

What are chronic complications of diabetes?
Retinopathy, nephropathy, neuropathy, cerebrovascular disease, coronary artery disease (CAD), peripheral vascular disease

What type of fatal fungal infection can diabetics get?
Mucor**,** especially **sinusitis** (Note: They love to ask this on the boards!)

What is the histologic description of *Mucor?*
Nonseptate hyphae with branching at 90° (looks like the letter M)

What are the diagnostic criteria for diabetes?
Both types of diabetes are diagnosed based on the same criteria.
Fasting glucose over 126 two separate times
Random glucose over 200 with symptoms of diabetes
Or
Glucose tolerance test (2-hour test with 75-g glucose load) over 200

What is the treatment for type 1 diabetes?
Insulin replacement. Since these individuals do not have insulin, hypoglycemics will not work.

For each of the following types of insulin, describe the peak and duration of action:

Lispro (Humalog)

NPH

Glargine (Lantus)

Lente

Levemir

Regular insulin

Ultralente

Aspart (NovoLog)

Rapid Acting	**Peak**	**Duration**
Lispro	30-90 min	3-5 h
Aspart	40-50 min	3-5h
Short Acting		
Regular	2-5 h	5-8 h
Intermediate Acting		
NPH	4-12 h	18-24 h
Lente	3-10 h	18-24 h
Long Acting		
Lantus	No peak	20-24 h
Levemir	6-8 h	Up to 24 h
Ultralente	10-20 h	20-36 h

Define each of the following complications of insulin treatment:

Somogyi effect

Nocturnal hypoglycemia causing elevated morning glucose due to release of counterregulatory hormones; treat with less insulin

Dawn phenomenon

Early morning hyperglycemia secondary to nocturnal growth hormone (GH) release

What is the first-line treatment for type 2 diabetes?

Metformin

In what patients would metformin be absolutely contraindicated?

In patients who have compromised kidney function because of concern for lactic acidosis

How do we believe metformin works?

Increases sensitivity to insulin

Give an example of each of the following classes of hypoglycemic agents, how they work, and major side effects:

Sulfonylureas	Examples: glipizide, glyburide (Note: **Start** with GL or end with IDE.) How they work: increased insulin secretion by B cells Side effects: hypoglycemia and teratogenic (except glyburide)
Thiazolidinediones	Examples: rosiglitazone (Avandia), pioglitazone (Actose) (end with glitazone). How they work: increases sensitivity to insulin. (Note: The **zone** for sensitivity to insulin is increased.) Side effects: Hepatitis—patients on this class of drugs should have liver enzymes monitored for first year that they are on the drug. Exacerbation of CHF—contraindicated in class III and IV CHF.

When is it most appropriate to treat a type 2 diabetic with insulin?
Refractory to oral hypoglycemic agents

What medication slows the progression of nephropathy in diabetes?
Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)

Other than medication, what other therapy is important in diabetes?
Nutrition education

What is HgA1c?
Blood marker of glucose control over the last 3 months. HgA1c <7 is ideal.

What preventative measures are recommended to minimize diabetic complications?
Lipid control (low-density lipoprotein [LDL] <70, TG <150).
BP control <130/80.
HgA1c <7.
Annual foot examinations.
Check for microalbuminuria and proteinuria.
Annual funduscopic examination.

What is the appropriate treatment in a diabetic patient with microalbuminuria?
ACE inhibitor or ARB

What is the major complication of type 1 diabetes?
Diabetic ketoacidosis (DKA)

What are the signs and symptoms of DKA?

Severe hyperglycemia (glucose often >500), ketoacidosis, hyperkalemia, fruity breath, slow deep breaths, abdominal pain, dehydration, lethargy

What are slow deep breaths in DKA called?

Kussmaul hyperpnea

What is the most important treatment in DKA?

Intravenous (IV) fluid hydration (usually with normal saline)

What are the other treatments in DKA?

Insulin drip. Add potassium if potassium is low or normal **and** add glucose when blood sugar reaches 250 because insulin needs to be continued to be given despite normal glucose until ketones are no longer present.

What are the most severe complications of DKA treatment?

Cerebral edema or cardiac arrest due to hyperkalemia

What is the major complication of type 2 diabetes?

Hyperosmolar hyperglycemic nonketotic (HHNK) coma; although on rare occasions type 2 diabetics can also go into DKA

What are some of the signs and symptoms of HHNK?

Hypovolemia, hyperglycemia (glucose can be >1000), **no ketoacidosis**, renal failure, altered mental status, seizure, disseminated intravascular coagulation (DIC); often precipitated by acute stress such as trauma or infection.

The difference between HHNK and DKA is that in HHNK there is no ketoacidosis.

What is the treatment for HHNK?

The mortality is >50%; as a consequence, immediate treatment is urgent.

Treatment includes rapid IV fluid resuscitation; insulin and potassium are usually needed earlier than in DKA because the intracellular shift of plasma potassium during therapy is accelerated in the absence of acidosis.

PITUITARY

What hormones are secreted from the anterior pituitary?

Follicle-stimulating hormone (FSH), luteinizing hormone (LH), adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), prolactin, GH

(Note: **FAST P:G**)

What hormones are secreted from the posterior pituitary?

Vasopressin (antidiuretic hormone), oxytocin

What is the action of each of the following hormones?

FSH	Spermatogenesis in males, ovarian follicle growth in females
LH	Testosterone secretion in males and ovulation in females
ACTH	Stimulates adrenal cortex to make cortisol, aldosterone, and sex hormones
TSH	T3 and T4 production as well as thyroid gland maturation
Prolactin	Milk production (lactation)
GH	Insulin-like growth factor secretion causing protein and fat metabolism
Antidiuretic hormone (ADH), vasopressin	Production of concentrated urine by sodium and water retention
Oxytocin	Uterine contractions, milk letdown

What is the most common type of pituitary tumor?
Prolactinoma

What type of tumor is a prolactinoma?
A pituitary adenoma which secretes prolactin

What are the two mechanisms by which a prolactinoma causes symptoms?
1. Endocrine effect: due to hyperprolactinemia
2. Mass effect: pressure of the tumor on surrounding tissues

What are some signs and symptoms of a prolactinoma?
Headache, diplopia, hypogonadism, amenorrhea, gynecomastia, galactorrhea, hypopituitarism

What cranial nerve (CN) can be affected by a prolactinoma?
CN III

How is a prolactinoma diagnosed?
Magnetic resonance imaging (MRI)/computed tomography (CT)

What is the first-line treatment for a prolactinoma?
Dopamine agonist such as bromocriptine

What are other treatment options?
Surgical resection or radiation therapy if tumor is very large or refractory to medical treatment

Other than a prolactinoma, what are other causes of hypopituitarism?
Sheehan syndrome (postpartum pituitary necrosis), hemochromatosis, neurosyphilis, tuberculosis (TB), surgical destruction of pituitary

What disorder is seen with elevated levels of GH?

Acromegaly

What is the most likely underlying cause of acromegaly?
Pituitary adenoma secreting GH

When must there be an elevation in GH in order for acromegaly to result?
Elevated levels of GH must be present after epiphyseal closure.

What results if there is excess GH secretion before epiphyseal closure?
Gigantism

What are the signs and symptoms of acromegaly?
Coarse facial features, large hands and feet, large jaw, deepening of voice, decreased peripheral vision due to compression of optic chiasm, hyperhidrosis

How is acromegaly diagnosed?
1. MRI/CT demonstrating pituitary tumor,
2. Nonsuppressiblity of GH after an oral glucose challenge
3. Elevtated IGF-1 (insulin-like growth factor)

What are the treatment options for acromegaly?
Surgery or radiation of pituitary tumor, or medical treatment with octreotide or somatostatin, which blocks GH or dopamine agonists

What malignancy are patients with acromegaly at increased risk for?
Colon cancer

THYROID

What is hyperthyroidism?
Increased secretion of thyroid hormones

In what sex is hyperthyroidism more common?
Ten times more common in women than men

What is the most common cause of hyperthyroidism?
Graves disease (80%-90% of US cases)

What are some other causes of hyperthyroidism?
Plummer disease; toxic multinodular goiter; subacute thyroiditis; amiodarone therapy

What are some of the signs and symptoms of hyperthyroidism?
Heat intolerance, weight loss, exophthalmos, tachycardia, anxiety, palpitations, atrial fibrillation, tremor, sweating, fatigue, weakness, diarrhea, increased reflex amplitude

What is Graves disease?
Autoimmune disease causing hyperthyroidism. It is due to antibody stimulation of TSH receptors causing excess secretion of free thyroid hormone.

What are the two symptoms only seen in Graves disease?
1. Pretibial myxedema

2. Infiltrative ophthalmopathy (exophthalmos)

What is pretibial myxedema?

Pruritic, nonpitting edema found on shins that usually remits spontaneously

What is infiltrative ophthalmopathy?

Exophthalmos that may not resolve despite treatment of Graves disease most likely due to autoimmune damage in extraocular muscles

How is Graves disease diagnosed?

All hyperthyroidism is diagnosed via measurement of TSH, free T4, and free T3. In Graves disease, since there is excess stimulation of the thyroid gland causing increased production of thyroid hormone, laboratory tests show high levels of free T4 and free T3, and low levels of TSH (because of negative feedback) (Table 9-1). Also, a radioactive iodine uptake scan should be done. If uptake is low, then thyroiditis or medication-induced hyperthyroidism is considered.

Table 9-1 Thyroid Function Evaluation

Hyperthyroid	TSH	Free T4	TRH
Graves disease	↓	↑	↑
Pituitary tumor	↑	↑	↓
Plummer disease	↓	↑	↑
Hypothyroid			
Primary	↑	↓	↑
Secondary	↓ or normal	↓	↑
Tertiary	↓ or normal	↓	↓
Hashimoto	↑	↓	↑ or normal

TRH, thyrotropin-releasing hormone.

What is another name for toxic multinodular goiter?

Plummer disease

What is the underlying cause of hyperthyroidism in Plummer disease?

Multiple thyroid nodules develop autonomous T4 secretion and, therefore, more T4 is released.

How is Plummer disease diagnosed?

Radioactive iodine uptake tests show “hot” nodules with the rest of the gland being “cold”; also, clinically, nodules can sometimes be felt.

What is another name for subacute thyroiditis?

de Quervain thyroiditis

What are the signs and symptoms of subacute thyroiditis?

Prodrome of viral upper respiratory infection (URI) followed by rapid onset of thyroid swelling and **tenderness** as well as hyperthyroid symptoms that can later turn into a hypothyroid state

What is the treatment for de Quervain thyroiditis?

Usually self-limiting, but aspirin and corticosteroids may be indicated to control inflammation.

What are the treatment options for a hyperthyroid state?

1. Medication: propylthiouracil (PTU) or methimazole
2. Radioactive iodine ablation
3. Surgery: subtotal thyroidectomy

What is the first-line treatment for Graves disease?

Radioactive iodine ablation except in children and pregnant women

What is radioactive iodine ablation?

Radioactive iodine is concentrated in the gland and destroys tissue.

What are the possible side effects of radioactive iodine ablation?

Hypothyroidism; thyrotoxic crisis secondary to the release of thyroid hormone into the blood stream

What is the mechanism by which PTU works?

It inhibits the peripheral conversion of T4 to T3, decreases iodine uptake, and decreases T4 synthesis.

Do patients need to be on therapy for the rest of their lives?

No. After a 1-2 year course of treatment about 50% no longer need to be treated.

What are the potential side effects of PTU?

Leukopenia, rash, nausea

What other adjunctive treatment is given to patients with hyperthyroidism?

Beta-blocker, usually propranolol, to control symptoms

What is the most serious complication of hyperthyroidism?

Thyroid storm

What can induce thyroid storm?

Infection, surgery, trauma, abrupt stop of antithyroid medication, serious acute medical problems such as cerebrovascular accident (CVA) or myocardial infarction (MI)

What are the signs and symptoms of thyroid storm?

Exaggerated symptoms of hyperthyroidism are tachycardia, high output **congestive heart failure (CHF),** abdominal pain, hyperpyrexia >104, altered mental status (ultimately coma)

What is the mortality rate of thyroid storm?

Up to 50%

What is the initial treatment for thyroid storm?

It is an emergency, so think of the ABCs:

Airway stabilization

Breathing/oxygen administration
Circulation (check pulse/blood pressure [BP]) and start IV fluids

After primary stabilization of the patient, what is the medical management of thyroid storm?
The goal of therapy is to decrease circulating thyroid hormone and treat the patient's symptoms.
1. Prevent hormone synthesis: methimazole or PTU
2. Prevent hormone release: cold iodine (about 2 hours after PTU to prevent worsening symptoms)
3. Prevent conversion of T4 to T3: glucocorticoids and beta-blockers
4. Symptomatic treatment: beta-blockers and Tylenol (for fever)

What are the signs and symptoms of hypothyroidism?
Cold intolerance, fatigue, lethargy, weakness, **constipation, weight gain,** arthralgias, hoarse voice, skin is dry, coarse, and with nonpitting edema, loss of outer third of eyebrows, delayed relaxation phase of deep tendon reflexes

What is primary hypothyroidism?
Thyroid gland dysfunction

What are some examples of primary hypothyroidism?
Hashimoto thyroiditis, thyroid ablation or neck radiation therapy in the past, subacute thyroiditis, iodine excess or deficiency, medication-induced

What medication can cause hypothyroidism?
Lithium

What is the most sensitive lab test for primary hypothyroidism?
Elevated TSH

What other lab results are present in primary hypothyroidism?
Low T3 and T4

What is Hashimoto thyroiditis?
Painless chronic autoimmune thyroid inflammation of autoimmune etiology

What lab results can help diagnose Hashimoto thyroiditis?
Elevated antithyroglobulin and antimicrosomal antibody titers

What is subacute thyroiditis?
Tender, enlarged thyroid; often postviral infection can begin with hyperthyroid symptoms, then hypothyroid symptoms

How can you distinguish Hashimoto from subacute thyroiditis?
On clinical examination, in Hashimoto the thyroid gland is **not** tender to palpation but in subacute thyroiditis it is **tender** to palpation.

How can Graves disease and Hashimoto thyroiditis be distinguished?
Radioactive iodine uptake is **increased** with Graves and **decreased** with Hashimoto.

What is secondary hypothyroidism?
Hypothyroidism caused by pituitary dysfunction

What are some examples of secondary hypothyroidism?
Sheehan syndrome, pituitary neoplasm, TB

What is Sheehan syndrome?
Postpartum pituitary necrosis

What lab results indicate a secondary hypothyroidism?
Low to normal TSH as well as **normal thyrotropin-releasing enzyme (TRH),** low levels of T3 and T4

What is tertiary hypothyroidism?
Deficiency of TRH

What is an example of tertiary hypothyroidism?
Hypothalamic radiation

Other than TSH, TRH, T3, T4, what other abnormal lab tests may be found in a hypothyroid patient?
Elevated serum cholesterol (TG, LDL, total cholesterol); elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT); anemia; hyponatremia

What is the treatment for hypothyroidism?
Levothyroxine

What is subclinical hypothyroidism?
Elevated TSH levels but with normal thyroid hormone levels and with no clinical symptoms

What is the life-threatening complication of hypothyroidism called?
Myxedema coma

What are the signs and symptoms of myxedema coma?
Severe lethargy or coma, hypothermia, areflexia, bradycardia

What causes myxedema coma?
Prolonged cold exposure, infection, sedatives, narcotics, trauma, or surgery

What is the treatment for myxedema coma?
This is an emergency, so start with ABCs (airway, breathing, circulation); IV fluids, steroids, levothyroxine, treat any precipitating causes

What is the initial appropriate workup of a thyroid mass?
Fine-needle biopsy and TSH

What other studies are done to workup a thyroid mass?
Thyroid ultrasound to determine the number and sizes of masses; and thyroid technetium 99m scan

What is a hot nodule and a cold nodule on a thyroid scan?
Hot nodule indicates a hyperactive nodule and is **less** likely to be malignant. A cold nodule indicates a hypoactive nodule that is **more** likely to be malignant.

What is the most common type of thyroid cancer?
Papillary cancer

What is the prognosis for papillary cancer?
85%, 5-year survival

What is seen on pathology?
Psammoma bodies, Orphan Annie nucleus

Which type of thyroid carcinoma is associated with multiple endocrine neoplasia types 2 and 3 (MEN 2 and 3)?

Medullary cancer

What can be used to monitor medullary carcinoma?

Calcitonin, because it is a calcitonin-secreting tumor

Which type of thyroid carcinoma has the worst prognosis?

Anaplastic cancer

In what patient population is anaplastic carcinoma usually found?

Older patients

What is the 5-year prognosis for anaplastic carcinoma?

5%-14% survival at 5 years

Which thyroid cancer has the second worst prognosis?

Medullary cancer

Which thyroid carcinoma often has metastasis to the bone and lungs?

Follicular cancer

Name the tumors that are part of each of the MEN syndromes.

1. MEN 1: Wermer syndrome: three Ps: **prolactinoma, parathyroid, pancreatoma**
2. MEN 2: Sipple syndrome: **pheochromocytoma, medullary thyroid, parathyroid**
3. MEN 3: same as MEN 2B: **pheochromocytoma, medullary thyroid, mucocutaneous neuromas**

PARATHYROID

What is primary hyperparathyroidism?

Increased secretion of parathyroid hormone (PTH)

What is the most common cause of primary hyperparathyroidism?

Adenoma is the most common cause; however, other etiologies include hyperplasia, carcinoma, MEN 2 or 3.

What does elevated PTH cause?

There is an ultimate increase in serum calcium (**hypercalcemia**) because PTH leads to increased vitamin D hydroxylation and, therefore, increased calcium resorption as well as decreased resorption of phosphate (**hypophosphatemia**). Calcium levels are also increased because of increased osteoclastic activity (**osteoporosis**).

What are the signs and symptoms of hyperparathyroidism?

Same as those for hypercalcemia: **"Stones, moans, groans, and psychiatric overtones."** Because of the osteoclastic activity it can also lead to osteoporosis.

What EKG finding could you expect with hyperparathyroidism?

Shortened QT, because of hypercalcemia

How is hyperparathyroidism diagnosed?

Hypercalcemia, hypophosphatemia, hypercalciuria, and PTH level

What other differential diagnoses should be considered with hypercalcemia?

Neoplasm, sarcoidosis, thiazide diuretic treatment, Paget disease, vitamin D intoxication, milk alkali syndrome, myeloma

What is the acute medical treatment for hyperparathyroidism?

Asymptomatic patients with calcium levels below 13 should just be watched. However, symptomatic patients or those with higher calcium levels should be treated with furosemide and bisphosphonates to decrease bone resorption and prevent osteoporosis. Calcitonin can be used as well.

What long-term treatment must be considered in hyperparathyroidism?

Surgical treatment. Adenomas should be removed. In hyperplasia, all four parathyroids are removed and a small piece is placed usually near the sternocleidomastoid for functionality.

What are the most common complications of parathyroidectomy?

Hoarseness because of damage of the recurrent laryngeal nerve and hypocalcemia

What is secondary hyperparathyroidism?

Increased PTH secretion secondary to chronic renal failure or vitamin D deficiency

What is hypoparathyroidism?

Decreased PTH

What are the causes of hypoparathyroidism?

Idiopathic, DiGeorge syndrome, hypomagnesemia, secondary to surgery or neck irradiation

Why does hypomagnesemia lead to hypoparathyroidism?

Because magnesium is necessary for the parathyroid to secrete PTH.

In what conditions is low magnesium seen?

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH), pancreatitis, alcoholism

How is hypoparathyroidism diagnosed?

Hypocalcemia, hyperphosphatemia, low PTH

What are the signs and symptoms of hypoparathyroidism?

Same as that for hypocalcemia: perioral paresthesias, tetany, seizures, Trousseau sign, Chvostek sign, anxiety

What EKG findings could you expect in hypoparathyroidism?

Prolonged QT interval because of the hypocalcemia

What is Trousseau sign?

Carpal spasm with arterial occlusion with BP cuff

What is Chvostek sign?

Spasm of the facial nerve upon tapping

How is hypoparathyroidism treated?

Emergently treat with IV calcium, then treat with vitamin D and oral calcium for maintenance treatment.

ADRENALS

What are the two main parts of the adrenal gland and what is the secretory product of each part?

1. Adrenal cortex
2. Adrenal medulla

The cortex secretes aldosterone, cortisol, and sex hormones and the medulla secretes the catecholamines including epinephrine and norepinephrine.

What is the function of aldosterone?

Kidney resorption of sodium and secretion of potassium and hydrogen ions

What is Addison disease?

Primary adrenal insufficiency caused by the destruction of the adrenal cortex leading to a deficiency in both mineralocorticoids as well as glucocorticoids

What is secondary adrenal insufficiency?

Decreased secretion of ACTH by the pituitary gland; the adrenal gland is functional

What is the cause of tertiary adrenal insufficiency?

Decreased hypothalamic function

What is the most likely etiology of Addison disease in the United States?

Autoimmune destruction of the adrenal gland

What are some other causes of Addison disease?

TB, amyloidosis, sarcoidosis, HIV, adrenal hemorrhage secondary to DIC or trauma, Waterhouse-Friderichsen syndrome, congenital adrenal hyperplasia, metastasis to the adrenals

What is Waterhouse-Friderichsen syndrome?

Endotoxin-mediated adrenal hemorrhage usually caused by meningococcemia that leads to fulminant adrenal failure

What is the most likely cause of secondary adrenal insufficiency?

Hypothalamic-pituitary axis disturbance, usually by sudden cessation of exogenous corticosteroids, which leads to decreased ACTH secretion

What are some other causes of secondary adrenal insufficiency?

Pituitary infarction, Sheehan syndrome, pituitary adenoma

What are some signs and symptoms of Addison disease?

Because of low aldosterone and cortisol there are hyponatremia, hyperkalemia, pica (craving for salt), weakness, anorexia, hypotension, nausea, vomiting, and hyperpigmentation.

What is the test used to diagnose adrenal insufficiency?

Hyperpigmentation, ↑ACTH,↓ cortisol and aldosterone response to ACTH challenge

Why do patients get hyperpigmentation?

ACTH stimulates melanin secretion.

What are the diagnostic findings in primary adrenal insufficiency?

ACTH (Cortrosyn) test in which a dose of ACTH is given to the patient and then serum cortisol levels as well as serum ACTH levels are measured about half an hour later

Primary adrenal insufficiency: ↑**cortisol** levels in response to ACTH and ↑**aldosterone** levels

Secondary adrenal insufficiency: ↑**cortisol** levels (more than double normal limits) in response to ACTH and **normal aldosterone** levels

How is the diagnosis of secondary adrenal insufficiency distinguished from primary adrenal insufficiency?

No hyperpigmentation, ↑cortisol response, ↑ACTH

What kind of metabolic disturbance is seen in primary adrenal insufficiency?

Metabolic acidosis due to aldosterone and cortisol deficiency and, therefore, lack of secretion of hydrogen ions

What is the treatment for adrenal insufficiency?

Glucocorticoid replacement. Extra glucocorticoids should be given in times of physical stress such as infection. You should instruct patients to taper off this extra replacement slowly as to prevent an adrenal crisis.

What is Cushing syndrome?

A term used to describe the symptoms caused by hypercortisolism

How is Cushing *syndrome* different from Cushing *disease?*

Cushing disease refers to a type of Cushing syndrome caused specifically by ACTH hypersecretion by the pituitary.

What are the different causes of hypercortisolism?

Exogenous glucocorticoids Pituitary hypersecretion of ACTH Hypersecretion of cortisol due to adrenal hyperplasia/neoplasm Ectopic ACTH production such as with small cell lung carcinoma

What is the most common cause of Cushing syndrome?

Exogenous corticosteroids

What is the most common cause of endogenous hypercortisolism?

Cushing **disease** (pituitary hypersecretion of ACTH)

What are the signs and symptoms of Cushing syndrome?

Buffalo hump, moon facies, truncal obesity, striae, virilization/menstrual disorders, hyperglycemia, hypertension, hypokalemia, immune suppression, osteoporosis, hirsutism, acne

What tests are used to diagnose hypercortisolism?

24-hour urine-free cortisol and the dexamethasone suppression tests, ACTH level, diurnal cortisol variation

What is the dexamethasone suppression test?

First a low dose of dexamethasone is given and cortisol is measured. If cortisol is not elevated then Cushing is ruled out; if it is elevated then a high-dose dexamethasone suppression test is done and ACTH is measured. If ACTH is decreased then the pituitary has good feedback and, therefore, it must be an adrenal etiology. However, if the ACTH is high or normal then it is probably ectopic ACTH; and if it is only partially suppressed, then the pituitary is the etiology. Dexamethasone → ↑ACTH (ectopic/pituitary) ↓ACTH (adrenal)

What are some other studies to consider to localize the lesion in hypercortisolism?

A CT scan can look for an adrenal mass and an MRI can look for a pituitary mass.

What is the treatment for hypercortisolism?

Treat the underlying cause. If it is a resectable tumor, tumor resection with postoperative glucocorticoids. In nonresectable tumors, medical therapy with ketoconazole, mitotane, metyrapone, or aminoglutethimide. If the etiology is exogenous glucocorticoids; taper off the glucocorticoids and eventually stop.

What is Conn syndrome?

Primary hyperaldosteronism

What is the etiology of Conn syndrome?
Either hyperplasia of the zona glomerulosa or aldosterone-producing adenoma

What are the signs and symptoms of Conn syndrome?
Hypertension, muscle cramps, palpitations, polyuria, polydipsia, hypokalemia

What percent of hypertensive patients have Conn syndrome?
1%-2%

What are some of the laboratory findings in Conn syndrome?
↑Na, ↑Cl, ↓K (muscle cramps, palpitations), ↓renin-angiotensin feedback, metabolic alkalosis

What are some ways to diagnose Conn syndrome?
Captopril stimulation test; fludrocortisone suppression test; sodium loading

What is the captopril stimulation test?
Captopril (an ACE inhibitor) is administered and then serum renin and aldosterone levels are measured. ↑aldosterone and ↓ **renin** confirm the diagnosis.

What is the fludrocortisone suppression test?
Fludrocortisone, a synthetic corticosteroid, is administered to the patient. Serum aldosterone levels are then measured. In a normal patient it would be expected that aldosterone levels would be suppressed but not in a patient with Conn syndrome.

What is the sodium loading test?
The patient is loaded with sodium via IV saline and then urinary aldosterone levels are tested. No decrease in urinary aldosterone confirms diagnosis.

What is the renin level in Conn syndrome?
Low renin

What other study can help in the diagnosis of Conn syndrome?
CT demonstrating an adrenal nodule or hyperplasia

What is the treatment for Conn syndrome?
Adrenal adenoma: resection of tumor; unilateral adrenal hyperplasia: unilateral adrenalectomy; bilateral adrenal hyperplasia: spironolactone (potassium-sparing diuretic) or ACE inhibitor to control blood pressure

What is secondary hyperaldosteronism?
Elevated aldosterone levels due to elevated renin levels secondary to renal ischemia in CHF, renal artery stenosis, shock, renal tumor.

How is secondary hyperaldosteronism diagnosed?
↓Renin

What can be measured to differentiate primary from secondary hyperaldosteronism?
Renin (this is very important)

What is the treatment for secondary hyperaldosteronism?
Treat the hypertension with a potassium-sparing diuretic, a beta-blocker, and treat the underlying cause.

What is a pheochromocytoma?
Tumor of the adrenal **medulla** that produces excess **catecholamines**

What percentage of people with hypertension have a pheochromocytoma?
0.5%

What are the possible etiologies for a pheochromocytoma?
MEN 2 or 3, von Hippel-Lindau disease, Recklinghausen disease, neurofibromatosis

What are the five Ps of pheochromocytoma?
1. Pain (headache)
2. Pressure
3. Perspiration
4. Palpitation
5. Pallor and hypertension

What is the most common sign of a pheochromocytoma?
Hypertension

What is the diagnostic test for a pheochromocytoma?
Urine screen for elevated **VMA** (vanillylmandelic acid), a urine catecholamine; as well as elevated urine and serum epinephrine and norepinephrine levels

What other test can be done to localize a pheochromocytoma?
A CT scan can identify a **suprarenal mass** (adrenal mass).

What are some other laboratory findings in a pheochromocytoma?
Hyperglycemia, polycythemia

What is the "rule of 10s" for a pheochromocytoma?
10% malignant
10% bilateral
10% extrarenal
10% familial
10% in kids
10% multiple tumors
10% calcified

What must be ruled out in a patient with a pheochromocytoma?
MEN type 2 or 3 or

What is the treatment for a pheochromocytoma?
In operative cases preoperative alpha-blockers and beta-blockers, then surgical resection; in inoperable cases **ph**enoxybenzamine **or ph**entolamine

Why treat with preoperative alpha-blockers and beta-blockers?
To prevent unopposed vasoconstriction, and thus volume depletion

BONES

What is osteoporosis?

Reduction in bone mass leading to increased risk of fracture

What are the risk factors for osteoporosis?
Female, postmenopausal or low estrogen state, hypercortisolism, hyperthyroidism, calcium deficiency, low physical activity, smoking

What are the typical fractures that occur in osteoporosis?
Hip, vertebrae, and Colle fractures

How is osteoporosis diagnosed?
Dual-energy x-ray absorptiometry (DEXA) scan which shows low bone density or an incidental fracture in the elderly

What are the treatments for osteoporosis?
Bisphosphonates, calcitonin, selective estrogen receptor modulators, calcium

How much calcium should be taken daily?
1500 mg daily with vitamin D

What is the calcitonin most useful for?
Treating bone pain; however, it cannot be used chronically because the effects wear off

What are some examples of selective estrogen modulators?
Tamoxifen, raloxifene

What do the selective estrogen modulators increase the risk for?
Thromboembolism

What is osteomalacia?
Vitamin D deficiency in adults

What is osteomalacia called in children?
Rickets

What are the signs and symptoms in children?
Pigeon breast, craniotabes (thin skull bones), **rachitic rosary** (costochondral thickening)

How is osteomalacia diagnosed?
Low levels of vitamin D as well as diffuse osteopenia on x-ray

How is osteomalacia treated?
Vitamin D supplementation

What is Paget disease of the bone?
Localized hyperactivity of the bone which leads to disordered bone matrix being replaced with soft, enlarged bone

What is the etiology of Paget?
Unknown, but some think it may be viral

What are the signs and symptoms of Paget disease of the bone?
Hearing loss (impingement of cranial nerve [CN] VIII), multiple fractures, bone pain, high-output cardiac failure, **increased hat size**

What is the typical finding on x-ray?

Hyperlucent area surrounded by hyperdense border-sclerotic lesions

How is Paget diagnosed?

Elevated alkaline phosphatase, sclerotic lesions on bone scans/x-rays

What are the complications associated with Paget disease of the bone?

Pathologic fractures, high-output cardiac failure, hearing loss, kidney stones, sarcoma, spinal cord compression

What is the treatment for Paget disease?

Most patients do not need treatment; however, patients with complications associated with Paget disease are treated with bisphosphonates as first line and calcitonin as second line.

CLINICAL VIGNETTES

You diagnose a patient with type 2 diabetes. You check a urine microalbumin and find that it is elevated. With what class of medication would you treat this patient?

ACE inhibitor

A 24-year-old male comes to your office complaining of terrible headaches over the past several months. His only past medical history is GERD. He has no past surgical history. The only family history is prostate cancer in his grandfather, otherwise the rest of his family is healthy. On review of systems, he complains of chest palpitations and says that he sweats a lot. His vitals demonstrate a BP of 173/98. On examination you notice that he appears somewhat pale. His cardiovascular, pulmonary, and abdominal examinations are unremarkable. His electrolytes are within normal limits. You suspect a secondary cause of hypertension. What specific diagnostic test would help you screen for your suspected diagnosis?

Urine VMA to screen for pheochromocytoma

Your patient has weight loss, heat intolerance, and palpitations. She complains of swelling and tenderness of her neck. She just got over a head cold. What is the suspected diagnosis?

Subacute thyroiditis

Your diet-controlled diabetic patient presents for a follow-up. The only medication he currently takes is lisinopril. His vitals are as follows: BP: 125/70; P: 73; RR: 15; Temp: afebrile. You review his most recent laboratory tests with him. His HgA1c is 6.8. His urinalysis shows no protein. The lipid profile demonstrates LDL : 110, HDL: 45, TG: 100. His most recent fundoscopic examination was 4 months ago and was normal. You do a foot examination and that is normal. What medication change do you suggest?

Add a statin to bring the LDL down below 100.

A 34-year-old male with hypertension presents to your clinic trying to seek your advice regarding his recent weight gain He has gained 20 lb over the course of the last 3 months but denies any change in his diet. He appears to have quite a bit of abdominal girth as well as noticeable striae on his abdomen. His face is also noticeably round and with significant acne. What do you suspect is this patient's condition?

Cushing syndrome