Endocrine

DIABETES

- **Type I** = insulin-deficient (10%) → autoimmune dz resulting in destruction of pancreatic beta-cells
  - Autoantibodies present: anti-islet cell, antiglutamic acid dehydrogenase (not required)
  - Association with HLA DR3-DQ2 & DR4 genes
- **Type II** = insulin-resistant (90%) → resistant to the effects of insulin, eventually results in beta-cell failure
- S/sx: polyuria, polydipsia, unexplained weight loss, blurry vision, fatigue, weakness, pruritus, poor wound healing, increased susceptibility to infections (esp. fungal)

**Metabolic Syndrome**
- HLD <40 in males, or <50 in females, Triglycerides >150
- BP >135/85 mmHg
- Fasting blood sugar 100-125, or OGTT 140-199
- Waist circumference >35 inches for females, >40 inches for males

**Exam considerations:**
- Monofilament test (checks for peripheral neuropathy)
- Check for microalbuminuria (often first sign of diabetic kidney damage)
- Foot exam → skin breaks, ulcers, decreased pulses, delayed cap refill, bony deformities

**Complications:**
- Diabetic retinopathy → blindness, cataracts, glaucoma
- Diabetic nephropathy → half of the cases of end stage renal disease in the US
- Accelerated large vessel atherosclerosis (increases CAD and stroke risk)
- Peripheral vascular disease → half of lower leg amputations in the US
- Neuropathy is the most common complication of DM (peripheral and autonomic)
  - Peripheral - symmetric sensory dysfunction, distal sensory loss, paresthesias
  - Autonomic - gastroparesis, orthostatic hypotension, impotence, neurogenic bladder
- Skin changes → candida infections, slow wound healing necrobiosis lipoidica diabeticorum, and acanthosis nigricans
- Periodontal disease

**Screen Population** → Adults aged 40 to 70 years who are overweight or obese

**Risk assessment** → Obesity/high percentage of abdominal fat, physical inactivity, and smoking. Abnormal glucose metabolism is also frequently associated with hyperlipidemia and hypertension.

**Screening tests** → A1C or fasting plasma glucose or with OGTT, repeated testing on different day

**Screening interval** → Screen every 3 years.

**Other screening** → Other modifiable risk factors: overweight and obesity, physical inactivity, abnormal lipid levels, high blood pressure, and smoking

<table>
<thead>
<tr>
<th></th>
<th>Diabetes</th>
<th>Prediabetes</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose</td>
<td>≥126</td>
<td>100-125</td>
<td>&lt;100</td>
</tr>
<tr>
<td>OGTT</td>
<td>≥200</td>
<td>140-199</td>
<td>&lt;140</td>
</tr>
<tr>
<td>Random glucose</td>
<td>≥200 w/ classic sx</td>
<td>126-199 (needs follow up fasting)</td>
<td>≤125</td>
</tr>
<tr>
<td>HbA1c (%)120d</td>
<td>≥6.5</td>
<td></td>
<td>&lt;6.5</td>
</tr>
</tbody>
</table>

**Management**
- Metformin should be used as first-line therapy to reduce microvascular complications, assist in weight management, reduce the risk of cardiovascular events, and reduce the risk of mortality in patients with type 2 diabetes mellitus.
- Pre-DM or new-onset diabetes should undertake extensive lifestyle changes to slow the progression
- Patients with existing cardiovascular disease, two or more cardiovascular disease risk factors, or duration of diabetes of 10 years or more should have higher A1C goals because of a lack of benefit and the potential for increased risk of mortality compared with lower A1C goals
- **Initiate treatment** → A1C >6.5, fasting plasma glucose >126, random plasma glucose >200 w/ symptoms of hyperglycemia, 2-hr plasma glucose >200 during OGTT, START METFORMIN
- If target not reached in **3 months**, start second drug (SU, TZD, DPP-4 Inhibitor, GLP-1 receptor agonist, insulin (basal))
- If target is STILL not reached **3 months later**, add a third drug from the same list

***Hypoglycemia → symptoms begin <60, cognitive impairment <50***
Initial Therapy (Step 1):

- **Lifestyle modifications** - decrease weight & increase activity (1-2% ↓ in A1c) – 5-7% weight loss
  - Exercise: 30-60 min. of moderate-intensity aerobic activity (40-60% of VO2 max) on most days of the week (>150 min/week) with resistance training 2x/wk
  - Diet: caloric restriction, decrease carbs, eliminate sugars

- **Biguanides**: Metformin (Glucophage, Glumetza) → First-line, suppresses hepatic glucose production without risk of hypoglycemia. It may promote weight loss and decrease triglycerides (1-2% ↓ in A1c)
  - S/E: GI/N/D that will go away over time, B12 deficiency may occur over time
  - **Contraindicated in renal insufficiency; stop if Scr >1.5 M or >1.4 F**
    - Use Glipizide, incretin for pts in which metformin is contraindicated
  - **Dosing**: 1500-2550 mg/d - **Immediate-release tablet or solution (adults ≥17 years)**:
    - Initial: 500mg 2xd or 850mg 1xd; titrate up 500mg/wk

Additional Therapy (Step 2):

- **Insulin therapy** → In the past, insulin therapy was used as a last resort, but today it’s often prescribed sooner because of its benefits. Often, people with type 2 diabetes start insulin use with one long-acting shot at night. (1.5-3.5% ↓) → initial therapy if A1c far from goal (>8.5), fasting blood sugar >250
  - *Initial therapy* = bedtime basal insulin (then add prandial short acting prn)
    - NPH insulin or Detemir @ bedtime, OR Glargine @ bedtime or morning
    - 0.2 units/kg/day (minimum 10 units), then titrated upward
  - **Rapid Short-Acting**: Aspart (NovoLog), Lispro (Humalog) → Take 3xd before meals
  - **Regular Short-Acting**: Humulin R, Novolin R → Take 3xd before meals
  - **Intermediate-Acting (Basal)**: NPH (Humulin 70-30 N, Novalin N) → Take 2xd, 6-10 hr peak
  - **Long-Acting (Basal)**: Detemir, Glargine
    - Take 1-2xd; no peak (mimics natural insulin), 20-24hr duration
    - Degludec = once daily dosing, lasts longer than 24 hrs

- **Sulfonylureas** → Increase insulin secretion. SE: low blood sugar and weight gain.
  - (1-2% ↓) = Glipizide**, Glimiperide, Glyburide
  - Increase insulin secretion by pancreatic beta cells (avoid in type I)
  - May cause weight gain and increase risk of hypoglycemia

Additional oral hypoglycemics (less well validated)

- **Meglitinides (repaglinide)** → Similar sulfonylureas
  - SE: weight gain, hypoglycemia but this risk is lower than with sulfonylureas

- **DPP-4 inhibitors** → (sitagliptin (Januvia), saxagliptin (Onglyza) and linaglizptin (Tradjenta))
  - They don’t cause weight gain, may cause headaches or pancreatitis (rare), or urticarial/angioedema
  - No associated hypoglycemia

- **GLP-1 receptor agonists** → Exenatide (Byetta), Liraglutide (Victoza), Albiglutide (Tanzeum), Dulaglutide (Trulicity)
  - (0.5-1% ↓)
  - Enhances insulin secretion, slows gastric emptying, suppresses glucagon
  - Weight loss
  - Disadvantages: requires injection, GI side effects, nausea and an increased risk of pancreatitis.

- **SGLT2 (sodium-glucose co transporter 2 inhibitors)** → Invokana, Farxiga, Jardiance (–gliflozins)
  - New, prevent kidneys from reabsorbing sugar (it is excreted in the urine). SE: yeast infections and urinary tract infections, increased urination and hypotension.
  - (0.5-0.7% ↓)
  - Weight loss, reduction in SBP
  - Disadvantages: UTIs, vulvovaginal candidiasis

- **Alpha-glucosidase inhibitors** = Acarbose, Miglitol (0.5-0.8% ↓)
  - Decrease glucose absorption in intestines (causes diarrhea, bloating & gas), Avoid when CrCl < 25

- **Thiazolidinediones** → rarely used = Pioglitazone or Rosiglitazone
  - May cause weight gain and other more-serious side effects, such as an increased risk of heart failure and fractures. Contraindicated in patients with class III or IV CHF
  - Disadvantages: edema, weight gain, pioglitazone is associated with bladder caner

- **Pramlintide** = Symlin, injectable (only used with insulin)
  - Amylin Analogue - can be combined w. Insulin in Type I or Type 2
  - slows down gastric transit (= feel full, less glucose absorbed), weight loss
  - Rarely used -only fine tunes BG control, doubles # of injections, GI sx, expensive

- **Bile Acid Sequestrants**: Colesevelam – ONLY used if pt needs lipid management TOO and can’t take statin
- **Daily aspirin** in those with an increased 10 yr cardiovascular risk (HTN, smoking, HLD, albuminuria)
**Thyroid**

### Hypoparathyroidism
- Can be acquired post thyroidectomy / parathyroidectomy
- Can also occur due to autoimmune disease → heavy metal toxicity (Wilson's disease, hemochromatosis), thyroiditis, or hypomagnesemia (chronic alcoholism)
- DiGeorge syndrome is a congenital cause of hypocalcemia arising from parathyroid hypoplasia

**Clinical features**
- Hypocalcemia → tetany, carpopedal spasms, muscle cramps, paresthesias, teeth, nail, hair defects, and hyperreflexia
- Chvostek sign is a contraction of the eye and mouth elicited by tapping along the facial nerve
- Trousseau sign produces a spasm in the hand/wrist when compressing the forearm
- Chronic findings → lethargy, anxiety, parkinsonism, mental retardation, personality changes, and blurred vision caused by cataracts

**Diagnostic Studies**
- Hallmark = decreased PTH and serum calcium and increased phosphate levels
- Serum magnesium may be low, Alk phos is normal
- ECG may have prolonged QT and T-wave abnormalities
- Xray may show increased bone mineral density, especially in the lumbar spine and skull

**Treatment**
- PTH has not been approved for hypoparathyroidism
- Correct hypocalcemia: calcium & vitamin D, calcitriol
- Monitor via serum and urine calcium levels
- Avoid furosemide + phenothiazines
- Monitor via serum and urine calcium levels
- Emergency tx for tetany is airway maintenance + slow admin of IV calcium gluconate

### Hyperparathyroidism
- Inappropriate production of PTH from parathyroid glands
- F>M, more common in post-menopausal females
- Poor feedback control of PTH by extracellular ionized Ca
- Benign PT adenomas (85%), PT gland hyperplasia (15%), Carcinomas (<3%), MEN, Familial isolated hyperPT

**Clinical Features**
- Hypercalcemia → “stones, bones, abd groans, psychic moans”
  - Stones d/t renal loss of calcium
  - Bone pain from demineralization, lesions (jaw)
  - Groans: increased abdominal absorption (cramps)
  - Moans: irritability, psychosis, depression
  - Other: renal failure, pancreatitis, gastric ulcers, weakness, fatigue, anorexia, polydipsia & polyuria

**Diagnosis**
- Routine chem panel in asymptomatic patients
- Serum calcium >10.5, PTH >55 (if PTH is low as well, this suggests secondary cause like cancer)
- Screen all patients for familial syndrome of hypercalcemia before treating
- Vitamin D deficiency common
- ECG → shortened QT, prolonged PR, brady
- Sestamibi scan, US, CT, MRI

**Treatment**
- Parathyroidectomy (if sx), low Ca+ and Vit D intake
- Bisphosphonates, Calcitriol
- Avoid lithium, thiazide diuretics, volume depletion

### Hypothyroidism
- Primary: Hashimoto’s (aka autoimmune/lymphocytic - m/c in US), iodine deficiency (m/c worldwide), congenital, thyroidectomy, meds (lithium, amiodarone, I-131 therapy)
- Central: pituitary/hypothalamic neoplasms, congenital, pituitary necrosis (Sheehan syndrome)

**Clinical Features**
- Weakness, fatigue, lethargy, cold intolerance, dry skin, hair loss, coarse hair, constipation, brittle fingernails, slow HR, leg cramps, depression, heavier menses, ED, weight gain, slower thinking, eyelid & facial edema, hyporeflexia, pretibial myxedema
- Bradycardia
- Hyponatremia may occur due to renal problems
- Increased risk of HLD, CAD, anemia can result
- 30% of downs patients have hypothyroidism

**Diagnosis**
- Primary: ↑ TSH, ↓ T3/T4 (normal T3/T4 if no sx)
- Secondary: ↓ TSH, ↓ T3/T4
- Anti-thyroid peroxidase + anti-thyroglobulin Abs (TPO and TG abs) → seen in Hashimoto
- Only image if concern for malignancy

**Treatment**: Levothyroxine sodium (LT4), higher dose in pregnancy

**Complications** = hyperlipidemia, atherosclerosis, fetal death
- myxedema coma → high mortality
- AMS/coma, hypotension, hypothermia, hypoventilation, AKI

### Hyperthyroidism
- Excess production of T3/T4 (thyrotoxicosis)
- F:M = 8:1, 20-40yr age of onset
- Primary: Grave’s dz (80%), goiter, toxic nodule, hashimotos thyroiditis, post-partum thyroiditis, inflammatory process, pregnancy, excessive iodine intake, can be caused by radiographic contrast or amiodarone
- Secondary: TSH-secreting pituitary adenoma

**Clinical Features**
- Weight loss despite good intake
- Anxiety, warm moist skin, onycholysis, insomnia, tremor, fatigue, cramps, irregular menses, pretibial myxedema
- Tachycardia, palpitations, PVCs, AFIB
- Change in bowel pattern, brittle hair, heat intolerance, thyroid enlargement/goiter
- Brisk hyperreflexia
- Graves dz is the only type that is associated with exophthalmos (more common in smokers)
- ED or loss of libido, enlarged thyroid
- May cause osteoporosis, clubbing, or finger swelling
- Gynecomastia, nephrocalcinosis, thyroid storm

**Dx:**
- Primary: ↓ TSH, ↑ T3/T4 (normal T3/T4 if subclinical)
- Secondary: ↑/N TSH, ↑ T3/T4
- Radioiodide uptake scan to differentiate cause

**Tx:** Anti-thyroid drugs → Thionamides (Methimazole, PTU)
- Beta-blockers (sx control), radioactive iodine ablation, thyroidectomy
- Complications: Afib, hypercalcemia, osteoporosis, impotence, decreased libido
<table>
<thead>
<tr>
<th>Thyroid Storm</th>
<th>Myxedema Crisis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life threatening form of extreme hyperthyroidism</td>
<td>Life threatening severe hypothyroidism</td>
</tr>
<tr>
<td>May be precipitated by illness, sepsis, trauma, surgery, RAI administration, and pregnancy</td>
<td>This can be precipitated by sepsis, cardiac disease, respiratory disease, CNS disease, cold exposure, drug use, or non-compliance with treatment</td>
</tr>
<tr>
<td><strong>Clinical features</strong></td>
<td><strong>Clinical Features</strong></td>
</tr>
<tr>
<td>o High fever, tachycardia, agitation, sweating, tremor, instability, delirium, vomiting, diarrhea</td>
<td>o Obtundation, CO2 retention, coma</td>
</tr>
<tr>
<td>o Mortality is high and these patients should go to the ICU</td>
<td>o AMS is the hallmark</td>
</tr>
<tr>
<td></td>
<td>o Mortality is between 20-50%, patient should go to ICU</td>
</tr>
<tr>
<td></td>
<td>o Patients may have severe hyperthermia, hypoventilation, hyponatremia, hypoglycemia, hypotension, rhabdlo, and AKI</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Treatment</strong></td>
</tr>
<tr>
<td>o PTU may be given orally, but monitor for liver dysfunction (also MMI)</td>
<td>o Thyroxine IV bolus, consider hydrocortisone if adrenal insufficiency is suspected</td>
</tr>
<tr>
<td>o IV sodium iodide</td>
<td>o Patients are overly sensitive to morphine which can lead to death</td>
</tr>
<tr>
<td>o IV hydrocortisone</td>
<td></td>
</tr>
<tr>
<td>o Iodide (as lugols solution)</td>
<td></td>
</tr>
<tr>
<td>o Propranolol for heart rate</td>
<td></td>
</tr>
<tr>
<td>o Avoid IV dextrose or oral carbohydrates</td>
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<td></td>
<td></td>
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<tr>
<td>Thyroiditis</td>
<td>Thyroid cancer</td>
</tr>
<tr>
<td>Thyrotoxicosis from leakage of stored thyroid hormone, thyroid cells get broken down. Acute thyroiditis is rare</td>
<td>Fastest growing cancer in US</td>
</tr>
<tr>
<td>Suppurative (bacterial) ➔ most commonly staph aureus</td>
<td>F:M = 3:1, worse prognosis for men</td>
</tr>
<tr>
<td>o Tender gland, fever, pharyngitis, overlying erythema, leukocytosis, elevated ESR</td>
<td>Papillary thyroid cancer (75%)</td>
</tr>
<tr>
<td>o FNA with gram stain and culture is required</td>
<td>Risk Factors</td>
</tr>
<tr>
<td>o Tx includes abx &amp; drainage</td>
<td>o Childhood radiation (25-fold increase), family history, gardner syndrome, MEN type II</td>
</tr>
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<tr>
<td>Subacute Painful ➔ post-viral, giant cell, deQuervain’s, granulomatous</td>
<td>Symptoms</td>
</tr>
<tr>
<td>o Most common cause of painful thyroid gland, most common in women</td>
<td>o Painless thyroid nodule/mass discovered on routine exam or incidentally on US</td>
</tr>
<tr>
<td>o Preceding viruses = EBV, coxsackie, MMR, adenovirus, influenza</td>
<td>o Most pts euthyroid, axs</td>
</tr>
<tr>
<td>o Tender gland, fever, fatigue, dysphagia, otalgia</td>
<td>o Sx of more advanced disease = dysphagia, dyspnea, hoarseness</td>
</tr>
<tr>
<td>o Thyrotoxicosis followed by hypothyroid (resolves in 12 months)</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>o ESR is elevated, treat with aspirin</td>
<td>o Ultrasound, RAIU, Whole body scan, CT scans, PET scans</td>
</tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Drug induced (amiodarone) ➔</td>
<td>Treatment</td>
</tr>
<tr>
<td>o Causes thyroid dysregulation in 20% of patients</td>
<td>o Thyroidectomy or lobectomy</td>
</tr>
<tr>
<td></td>
<td>o Radioactive iodine (100+ mCi)</td>
</tr>
<tr>
<td>Chronic lymphocytic (hashimotos) ➔ most common cause of sporadic goiter in kids, starts as thyrotoxicosis</td>
<td>o TSH suppression w/ levothyroxine</td>
</tr>
<tr>
<td>Fibrous thyroiditis (Reidel) ➔ rarest form</td>
<td>Routine monitoring</td>
</tr>
<tr>
<td>o Formation of dense fiber in the gland, diagnosis is made by biopsy</td>
<td>o Follow serum thyroglobulin, Neck ultrasound</td>
</tr>
<tr>
<td>o “Woody thyroid”</td>
<td></td>
</tr>
<tr>
<td>o May respond to tamoxifen</td>
<td></td>
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<tr>
<td></td>
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</tr>
<tr>
<td>Symptoms</td>
<td>Approach to patient with a thyroid nodule:</td>
</tr>
<tr>
<td>o Lasts 6-8wks until stored thyroid hormone is depleted</td>
<td>Thyroid nodule ➔</td>
</tr>
<tr>
<td>o Usually swings to transient hypothyroidism</td>
<td>o If multiple nodules or history of radiation therapy, do a surgical excision</td>
</tr>
<tr>
<td>o Recovered by euthyroid state</td>
<td>o Otherwise: FNA</td>
</tr>
<tr>
<td></td>
<td>o If malignant ➔ surgical excision</td>
</tr>
<tr>
<td></td>
<td>o If benign ➔ T4 tx and re-aspirate in 1-2 yrs</td>
</tr>
<tr>
<td></td>
<td>o If hypercellular follicular neoplasm</td>
</tr>
<tr>
<td></td>
<td>o RAIU scan</td>
</tr>
<tr>
<td></td>
<td>o If cold ➔ surgical excision</td>
</tr>
<tr>
<td></td>
<td>o If hot ➔ observe</td>
</tr>
</tbody>
</table>
**Adrenal insufficiency (Addison disease)**

- The most common cause is autoimmune destruction (80%)
  - Glucocorticoid deficiency (adrenal etiology) → *loss of GC* + MC, *high ACTH levels*
- Secondary causes are pituitary based
  - ACTH deficiency (pituitary etiology) → *loss of GC*, normal MC, *low ACTH*
- TB is the leading cause of Addison’s in areas of prevalence, calcification of adrenal glands in a setting of symptoms is diagnostic
- Adrenal crises may be precipitated by infection, trauma, surgery, stress, lymphoma, metastatic cancer, amyloidosis, scleroderma, hemochromatosis, cessation of corticosteroids

**Clinical Features**

- Weakness, fatigue, anorexia, GI sx, *salt craving*, postural dizziness, muscle or joint pains, weight loss, *hyperpigmentation*, hypotension, *vitiligo*
- Primary specifically: Na loss & K retention (MC), hyperpigmentation (↑ ATCH – only found in primary disease)
- Delayed DTRs, orthostatic hypotension, small heart, hyperplasia of lymphoid tissues, scant axillary and pubic hair, hypogonadism, AMS (can be fatal)

**Diagnosis**

- Lab findings = hyperkalemia, hyponatremia, hypoglycemia, hypercalcemia, neutropenia, eosinophilia, anemia
- Low AM plasma cortisol & elevated ACTH in primary
- Will see a subnormal response to *Cosyntropin Stimulation Test (CST)* – if cortisol does not increase above 20 it is concerning
- CXR & CT may be indicated for secondary disease
- Abs to 21-hydroxylase

**Treatment**

- Primary disease is treated with a combination of corticosteroids and mineral-corticoids
  - Maintenance therapy: GC replacement (hydrocortisone or prednisone), and MC replacement (fludrocortisone), ↑ salt
- DHEA may be given
- Need medical alert bracelet
- Addisonian crisis requires aggressive IV saline, glucose, and glucocorticoids (as well as treating the underlying cause) → hypotensive shock unresponsive to fluids & pressors

---

**Adrenal Neoplastic disease**

- Most are benign (adrenal incidentalomas)
- Some are benign, hormone-secreting adenomas that cause *Cushing's syndrome, primary aldosteronism, or virilization*.
- Adrenocortical carcinomas (ACCs) are rare, often aggressive tumors that may be functional (secreting steroids independently) and cause Cushing’s syndrome and/or virilization, or nonfunctional and present as an abdominal mass or an incidental finding.
- Pheochromocytomas are catecholamine-secreting tumors that arise from *chromaffin cells* of the adrenal medulla. They may be benign or malignant.
- Imaging — The maximum diameter of the adrenal mass is predictive of malignancy. *Most adrenal adenomas are less than 4 cm in diameter. In contrast, most ACCs are greater than 4 cm in diameter when discovered.*

**ADRENOCORTICAL CARCINOMA**

- Rare
- Bimodal age distribution
- More common in females
- Clinical presentation
  - 60% create clinical syndromes (usually Cushing’s or virilization)
  - The clinical symptoms associated with glucocorticoid excess, such as *weight gain, weakness, and insomnia*, usually develop very rapidly (over three to six months).
- Diagnosis
  - (CT) scanning can usually distinguish ACCs
- Treatment
  - Adrenal adenoma → surgery
  - Adrenal carcinoma → surgery, anti-adenals, mitotane
  - Glucocorticoid replacement is necessary following resection of cortisol-secreting ACC
  - Postoperative radiation therapy (RT) for all patients is recommended

---

**Cushing syndrome**

- ACTH-secreting pituitary adenoma, 10% due to adrenal adenomas, exogenous cushing’s is commonly cause by corticosteroid use
- Less severe in patients >50 years of
- Impairment of normal feedback, ACTH secretion despite high cortisol levels → ↑ ACTH, cortisol, free plasma glucocorticoids

**Symptoms**

- Truncal obesity, thirst, polypuya, striae, moon faces, hirsutism, easy bruising, proximal muscle weakness, backache, headache, acne, depression, insomnia, menstrual issues, HTN, gonadal dysfunction, thyroid dysfunction, osteoporosis

**Dx:** ACTH levels detectable

- 24-hr urine free cortisol → >4x normal is diagnostic
- Late night salivary cortisol → expect lack of midnight nadir
- 1mg Dexamethasone suppression test → expect cortisol >1.8
- 8mg DST → ectopic vs. cushing’s dz (≈50% suppression of 1mg value)
- MRI, CT (look for small cell lung tumors, thymomas, pancreatic cancers), somatostatin scintigraphy

**Treatment:**

- 1st line = transphenoidal tumor resection (cures 75-90%), pituitary irradiation, antiadrenal agents, bilateral adrenalectomy
### Diabetes insipidus Type 1/Type 2

- **Deficiency of or resistance to vasopressin (ADH) → retains salt** (Specific Gravity with DI will be low ~1.00)

- **Central / Hypothalamic (Secondary) →** defect in ADH production
  - Head trauma, surgery, hereditary (aut. dominant), prolactinoma, pituitary adenoma
  - Primary or metastatic tumors, sarcoidosis, granulomatous (TB), idiopathic/autoimmune, infection (syphilis)

- **Nephrogenic (Primary) →** kidney resistance to ADH action
  - Chronic renal failure, lithium toxicity, hypercalciemia, hypokalemia, may be inherited, abnormal receptors in kidneys, no response to desmopressin

- **Others →** Craniophyngioma, Leukemia, lymphoma, Pregnancy (transient)

- **Clinical Features**
  - Thirsty constantly, Polyuria (>3 L/d), Polydipsia (>3.5 L/d), Hypernatremia, Dehydration, Dilute urine
  - Often acute presentation w/ unremitting sustained thirst & polyuria day and night, preference for cold liquids/H2O
  - At serum osm of 290mOsm/kg thirst kicks in

- **Diagnosis**
  - Check glucose, Ca, K, Cr, BUN might be low
  - Screen with 24-hr urine
  - **High serum osm, low urine osm**
  - ADH Levels
    - Central → low ADH levels
    - Nephrogenic → high ADH levels
  - **Water Deprivation Test**
    - Central → responds to DDAVP; urine osmolality (Na) increases
    - Nephrogenic → no response to desmopressin; urine osmolality does not significantly increase
  - Xray for bright spot (stored ADH), MRI for lesions

- **Treatment**
  - Desmopressin (increases water resorption) → treatment of choice for central DI or with pregnancy
  - Mild cases may just require adequate hydration
  - May respond partially to hydrochlorothiazide w/ K+ or amiloride supplementation
  - Nephrogenic may respond to indomethacin (+/- DDAVP, hydrochlorothiazide, amiloride)

### Pituitary adenoma

- **Types:**
  - Gonadotroph adenomas → nonfunctioning
  - Thyrotroph adenomas → hyperthyroidism
  - Corticotroph adenomas → Cushing’s disease
  - Lactotroph adenomas → hyperprolactinemia, which leads to hypogonadism in women and men
  - Somatotroph adenomas → acromegaly

- **Common presentation**
  - Visual defects — compression of the optic chiasm.
  - The most common complaint is diminished vision in the temporal fields (bitemporal hemianopsia)
  - Hormone deficiencies — The most common pituitary hormone deficiencies are of gonadotropins, resulting in hypogonadism in both men and women.

- **Evaluation**
  - MRI & Hormonal hypersecretion
    - A serum prolactin concentration >200 ng/mL generally identifies a lactotroph adenoma.
    - Test for acromegaly is measurement of serum IGF-1.
    - Elevated 24-hour urine cortisol excretion with high adrenocorticotropic hormone (ACTH) concentration = corticotroph adenoma.
    - Thyrotroph adenomas → hyperthyroid patient who has an inappropriately elevated serum TSH level

- **Treatment**
  - Transsphenoidal surgery
  - Can manage hormonally (Prolactin → dopamine agonist like cabergoline or bromocriptine)

---

### Acromegaly - Somatotroph Adenoma (GH)

- **Overproduction of Growth Hormone**
- **Excess GH secretion after epiphyseal plate closure at puberty** → allows excessive linear growth
- **MCC = pituitary adenoma**
- Patient will be complaining of increased head, glove, or shoe size
- **PE will show** coarse facial features, oily skin, visual field deficits, diabetes
- At diagnosis, 10% have heart failure with dilated LV and reduced EF

- **Symptoms**
  - Acral enlargement, frontal bossing, prognathism (protruding jaw), jaw malocclusion, soft tissue swelling, arthralgia & arthritis, proximal myopathy, cardiac hypertrophy, HTN, DM, CAD, skin tags, hyperglycemia, sleep apnea, visceromegaly, kidney stones, hyperhidrosis, menstrual abnormalities, hirsutism

- **Diagnosis**
  - **Measure IGF-1 →** increased suggests acromegaly
  - **Confirmatory tests with OGTT or nadir glucose levels**

- **Treatment**
  - Somatostatin, Somatostatin analogue (ocreotide), GH receptor antagonists, Surgery (transphenoidal), Radiation (usually post-op)

**Pts have increased morbidity & mortality from CV disorders and progression of acromegalic sx**
### Prolactinoma
- Pituitary tumor (40-50% of cases)
- Increased prolactin levels

#### Etiology
- Diminished dopamine levels (DA blocks prolactin)
- Pregnancy
- Hypothyroidism
- Renal failure
- Stalk effect (DA effects decreased by stalk injury)

#### Clinical Features
- Signs of increased prolactin
- Women: infertility, amenorrhea, galactorrhea
- Men: headache, visual abnormalities, libido loss, ED

#### Diagnosis
- Screen –
  - Women: pregnancy test, thyroid function, Cr, prolactin
  - Men: prolactin, testosterone, LH/FSH, thyroid function, Cr, visual field check

#### Treatment
- Dopamine agonists → Bromocriptine, Cabergoline

### SIADH
- Elevated ADH
- Leads to water retention & volume expansion

#### Ectopic production:
- Malignancy (small cell lung ca)
- Baroreceptor dysregulation
- CNS (infx, masses, hemorrhage)
- Pulmonary (pneumonia, TB)
- Transient (pain, nausea, surg)

#### Multifactorial
- Drugs, vigorous exercise

#### Symptoms
- Euvolemia (NO edema)
- Hyponatremia (<135)
- Moderate-severe = confusion, headache, nausea
- Severe = vomiting, somnolence, seizures, GCS <8

#### Diagnosis
- Decreased serum Na
- Increased urine Na loss

#### Treatment
- Restrict fluid intake
- Administer hypertonic fluids
- Drugs that impair renal response to ADH → demeclocycline, lithium
- Vasopressin antagonists

### DKA/hyperosmolar state
- Patient will be a diabetic
- With a history of Infection, Ischemia (cardiac, mesenteric), Infarction, Ignorance (poor control), Intoxication (FIVE I’s)
- Complaining of abdominal pain, vomiting, and fatigue
- PE will show hyperglycemia and ketonemia
- Labs will show anion gap metabolic acidosis
- Caused by precipitating factor in known diabetic
- Hyperglycemia + ketonemia + acidosis
- Anion gap metabolic acidosis with respiratory compensation
- K⁺: monitor and replace as needed
- Mortality in children: cerebral edema
- Mortality in adults: sepsis, cardiopulmonary complications
- Treatment is IV fluids & insulin infusion
- Comments: Corrected sodium add 1.6 mEq/L for each 100mg/dL in serum glucose

### Hypoglycemia
- Usually glucose <60
- Confusion, agitation, unresponsiveness
- Tachycardia, diaphoresis, tremulousness
- Focal neurologic deficit
- Dextrose, thiamine, glucagon

### Pituitary neoplasm
- Paget’s disease of the bones