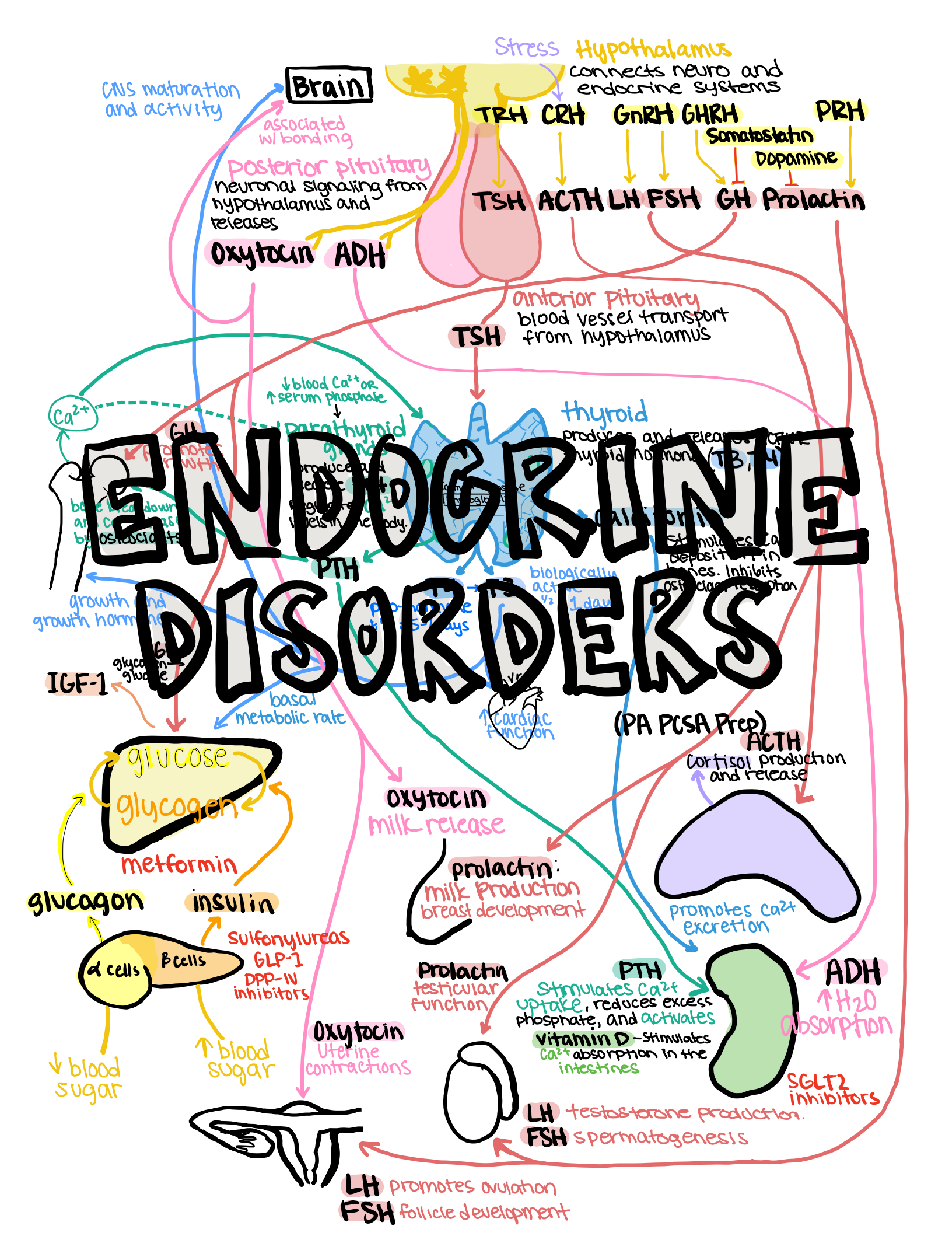

ENDOCRINE DISORDERS
Stress
Hypothalamus
connects neuro and endocrine systems
Brain
CNS maturation and activity
associated w/ bonding
TRH
CRH
GnRH
GHRH
PRH
Somatostatin
Dopamine
Posterior pituitary
neuronal signaling from hypothalamus and releases
Oxytocin
ADH
TSH
ACTH
LH
FSH
GH
Prolactin
Anterior pituitary
blood vessel transport from hypothalamus
TSH
↓blood Ca2+ OR ↑serum phosphate
Ca2+
Parathyroid
thyroid
PTH
IGF-1
growth and growth hormone
basal metabolic rate
1 cardiac function
(PA PCSA Prep)
ACTH
Cortisol production and release
glucose
glycogen
metformin
glucagon
insulin
α cells
β cells
sulfonylureas
GLP-1
DPP-IV inhibitors
↓blood sugar
↑blood sugar
Oxytocin
milk release
prolactin:
milk production
breast development
promotes Ca2+ excretion
Prolactin
testicular function
PTH
Stimulates Ca2+ uptake, reduces excess phosphate, and activates
vitamin D - stimulates Ca2+ absorption in the intestines
ADH
↑H2O absorption
SGLT2 inhibitors
Oxytocin
Uterine contractions
LH testosterone production.
FSH spermatogenesis
LH promotes ovulation
FSH follicle development

ADRENAL INSUFFICIENCY

Causes: autoimmune, surgery (adrenalectomy), infections (TB, fungal, CMV, HIV), tumors

	1°-Addison's disease	2°-hypopitoltarism / ↓ACTH	
Clinical	Salt craving, vitiligo, skin hyperpigmentation, hypotension (<110 systolic)	weakness, fatigue, anorexia, nausea, vomiting, weight loss, cachexia, abdominal pain, dizzy/lightheaded, depressed, muscle and joint pain	signs of pituitary tumor (headache, visual field defects)
BMP	hyperkalemia	hyponatremia, hypoglycemia	—
CBC	normocytic anemia	—	± anemia
Ald/renin	low	—	normal
Cortisol	—	level <30ng/mL POSITIVE	—
ACTH Stim.	—	inject ACTH → cortisol <550ng/mL	—
	↑ACTH		↓ACTH
Treatment	Glucocorticoid AND mineralcorticoid replaced fludrocortisone	Glucocorticoid replacement: 1st: hydrocortisone (2-3x daily) 2nd: long-acting (prednisone) Side effect → osteoporosis	MRI to assess for tumor. ONLY Glucocorticoid replacement

ADRENAL CRISIS: acute onset of adrenal insufficiency that most commonly presents as shock. Abdominal tenderness, N/V, fever.

Treatment: 1-3L normal saline (first 12-24hrs)
Hydrocortisone 100mg IV bolus → 50mg IV every 6 hours for maintenance

CUSHING SYNDROME: HYPERCORTISOLISM

may or may not be ACTH-dependent

ACTH-dependent: pituitary tumor (cushing's disease) or ectopic ACTH production
ACTH-independent: exogenous glucocorticoids or cortisol producing adrenal tumor
Other causes → alcoholism, depression, obesity, pregnancy

Clinical Presentation: GI distress, edema, personality changes, weight gain.
On exam: central obesity, purple striae, buffalo hump, thin skin, gynecomastia (men), amenorrhea/hirsutism (women)

Diagnosis: Should have two first line tests to confirm.
1. low dose dexamethasone suppression test → >1.8mg/dL
2. 24 hr urinary free cortisol excretion
3. Late night salivary cortisol

ACTH
- high → ACTH-dependent cushings syndrome → high dose dex → normal cortisol
  - **Cushing's disease**: 1-2cm pituitary tumor
  - CT → bilateral adrenal hyperplasia
  - MRI → tumor
  - Transsphenoidal microadenomectomy
  - high cortisol: ectopic ACTH-producing tumor not suppressed by dex tests (lung cancer)
- normal → CRH stim test → + response ↑cortisol; no ACTH response → ACTH-independent Cushing Syndrome → adrenal CT to assess for adrenal tumor
- low → ACTH-independent Cushing Syndrome → adrenal CT to assess for adrenal tumor

Treatment: adrenalectomy + glucocorticoid/mineralcorticoid = definitive
- **Surgery**: resection of ACTH-secreting tumor, Pituitary resection (cushing disease)
- **Medical**: adrenal enzyme inhibitors adrenolytic agents, Cabergoline (targets corticotroph)

DIABETES MELLITUS

a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion and/or action.

Criteria: Symptoms plus bg > 200 mg/dl, fasting bg > 126 mg/dL, OR 2hr bg > 200 mg/dL
- diagnosis if asymptomatic → 2 abnormal tests

Symptoms: polyuria, polydipsia, weight loss

Monogenic: one gene defect

① **neonatal DM**: occurs in first six months of life. RARE.
insufficient insulin production → 50% permanent

② **MODY**: diagnosed in adolescence/early adulthood. FAM HX
several different gene mutations - monogenic diabetes
- patients rarely obese

Polygenic: multi-gene defect. Type 1 and Type 2

TYPE 1: B-cell destruction → absolute insulin deficiency. Autoimmune

Epidemiology: ≤ 19 yo. Caucasian.
5% with relative w/ same disease.

Pathophys: immune activation (B-cells attacked) → immune response (Ab development) → stage 1 → 2 → 3 No insulin production

Presentation: not overweight and have recent weight loss, polyuria, polydipsia.
- short duration
- frequently have ketoacidosis

Diagnosis: + antibodies (islet cell, GAD, IA-2, insulin antibodies)

Treatment: **insulin**

Basal: necessary to maintain function
NPH, glargine, detemir, or pump

Bolus: needed to cover ingested food

First 1-2 years → 0.2-1 u/kg/day

After complete failure to secrete insulin
pre-puberty → 0.7-1 u/kg/day
during puberty → 1-1.5 u/kg/day

Twice daily: NPH/Reg or insulin (AM 70/20 PM)

Multidose: basal: detemir, glargine, degludec
bolus: fiasp, lispro, aspart, glulisine

Pump: fiaspro, lispro, aspart, glulisine

TYPE 2: insulin resistance with relative insulin deficiency.
- Progressive insulin secretory defect

Epidemiology: 45+, inactive, fam hx, ↑bp, overweight, gestational diabetes hx

Pathophys: ↓postprandial insulin secretion PLUS ↑insulin resistance → postprandial hyperglycemia → exhaust B-cells → apoptosis

Presentation: ↑urination, ↑thirst, blurred vision, dizzy, ↑hunger, irritable, tingling, weight changes, ↓wound healing

If asymptomatic, Screen IF:
>45, overweight, 1+ risk factor, HIV, prediabetes pts, woman w/ GDM

Treatment: goal is glycemic control-
A1C < 7%, fasting bg 80-130 mg/dL, peak < 180
└ 8-8.5% for elderly, frail, ↓life expectancy

CV risk reduction - lifestyle modifications
- weight management
- physical activity (150 min/wk + 2 days strength)

Medication

monotherapy: **metformin** - acts at liver to ↓ glucose production and ↑ insulin sensitivity

dual therapy: do initially if A1C ≥ 9%. ADD:

(-flozin) SGLT2i ↑glucose and sodium excretion. yeast infections

(-glitpin) DPP41 ↑ insulin release, ↓ glucagon release, ↑ satiety,
(-tide) GLP1 slow gastric emptying to ↑ glucose absorption

(-glitazone) TZD ↑ insulin sensitivity in muscle.

insulin: usually in combo w/ metformin. Helps overcome resistance

If A1C > goal after 3 more months → triple therapy

MICROVASCULAR COMPLICATIONS

① Eyes → retinopathy - capillary damage due to persistant hyperglycemia

- non-proliferative: aneurisms, hemorrhage, hard exudates, cotton wool spots
- proliferative: growth of new blood vessels 50% chance of blindness if untreated
- Clinically-significant macular edema: MC vision loss in DR. Leakage + accumulation of fluid

Treatment: **glycemic control**
Lipid / bp management, laser, injections

② Kidneys → nephropathy - albuminuria and/or decreased eGFR

macro >300 Stage1 >90 ESKD<15

Screen w/ yearly urine microalbumin
2 out of 3 tests at least 1 mon apart

Treatment: **glycemic control**
blood pressure management, ACE/ARB, ↓protein

③ Nerves → neuropathy

Peripheral is most common. Disease of the axon. "Stock and glove pattern" usually in feet first.
- Vibration - first loss sense

Autonomic: orthostatic hypotension, ED, gastroparesis, neurogenic bladder

Foot disease: ulcer → surgically debride. may lead to amputation.

MACROVASCULAR COMPLICATIONS

① Brain → cerebrovascular disease
② Heart → coronary heart disease
③ Vessels → peripheral arterial disease

Cardiovascular disease is the #1 cause of mortality in diabetes.
- diabetes is as great a risk factor for MI as a hx of prior MI in non-diabetic

Key considerations
- Controlling blood glucose has **NOT** been shown to ↓ risk of macro comps
- **early glycemic control DID** ↓ risk of macrovascular complications
- control of other risk factors ↓ comps
  - smoking cessation, anti-platelet therapy, anti-hypertensives, statins

HYPERGLYCEMIC EMERGENCIES

Diabetic Ketoacidosis

more common in Type 1

Hallmark: **hyperglycemia, anion gap, bicarb<18** (>12 is severe)

May be precipitated by: infection, new onset T1DM, gastroenteritis, meds, cocaine use, eating disorders

Signs/Symptoms: N/V from ↓ peristalsis, altered mental state. **ABDOMINAL PAIN**

On exam: Kussmaul resp, fruity odor, volume deplete lethary, coma

Management: **IV fluids** - 0.9 NS 15-20 ml/kg/hr. 0.45 NS if corrected Na.
Add dextrose if bg<200
Continuous insulin drip
Replace K if **<5.3** (KCl)
Monitor bg hourly. Bicarb **ONLY IF pH≤6.9**

HHS: relative insulin def.

type II and insidious onset

Hallmark: hyperglycemia, ↑osmolarity >300.
Absence of significant ketoacidosis
precipitated by: acute illness → counterregulatory hormones

Presentation: neurologic deterioration (can look like a stroke)
- normal arterial pH

NO significant ketoacidosis

Management: **IV fluids**
Insulin - reg/short acting
electrolytes

Resolution → mentally alert, plasma osmolarity <315
- tolerating po

Euglycemic DKA

Starvation resulting in ketosis while maintain normoglycemia

serum glucose <250 AND metabolic acidosis, ketonemia (positive for ketones)

Seen in pts with:
- **SGLT2 inhibitors** (not indicated for T1)
- poor intake
- pregnancy
- incomplete treatment

Treatment:
Insulin if K>3.3
IV fluids **+dextrose immediately**
STOP SGLT2 inhibitor

THYROID MASSES/NODULES

Very common. ↑ with age. Often multiple.

BENIGN

1. Hyperplastic nodules
2. Adenoma (neoplastic): may be autonomously functional
3. Cysts
4. Nodules associated w/ thyroiditis

Nontoxic Goiter

- **Multinodular**: hyperplastic growth of thyroid. Tends to grow slowly over multiple years associated with iodine deficiency. More common in women. thyroid function → normal but may cause compressive symptoms.
- **Substernal**: indication for operation even if asymptomatic due to risk of airway compromise. Removed transcervically (through neck)

Treatment: TSH suppression to decrease mass. Levothyroxine at low dose → increase to keep TSH low. BUT risk of arrhythmia.

CANCER

Clinically silent thyroid cancer is very common
Increasing incidence → incidental detection.

1. **Papillary** (80-85%): >50% w/ lymph node mets. Often multifocal. Diagnosed w/ FNA.
   Aggressive variants: insular (unencapsulated) and tall cell
2. **Follicular** (10-15%): typically present w/ distant mets. unifocal. NOT diagnosed w/ FNA.
   Histology: similar to follicular adenoma but MUST see vascular/capsular invasion.
   Hürthle cell cancer – mitochondrial DNA mutations. Worse prognosis.

MACIS for prognosis: based on age, tumor size, resection, local invasion, distant mets
<6 → 99% chance of survival. >8 → 24% survival

Treatment for differentiated: Observation → Surgery → adjuvent TSH suppression, RAI → drugs

3. **Medullary** (5%): derived from neuroendocrine C-cells (synthesize Ca^{2+}). RET mut.
   total thyroidectomy, central neck dissection
4. **Anaplastic** (1%): highly undifferentiated. FATAL. Surgery, chemo, radiation

Detection:

- Thyroid function tests → **TSH**, free T4
- radioactive iodine uptake scans → most nodules cold
- **Ultrasound** → highly useful in determining size and characteristics | heterogeneous nodule echogenicity

  Features of malignancy: microcalcifications, hypoecoic (appear dark but internally homogenous), increased vascularity, infiltrative margins (irregular), taller than wide

FNA: fine needle aspiration is test of choice for the thyroid to obtain tissue
Ultrasound guided. Rarely need core biopsy. >4cm have high incidence of cancer

- I non-diagnostic → 1-4% risk → repeat FNA
- II benign → 0-3% risk → Clinical FU
- III atypia of unknown sig. → 5-15% risk → repeat FNA
- IV follicular neoplasm suspicion → 15-30% risk → surgical lobectomy
- V malignancy suspicion → 60-76% risk → lobectomy OR total thyroidectomy
- VI malignant → 97-99% risk → total thyroidectomy

Risk of injury to recurrent laryngeal nerve

HYPOTHYROIDISM

deficiency of thyroid hormone

1° - caused by thyroid gland dysfunction, failure or absence

2° - caused by pituitary or hypothalamic disease

Epidemiology: women > men. ↑ w/ age.

Causes

① Loss of thyroid tissue

autoimmune (Hashimotos thyroiditis)

TPO antibodies → destruction of thyroid tissue → extensive infiltration of lymphocytes/plasma cells.

Permanent hypothyroidism

- **De Quervain's**: painful mass. No thyroid antibodies.
- **Silent/lymphocytic**: painless. +antibodies.
- **Acute/suppurative**: S.aureus. painful. ILL. abx.
- **Reidel's**: firm, hard, "woody"

post-surgical, post radioiodine ablation, congenital

② Decreased thyroid hormone production

medications (lithium, amiodarone)

iodine deficiency

Clinical

fatigue, weight gain, cold intolerance, hair loss, constipation, dry skin/hair, poor memory **due to**

1. slowing of metabolism and target organ function
2. accumulation of glycoaminoglycans

Diagnosis

test if multiple sx, famhx, women>60, use of above meds, exposures

	TSH	FT4	T3
Primary -	↑	↓	N/↓
Subclinical -	↑	N	N
Secondary -	↓/N	↓	N/↓

Treatment

levothyroxine daily in AM separate from antacids. NO BIOTIN.

1.6 mcg/kg for full replacement

25-50 mcg empirically and titrate

Monitor TSH every 6-8 weeks.

HYPERTHYROIDISM

excess thyroid hormone

Causes

endogenous

① excess thyroid hormone production

- graves disease - women 20-5 yo
- toxic multinodular goiter - elderly, f.
- toxic adenoma - 20-40 yo "hot" nodule
- TSH secreting tumor (2°) - rare (mental disturbances)

② excess thyroid hormone release - thyroiditis

exogenous: excess thyroid hormone dosage or surreptitious use

Clinical

: due to accelerated metabolism and target organ hyperfunction

- weight loss, ↑HR, heat intolerance, sweating, anxiety, fatigue, ↑appetite

GRAVES DISEASE: autoimmune disorder

TSI (immunoglobulin) activate TSH receptor on thyroid gland → enlargement of gland → ↑TH + goiter + exophthalmos

Epidemiology: 20-50 yo female

Clinical: diffusely enlarged, painless goiter ± thyroid bruit.

- graves ophthalmopathy → proptosis
- graves dermopathy → skin swelling
- acropachy → finger clubbing, hands swell

Toxic Multinodular Goiter: nodules become autonomous over years. Monoclonal expansion of follicles ± activating mutations in TSH-R

Epidemiology: older. F>M.

Clinical: asymmetric, enlarged nodular gland

- compressive symptoms (dysnea, dysphasia)

Diagnosis

	TSH	FT4	T3
Primary -	↓	↑	↑
Subclinical -	↓	—	—
Secondary -	↑	↑	↑

Antibody testing: ↑TSI/TSH-R in graves

Nuclear studies: radioactive iodine uptake scans

Treatment

methimazole (for graves) and propylthiouracil (preg)

radioactive iodine, surgery (for toxic nodules)

- Ancillary/adjunctive: iodine (SEVERE), b-blockers for cardiac sx

MYXEDEMA COMA

High mortality rate

Severe hypothyroidism

Chronic non-compliance or undiagnosed hypothyroidism, after precipitating event:

- severe illness
- surgery, sedatives, anesthetics
- Elderly women in winter

Clinical: bradycardia, hypotension, hypothermia, hypoventilation, coma

Diagnosis: Clinical

Treatment: IV thyroid hormone

- treat underlying cause
- ICU admission
- aggressive supportive care
- passive warming

THYROID STORM

Severe hyperthyroidism

In borderline or untreated disease after precipitating event:

- severe illness, infection
- surgery, trauma, sepsis
- iodine loads
- post-partum

Clinical: fever, mental status changes, palpitations, tachy, afib, n/v, psychosis, tremors

Diagnosis: Clinical

Treatment: high dose IV PTU then iodine, propranolol, dexamethasone

treat underlying cause

THYROIDITIS inflammation of thyroid

1. Chronic lymphocytic (autoimmune) → Hashimotos → Levothyroxine
   main cause of hypothyroidism
2. Non-specific: transient hyperthyroidism → B-blockers for Sx
   Painless thyroiditis
   Postpartum thyroiditis
3. Granulomatous: tender, swollen, ↑ESR, post-viral → NSAID/prednisone for pain
   subacute, painful subacute, De Quervains
4. Reidel's → firm, hard, woody
5. Acute/supperative: S. aureus. Painful, ill, febrile → antibiotics
   - no change in thyroid function

PHEOCHROMOCYTOMA Catecholamine-secreting tumor arising from the chromaffin cells of the adrenal medulla

Paraganglioma: catecholamine-secreting tumor arising from the sympathetic ganglia ("extra-adrenal pheochromocytoma")
Do NOT make epinephrine

Epidemiology: rare. Diagnosed at 40-50 yo. Associated w/ MEN2, fam disorders

Presentation: CLASSIC TRIAD - headache, sweating, tachycardia

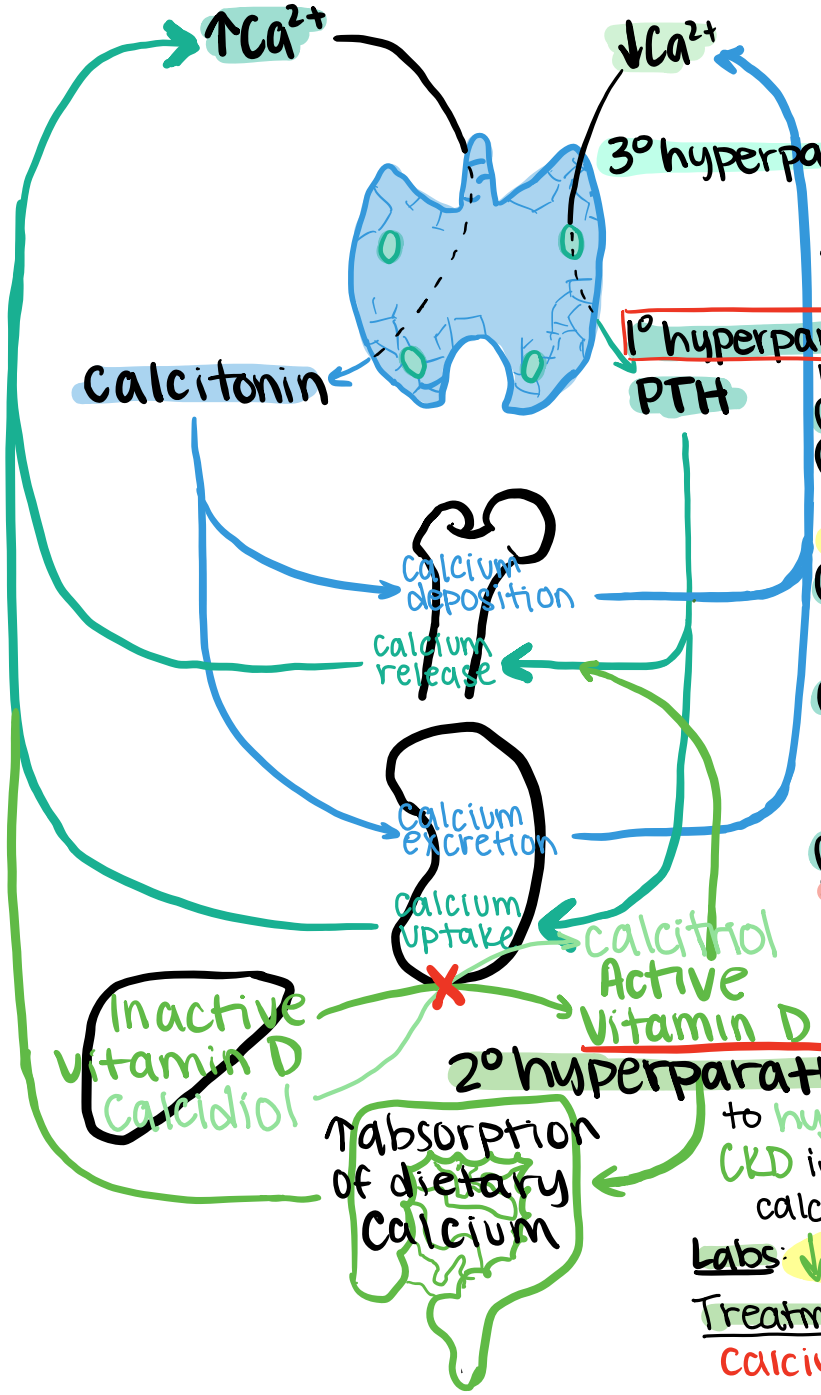
- Palpitations, tremor, pallor, dyspnea, panic-attack like sx, weight loss

on exam: paroxysmal hypertension

Diagnosis: POSITIVE urine and serum metanephrines (2x ULN)
Abdominal CT/MRI → intraadrenal tumor

Treatment: α-block x 7days → ↑sodium → β-block x 2-3days → Surgery
phenoxybenzamine; diet x 3days; propranolol or metoprolol

"Rule of 10s": 10% extra adrenal, bilateral, malignant, familial



3° hyperparathyroidism: autonomous overproduction of PTH following long term stimulation
Chronic kidney disease ± renal transplant
Treatment: Surgery ↑serum phosphate

1° hyperparathyroidism: most common cause of hypercalcemia. Excess PTH production
① 60-70yo. Female > male.
② 80-90% single adenoma
10-20% hyperplasia >2 glands
<1% carcinoma → Ca^{2+} >14. age <30yo. Palpable.
③ Stones, bones, groans, moans
If SEVERE, osteitis fibrosa cystica - cystic, bony spaces fill w/ "brown tumor" osteoclasts
④ ↑Ca^{2+} ↑PTH ↑24hr urine Ca ↓Phosphate ↑VD
Nuclear imaging for localization
Determination of **iPTH** is the most important serological test for 1° hyperparathyroid diagnosis
⑤ Parathyroidectomy
Severe: IV saline (until 200 mL/urine) + furosemide to ↓ Calciu
Ca >14 or Symptomatic
Mild: furosemide (lasix), hydration, activity ± estrogen for post-menopausal woman

2° hyperparathyroidism: normal parathyroid response to hypocalcemia.
CKD impairs vitamin D activation, lowering calcium absorption in gut → Parathyroid Compensation
Labs: ↓Ca^{2+} ↑PTH ↑phos
Treatment: phos binders, vitamin D analog, Calcium and parathyroidectomy if severe (PTH >800)

Hypoparathyroidism

Causes: low PTH or insensitivity to PTH
- accidental removal/damage during surgery (post surgical is most common cause)
- autoimmune destruction of gland
- congenital
- Mg deficiency: ↓Mg → ↑PTH BUT ↓↓↓Mg → ↓PTH. Treat w/ Mg^{2+}. Mg acts like Ca.

Diagnosis: ↓Ca^{2+} ↓PTH ↑phosphorus

Treatment: acute → IV calcium Chronic → oral calcium + vitamin D supplementation

DiGeorge Syndrome: autosomal dominant 22q11.2 deletion

Cardiac abnormality **A**bnormal facies **T**hymic aplasia **C**left palate **H**ypocalcemia/ hypoparathyroidism

GROWTH HORMONE EXCESS

Gigantism: the result if the disease mechanism starts in childhood prior to closure of epiphyses. VERY RARE

Etiology: pituitary adenoma.

Presentation: excess growth of long bone

Acromegaly: the result if disease mechanism starts after puberty. Onset 30s

Presentation: enlargement of hands, feet, jaw

Physical complications: jaw protrusion, joint pain, peripheral neuropathy, cardiac disease, impaired glucose tolerance

Diagnosis: elevated IGF-1 (5x normal)

Glucose tolerance test: ↑GH. glucose bolus normally decreases GH levels

Treatment: ↓GH production, ↓negative effects of tumor on pituitary gland and tissue.

- Pituitary adenoma → surgical resection
- Medications → somatostatin analogs, dopamine D2 agonists, GH receptor antagonist

GROWTH HORMONE DEFICIENCY

Dwarfism: short stature. 4'10" or less.

- disproportionate: some average-size parts of the body and some shorter than normal
- proportionate: individual is smaller than average overall

Pituitary dwarfism: deficiency of GH secreted by anterior pituitary

Congenital: slowed height velocity. May not show immediate growth failure.

Acquired: SEVERE growth failure, ↓bone age, ↑weight:height ratio. tumor or trauma.

Pituitary dwarf	vs.	hypothyroid dwarf
• skeletal/dental developmental delay • plump, immature face		• mental/physical developmental delay • potbelly, tongue protrudes

Diagnosis: ↓IGF-1/IGFBP-3 (binding protein) not as affected by age/nutrition ↑

GH stim – fast → bolus → measure GH btwn 0 and 3 hours

Treatment: daily subq recomb. GH based on weight and IGF-1 levels until <1in/yr growth velocity

SIADH Syndrome of inappropriate ADH

Pathophys: excess ADH secreted from PP or ectopic

- malignancy, drugs/meds, brain injury, infection, hypothyroidism

ADH causes ↑water reabsorption at kidneys.

Presentation: hyponatremia symptoms

confusion, fatigue, seizures, edema, n/v

Diagnosis: ↓serum osmolarity ↓BUN ↓serum Na^+ ↑urine osmolarity

Treatment: underlying cause. Water restriction.

Severe → IV saline w/ furosemide

DIABETES INSIPIDUS

ADH Deficiency - hypothalamic (central)

Causes: idiopathic, autoimmune, tumor, trauma

ADH Insensitivity - nephrogenic

Causes: meds, hypercalcemia, hypokalemia

Presentation: dehydration, polyuria, orthostasis, occur w/ decreased free water intake

Diagnosis: ↑serum osmolarity ↑BUN ↑serum Na^+ ↓urine osmolarity fluid deprivation test

Treatment: central - desmopressin (DDAVP)

nephrogenic - HCTZ, indomethacin, ↓Na diet

PITUITARY TUMORS

functioning → hormone secreting. Non-functioning → non-secreting

Symptoms depend on hormone involved. **Diagnosed** by mri of brain (sellar mass)

1. **Prolactin**-secreting (Prolactinomas): cause ↓ sex hormone.

   Treat with dopamine agonist - **Cabergoline** (Bromocriptine for pregnancy)

   - Women: ↓estrogen → irregular menses, amenorrhea, galactorrhea, infertility
   - men: ↓testosterone → ED, low sperm count, ↓libido, gynecomastia
2. **ACTH**-secreting: excess ACTH production stimulates adrenal glands to make cortisol. ↑Cortisol → Cushing's Syndrome
   - ↑fat, ↑bp, ↑bg, striae, buffalo hump, facial roundness, bruising
3. **GH**-secreting: can cause acromegaly
4. **TSH**-secreting: similar to primary hyperthyroidism (weight loss, sweating)

Treatment: transsphenoidal surgery. Observe small, non-functional except prolactinomas