ABIM Examination Blueprint

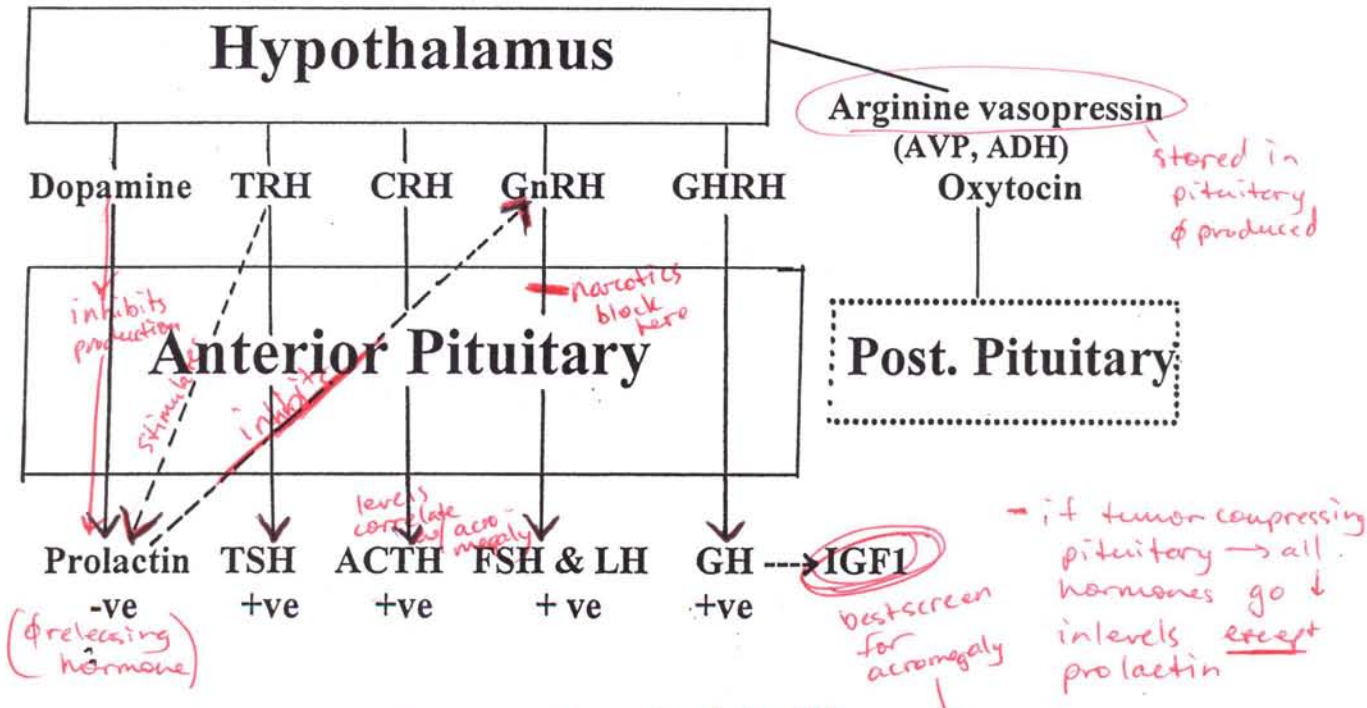
(Certification and Recertification)

Cardiology 14%	Gastroenterogy 10%	Pulmonary 10%
Infectous Disease 9%	Rheumatology 8%	Endocrinology 7%
Oncology 7%	Hematology 6%	Nephrology 6%
Immunology 5%	Psychitry 4%	Neurology 4%
Dermatology 3%	OB/GYN 2%	Opthalmology 2%
Miscellaneous 3%		

Cross-Content Area

Critical Care 10%	Geriatrics 10%	Prevention 6%
Women's health 6%	Clinical Epidemiology 3%	Ethics 3%
Nutrition 3%	Palliative Care 3%	Adolescent Medicine 2%
Occupational Medicine 2%	Substance Abuse 2%	

Pituitary Disorders



Causes of Hyperprolactinemia

1. Hypothalamic disease
2. Pituitary stalk disease
3. Pregnancy (↑FSH/LH)
4. Hypothyroidism (very common cause)
5. Renal Failure
6. Pituitary tumors (prolactinoma or non-prolactinoma → amenorrhea galactorrhea HAS)
7. Cirrhosis
8. Acromegaly
9. Idiopathic
10. Drugs:

Phenothiazines, metoclopramide, reserpine, methyldopa, estrogens, opiates, fluoxetine, cocaine, risperidone, MAO inhibitors, tricyclics, verapamil

prolactin > 100 → prolactin-secreting tumor

- prolactin level correlates w/ tumor size

Hyperprolactemia

most common cause of amenorrhea after stopping OCP's

Rule Out Secondary Causes (Ex. TSH, drugs - as above)

MRI

Microadenoma (< 10 mm)

- Regular Menses → No treatment
- Infertility → Bromocriptine
- Amenorrhea → Bromocriptine or Cabergoline or Estrogen-progesterone

Macroadenoma (> 10mm)

- Intrasellar
  - Infertility → Bromocriptine
  - Amenorrhea → Bromocriptine or Cabergoline
- Suprasellar → Do visual field testing, Evaluate ant. pituitary function
  - Infertility → Bromocriptine
  - Amenorrhea → Bromocriptine or Cabergoline
  - No response → Surgery

Bromocriptine, Cabergoline → Dopamine Agonists Tx

medical tx first then surgery

stop Bromocriptine in pregnancy

Complications of Acromegaly

- If acromegaly suspected but MRI OK → CT chest/Abd/Pelvis

1. Sleep apnea
2. Carpal tunnel Syndrome
3. CHF, LVH, ↑BP, Cardiomegaly
4. Colon polyps
5. Osteoarthritis
6. Pseudogout
7. Diabetes and insulin resistance
8. Hyperprolactinemia, hypogonadism
9. Visual field defects
10. Gigantism → prior to epiphyseal closure

- enlarging shoe size
- prominent jaw

Tx: surgery (trans-sphenoidal)

If Sx does not achieve biochemical remission → octreotide ± Rad Tx

Post-op Follow w/ annual:
- IGF-1
- GH after glucose load
- pituitary MRI

Causes of Deficiency of GnRH

most common

1. Kallman's syndrome — x-linked hypothalamic hypogonadism w/ ↓FSH/LH, hypogonadism, anosmia (lost sense of smell) — Tx: Testosterone Replacement
2. Mutation in the GnRH receptor gene
3. Long distance running → inducing amenorrhea
4. Anorexia nervosa
5. Starvation & stress
6. Hyperprolactinemia

least common

Hypopituitarism

think of when there is multiple hormonal abnorms

Clinical Manifestation

Young children: Growth retardation (↓growth hormone)
Older Children: Delayed puberty (↓LH/FSH)
Premenopausal women: Amenorrhea (↓LH/FSH)
Men: Hypogonadism (loss of libido, infertility, impotence)
hypothyroidism, secondary hypocortisolism

Growth Hormone Deficiency

↑fat mass, ↓lean body mass, ↓bone density, ↓quality of life

Prolactin Deficiency: Inability to lactate after pregnancy

ACTH Deficiency ★ → most critical function to determine for hypopituitarism

Secondary hypocortisolism (hypoglycemia, fatigue, anorexia).
Aldosterone is normal, so no salt wasting or ↑K or volume contraction. No skin pigmentation

Thyrotropin deficiency → Hypothyroidism

Weight gain, dry brittle hair, hair loss, constipation, fatigue, cold intolerance, cognitive complaints, dry skin

Evaluation:

IGF-1, freeT4, TSH, morning cortisol, ACTH, testosterone, estradiol, LH/FSH
TSH, LH/FSH can be normal or low in hypopituitarism
MRI of the pituitary gland

Pituitary Apoplexy
- pituitary hemorrhage/infarction
leads to
char by:
- sudden-onset HA's
- visual Δ's
- ophthalmoplegia (ocular muscle paralysis)
- delirium
- usually acute-onset adrenal insuff. + hypothyroidism
↓
hypotension
hyponatremia
Tx: IV hydrocortisone ± surgery (if severe)

Normal TSH w/ ↓ FTH
↓
pituitary dis. (2nd-ary hypothyroidism)

Tx: Cortisol
Synthroid
TSH Replacement
Estrogen/Testost

- follow TSH for hypothyroidism but follow FT4 for hypopituitarism

follow FT4 to monitor adequate supplementation

Common Causes of Hypopituitarism

1. Tumors
2. Brain radiation
3. Hemochromatosis
4. Amyloidosis
5. Autoimmune
6. Sarcoid
7. Sheehan's syndrome
8. Empty sella syndrome

char by:
- failure of post partum lactation
- fatigue/cold intol.
- weakness

- post-delivery hypotension during labor
↓
pituitary necrosis

Tx: Hormone-Replacement Tx.

5/10% may develop hypopituitarism but most are normal w/ normal pituitary function

Evaluation of Patient with Polyuria

	(1) Central D. Insipidus	(2) Nephrogenic D. Insipidus	(3) Psychogenic Polydypsia
Urine Osmolality after water deprivation	No change	No change	Increases (start concentrating)
Urine osmolality after 5 U of vasopressin or 1 ug of desmopressin (ADH)	Increases > 50% (Difference)	No change or slight↑ (< 10%) (Difference)	No change or slight↑
BUN	N/↑	N/↑	N
Na	N/↑	N/↑	↓ (Dilutional Hyponatremia)

Causes of Nephrogenic Diabetes Insipidus

1. Congenital and familial
2. Hypokalemia
3. Hypercalcemia
4. Renal Disease
5. Drugs : Lithium, demeclocycline

Tx: Diuretics (Thiazides or Amiloride)

Minimal response to Desmopressin → b/c problem is ϕ making ADH problem is that kidneys don't respond to the made ADH

SIADH

Diagnosis: Na↓, Urine osmolality↑, Urine Na↑
No edema & absence of severe pain, hypotension or hypovolemia

Pain (esp. post-op) → ↑ADH → ϕSIADH

Classic case: post-op abd. surgery now w/ Na 130 → ϕ SIADH → still tx w/ fluid restriction though

Causes:

1. Tumors
2. Pulmonary Disease
3. CNS disorders
4. Hypothyroidism
5. Positive pressure breathing
6. Drugs : Chlorpropamide, vincristine, vinblastine, tricyclics, Cyclophosphamide, narcotics, carbamazepine, HCTZ, SSRIs, phenothiazines, MAO inhibitors

Tx: Fluid Restriction or Hypertonic saline (if acutely ill) 200-300 cc's over 3 hrs.

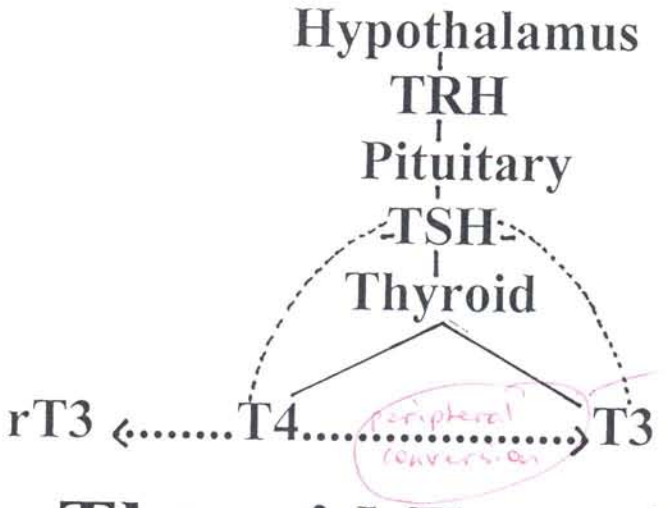
Correct Na ↓ ϕ more than 0.5 mEq/hr rise

Rapid correction can cause Central pontine myelinosis

Quadriplegia ← Pseudobulbar Palsy

if ϕ response then Demeclocycline ↑

Thyroid Function Tests



Central Hypothyroidism
↓ FT4 w/ a ↓ TSH

Impaired in acute illness
Instead T4 shifted to ↑ rT3

Thyroid Function Tests

↑ Binding globs → ↑ total levels

	Thyrotoxicosis	Hypothyroidism	↑TBG	↓TBG
1. Total T4	↑	↓	↑	↓
2. Total T3	↑	↓	↑	↓
3. Free T4 (FT4)	↑	↓	N	N
4. Free T3 (FT3)	↑	↓	N	N

- estrogen ↓ ↑ TBG

5. TSH (most sensitive test for hypothyroidism)
6. RAI uptake (5-30%) — only for thyrotoxicosis
7. Thyroglobulin levels — ↑'d in thyroid ca. except medullary carcinoma
8. Thyroid Antibodies — ↑ thyrotoxicosis

Thyroid Antibodies

Hashimoto's
- ↑ risk of other autoimmune endocrine D/O's
  - Adrenal Insuff
  - Pernicious Anemia
  - DM (Type 1)
  - vitiligo
  - Premature ovarian failure

1. Thyroid peroxidase antibodies (TPOAB)
2. Thyroglobulin antibodies
3. TSH receptor antibodies
   - Thyroid stimulating immunoglobulin (TSI) → Grave's dis.
   - TSH binding inhibitor immunoglobulin (TBII) → atrophic thyroiditis

TBG

Increase (↑ Total T_3 + T_4)

1. Pregnancy
2. Estrogens
3. Tamoxifen
4. Genetic
5. Hepatitis
6. Biliary cirrhosis
7. Methadone

Decrease (↓ Total T_3 + T_4)

1. Androgens
2. Nephrotic syndrome
3. Glucocorticoids
4. Chronic liver disease
5. Severe systemic illness
6. Acromegaly
7. Genetic

Celiac Dis.
- malabsorptive process
↓
Pt's may require ↑'d Synthroid doses to achieve euthyroidism

Pendred's Syndrome
- AR inheritance
- congenital SNHL
- goiter
- char. by mutation in pendrin → iodide transport protein

Dx: (+) Perchlorate D/C Test

Suspect Thyroid Disease

↓

Measure FT4 and TSH

↓

FT4

High (Hyperthyroidism) → **TSH**

- **Low** → **Primary Hyperthyr.**
- **normal or ↑** → **Secondary Hyperthyr.**
  - TSH producing tumor → ✓MRI
  - Thyroid hormone resistance syndrome

↑'d metabolism of coumadin BUT ↑↑↑'d metabolism of clotting proteins
↓
Result → ↑ coumadin dose in hyperthyroidism

↑'d Digoxin metabolism in Hyperthyroidism
↓
↑ Dig doses

RAI uptake

- **Diffuse ↑** → **Graves**
- **Focal ↑** → **Toxic adenoma**
- **uptake ↓** → 1. Subacute or Lymphocytic thyroiditis Disease
  2. Factitious Thyrotoxicosis
  3. Iodine excess
  4. Struma ovarii

Low (Hypothyroidism) → **TSH**

- **High** → **Primary Hypothyr.**
  - **TPOAB+** (Hashimoto's)
  - **TPOAB-** (Other causes of hypothyroidism)
- **Normal or ↓** → **Secondary Hypothy.** → **CT & MRI** Measure other Hormones

- Delayed DTR's (most sensitive PExam finding)

Tx: young w/out CHD
- will also ↓ LDL levels
- 50 mcg Synthroid
- elderly 12.5-25 mcg
- re-eval Q 6 wks
- ✓ TSH to normalize it

Pregnant woman on synthroid
↓
↑ dose by 30%
monitor TSH Q Month during pregnancy then ↓ level post-partum

Thyroid Storm
- Known h/o Grave's dis.
- Took anti thyroid meds in past
- fevers
- tachycardia
- hypotension
- SOB

Tx: High-dose PTU
Dexamethasone
K-Iodide

Euthyroid Sick Syndrome

-usually normal TSH w/ low FT4

-remeasure TFTs a couple wks. after recovery

Total T4 ↓ or N

T3 RIA ↓ (impaired T4 to T3 conversion)

peripherally via inhibition of type 1 deiodinase

FT4 ↓ or N

TSH N or ↓ (may ↑ during recovery)

rT3 ↑ → T4 shunted to rT3 as peripheral T4 → T3 conversion is impaired

Hyperthyroidism

✓ T3 levels when suspecting thyrotoxicosis

Causes	FT4	FT3	TSH	RAI
1. Grave's disease	↑	↑	↓	↑ Diffuse uptake
2. Toxic adenoma	↑	↑	↓	↑ Focal uptake
3. Multinodular goiter	↑	↑	↓	↑
4. T3 thyrotoxicosis	N	↑	↓	↑
5. Subclinical	N	N	↓	↑/N
6. TSH producing tumor	↑	↑	↑/N	↑ ✓ MRI
only causes that ↑ TSH: 7. Thyroid hormone Resistance syndrome	↑	↑	↑	↑
8. Thyroditis	↑	↑	↓	↓
9. Thyrotoxicosis factitia				
T4 (exogenous sources)	↑	↑	↓	↓
T3 (exogenous sources)	↓	↑	↓	↓
10. Struma ovarii	↑	↑	↓	↓

→ differentiates from Grave's

Generalized or thyroid-specific

Thyroditis

↑'d cancer ↑ lymphoma

1. **Hashimoto's** (most common cause of hypothyroidism) painless firm symmetrical
2. **Painless postpartum** (Lymphocytic) - enlarged nontender
3. **Painless sporadic** (Lymphocytic) - if hyperthyroidism → Tx: Propranolol usually hypothyroidism → IFN can cause
4. **Painful subacute** enlarged thyroid ↑ ESR, CRP
5. **Suppurative** → abscess Tx - Drainage, Abx
6. **Drug-induced** (Amiodarone, Lithium, Interferon Alfa, Interleukin-2) - cold nodule
7. **Riedel's** - stone-hard gland

Steps
① Thyrotoxicosis early
② Transient hypothyroidism
③ Improvement

- can use NSAIDs or Prednisone for pain

vs. acute
- fever
- abscess
- bacteremia

Apathetic Thyrotoxicosis
- apathy
- ↓ hyperactivity
- lethargy
- wt. loss
- somnolence
- droopy eyelids
- constipation
- AFib
- myopathy

Prominent Thyroid Nodule
- FNA Bx

Post partum Thyroiditis
- can differentiate from Grave's dis via RAI scan but RAI is secreted in breast milk → avoid if breastfeeding
- instead ✓ TSH Ig's

Treatment of Hyperthyroidism Due to Grave's Disease

↑ FT4/FT3
↓ TSH
↑ RAI uptake (diffusely)

RAI

1. Severe hyperthyroidism
2. Very large goiter (> 4 times normal)
3. T3/T4 ratio > 20
4. ↑Baseline levels of antithyrotropin antibody
5. Other Adults
6. Contraindicated in pregnant and lactating women

Antithyroid-drug therapy (PTU or methimazole)

1. Children
2. Adolescents
3. Pregnancy (PTU preferred)
4. Lactating women
5. Option for initial therapy in adults with:
   a) Severe eye disease
   b) Mild to moderate hyperthyroidism
   c) Small goiters
   d) T3/T4 ratio < 20
   e) Negative antithyrotropin antibody

Treat 12-18 months

Relapse

- RAI
- Second course in children and adolescents

Multinodular Goiter
- complications:
  (1) ↑'d Iodine load → induces thyrotoxicosis (Ex. Jod-Basedow phenomenon) → post-cath
  (2) or w/ Amio(Iodine)

Graves Ophthalmopathy
- blurry vision
- afferent pupillary defect (Marcus Gunn pupil)
- dry eyes
- Diplopia
- ↓ unilateral acuity
- Severe cases → optic nerve impingement

Side Effects of Antithyroid Drugs

1. Agranulocytosis
2. Arthralgias
3. Polyarthritis
4. ANCA-positive vasculitis
5. Immunoallergic hepatitis (PTU)
6. Cholestasis (methimazole)
7. Hypoglycemia-Insulin autoimmune syndrome (methimazole)

Amiodarone
- rule euthyroid prior to the initiation:
  ↑ F-T4
  ↑ Total T4
  ↑/normal TSH
  ↑/normal T3
  ↓/normal T3

Thyroid Carcinoma

Substernal Goiter
- assoc w/ Pemberton's sign
- great veins of neck compression due to narrowed thoracic inlet (anterior mediastinum)
- symptoms worse w/ extension of arms over the head
leads to facial plethora

1. Medullary (most common)
2. Anaplastic : Rapidly fatal
3. Follicular : Distant mets.
4. Papillary

Thyroid Lymphoma
- elderly women
- thyroiditis
- rapidly expanding thyroid mass

Treatment of Thyroid Cancer

Near total thyroidectomy
↓
RAI scan after 6 weeks when TSH↑
↓
RAI ablation of thyroid remnants
↓
Thyroid hormone replacement (TSH < N) (keep)
↓
Repeat scan 6-12 months later
↓
Follow by serial thyroglobulin levels

Features Suggestive of Thyroid Carcinoma in a Nodule

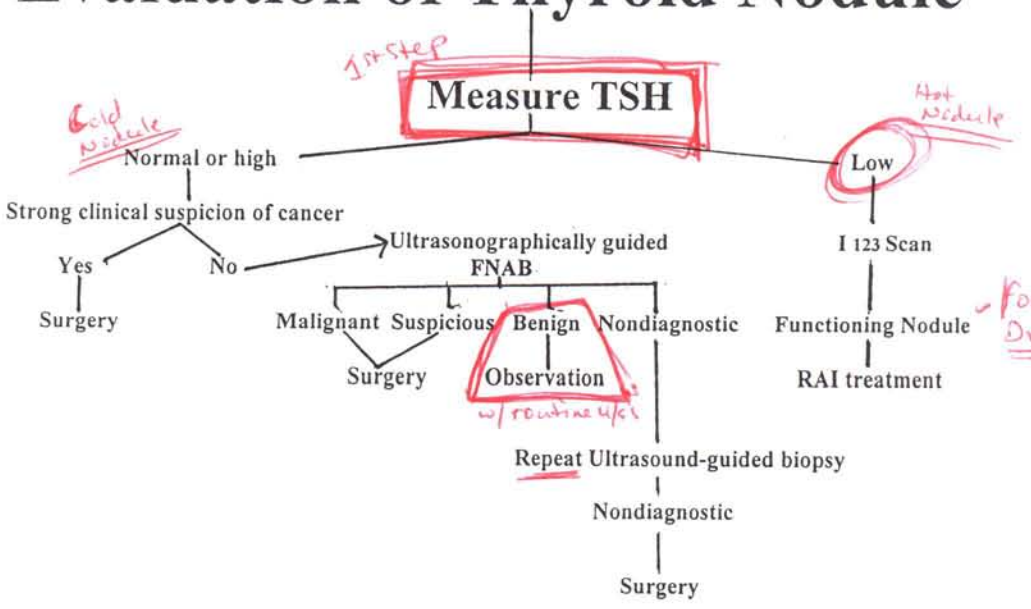
High Suspicion

- Nodule that is firm or hard or fixed to adjacent structures
- Rapid growth
- Regional lymphadenopathy or distant metastasis
- Paralysis of vocal cords
- Family H/O of medullary carcinoma or MEN syndrome

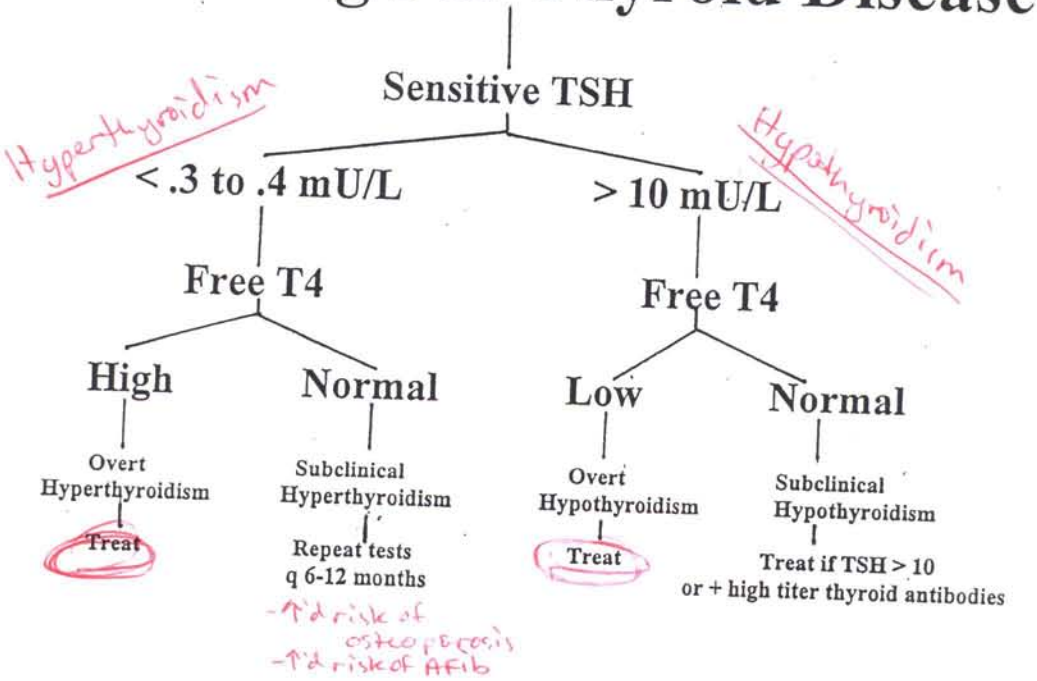
Moderate Suspicion

- Size >4cm or partially cystic
- Male sex, Age <20yrs or >70yrs
- H/O head and neck radiation
- Associated with dysphagia, hoarsness, dyspnea, and cough

Evaluation of Thyroid Nodule



Screening For Thyroid Disease



Effect of Amiodarone on Thyroid Functions

(AIT) Amio-Induced Thyroiditis

1. **Hypothyroidism** (↑iodine↓synthesis and secretion of thyroid hormone)
2. **Hyperthyroidism in patients with preexisting Graves or multinodular goiter** (Type 1 AIT) → ↑'d iodine load
3. **Hyperthyroidism due thyroditis** (Type 2 AIT)

Tx: STOP Drug corticosteroid

Diabetes

Results of DCCT Trial:

Intensive therapy to achieve near normal glucose delays the onset and slows the progression of microvascular complications of diabetes (retinopathy, nephropathy, and neuropathy) and macrovascular complications (MI, stroke)

Elevated HbA1c is an independent risk factor for cardiovascular disease

Microalbuminuria (Incipient nephropathy)

Abnormal Ranges:
- 30-300 ug/minute or 30-300 mg/day in a 24-hour urine collection
- 20-200 ug/minute in a overnight urine collection
- 30-300 mg /Gm of Cr on random sample

- BP control < 130/80
- ACEI/ARB
- Intensive glucose control

Criteria for the Diagnosis of Diabetes Mellitus

1. Symptoms of diabetes + random blood glucose > 200 mg/dL
2. 8 hour fasting blood glucose > 126 mg/dL on two occasions
3. 2 hour plasma glucose level > 200 mg/dL during a oral glucose tolerance test with 75 gm of glucose

Impaired Glucose Tolerance

FBS < 126 + 2hour plasma glucose 140-199 mg/dL

Impaired Fasting Glucose (Prediabetes)

FBS >100 to 125 mg/dL

↳ Lifestyle Δ's ± Drugs

Management of Diabetes

1. Annual urine microalbumin
2. Blood pressure measurement quarterly
3. Annual lipid profile
4. HbA1C 2-4 times a year
5. Annual eye examination
6. Foot examination 1-2 times a year by physician and daily by patient

Beginning initially for DM2 for DM1 age >30 or 5 yrs. after Dx (whichever comes first)

End-organ Diabetes
- causes:
  - CF
  - Pancreatitis
  - Pancreatic Ca.
  - Cushings Synd.

Latent Autoimmune (LADA) Diabetes of Adulthood
- lean, older patients
- severe insulin defic. d/t autos type I DM's
- labile sugars

(GLP) glucocorticoid-like peptide

Treatment of Diabetes

- Diet & Exercise
- Sulfonylureas — ↑'d pancreatic insulin release; side effect: wt gain
  Glipizide, glyburide, glimepiride
- Biguanide (Metformin) (see below)
- Alpha-glucoside inhibitor (Acarbose & Miglitol)
- Thiazolidinediones (Glitazones) — lower insulin resistance; side effect: fluid retention, ALT/AST ↑'s
  Rosiglitazone (Avandia), Pioglitazone (Actos)
- Meglitinides (Repaglinide , Nateglinide) → stimulate insulin release (short-acting)
- DPP-4 Inhibitor (Sitagliptin...Januvia) → potentiate insulin synthesis + release
- Exenatide (synthetic GLP-1 like hormone) given SQ → ↑GLP-1 levels → stimulates β-cell insulin production
  - can be used in renal failure
  - ↓ preferred as initial tx
  - cannot be used w/ Sulfonylureas
- Insulin

- Gout in Hosp. pts 90-130
- Acute illnesses 80-110 fgtt

once reached 50% of drug max's → add another drug as drug-response curve plateaus

Type I DM w/ acute pancreatitis
Gluc: 450
Trigs: 5000

Best tx for trigs?
IV insulin

Nutritional Recommendations For Diabetes

Protein:	**10-20% of total calories**
Saturated Fat	**< 10% (< 7% if LDL↑)**
Polyunsaturated	**⩽ 10%**

Remaining calories from carbohydrates and monosaturated fat depending on personal tolerance and medical needs

Fiber	20-35 g/d
Na	< 3000 mg/d
Cholesterol	< 300 mg/d

Total calories to maintain desirable weight

Metformin

- preferred initial tx

Actions

↓ Glucose production in the liver
↑ Uptake & utilization of glucose by adipose tissue & muscles
No effect on insulin release
Promotes weight loss & ↓lipids
↓macrovascular complications (MI, stroke)

Toxicity

Lactic acidosis

Contraindications

Renal disease (Cr > 1.5 M, Cr > 1.4 F)
Impaired liver functions, CHF, severe hypoxia
Chronic alcoholism or binge drinking
Discontinue prior to radiocontrast x-ray procedures → restart 48 hrs. if creat ok
Discontinue prior to surgery or in critically ill patients or if patient develops nausea and vomiting

also hold Sulfonylureas if on them

Various Insulin Preparations

Rapid-acting

Insulin lispro (Humalog), aspart (Novolog), glulisine (Apidra),
Inhaled insulin – contraindicated in asthma + COPD – monitor PFT's

Short-acting

Regular

Intermediate-acting

NPH, lente

Long-acting

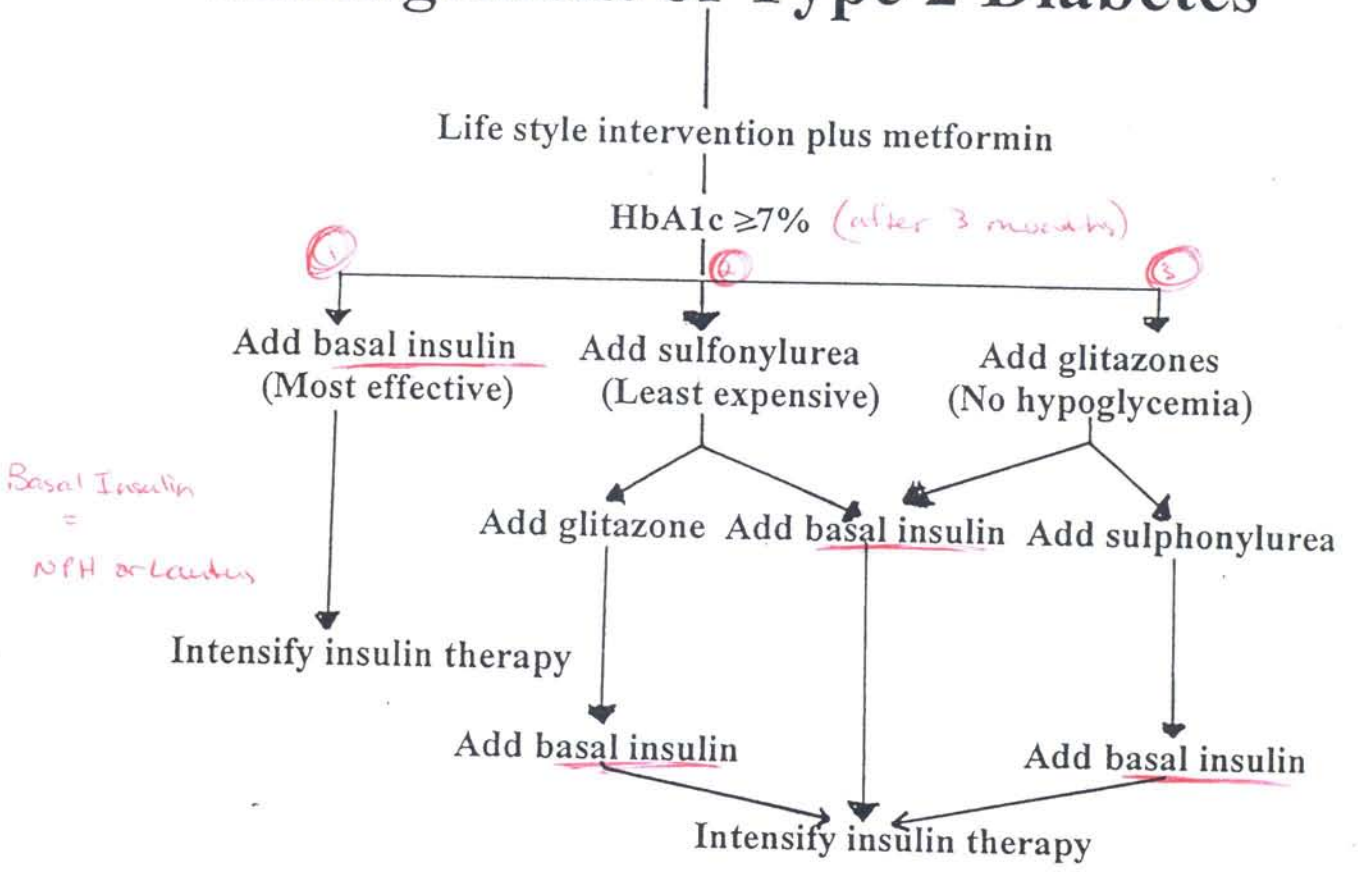
Insulin glargine (Lantus), ultralente

Pre-mixed

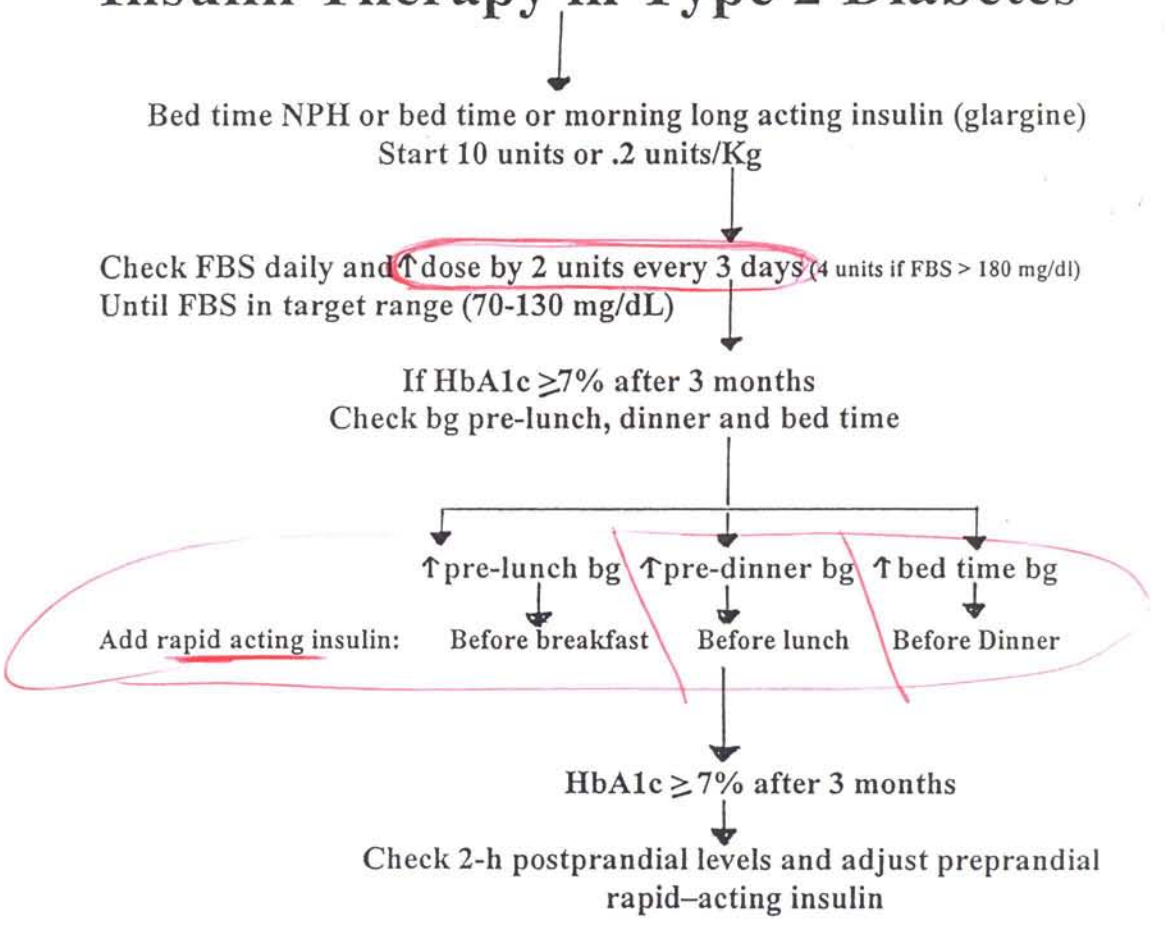
NPH/Reg (70/30, 50/50)
Insulin aspart protamine suspension/aspart (70/30)
Insulin lispro protamine suspension/lispro (75/25)

- addition of metformin / Glitazones may allow ↓'d insulin doses w/ better control

Management of Type 2 Diabetes



Insulin Therapy in Type 2 Diabetes



Current Goals for the Treatment of Diabetes

Hemoglobin A1c	< 7%
Preprandial	90-130 mg/dL
Peak postprandial (1-2h after meals)	< 180 mg/dL
BP	≤ 130/80 (≤ 125/75 with proteinuria)
LDL	< 100 mg/dL, < 70 mg if + CAD
HDL	> 40 mg/dL in M, > 50 mg/dL in F
TG	< 150 mg/dL
Non HDL Cholesterol	< 130 mg/dL
Aspirin (75-325mg)	+ Macrovascular disease, age > 40 yrs, one or more cardiovascular risk factors (Family H/O CVD, ↑BP, ↑lipids, albuminuria, smoking, obesity)
Influenza vaccine	Yearly
Pneumococcal vaccine	Once

ACES or ARBS to treat hypertension and reduce urinary protein < .3g/24hr

Insulin Therapy

Conventional

Single NPH in AM
Split NPH (2/3 AM & 1/3 PM)
NPH+R AM & NPH+R PM
70/30 Insulin (2/3 AM & 1/3 PM)

Somogyi Phenomenon
- ↓ NPH @ night time
- Hypoglycemia overnight
- Suspect w/ hunger, wt gain
- wide swings in Fingersticks

Multiple Injections

25% NPH, ultralente or glargine (HS) & 75% regular or lispro(40 % B, 30 % L, 30% D)

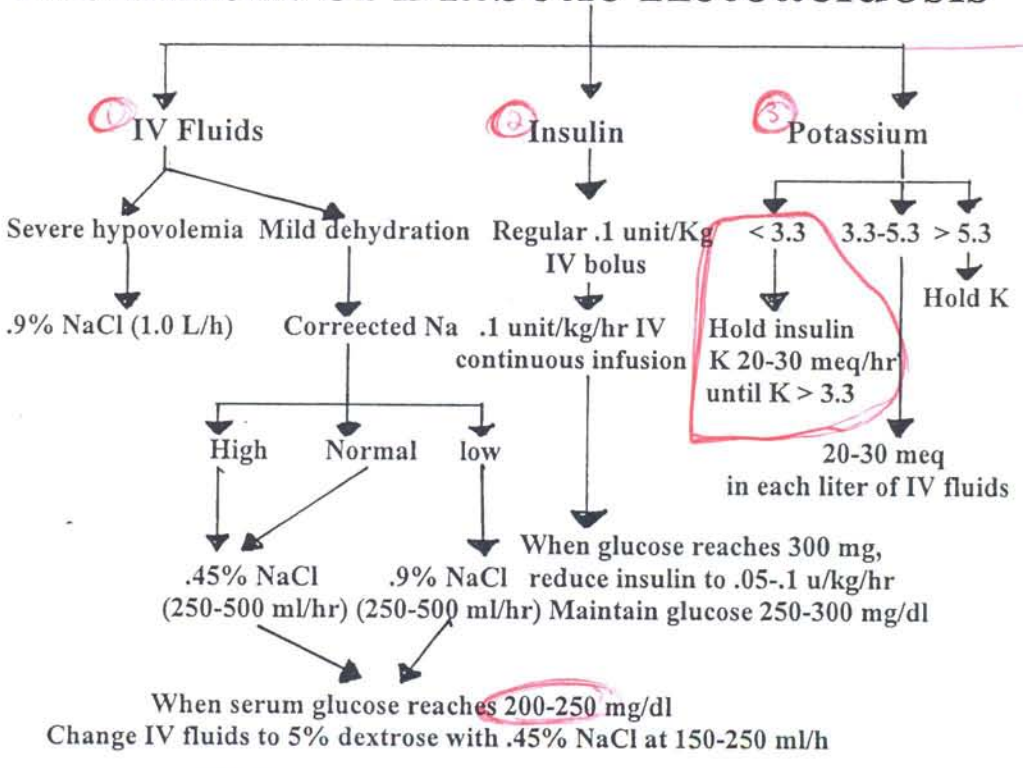
Continuous Infusion Pump

Diabetic Ketoacidosis

Insulin deficiency & Glucagon excess
↑Gluconeogenesis & ↓peripheral glucose utilization
Release of fatty acids from adipose tissue
Accelerated fatty acid oxidation in the liver
↑Ketones (B hydroxybutyrate/ acetoacetic acid)

- do not follow in DKA (↳ 3 : 1 ratio normally in DKA)
- follow A Gap

Treatment of Diabetic Ketoacidosis



HCO3: Use only if severe acidosis ph <7.0 or HCO3 < 5 meq/L
Follow ph and anion gap rather than ketones

Complications During Treatment of Diabetic Ketoacidosis

Hyperosmolar (HONK) Non-Ketosis
- seizures or focal neurofindings may develop
- Tx: IVF's (NS)

1. Accelrated coagulopathy
2. Cerebral edema
3. Hyperchloremic acidosis
4. Hypokalemia
5. Hypophosphatemia → muscle weakness, resp failure + reversible CM
6. Hypoglycemia

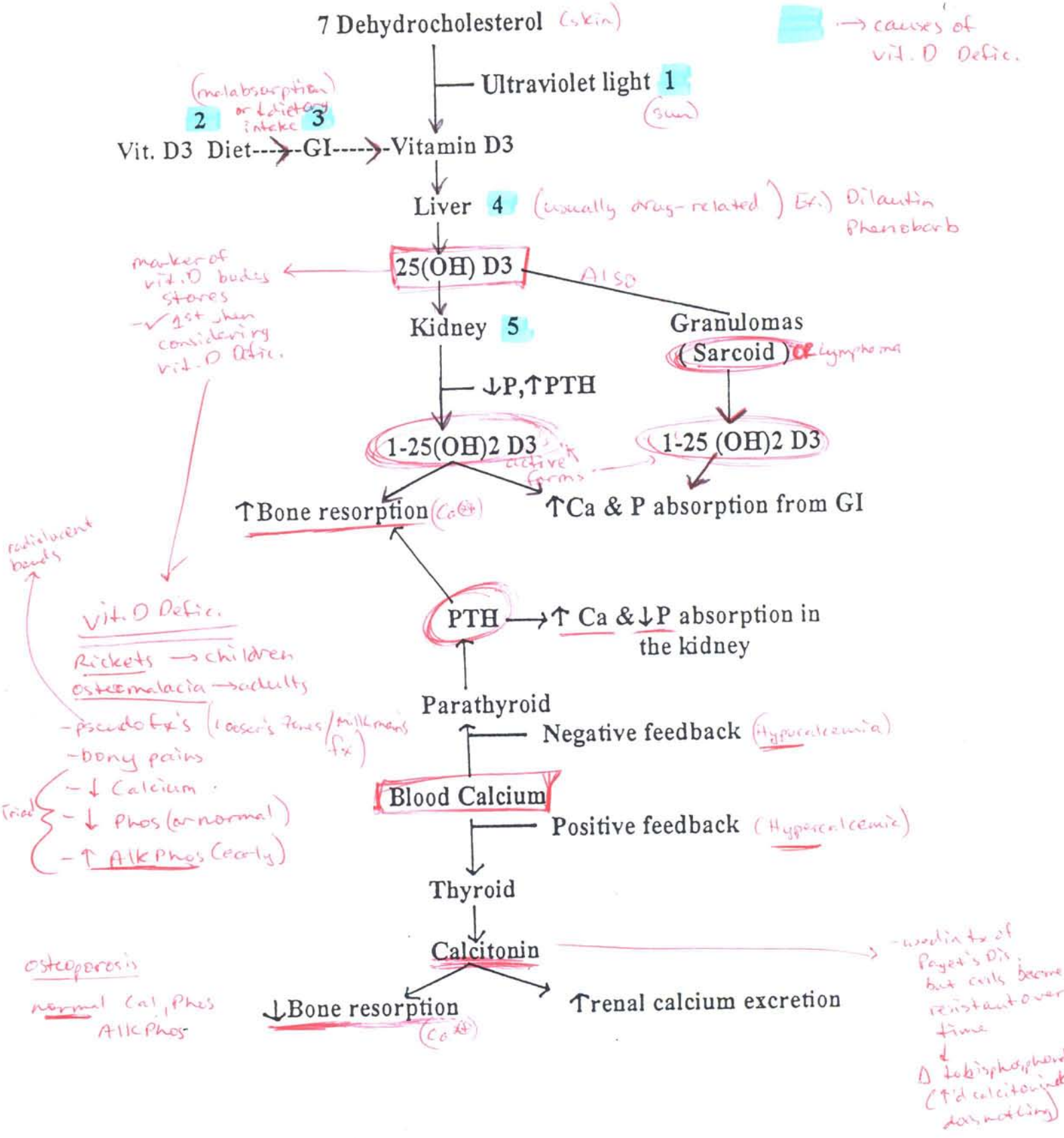
Autonomic Neuropathy in Diabetes

Gastroperesis → Tx: Metaclopramide / Reglan + frequent meals
Alternating diarrhea & constipation
Urinary incontinence or retention
Impotence
Orthostatic hypotension without reflex tachycardia
Persistent sinus tachycardia

Risk Factors For Diabetic Foot Ulcers

1. ↑Formation of keratin
2. Loss of pressure sensation
3. Loss of pain and temperature sensation
4. Weakness of intrinsic muscles
5. Loss of sweating

Disorders of Calcium



Hypercalcemia

Tertiary Hyper-Ca
- CKD plus secondary hyperpara
↑PTH, ↑Ca, ↑Phos
↑BUN/creat
Tx: Cinacalcet (Sensipar)
- calcimimetic

PTH (intact)

High or Normal

1. Hyperparathyroidism (↑Ca, ↓Phos)
2. Lithium
3. Familial hypocalciuric hypercalcemia
   - AD
   - asymptomatic

Differentiate via ↑FH and urine Ca

DO NOT REQUIRE SURGERY

Low or undetected

Chronic

Sarcoid and other causes

Acute

Malignancy

Other Causes:
Thyrotoxicosis, Adrenal insufficiency, Immobilization
Drugs: Thiazides, Vitamin A & D, calcium carbonate

- Ca↑P↓ → Humoral (PTHrP)
- Ca↑P N → Metastatic Myeloma

Multiple Endocrine Neoplasia

MEN 1 : Hyperparathyroidism, pituitary & pancreatic tumors

MEN 11a : Hyperparathyroidism, pheochromocytoma, medullary carcinoma

MEN 11b : Pheochromocytoma, medullary carcinoma, mucous neuromas, marfanoid habitus

RET Mutation

Triad:
1. HA's
2. palpitations
3. diaphoresis

Dx: urinary or plasma free catecholamines

Indication for Surgery in Hyperparathyroidism

1. Age < 50 years
2. Symptomatic hypercalcemia
3. Renal Stones
4. Calcium > 1 mg above normal
5. ↓Bone mass
6. No Adequate follow-up
7. Urine Ca > 400 mg/d
8. H/O Life threatening hypercalcemia
9. Impaired renal function (creatinine clearance < 70%)

T-score <-2.5 @ any site (osteoporosis)

pre-op localization procedures needed (unless minimally invasive strategy)
- if needed best is: Technetium-99 scan

Hypercalcemia of Malignancy

1. **Humoral** (PTHrP- Ca↑P↓) → normal PTH intact or suppressed
   - Squamous cell carcinoma of lung and other sites
   - Other tumors: Renal, breast, ovary and endometrium

   Carcinoid too → -flushing, -palp's, -dermatographism, -hepatomegaly, -diarrhea
2. **Metastatic** (Breast, prostate, thyroid, kidney, lung)
3. **Osteoclast Activating Factors**
   - Interleukin 1
   - TNF
   - 1-25 $(OH)_2$ vitamin D (1 alpha hydroxylase converts 25 vit D to 1-25 vit.D)
4. **Ectopic PTH secretion (rare)**
5. **Coexisting primary hyperparathyroidism**

Treatment of Hypercalcemia

1. **Hydration with N. saline**
2. **Loop diuretics** ↓ thiazides
3. **Phosphate repletion** (if serum P ≤ 3.0 mg/dl)
4. **First-line medications** → especially useful in hypercalcemia of malignancy
   - Inravenous bisphosphonates (IV palmidronate or zolendronate)

   faster-acting than →
5. **Second-line medications**
   - Glucocorticoids, mithramycin, calcitonin, gallium nitrate

   Lymphoma sarcoid or myeloma → ↑'d active 1,25-dihydroxy vit. D_3)

Diseases Associated With Hypoparathyroidism

↓ Calcium, ↑ Phos, ↓ PTH

1. **Addison's disease**
2. **Premature ovarian failure**
3. **Autoimmune thyroid disease**
4. **Pernicious anemia**
5. **Mucocutaneous candidiasis**

Paget's Disease
- ↑ Alk Phos
- ↑'d risk of osteogenic sarcoma ("starburst" appearance)

Consequences
- ↑ Ca^{++}
- ↑-output CHF
- deafness
- excessive bleeding w/ surgery → hypervascular bone

Hypocalcemia

PTH Absent

- Hypoparathyroidism
- Hypomagnesemia

PTH Ineffective

- Pseudo hypoparathyroidism

PTH Overwhelmed

- Severe acute hyperphosphatemia
  (Tumor lysis, rhabdomyolysis, ARF)
- Hungry bone syndrome

Interpretation of Calcium Values

	Ca	P	PTH	Diagnosis
1.	↑	↓	↑	Primary hyperparathyroidism
2.	↑	↓	↓	Humoral hypercalcemia
3.	↑	N	↓	Metastatic disease, myeloma
4.	↑	↑	↓	Vit. D intoxication, sarcoid
5.	↓	↑	↓	Hypoparathyroidism, ↓Mg
6.	↓	↑	↑	Pseudohypoparathyroidism
7.	↓	↑	↑	Renal failure
8.	↓	↓	↑	Vit. D deficiency (osteomalacia)

Risk Factors for Osteoporosis

1. Increasing age >65
2. Female gender
3. White, asian, hispanic
4. Body habitus (tall & thin)
5. Family history
6. Early menopause
7. Low calcium intake
8. Smoking
9. Alcohol abuse
10. Corticosteroid Rx
11. Hyperthyroidism
12. Hyperparathyroidism
13. Sedentary lifestyle
14. Multiple Myeloma
15. Hypogonadism
16. Personal H/O fracture
17. H/O fracture in a first degree relative

Management of Osteoporosis

Prevention

1. Calcium
2. Vitamin D (600-800 IU/d)
3. Exercise (weight bearing) 4+ weekly
4. Smoking cessation
5. Reduce alcohol intake

Treatment

1. Calcium
2. Vitamin D
3. Raloxifen
4. Bisphosphonates
5. PTH (Teriparatide)
6. Calcitonin → ↓s bone resorption of Ca++
7. Estrogens

Calcium Requirements

Males < 65,
Premenopausal females
Postmenopausal females on estrogens… 1000 mg/d

M or F > 65
Postmenopausal females not on estrogens … 1500 mg/d

Adolescent/young adults
Pregnant or nursing women … 1200-1500 mg/d

Raloxifene (evista)

1. Selective estrogen receptor modulator (SERM)
2. Approved by FDA for both prevention and treatment of Osteoporosis
3. Reduces risk of vertebral fractures by 40% but does not reduce the risk of non-vertebral fractures → use bisphosphonates
4. Does not increase risk of endometrial cancer
5. Reduces risk of breast cancer
4. May cause hot flashes and increase risk of thromboembolism
5. Lipids: Cholesterol ↓, LDL ↓, no change in TG & HDL
6. Contraindications: Pregnancy, h/o thromboembolism

Bisphosphonates

1. Potent antiresorptive agents and reduce the incidence of vertebral and nonvertebral fractures by 50% during first year of treatment
2. Increase bone mass about 1%/year for up to 8-10 years
3. Discontinuation after 5 years of use results in minimal bone loss
3. Reduces the number of active remodeling loci on bone surface which leads to decrease in bone fragility
4. Approved for both prophylaxis and treatment of osteoporosis

Side Effect: Chemical esophagitis (risk less with once a week preparations)
Osteonecrosis of jaw

Agents: Allendronate, risedronate, ibandronate

PTH (Teriparatide)

1. Anabolic agent and stimulates osteoblastic bone formation
2. Increases bone mass 8-10%/year for up to 2 years
3. Reduces risk of vertebral and nonvertebral fractures by 50%
3. It's use should be limited to patients with moderate to severe osteoporosis and in those at increase risk of fractures or previous osteoporotic fractures (do not use for > 2 years)
4. Combination therapy with PTH and bisphosphonates increases bone mass less than PTH alone
5. A Bisphosphonate should be started after completing 2 year of therapy with PTH, otherwise some or all the bone gained is lost

Postmenopausal Hormone Replacement Therapy

↑HDL, ↓LDL, ↓Lp(a), inhibit oxidation of LDL
↑TG, ↑factor VIII, prothrmbin and fibrinopeptide A

Benefits

1. Improves symptoms of menopause
2. ↑bone density
3. ↓risk of colan cancer
4. No benefit for primary or secondary prevention of CHD.

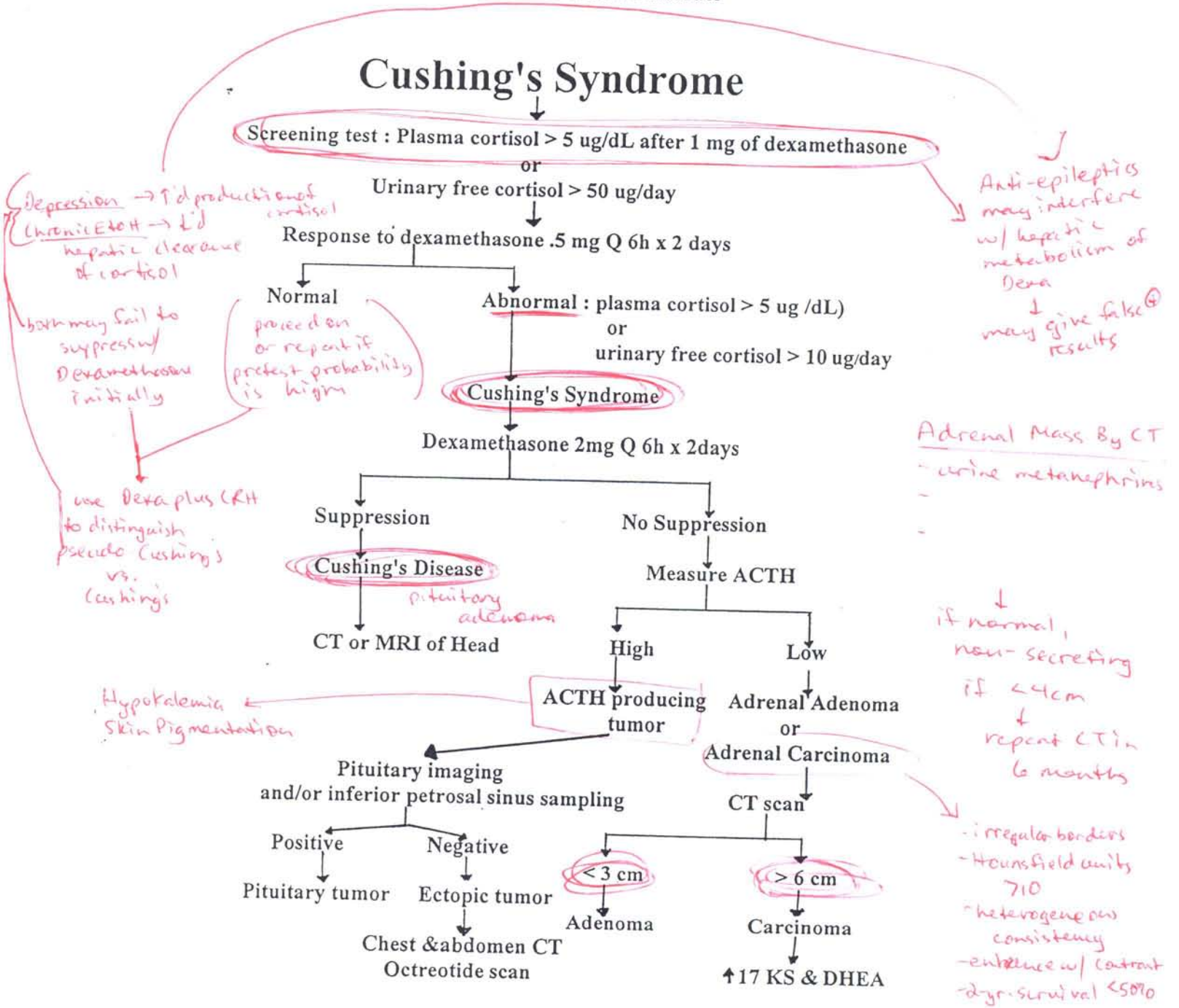
Risks

1. Endometral cancer
2. Venous thromboembolism
3. Breast cancer
4. Gall bladder disease
5. ↑ risk of stroke and coronary events

Contraindications for Hormonal Replacement Therapy

Absolute	Relative
Pregnancy	H/O thromboembolic disease
Unexplained vaginal Bleeding	Hypertriglyceridemia
Active or chronic liver disease	Family H/O breast cancer
Recent vascular thrombosis	Uterine leiomyoma
H/O breast or endometrial cancer	Gall bladder disease
Known CHD	Migraine headaches
	Seizure disorder

Cushing's Syndrome



Clinical Features of Adrenal Insufficiency

(Addison's Dis)

S/S: Weakness, vomiting, myalgias, arthralgia, postural hypotension and dizziness, salt craving, headache, memory impairment, skin pigmentation, fever, tachycardia, ↓body hair, amenorrhea or cold intolerance suggest hypopituitarism

Lab: ↓Na, ↑K, ↓glucose, eosinophilia

Best Dx Test: ACTH-stim test
peak level < 18
- confirmatory

Causes:

Primary: Autoimmune, TB or fungal infections, amyloid, hemachromatosis
Secondary: Pituitary and hypothalamic diseases
Functional: Acute illness, septic shock

Hypofunction of Adrenal Gland

	Primary	Secondary
Plasma cortisol	↓	↓
ACTH level	↑	↓
Skin pigmentation	Yes	No
Hyperkalemia	Yes	No
Volume contraction	Yes	No
Salt wasting	Yes	No
Aldosterone level	Low	Normal
Hyponatremia	Yes	Yes (SIADH)

Schmidt's Syndrome
- concomitant autoimmune thyroiditis (hypothyroid) + adrenal insufficiency
- Frequently ⊕ anti-CYP 21 Ab's
- patients usually present w/ hypothyroidism, get treated, become euthyroid and then adrenal insufficiency reveals head

Tx: Hydrocortisone plus Fludrocortisone

Corticosteroid Insufficiency in Acute Illness

Increases mortality if untreated

Causes:

a) Preexisting conditions affecting the hypothalamic pituitary adrenal axis (Ex Hypopituitarism)
b) Exogenous corticosteriod therapy (> 30 mg hydrocortisone, 7.5 mg prednisone or .75 mg dexamethasone/day for > 3 weeks in the prior year)
C) Functional deficiency during acute illness or septic shock
d) Adrenal hemorrhage
e) Corticosteroid resistance due to inflammatory cytokines
f) ↑risk with head injury, CNS depressants, pituitary infarction
g) ↑risk with use of ketoconazole, rifampin, megestrol, etomidate

Stress-Dose Steroids:
(1) Used steroids > than 3 wks in past 12 months
(2) Hypopituitarism
(3) Addison's Dis.

50 mg Hydrocortisone Q6H

S/S: Hemodynamic instability despite adequate fluid replacement (usually associated with hyperdynamic circulation), ongoing evidence of inflammation without an obvious source that does not respond to adequate treatment

Diagnosis:

Cotisol level: < 15 ug/dL…Insufficiency likely…Rx
> 34 ug/dL…Insufficiency unlikely…No Rx
15-34 ug/dL… Measure response to corticotropin (250 ug IV and cortisol measured at 0, 30 & 60 minutes)
< 9 ug/dL increase…Insufficiency likely…Rx
> 9 ug/dL increase… Insufficiency unlikely…No Rx

Treatment: Hydrocortisone 50 mg IV q 6h ± 50 ug of fludrocortisone/day
Rx for 7 days in septic shock or until response to ACTH stim test is normal
In other situations reduce dose by 50% each day

Hyperaldosteronism

Aldosterone/Renin ratio
720 → suggestive

-once Dx'd ↓ CT to look for tumor

	Primary	Secondary
Aldosterone level	↑	↑
Renin level	↓	↑
K level	↓	↓

Hyporeninemic Hypoaldo
↓Renin
↓Aldo
-hyperkalemia
Tx - ↓ K+ diet
-loop diuretics
-fludrocortisone

Potency of Various Steroids

	Potency
Short Acting (1/2 life < 12hrs)	
Hydrocortisone	1
Intermediate Acting (1/2 life 12-36 hrs)	
Prednisone	4
Methylprednisolone	5
Long Acting (1/2 life > 48 hrs)	
Dexamethasone	30

Pheochromocytoma
-HA's
-Palp's
-orthostasis
-tremors (hands)

-Dx: plasma free metanephrines or 24-hr urinary metanephrines
-localize w/ MRI or I^{123} scan

Tx: α-blockers
β-blockers
Sx

Evaluation of Hypoglycemia

Normal 5-25

measure endogenous insulin production

	Insulin (uU/ml)	C-Peptide (pmol/L)	Proinsulin (pmol/L)	Diagnosis
1.	↓(<6)	↓(<200)	↓(<5)	All causes of hypoglycemia except hyperinsulin states
2.	↑(>6)	↑(>200)	↑(>5)	a) Insulinoma b) Sulfonylurea
3.	↑(>6)	↓(<200)	↓(<5)	Exogenous insulin

hyperinsulin state

Differentiate via sulfonylurea in urine test

Hypoglycemia awareness
-complication of long-term diabetes
-↓ symptoms w/ hypoglycemia
Tx: ↓ insulin + ↑ monitoring

Hirsutism & Virilization

	Testosterone	DHEA	17 OH Progesterone	Diagnosis
1.	↑↑	↑↑	N	Adrenal Tumor
2.	↑↑	N	N	Ovarian tumor
3.	↑	↑/N	N	Polycystic Ovary Disease
4.	↑	↑	↑	Congenital adrenal hyperplasia (21 hydroxylase deficiency) (CAH)

Evaluation of Male Hypogonadism

	Testosterone	LH	FSH	Prolactin	Diagnosis
1.	↓	↑	↑	N	Primary Testicular Failure
2.	↓	N/↓	N/↓	N	Pit. & Hypothalamic Causes
3.	↓	N/↓	N/↓	↑	Hyperprolactinemia

Evaluation of Erectile Dysfunction

Psychogenic (25 %)	Organic (75%)
Normal nocturnal & early morning erection	Abnormal
Erection may occur in some circumstances	Rigid erection under no circumstances
Nocturnal penile tumescence : Normal	Abnormal
Causes	1. Hypogonadism 2. Vascular 3. Neurogenic 4. Drugs : B blockers, thiazides, spiranolactone, cimetidine

Treatment of Erectile Dysfunction

1. **Testosteron replacement for hypogonadism** (I/M or patch)
2. **Phosphodiesterase-5 inhibitors (PDE-5)**
   Sidenafil (Viagra), Vardenafil (Levitra), Tadalafil (Cialis)
3. **Yohimbine** (Alpha 2 adrenergic receptor antagonist)
4. **Transurethral alprostadil** (prostaglandin E1)
5. **Intracavernous therapy**
   Alprostadil, papaverine, phentolamine or combination therapy
6. **Vacumm constriction device**
7. **Penile prosthesis**

Rarely used

Phosphodiesterase-5 Inhibitors (PDE-5)

TOC for Psychogenic, Neurogenic or Vascular causes

Actions

Increases cyclic GMP levels
No effect in absence of sexual stimulation

Duration of Action

Sidenafil & Vardenafil: Effective as early as 30 minutes and up to 4 hours
Tadalafil: Effective as early as 16 minutes and up to 36 hours

Contraindications

Patient on nitrates, multiple BP medications
Drugs that inhibit CYP3A4 (erythromycin, cimetidine, ketokonazole, protease inhibitors or grapefruit juice)
Tadalafil should not be used with alpha antagonists (except Tamulosin .4 mg/d)

Side effects

Headache, flushing, dyspepsia, dizziness, lightheadedness, syncope, visual disturbance (blue tinge to vision...seen with sidenafil only), myocardial infarction, rarely non-arteritic ischemic optic neuritis

↓ not due to drugs itself but rather underlying dis.

Causes of Gynecomastia

Caused by imbalance between free estrogen and free androgen actions in the breast tissue (↑estrogen or ↓androgen)

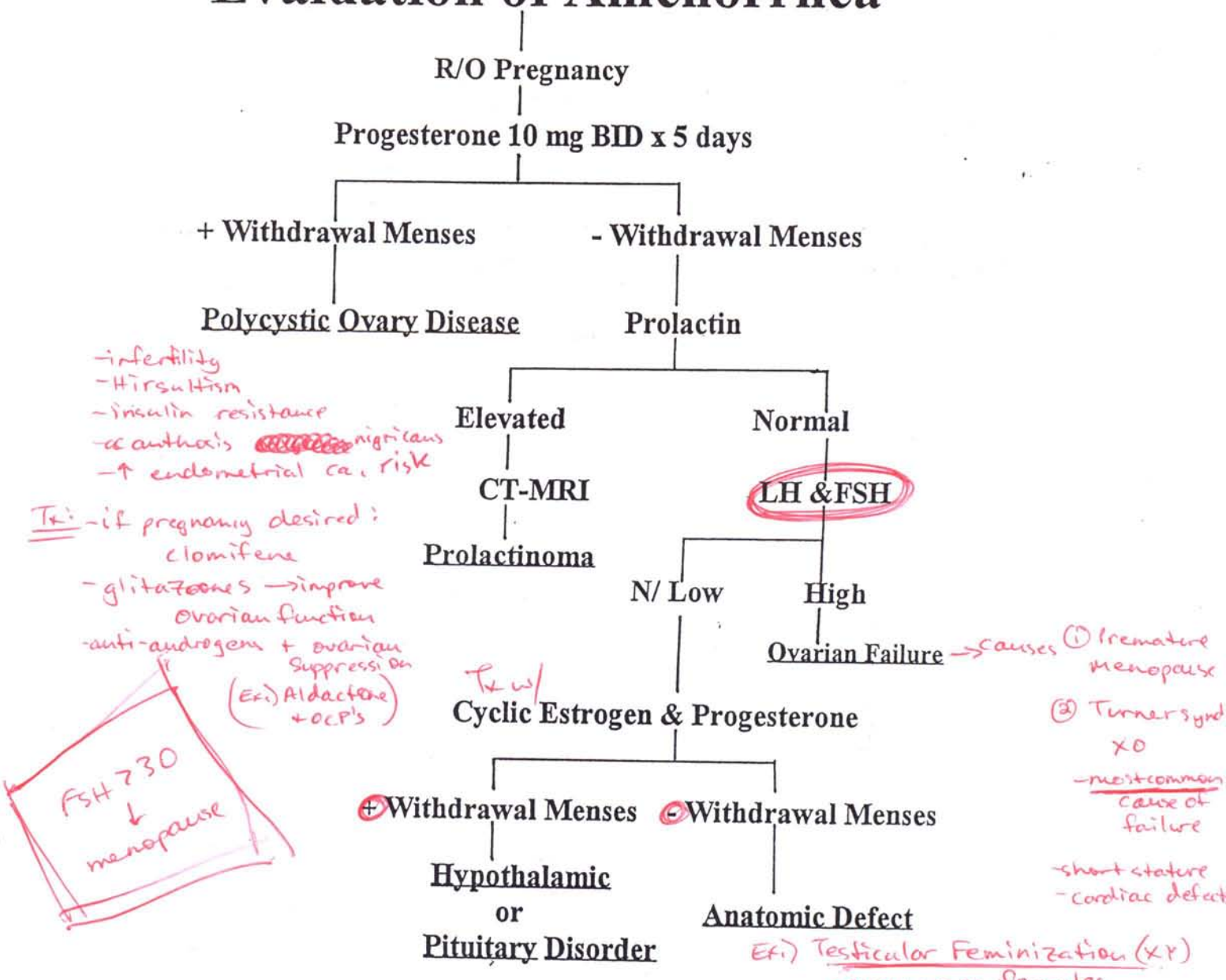
1. Primary or secondary hypogonadism
2. Estradiol producing tumors
   Leydig or sertoli-cell tumor of testes, adrenal tumor
3. HCG producing tumors
   Testicular or exragonadal germ-cell tumor, nontrophoblastic neoplasm
4. Hyperthyroidism
5. Liver or kidney disease
6. Androgen insensitivity
7. Familial or sporadic aromatase excess syndrome
8. Physiological pubertal gynecomastia
9. Obesity
10. Drugs: Anabolic steroids, antiandrogens used for prostate cancer, spiranolactone, cimetidine, protease inhibitors, alcohol, marijuana, opioids

Try Eplerenone if painful gynecomastia w/ spironolactone

Evaluation of Gynecomastia

	Testosterone	LH	Estradiol	HCG	Diagnosis
1.	↓	↑	N	N	Primary Hypogonadism → Tx: Testosterone Replacement
2.	↓	↓/N	N	N	Secondary Hypogonadism or ↑Prolactin
3.	↓	↓/N	↑	N	Estradiol producing tumor (Testicular ultrasound, adrenal CT or MRI) ✓ MRI of pituitary
4.	↑	↑	↑	↑	HCG producing tumor (Testicular ultrasound, chest x-ray, CT abdomen)
5.	↑	↑	N	N	Thyrotoxicosis or androgen resistance (Free T4 and TSH)
6.	N	N	N	N	Idiopathic

Evaluation of Amenorrhea



Side effects of Anabolic/Androgenic Steroids

1. Gynecomastia, testicular atrophy, ↓sperm count
2. Menstrual irregularity, ↓breast size, voice change
3. Liver : Jaundice, tumors & cysts
4. Acne
5. ↑LDL, ↓HDL, ↑CAD risk
6. Withdrawal : Depression, muscle pain

also ↑'s PSA ~50% by Exogenous Testosterone

↑ sperm count → tx infertility w/ gonadotropins (Ex) HCG injex