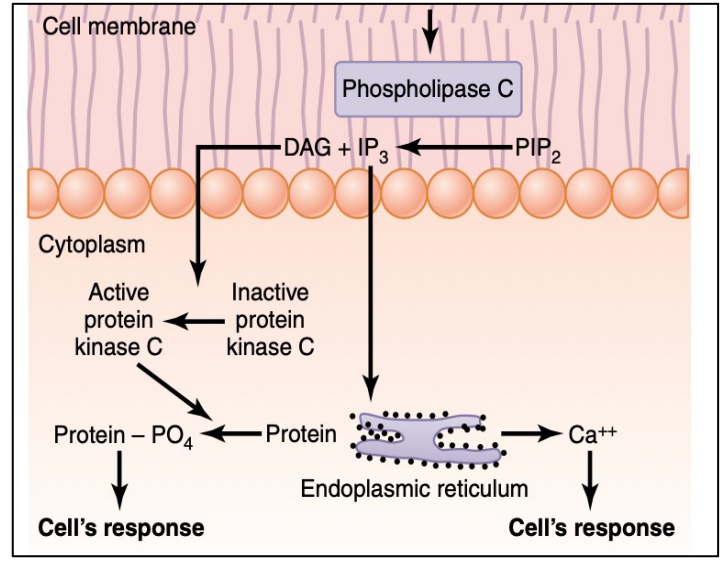
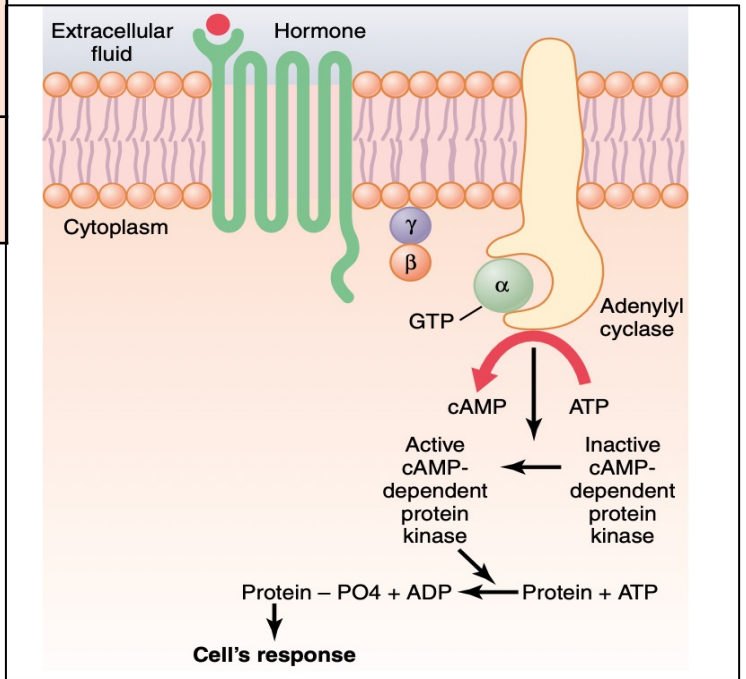
INTEGRATED ENDOCRINE SYSTEM

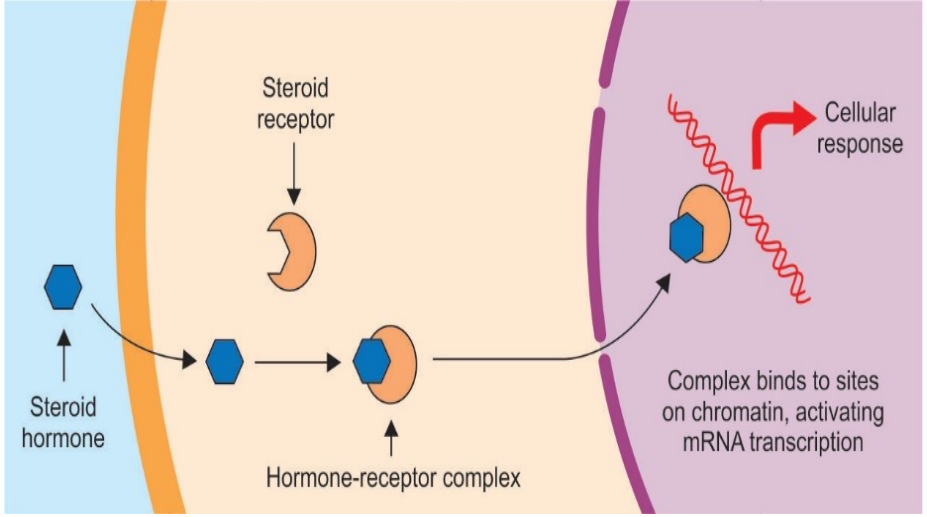
Hormone Actions

G-protein	Receptor and ligand	Second messenger
G_q-alpha subunit	"Hav1 M and M-GOT"	↑IP3 ↑DAG
G_s-alpha subunit	FSH, LH, ACTH, TSH, CRH, hCG, ADH-V_2, MSH, PTH, Calcitonin, H2, Glucagon, GHRH All B receptors	↑cAMP
G_i-alpha subunit	MAD 2	↓cAMP
Receptor Guanyl cyclase	BAN	↑cGMP

Glutamate	Ligand-gated ion channels: NMDA, AMPA
GABA	Ligand-gated: GABA A, GABA C (B-GPCR)
Acetylcholine	Nicotinic → Ligand-gated
Norepinephrine, 5HT, Dopamine, Ach-M	GPCR (*except 5HT3 which is ligand-gated)*



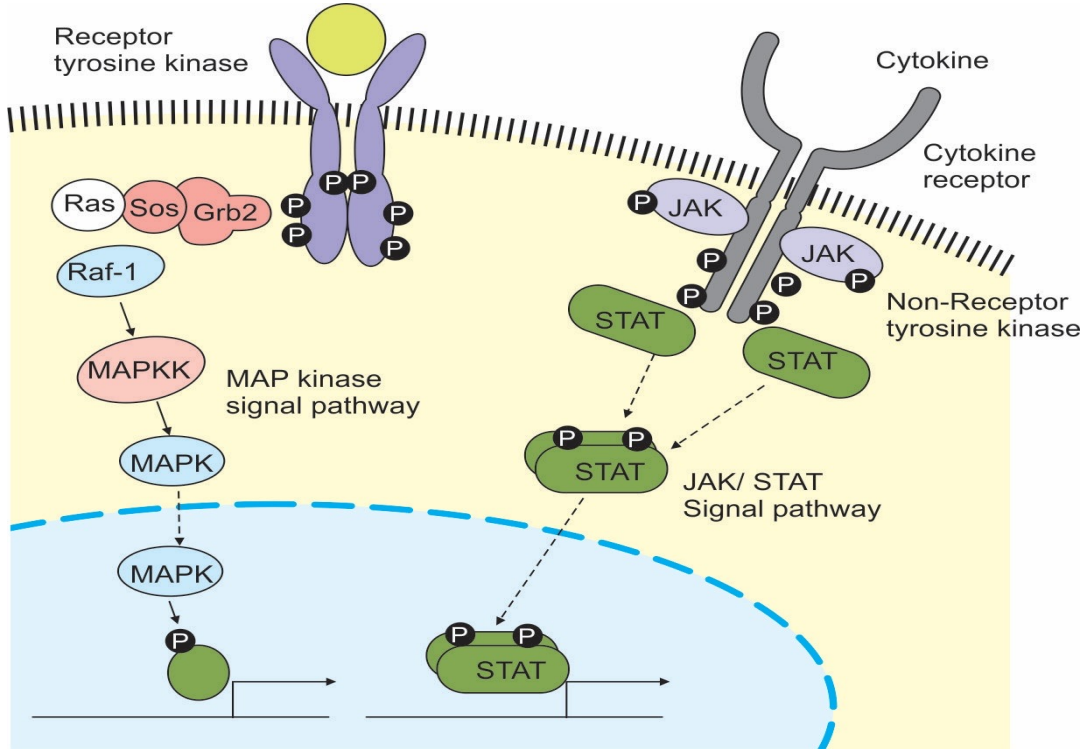




STEROIDS PREP TV

Intranuclear:

Cytoplasmic:



INSULIN PIFE

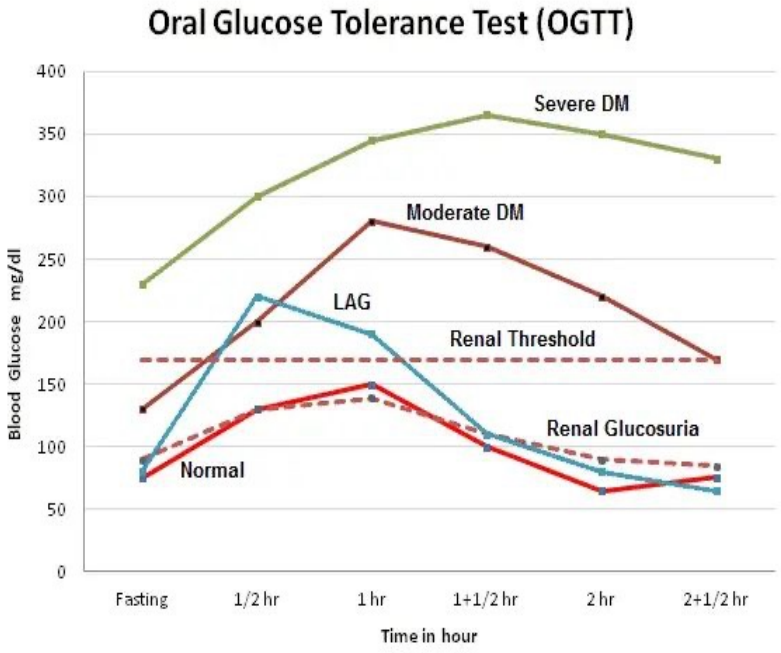
PIGGLET

Diabetes mellitus - Diagnosis

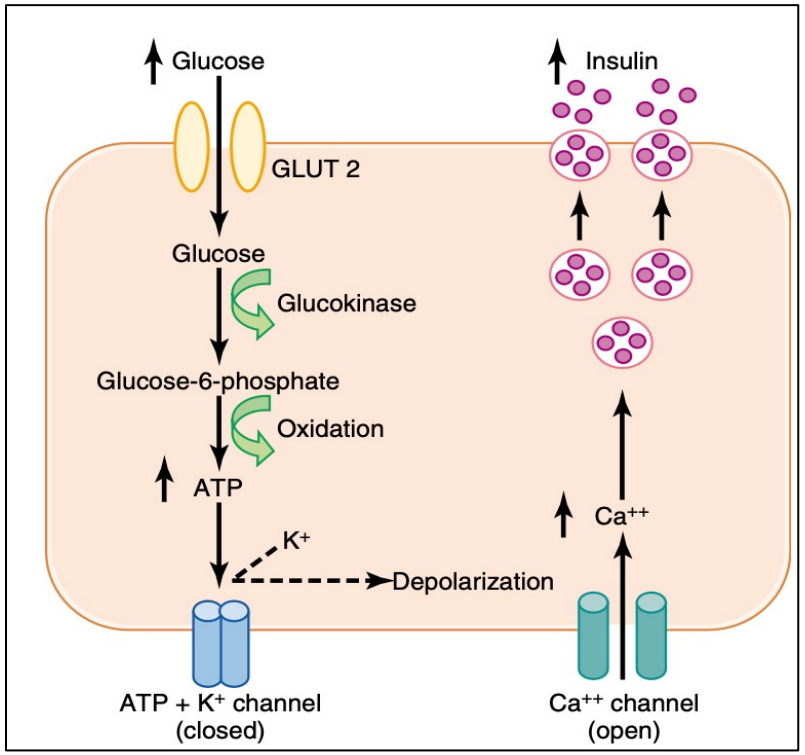
HbA1c	FBS	RBS	OGTT-75g

Stages of Type 1 DM
Stage 1: Auto-Ab
Stage 2: Auto-Ab + Dysglycemia
Stage 3: Auto-Ab + Dysglycemia + Symptoms

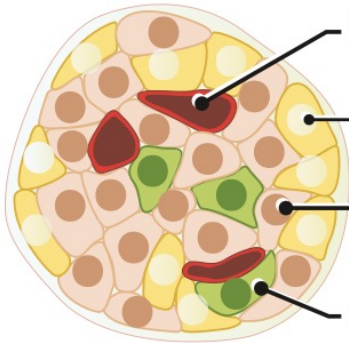
	Type 1 DM Adult onset: LADA Antibodies:	Type 2 DM	MODY AD MC type: Gene:
Age of onset			
Habitus			
Insulin levels			
B cell mass			
OHG			



Insulin



Increase Insulin Secretion	Decrease Insulin Secretion
Increased blood glucose/ FFA / AA	Decreased blood glucose / fasting
Gastrointestinal hormones (gastrin, cholecystokinin, secretin, GIP)	Somatostatin
Glucagon, growth hormone, cortisol	Leptin
β-Adrenergic stimulation	α-Adrenergic activity
Insulin resistance (obesity)	

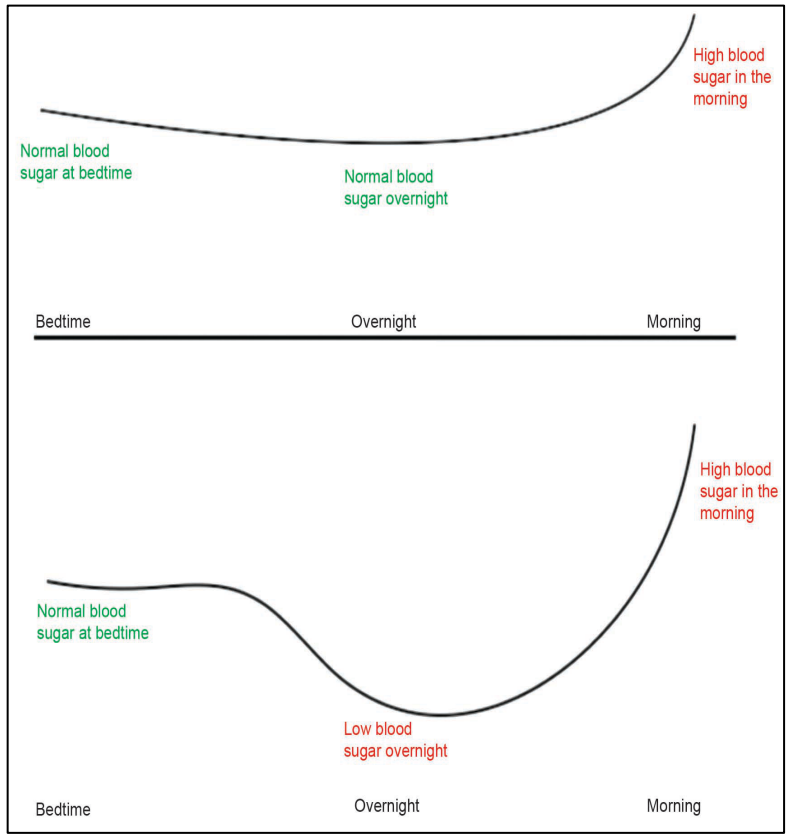


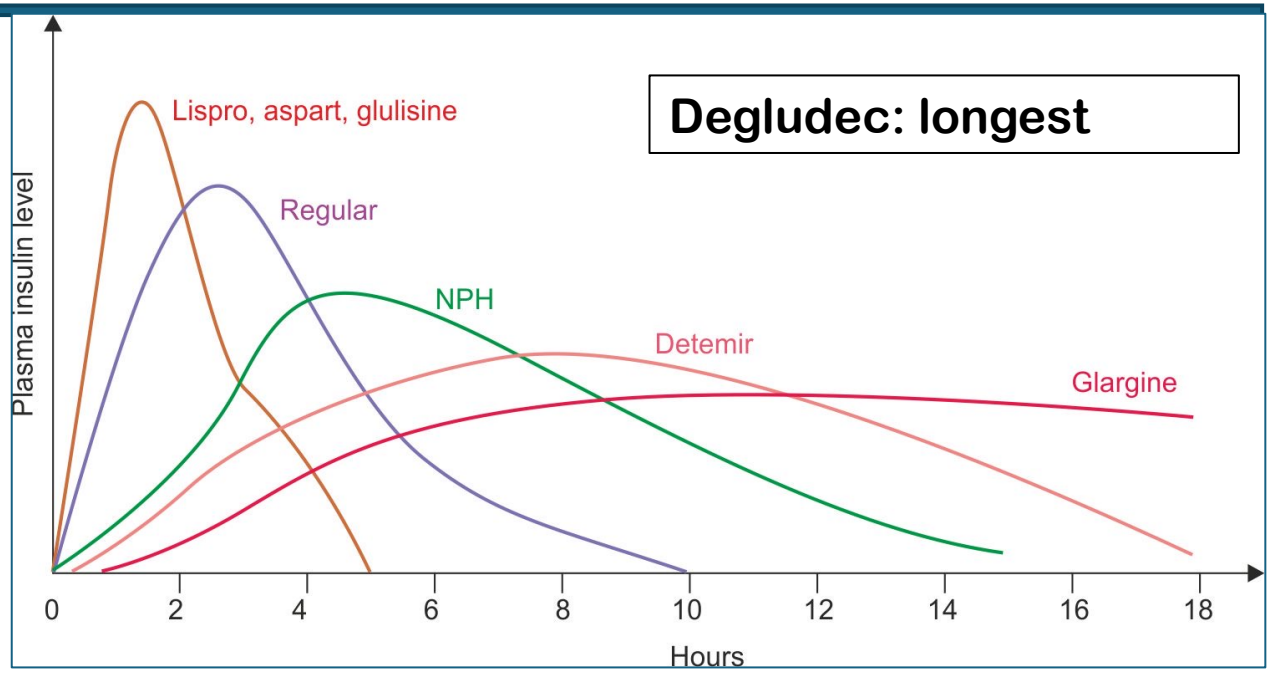
Preproinsulin (RER)
Proinsulin (stored in secretory granules)
Insulin (51aa) and C-peptide
Biphasic release:

Metabolic syndrome: NCEP-ATP III

1. Central obesity:
>102 cm (India-90cm) in men
>88 cm (India-80cm) in women
2. Elevated triglycerides: >150 mg/dL
3. HDL
< 40 mg/dL in men
< 50 mg/dL in women.
4. Blood pressure: >130/85 mm Hg
5. Fasting glucose: >100 mg/dL

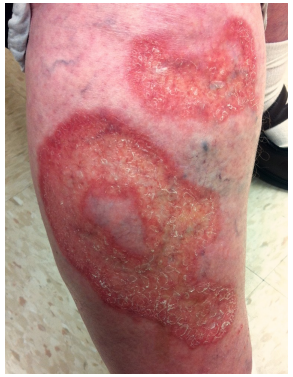
DM





Degludec: longest

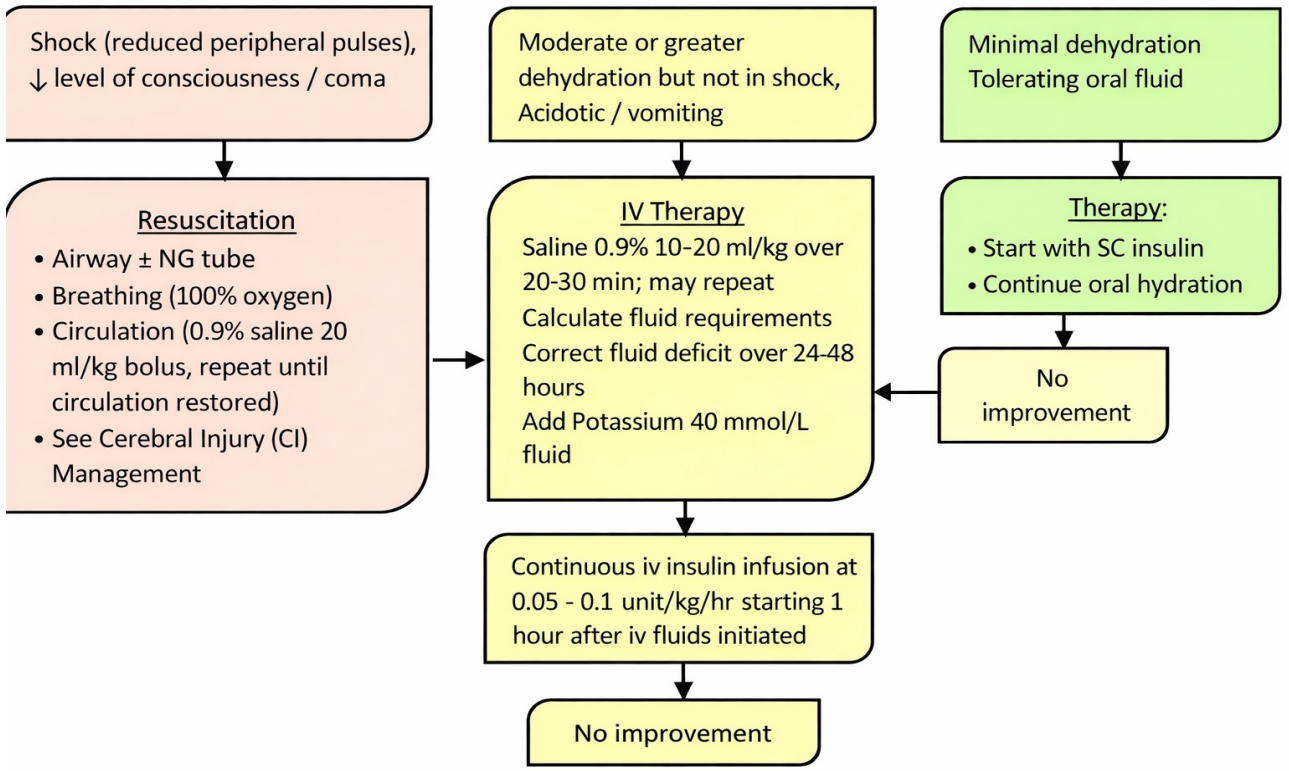
Affreza: Inhalational –Postprandial
Good glycemic control can reduce:
Mortality:
MC microvascular complication:
MC type:



Drugs causing DM:
Steroids
Thiazide
Niacin
Phenytoin
PI
Clozapine
B Agonists
IFN alpha

DKA-HHS

ISPAD guidelines for DKA



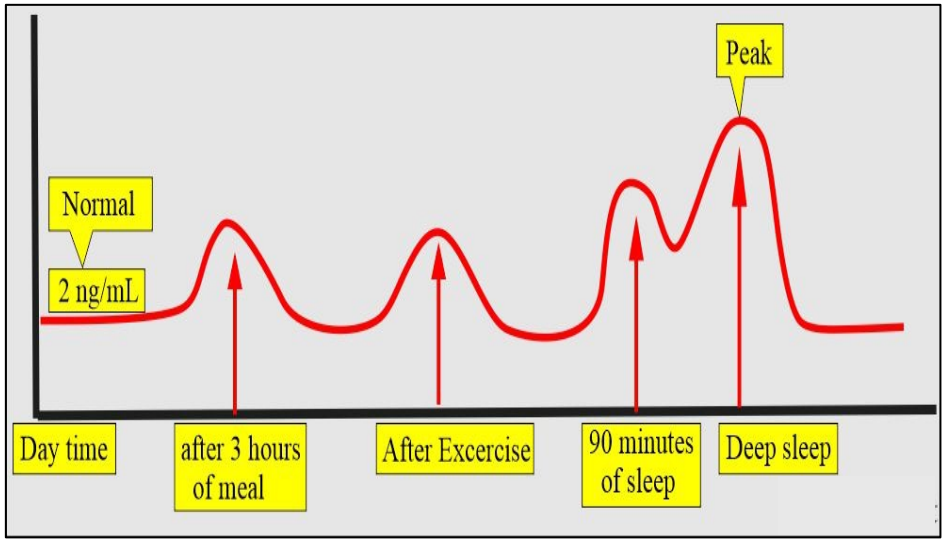
	DKA	HHS
Glucose		
ABG		
Ketones		
Demographic		
Pathophysiology		
Mortality		

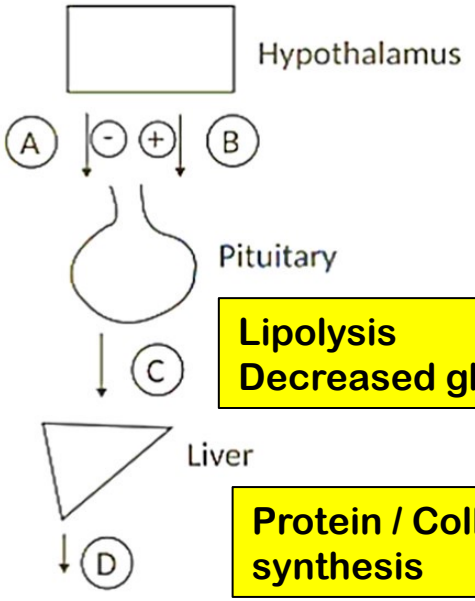
- Add IV potassium if serum K ≤5.2 mEq/L
- Hold insulin for serum K <3.3 mEq/L
- Hco3 if pH <6.9

OHG

Agent	Mechanism of action	Side effects
Sulfonylureas Chlorpropamide,Glipizide, Glyburide Meglitinides Repaglinide, Nateglinide	Increases insulin secretion by inhibiting B-cell K+ ATP channels	Hypoglycemia , Weight gain Safe in renal failure (Max-Glipizide/ Glicazide) Chlorpropamide:
Biguanides Metformin	Stimulates AMP kinase, decreasing insulin resistance	Lactic acidosis, Weight loss, Vit B12 deficiency, Diarrhea Max reduction in HbA1c
Thiazolidinediones Pioglitazone, Rosiglitazone	Activates transcription regulator PPAR-g, decreasing insulin resistance	Weight gain, Heart failure, Hepatotoxic, Fractures, CME Risk of bladder cancer - MI-
GLP-1 agonists Exenatide, Liraglutide, Tirazepatide-SC Semaglutide-Oral / SC DPP4 inhibitors : ORAL Sitagliptin, Saxagliptin, Linagliptin	Increases glucose-dependent insulin secretion, decreases glucagon secretion, delays gastric emptying Useful in CV risk mortality GLP-2 agonist: GLP-1 + GLP-2 agonist:	Increase satiety, Weight loss Pancreatitis, MTC – Nasopharyngitis- GLP1- safe in renal failure except: DPP4 - CI in renal failure except: Monitor LFT: Vidagliptin CYP metabolized:
Amylin Analogue Pramlintide	Decreases glucagon secretion, delays gastric emptying	Increase satiety
α-glucoside inhibitors Acarbose , Miglitol, Voglibose	Reduces intestinal disaccharide absorption	Diarrhea, Flatulence CI in IBD
SGLT2 Inhibitors Canagliflozin, Dapagliflozin Sotagliflozin:	Increases renal glucose excretion Useful in CV risk mortality Only if eGFR >20	Urinary tract infections, Fournier gangrene, Polyuria Weight loss, Fractures Euglycemic ketoacidosis
Bromocriptine, bile acid sequesterant (colesevalam, ranolazine)		

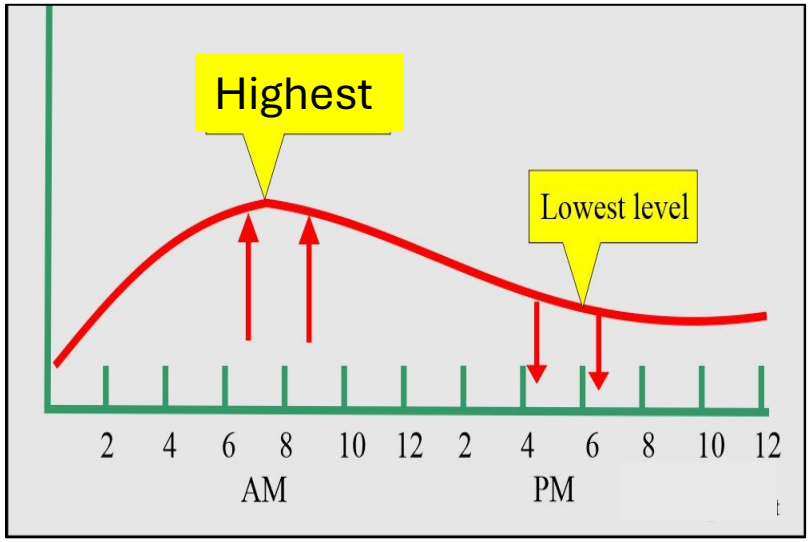
Hormone-Graphs





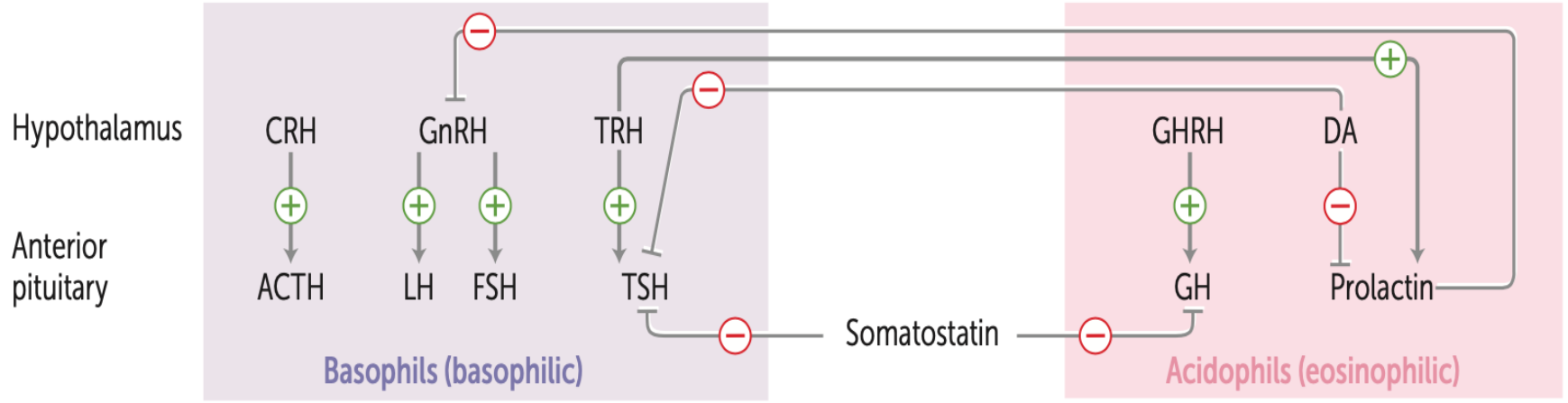
Lipolysis
Decreased glc uptake

Protein / Collagen synthesis



Autocrine
Paracrine
Endocrine

Pituitary hormones



GnRH agonists-Goserelin, Nafarelin, Leuprolide

Continuous :

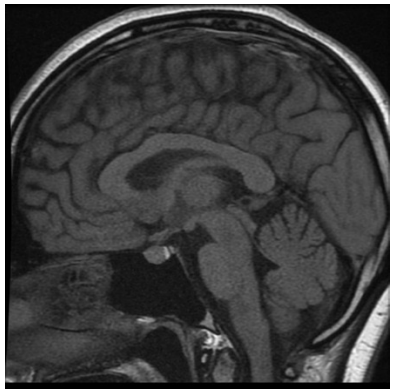
Pulsatile:

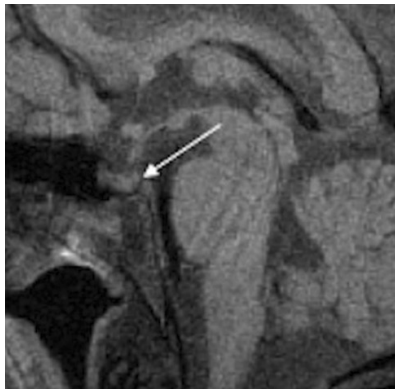
GnRH antagonists-Ganirelix, Cetrorelix

GHRH analog- Tesamorelin

Mecasermin:

Hypopituitarism + Hyperprolactinemia + Central Diabetes Insipidus
Triphasic response:

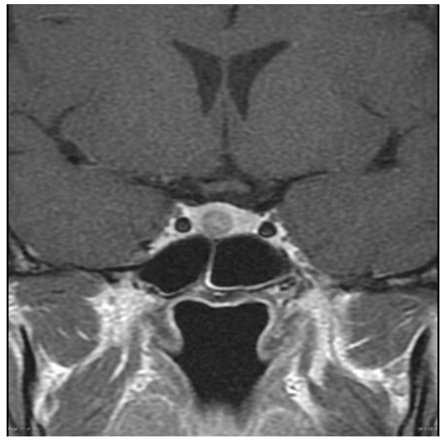




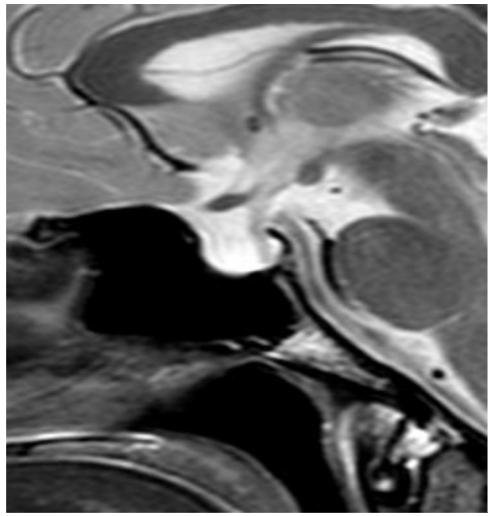
Anterior Pituitary

Amenorrhea, infertility, galactorrhea

PRL:
RULE OUT:
TSH
RFT
UPT
Drugs

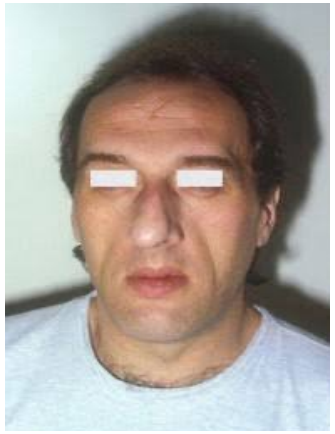


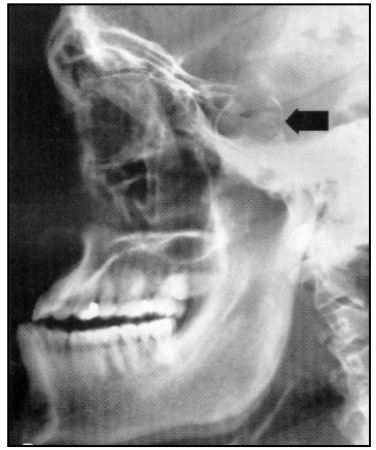
Post-partum Failure to lactate, Amenorrhea, Fatigue, Hypoglycemia
PRL / GH/ TSH

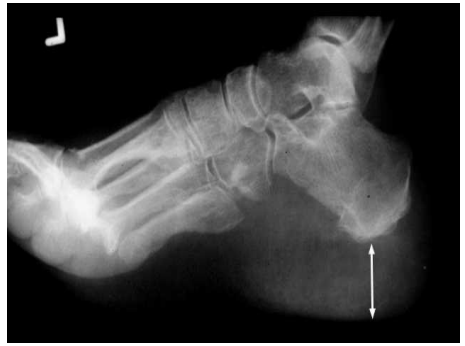


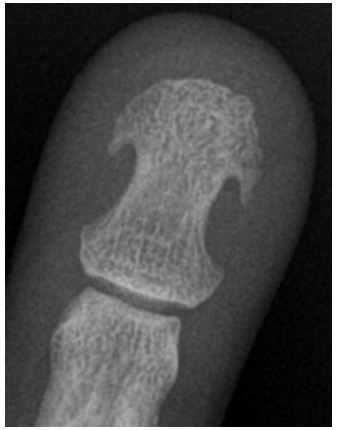
Insulin tolerance test

Sudden headache, visual deficit
Pre-existing adenoma



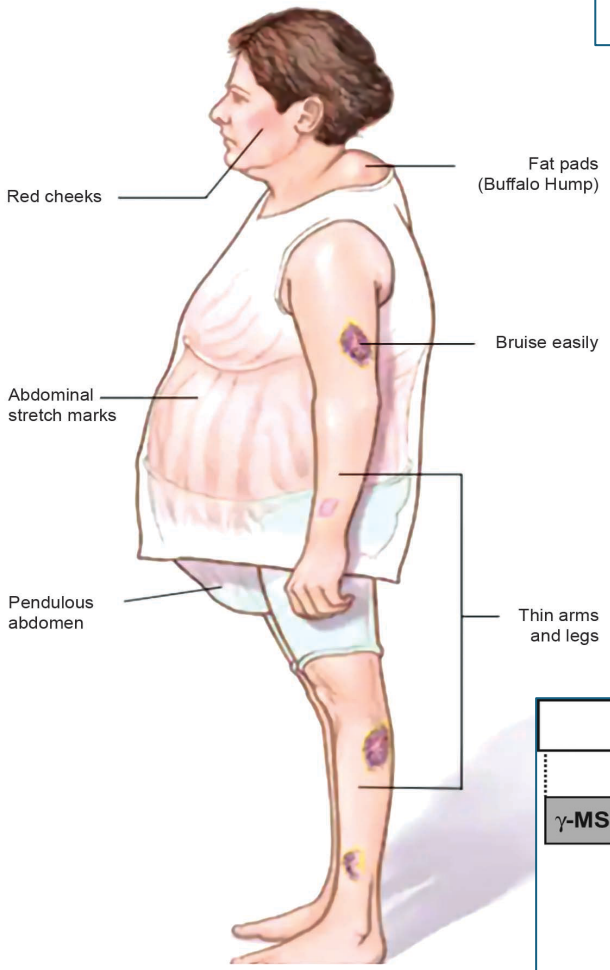






Initial:
Confirmatory:
Management:
Unresectable:

CUSHING SYNDROME



"A BIG FIB"

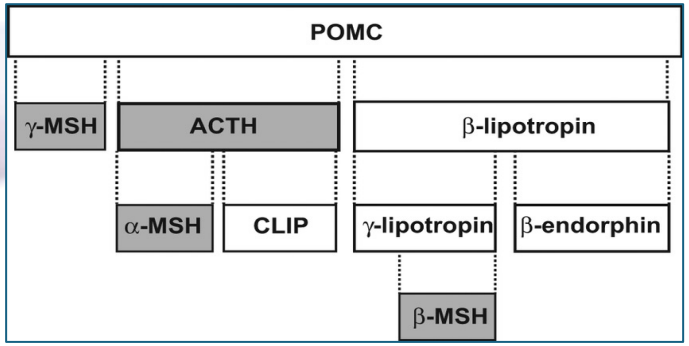
CUSHING SYNDROME:
MCC:
IOC to confirm-

ACTH

Low

High

High dose DMS:



Supress

Not supressed

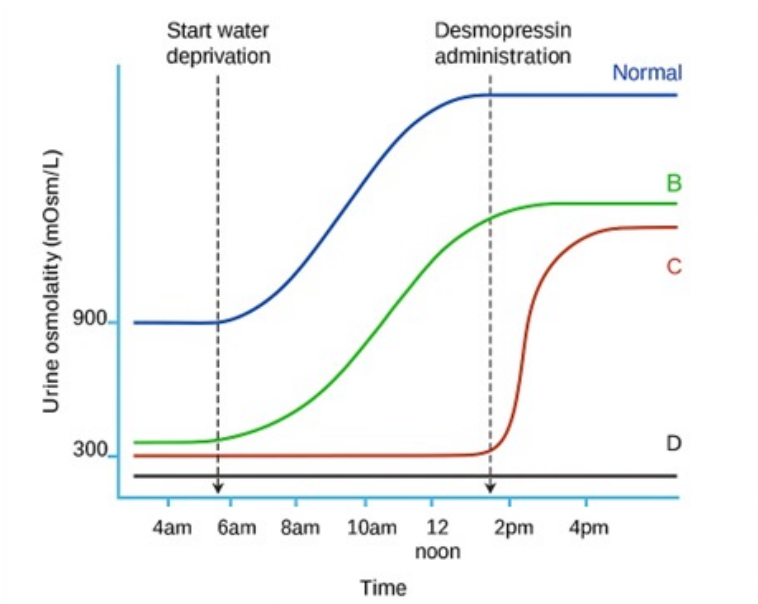
Neutrophil:
Eosinphil:
Lymphocytes:

Nelson syndrome: Hyperpigmentation + Headache/visual symptoms
H/o B/L adrenalectomy for Cushing syndrome

Posterior Pituitary

Polydipsia-Polyuria

	SIADH	Central DI	Nephrogenic DI	Primary polydipsia
Urine Osm				
Plasma Osm				
Serum Na				
Uric acid				
Diagnosis	Water loading test: ADH high	Water deprivation test: Osm low	Water deprivation test: Osm low	Water deprivation test: Osm >600 mosm/kg
Management				



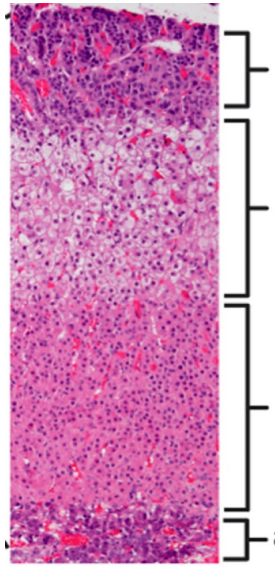
D/D:
Hypovolemic HypoNa + SAH
High BNP→ Natriuresis→ Increased Urinary Na+

Barter-Schwartz Criteria for SIADH:
- Clinically Euvolemic
- Low Serum Osmolality <275
- Urine Osmolality >100 or Urine Na+ > 40meq/L
- Absence of Any Renal, Thyroid disease, diuretic use
- Correction with fluid restriction

ADH: V1-
V2
V3-

SIADH causes: Chlorpropamide, Oxcarbamazepine, Cyclophosphamide, Vincristine, SSRI, Small cell ca lung, Pneumonia, Encephalitis

ADRENAL INSUFFICIENCY



IOC:
COSYNTROPIN TEST

HIGH CORTISOL

LOW CORTISOL <20ug/dl

ACTH

LOW

HIGH

Primary versus central adrenal insufficiency		
	Primary	**Secondary**
Most common cause	Autoimmune/ Granulomatous	Chronic glucocorticoid therapy
Cortisol		
ACTH		
Aldosterone		
Clinical features	• Severe symptoms • Hyperpigmentation • Hyperkalemia	• Less severe • No hyperpigmentation • No hyperkalemia

HYPERALDOSTERONISM

CAUSES

- Bilateral nodular hyperplasia
- Hyperfunctioning adrenal adenoma

↑ Aldosterone

EFFECTS ON ELECTROLYTES

- ↑ K^+ excretion → Hypokalemia
- ↑ H^+ excretion → Metabolic alkalosis
- ↑ Na^+ reabsorption → Hypertension + Blood volume

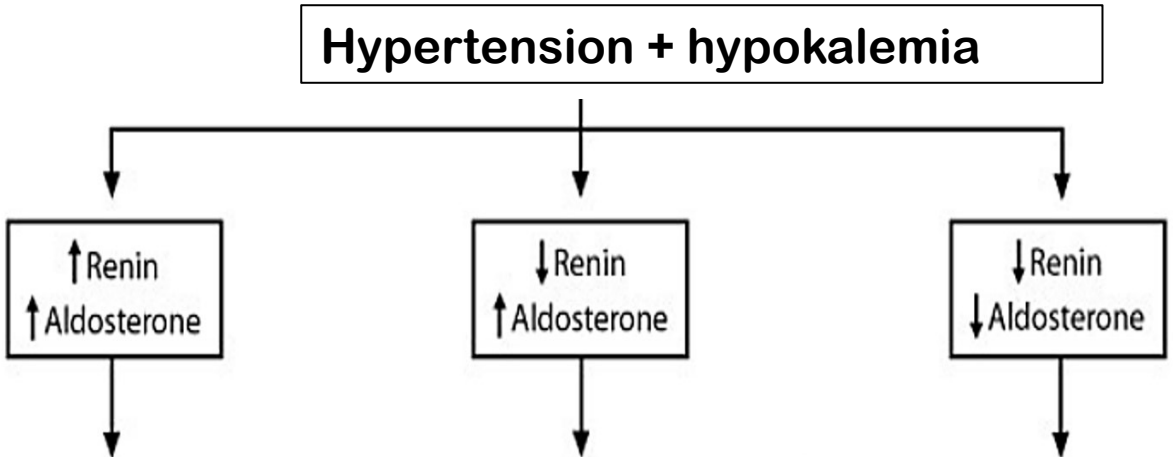
RAAS EFFECT

- ↓ Renin
- ↓ Angiotensin II

ALDOSTERONE ESCAPE

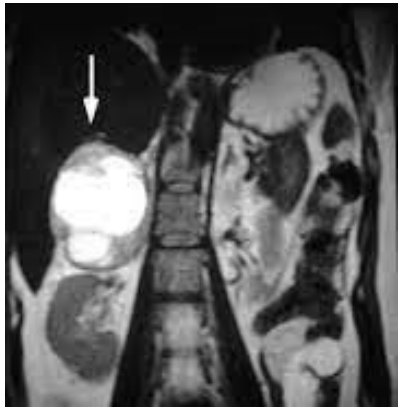
- Limits edema
- Limits hypernatremia

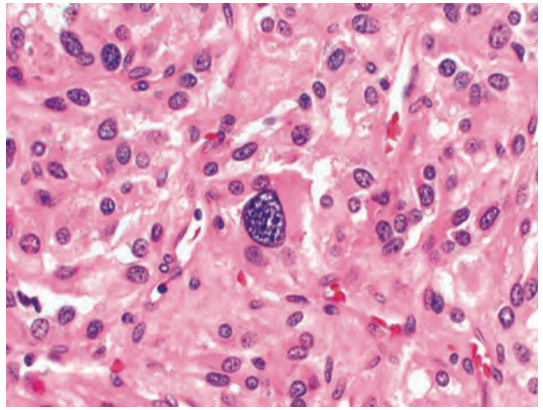
↑ Na^+ excretion



Pheochromocytoma

Headache / Sweating / Palpitation
Initial Ix-
Confirm Ix-
Best to localize-
Biopsy/ FNAC-
Best for mets-
Best for extraadrenal pheo-
MC site for extradrenal pheo-
Rule of 10 :
-Extradrenal/ No hypertension/ Children
-B/L But 50% in
-Malignant But 40% in
-Familial
Treatment:

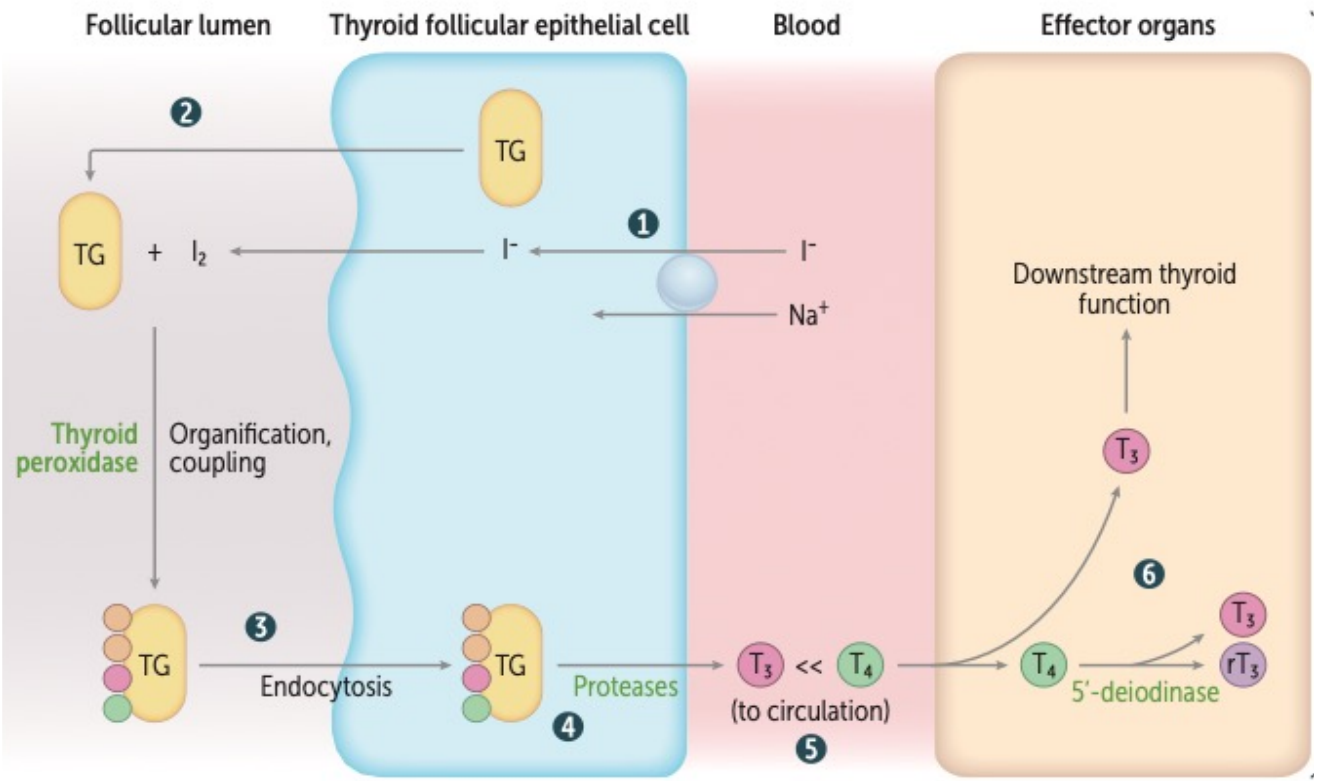


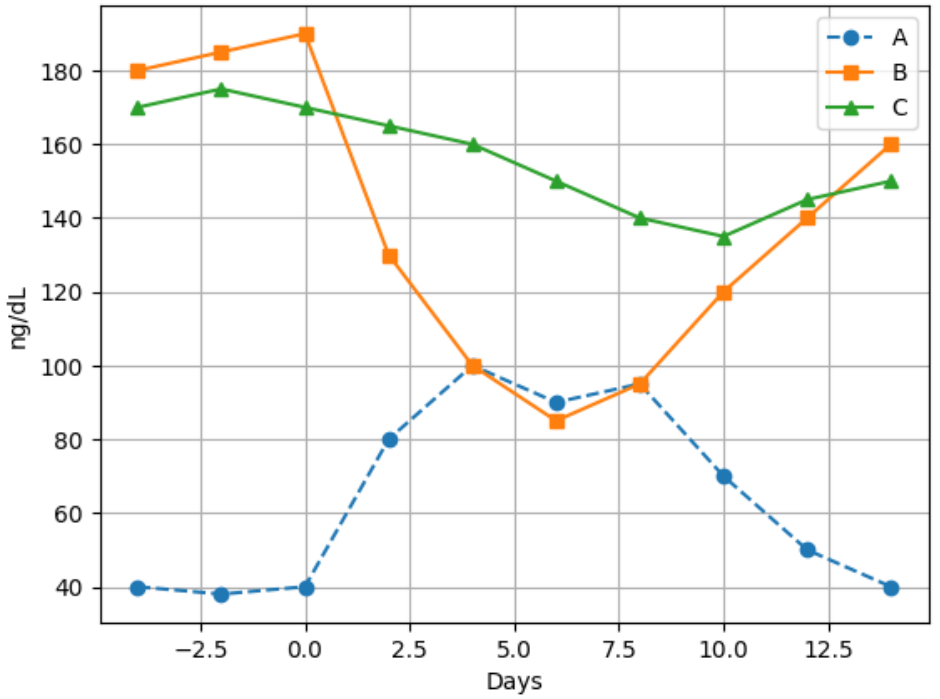


Carcinoid tumor

Origin:
MC site:
Urinary:
Skin flushing
Heart valve disease
Intestinal diarrhea
Vasospasm
Asthma
Rx:
Telotristat-
Rule of 1/3: Mets, 2nd malignancy, multiple

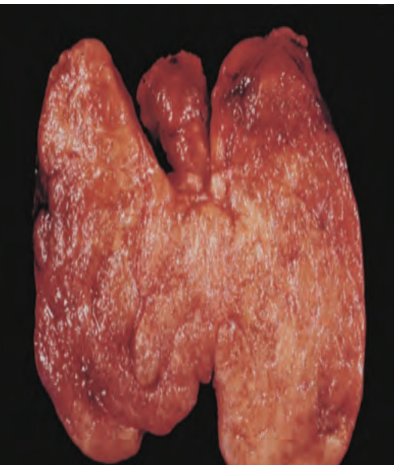
Thyroid hormone

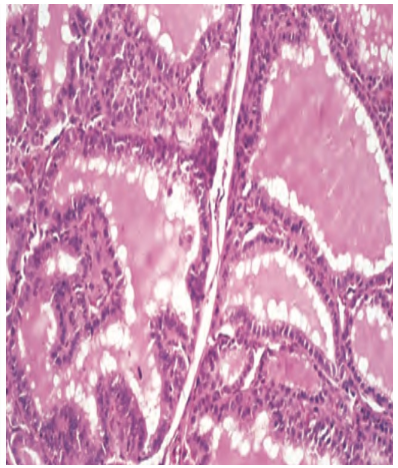


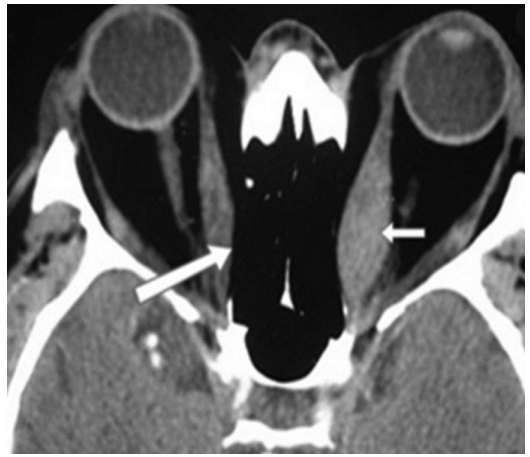


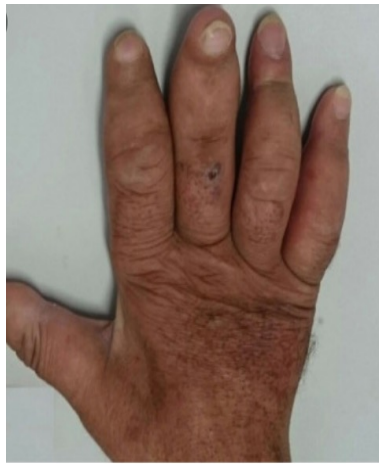
- **Brain maturation**
- **Bone O'clast +**
- **↑ β_1 receptors in heart**
- **Basal metabolic rate ↑ (via ↑ Na^+/K^+-ATPase)**
- **Blood sugar ↑ (↑ glycogenolysis, gluconeogenesis)**
- **Break down lipids ↑ (↑ lipolysis)**
- **Babies: stimulates surfactant synthesis**

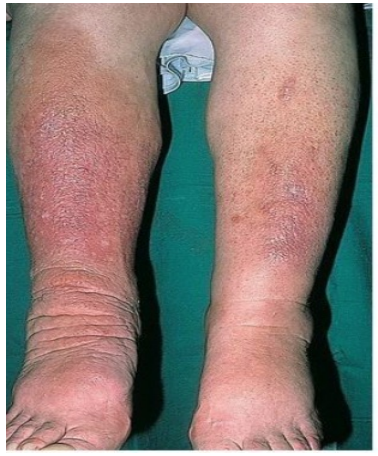
Graves Disease











1-Only signs

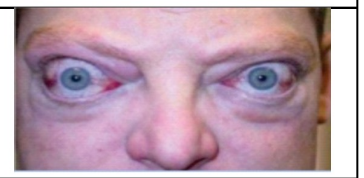
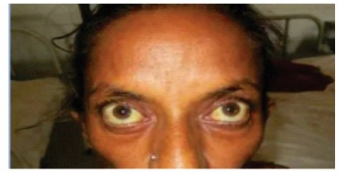
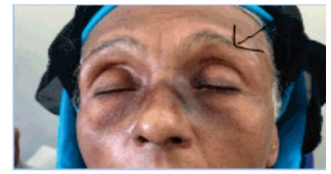
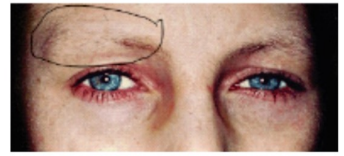
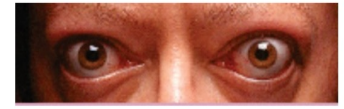
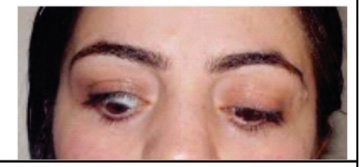
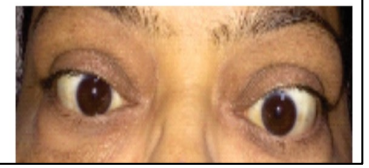
2-Soft tissue involvement

3: Proptosis

4: Extraocular muscle involvement

5: Corneal involvement

6: Sight loss (optic nerve involvement)

Staring look	
Absent creases in the forehead on superior gaze	
Hyperpigmentation of the superior eye folds	
Loss of the lateral third of eyebrows	
Retraction of upper eye lid	
Lid lag of the upper eyelid on downward gaze	
Inability to converge	

Treatment

Management of Graves

RADIO-IODINE ABLATION

DRUGS

SURGERY

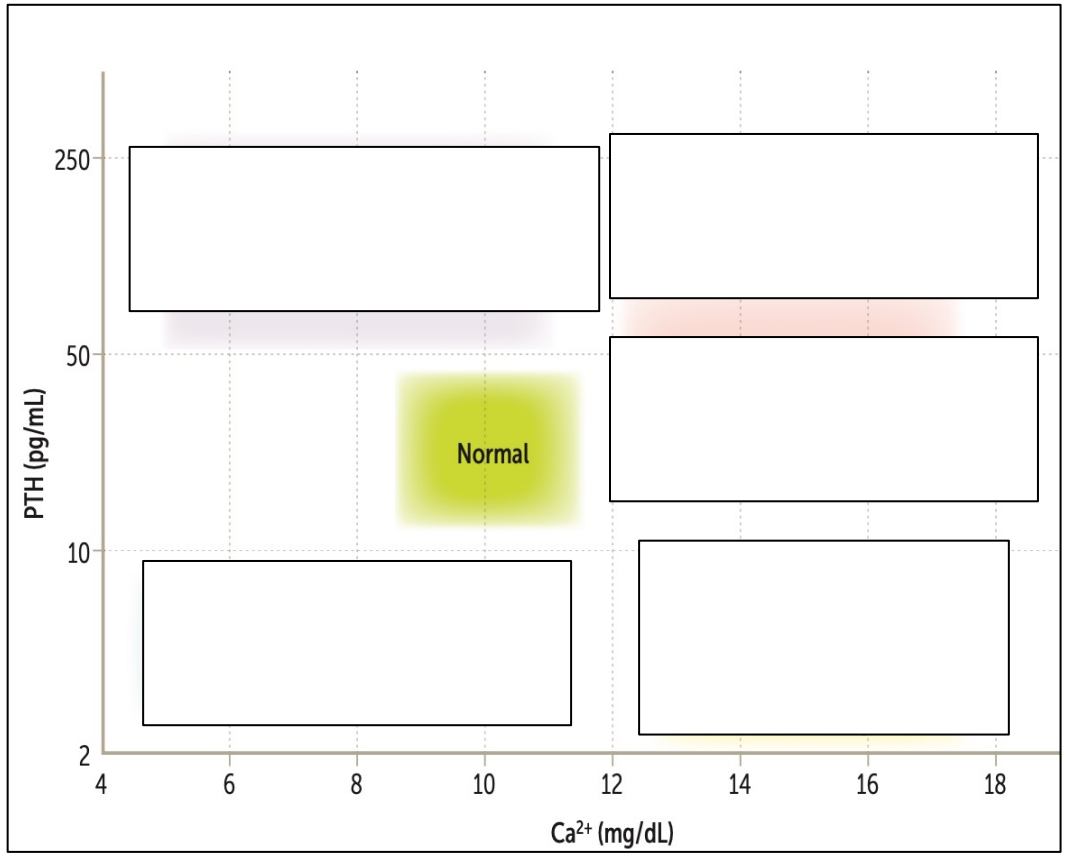
Thyroid storm

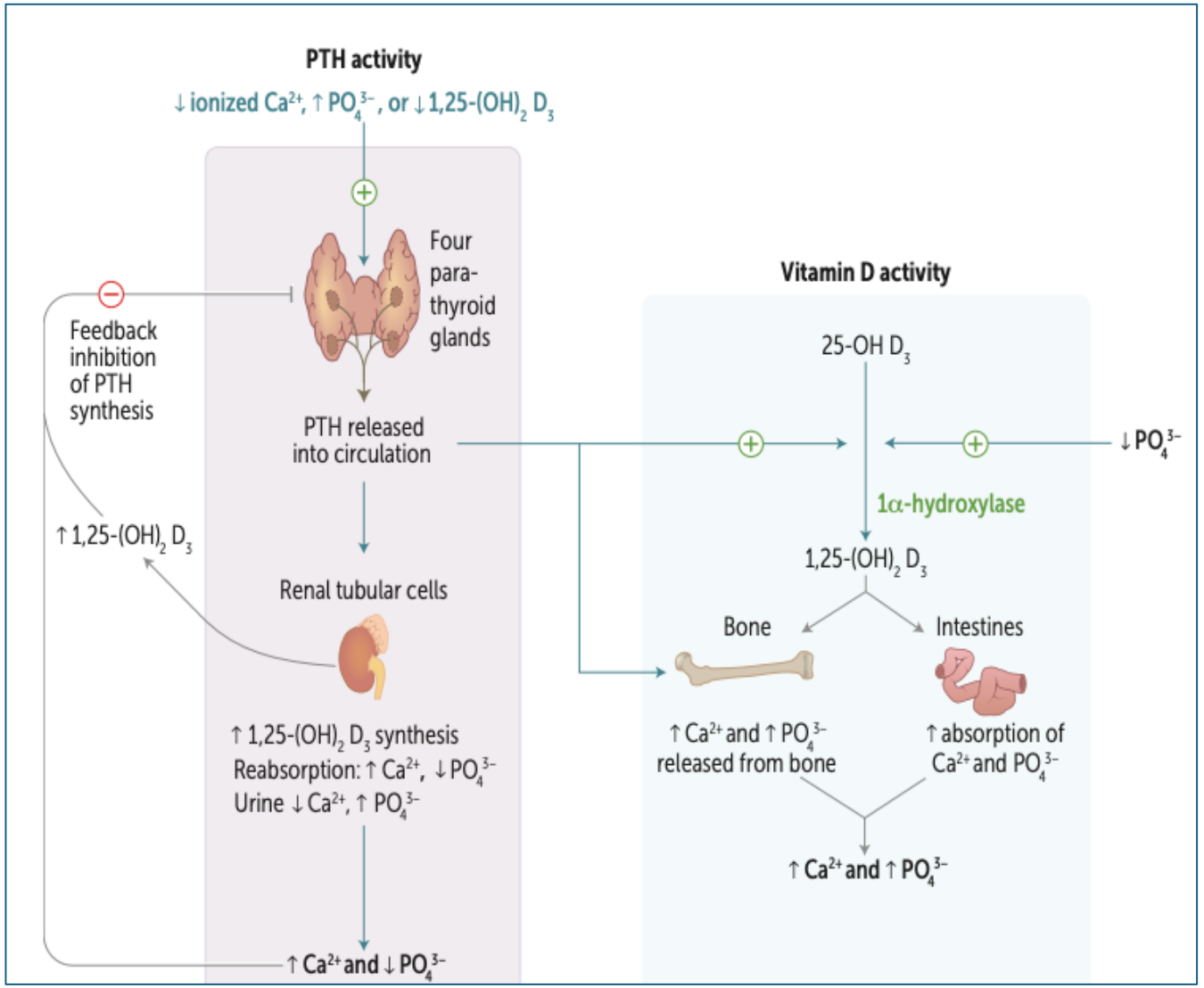
- Beta blockers
- PTU
- Glucocorticoids
- Sodium iodide
- If asthma + A-fib:

Myxedema coma

IV T3 and/or L-thyroxine (T4)
IV Hydrocortisone
0.9% NaCl if Na^+ < 120 mEq/L
Treat hypothermia (temperature < 35 °C)

Parathyroid and calcium

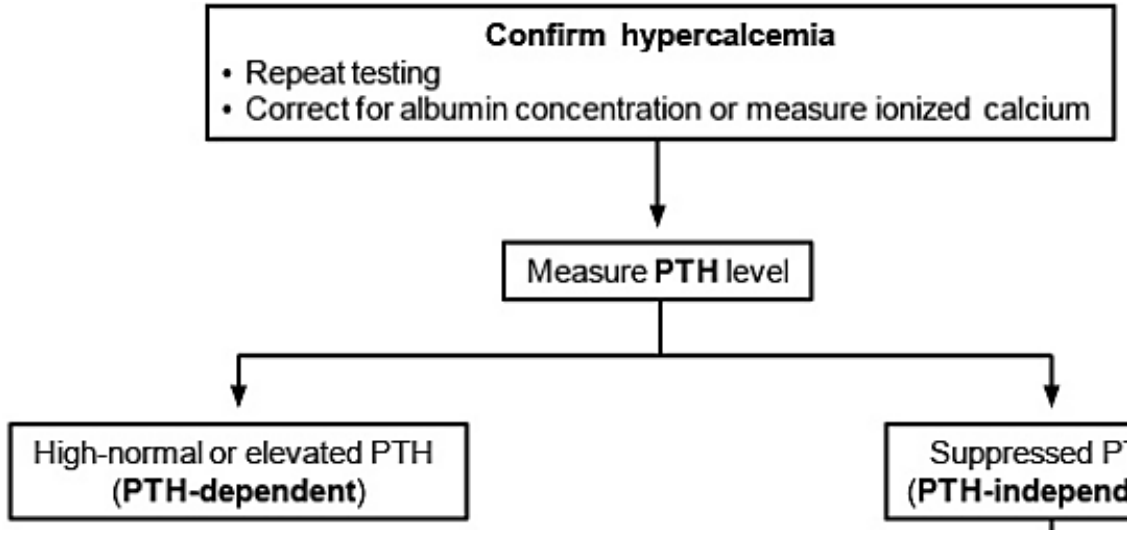




↑ Serum Ca^{2+} → stimulation of parafollicular (C) cells of the thyroid → ↑ calcitonin
Inhibits osteoclastic bone resorption

Intermittent/ 1-34 aa chain PTH:

Hypercalcemia



- Primary (or tertiary) hyperparathyroidism
- Familial hypocalciuric hypercalcemia
- Lithium

- Malignancy
- Vitamin D toxicity
- Granulomatous diseases
- Thiazides
- Milk-alkali syndrome
- Thyrotoxicosis
- Vitamin A toxicity
- Immobilization

Management:
Severe (Calcium > 14 mg/dL) or Symptomatic
- Normal saline hydration plus calcitonin
- Avoid loop diuretics unless volume overload (heart failure) exists

Long-term treatment: Bisphosphonate