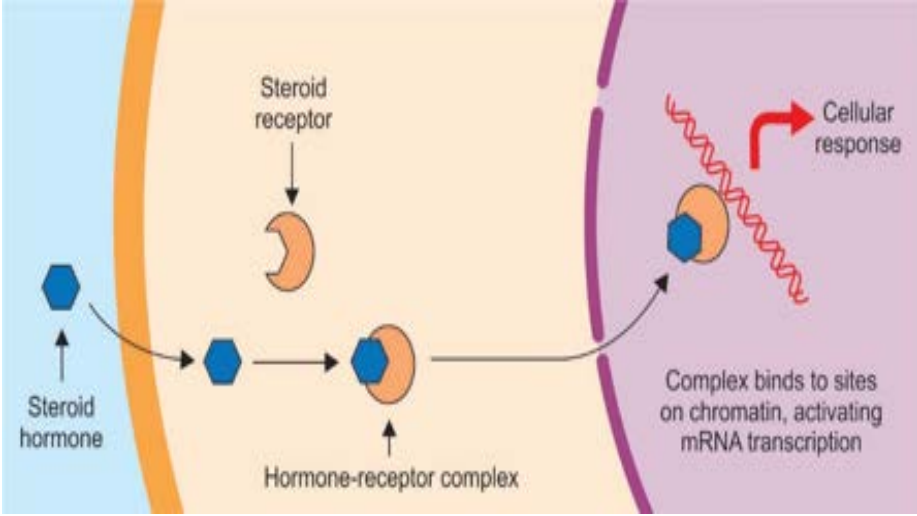


INTEGRATED ENDOCRINE SYSTEM

Hormone Actions - GPCR

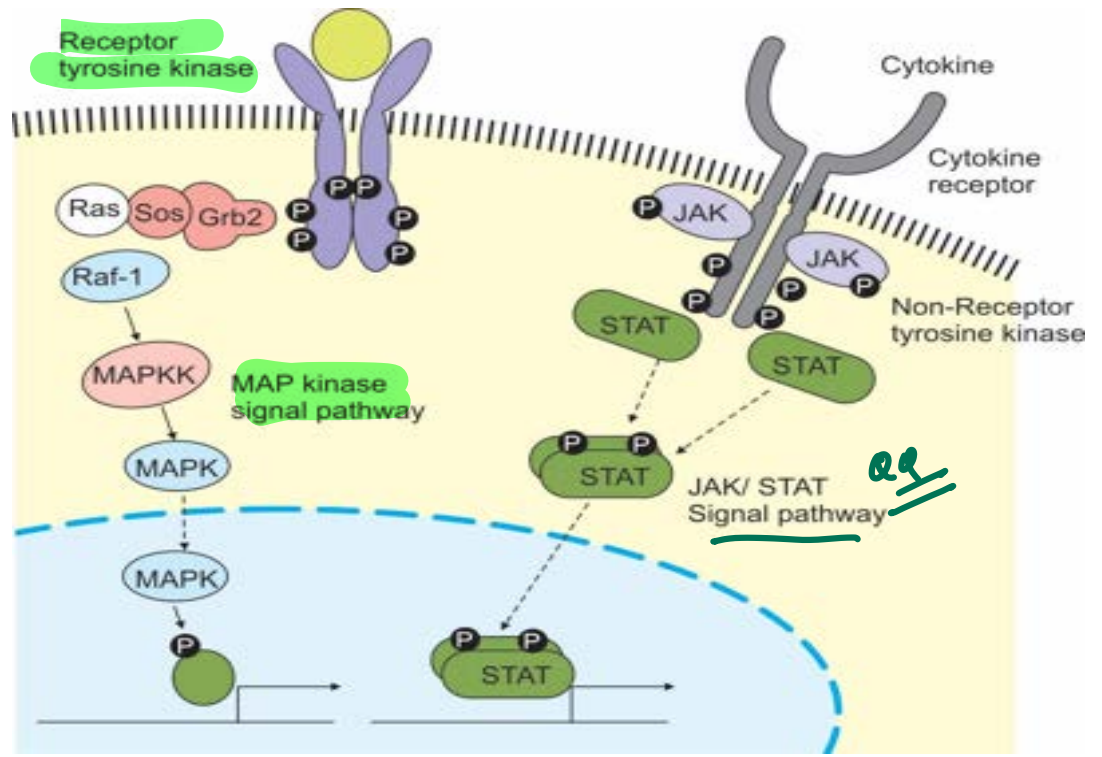
G-protein pathway	Receptor and ligand	Second messenger
G-protein (G_q -alpha subunit) =	"Hav1 M and M-GOT" $H_1, \alpha_1, V_1, M_1, M_3, ATII$ - Gastrin - GnRH - oxytocin - TRH	$\uparrow IP3$ $\uparrow DAG$ ← Phospholipase → \oplus Protein kinase C
G-protein (G_s -alpha subunit)	FSH, LH, ACTH, TSH, CRH, hCG, ADH- V_2 , MSH, PTH, Calcitonin, H_2 , Glucagon, GHRH All B receptors	$\uparrow cAMP$
G-protein (G_i -alpha subunit)	MAD 2 M_2, α_2, D_2	$\downarrow cAMP$
Receptor Guanyl cyclase	29 "BAN" BNP ANP NO	$\uparrow cGMP$

arginine → EDRF & PAN → iNO



STEROIDS PREP TV

Cytoplasmic: *steroids / vit D*
 Intranuclear: *Estrogen vit A T3/T4*
NEAT
Progestone : both



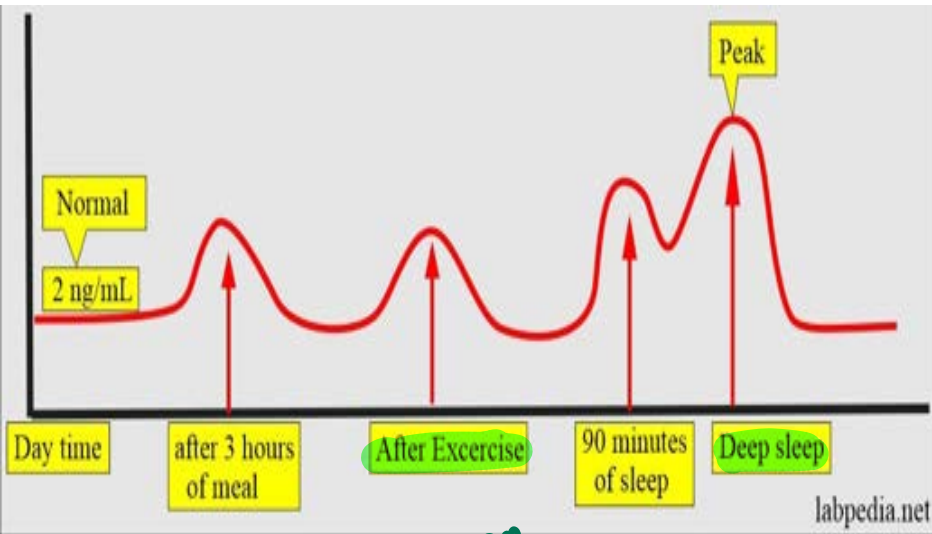
INSULIN PIPE

- PDGF
- IGF
- FGF
- EGF

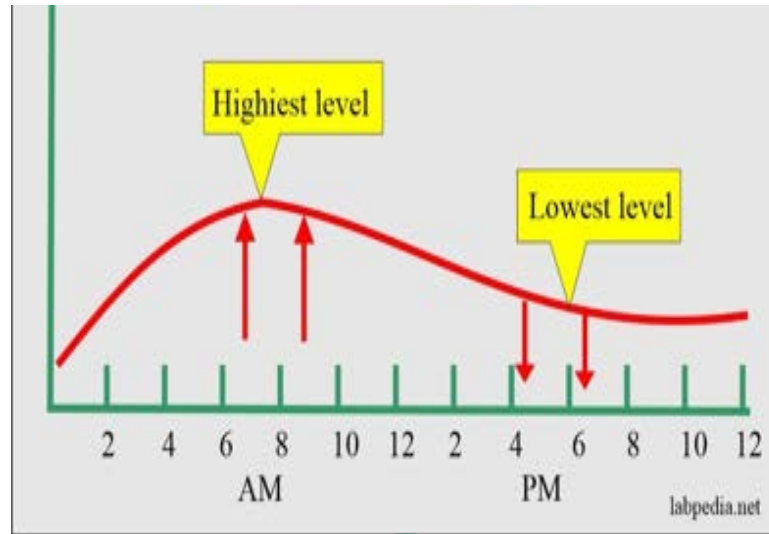
PIGGLET

- PAL
- IL
- GM-CSF
- GH
- Leptin^{RR}
- EPO
- TPO

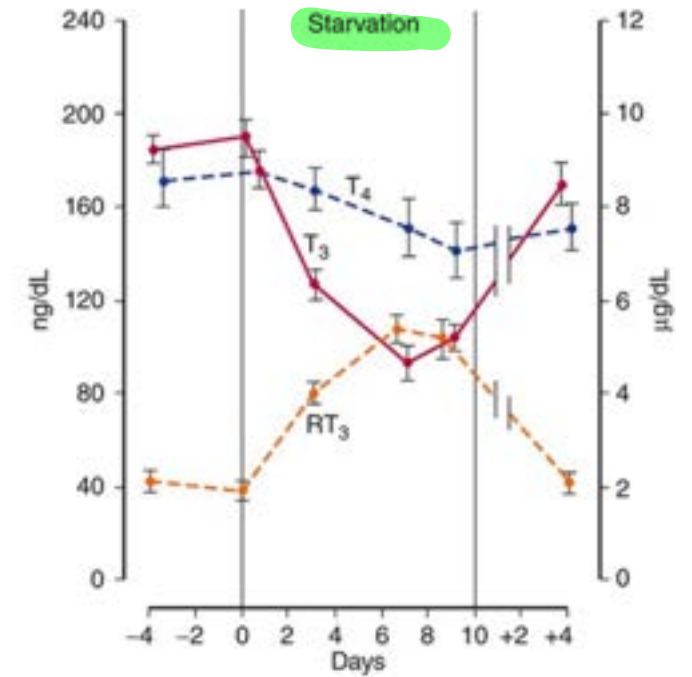
Graphs



GH



Cortisol



$\downarrow T_4$ \rightarrow T_3 (active) \downarrow
 \rightarrow rT_3 (inactive) \uparrow

Diabetes mellitus - Screening

HbA1c	FBS	RBS	OGTT-75g
<p>5.7 - 6.5</p> <p>↙ ↘</p> <p><5.7 >6.5</p> <p>Ⓝ </p> <p>impaired </p> <p>glc </p> <p>tolerance </p> <p>DM</p>	<p>100 - 126</p> <p>Ⓝ ></p> <p>IGT DM</p>	<p>140 - 200</p> <p><Ⓝ ></p> <p>IGT DM</p>	<p>140 - 200</p> <p><Ⓝ ></p> <p>IGT DM</p>

	Type 1 DM Adult onset: LADA Antibodies: anti-islet, anti-GAD	Type 2 DM	MODY AD MC type: 3 Gene: HNF1α
Age of onset	childhood	adults	<u>< 25 yrs</u> <u>≥ 2 family</u>
Habitus	thin	obese	(N) (N) — ↓ (N) — ↓
Insulin levels	(↓)	(↑) — ↓	(N) — ↓
B cell mass	(↓)	(↑) — ↓	(N) — ↓
OHG	NO	Yes ≈	✓

H/P: ^{leukocytic} infiltration

R₀ - insulin

LADA:

Latent AI DM adults

H/P: IAPP
amyloid

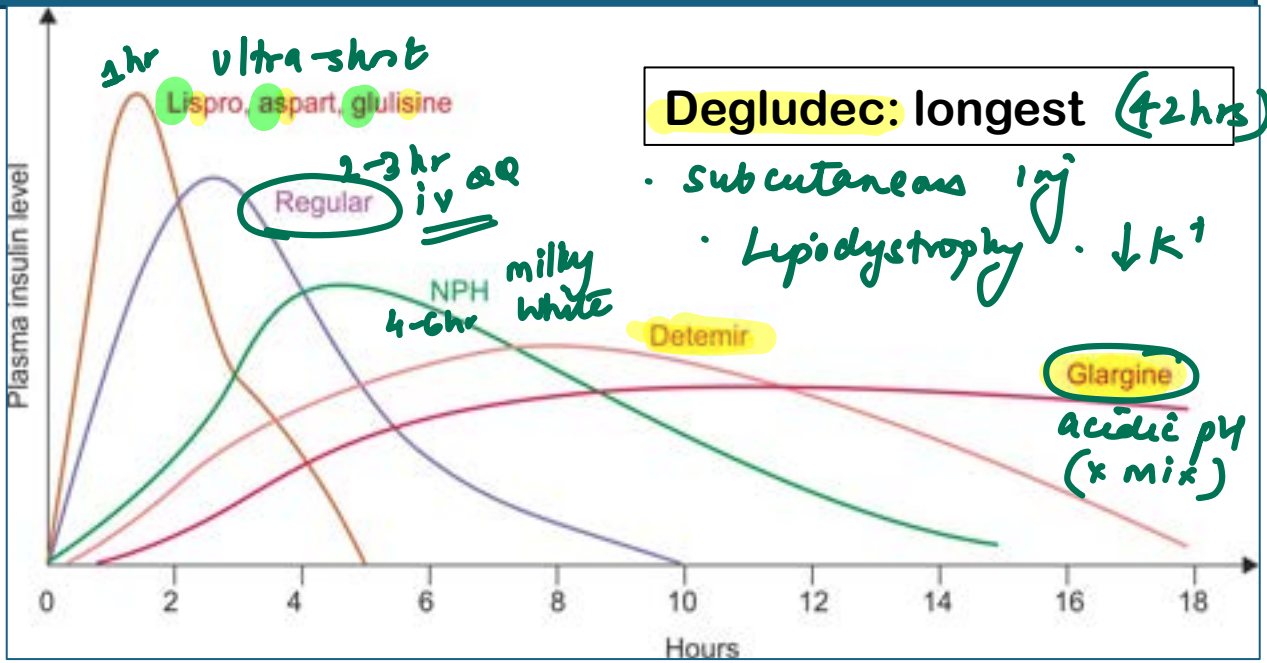
islet associated
polypeptide

DM

Metabolic syndrome: NCEP-ATP III ~~OR~~

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

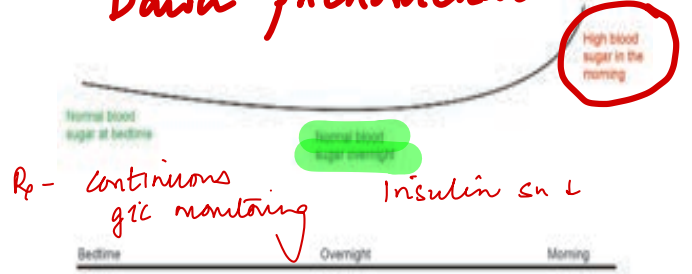
LDL



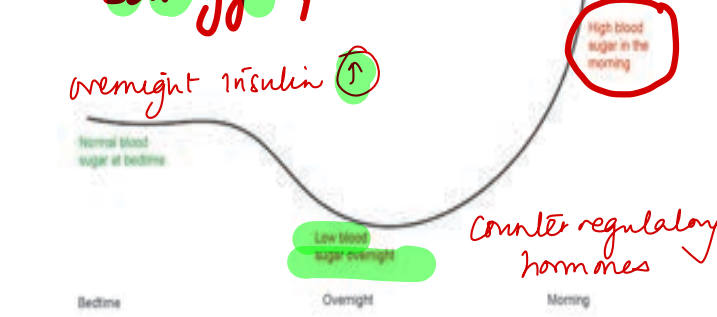
Degludec: longest (42hrs)

- subcutaneous inj
- Lipodystrophy ↓K⁺

Dawn phenomenon



Somogyi phenomenon



Affrezza: Inhalational - Postprandial CI - COPD/asthma

Good glycemic control can reduce: **microvasc amphi**

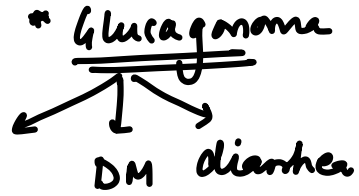
Mortality: **No change → CVS**

MC microvascular complication: **neuropathy**

MC type: **glove & stocking - sensorimotor distal**



Necrobiosis lipodica diabetorum



- Drugs causing DM:**
- Steroids
 - Thiazide } ↑uricemia
 - Niacin } ↑uricemia
 - Phenytoin
 - PI
 - Clozapine
 - B Agonists
 - IFN alpha

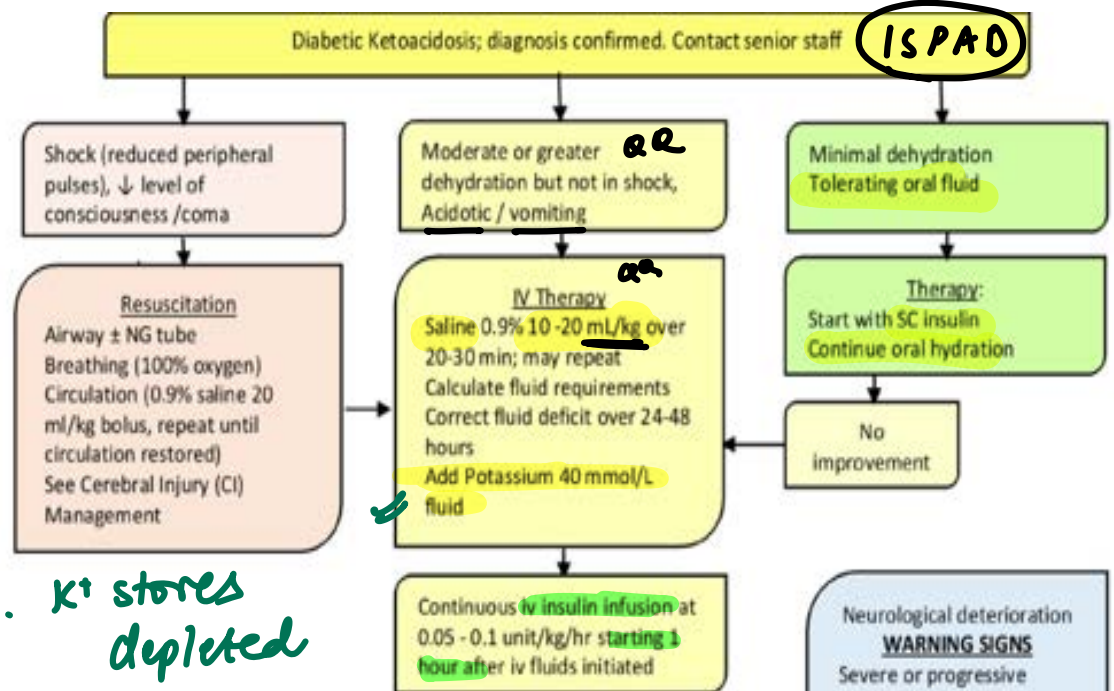
DKA-HHS

iv fluids + insulin → iv fluids

	DKA	HHS
Glucose	250 - 400 mg/dl	500 - 600 mg/dl
ABG	HAGMA	⊖
Ketones	fatty odour (↑↑)	⊖
Demographic	type I DM	type II DM
Pathophysiology	illness (+)	dehydration (↑↑)
Mortality	↓	↑↑

Euglycemic DKA

- stress
 - illness
 - SGLT2 ⊖
- < 250 mg/dl



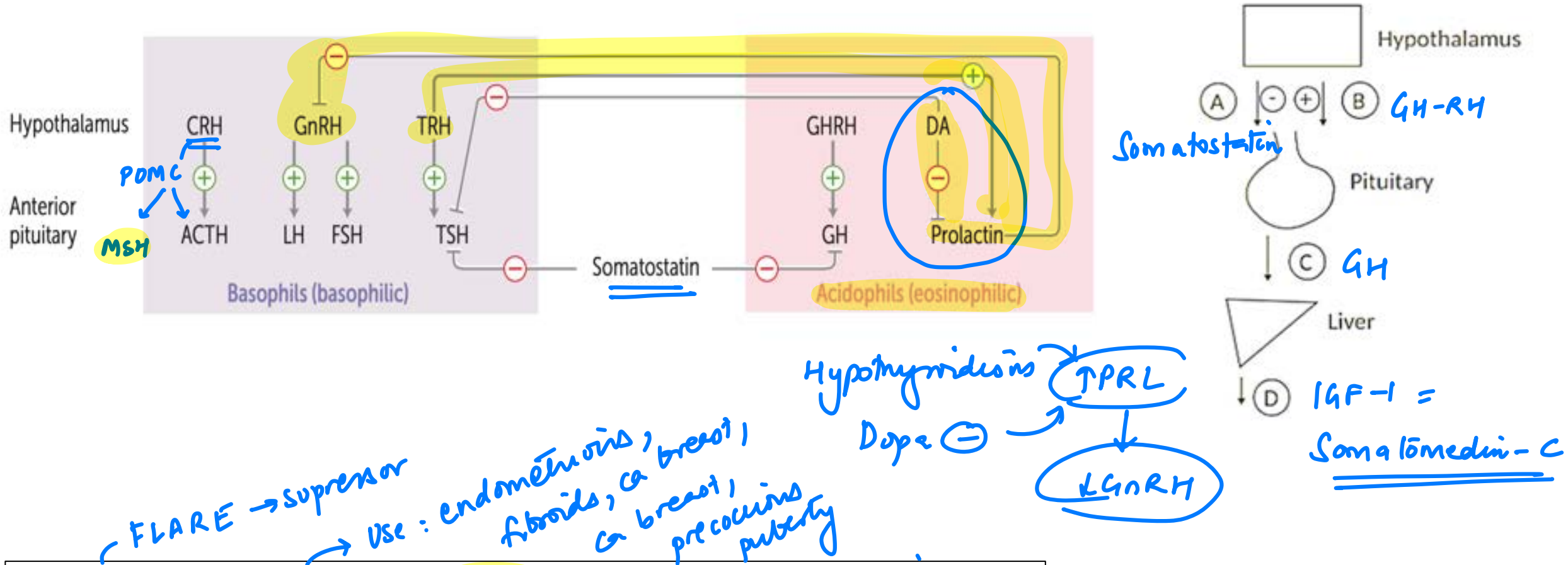
K⁺ stores depleted

- 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 QQ

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 Chlorpropamide: <u>SIADH</u> , disulfiram-like rxn
Biguanides Metformin <i>1st line</i>	Stimulates AMP kinase, decreasing insulin resistance Useful in CV risk mortality	Lactic acidosis, Weight loss, Vit B12 deficiency, Diarrhea <i>CI in renal failure</i> Max reduction in HbA1c
Thiazolidinediones Pioglitazone Rosiglitazone	Activates transcription regulator PPAR-g, decreasing insulin resistance	Weight gain, Heart failure, Hepatotoxic, Fractures Risk of bladder cancer - <u>Pio</u> MI- <u>ROSI</u>
GLP-1 agonists Exenatide, Liraglutide, Tirazepatide-SC Semaglutide- <u>Oral</u> / SC DPP4 inhibitors: <u>ORAL</u> (<i>wt neutral</i>) Sitagliptin, Saxagliptin, <u>Linagliptin</u>	Increases glucose-dependent insulin secretion, decreases glucagon secretion, delays gastric emptying Useful in CV risk mortality GLP-2 agonist: <u>Teduglutide</u> - short bowel <u>INCRETIN</u>	Increase satiety, Weight loss Pancreatitis - <u>GLP 1</u> (+) MTC Nasopharyngitis- <u>DPP4</u> (-) DPP4 - : CI in renal failure except: <u>Linagliptin</u>
Amylin Analogue Pramlintide	Decreases glucagon secretion, delays gastric emptying	Increase satiety
α-glucoside inhibitors Acarbose, Miglitol	Reduces intestinal disaccharide absorption	Diarrhea, Flatulence CI in IBD
SGLT2 Inhibitors Canagliflozin, Dapagliflozin <u>QQ</u>	Increases renal glucose excretion Useful in CV risk mortality	Urinary tract infections, Polyuria (osmotic diuresis) Weight loss <u>Candidiasis / Fournier</u> <u>QQ</u>

Pituitary regulation of hormones



- GnRH agonist continuous:** Goserelin / Nafarelin / Leuprolide
- GnRH agonist Pulsatile:** ⊕⊕ - use: delayed puberty
- GnRH antagonist:** Cetrorelix, Ganirelix
- GHRH analog:** Tesamorelin - HIV atrophy use

Anterior Pituitary

GnRH ⊖

Amenorrhea, infertility,
galactorrhea or

PRL ↑

PRL: >20 uIU PRLoma: >200

RULE OUT:

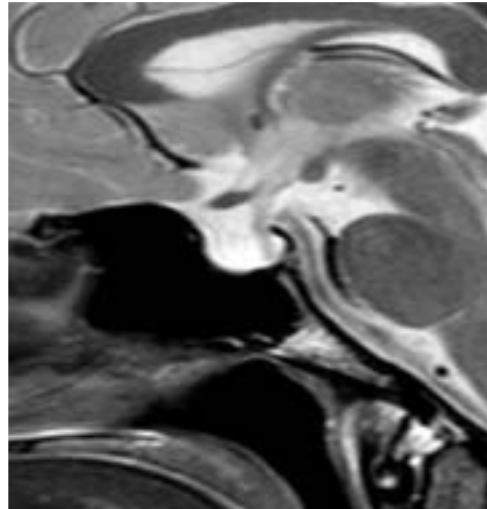
TSH Hypothyroidism TRH ⊕ PRL

RFT

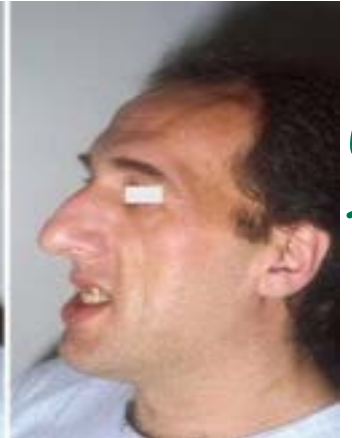
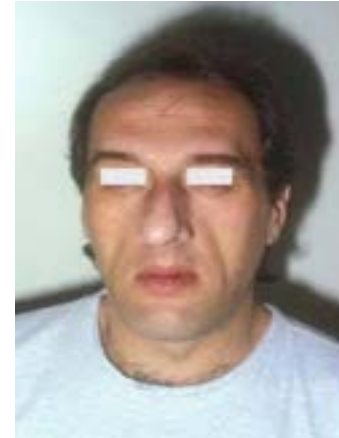
UPT

Drugs D2 ⊖ typical AP
Metoclopramide

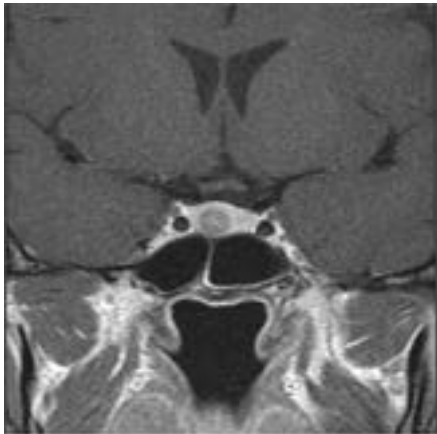
Post-partum Fatigue, h/o PPH
Hypoglycemia, Failure to lactate,
Amenorrhea



ischemic
necrosis



Coarse
features



CE-MRI
pituitary

<10mm: adenoma
>10mm: macroadenoma

↓
mass effect

Insulin tolerance test

SHEEHAN'S
Empty sella Sx

Mx: Medical Mx

Doc - Cabergoline (D+)

Pregn: ↑ suppress lactation } → Sx (TSR)

Bromocriptine (D+) DM use: sle: valvular fibrosis

Ⓝ - cortisol ↑
ACTH ↓



Increase heel pad
thickness



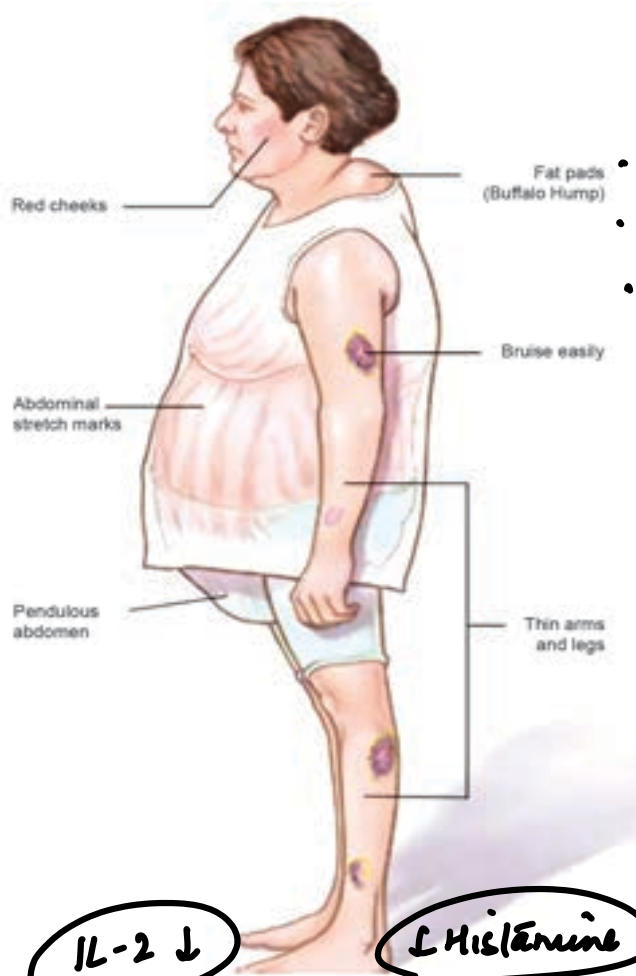
prognathism

↑ GH

ACROMEGALY

Initial: IGF-1
Confirmatory: OGTT or glc → GH ↓
Management: Sx (1st - TSR)
Unresectable: Somatostatin / Pegvisomant
visual sle

CUSHING SYNDROME

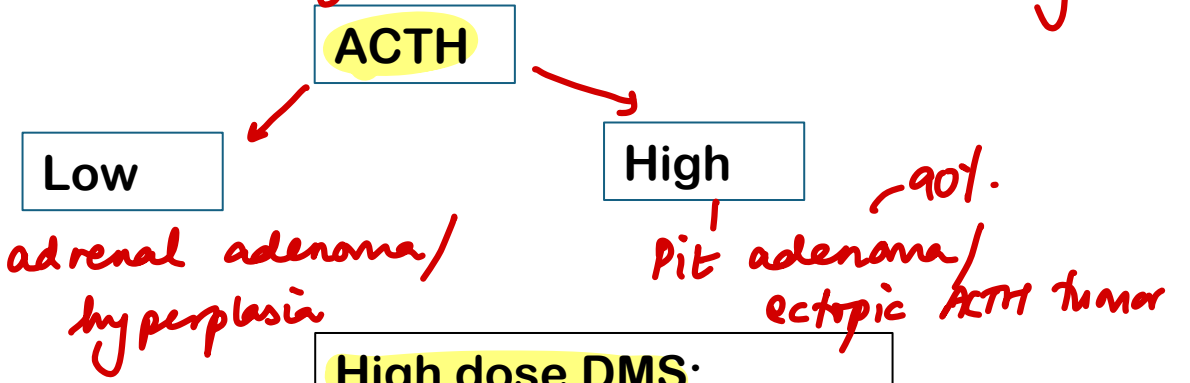


Cortisol:
 • ↑BP
 • DM
 • myopathy

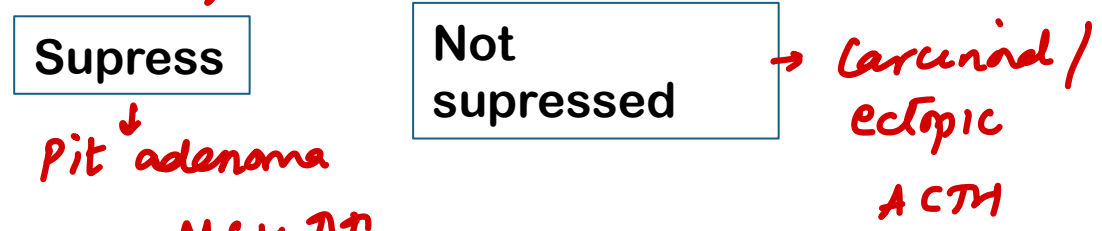
IL-2 ↓
 ↓ Histamine

Neutrophil: ↑
 Eosinophil: ↓
 Lymphocytes: ↓
 ⊖ chemotaxis

CUSHING SYNDROME:
 MCC: *exogenous steroid*
 IOC to confirm - Low dose DMS: (N) - Cortisol
 1mg dexamethasone - remains high



High dose DMS:
 2mg dexam 6hly x 48hrs



Nelson syndrome: Hyperpigmentation + Headache/visual symptoms
 H/o B/L adrenalectomy for Cushing syndrome ACTH ↑↑ pit
 -ve feedback LOST

Posterior Pituitary

Polydipsia-Polyuria

	<u>SIADH</u>	<u>Central DI</u>	<u>Nephrogenic DI</u> <i>end organ R</i>	Primary polydipsia	Diabetes mellitus
Urine Osm	↑	↓	↓	↕	↑↑
Plasma Osm	↓	↑	↑	↓	-
Serum Na	↓ <i>euvolemic</i>	↑	↑	N	-
Uric acid	↓	↑	↓	-	-
Diagnosis	Water loading test: <u>ADH high</u> (N) - ↓	Water deprivation test: test: <u>Osm low</u>	Water deprivation test: test: <u>Osm low</u>	Water deprivation test: test: <u>Osm >600 mosm/kg</u>	-
Management	<i>Fluid restrictⁿ</i> ↳ $V_2 \ominus$ <u>vaptan</u>	<u>Desmopressin</u>	<u>Thiazides</u>	-	-

Euvolemic ↓ Na ← SIADH
 ↳ *vaptan*
 ↳ *Hypothyroidism*
 ↳ *nocturnal enuresis*

NDI Causes

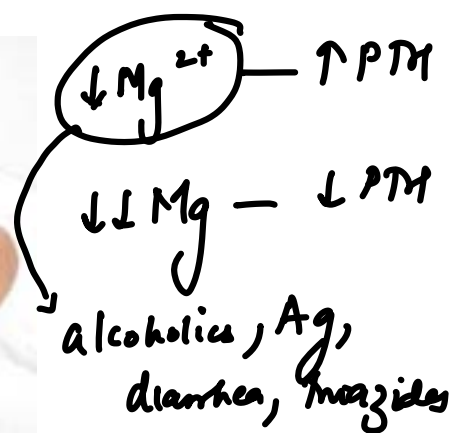
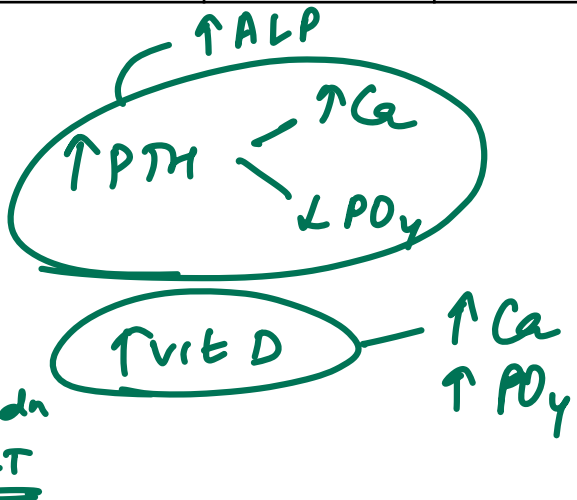
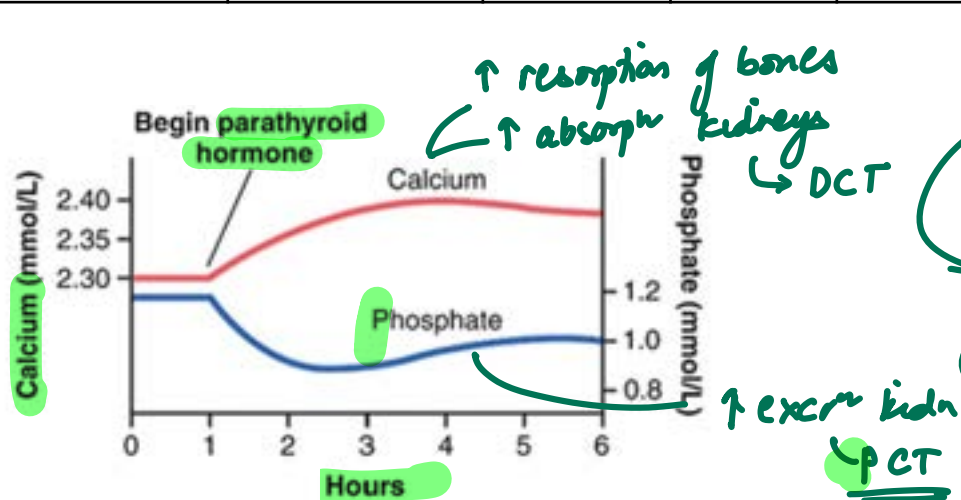
- Li → *A₁: amiloride*
- Demeclocycline*
- $\uparrow Ca^{2+}$ / $\downarrow K^+$

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

Calcium metabolism

AD: GNAS mutation
 maleins
 AD paternal

	Rickets Osteomalacia	1 HPT PTM Adenoma	2 HPT Id DM ⊖	Hypercalcemia of malignancy sq cc PTHrp	Sarcoidosis Id DM ⊕ granulom	Hypo PTH	Pseudo-hypoPTH type IA	Pseudo-pseudo-hypoPTH	Paget's	Osteoporosis <u>BMD ↓</u>
Calcium 8.5-10.5 mg/dl	↓	↑	↓	↑	↑	↓	↓	Ⓝ	-	Ⓝ
Phosphate 2.5-5 mg/dl	↓	↓	↑ ^{cor}	↓	↑	↑	↑	Ⓝ	-	Ⓝ
PTH	↑	↑↑	↑	↓	↓	↓	↑	Ⓝ	-	Ⓝ
ALP	↑	↑	↑	↑	Ⓝ	Ⓝ	Ⓝ	Ⓝ	↑	Ⓝ





acidosis ($\uparrow \text{H}^+$) \rightarrow \uparrow free Ca^{2+}

alkalosis ($\downarrow \text{H}^+$) \rightarrow \downarrow free Ca^{2+}

Osteoporosis treatment ^{qq}

Inhibit Osteoclasts

BISPHOSPHONATES: Farnesyl pyrophosphate synthase -

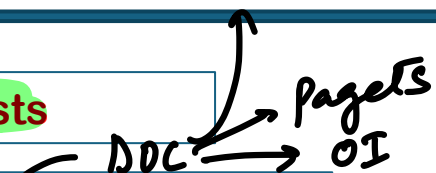
Adverse effect-

1. esophagitis
2. osteonecrosis jaw ^{qq}
3. atypical femur #

Longest acting- Zoledronate

s/e: renal failure

Alendronate/Risedronate: ORAL



Stimulate Osteoblasts

PTH 1-34

Teriparatide

Abaloparatide ^{qq}

Max: 2yrs ~~qq~~ R/o osteosarcoma



Dual Action

Romosozumab ^{qq}

Sclerostin ⊖

Strontium

SERM : Raloxifene s/e: DVT

Denosumab RANK ligand ⊖

Calcitonin: Intranasal

s/e: liver toxicity
Ca breast

Cinacalcet-CasR agonist
Used in HyperPTH



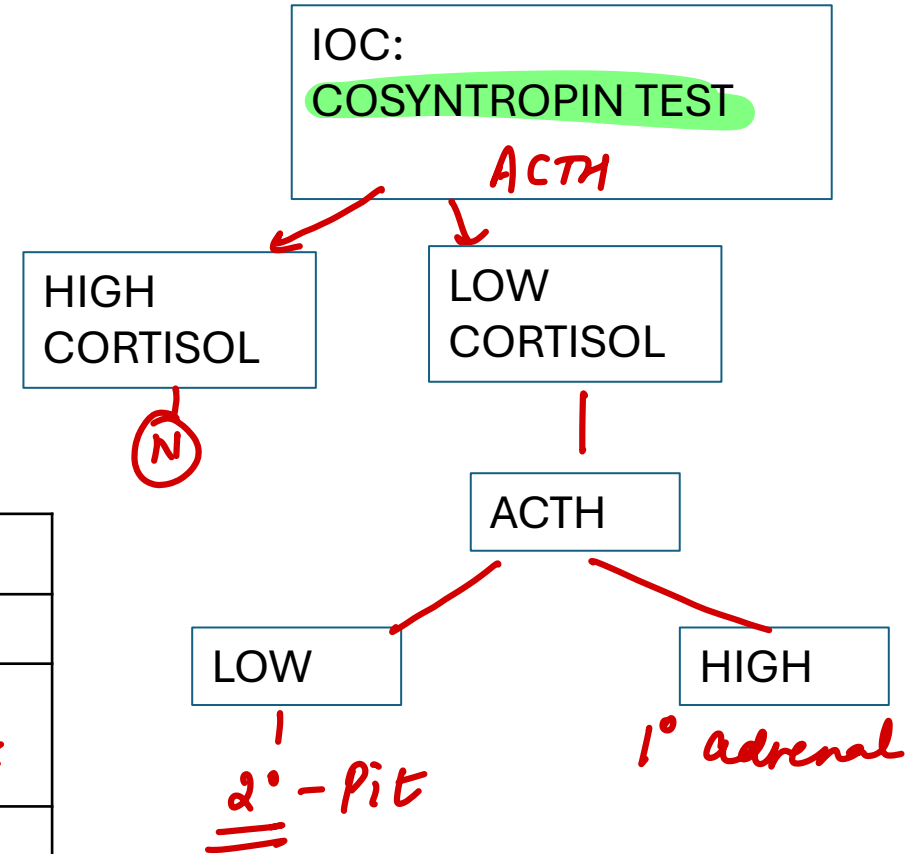
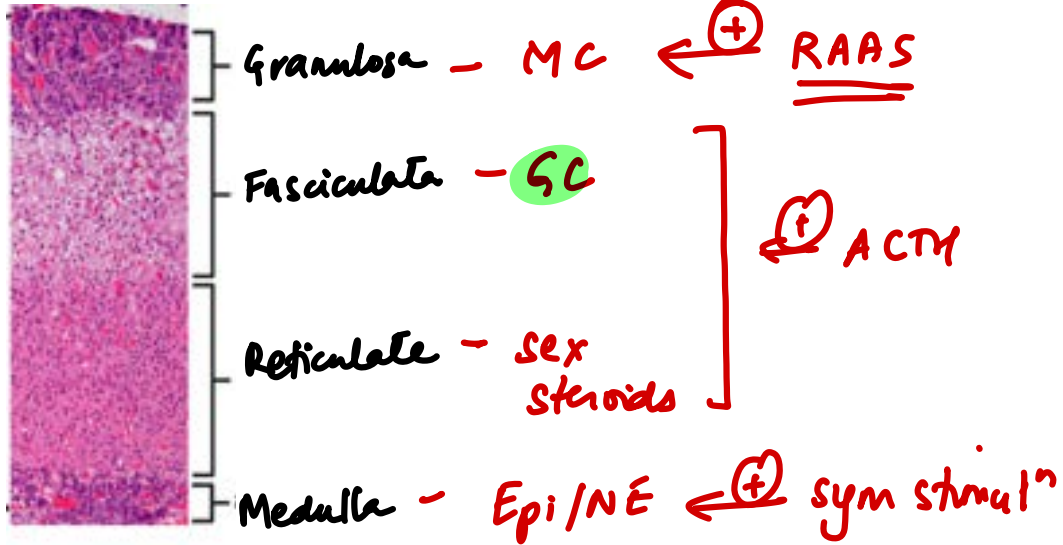
osteonecrosis Actinomyces
mandible → Sinuses

Phossy
jaw

Bisphosphonates

RT

ADRENAL INSUFFICIENCY



Primary versus central adrenal insufficiency

	Primary	Secondary
Most common cause	Autoimmune/ Granulomatous \leftarrow TB Histo	Chronic glucocorticoid therapy / Pit x
Cortisol	\downarrow	\downarrow (circled)
ACTH	\uparrow (circled)	\downarrow (circled)
Aldosterone	\downarrow	\downarrow (circled N)
Clinical features	<ul style="list-style-type: none"> Severe symptoms Hyperpigmentation Hyperkalemia \downarrow Na⁺ <p>Salt craving</p>	<ul style="list-style-type: none"> Less severe No hyperpigmentation No hyperkalemia

Pheochromocytoma

Headache / Sweating / Palpitation

MC symptom- *Headache*

MC sign- *Hypertension*

Initial Ix- *Urinary metanephrines / VMA*

Confirm Ix- *Plasma metanephrines*

Best to localize- *MRI abdomen*

Biopsy/ FNAC- *NO*

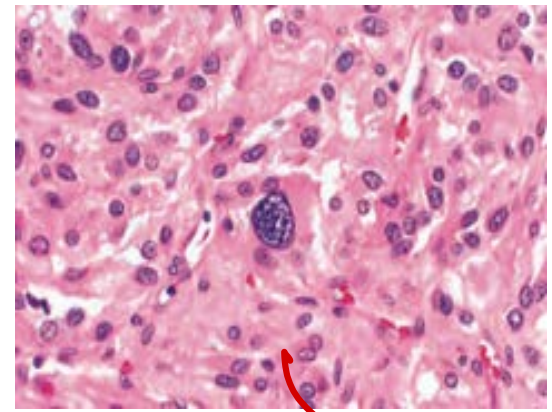
Best for mets- *MIBG scan*

Best for extraadrenal pheo- *Tc 99m - DOPA PET*

MC site for extraadrenal pheo- *Organs of Zuckerkanndl*

Treatment: *α blocker → β blocker*

Ⓢ



Light bulb sign
T2 ↑↑

Hemangioma
Zellballen appear

Rule of 10 :

- Extradrenal
- No hypertension
- Children
- B/L But 50% in *syndromic*
- Malignant But 40% in *familial*
- Familial

MEN 2a, 2b
UHL
NF 1
SDH

257.