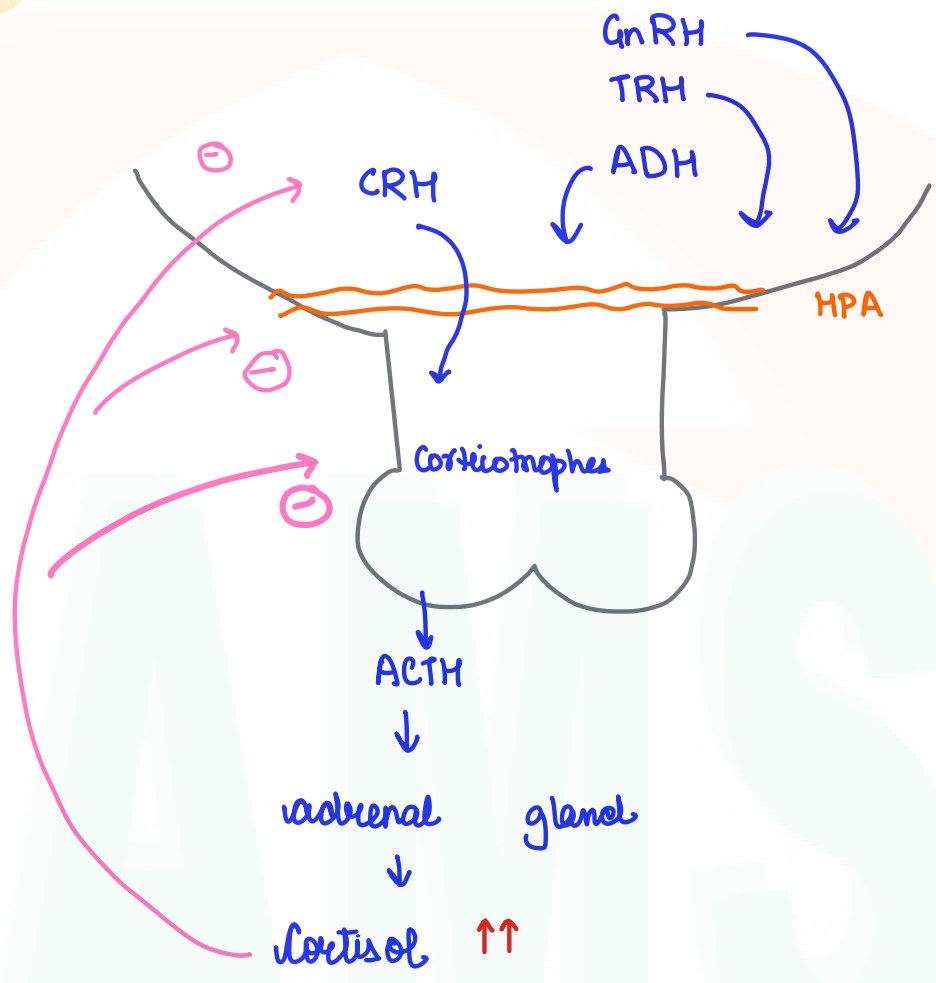
# ACTH

→ Adrenocorticotrophic hormone.

∴ normal secretion




∴ normal actions -

→ ↑ses lipolysis of peripheral fat

→ depos$^{n}$ of fat centrally

→ ↑ses routine catabolism

→ ↑ ses gluconeogenesis

→ ↑ ses anti- Inflamm. response

→ ↑ ses hunger.

→ stimulates adrenaline synthesis.

# ACTH - deficiency

∴ Causes -

Suppression of HPA.

m/c cause - abrupt withdrawl of steroids.

∴ C/F -

Hypoglycemia
wt. loss (↓se hunger)

∴ $I_x$ -

↓ ACTH
↓ Cortisol

∴ $M_x$ -

Glucocorticoid Replacement
- → Hydrocortisone
- → Prednisone

c/o Rheumatoid arthritis
↓
steroid (60 mg)
↓
Pt. won't Experience any Symptom during Therapy.

60 → 50 → 40 → 30

gradual ↓se
↓
active axis

Abrupt ↓se

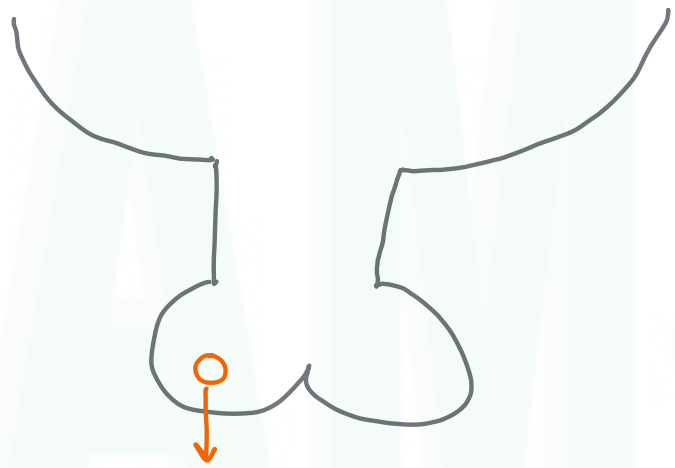
axis will remain Inactive

## CUSHING's SYNDROME

→ CF due to chronic exposure to any Etiology.
excess gluco-corticoids of

## CUSHING's DISEASE

→ Cushing's syndrome because of Pituitary adenoma.



ACTH
↓
adrenal gland ⟶ Cortisol .

∴ Causes →

- Iatrogenic Cushing's
  - Drugs (steroids)
- Ectopic ACTH prod$^{n}$
  - Small cell Ca. of lung.
  - medullary Ca. of Thy.
  - Pancreatic Ca.
  - Pheochromocytoma.

# Causes of Cushing's Syndrome

## ACTH - dependent (90%)
(ACTH ↑ Cortisol ↑)

- Cushing's vole.
- Ectopic ACTH

## ACTH - Independent (10%)
(ACTH ↓ Cortisol ↓)

- adreno - Cortical adenoma / Carcinoma

C|F →

Face - Acne
Hirsutism
Rounded face (moon)

Cortisol (+) → Oil - secretory glands
ACTH (+) → Androgen produc°

Neck - Buffalo hump (Cortisol → lipolysis of p/ fat)

Skin - thin & brittle
purple striae
Easy bruising

Rapid depos° of ↓ fat below skin
stretching of skin
Injury to epithelium → healing

Bone - Osteoporosis

Cortisol (−) → Int. $Ca^{2+}$ absop°
Cortisol (−) → Osteoblasts
Cortisol (+) → Osteoclasts
Cortisol (+) → Renal $Ca^{2+}$ excr°.

Diabetes - ↑se gluconeogenesis

↓se Immunity - Infections

Hyperpigmentation - ACTH (+) → melanocytes

CVS - Hypertension
Hypokalaemia

Excess of Cortisol
↓ ⊕
mineralo - Corticoid ®

absorp$^{n}$ of
$Na^{+}$ & $H_2O$
↓
↑ Intra - vasc. - volume
↓
HT$^{n}$

excr$^{n}$ of
$K^{+}$
↓
Hypokalaemia

Repro - ↓ Sex libido
amenorrhoea

Cortisol
↓ ⊖
GnRH

## ∴ Management -

### Protocol for suspected Cushing's Syndrome

- Symptoms +
- rule out Iatrogenic Pts.
- Investigations to prove Cortisol - ↑sec.

1st Inv. → 24 hour urinary free Cortisol > 3N
2nd → mid - night Plasma Cortisol > 130 nmol/L
3rd → mid - night Salivary Cortisol > 5 nmol/L
4th → Dexamethasone Overnight test
1mg of dexamethasone at 11 pm (night)
↓

↳ These Invn done by MRI bcz. the structure can be

non - secreting too.



Plasma cortisol at 8 am to 9 am (morn.)

↓

> 50 nmol / L ⊕

If further confirmation needed ;

low dose DEX. Test

0.5 mg of dexamethasone 6 hrly for 2 days

Plasma cortisol > 50 nmol/L

+ → Cushing's → measure ACTH levels

↑ Seal

1) MRI - Brain
2) CRH - Test

Inj. CRH 100 mg (i.v)

- ACTH ↑ses > 40 %. at 15 - 30 mins
- Cortisol ↑ses > 20 %. at 45 - 60 mins

Case - Cushing's ds.

↓ Seal → CT - Abdomen

Bi - micro nodular or macro nodular adrenal hyperplasia → B/L Adrenelectomy

U/L adrenal mass → U/L Adrenelectomy

3) High dose Dexamethasone Test

Cortical suppres^n > 50 %.

⊕ Cushing's ds.

⊖ Ectopic ACTH producing tumor.

Mx: Trans - Sphenoidal
Surgical - resection

CT- Abdomen
CT- chest
↓
Surgical resection

Equivocal results = Inferior - Petrosal - sinus sampling
+
Peripheral vein sampling

$\frac{\text{Petrosal ACTH}}{\text{Perip. ACTH}}$ > 2 at baseline

or

Ratio > 3 at 2 to 5 mins after Inj. of CRH 100 mcg i.v.

⊕ Cushing's dz.

⊖ Ectopic tumor.

Note :- proliferations in pit. & Adrenal can be non-Secreting too ; so Cortisol level Ix - necessary.

(> stronger)

| Cushing's dz. | Ectopic ACTH secretion |
|---|---|
| Sex - ♀ > ♂ | ♂ > ♀ |
| C/F - Slow onset | Rapid onset<br>Pigmentation<br>Severe myopathy |
| Sr. $K^+$ < 3.3 mcg/L < 10 %. | 75%. |
| High dose dexamethasone test - Sr. Cortisol ∨ 5 mcg/dl | Serum Cortisol ∨ 5 mcg/dl |

∴ Drugs -

Metyrapone

Ketoconazole

**TABLE 403-8 DIFFERENTIAL DIAGNOSIS OF ACTH-DEPENDENT CUSHING'S SYNDROME[a]**

| | ACTH-Secreting Pituitary Tumor | Ectopic ACTH Secretion |
|---|---|---|
| Etiology | Pituitary corticotrope adenoma<br>Plurihormonal adenoma | Bronchial, abdominal carcinoid<br>Small cell lung cancer<br>Thymoma |
| Sex | F > M | M > F |
| Clinical features | Slow onset | Rapid onset<br>Pigmentation<br>Severe myopathy |
| Serum potassium <3.3μg/L | <10% | 75% |
| 24-h urinary free cortisol (UFC) | High | High |
| Basal ACTH level | Inappropriately high | Very high |
| Dexamethasone suppression | | |
| 1 mg overnight | | |
| Low-dose (0.5 mg q6h) | Cortisol >5 μg/dL | Cortisol >5 μg/dL |
| High-dose (2 mg q6h) | Cortisol <5 μg/dL | Cortisol >5 μg/dL |
| UFC >80% suppressed | Microadenomas: 90%<br>Macroadenomas: 50% | 10% |
| Inferior petrosal sinus sampling (IPSS) | | |
| Basal | | |
| IPSS: peripheral | >2 | <2 |
| CRH-induced | | |
| IPSS: peripheral | >3 | <3 |

[a]ACTH-independent causes of Cushing's syndrome are diagnosed by suppressed ACTH