

## SUMMARY

Adrenocorticotropin Hormone (ACTH):

a polypeptide secreted in a pulsatile fashion from the anterior pituitary with Diurnal Variability. Part of pro-hormone ( Pro - opiomelanocrticotropin POMC ) which contains alpha, beta and gamma Melanocytes- Stimulating hormones, beta- endorphins and beta-lipotropins as well as ACTH.

Secretion of ACTH regulated by corticotropin - releasing Hormone (CRH) and arginine vsopressin.

Stimulates growth of adrenal cortex and secretion of its hormones via cAMP.

Stimulates release of glucocorticoids, androgens and to a limited extent, mineralocotriciods  
some melanocyte stimulating activity.

- Cortisol:

### Physiological Effects of Glucocorticoids:

Stimulatory effect	Inhibitory effect
Stimulate hepatic glucose production ( gluconeogenesis )	Inhibit bone Formation, stimulates bone resorptions
Increase insulin resistance in peripheral tissue	inhibits fibroblasts, causing collagen and connective tissue loss
Increase Protein Metabolism	Suppress Inflammation, impair cell mediated immunity
Stimulates leukocytes and lymphopenia	Inhibit growth hormones xis
Increase cardiac output, vascular tone + Na retention	Inhibit reproductive axis
increase PTH, urine calcium excretion	inhibit Vitamine D3 and calcium uptake

### Tests of adrenocortical Function:

Plasma Cortisol	Diurnal Variation ( Random level less useful ) Response to stimulation or suppression
25 hour urinary free cortisol	correlates well with secretory rates Good screening test for adrenal hyperfunction
Serum Morning ACTH	High in Primary Adrenal Insufficiency Low in secretory adrenal insufficiency
Serum DHEA-S	The main adrenal androgen

### Dexamethasone (DXM) Suppression Test:

- Gold standard to determine presence and etiology of Hypercortisolism.

- Principle: DXM suppresses pituitary ACTH, so plasma cortisol should be lowered by negative feedback if HPA axis were normal.

- single dose DST: screening test

- 1- DXM 1 mg given at 23:00 would suppress pituitary ACTH production in healthy individuals, so that the normal 08:00 peak of plasma cortisol would fail to develop.

- 2- 95% of Cushing's syndrome patients would fail to suppress

- 3- <20% false positive results due to obesity, depression, alcohol, other medications

- Confirmatory Tests:

- 1- Low Dose DST : 0.5 mg of DXM for 48 hr, then urinary free cortisol (UFC)

- Normally, UFC level would be reduced to <54 nmol/day

- 2- High Dose DST ( 8 mg/day ): 70-80%

- suppressed UFC: adrenal cortex hyperplasia due to hypersecretion of Pituitary ACTH.

- No change in UFC or serum cortisol: adrenal cortisol- producing adenoma/ carcinoma.

- however, 30-40% of ectopic ACTH tumors may partially suppress UFC

- Plasma ACTH assay supplements DST for differential of the various etiologies of Cushing's.

Done ..