بسم الله الرحمن الرحيم

Adrenal Gland Disorders
Adrenocortical insuffuciency

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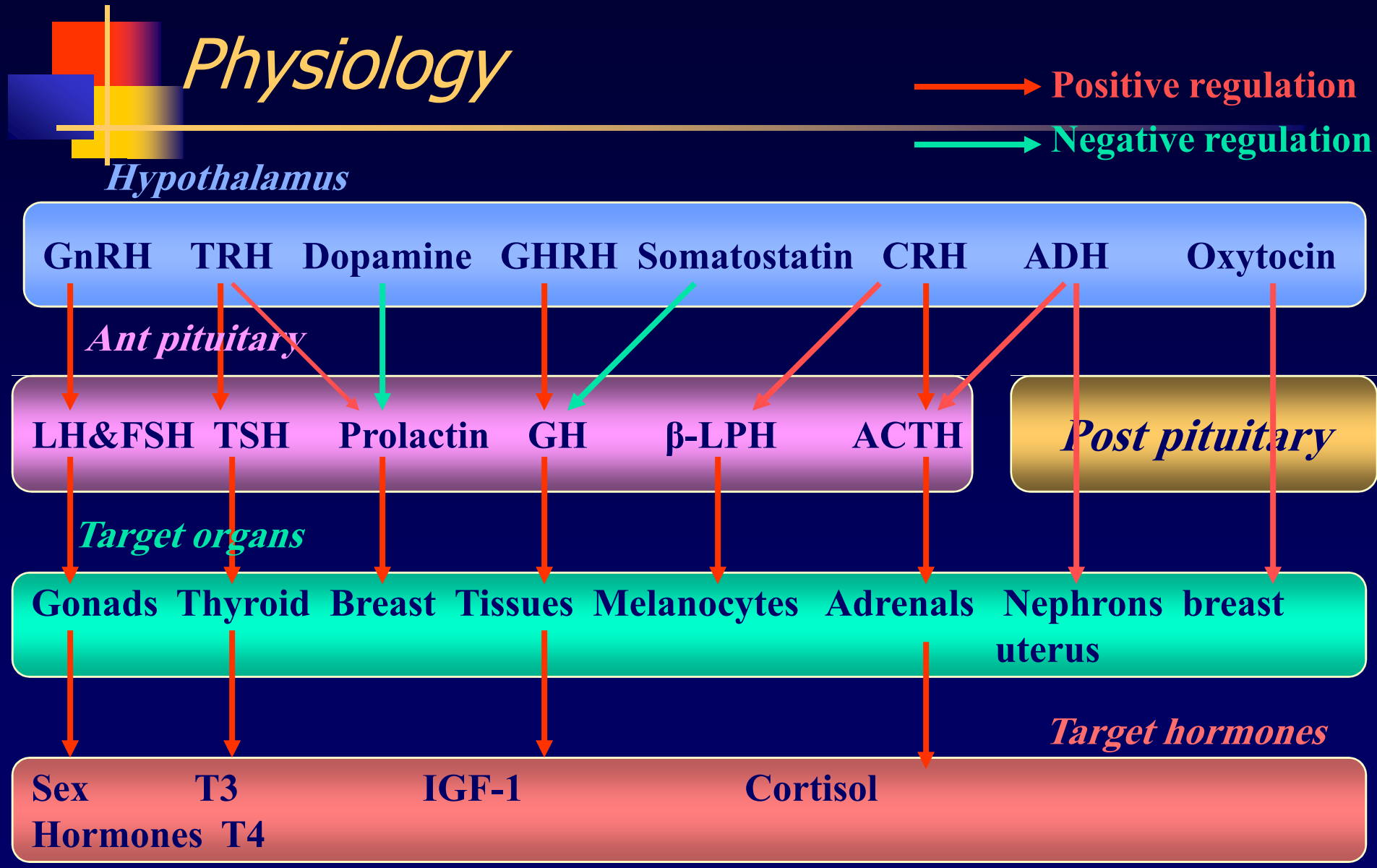
Physiology


Positive regulation
Negative regulation
Hypothalamus
GnRH TRH Dopamine GHRH Somatostatin CRH ADH Oxytocin
Ant pituitary
LH&FSH TSH Prolactin GH β-LPH ACTH
Post pituitary
Target organs
Gonads Thyroid Breast Tissues Melanocytes Adrenals Nephrons breast uterus
Target hormones
Sex Hormones T3 T4 IGF-1 Cortisol

Functional Anatomy and Physiology

- *Adrenal cortex*

1. Zona glomerulosa → Aldosterone
2. Zona fasciculata } → Cortisol
3. Zona reticularis } → Adrenal androgens

- *Adrenal Medulla*

Component of the sympathetic nervous system
→ Catecholamines.

Functional Anatomy and Physiology

- *Glucocorticoids*
- Major one in human is cortisol.
- Diurnal pattern of secretion via ACTH stimulation.
- Rise dramatically during stress.
- 95% bound to cortisol-binding globulin.
- Has a minimal mineralocorticoid activity.
- *Principal functions:*

1. Regulation of carbohydrate metabolism.
2. Increase protein catabolism.
3. Immunomodulation.
4. CV regulation.

Functional Anatomy and Physiology

- *Mineralocorticoids*

- Major one is Aldosterone.
- It is the most important sodium-retaining hormone.
- The principle stimulus is Angiotensin-II (renin-angiotensin system).
- *Principal functions:*

1. Sodium retention.
2. Patassium excretion.

Functional Anatomy and Physiology

- *Catecholamines*
- Small proportion of circulating noradrenaline is secreted from adrenal medulla, much more is released from the nerve endings.
- Conversion of noradrenaline to adrenaline is induced by glucocorticoids.
- *Principal functions:*

1. Increase heart rate.
2. Regulation of vascular tone.
3. Antagonise insulin action.

Actions of glucocorticoids:

Increase:

- Gluconeogenesis
- Protein catabolism
- Sodium retention
- Potassium loss
- Circulating neutrophils

Decrease:

- Protein synthesis
- Host response to infections
- Circulating lymphocytes
- Circulating esinophils

Glucocorticoid excess; Cushing's syndrome

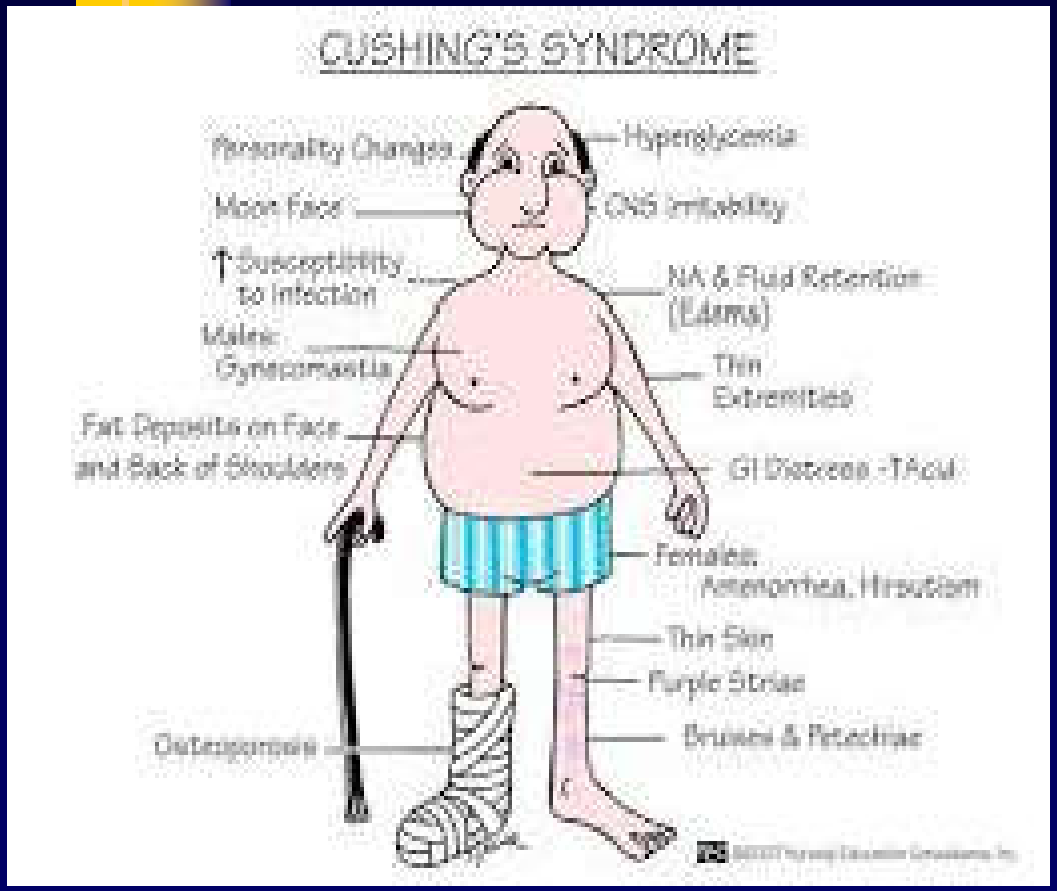
Etiological classification

1. ACTH dependent:
- Pituitary- dependent (Cushing's disease).
- Ectopic ACTH secretion.
- Iatrogenic.
2. Non-ACTH-dependent:
- Adrenal hyperplasia, adenoma or carcinoma.
- Glucocorticoid administration
2. Others
- Alcohol-induced pseudo-Cushing's syndrome

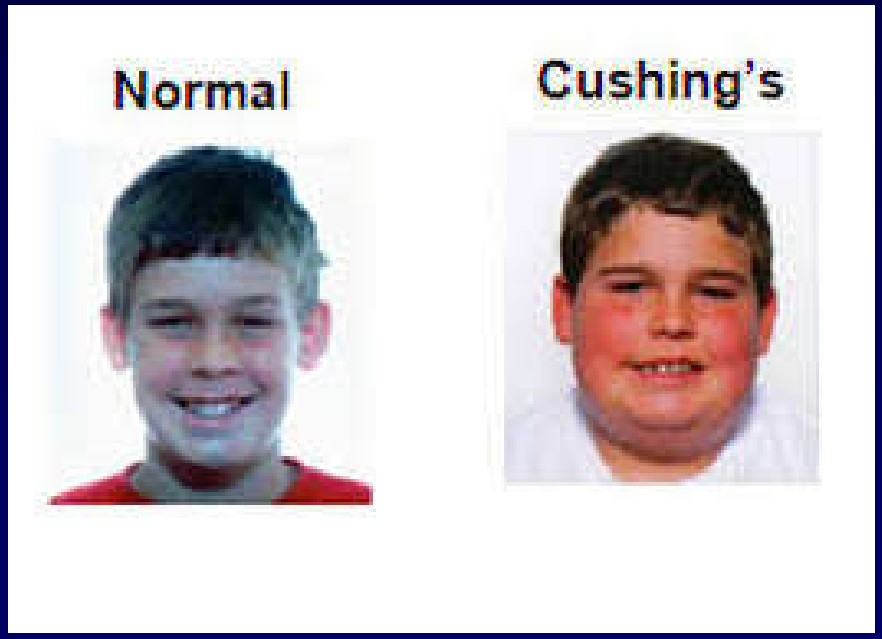
Cushing's syndrome
Clinical features

1. Weight gain (central obesity), moon face, dorsal fat pad.
2. Plethora, acne, Hirsutism, scalp hair-thinning, frontal balding.
3. Depression/ psychosis, insomnia.
4. Skin; thin skin, infections, easy bruising, striae, pigmentations, poor wound healing.
5. Musculoskeletal; back pain, osteoporosis, kyphosis, muscular weakness, proximal muscle wasting, pathological fractures.
6. Menstrual irregularities, decreased libido.
7. Hyperglycemia, hypertension.

Central obesity and dorsal fat pad



Moon face



Striae

Figure 1. Typical striae as seen in a case of Cushing's Syndrome

Acne and Hirsutism

Cushing's syndrome; Clinical features

1. Pigmentation occurs only with ACTH – dependent causes.
2. Pseudo-cushing; cushignoid appearance can occur with excess alcohol consumption.
3. Impaired glucose tolerance and hypokalemia are more common with ectopic ACTH secretion.

Cushing's syndrome Investigations:

- *Investigations to confirm the diagnosis:*

1. 24-h urinary cortisol level.
2. Diurnal rhythm of plasma cortisol.
3. Low dose Dexamethasone suppression tests; (0.5 mg/6h for 48 h). Normal response: plasma cortisol less than 50nmol/L by the end of the test.

Cushing's syndrome Investigations

- *Investigations for the cause:*

1. Adrenal CT or MRI
2. Chest x-ray
3. High-dose dexamethasone-suppression test; 2mg/6h for 2 days; in pituitary dependent disease; plasma cortisol on day 2 is less than 50% that on day 0, failure of suppression suggests ectopic source or adrenal tumor.
4. Plasma ACTH level
5. CRH test; 100μg iv. And monitor ACTH and plasma cortisol.

Cushing's syndrome Treatment

- *Medical treatment*

1. Metayrapone; 11-B hydroxylase blocker. Given in doses of 750-4 g daily in 3-4 divided doses.
2. Ketoconazole (200mg 3times/day); synergestic to metyrapone to reduce its dose.
3. Aminoglutethimide and trilostan; inhibit several side-chain enzymes
4. Treatment of Hypertension and diabetes

- *Treatment of the cause*

Adrenocortical insuffuciency

- Addison's disease;

- Rare disease in which there is destruction of the entire adrenal cortex, thus, glucocorticoids, mineralocorticoids and sex steroids all are reduced. It differs from pituitary disease where mineralocorticoids remains largely intact.
- Increased CRH and ACTH production are responsible for the hyperpigmentation.

Incidence:

- It is rare disease
- Incidence 3-4/million/year
- Female predominance (F:M 2:1)
- Common in 30-50 years
- 90% in UK is autoimmune disease
- Previously most common cause was TB

Causes of adrenocortical insuffuciency

1. Primary (increased ACTH)
   - Autoimmune (sporadic or polyglandular syndrome).
   - TB.
   - Other infections; fungal (Most of systemic fungal infections can involve and destroy the adrenal cortex), CMV, AIDS.
   - Meningococcal septicemia
   - Surgical removal
   - Rare; metastatic carcinoma , adrenal heamorrhage or infarction,
   - Infiltrative: amyloidosis, heamochromatosis.
   - Drugs: Ketoconazole, metyrapone
2. Secondary (decreased ACTH)

Addison's disease; clinical features

1. *Chronic presentation*

- Symptoms :
- Non-specific; malaise, fatigue, anorexia, nausea, vomiting, weakness
- Weight loss
- Myalgia and may be flaccid muscle paralysis due to hyperkalemia
- Impotence
- Amenorrhoea

Clinical features

Signs:

- Hypotension present in about 90% of cases (dizziness)
- Hypoglycemia.
- Hyperpigmentation (is one of the earliest manifestations of Addison disease, it is increased in sun-exposed areas and accentuated over pressure areas such as toes, elbows, and knees.
- Buccal pigmentation, increased pigmentation of the palmar creases, nail beds, nipples, areolae.
- Decrease in body hairs.
- Dehydration

Addison's disease; Investigations

- *Assessment of glucocorticoids*

1. Random cortisol level is of little value (but level less than 100 nmol/L is highly suggestive.
2. Primary or secondary failure?

- ACTH measurement.

1. - Short ACTH stimulation test; 250µg synacthen im., S. cortisol measurement at 0, 30 min. normal response > 550 nmol/L.
2. - Long ACTH stimulation test; is no longer used.

Addison's disease; Investigations

1. In primary failure; hyponatremia, hyperkalemia.
2. In secondary failure; aldosterone secretion is intact.
3. Blood glucose may be low
4. CBC
5. Adrenal antibodies are present in autoimmune disease
6. Chest and abdominal x rays : TB or calcified adrenals
7. High plasma renin

Addison's disease; management

- Glucocorticoid replacement with hydrocortisone (20-30 mg/day) or prednisolone (7.5 mg /day)or rarely dexamethane (0.75 mg/day)
- Be careful about:

- diurnal variation.
- increase the dose during stressful conditions.
- adjust the dose by:

1-Clinical well being

2 - Restoration of serum electrolytes.

3- Blood pressure response to posture

Addison's disease; management

- *Mineralocorticoid replacement*

1. Aldosterone is not available, fluodrocortisone is used 0.5-1 mg daily.
2. Adequecy of replacement is assessed by measurement of s. electrolytes, blood pressure and plasma renin activity.

2-Acute presentation (acute adrenal crisis)

- Severe hypotension.
- Hyponatremia, hyperkalemia. hypoglycemia, and dehydration.
- Anorexia, nausea and vomiting increase and worsen the volume depletion and dehydration.
- Hypovolemic shock frequently occurs, and adrenal insufficiency should be considered in any patient with unexplained vascular collapse.

Cinical features

- Abdominal pain may occur and mimic an acute abdominal emergency.
- Weakness, apathy, and confusion are common.
- Fever is also common and may be due to infection.
- Additional findings that suggest the diagnosis are lymphocytosis, and eosinophilia.

Causes

- occurs in patients with Addison disease who are exposed to the stress of:

1. infection,
2. trauma,
3. surgery,
4. or dehydration due to salt deprivation, vomiting, or diarrhea.

Management of acute crisis:

- Assessing of CVP(central venous pressure).
- Saline 0.9%
- Treatment of hypoglycemia
- I.V. bolus of 100 mg hydrocortisone then 100 mg IM/6 hs until the patient is clinically stable then replacement with oral medications.
- Fludrocortisone should be introduced later
- Treatment of infection if present and other precipitating factors.

Hyperaldosteronism

Hyperaldosteronism

- *Primary hyperaldosteronism*

Causes

1. Adrenal adenoma (Conn's syndrome); 60%
   often very small, occur in young females.
2. Bilateral adrenal hyperplasia;
   more common in males, rare before 40ys.

Secondary Hyperaldosteronism

- Causes

1. Accelerated hypertension
2. Renal artery stenosis.
3. Heart failure.
4. Liver cirrhosis

Primary Hyperaldosteronism

- *Clinical features*

1. Hypertension ; almost invariable but it is a rare cause of secondary hypertension (<1%).
2. Hypernatremia and increased potassium excretion. Hypokalemia ⟶ muscle weakness, polyuria, secondary to tubular damage (nephrogenic diabetes insipidus).
3. Peripheral edema may occur.

Primary Hyperaldosteronism

- Investigations

1. Hypokalemia, increased urinary potassium excretion. (diuretic therapy should be stopped).
2. Increased plasm aldosterone/ renin ratio.
3. High plasma aldosterone not suppressed by 0.9% saline infusion or fluodrocortisone injection.
4. Investigation for the cause; adrenal CT or MRI, venous catheterization of the adrenal glands for aldosterone level.

Primary Hyperaldosteronism

- *Treatment*

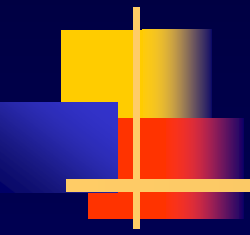
1. Adenoma; surgical removal.
2. Aldosterone antagonist; spironolactone 100-400 mg/day. Side effects; skin rash, nausea, gynecomastia.
3. Aldosterone receptor antagonist eplerenone can be use if there is side effects of spironolactone.

Inications of glucocorticoids:

- Cardiac: rheumatic fever, Post-myocardial infarction syndrome
- Respiratory: asthma- sarcoidosis-Chronic obstructive pulmonary disease -ARDS
- Blood disorders: hemolytic anemias- hematological malignancy
- Renal: nephrotic syndrome- some GN
- GIT: UC- Chrons disease- autoimmune hepatitis
- Rheumatology: SLE- vasulitis- RA
- Neurological disease: Cerebral oedema
- Skin: eczema
- After organ transplantation

Side effects of glucocorticoids:

- Adrenal and pituitary suppression
- CVS: increase blood pressure
- GIT: pancreatitis
- CNS: depression- psychosis- insomnia
- Endocrine: weight gain- hyperglycemia- amenorrhoea
- Bone and muscle: osteoporosis-proximal myopathy-pathological fractures
- Skin: thinning and easy bruising
- Eye: cataract
- Increase susceptibility to infections



Thank you