Adrenal Cortical Hormones
Part 2
(Glucocorticoids)

Objective:

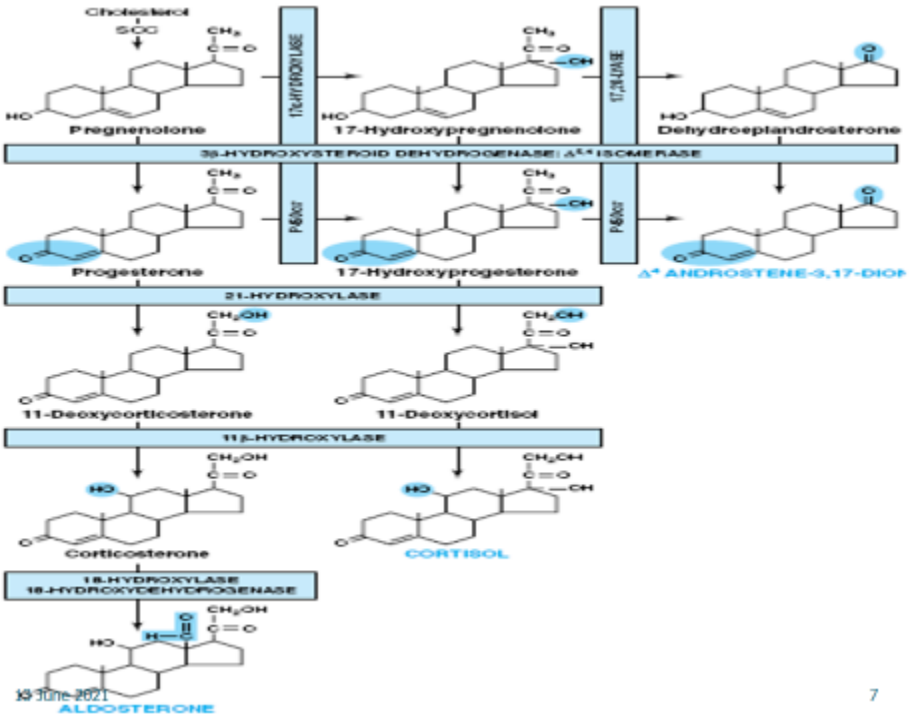
To illustrate the effects of glucocorticoids and the disorders of their secretion.

Glucocorticoids

Clucocorticoids secretion is controlled by ACTH. They are C21 steroids.

Cortisol is the predominant glucocorticoid in humans and is made mainly in ZF.

Corticosterone is less abundant in humans.



Granner DK. Diversity of the endocrine system. In: Murray RK, Granner DK, Mayes PA, Rodwell VW,eds. Harpers's Illustrated Biochemistry. 26th edn, New York: Lange Medical Books/McGraw-Hill; 2003: 434-455.

Effects of Glucocorticoids:

A: On Carbohydrate metabolism :-

1. Increases glucose production via gluconeogenesis.

2. **Increases hepatic glucose deposition by increasing glycogen synthetase activity.**

B: On Lipid metabolism :-

Promotes lipolysis (in extremities), but causes lipogenesis in the face and trunk especially at higher than physiological levels.

C: On Protein metabolism :-

They are anabolic at physiological levels, but can be catabolic at higher levels.

D: On host mechanisms: :-

1. Suppress the immune response.

2. Suppress the inflammatory response.

E: Other effects:-

1. Necessary for maintenance of normal blood pressure and cardiac output.

2. Required for maintenance of normal water and electrolyte balance.

3. Necessary, with hormones of adrenal medulla, in allowing the individual to respond to stress.

Pathophysiology

A:- Glucocorticoids insufficiency (Under production of glucocorticoids)

Types of adrenocortical insufficiency:

1. **Primary (Addison's disease) "↑ ACTH":-**
   Due to primary adrenocortical failure. There is both Cortisol and Aldosterone deficiency.
   It is characterized by postural hypotension, hyponatraemia, hyperkalaemia, and hyperpigmentation.

2. **Secondary " ↓ ACTH" :-**

   Due to hypothalamic or pituitary disease, or most commonly due to withdrawal of suppressive glucocorticoid therapy.

   Hypotension is less marked. There is no pigmentation.

Investigations of adrenocortical insufficiency:

1. **Electrolytes: Hyponatraemia and hyperkalaemia.**
2. **Serum Cortisol and ACTH.**
3. **Stimulation tests:**
   A. **Short synacthen test (ACTH stimulation test).**
   B. **Long (Depot) synacthen test.**

B:- Glucocorticoids Excess (Overproduction of glucocorticoids):

Causes a syndrome called Cushing's Syndrome

Types of Cushing's syndrome:-

A. ACTH – dependent:-

1. **Pituitary adenoma secreting ACTH " Cushing's disease"**
2. **Ectopic ACTH secretion.**
3. **Iatrogenic " ACTH therapy"**

B. Non –ACTH - dependent:-

1. **Iatrogenic " Glucocorticoid therapy"**
2. **Adrenal tumour secreting glucocorticoids**

C. Pseudo – Cushing's syndrome:-

Cortisol excess as part of another illnesses like: alcohol excess , obesity or major depressive illness.

The metabolic manifestations in Cushing's syndrome:-

1. **Negative nitrogen, K^+ and P^- balance**
2. **Na^+ retention which cause hypertension , oedema or both .**
3. **Glucose intolerance or Diabetes mellitus**
4. **↑ plasma fatty acids.**

Diagnosis of Cushing's Syndrome

A. Screening of Cushing's Syndrome:-

1. **24 hr urinary cortisol**
2. **Overnight dexamethasone suppression test**

B. Confirmation of diagnosis of Cushing's Syndrome:-

Low dose dexamethasone suppression test

C. Determining the cause of Cushing's Syndrome :-

High dose dexamethasone suppression test with inferior petrosal sampling to measure central: peripheral ACTH ratio.