**Adrenal Hormone**

1. **Adrenal gland**
   - Cortex: 80%
   - Medulla: 20%

2. **Adrenal cortex hormones**
   - Glucocorticoid
   - Mineralocorticoids
   - Sex hormones

3. **Adrenal medulla**
   - Norepinephrine ≈ 20%
   - Epinephrine ≈ 80%

4. **Adrenal steroids biosynthesis**

5. **Adrenal-pituitary feedback regulation**
   - ACTH
   - Stress
   - Sleep/awake
   - CRH
   - Adrenocorticotropic hormone (ACTH)
   - Cortisol
   - DHEA
   - Anxiety
   - Depression
   - Neurotransmitters
   - FEEDING
   - ANXIETY
   - DEPRESSION
   - Neurotransmitters

- **Cholesterol**
  - Dehydroepiandrosterone (DHEA)
- **Pregnenolone**
  - 17α-Hydroxypregnenolone
- **Progesterone**
  - 17α-Hydroxyprogesterone
- **11-Deoxycorticosterone**
  - Androsterone
- **Cortisol**
  - Testosterone
  - Estrogen
- **Aldosterone**
  - Stimulation
  - DHEA
  - Cortisol
  - Inhibition
  - Aldosterone
Major Glucocorticoids actions

- **Adipose tissue**
  - Lipolytic hormones
  - FFA
- **Liver**
  - Glucose,
  - Amino acids
  - Insulin
- **Muscle**
  - Glucose,
  - Amino acids
  - Insulin

Actions

- Lipolysis
- Redistribution of fat
- Gluconeogenesis
- Glucose utilization
- Insulin sensitivity

Diabetogenic effects
- Protein breakdown

Glycogen
Glucose precursors

**Glucocorticoids actions**

- **CVS** → Vasoconstriction
- Maintain ECF volume & capillary integrity
- Free water clearance (GFR)

**Mineralocorticoid effects**
- Na+ retention/ K+ excretion
- Normal muscle contraction (skeletal & cardiac M)
- Collagen synthesis: skin, blood vessels

**Glucocorticoids actions**

- Anti-inflammation
  - PGs, TXs, LTs
  - Interleukin
- Capillary permeability
- Phagocytosis
- Anti-allergic action
- Immuno-suppressant
- T-lymphocytes
- Suppress antibody

**Glucocorticoids actions**

- Bone protein matrix/
- GI Ca2+-absorption.
- Renal Ca2+-excretion

Blood calcium
- PTH
- Bone formation
- Bone reabsorption
- Osteoporosis

**Abnormal glucocorticoids secretion**

- Glucocorticoids excess
  - Cushing's disease
  - Cushing's syndrome (drug)
- Glucocorticoids deficit
  - Addison's disease (Adrenal insufficiency)
Cushing's syndrome

- High risk infection
- Delayed wound healing
- Steroid diabetes
- Muscle wasting
- Osteoporosis
- Hyper tension
- ↑ Appetite
- Steroid psychosis

Cushing's disease

- Moon face
- Buffalo hump
- Abdominal striae

Addison's disease

- ↓ Appetite
- Hyper pigmentation or dark tanning of skin both exposed and nonexposed parts of body
- Fainting / dizziness (↓ BP)
- Salt craving
- Hypoglycemia

Mineralocorticoids (aldosterone)

- Increase the reabsorption of Na+ from the urine, sweat, saliva and the contents of gastrointestinal tract.
- Increase the reabsorption of water (↑ ECF). This is an osmotic effect directly related to increased resorption of sodium.
- Increase the renal excretion of K+.
Regulation of Mineralocorticoids secretion

Mineralocorticoids deficit
- Usually occur with glucocorticoid deficit
- Salt and water depletion
  - Postural hypotension
  - Dehydration
  - Hypovolemia
- Hyperkalemia
- Metabolic acidosis
- Primary case with increased ACTH
  - Hypovolemic shock
  - Hyperpigmentation

Adrenal medulla

Adrenal E & NE
- Marked deviation of homeostasis
- Adrenal cathecolamines ~ 10% of sympathetic activity

Sympathetic NE
- Fine regulation ➞ Neurotransmitter (local hormone)
- Intense stimulation ➞ circulation

Cathecolamine actions
- NE and E act via
  - $\alpha_1$, $\alpha_2$, $\beta_1$, $\beta_2$ Adrenergic receptors
    - (Cell-surface receptor)
- Different receptors
  - Different intracellular mechanisms
**Flight or fight response**
- Pupils dilated
- Salivation inhibited
- Increased respiration
- Bronchial passages dilated
- Increased heart rate
- Digestion inhibited
- Secretion of adrenal hormones
- Increased secretion by sweat glands
- Hair follicles raised
- Bladder sphincter relaxed

**Stress Response**
- Heart rate
- Force of contraction of the heart muscle
- Constriction of blood vessels
- Dilation of bronchioles
- Increased metabolic rate
- Lipolysis in fat cells

**Endogenous opioid peptides (EOP)**
- Pro-opiomelanocortin
  - POMC, 265 amino acids
  - alpha-MSH
  - beta-endorphin
  - Met-enkephalin
  - Leu-enkephalin
  - Dynorphins
  - Neo-endorphins

**Humans**
- MSH-like activity: ACTH & b-LPH
  - Anterior pituitary
  - Skin hypopigmentation
  - Skin hyperpigmentation

**Role of EOP**
- Opioid receptors: d, k, s, e, m
  - Neurotransmitter
  - Pain transmission
  - Substance P
  - Pain threshold
  - Anti-stress hormone
  - Moods
  - Gn/PRL, ACTH, ADH
Islet of Langerhans

- A, α: 20-30% Glucagon
- B, β: 60-80% Insulin
- D, σ: ~8% Somatostatin
- B cells
- A cells
- Parasympathetic fibers
- Sympathetic fibers
- Pancreatic polypeptide

Normal blood glucose: ~100 mg/dl (3-5 mM)
Basal plasma insulin concentration: ~10 microU/ml
**Insulin signaling**

- **a-subunit**
- **b-subunit**
- Insulin
- Insulin receptor

**Glucose transport**
**Protein synthesis**
**Lipid synthesis**
**Glycogen synthesis**
**Growth and Gene expression**

**Insulin actions**

- Muscle
- Liver
- Glycogen
- Glucose
- Glucose synthesis
- Free fatty acids
- Ketonoids
- Gluconeogenesis
- Pyruvate
- CO

**Protein**
- Amino acid uptake & protein synthesis
- Amino acid output & amino acid oxidation

**CHO**
- Glycogen synthesis
- Glycogenolysis

**Lipid**
- Triglyceride synthesis
- Lipolysis

**Factor affecting insulin secretion**

- **Glucose**
- **Amino acids**
- **GI hormones**
- **Diabetogenic H**

- **Vagus N**
- **a-Adrenergic**
- **Insulin**
- **Somatostatin**

**B cells**

**Insulin deficit ➔ Diabetes Mellitus**

- **Absolute:** Insulin dependent diabetes mellitus (IDDM)/ Type I ~ 5-10%
- **Relative:** Non insulin dependent diabetes mellitus (NIDDM)/ Type II ~ 90-95%

- Defect in insulin secretion
- Insulin resistance
- Receptor
- Postreceptor

**Diagnosis Diabetes Mellitus**

- A casual plasma glucose level (taken at any time of day) of 200 mg/dL or greater when the symptoms of diabetes are present.

- A fasting plasma glucose value of 126 mg/dL or greater.

- An OGTT value in the blood of 200 mg/dL or greater measured at the 2-hour interval.

**Signs and symptoms of diabetes mellitus**

- **Hyperglycemia ➔ Glucosuria** (Osmotic diuresis)
- **Hyperlipidemia ➔ Ketonemia**
- **Protein wasting ➔ Weight loss**
**Insulin excess**
- Overdose insulin
- Insulinoma
  - Hypoglycemia
  - Neuroglycopenia
    - Hunger
    - Dizziness
    - Coma
  - Cathelic: anxiety, sweating, tachycardia

**Glucagon**
- 29 amino acids identical to enteroglucagon
- Glucagon acts by binding to its receptor and activated G protein which cause an increase in cAMP.
- Glucagon has the effect of increasing blood glucose levels (opposite effect of insulin)

**Glucagon actions**
- CHO
- Glycogen synthesis
- Glycogenolysis
- Gluconeogenesis
- Hepatic glucose production
- Lipid
- Lipolysis

**Factor affecting glucagon secretion**
- Sympathetic activity
- Secretin
- CCK
- Amino Acids
- Insulin

**Insulin and glucagon cause the tight control of blood glucose concentration**
- Blood Glucose Concentration
- Insulin
  - Normal Range
  - Catecholamines
  - Corticosteroids
  - Growth H
Glucagon excess and deficit are rare

- Glucagon excess: cancer of alpha cells (glucagonomas)
- There is no report of glucagon deficit.

Somatostatin

- Somatotrophin-release inhibiting factor (SRIF)
- Also found in nerve terminals and other tissues.
- Somatostatin is a local inhibitor of insulin and glucagon secretion.
- Also function as a neurotransmitter/neuromodulator in the control of moter activity and cognitive functions.

Pancreatic polypeptide (PP)

- 36 amino acids
- Secretion of PP is mainly under autonomic control.
- PP is released following feeding or during hypoglycaemia
- Role of PP is still not understood.