



Introduction to Clinical Biochemical Endocrinology (LAB)

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LEVEL 3



OBJECTIVES:

- 1) Review endocrinology (Level II)
 - Definitions
 - Names of endocrine glands and the hormones they produce
 - Endocrine control---AXIS
 - Biochemical alterations related to Endocrinopathies
 - Aetiological factors



OBJECTIVES CONTINUED

2) Review of:

- Hypothalamus
- Anterior pituitary
- Thyroid gland
- Adrenal cortex



OBJECTIVES CONT.

- ▶ Ovary/Testis
- ▶ Pancreas/adrenal medullar (CHO metabolism)-



OBJECTIVES CONT.

- ▶ 3) Symptoms and signs of common endocrinopathies
- ▶ 4. Describe the biochemical investigations of the endocrinopathies
- ▶ **5. Use of endocrine lab**
- ▶ 6. Interpretation of results and differential diagnosis



OBJECTIVES CONTINUED

- 7. Role of the health provider:
 - Internal Medicine
 - Obs/Gyn
 - Paediatrics
 - Pathology
 - Surgery
 - GP
 - Dentists –referral system
- 8. Pass exams



DEFINITIONS

- ▶ **ENDOCRINOLOGY** is the study of COMMUNICATION and CONTROL within a living organism by means of CHEMICAL MESSENGERS OR HORMONES that are synthesized in whole or part by that organism in order to maintain the HOMEOSTATIC environment of the organism through metabolic processes.



DEFINITIONS and examples

- ▶ METABOLIC PROCESSES:
- ▶ **METABOLISM** is the study of biochemical control mechanisms that occur in the living organism with example such as:
 - ▶ Gene expression/reproduction
 - ▶ Biosynthetic pathways and enzymatic catalysis



DEFINITIONS and examples

- Modification, transformation and degradation of biological compounds
- Biochemical mediations of such compounds
- Means of obtaining, storing and mobilizing energy




EXAMPLES OF PHYSIOLOGICAL FUNCTIONS CONTROLLED BY HORMONES

- Muscular activity
- Respiration
- Digestion
- Haemopoiesis
- Sense organs and functions
- Thought



EXAMPLES CONT.

- Mood
- Behaviour
- Sexuality
- Gametogenesis
- Nourishment
- Parturition
- Others



PATHOLOGICAL CONDITIONS IN ENDOCRINE SYSTEM

- ▶ Emergency energy demand
- ▶ Starvation
- ▶ Infections
- ▶ Trauma
- ▶ Stress
- ▶ Others
- ▶ ENDOCRINOPATHIES/HORMONAL IMBALANCE
 - ▶ HYPOFUNCTION
 - ▶ HYPERPERFUNCTION



OVERALL FUNCTIONS OF THE ENDOCRINE SYSTEM IN MAN

- ▶ a) Maintaining the homeostatic environment of the multicellular organism in a constantly changing and threatening environment
- ▶ b) Organism can:
 - Live
 - Thrive
 - Reproduce



MODE OF ACTION OF THE HORMONES

- Coordination
- Regulation
- Interactive through e.g. neurohormones, releasing hormones, cytokines with:
 - CNS
 - Environment - neurohormones
 - Immunological reactions- cytokines
- Stimulatory
- Suppressive---FEED BACK MECHANISMS



FEATURES OF THE ENDOCRINE SYSTEM VS CNS

- ▶ 3 Distinguishing features:
 - ▶ Speed
 - ▶ Mode of conveying the message
 - ▶ Self-regulatory
- ▶ (i) SPEED is slow compared to the CNS
 - ▶ Minutes
 - ▶ Days e.g. in the menstrual cycle
 - ▶ Months e.g. gestation



FEATURES OF THE ENDOCRINE SYSTEM VS CNS

- (ii) Information is conveyed via **HORMONES** or **BIOCHEMICAL MESSENGERS**
- Circadian rhythm, diurnal rhythm release (24 hours)- cortisol
- Pulsatile release
- Cyclic - menstrual cycle
- RECEPTORS- specificity to each hormone



AXIS

(iii) Self- regulation

AXIS

- ▶ Stimulatory (+) and inhibiting (-) substances
- ▶ Feedback mechanisms with loops

▶ Hyperfuction (hyperthyroidism)

↑

Eu. (Euthyroidism)

↓

Hypofuction (hypothyroidism)

Hypothalamic-anterior pituitary-thyroidal axis (H-P-T axis)

► H :Thyrotropin Releasing Hormone (TRH)

► + -ve

► AP: Thyroid Stimulating Hormone (TSH)

► +ve -ve

► T: Thyroxine (T4)/Triiodothyronine (T3)

► -



AXIS

Interpretation of hormonal profiles

-TSH T4
T3
- a) Euthyroidism →TSH →T4 →T3
- b) 1° hypothyroidism ↑TSH ↓T4 ↓T3
- c) 2° hypothyroidism ↓TSH ↓T4 ↓T3
- d) 1° hyperthyroidism ↓TSH ↑T4 ↑T3
- e) 2° hyperthyroidism ↑TSH ↑T4 ↑T3

Interpretation of results level

II

- f) Compensated/ sub clinical states
- Sub clinical hypothyroidism \uparrow TSH
 \rightarrow T4 \rightarrow T3
- Sub clinical hyperthyroidism \downarrow TSH
 \rightarrow T4 \rightarrow T3



EFFECTS ENDOCRINE SECRETION (HORMONES)

- ▶ A specific effect on an organs
- ▶ General effects e.g. Thyroid hormones on BMR
- ▶ Rates of metabolism of specific substances e.g. CHO



EFFECTS ENDOCRINE SECRETION (HORMONES)

- Growth and development
- Secretory activity of other endocrine glands
- Development and functioning of the reproductive glands
- Sexual characteristics and libido



EFFECTS ENDOCRINE SECRETION (HORMONES)

- Development of personality
- Nervous system functions
- Ability to cope with stress
- Resistance to diseases
- Others



AETIOLOGICAL FACTORS OF ENDOCRINE DISORDERS

Causes of hormonal imbalance:

- Amount secreted
- Failure of the hormonal response
- Structure of the hormone
- Malfunctioning receptor hormonal mechanisms
- Ineffective translational mechanisms
- Dysfunctioning organs
 - Hypofuction
 - Hyperfuction



AETIOLOGICAL FACTORS LEADING TO ENDOCRINOPATHY

- Tumours- adenomas
- Destructive disorders- sarcoidosis, amyloidosis, cancers
- Trauma to the endocrine gland
- Congenital anomalies- lack of enzymes
- Developmental disorders- aplasia, agenesis
- Infections-TB, HIV etc



AETIOLOGICAL FACTORS LEADING TO ENDOCRINOPATHY

- ▶ Autoimmune diseases- hormone mediated endocrinopathies
- ▶ Receptor/hormone defects
- ▶ Surgical or irradiation
- ▶ Multiple Endocrine Neoplasia (MEN)
- ▶ Paraneoplastic Endocrine syndrome (PNES) /ECTOPIC




Investigations of endocrinopathies

- **Clinical: symptoms and signs (Hx/PE)**
- Laboratory
 - Clinical history is very important for interpretation of results
 - Technique of immunoassays
 - Analysis with quality control to give out **VALID** results
 - Interpretation of results



Use of endocrine laboratory

- Screening
 - Diagnosis
 - Monitoring during treatment
 - Monitoring for complications
 - Assessing success of treatment
 - Research
 - Training
- 



Factors to consider in interpreting hormonal levels

- ▶ Age= **different reference ranges**
 - ▶ Utero
 - ▶ Neonatal
 - ▶ Pre-purbertal
 - ▶ Pubertal
 - ▶ Adults
 - ▶ menopause
- ▶ Gender = **different references for some hormones**
 - ▶ Female
 - ▶ male



Factors to consider in interpreting hormonal levels

- Physiological status= **changes over a period of time**
 - Pregnancy = gestational age (week/trimester)
 - Menstrual cycle- follicular, mdphase, luteal phase)
- Time- **diurnal changes**
 - AM, Afternoon, night
 - Stimulation tests



Factors to consider in interpreting hormonal levels

- ▶ Assay systems –**immunoassays**
- ▶ Laboratory performance- **reliability of results**
- ▶ Interference in assay system
 - ▶ Drugs
 - ▶ Diet
- ▶ Pathological states- **different reference ranges**
 - ▶ menopause



Endocrine glands and dysfunctions

- Hypothalamus
- Anterior pituitary
- Thyroid gland
- Adrenal cortex
- Adrenal medulla
- Gonads- ovaries and testis

1. Hypothalamic control of anterior pituitary secretions

n	Hormones	Effect on Ant Pituitary
1.	Thyrotropin-releasing hormone (TRH)	(+) TSH & Prolactin
2.	Corticotropin-releasing hormone (CRH)	(+) ACTH
3.	Growth hormone releasing hormone (GHRH)	(+) GH
4.	Growth hormone inhibitory hormone (GHIH) "Somatostatin (SS)"	(-) GH
5.	Gonadotropin-releasing hormone (GnRH)	(+) Gonadotropic hormones (LH, & FSH)
6.	Prolactin releasing hormone (PRH)	(+) Prolactin
7.	Prolactin releasing inhibitory hormone (PRIH) "Dopamine"	(-) Prolactin



2. Anterior pituitary

- ▶ Engine for the endocrine system
- ▶ Influenced by hypothalamus
- ▶ Affects many functions in the body

Anterior Pituitary (AP) Hormones

Hormones	Target tissue	Principal action
1. Growth hormone (<u>GH</u> , or somatotropin)	Most tissue	(+) protein synthesis & growth; lipolysis; ↑ bl glucose
2. Thyroid-stimulating hormone (<u>TSH</u> , or thyrotropin)	Thyroid gland	(+) thyroid hormones (T4/T3)
3. Adrenocorticotrophic hormone (<u>ACTH</u> , or corticotrophin)	Adrenal cortex	(+) glucocorticoids- CORTISOL
4. Follicle-stimulating hormone (<u>FSH</u>)	Gonads	(+) gamete production, (+) estrogen in ♀
5. Luteinizing hormone (<u>LH</u>)	Gonads	(+) sex hormones; ovulation & corpus luteum formation in females; (+) testosterone in ♂
6. Prolactin (PRL)	Mammary glands	(+) milk in lactating ♀; regulates ♂ reproductive system



Endocrinopathies





1. HYPOTHALAMUS DISORDERS.

- ▶ Lack of releasing hormones
 - ▶ Leads to hypo functioning AP
- ▶ Over production of releasing hormones
 - ▶ Leads to hyper functioning AP



2. Dysfunctions of AP.

- ▶ A) Hyper- function- Increased production of the hormones- adenomas
- ▶ B) Hypo- function- decreased production of the hormones
 - ▶ Destruction of AP
 - ▶ Isolated deficiency e.g GH- Dwarfism



H-AP Disorders

- ▶ A) Hyperfunction of AP:
 - ▶ Hyper-prolactinemia- \uparrow PRL- Galactorrhea
 - ▶ Acromegaly /giagantism- \uparrow GH
 - ▶ Cushing's disease – \uparrow ACTH
 - ▶ Precocious puberty – \uparrow FSH/LH
 - ▶ Secondary hyperthyroidism - \uparrow TSH



H-AP Disorders

➤ B. HYPOFUNCTIONING AP

- Panhypopituitarism- All hormones are low
- Dwarfism- ↓GH
- Hypogonadotropic hypogonadism-
↓FSH/↓LH
- Secondary adrenocortical insufficiency-
↓ACTH
- Lack of lactation- no ↓Prolactin
- Secondary hypothyroidism-↓TSH



➤ start






TESTS USED TO ASSESS H-P functions/dysfunction

- ▶ Hormones produced in AP:
- ▶ Investigate the axis
 - ▶ **LH/FSH**/Estradiol (E2) and Progesterone for females in the axis,
 - ▶ **LH/FSH**/Testosterone for males in the axis
 - ▶ **TSH/T4/T3/FT4/FT3**



TESTS USED TO ASSESS H-P functions/dysfunction

- ▶ **ACTH/Cortisol**
 - ▶ **GH**
 - ▶ **Prolactin (PRL)**
- 



TESTS USED TO ASSESS H-P functions/dysfunction

- ▶ Other tests to indicate that the AP is functioning-
indirect tests
 - ▶ FT3/FT4----**TSH**
 - ▶ E2/P4---**FSH/LH**
 - ▶ Testosterone- **FSH/LH**
 - ▶ Cortisol---**ACTH**
 - ▶ **Others- semen analysis- male**

3. Thyroid disorders

► H-AP-T AXIS-

► Hypothyroidism

► Primary: \uparrow TSH \downarrow **T4** \downarrow **T3**

► Secondary : \downarrow **TSH** \downarrow T4 \downarrow T3

► Hashimotos thyroiditis : immune mediated endocrinopathy antibodies are produced e.g Antithyroglobulin Abs

H-AP-T Axis cont.

► Hyperthyroidism

- Primary : ↓ TSH ↑ **T4** ↑ **T3**
- Secondary : ↑ **TSH** ↑ T4 ↑ T3
- Grave's disease- immune mediated endocrinopathy:
Thyroid Stimulating immunoglobulin (TSI)



TESTS FOR H-AP-T AXIS

- **TSH**
- TT4
- TT3
- **FT4**
- FT3
- Used more often
- Others



4. H-AP-Adrenal Cortical AXIS



➤ A) **Hyperfunction**

➤ B) **Hypofunction**

➤ **HYPERFUNCTION:**

➤ Cushing's syndrome :- **↑cortisol**

➤ H- **↑ CRH↑ ACTH↑cortisol**

➤ AP- **↑ ACTH↑cortisol**

4. **H-AP-Adrenal Cortical AXIS**

➤ Ectopic production of **↑ ACTH↑cortisol**

➤ Adrenal Cortex- **↑cortisol ↓ ACTH**

➤ Adenoma

➤ carcinoma

4. H-AP-Adrenal Cortical AXIS

- ▶ **HYPOFUCTION: Low cortisol**
- ▶ Addison's disease- destruction of adrenal cortex – ↓
cortisol, ↑ ACTH
- ▶ Secondary adrenal cortisol insufficiency : ↓ **ACTH** ↓
cortisol



4. H-AP-Adrenal Cortical AXIS

- ▶ Congenital adrenal hyperplasia (CAH)
 - ▶ Enzyme deficiencies e.g 21 hydroxylase deficiency :
overproduction of cortisol and aldosterone **precursors**
e.g 17hydroxy progesterone (17OHP4)
 - ▶ Androgens- testosterone
 - ▶ Low cortisol and aldosterone levels



Tests used to assess AC axis

- ▶ ACTH
- ▶ Cortisol
- ▶ Aldosterone
- ▶ Androgens e.g testosterone

5. Adrenal medullar

- ▶ Function is production of catacholamines
 - ▶ Adrenaline/epinephrine
 - ▶ Nor-adrenaline/nor-epinephrines
- ▶ Glucose metabolism



5. Adrenal medullar

- ▶ Major disorder:
 - ▶ Pheochromocytoma- ↑catecholamines
 - ▶ Tests:
 - ▶ Vanillyl mandelic acid –**VMA in urine**
 - ▶ Catecholamines and their products in blood or urine

6. H-AP-Gonadal axis

- ▶ Hormonal imbalance lead to:
- ▶ Infertility
 - ▶ Axis :
 - ▶ Females: GnRH, LH/FSH, Estrogens,P4
 - ▶ Males: GnRH, LH/FSH androgens, Testosterone

6. H-AP-Gonadal axis

- ▶ Females:
- ▶ Primary ovarian failure: \uparrow FSH $>$ \uparrow LH \downarrow **Es**
 - ▶ e.g. menopause/premature menopause

6. H-AP-Gonadal axis

▶ Secondary ovarian failure:

▶ ↓ LH ↓ FSH, ↓ Estrogens: **hypogonadotropic-hypogonadism**

6. H-AP-Gonadal axis

- ▶ **males**

- ▶ Primary testicular failure: \uparrow LH \uparrow FSH \downarrow **androgens**

- ▶ Secondary testicular failure: \downarrow **LH** \downarrow **FSH** \downarrow
androgens: **hypogonadotrophic-hypogonadism**



Assessing H-AP-G axis

- ▶ Females
 - ▶ LH
 - ▶ FSH
 - ▶ E2
 - ▶ P4
- ▶ Others PRL



Assessing H-AP-G axis

- ▶ Males
 - ▶ LH
 - ▶ FSH
 - ▶ Testosterone
- ▶ Others PRL
- ▶ semen analysis



Evaluation of male infertility

- Semen analysis- semen as a sample
- Parameters assessed:
 - Time of liquefaction
 - Consistence- droplets
 - Volume
 - Concentration of sperms- **how many sperms per ejaculate**
 - Motility of sperms- **speed of sperms**
 - Morphology of sperms- **shape of sperms**
 - Presence of infection- **WBCs**
 - others



Classification of semen results

- ▶ Normozoospermia- all parameters are within reference ranges
- ▶ Oligozoospermia- reduced sperm count
- ▶ Asthenozoospermia – reduced motility
- ▶ Teratozoospermia- poor morphology
- ▶ combination

7. Pancreatic endocrine disorders

- ▶ DM- type 1
 - ▶ ↓ Insulin
 - ▶ ↓ C-Peptide
- ▶ Type II DM
 - ▶ ↑ ↓ Insulin
 - ▶ ↑ C-peptide
- ▶ Insulinoma
 - ▶ ↑ Insulin
 - ▶ ↑ C-Peptide



7. Pancreatic endocrine disorders

- ▶ Glucagonoma
 - ▶ ↑ Glucagon- hyperglycemia
 - ▶ ↓ glucagon-hypoglycemia



Conclusion

- ▶ Enjoy endocrinology
 - ▶ Pathology
 - ▶ Medicine
 - ▶ Surgery
 - ▶ Peadiatrics
 - ▶ Radiology
 - ▶ Dental- REFERRAL SYSTEM



Conclusion

- ▶ ALWAYS USE THE LAB WHEN DEALING WITH ENDOCRINOPATHIES!!!!!!!
- ▶ MORE IN LEVEL IV