Principles of laboratory investigations in endocrine disorders

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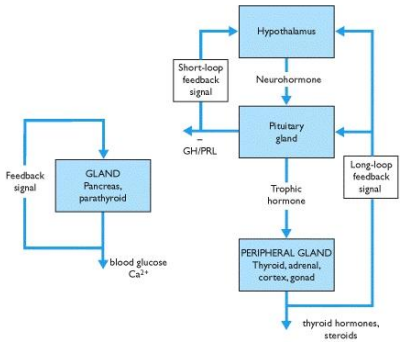
Introduction

- Unique feature of the endocrine system is it's ability to regulate itself
- This is done by providing (-) ve and (+) ve feedback stimuli to each gland that produces a secretory hormone
- All hormone production comes under some form of feedback control

Feedback control



Commonly measured hormones

- FT_4, FT_3, TSH
- GH
- Insulin
- PTH, Calcitriol
- Prolactin
- Cortisol, ACTH
- Renin, Aldosterone
- LH, FSH
- Oestrogen, Progesterone
- Testosterone
- hCG
- Gastrin

Endocrine disorders can result from

- Dysfunction originating in the peripheral endocrine gland (primary disorders) or
- Understimulation or overstimulation by the pituitary (secondary disorders)
- Accelerated degradation
- Hormone resistance (receptor/target organ)

Hyperfunction

- May result from
  - Hyperplasia of gland
  - Neoplasia of gland
  - Overstimulation by the pituitary
  - Ectopic hormone production
  - Exogenous hormone administration
  - Antibody stimulation of gland

Hypofunction

- Destruction of gland
  - Autoimmune disorders
  - Tumors
  - Infections
- Understimulation by the pituitary
- Increased degradation
- Genetic disorders
- Abnormalities of the receptor

Why tests are important?

- Because symptoms can begin insidiously and may be nonspecific, clinical recognition is often delayed.
- For this reason, biochemical diagnosis is usually essential.
- It requires measuring levels of the peripheral endocrine hormone, the pituitary hormone, or both.

Difficulties

- The main problem – Small quantities 100 nmol/L (10^{-9} moles)
- Two fractions
  - Free
  - Bound
- The active form is free fraction even smaller levels 20 pmol/L (10^{-12} moles)

Difficulties

- Measured by immunoassays
- Lab to lab differences

Which sample?

- Blood
  - direct assessment of circulating hormones
  - relatively accurate values
  - well-established reference ranges
- Urine
  - 24-hour urine sample
  - non-invasive
  - provides a stable indicator of output
  - not susceptible to the hour-to-hour fluctuations
- Saliva
  - Simple, non-invasive, economical and can be collected at home

Sampling

- Patient preparation
- Correct sample collection
- Sample storage and transport

Indirect estimates

- GH may be assessed indirectly by measuring IGF-1 levels.
- Diabetes insipidus-urine and serum osmolality

Paired testing

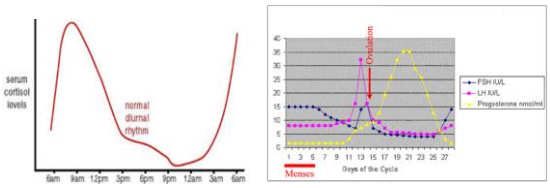
- PTH, Serum calcium

	Serum Ca	PTH
Hyperparathyroidism	High	High
Vit D toxicity	High	Low
Hypoparathyroidism	Low	Low
Vit D deficiency	Low	High

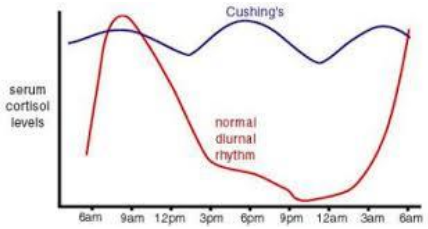
- Insulin, Blood glucose
- ACTH, Cortisol
- TSH, T4

What's wrong with a single measurement?

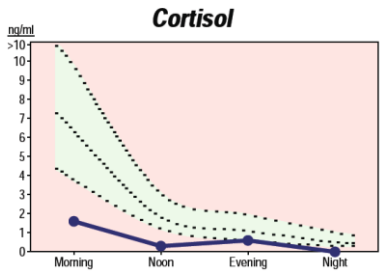
– Episodic and circadian output
– Normal level may differ during the menstrual cycle
– Abnormal function may fall into normal range



Abnormal function may fall into normal range cont.



Abnormal function may fall into normal range



Interpretation of hormone levels

- Interpretation of the results should always take into account three factors
  – the clinical features of the patient,
  – the concentration of the variable regulated by the hormone, and
  – the concentration of other hormones in the feedback loop.

Dynamic function tests

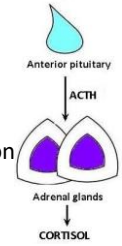
- In some cases, a dynamic test is necessary to diagnose a hormonal disorder.
- Involve either stimulating or suppressing a particular hormonal axis, and observing the appropriate hormonal response.
- If a deficiency is suspected→a stimulation test
- If an excess is suspected →a suppression test

Stimulation tests

- Glucose tolerance test - diabetes mellitus
- Insulin tolerance test - growth hormone deficiency
- Short synacthen test - adrenal insufficiency
- Water deprivation test - diabetes insipidus

Short synacthen test

- A synacthen test uses Synacthen to test how well the adrenal glands produce cortisol.
- It involves stimulating the adrenal glands and then checking to see if they respond.
- This is performed for the investigation of adrenal insufficiency.

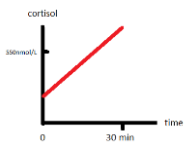


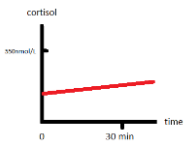
Short synacthen test

- Adrenal glucocorticoid secretion is controlled by adrenocorticotrophic hormone (ACTH) released by the anterior pituitary.
- This test evaluates the ability of the adrenal cortex to produce cortisol after stimulation by synthetic ACTH (Synacthen).
- The short test assesses the ability of the adrenal gland to respond to ACTH.

Short synacthen test

- At 0900
  - take blood for cortisol
- inject Synacthen iv or im
- At 0930
  - take further sample for cortisol



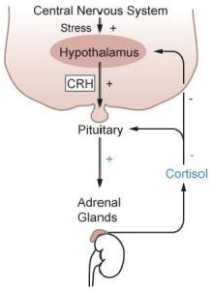


Suppression tests

- Dexamathasone suppression test- Cushing's
- Glucose tolerance test - Acromegaly

Overnight dexamathasone suppression test

- Dexamethasone is a cortisol look-alike.
- It suppress pituitary ACTH causing a fall in cortisol levels.



Overnight dexamathasone suppression test

- The patient takes 1 mg dexamethasone orally at 2300h and the following morning at 0900h a blood sample is taken for plasma cortisol.
- A normal response is shown by suppression of 0900 h cortisol to < 50 nmol/L.

Thank you