Investigations of Endocrine Diseases Part 1

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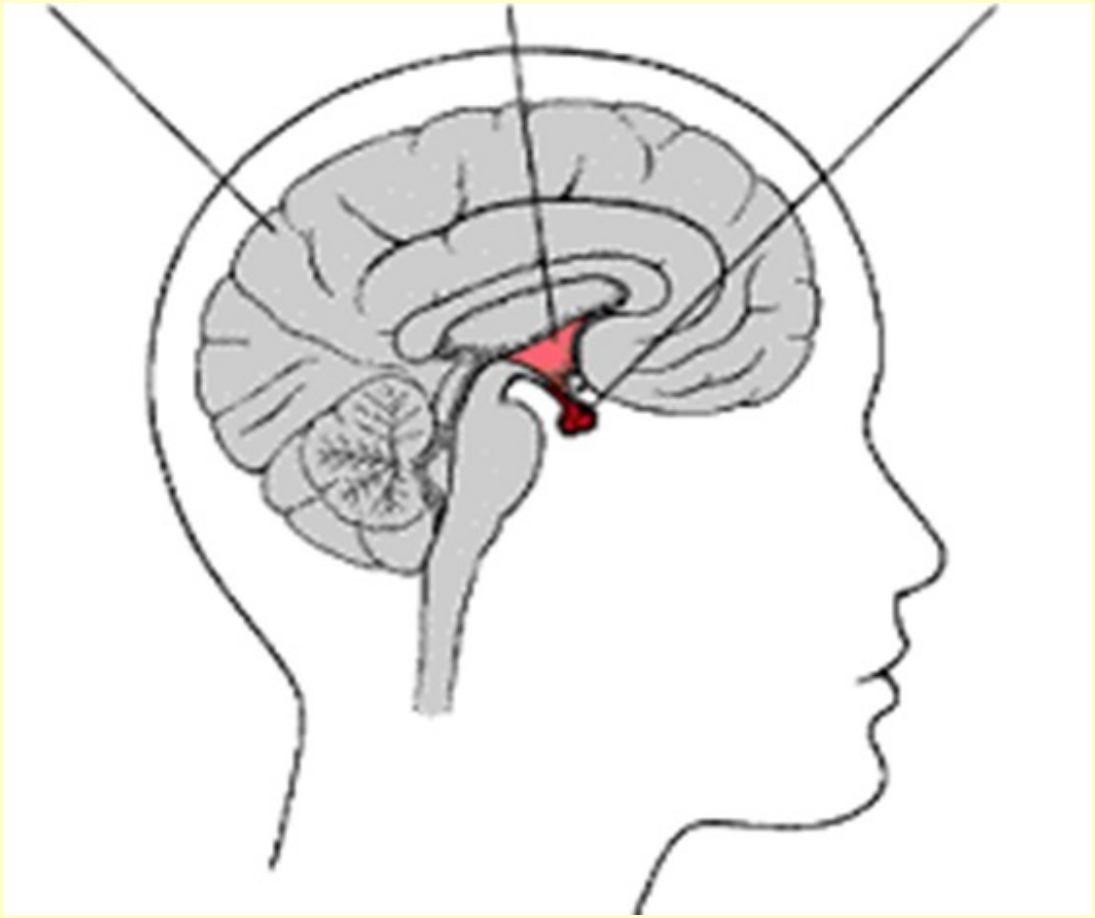
Endocrinology Objectives

- What is the pathological basis of endocrine dysfunction?
- What are the principles of laboratory investigations?
- What are the primary and secondary investigations for common endocrine diseases?
- What are the expected biochemical abnormalities in common endocrine disorders?

Pituitary gland

Brain Hypothalamus Pituitary



Hypophysiotrophic hormones

Hormone	Action
Thyrotropin releasing hormone (TRH)	Releases TSH and prolactin
Gonadotropin releasing hormone (GnRH)	Releases LH and FSH
Corticotropin releasing hormone (CRH)	Releases ACTH
Growth hormone releasing hormone (GHRH)	Releases GH

Inhibiting Hormones:
Somatostatin
Dopamine

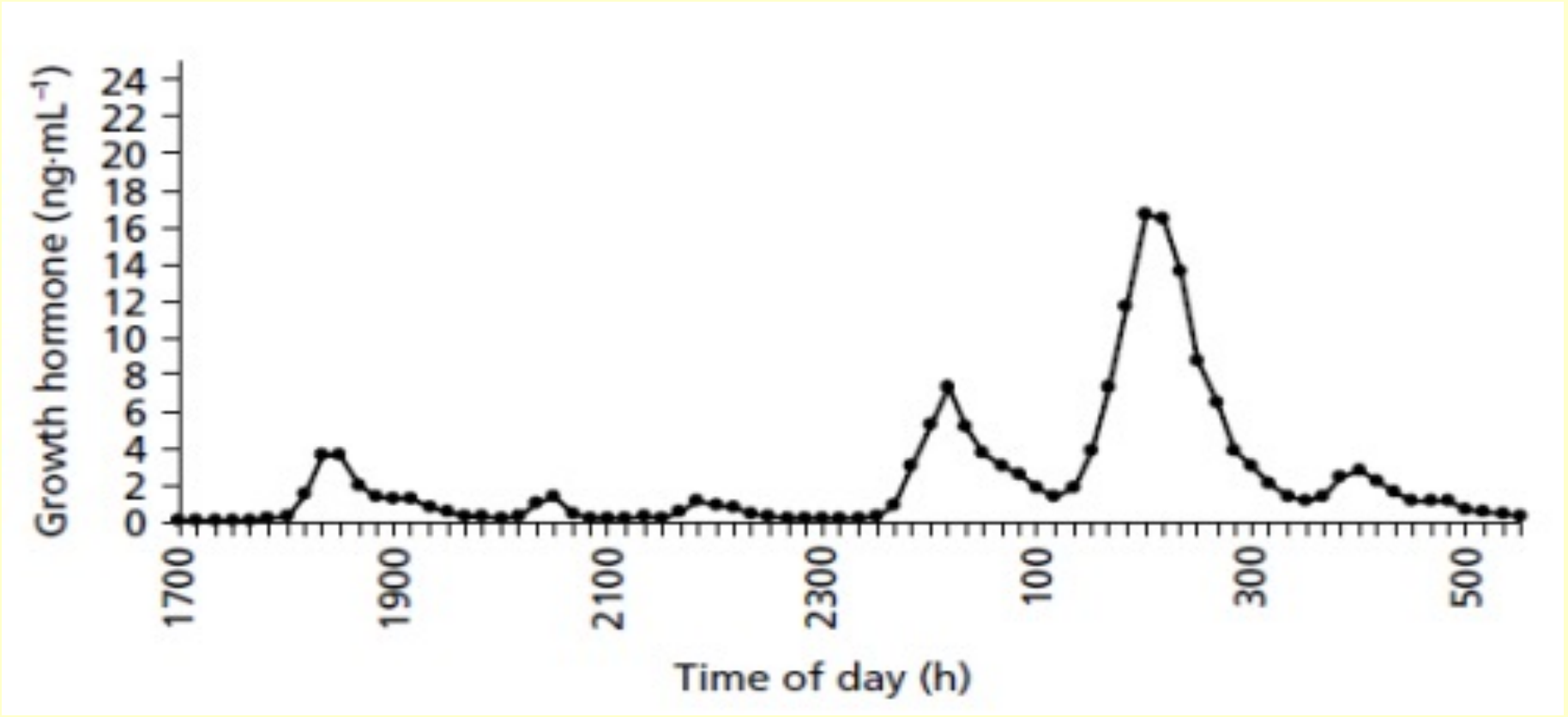
Pituitary Hormones

Anterior pituitary	Posterior Pituitary
Luteinizing hormone (LH)	Vasopressin (Anti diuretic hormone)
Follicle stimulating hormone (FSH)	Oxytocin
Thyroid stimulating hormone (TSH)	
Adrenocorticotropic hormone (ACTH)	
Growth hormone (GH)	
Prolactin (PRL)	

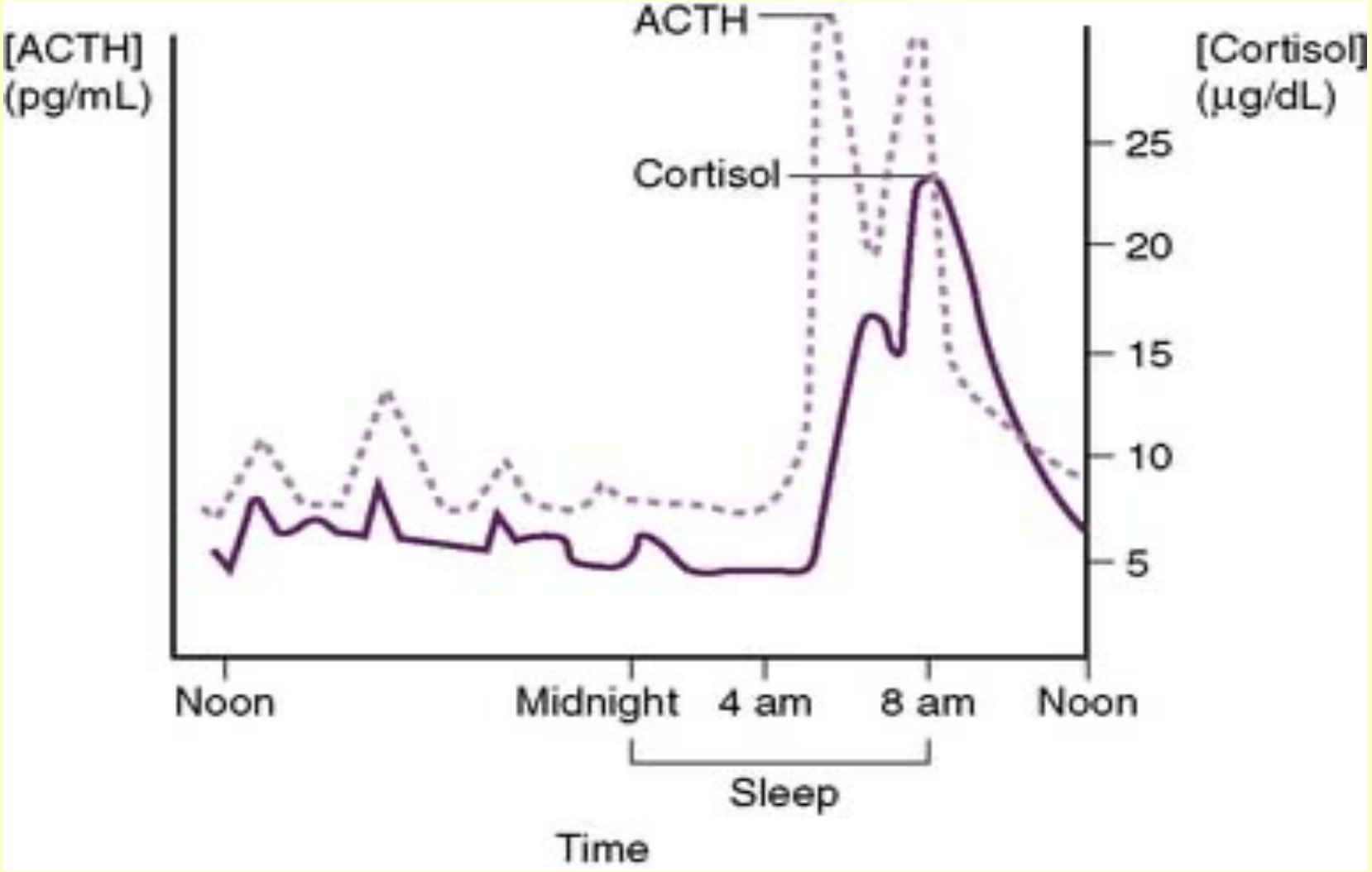
Secretary Patterns of Hormones

- Continuous secretion e.g. thyroid hormones under the control of TSH
- Pulsatile secretion e.g. growth hormone, prolactin
- Diurnal secretion e.g. ACTH (highest at 8.00 a.m. lowest at midnight),cortisol

Pulsatile Secretion



Diurnal secretion



What is the basis of endocrine dysfunction?

- Hypothalamic/pituitary or target gland pathology
- Failure of regulatory mechanisms
- Results in Hyperfunction or Hypofunction

What are the causes of endocrine dysfunction

- Hyperfunction

❑Neoplasms which are autonomous

❑Failure in regulatory mechanisms

- Hypofunction

❑Autoimmume diseases

❑Infectious/infiltrative diseases

❑Pressure atrophy

❑Iatrogenic

Tests of Endocrine Function

Basal secretion – single blood or urine sample

Dynamic tests - two or more samples and used to test the integrity of the control mechanism of the hypothalamic-pituitary-end organ axis

Testing Anterior Pituitary Function

- Stimulatory tests used in cases of suspected insufficiency.

- Suppression tests for hyperfunction.

Samples for hormone assay

- Serum, plasma, urine
- Serum commonly
- Exceptions

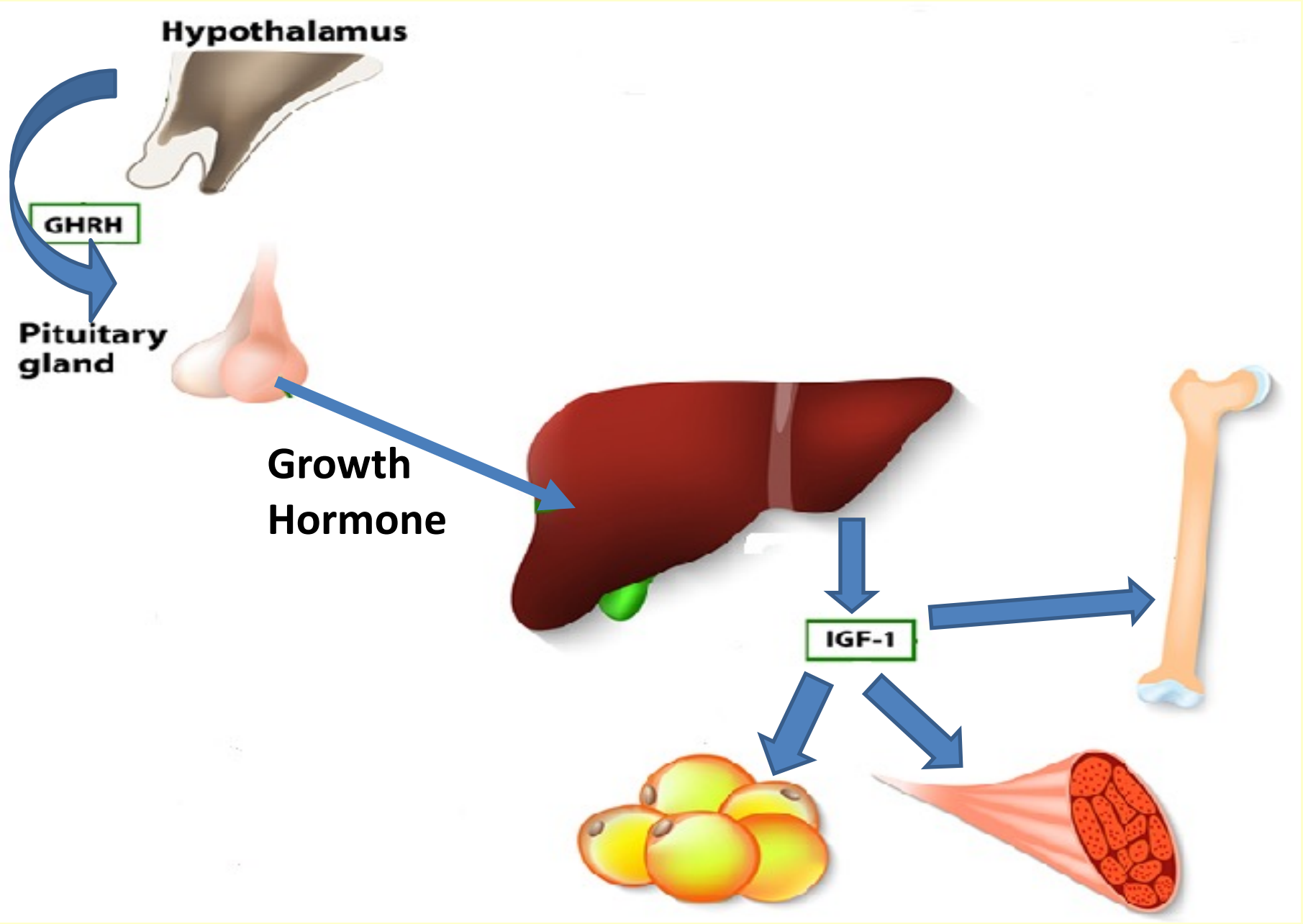
ACTH - EDTA plasma

PTH - EDTA plasma

Growth Hormone

- Secreted in 6 – 12 pulses/day
- Natural increases seen
  - After exercise
  - During sleep
- Exerts effects via IGF -1

  (Insulin-like growth factor 1)
- Basal levels very low or undetectable
- Random specimens are not useful


Hypothalamus
GHRH
Pituitary gland
Growth Hormone
IGF-1

Tests for GH Reserve (Deficiency) Investigation of Short Stature

- Basal growth hormone (GH) is usually < 1 mU/L in normal individuals except during pulses of secretion.
- Measurement of random growth hormone level is unhelpful.
- Therefore stimulation tests are required to confirm existence of GH deficiency.
- **Children (< 18 yrs)** – Glucagon/Arginine stimulation test
- Second line test
  - Clonidine stimulation test
  - Exercise stimulation test

Adults

- Insulin hypoglycaemic test (IHT)
- Glucagon stimulation test

Second line test

- Clonidine stimulation test

Insulin Hypoglycaemic Test (IHT)

Time (min)	Growth Hormone	Plasma Glucose
0	√	√
30	√	√
60	√	√
90	√	√
120	√	√

Interpretation - IHT

- If adequate hypoglycaemia wasn't achieved cortisol or GH deficiency cannot be diagnosed.

Normal response

- Venous plasma glucose concentration fallen to < 2.2 mmol/L is a satisfactory evidence of sufficient stress.

- Serum cortisol rises by > 200 nmol/L to at least 550 nmol/L
- Serum GH rises to > 20 mU/L

- Peak GH response

< 10 mU/L	GH deficiency
10 - 20 mU/L	Partial GH deficiency
> 20 mU/L	Normal

Exercise stimulation test for GH

- Exercise is a physiological stimulant of GH secretion.
- Pre exercise blood for growth hormone
- Exercise vigorously for 20 min

➢ Running on a tread mill

➢ Climbing stairs up and down

- Adequate exercise confirmed by

➢ Increased heart rate > 140 bpm

Interpretation- exercise stimulation test

- Peak GH response < 10 mU/L suggest GH deficiency
- Responses 10 - 20 mU/L suggest Partial GH deficiency
- Normal > 20 mU/L

- GH deficiency must be confirmed with at least 2 stimulation tests before starting growth hormone administration.

- IGF – 1 levels will be low.

Tests for GH excess (Acromegaly/Gigantism)

- IGF-1 if done will be high.
- Dynamic function test by suppression
- Growth hormone is naturally suppressed by glucose.
- Perform an oral glucose tolerance test (OGTT) (75 g glucose load)
- Blood for glucose and growth hormone
- GH producing tumors will not be suppressed.

Oral Glucose Tolerance Test (OGTT)

- Overnight fast 8 hrs. Patient at rest throughout. Drink of water is allowed.
- Baseline sample for fasting plasma glucose (FPG) and growth hormone (GH) taken.
- Administer 75 g of glucose in 300 mL of water to drink within 5 minutes.
- Draw sample at 30,60,90 and 120 min.
- Serum GH suppression < 1 mU/L exclude possibility of excess growth hormone.

Prolactin

- Secretion is under the inhibitory effect of hypothalamic dopamine.
- Secretion is pulsatile and increase during sleep,exercise and stress.
- High levels during pregancy and lactation.

Test for prolactin

- Blood should be taken about 3 hours after waking up.
- Avoid pain and stress during sampling.
- Serum is preferred. Take 2 mL of blood to a plain tube after an overnight fast.(Protein rich diet stimulate prolactin release).

Causes for hyperprolactinaemia

- Prolactinoma
- Damage to pituitary stalk
- Drugs
  - Oestrogens
  - Dopaminergic receptor blockers (phenothiazines,haloperidol)
  - Dopamine depleting agents e.g. methyldopa,reserpine
- Hypothyroidism
- Chronic kidney disease

Hyperprolactinaemia clinical features

Premenopausal women

- Delayed menarche
- Menstrual irregularities
- Subfertility
- Galactorrhea

Men

- Hypogonadism and subfertility

Diagnosis

- Serum prolactin
- Investigate further > 700 mIU/L
- Very high levels are suggestive of prolactinoma (> 5000 mIU/L)
- Check visual fields
- Assess the rest of the pituitary function

Reproductive Hormones

- Pituitary
  - LH
  - FSH
- Gonads
  - Male -Testosterone, inhibin
  - Female - Progesterone,oestrogen

Primary gonadal failure
Hypergonadotrophic hypogonadism

- LH and FSH – High
- Testosterone/estrogens,progesterone –low
- Physiological - menopause

Secondary gonadal failure
Hypogonadotrophic hypogonadism

- LH and FSH – low
- Testosterone/Estrogen, Progesterone – low

  e.g.Sheehan's syndrome

Causes of Hypopituitarism

1. Tumours e.g. non functioning (Craniopharyngioma) or functioning pituitary tumours, hypothalamic tumours
2. Post traumatic – e.g. fracture base of skull
3. Post infection e.g. after bacterial or T.B meningitis
4. Vascular – necrosis following post partum haemorrhage (Sheehan's syndrome)
5. Infiltration e.g. Haemochromatosis, Sarcoidosis
6. Iatrogenic e.g. post pituitary surgery, radiation

Clinical Features in Hypopituitarism

Hormone	Features of deficiency
Growth hormone	**Adults:** decreased muscle bulk **Children** : growth retardation
Prolactin	Failure of lactation
Gonadotropins	**Children** : delayed puberty **Females** : oligomenorrhoea, infertility, atrophy of breasts and genitalia **Males** : impotence, azoospermia, testicular atrophy
ACTH	Weight loss, weakness, hypotension, hypoglycaemia, decreased pigmentation
TSH	Weight gain, cold intolerance, fatigue
ADH	Thirst, polyuria

Investigations for hypopituitarism

- Measurement of anterior pituitary gland hormones at 9 am

GH
ACTH
Prolactin
TSH
FSH
LH

- Measurement of target gland hormones at 9 am

Cortisol
Free T4
Estradiol
Testosterone

Posterior Pituitary Hormones

- Vasopressin/ADH – Controls the tonicity of the Extracellular fluid

Clinical syndromes:

- Inappropriate ADH secretion - Can cause severe hyponatremia

- Diabetes Insipidus - D/D of polyuria

SIADH

- Causes significant dilutional hyponatremia
- Investigations

✓ Serum electrolytes

✓ Plasma and urine osmolality

- Exclude renal, adrenal and thyroid dysfunction

D/D of Polyuria

- Diabetes Mellitus
- Hypokalaemia
- Hypercalcaemia
- Chronic renal failure
- Primary polydipsia
- Diabetes Insipidus

Investigations for patients with polyuria

- Plasma glucose
- Serum creatinine
- Blood urea
- Serum electrolytes
- Urine osmolality
- Water deprivation test

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Thank you !