

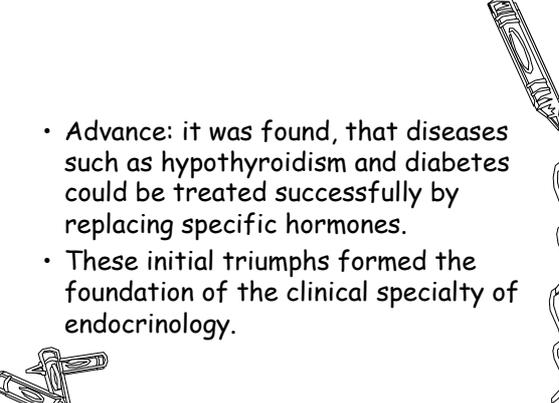
Introduction to endocrinology

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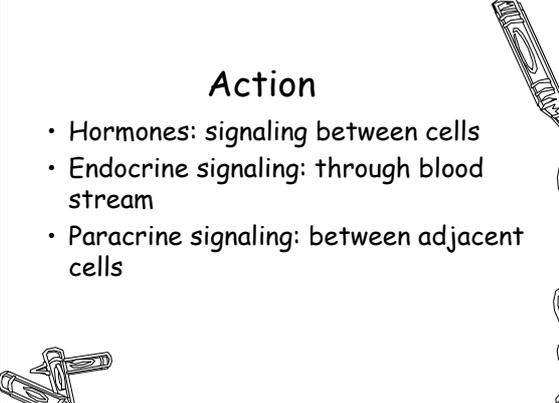


History

- One century ago - Starling coined the term `hormone`, first described hormone: secretin (secreted by the small intestine, stimulate pancreatic secretion)
- In the next decades, more and more hormones were identified

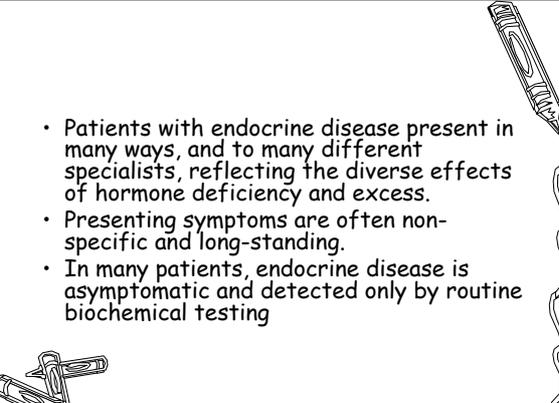


- Advance: it was found, that diseases such as hypothyroidism and diabetes could be treated successfully by replacing specific hormones.
- These initial triumphs formed the foundation of the clinical specialty of endocrinology.

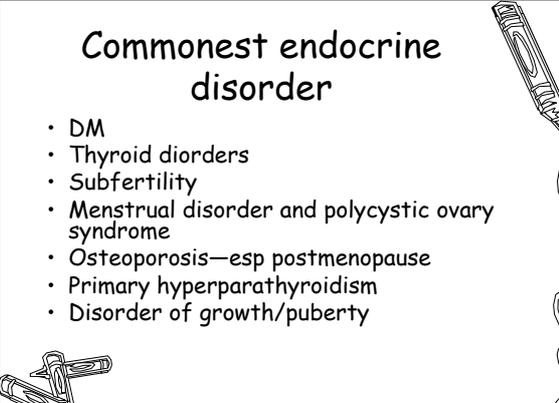


Action

- Hormones: signaling between cells
- Endocrine signaling: through blood stream
- Paracrine signaling: between adjacent cells



- Patients with endocrine disease present in many ways, and to many different specialists, reflecting the diverse effects of hormone deficiency and excess.
- Presenting symptoms are often non-specific and long-standing.
- In many patients, endocrine disease is asymptomatic and detected only by routine biochemical testing

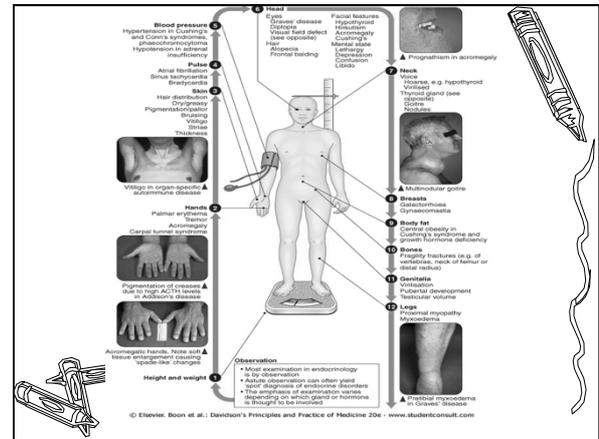


Commonest endocrine disorder

- DM
- Thyroid disorders
- Subfertility
- Menstrual disorder and polycystic ovary syndrome
- Osteoporosis—esp postmenopause
- Primary hyperparathyroidism
- Disorder of growth/puberty

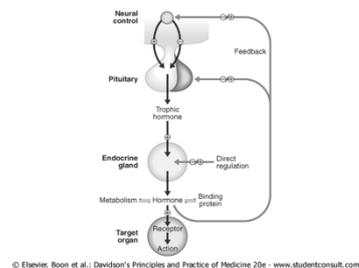
Hormones as therapy

- Oral contraceptive: 20-30% women aged 18-35
- Hormone replacement Tx:
- Steroid therapy in non-endocrine disorder--- asthma etc



Control and feed back

- Most hormones are controlled by some form of feedback
- Hypothalamic-pituitary-thyroid axis
- TRH (thyrotrophin releasing hormone)---TSH---T3/T4



ENDOCRINE DISEASES

Five categories:

- (1) hormone overproduction
- (2) hormone underproduction
- (3) hormones hypersensitivity
- (4) hormones resistances
- (5) tumors of endocrine glands.

Hormone Overproduction

- Primary gland over-production
- Secondary to excessive trophic substances
- Eg. in Graves' disease, antibodies mimic TSH → TSH receptor activation → increase in thyroid cell proliferation and increased synthesis and release of thyroid hormone (polyclonal expansion of the thyroid cells)
- most endocrine tumors: monoclonal expansions of one mutated cell

Hormone Underproduction

Can be the result from a wide variety of processes

- Primary gland failure eg: surgical removal; tuberculous destruction; **autoimmunity**
- Secondary to deficient trophic hormones



Hormones hypersensitivity

- Failure of inactivation of hormones
- Target organ over activity/ hypersensitivity



Hormones resistance

- Failure of activation of hormones
- Target organ resistances
- Resistance to hormones can be caused by a variety of genetic disorders.
- The insulin resistance in muscle and liver--appears to be polygenic in origin- T2DM.
- Mutations in signal reception and propagation. Eg. activating mutations in TSH, LH, and PTH receptors can cause increased activity of thyroid cells, Leydig cells, and osteoblasts, even in the absence of ligand.



Tumors of Endocrine Glands

- often results in hormone overproduction
- some tumors of endocrine glands produce little if any hormone but cause disease by their local compressive symptoms or by metastatic spread
- Eg. pituitary tumors can cause a variety of symptoms due to compression on adjacent structures,
- thyroid cancer, which can spread throughout the body without causing hyperthyroidism



SPECIAL FEATURES OF ENDOCRINE ILLNESS

- Discovery through Screening
- Quantitative Rather Than Qualitative Abnormalities
- Overlap with Other Diseases
- Evolve gradually over months to years instead of appearing suddenly
- Unique Features of Reproductive Disorders



COMMON PRESENTATIONS IN ENDOCRINOLOGY

- Obesity
 - Cushing's syndrome,
 - hypothyroidism,
 - pancreatic insulinoma,
 - growth hormone deficiency,
 - menopause,
 - metabolic syndrome,
 - polycystic ovary syndrome,
 - hypothalamic lesions



Unintended Weight Loss

- Uncontrolled diabetes mellitus
- Hyperthyroidism
- Hypothyroidism (↓ appetite)
- adrenal insufficiency (due either to pituitary ACTH deficiency or to Addison's disease)
- Diabetes insipidus
- Pheochromocytoma
- Cushing's syndrome (muscle wasting)



Abnormal Skin Pigmentation

- Addison's disease (ACTH ↑)
- POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes);
- Hemochromatosis
- porphyria
- Chronic renal failure
- Chronic liver failure



Bone Pain & Pathologic Fractures

- Hyperparathyroidism
- Hyperthyroidism
- Cushing's syndrome
- malignancy
- rickets
- osteomalacia



Muscle Cramps & Tetany

- Hyperthyroidism
- Hypothyroidism
- Diabetes mellitus
- Hypocalcemia
- Hypomagnesemia



Others

- Gynecomastia
- Galactorrhea
- Erectile Dysfunction & Diminished Libido in Men
- Cryptorchism
- Mental changes



PRINCIPLES OF ENDOCRINE INVESTIGATION

Timing of measurement: Release of many hormones is rhythmical (e.g. pulsatile, circadian or monthly), so random measurement may be invalid and sequential or dynamic tests may be required

Choice of dynamic biochemical tests

- Abnormalities are often characterised by loss of normal regulation of hormone secretion
- If hormone deficiency is suspected, choose a stimulation test
- If hormone excess is suspected, choose a suppression test
- The more tests there are to choose from, the less likely it is that any single test is infallible, so avoid interpreting one result in isolation



PRINCIPLES OF ENDOCRINE INVESTIGATION

Imaging

- Secretory cells also take up substrates, which can be labelled
- Most endocrine glands have a high prevalence of 'incidentalomas', so do not scan unless the biochemistry confirms endocrine dysfunction or the primary problem is a tumour

Biopsy

- Many endocrine tumours are difficult to classify histologically (e.g. adrenal carcinoma and adenoma)



Stimulation and suppression tests

- These tests are used when basal levels are equivocal
- stimulation tests are used to confirm suspected deficiency
- suppression tests are used to confirm suspected excess of hormone secretion



- if the secretory capacity of a gland is damaged, maximal stimulation by the trophic hormone will give a diminished output
- synacthen (SYNthetic-ACTH-en) test for adrenal reserve, the healthy subject shows a normal response while the subject with primary hypoadrenalism (Addison's disease) demonstrates an impaired cortisol response to ACTH



Short tetracosactide (synacthen) test

- **Indication**
- Diagnosis of Addison's disease
- Screening test for ACTH deficiency
- **Procedure**
- Intravenous cannula for sampling
- Any time of day, but best at 0900 h; non-fasting
- Tetracosactide 250 µg, i.v. or i.m. at time 0
- Measure serum cortisol at time 0 and time +30 min
- **Normal response**
- 30 min cortisol > 600 nmol/L* (400-600 nmol/L borderline and may indicate deficiency)



Suppression test

- A patient with a hormone-producing tumour usually fails to show normal negative feedback
- A patient with Cushing's disease (excess pituitary ACTH) will thus fail to suppress ACTH and cortisol production when given a dose of synthetic steroid, in contrast to normal subjects
- a normal subject given dexamethasone 1 mg at midnight, cortisol is suppressed the following morning, while a subject with Cushing's disease shows inadequate suppression



Thank you

