Hypothalamic and pituitary disorders
Diseases of the adrenal cortex

Timea Balo MD
IIIrd Dept of Internal Medicine
23 Nov 2015
Oh, NO!
Monday again
Content

Pituitary
- Hyperpituitary syndromes
- Anterior pituitary insufficiency
- Diabetes insipidus

Adrenal cortex
- Cushing’s syndrome
- Addison’s disease
Pituitary diseases
Normal pituitary

- MR is the optimal imaging technique for evaluating the pituitary gland
- The coronal plane offers the best single view for assessing the sella and allows the pituitary gland to be distinguished from the surrounding structures
- Sagittal views are particularly helpful for evaluating midline structures
- Slice thicknesses must be 3 mm or less, and the field of view must cover only the sellar and immediate parasellar regions
The primary function of the pituitary gland is hormone production. It is considered as the "Master Gland" because it regulates growth, development, and reproduction.
Anterior pituitary

- Non-neural tissue
- Unlike the posterior pituitary it has no direct nervous connection with the hypothalamus
- The tropic hormones secreted by the neurosecretory cells of the hypothalamus reach the target cells of the anterior pituitary by the hypothalamic-pituitary portal system
Characteristics of hypothalamic releasing hormones

- Secretion in pulses
- Act on specific membrane receptors
- Transduce signals via second messengers
- Stimulate release of stored pituitary hormones
- Stimulate synthesis of pituitary hormones
- Stimulates hyperplasia and hypertrophy of target cells
- Regulates its own receptor
Hypothalamic-pituitary axis

Hypothalamus

Hypothalamic tropic hormone
PRH (dopamine)
PIH
TRH
CRH
GHRH
GHIH (somatostatin)
GnRH

Hypothalamic-pituitary portal vein

Anterior pituitary

Prolactin
TSH
ACTH
GH
LH
FSH

Endocrine cells

Systemic circulation

Breasts
Thyroid gland
Adrenal cortex
Liver
Cells throughout body
Gonads

TH
Cortisol
Insulin-like growth factors
Cells throughout body
Estrogens, progesterone
Androgens

© 2011 Pearson Education, Inc.
Modern classification of Adenohypophyseal cells

- **SOMATOTROPHS**
  - Secrete Growth Hormone

- **MAMMOTROPHS**
  - Secrete Prolactine

- **THYROTROPHS**
  - Secrete TSH

- **GONADOTROPHS**
  - FSH type: Secrete FSH
  - LH type: Secrete LH

- **CORTICOTROPHS**
  - Secrete ACTH and MSH
Function of the pituitary

- The output of the hypothalano-pituitary unit regulates the function of the thyroid, adrenal and reproductive glands and also controls somatic growth, lactation, milk secretion and water metabolism.
Regulation of hypothalamus
**Posterior pituitary**: neurohypophysis

- Posterior pituitary: an outgrowth of the hypothalamus composed of neural tissue.
- Hypothalamic neurons pass through the neural stalk and end in the posterior pituitary.

<table>
<thead>
<tr>
<th>Posterior Lobe <em>(Neurohypophysis)</em></th>
<th>Anterior Lobe <em>(Adenohypophysis)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Posterior Lobe Diagram" /></td>
<td><img src="image" alt="Anterior Lobe Diagram" /></td>
</tr>
</tbody>
</table>
Hyperpituitary syndromes
Pituitary tumors
How sellar masses present?

Symptoms of a Pituitary Tumor

- Blurred vision
- Double vision
- Loss of peripheral vision
- Sudden blindness
- Headaches
- Facial numbness
- Facial pain
- Dizziness
- Loss of consciousness
- Facial flushing
- Irritability
- Anxiety
- Depression
- Runny nose
- Affected hormones
- Nausea
- Weakness
- Unexplained weight loss or gain
- Feeling cold
- Feeling tired
- Muscle & bone weakness
- Hypertension
- Menstrual changes
- Erectile dysfunction
- Decreased interest in sex
Clinical manifestations

• Neurologic symptoms – visual defects leading to compression of the optic chiasm
  • Onset of the visual deficit
  • Headaches
  • Diplopia – oculomotor nerve compression – lateral extension
  • Pituitary apoplexia – sudden hemorrhage into the adenoma – headache
  • Cerebrospinal fluid rhinorrhea
Causes of sellar masses

- Pituitary adenoma – from the third decade; 10% of all intracranial neoplasms
- Other: physiologic enlargement of the pituitary, benign and malignant tumors

<table>
<thead>
<tr>
<th>Benign tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pituitary adenoma (most common sellar mass)</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
</tr>
<tr>
<td>Meningiomas</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pituitary hyperplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactotroph hyperplasia (during pregnancy)</td>
</tr>
<tr>
<td>Thyrotroph and gonadotroph hyperplasia</td>
</tr>
<tr>
<td>Somatotroph hyperplasia due to ectopic GHRH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Malignant tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
</tr>
<tr>
<td>Germ cell tumor (ectopic pinealoma)</td>
</tr>
<tr>
<td>Sarcoma</td>
</tr>
<tr>
<td>Chordoma</td>
</tr>
<tr>
<td>Pituitary carcinoma (rare)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
</tr>
<tr>
<td>Breast</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rathke’s cleft</td>
</tr>
<tr>
<td>Arachnoid</td>
</tr>
<tr>
<td>Dermoid</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pituitary abscess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphocytic hypophysitis</td>
</tr>
<tr>
<td>Carotid arteriovenous fistula</td>
</tr>
</tbody>
</table>
Classification

• By size and the cell of origin
  • < 1 cm: microadenomas
  • > 1 cm: macroadenomas
• The tumors can arise from any of cell of the anterior pituitary
• May result in increased secretion of hormone produced by the cell
• Decreased secretion of other hormones due to compression
Pituitary adenomas

• Gonadotroph adenomas - clinically nonfunctioning sellar masses

• Thyreotroph adenomas - can present clinically nonfunctioning, or may cause hyperthyreoidism

• Corticotroph adenomas – Cushing’s disease

• Lactotrophs – hyperprolactinaemia, which leads to hypogonadism in women and men

• Somatotrophs – acromegaly

• Sometimes mixed
Clinical manifestations II.

- **Hormone deficiencies** – detailed questions
- **Most common** – gonadotropins: hypogonadism
- **Hormone overproduction**
Evaluation of the pituitary incidentalomas

- Radiologic evaluation
- Hormonal evaluation
- Clinical evaluation
Radiologic evaluation: MRI

- Preferred imaging study for the pituitary
- Better visualization of soft tissues and vascular structures than CT
- No exposure to ionizing radiation
Hormonal evaluation

- May include both basal hormone measurement and dynamic stimulation testing
- All pituitary masses should have screening basal hormone measurements, including:
  - Prolactin
  - TSH, fT4
  - ACTH, midnight salivary cortisol
  - LH, FSH, estradiol or testosterone
  - Insulin-like growth factor 1 (IGF1)

Balance is the Key to Life
Clinical evaluation

• All patients with macroadenomas should have formal visual field testing

• In addition to radiographic and hormonal evaluation, patients should be asked and examined for any clinical signs suspicious for pituitary hyper-or hypofunction
Management of pituitary tumor

- Observation
- Pharmacotherapy
- Surgery
- Radiation therapy
Hyperprolactinaemia
Causes

- Prolactinoma
- Disruption of dopamine - pituitary stalk compression
- Primary hypothyroidism (increases TRH)
- Acromegaly
- Estrogen increase (pregnancy), lactation
- Liver cirrhosis
- PCOS
- Chest wall burns-neuronal effect like suckling
- Chronic renal failure
- Drugs (verapamil, H2 blockers, estrogens, opiates, dopamine receptor antagonists)
Prolactinomas

- Most common functional pituitary tumor
- 25-30% of all pituitary adenomas
- Annual incidence 3/100,000
- 10% are lactotroph and somatotroph such as GH producing
- Presents with amenorrhea and infertility
- Prolactinomas lose TRH response
- Microadenomas < 10 mm on MRI (90% of women)
- Macroadenomas > 10 mm (up to 60% of men)
Clinical Features

- Macroadenoma: neurological symptoms
- Amenorrhea (primer/sec)
- Galactorrhea (true galactorrhoea is uncommon in men)
- Infertility
- Osteoporosis (hypoestrogenaemia)
- Weight gain
- Mild hirsutism
Laboratory investigation

• Basal fasting morning PRL levels (norm: < 20 ug/L)

• Falsely elevated values may be caused by aggregated forms of circulating PRL, which are biologically inactive (macroprolactinaemia)

• Hypothyreoidism should be excluded
Treatment pregnancy not desired

- Treat only if symptomatic (headache, vision changes)
- Dopamin agonist (Bromocriptine, Cabergoline/Quinagolid)
- Not recommended for breastfeeding
- Transsphenoideal surgery if unsuccessful
Treatment pregnancy desired

- Therapeutic goals include control of hyperPRL, reduction of tumor size, restoration of menses and fertility, improvement of galactorrhoea
- Dopamine agonists (bromocriptine, cabergoline)
- If causing major visual defect and unresponsive, consider transsphenoidal surgery
- Bromocriptine until preg occurs, then stop
During pregnancy

- Microadenomas can significantly increase in size
- Visual field check 2-3 mos. MRI prn
- If neurologic symptoms occur during preg, usually about 14 wga, restart treatment

- If severe and unresponsive: 2nd trimester consider surgery

: 3rd trimester: Wait until pp
GH overproduction

Adults: Acromegaly
Infants: Gigantism
Acromegaly

- A disorder caused by excess production of GH

- Is rare with prevalence of 36-96 / million

- The onset is insidious and very slow leading to delay in diagnosis by mean of 9 years

- Reduced overall survival by an average of 10 years
Facial dysmorphia
ABC of Acromegaly

- A: Arthropathy
- B: Big Boggy Hands
- C: Carpal Tunnel Syndrome
- D: Diabetes Mellitus
- E: Enlarged Tongue - Heart (Cardiomegaly) - Throat
- F: Field defect on vision (Bitemporal Hemianopia)
ABC of Acromegaly II.

G: Gynecomastia, Galactorrhoea, Greasy skin

- H: Hypertension: 20-50% of cases
- I: Increasing size of shoes, hats, gloves, dentures, rings
- J: Jaw enlarged: prognatism
- K: Kyphosis: Vertebral deformity
Co-morbid conditions associated with acromegaly

- Dysmorphic syndrome
- Cardiomyopathy
- Hypertension
- Colon cancer
- QoL
- Diabetes mellitus
- Arthropathy

Chanon et al. Best Pract Res Endocrinol Metab 2009
Giustina et al Nat Rev Endocrinol 2013
Cushing’s Disease
Clinical Features

• Weigh gain, muscle weakness, loss of scalp hair, backache, fractures, menstrual irregularity, hirsutism
• Truncal obesity with thin limbs
• Rounded plethoric face
• Dorsocervical and supraclavicular fat pad (Buffalo’s hump)
• Hirsutism
Clinical features II.

• Skin:
  – Atrophied, thin cigarette paper-like
  – Easy bruising
  – Purplish abdominal striae
  – Hyperpigmentation
  – Fungal infection of skin and nails

• Myopathy

• Hypertension

• Diabetes mellitus

• Osteoporosis

• Hypogonadism
Diagnosis

- Urinary free cortisol
- ACTH
- Serum Cortisol (08:00 and 22:00)
- Dexamethasone Suppression Test
- MRI pituitary
- Inferior petrosal sinus sampling

![Graph showing normal diurnal cortisol range and examples of abnormal cortisol levels in Cushing's syndrome.](image)
Nonfunctioning and gonadotropin producing adenomas

- Secrete little or no pituitary hormones
- Macroadenomas with mass effect
- Most common pituitary tumors
- Originate from gonadotrop cells (immunohistochemistry)
- Produce intact gonadotropins, and LH-FSH β subunits
- hypogonadism
- Menstrual disturbances
TSH secreting adenoma

- Macroadenomas
- Rare but often large and locally invasiv
- Patients present with thyroid goiter and hyperthyroidism
- Dg: MRI, ↑TSH, T4
- **Treatment**: debulk the tumor mass, thyroid ablation, or antithyroid drugs
- Dopamine agonists are rarely effective
- Somatostatin analogue treatment
Hypopituitarism

Deficiency of one or more hormone produced by anterior lobe of pituitary
Hypopituitarism

- A disorder in which the pituitary gland fails to produce one or more of its hormones partially or completely.
- Inherited or acquired
- Reflects the mass effect of tumours, consequences of inflammation or vascular damage
- Prevalence is 45.5 per 100,000
Etiology

- Development/structural
- Tumors
- Trauma (surgical, radiation, head injuries)
- Infarction
  - Sheehan Syndrome
  - Pituitary apoplexy
- Autoimmune
- Infiltration and infection
Clinical Features

Major Clinical Manifestations of Hypopituitarism

- Pituitary necrosis
- Pallor (↓ MSH)
- Hypothyroidism (↓ TSH)
- Failure of lactation (↓ prolactin)
- Adrenal insufficiency (↓ ACTH)
- Ovarian failure with amenorrhea (↓ FSH, LH)
ACTH deficiency

- Pituitary ACTH deficiency causes secondary adrenal insufficiency
- Fatigue, weakness, anorexia, nausea, vomiting, hypoglycaemia
- Not accompanied with pigmentation changes or mineralocorticoid deficiency
- Isolated ACTH def. can occur after removal of an ACTH prod adenoma
- Mass effect of other pituitary tumors (usually in comb with other pituitary deficiencies)
- **Lab:** low basal cortisol, ACTH stimulation, CRH and metyrapone tests
TSH deficiency

- Features like in primer hypothyroidism, but less severe
- Cold intolerance, constipation, somnolence, fatigue, lethargy, weight gain, impaired memory, deafness, menstrual abnormalities
- Low basal TSH, low T4
- **TRH test:** Iv 200 ug TRH causes a 2-3x increase in TSH within 30 min
- Thyroid replacement therapy should be initiated after establishing adequate adrenal function
Gonadotropin deficiency

- Hypogonadotropic hypogonadism
- Common presenting feature of hyperprolactinaemia
- Inherited and acquired disorders
- Acquired forms of GnRH deficiency are seen in anorexia nervosa, stress, extreme exercise, can be idiopathic
- Women: amenorrhoea, infertility, breast atrophy, decreased libido
- Men: secondary testicular failure, infertility, decreased muscle mass, osteoporosis

Hypopituitarism:
- Infertility
- Pallor
- Low BMR
- Intolerance to stress
GH Deficiency

- Short stature and delayed puberty in children
- Increased abdominal obesity
- Fatigue
- Reduced muscle mass
- **Diagnosis**: screening with IGF-1
- Stimulation of pituitary with -ITT, CRH, ACTH test
- 2 positive tests are necessary for diagnosis
Hormon substitution

- Corticosteroid therapy – hydrocortison
- Thyroid hormone substitution – levothyroxine
- Sex hormone – testosteron, BUT! Improve fertility with HCG+FSH
- GH substitution (???)
Diabetes insipidus

- Central: Lack of ADH hormone
- Posterior pituitary is composed of nerve fibers, that have their cell bodies in the supraoptic and paraventricular nuclei of the hypothalamus

- The neurosecretory cells produce oxytocin, and vasopressin, which pass down to be stored in and released in the posterior pituitary
Regulation of ADH secretion

ADH release is stimulated by:

• Plasma osmolality > 280 mosm/kg
• A fall in plasma volume
• Emotional factors and stress
• Sleep
• Other factors
Symptoms

Polyuria

Nocturia

Dehydration
Diagnosis

- Electolytes
- BUN, kreatinin
- Plasma/urin osmolality
- Glucose, calcium
- 24 hour urin sample
- Hypophysis screen (TSH, fT4, PRL, cortisol, IGF1, FSH/LH)
- Visual field
- MRI
Specific gravity

A: Urine

When urine is diluted (1005) the bobber falls down, when it is concentrated (1030) it exceeds the lifting force is proportional to the urine’s specific gravity.
Specific gravity

- Morning urine: $>1022$; Osm $> 800$ mosm/l - normal
- Water deprivation test: in every hour Se Na$^+$ and osmolality, urine osm
- Physiologic response: urine osm $> 600$ m osm/l
- ADH deficiency: Urine osm: no change, Se osm: increase
- STOP: if body weight decreases by 3%
Water Deprivation Test

- Urine osmolality increases to 500 mOsm/L
  - Psychogenic polydipsia

- Urine osmolality doesn't change by much
  - Diabetes insipidus
    - Increase in urine osmolality upon desmopressin administration
      - Central diabetes insipidus
    - No change in urine osmolality upon desmopressin administration
      - Nephrogenic diabetes insipidus
Causes of central diabetes insipidus

• Idiopathic
• Head injury, brain operation
• Neoplasia: hypophysis tumor, craniopharyngeoma, dysgerminoma, metastasis
• Infectious diseases: meningitis, encephalitis
• Granulomatous diseases: sarcoidosis, histiocytosis X
• Vascular: Sheehan sy, aneurysma, sickle cell anaemia
• Drugs: naloxon, ethanol, phenytoin
Treatment

• Treat the underlying cause

• ddAVP nasal spray (desmopressin, a synthetic analogue, more potent, long duration of action 8-10 hrs)
The adrenal cortex
The Adrenal Gland
Zona glomerulosa-function

- The cells secrete **mineralcorticoids**, mainly aldosterone
- It’s essential for life
- Promotes sodium retention and potassium elimination by the kidney
- Expands ECF volume
Regulation of Aldosterone Secretion
Zona fasciculata-function

• Cells secrete **glucocorticoids** (important in lipid, protein and carbohydrate metabolism).

• The daily secretion of cortisol ranges between 40 and 80 umol (15-30 mg) with a pronounced circadian cycle.

• Free cortisol, protein bound cortisol, and cortisol metabolites
Glucocorticoid synthesis

1. Cholesterol → P450scc → Pregnenolone
2. Pregnenolone → P45017α → Progesterone
3. Progesterone → 3βHSD → Deoxytocorticosterone
4. Deoxytocorticosterone → P450c21 → Corticosterone
5. Corticosterone → P450aldo → 18-O-Corticosterone
6. 18-O-Corticosterone → Aldosterone
7. Progesterone → 3βHSD → Androstenedione
8. Androstenedione → P450arom → Estrone
9. Estrone → 17βHSD → Testosterone
10. Testosterone → P450arom → Estradiol

ADRENAL CORTEX

GONADS
Glucocorticoid physiology

- Enhance the production of glucose
- The effect is mediated by the GC receptor
- Raise blood glucose levels
- Protein catabolism (increased protein breakdown, and nitrogen excretion)
- GCs regulate fatty acid mobilization
- Anti-inflammatory effect
- Cortisol levels respond within minutes to stress
- Cortisol has major effect on body water (water goes into cells)
Cortisol: Role in Diseases and Medication

• Use as immunosuppressant
  – Hyperimmune reactions (bee stings)
  – Serious side effects
• Hypercortisolism (Cushing's syndrome)
  – Tumors (pituitary or adrenal)
  – Iatrogenic (physician caused)
• Hypocortisolism (Addison's disease)
Zona reticularis

- The major androgen secreted by the adrenal is dehydroepiandrosterone (DHEA) and its sulfuric acid ester (DHEAS)
- Approximately 15-30 mg of these compounds are secreted daily
- Smaller amounts of androstendion, 11-β-OH androstendione and testosterone are secreted.
- DHEA is the major precursor of urinary 17-ketosteroids
Androgen synthesis
Basic principles in the laboratory evaluation of adrenocortical function
Measurement of the adrenal steroids

**When?** Basal results (in the morning, fasting)  
Values after stimulation (specific endocrine tests)

**From what?**
- **Blood**: whole amount, annoying effect of the binding proteins
- **Urine**: random or collected
- **Saliva**: free fraction, easy implementation

**How?** Sensitivity and specificity depending upon the method
- Electrochemiluminescent immunoassay (ECLIA)
- Radioimmunoassay

**Evaluation**
Parameters to consider: diurnal rhythm, age and gender, effects of medication
Patient as a source of imprecision

Physiological states which influence hormone assays

- age
- pregnancy
- menstruation cycle (LH, FSH, E2, P ....)
- nutrition
- daily rythm of hormones (eg. cortisol, PRL...)
- stress (eg. renin activity, catecholamines)
Hyperfunction of the adrenal cortex

• Excess cortisol: Cushing’s syndrome
• Excess aldosterone: Hyperaldosteronism (Conn’s syndrome)
• Excess adrenal androgens: Adrenal virilism

• These syndromes do not always occur in pure form but may have overlapping features
Harvey Williams Cushing (1869-1939)
Cushing’s syndrome

Harvey Cushing
Etiology

• Exogenous steroids – commonest cause

• ACTH dependent - 80-90%
  Pituitary 80%, ectopic 20%

• ACTH independent - 10-20%
Common causes of ectopic ACTH secretion

- Small cell lung cancer 50%
- Endocrine tumors of foregut origin 35%
  - Thymic carcinoid
  - Islet cell tumor
  - Medullary thyroid carcinoma
  - Bronchial carcinoid
- Phaeocromocytoma 5%
- Ovarian tumors 2%
Symptoms and signs
FIG. 1. Algorithm for testing patients suspected of having Cushing's syndrome (CS)

Cushing's syndrome suspected (consider endocrinologist consultation)

Exclude exogenous glucocorticoid exposure

Perform one of the following tests:
- 24-h UFC (≥ 2 tests)
- Overnight 1-mg DST
- Late night salivary cortisol (≥ 2 tests)

Consider caveats for each test (see text)
Use 48-h, 2-mg DST in certain populations (see text)

ANY ABNORMAL RESULT
- Normal (CS unlikely)

Exclude physiologic causes of hypercortisolism (Table 2)
Consult endocrinologist

Perform 1 or 2 other studies shown above:
- Suggest consider or repeating the abnormal study
- Suggest Dex-CRH or midnight serum cortisol in certain populations (see text)

Discrepant (Suggest additional evaluation)

ABNORMAL
- Normal (CS unlikely)
- Cushing's syndrome

Treatment of Cushing’s syndrome

Ideal therapy of Cushing's syndrome would achieve the following goals:

• Reverse the clinical manifestations by reducing cortisol secretion to normal
• Eradicate any tumor threatening the health of the patient
• Avoid permanent dependence upon medications
• Avoid permanent hormone deficiency
Conn - syndrome

Prof. Jerome W. Conn (1907-1981)
Primary aldosteronism – causes

- Unilateral adenoma (small, may occur on either side)
- Bilateral cortical nodular hyperplasia = idiopathic hyperaldosteronism (the cause is unknown)
- Adrenal carcinoma - rarely
Signs and symptoms

• Progressive depletion of potassium, development of hypokalemia

• Diastolic hypertension, headaches

• Hypertension is due to the increased sodium reabsorption and extracellular volume expansion
Signs and symptoms

- EKG, X-ray: left ventricular enlargement

- EKG (low potassium): prominent U waves, cardiac arrhythmias, premature contractions

- In the absence of associated congestive heart failure, renal disease or preexisting abnormalities (thrombophlebitis) edema is absent
Complications

- Structural damage to the cerebral circulation, retinal vasculature and kidney
- Proteinuria may occur in 50% of patients
- Renal failure occurs in up to 15%
- Probably excess aldosterone production induces cardiovascular damage independent of its effect on blood pressure
When to screen aldosteronism?

- Hypertension and hypokalemia
- Hypertension and adrenal tumor
- Resistant hypertension (20% incidence)
- Onset of hypertension < 20 years of age
- Severe hypertension (> 160/100 mmHg)
- Whenever considering secondary hypertension
Adrenocortical hypofunction

- 1. Primary inability of the adrenal to elaborate sufficient quantities of hormones
- 2. Secondary failure due to inadequate ACTH formation or release
Addison’s disease

ADDISON’S DISEASE

- Bronze Pigmentation of Skin
- Changes in Distribution of Body Hair
- GI Disturbances
- Weakness

Adrenal Crisis:
- Profound Fatigue
- Dehydration
- Vascular Collapse (↓BP)
- Renal Shut Down
- ↓Serum Na
- ↑Serum K

Hypoglycemia
Postural Hypotension
Weight Loss
Thomas Addison (1793-1860)

- Adrenocortical deficiency and pernicious anaemia (1849): ‘Anaemia-disease of the suprarenal capsule in which the disease is not distinctly separated from a new form of anaemia’
- In Addison's day tbc was found at autopsy in 70-90% of cases.
Etiology and pathogenesis

• **Incidence:** acquired forms-rare, secondary: relatively common
• **Etiology:** progressive destruction of the adrenals > 90%
• Chronic granulomatosus diseases (tbc, histoplasmosis, cryptococcocosis, coccidioidomycosis)
• **Idiopathic atrophy-autoimmun mechanism**
• Rarely: adrenoleukodystrophy, haemorrhage, tumor metastases, HIV, CMV, amyloidosis, sarcoidosis, familiar adrenal insufficiency
Primary adrenal insufficiency

• Loss of all three types of adrenal steroids
• 90% of glands must be destroyed to manifest clinically
  - high functional reserve
Signs and symptoms

**Symptoms:**
- Fatigue, lassitude, malaise, weakness, anorexia
- Postural dizziness, syncope
- Gastrointestinal Symptoms
  - Nausea
  - Vomiting
  - Abdominal Pain
  - Diarrhea
  - Constipation
- Myalgias, arthralgias, rarely flexion contractures
- Decreased libido, amenorrhea

**Signs:**
- Weight loss
- Hyperpigmentation
- Hypotension
- Thinning of axillary and pubic hair
- Vitiligo
Addison’s Disease
Waterhouse- Friedrichsen syndrome

- bleeding into the gland
- Severe infection with meningococcus bacteria
- It can be caused by procoagulants
- Other causes: low platelet count, primary anti- phospholipid syndrome, renal vein thrombosis, steroid use
Diagnosis

• ACTH stimulation
  250 ug Synacthen iv – cortisol response 60 min after.
  Cortisol level should exceed 495 nmol/l (18 ug/dl)
If the response is abnormal, measure aldosterone levels (in secondary aldosterone increasement will be normal > 5 ng/dl)
Treatment

• Specific hormone replacement
• Careful education about the disease
• **Cortizol** 20-30 mg/d (it should be taken with meals)
• **Fludrocortizone** 0.05-0.1 mg/d
• Patient should be instructed to maintain an ample intake of sodium (3-4 g/d)
• Control blood pressure and serum electrolytes
The lecture ended.