ADRENAL GLAND (PART2)

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AGENDA:

- 1-ADRENAL INSUFFICIENCY
- 2-PHEOCHROMOCYTOMA

ADRENAL INSUFFICIENCY

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- Primary Adrenal Insufficiency is also known as Addison's Disease in honor of Dr. Thomas Addison
- Dr. Addison is also credited with the discovery of Pernicious Anemia
- **Addison's disease** is serious chronic disease, caused by partial or absolute abnormality of hormonal function of the adrenal cortex due to its two-sided disorder (first it was described by Tomas Addison in 1855).

EPIDEMIOLOGY

- *Addison's disease is a rare and chronic disease.*

6-110 cases diagnosed per 100,000 in the world per year.

1.4 million deaths per year around the world.

Usually effects 30-50 year-olds, but can be seen in all ages.

ADRENAL INSUFFICIENCY

- Arises when cortisol levels are not sufficient to meet the needs of the body
- May be primary or secondary
- May be congenital or acquired
- It develops at the age of 20-40 years old
- Can be fatal if left untreated

PRIMARY ADRENAL INSUFFICIENCY (HIGH ACTH) (ADDISON'S DISEASE)

- AUTOIMMUNE:
- ISOLATED AUTOIMMUNE ADRENALITIS (30- 40%)
- POLYGLANDULAR SYNDROME 1 &2 (60- 70%)
- INFECTION:TB, HIV, CMV, CRYPTOCOCCOSIS, HISTOPLASMOSIS, COCCIDIOIDOMYCOSIS
- AIDS
- METASTASES
- BILATERAL ADRENALECTOMY

CONT.

Secondary (low ACTH)

- *Hypothalamic or pituitary disease:*

- Chronic glucocorticoid excess (endogenous or exogenous)
- Pituitary tumors (active and inactive adenomas, carcinoma)
- Mass lesions affecting the hypothalamic-pituitary region: Craniopharyngioma meningioma, metastases
- Pituitary irradiation
- Autoimmune hypophysitis
- Pituitary apoplexy/hemorrhage
- Pituitary infiltration (TB, actinomycosis, sarcoidosis, histiocytosis X, Wegener's granulomatosis, metastases

ETIOLOGY

- Most commonly is of an autoimmune etiology, resulting from chronic destruction of the adrenal cortex
- Typical histologic feature is lymphocytic infiltration
- Antibodies to adrenal cortical antigens are present early in the disease process
- Patients with autoimmune adrenal disease are more likely to have polyglandular autoimmune systems causing deficiency of other endocrine glands

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- Several Other Mechanisms Exist:
  - Bilateral adrenal hemorrhage
  - Infection: Tuberculosis, CMV, Histoplasmosis,syphylis
  - Metastatic Disease
  - Deposition Diseases: Hemochromatosis, Amyloidosis, Sarcoidosis
  - Drug Induced: Ketoconazole, Etomidate, Rifampin, Anticonvulsants
  - Congenital Adrenal Hyperplasias

❖ idiopathic atrophy of adrenal cortex (antigens to mitochondrion and microsomal fraction);

❖ adrenal glands hemorrhage;

SECONDARY ADRENAL INSUFFICIENCY

- Caused by pituitary failure of ACTH secretion
- Etiologies include:
  - any cause of primary or secondary hypopituitarism
  - Exogenous Glucocorticoid Therapy
  - Megestrol, which has some glucocorticoid therapy

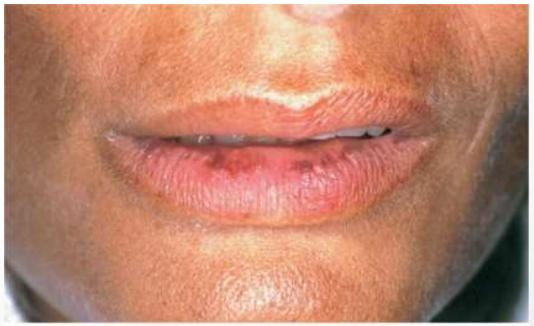
THE PATHOGENESIS

The deficiency of clucocorticoids leads to adynamia, the cardiovascular and gastrointestinal disorders:

- the sugar level in the blood is decreased;
- the development of eosinophilia, leukocytosis, and granulopenia;
- hyponatremia, hypochloremia, hyperkaliemia, which lead to dehydration and hypotonia;
- the decreasing of sex hormones production leads to the impotence in male, or the menstrual cycle disorder in female;
- the bronze color of the skin is caused by the melanin pigment deposit in the papillary layer of the dermis and mucous membranes.

CLINICAL PRESENTATION

- Symptoms may include weakness, weight loss, nausea, vomiting, anorexia, and postural hypotension,Hyperpigmentation,Hypotension,Orthostatic changes,Weak pulses,Shock
- Loss of axillary/pubic hair (women)
- Increased skin pigmentation can be seen with primary adrenal insufficiency secondary to melanocyte stimulating activity associated with ACTH
- Hyponatremia and Hyperkalemia may develop secondary to a lack of aldosterone



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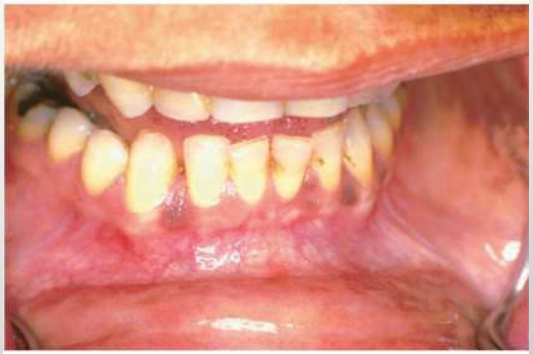

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LABORATORY DIAGNOSTICS

- In the blood analysis: lymphocytosis, eosinophilia, erythrocyte sedimentation rate is decreased, when the active tuberculosis is present this rate is increased;
- The electrolyte: hyponatremia, hypochloremia, hyperkaliemia;
- Baseline Cortisol and ACTH levels should be obtained in the early morning
- The content of ACTH is increased;
- The content of cortisol is decreased;
- The concentration of glucose in the blood is decreased;
- The glucose tolerance test – flat with marked hypoglycemic phase in three hours;
- The potassium flow with urine is decreased, the natrium and chlorine flow is increased.

PRIMARY ADRENAL INSUFFICIENCY: LABORATORY FINDINGS

- Hyponatremia
- Hyperkalemia
- Hypoglycemia
- Narrow cardiac silhouette on CXR
- Low voltage EKG

TREATMENT

- Replacement (always need glucocorticoids and usually mineralcorticoid therapy)
- Hydrocortison orally 15 mg at morning and 5 mg at evening
- Doses change according to lifestyle:

- doubling the routine oral dose in the case of intercurrent illness with fever
- IV hydrocortisone injection at a daily dose of 100 mg in cases of prolonged vomiting, surgery, or trauma

- Have to carry emergency injection of hydrocortisone and card/bracelet indentifying their condition

CONT..

- Mineralocorticoid replacement in primary AI (100–150 g fludrocortisone). The adequacy of treatment can be evaluated by measuring BP, sitting and standing to detect a postural drop indicative of hypovolemia, serum Na, k, and plasma renin should be measured regularly.
- Adrenal androgen replacement is an option in patients with lack of energy, and in women with loss of libido.

- It can be achieved by once-daily administration of 25–50 mg DHEA. Treatment is monitored by measurement of DHEAS, androstenedione, testosterone.

Special precautions

- During intercurrent illness,trauma,surgery, esp in fever, the dose of hydrocortisone should be doubled

- Increase the dose of fludrocortisone and to add salt in strenuous exercise with sweating, extremely hot weather, gastrointestinal upsets such as diarrhea

- Pts receiving long term steroid therapy have two deficits

1.adrenal atrophy secondary to the loss of endogenous ACTH

2.failure of pituitary ACTH release have low blood cortisol, ACTH levels, and abnormal ACTH stimulation test

COMPLICATIONS

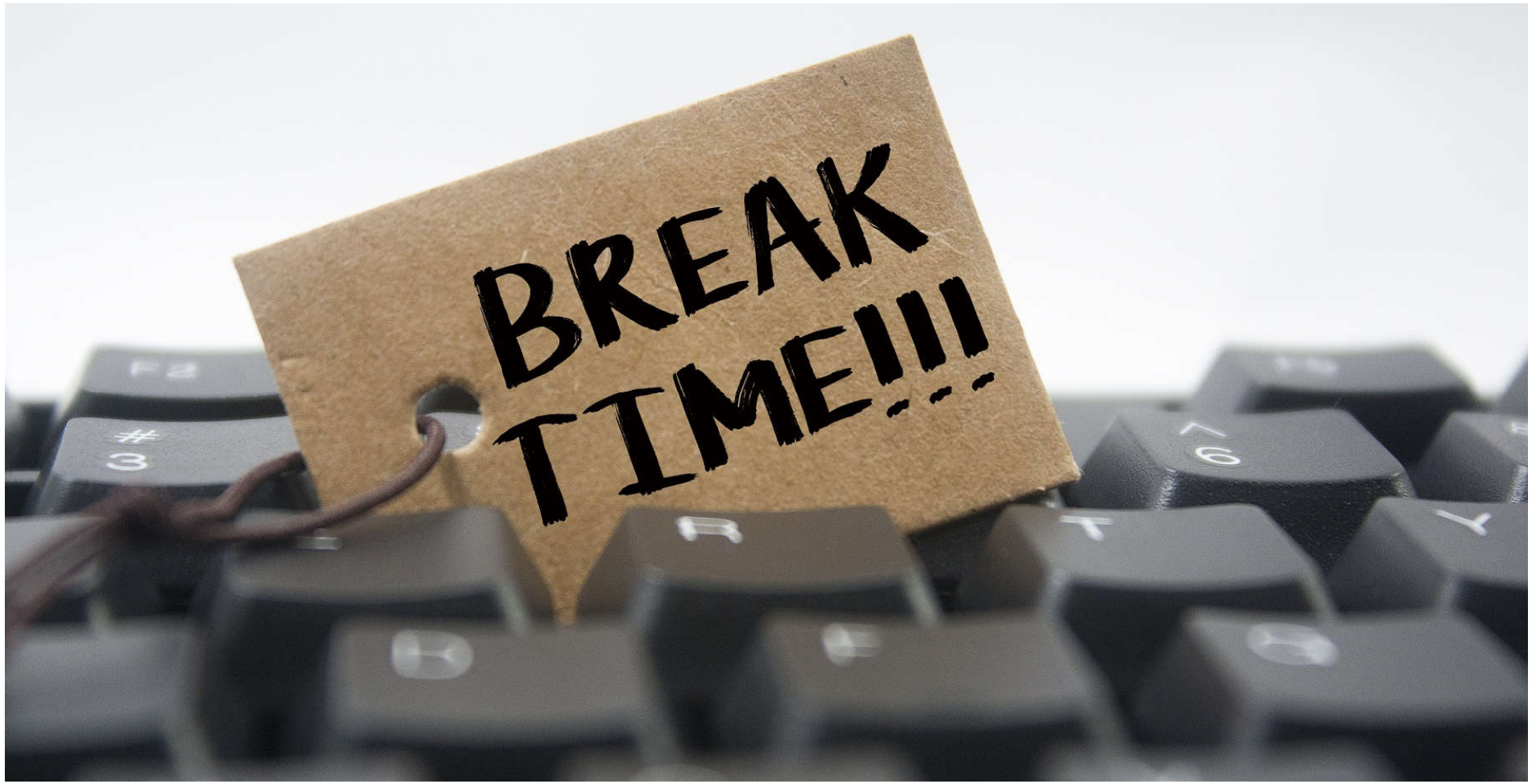
- Gastritis
- hypokalemia,
- sodium retention lead to hypertension,cardiac enlargement, and even congestive heart failure
- So Periodic measurements of body weight,serum potassium level, and blood pressure

ADDSONIAN CRISIS

- **Addisonian Crisis:**
  - Severely low blood pressure (shock)
  - Hyperkalemia
  - Hyponatremia
  - Hypoglycemia
  - Hypercalcemia
  - Unexplained fever, diarrhea, vomiting
  - Coma and death
  - Precipitated by infection, surgery or intercurrent disease

MANAGEMENT

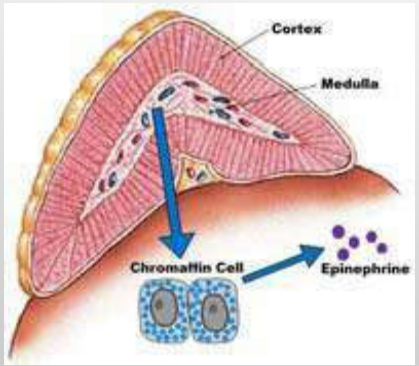
- It is a medical emergency
- IV fluid (normal saline 1 L/h with continuous cardiac monitoring and 10% dextrose)
- Hydrocortisone 100 mg bolus followed by 100–200 mg hydrocortisone over 24 h infusion or i.v doses until GI symptoms improve then start oral therapy
- Mineralocorticoid replacement can be initiated once the daily hydrocortisone dose has been reduced to <50 mg
- Treat precipitating cause


BREAK
TIME!!!

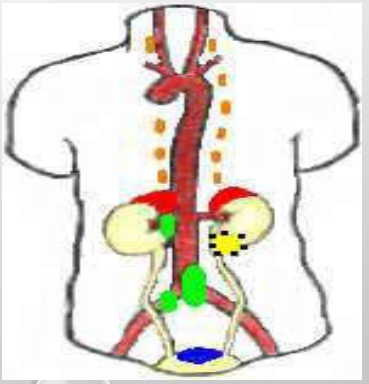
PHEOCHROMOCYTOMA

PHEOCHROMOCYTOMA

- Is a are neuroendocrine tumor of the medulla of the adrenal glands (originating in the chromaffin cells), or extra-adrenal chromaffin tissue that secretes excessive amounts of Catecholomines (epinephrine and norepinephrine) --hormones that regulate heart rate and bloodpressure



- May occur as a single tumor or as more than one growth. It usually develops in the center (medulla) of one or both adrenal glands.
- Sometimes this kind of tumor occurs outside the adrenal gland but 90% are in the adrenal glands .The extramedulary sites are;
- Within the sympathetic nervechain along the spinal cord
- Overlying the distal aorta
- Within the ureter
- Within the urinary bladder



FACTORS ASSOCIATED WITH PHEOCHROMOCYTOMA INCLUDES:

- A family history of pheochromocytoma
- Tumors in other glands of the body
- Other hormonal disorders
- Genetic diseases including:
    - Von Hippel-Lindau disease
    - Multiple endocrine neoplasia type 2
    - Neurofibromatosis type 1
    - Paraganglioma syndromes

ADRENERGIC RECEPTORS

- Alpha-Adrenergic Receptors
  - α_1: vasoconstriction, intestinal relaxation, uterine contraction, pupillary dilation
  - α_2: ↓ presynaptic NE (clonidine), platelet aggregation, vasoconstriction, ↓ insulin secretion
- Beta-Adrenergic Receptors
  - β_1: ↑ HR/contractility, ↑ lipolysis, ↑ renin secretion
  - β_2: vasodilation, bronchodilation, ↑ glycogenolysis
  - β_3: ↑ lipolysis, ↑ brown fat thermogenesis

SIGNS &SYMPTOMS

- The five P's:
  - Pressure (HTN) 90%
  - Pain (Headache) 80%
  - Perspiration 71%
  - Palpitation 64%
  - Pallor 42%
    - Paroxysms (the sixth P!)
- The Classical Triad:
  - Pain (Headache), Perspiration, Palpitations
  - Lack of all 3 virtually excluded diagnosis of pheo in a series of > 21,0000 patients

SIGNS & SYMPTOMS

- N/V, abdo pain, severe constipation (megacolon)
- Chest-pains
    - Anxiety
    - Angina/MI with normal coronaries:
        - Catecholamine induced: ↑ myocardial oxygen consumption or coronary vasospasm
- CHF
    - HTN → hypertrophic cardiomyopathy → diastolic dysfn.
    - Catechols induce dilated cardiomyopathy → systolic dysfn.
- Cardiac dysrhythmia & conduction defects
- Postural hypotension,Lypolisis[VLDL synthesis]

CONT

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- Hyperglycemia
- Tachycardia
- Anxiety
- Chest pain
- Palpitations
- Refractory hypertension
- Abdominal pain
- Increased appetite
- Weight loss

‘RULE OF 10’

- 10% extra-adrenal (closer to 15%)
- 10% occur in children
- 10% familial (closer to 20%)
- 10% bilateral or multiple (more if familial)
- 10% recur (more if extra-adrenal)
- 10% malignant
- 10% discovered incidentally

EXAMS AND TESTS

- **24 hr Urine Sample**
- **Plasma levels of Catecholamines**
- **Glucose test**
- **Adrenal biopsy**
- **Abdominal CT scan**
- **MRI of abdomen**
- **ultrasonography**

TREATMENT

PHARMACOLOGIC THERAPY

- **Decrease BP:**
  - Alpha-adrenergic blocking agents.-eg. Phentolamine (Regitine)
  - Smooth muscle relaxants.-eg. Na nitroprusside (Nipride
- **Before and During Surgery:**

  Long-acting alphablocker.-Phenoxybenzamine

  Ca Channel Blockers.-Nifedipine

  Beta-adrenergic blocking agents.-Propranolol

  Cathecholamine synths. inhibitors.-Methyrosine

SURGICAL MANAGEMENT

- Adrenalectomy

PROGNOSIS

- **•1/3 Patients continue to be hypertensive:**

1)Not all tissue removed

2)Recurrence

3)Blood vessels damaged by severe & prolonged hypertension

- The tumors come back in less than 10% of these patients.
- Release of the hormones norepinephrine and epinephrine returns to normal after surgery.
- Less than 50% of patients who have cancerous tumors that spread to the bones, liver, or lung are alive after 5 years.

ASSESSMENTS

- Blood sugar

- Hypoglycemia (after surgery)

- Hyperglycemia (before and during surgery)

- Blood pressure

- Hypertension (before and during surgery)

- Hypotension (after surgery)

THANK YOU