



המרכז הרפואי לגליל
קטואה מקצועית ואנושית

Cushing Syndrome

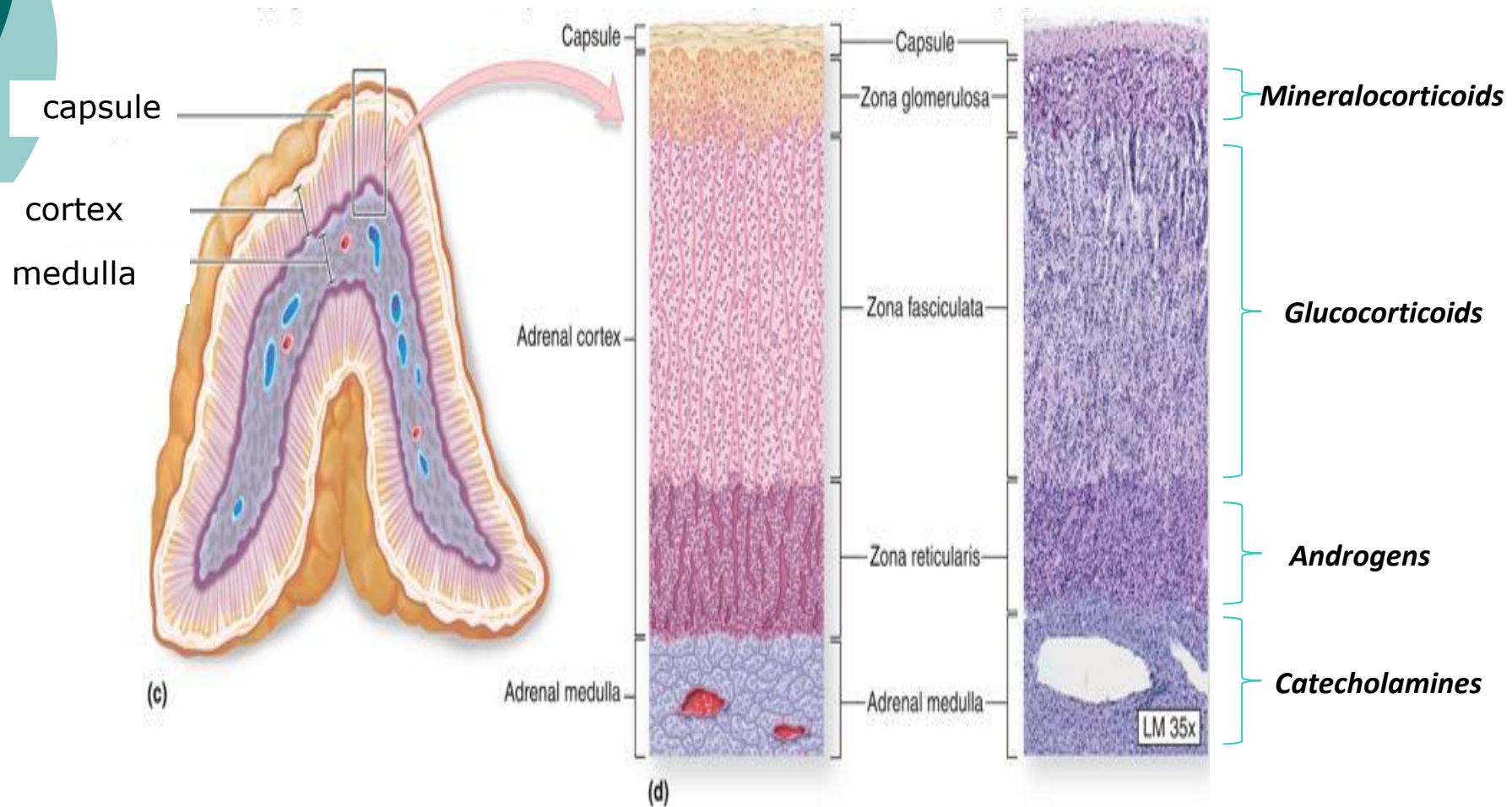
Dr. Nodelman Marina

Cushing Syndrome

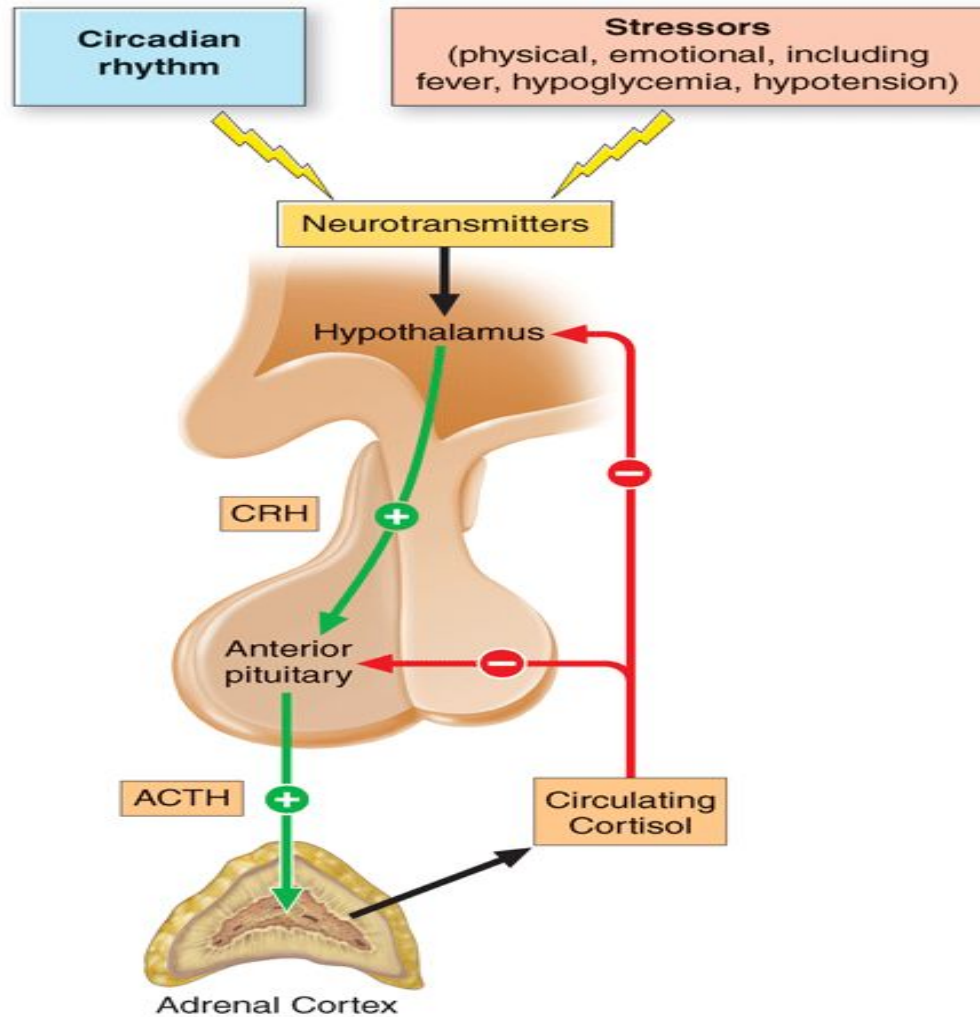
Cushing's syndrome is a collection of signs and symptoms due to prolonged exposure to cortisol

In pituitary Cushing's, a benign pituitary adenoma secretes ACTH. This is also known as **Cushing's disease** and is responsible for 70% of endogenous Cushing's syndrome.

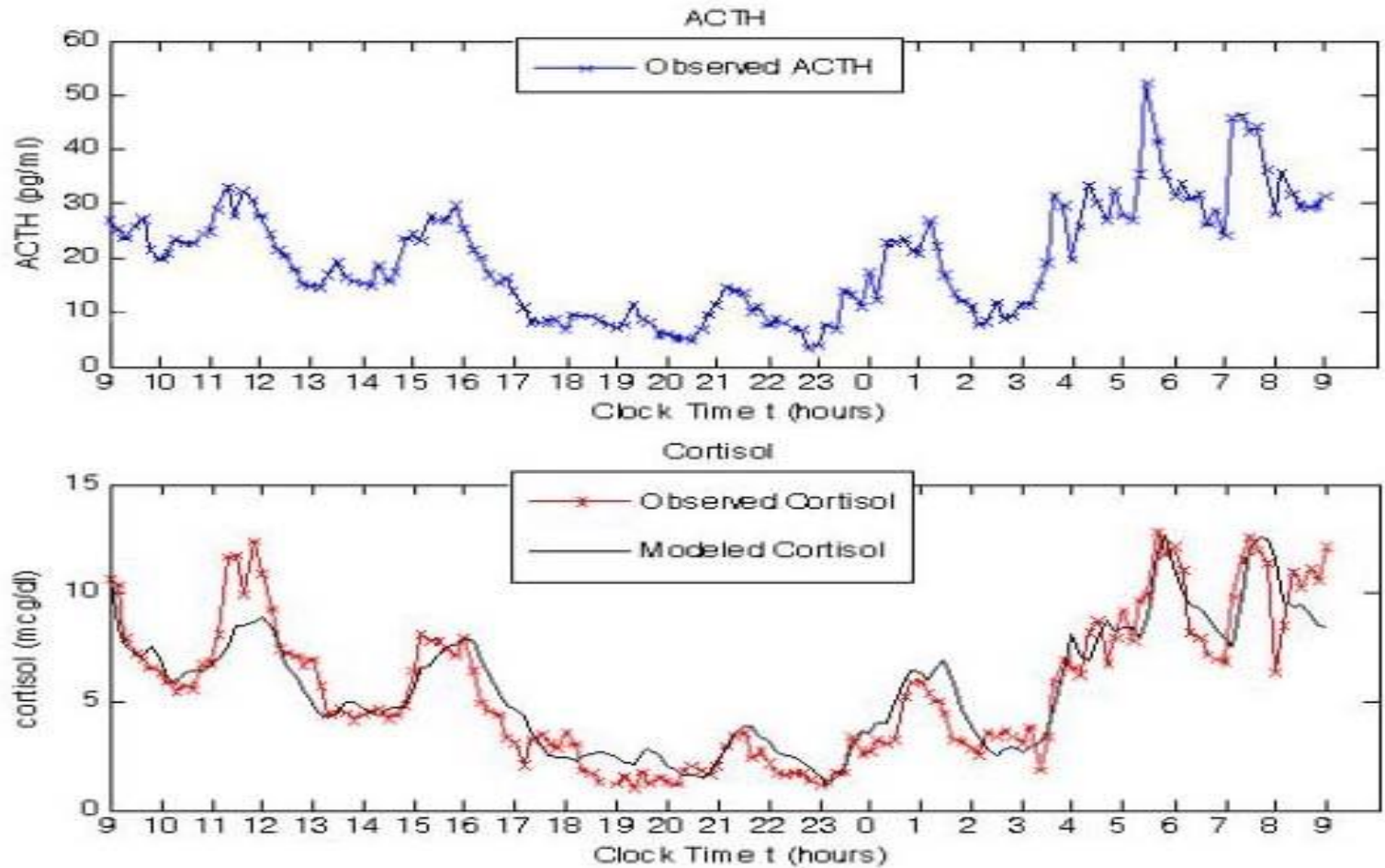
Adrenal gland anatomy



Hypothalamic pituitary adrenal axis



Circadian rhythm of cortisol secretion



Classification of Cushing syndrome

endogenous

exogenous

ACTH dependent

ACTH independent

80%

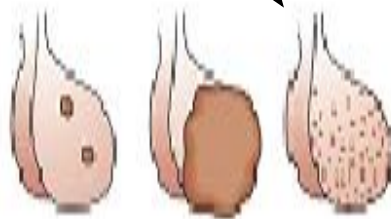
20%



ectopic

20%

SCCA
Carcinoid
Pancreatic Ca
Medullary Ca of thyroid
Pheochromocytoma



central

80%



adenoma

60%



carcinoma

40%



rare

2%

Macronodular adrenal hyperplasia
PPNAD
McCune-Albright

Epidemiology

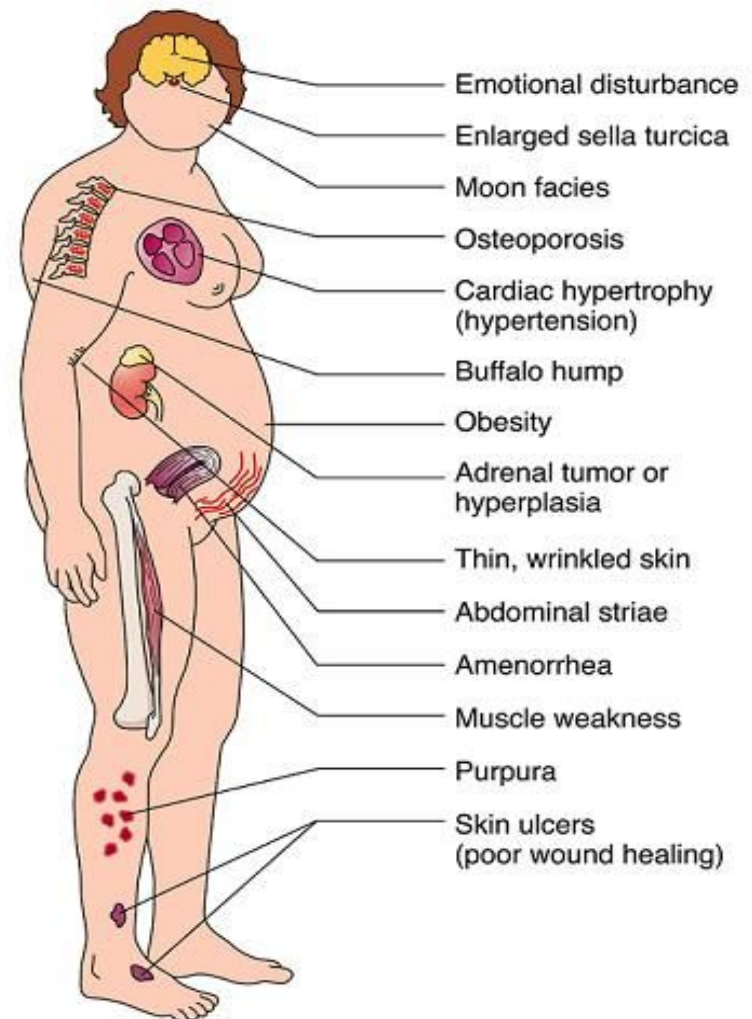
- Rare endocrine disorder 2.3/1,000,000/year
- Cushing's dis. 1.5/1,000,000/year, women >> men, 25-45
- Adrenal adenoma 0.6/1,000,000/year, women >> men
- Adrenal carcinoma 0.2/1,000,000/year, 50% Cushing syndr. in children
- Ectopic Cushing, 1% SSICA, men > women, after 50

Clinical picture

Presenting Symptoms & Signs of Cushing's Syndrome

Symptom	Frequency %
Weight Gain	90
Growth Retardation	83
Menstrual Irregularities	81
Hirsutism	81
Obesity (BMI > 85th percentile)	73
Violaceous skin striae	63
Acne	52
Hypertension	51
Fatigue-weakness	45
Precocious puberty	41
Bruising	27
Mental Changes	18
"Delayed" bone age	14
Hyperpigmentation	13
Muscle weakness	13
Acanthosis nigricans	10
"Accelerated" bone age	10
Sleep disturbances	7
Pubertal delay	7
Hypercalcemia	6
Alkalosis	6
Hypokalemia	2
Slipped femoral capital epiphysis	2

Adapted from Magiakou M, Mastorakos G, Oldfield EH, et al. Cushing's Syndrome in Children and Adolescents: Presentation, Diagnosis and Therapy. New England J Med 1994 331: 620-35.



Clinical picture



Central obesity

Clinical picture



Moon face

Clinical picture



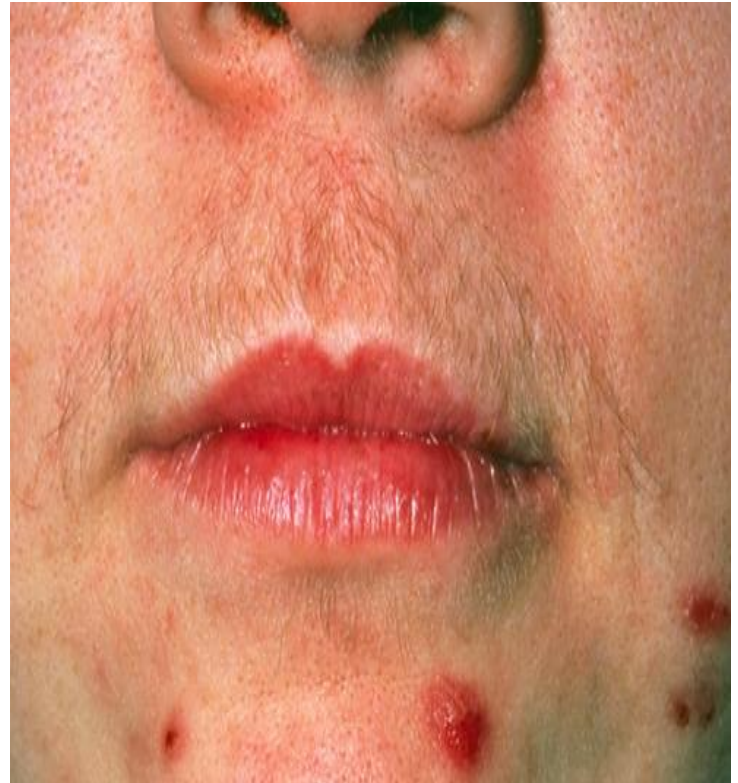
Buffalo hump

Clinical picture



Striae

Clinical picture



Hirsutism & acne

Complications

- Metabolic syndrome
- CVD
- Hypercoagulability & thromboembolism
- Bleeding
- Immunosuppression & opportunistic infections
- High mortality

Laboratory

- Hyperglycemia
- Hypokalemia
- Metabolic alkalosis
- Leucocytosis, neutropenia, eosinophilia
- High non-suppressible level of cortisol in blood/urine

Diagnosis

- ***UFC in 24 h urine collection*** (twice)
Normal less than 150 nmol (50 mkg)/24 h

- No

Specificity of one test 84-90%

Specificity of two tests 96%

- ***Late evening serum cortisol***
- ***Overnight Dexamethasone Test***
Normal less than 50 nmol/l (1.8 nmkg/dl)

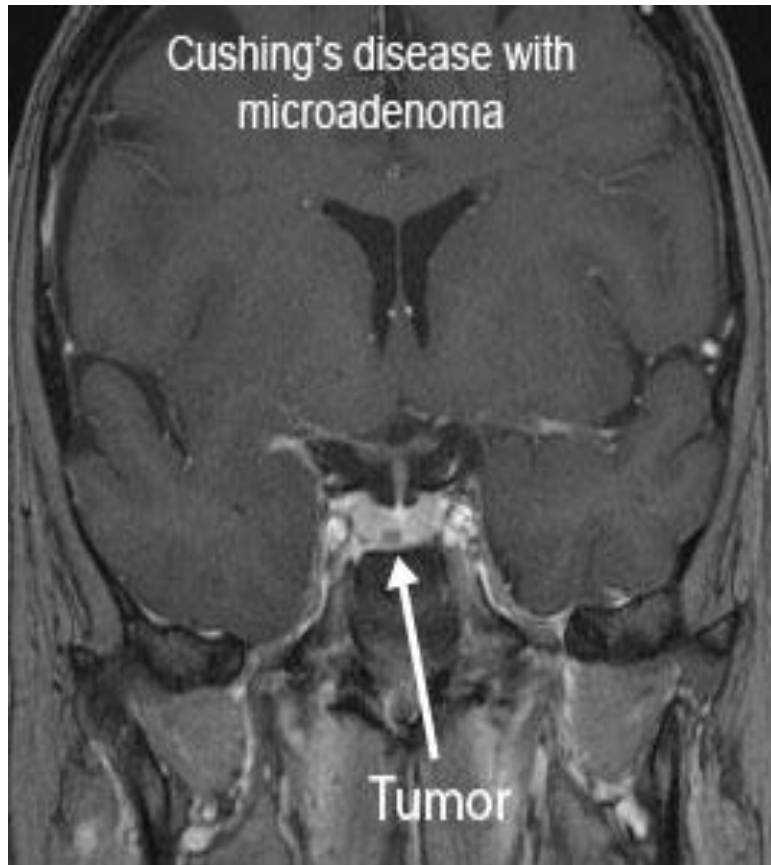
Diagnosis

- ***ACTH level in blood***

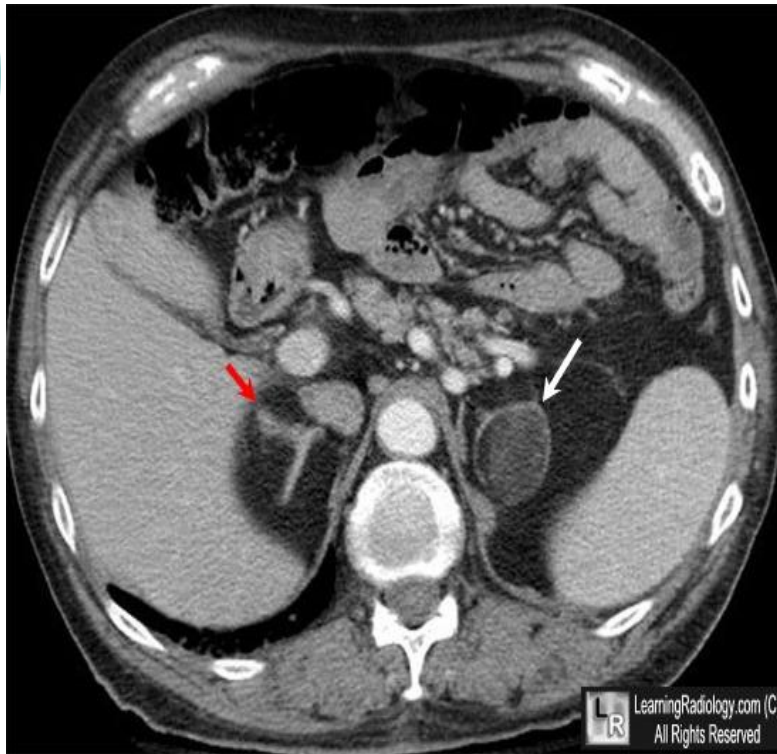
less than 5 pg/ml: ACTH independent (adrenal)

more than 5 pg/ml: ACTH dependent (central or ectopic)

Cushing's disease investigation



Adrenal Cushing investigation



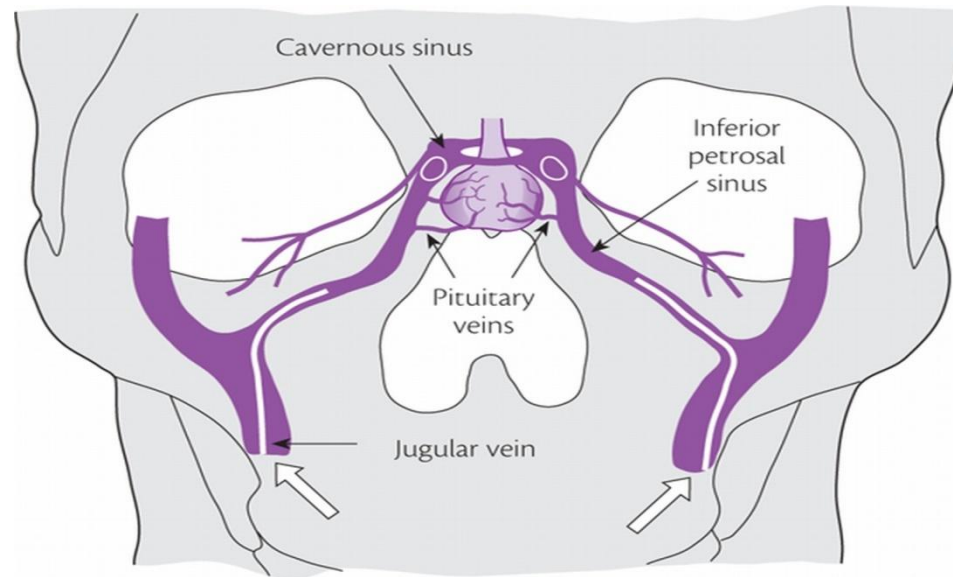
adenoma



carcinoma

Bilateral inferior petrosal sinus sampling

- Differential diagnosis of central and ectopic Cushings



Treatment of Cushing's disease

- **Transphenoidal surgery**
 - Cure after the operation 70-80%
 - 10-years cure 60-70%
- **Medical treatment**
 - Dopamine-agonist **Cabergoline**
 - Somatostatine-analog **Pasireotide**
- **Irradiation**
- **Adrenalectomy**
 - Surgery
 - drugs

Treatment of Adrenal Cushing

- **Adrenalectomy**
- **Medical treatment** (Ketoconazole, Metyrapone, Mitotane)
- **GK supplemental treatment**

!Thank You

