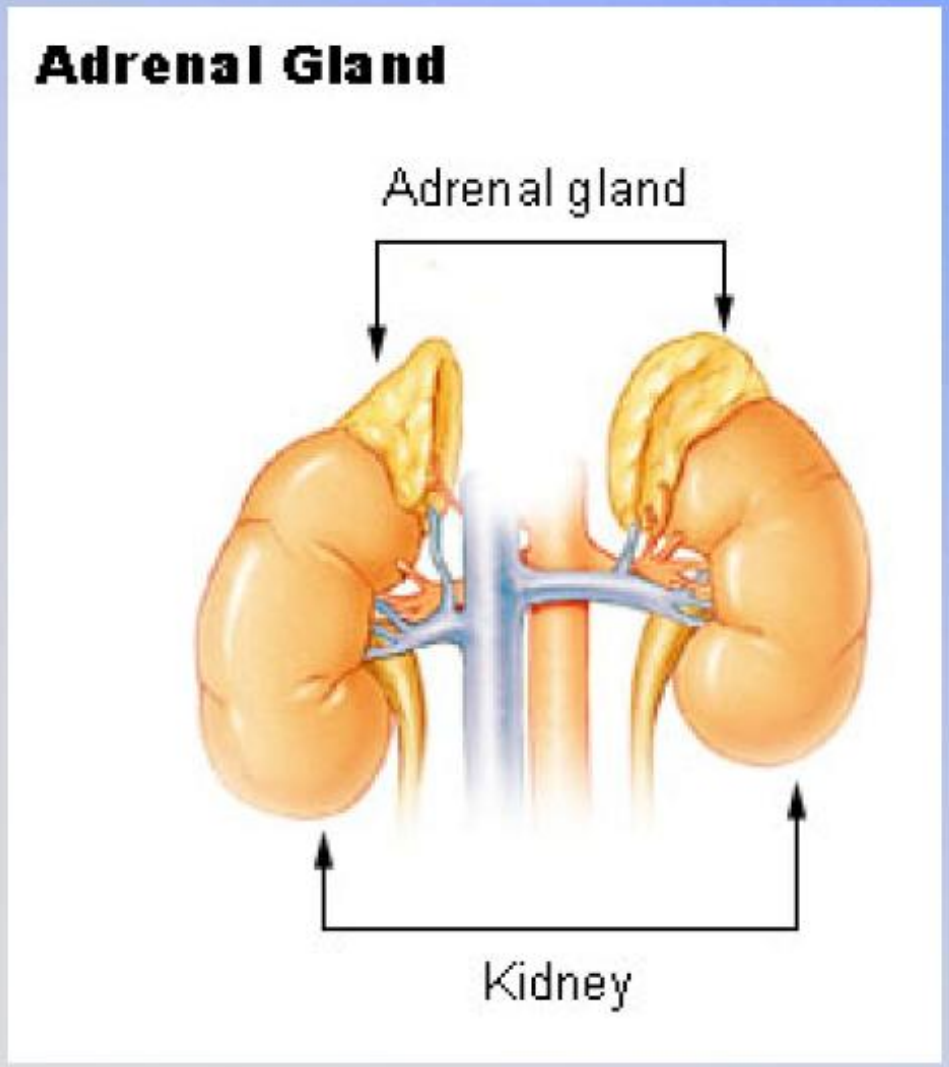
ΕΠΙΝΕΦΡΙΔΙΑ

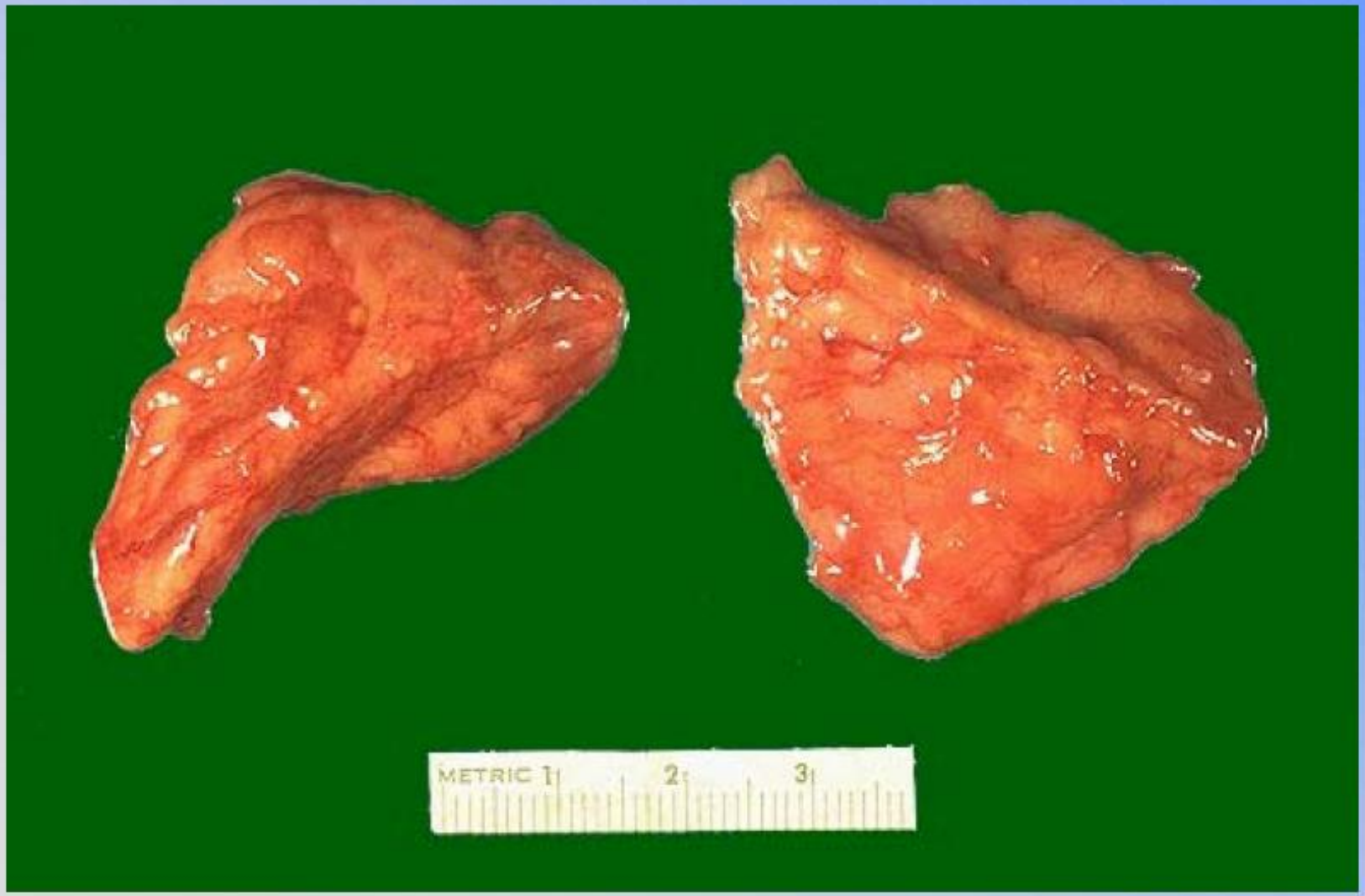
Σ Τσιόδρας

Adrenal Glands

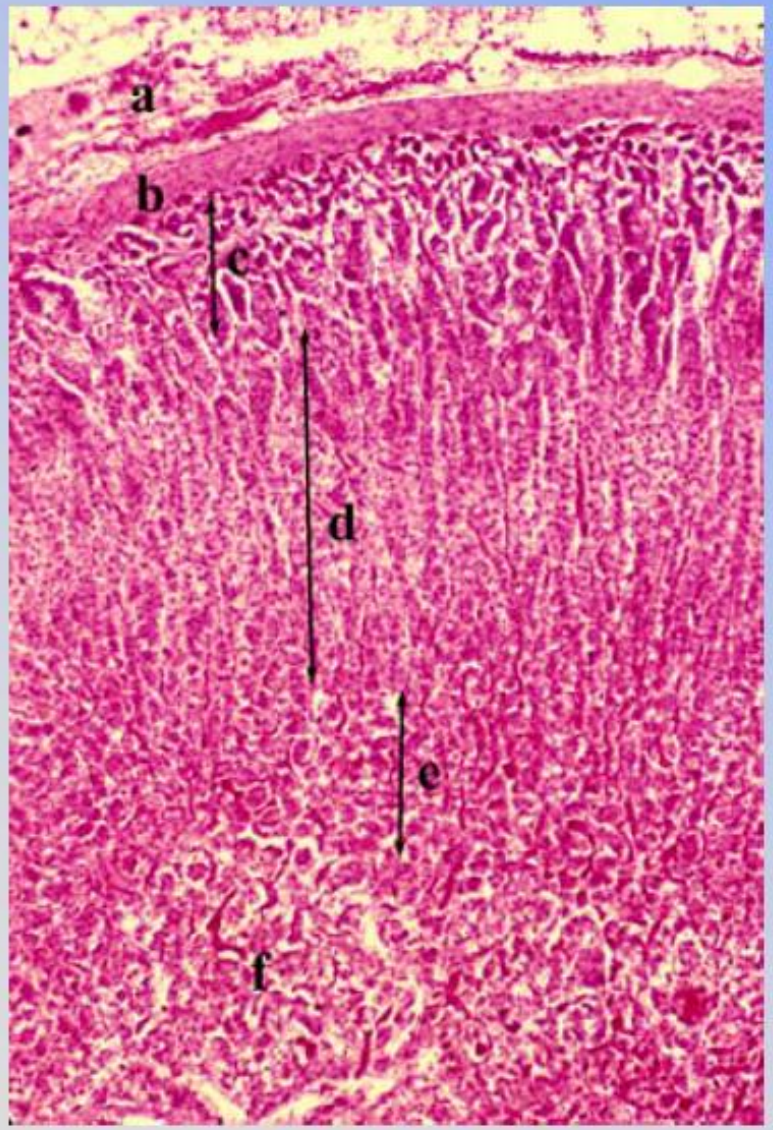


- paired organ
- 'supra-renal'
- pyramid shaped
- artery / vein from renal circulation

Normal Adrenal Glands



Adrenal Gland



CORTEX

c. zona glomerulosa

d. zona fasciculata

e. zona reticularis

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f. MEDULLA

THE ADRENAL GLANDS

- Adrenal cortex:
- Zona glomerioloza… Mineralocorticoids,
- Zona fasciculata……Glucocorticoids
- Zona reticularis…….Sex Hormones
- Adrenal medulla : Adrenaline
  Noradrenaline
  Dopamine

Functional Adrenal Abnormalities

- *Benign or malignant tumors or hyperplasia*
- ***Cortex** : Cortical tumors :*
  - *Cortisone secreting tumors-Cushing's Syndrome*
  - *Aldosterone secreting tumors- Conn's Syndrome*
  - *Sex hormone secreting tumors- Virilisation or Feminization.*

Diffuse Hyperplasia

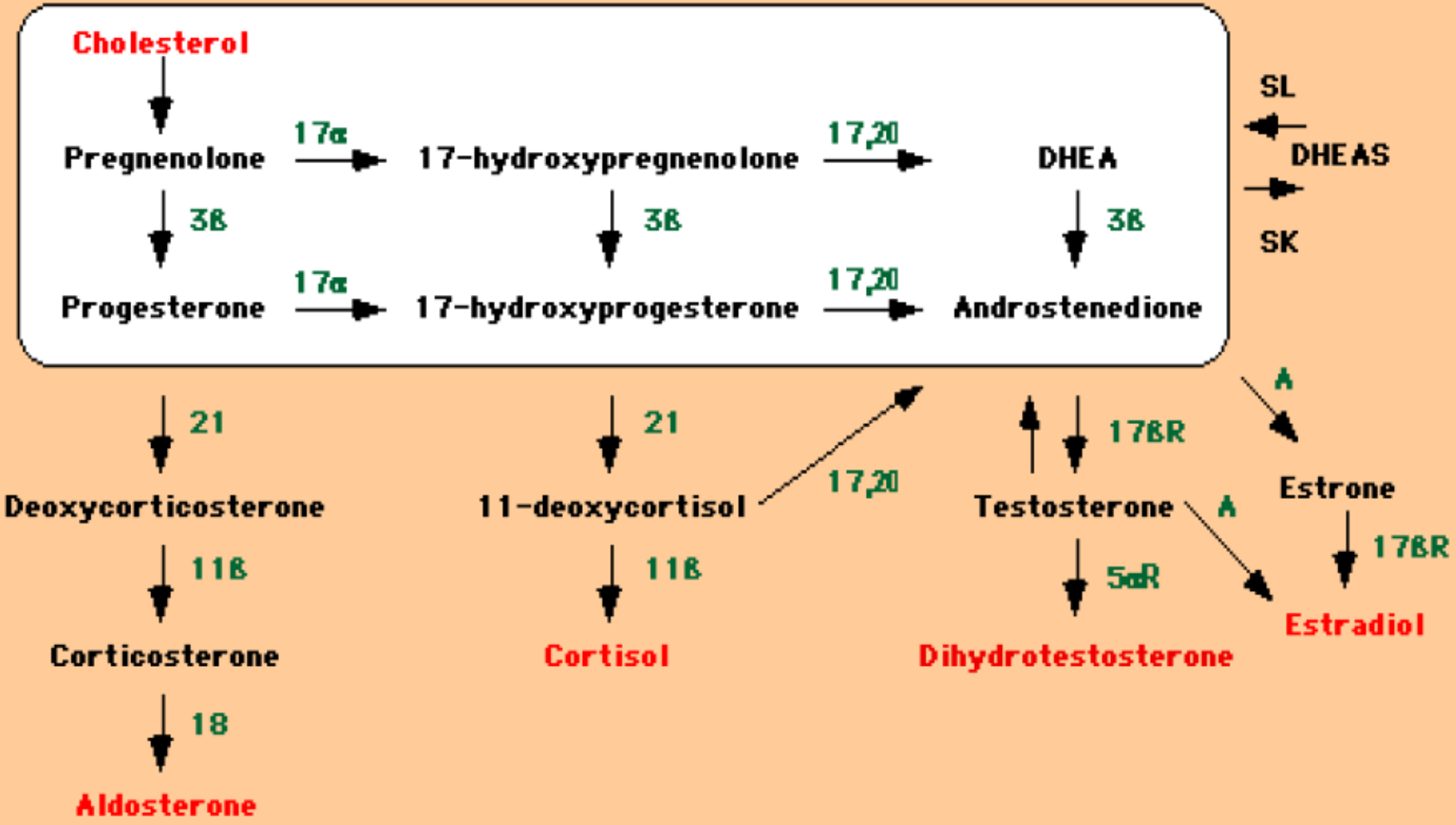
- ***Primary or a consequence of stimulation by trophic hormones leading to hypercortisolism , Conn's disease or Adrenogenital syndrome***

Medulla

- Tumors secreting adrenaline/nor-adrenaline

  (Phaeochromocytoma)

Sterol Biosynthesis



Mineralocorticoids

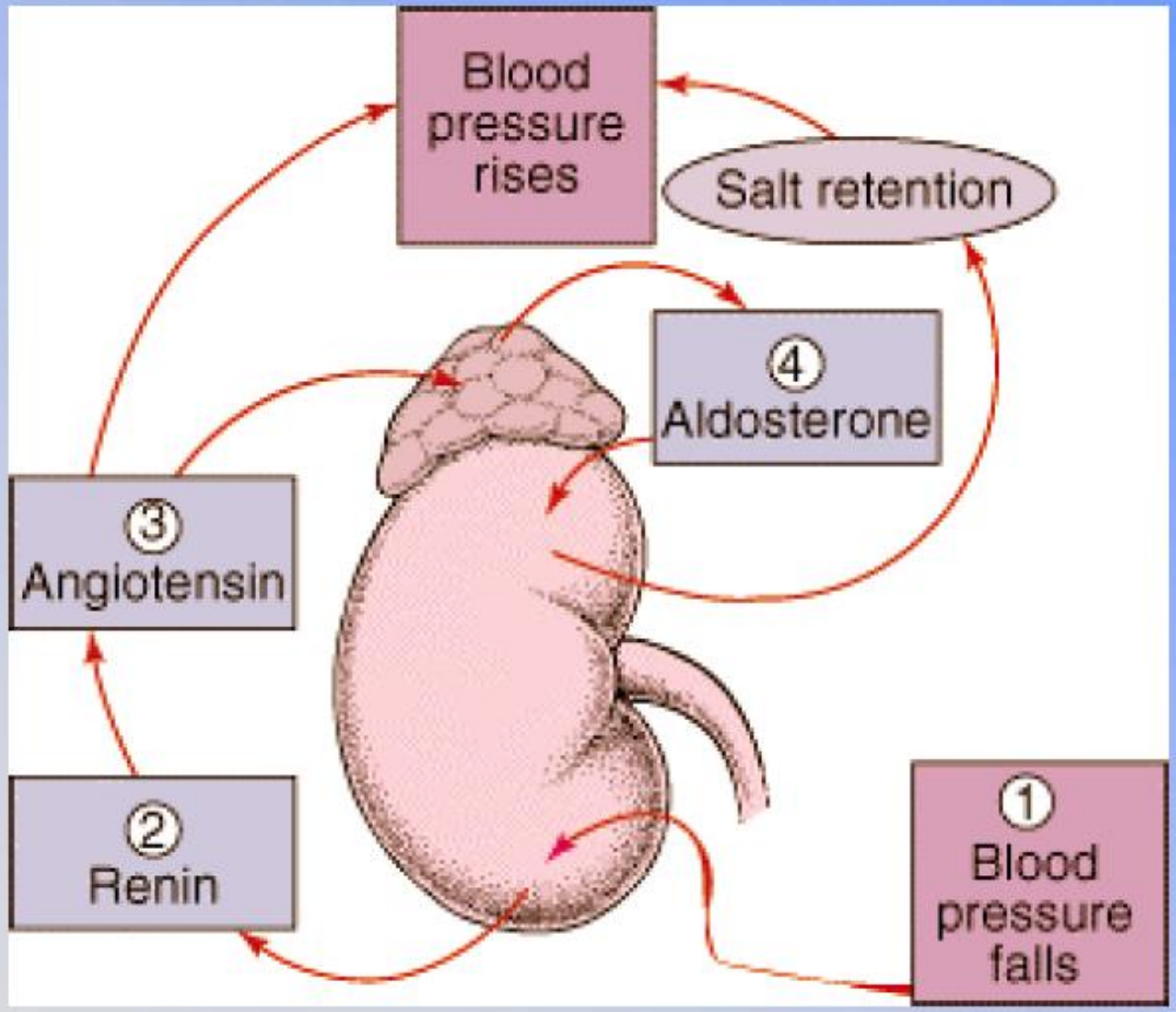
- Aldosterone
  - renin and angiotensin increases production
  - Increases Blood Pressure
  - Increases Salt (Na+) and Water Retention
  - Decreases potassium (kidney dumps K+)

Aldosterone

ACE-Inhibitors
captopril
enalipril
ramipril
lisinopril
benazepril
fosinopril
quinapril

Angiotensin Receptor Blockers
losartan
irbesartan
candesartan
telmisartan
valsartan

Aldosterone Blocker
spironolactone



Too Much Aldosterone

- Conn's Syndrome
  - tumor produces aldosterone
- Congenital Adrenal Hyperplasia
  - overactive production of aldosterone
- Atrophic Kidney
  - ischemic kidney makes angiotensin

Aldosteronism
* Conn's Syndrome*

- **Primary due to :** **tumor (Adenoma)**
  nodularity
  hyperplasia

Secondary due to:Excess stimulation by Angiotensin

Commonest cause is :

"Aldosterone producing Adenoma "

Incidence: Females more than males

30—60 years of age

1% of patients investigated for hypertension

Adrenocortical Carcinoma

- Rare
- Any age 4-5th decades
- 60% : no important secretory function
- Benign or Malignant ? Pain
  Weight loss
  Weakness
  Fever
- Functional tumors present depending on their type of secretion

Clinical features

Clinical suspicions should be raised when

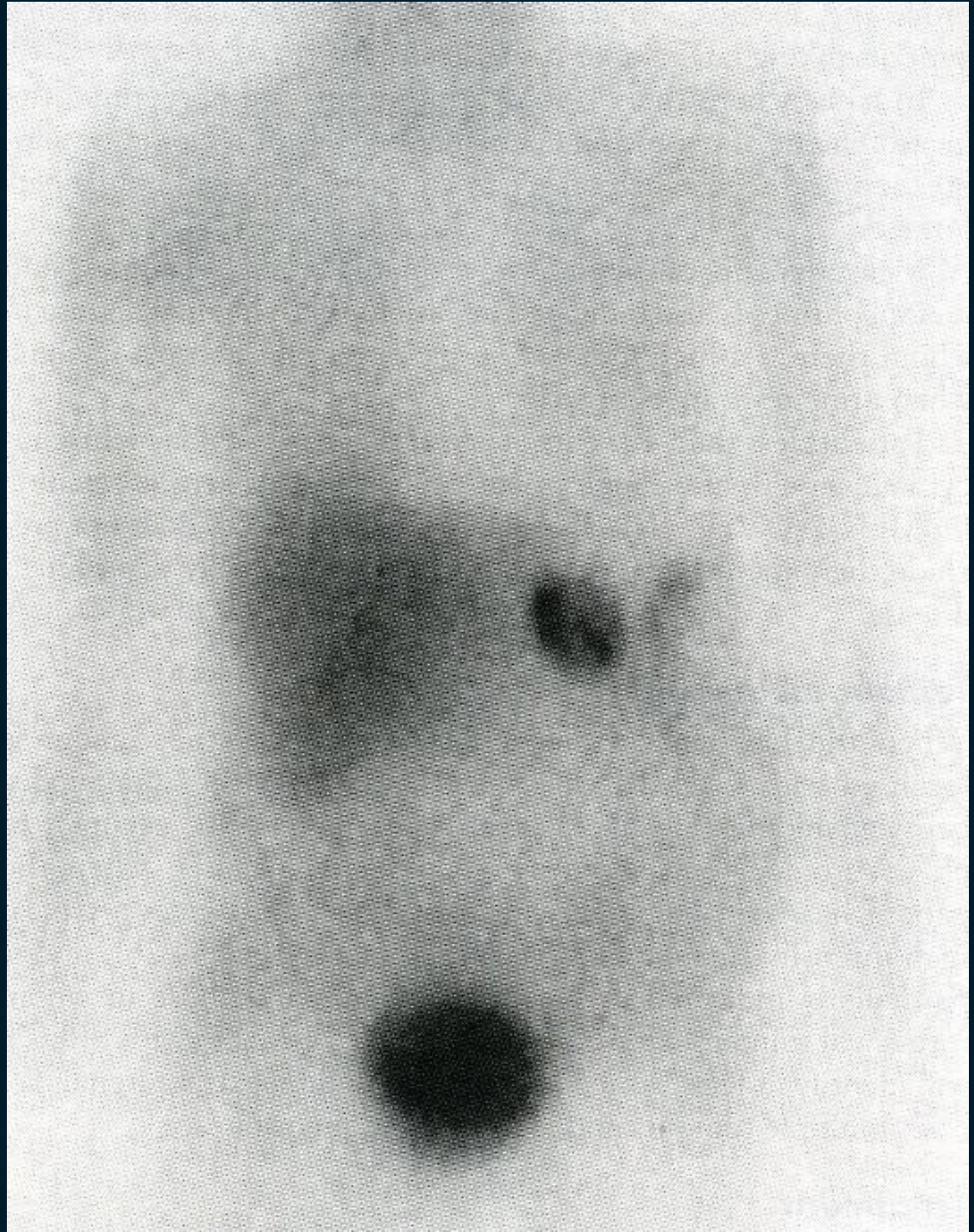
- Hypertension + hypokalemia.
- Muscle weakness
- Malaise
- Polyurea polydypsia

Conn’s Syndrome

- Laboratory assessment:
  ↑ aldosterone, ↓ renin
  ↑ plasma sodium, ↓ plasma potassium

Investigations

- Blood : Hypokalemia
  Plasma aldosterone
- Urine : Increase urinary potassium
- Imaging : U S
  C T
  M R I
  Iodocholesterol isotope scan
  Adrenal vein sampling

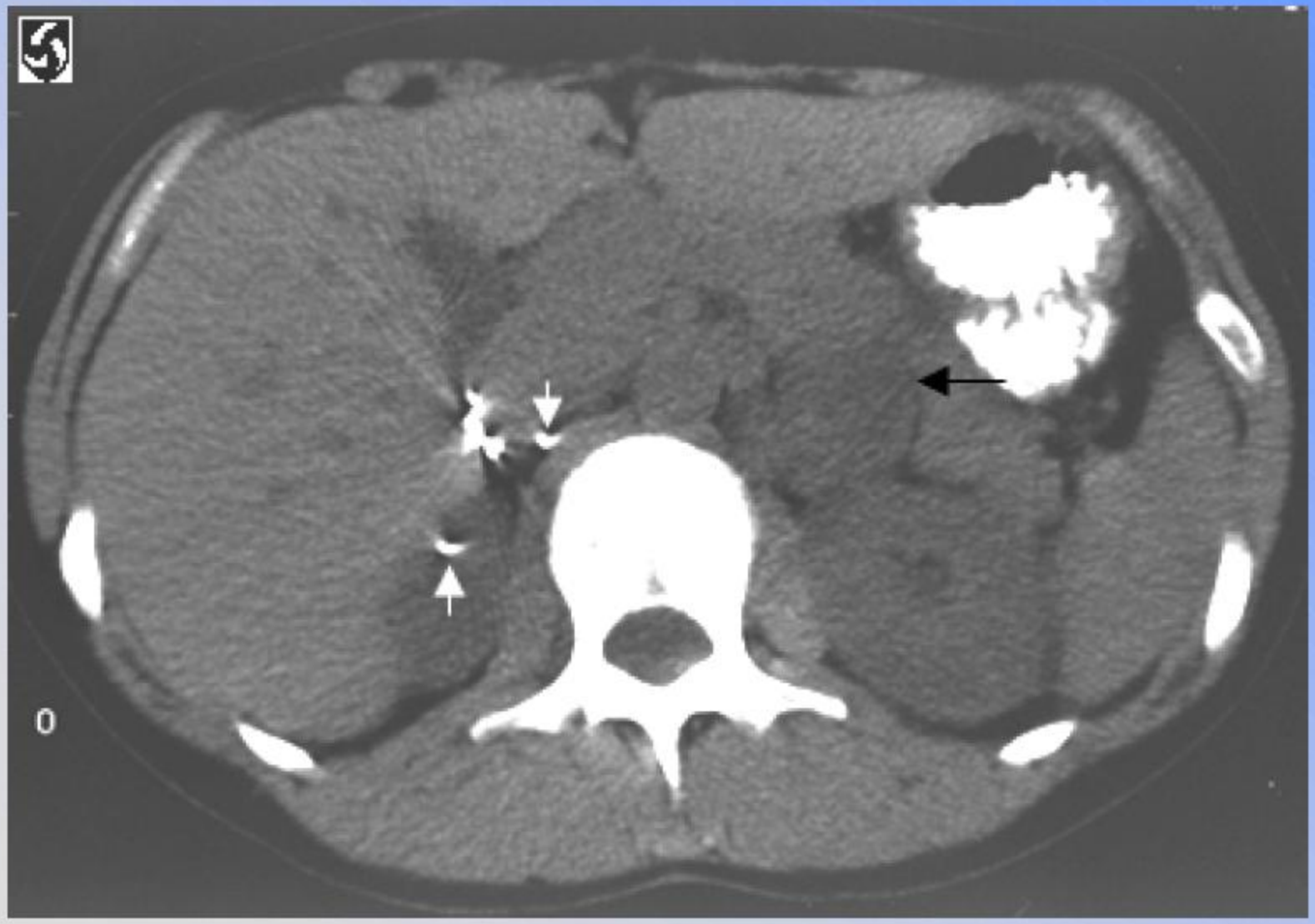


Secondary Hyperaldosteronism

- Causes:
  - Kidney disease causing increased renin output
  - Decreased BP causing increased renin output
  - Volume depletion causing increased renin output
  - Renin-secreting tumor

- Laboratory assessment:
  ↑ aldosterone, ↑ renin,
  ↑plasma sodium, ↓ plasma potassium

Adrenal Tumor

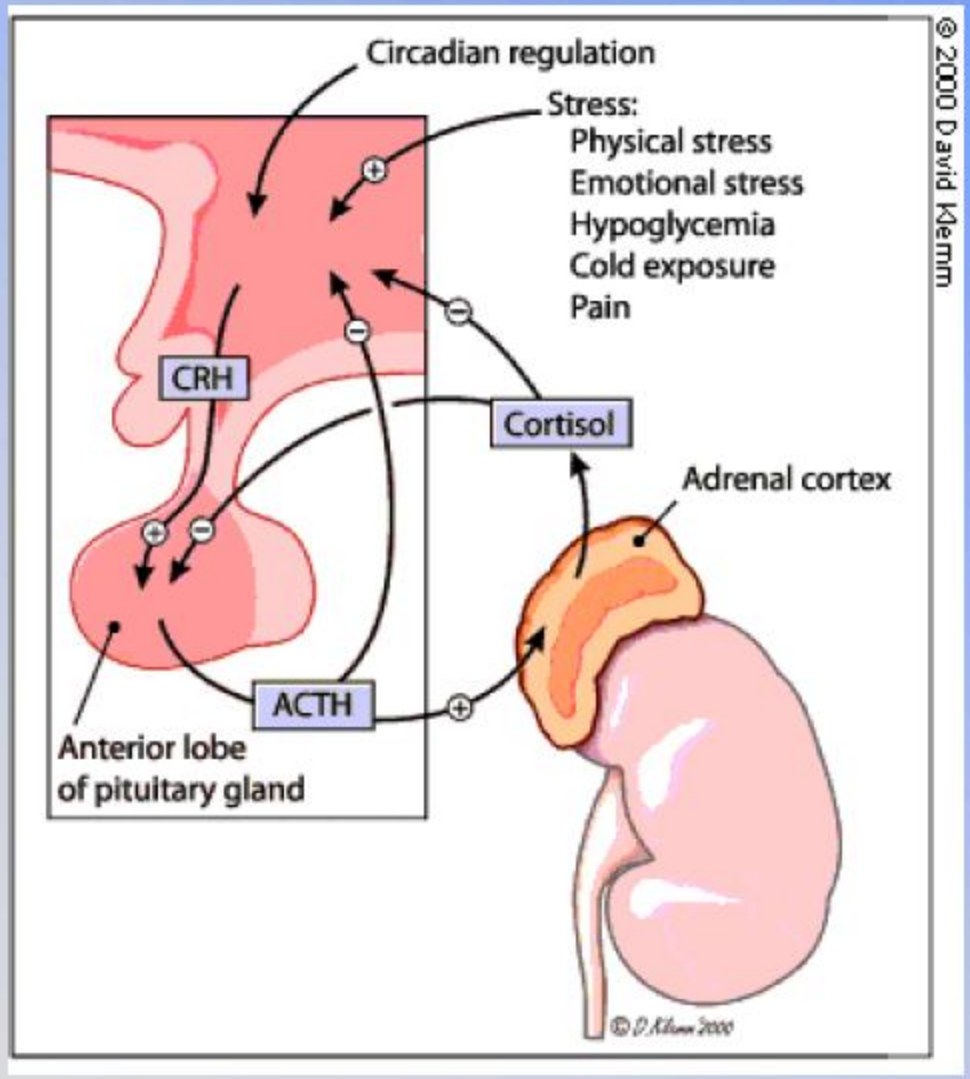


Too Much Cortisol

Glucocorticoids

- Cortisol (stress hormone)
  - increases available energy
  - increases protein breakdown
  - increases glucose production
  - increases fatty acid availability

Cortisol Regulation



Cushing's Syndrome

- ***Definition:***

  Excess circulating cortisol that occurs as a result of endogenous steroid hyper secretion, due to:

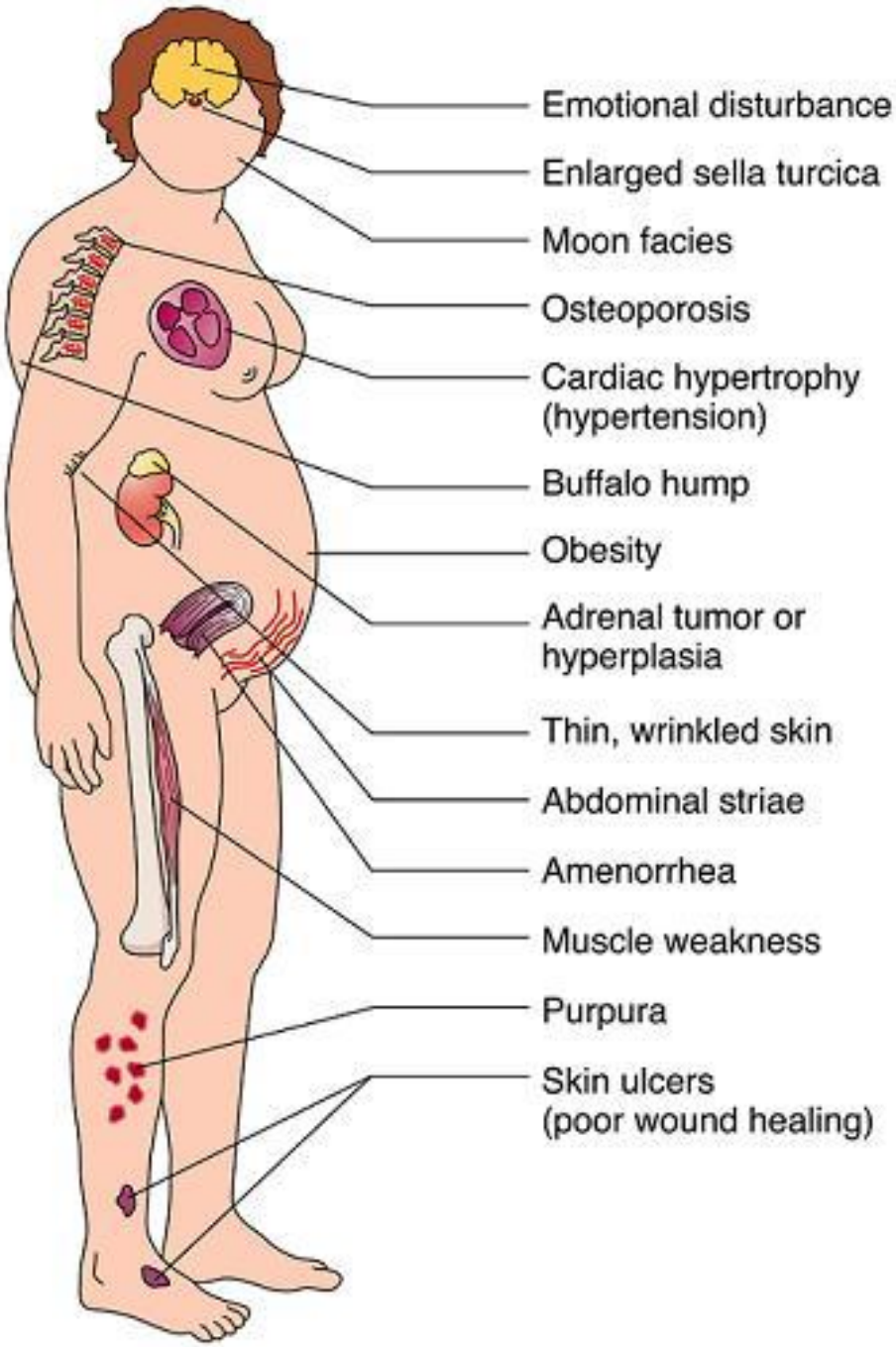
  ACTH dependent or

  ACTH_ independent disease

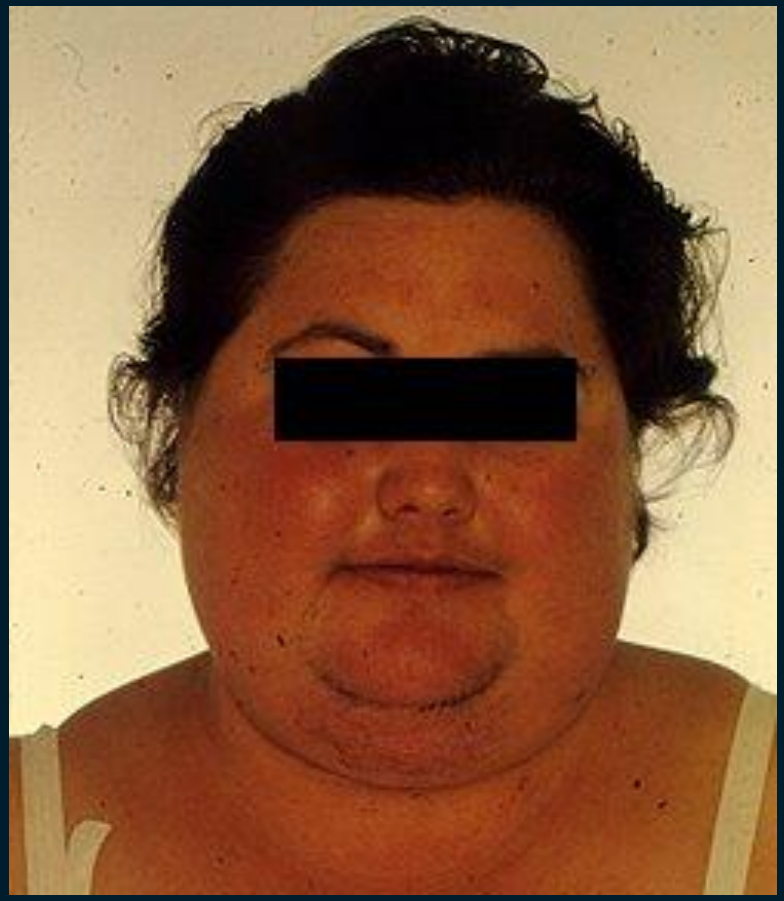
  Or exogenous steroid medication.

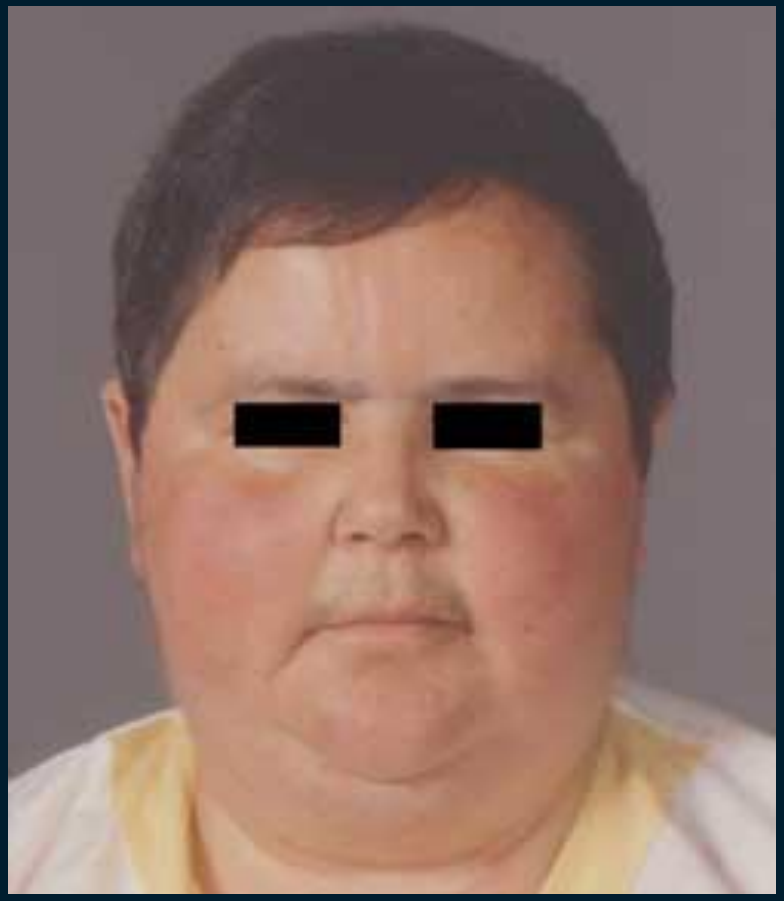
Too Much Cortisol

- Cushing's Syndrome
  - thin skin, bruises, striae
  - moon facies, buffalo hump
  - cataracts
  - increases blood pressure
  - thins bones (osteoporosis)
  - immune dysfunction
  - increases glucose and obesity
  - muscle loss
  - mental status changes

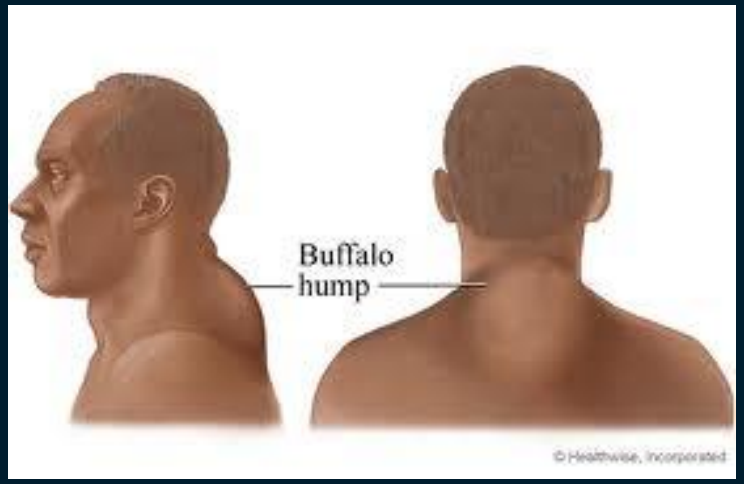

Emotional disturbance
Enlarged sella turcica
Moon facies
Osteoporosis
Cardiac hypertrophy (hypertension)
Buffalo hump
Obesity
Adrenal tumor or hyperplasia
Thin, wrinkled skin
Abdominal striae
Amenorrhea
Muscle weakness
Purpura
Skin ulcers (poor wound healing)

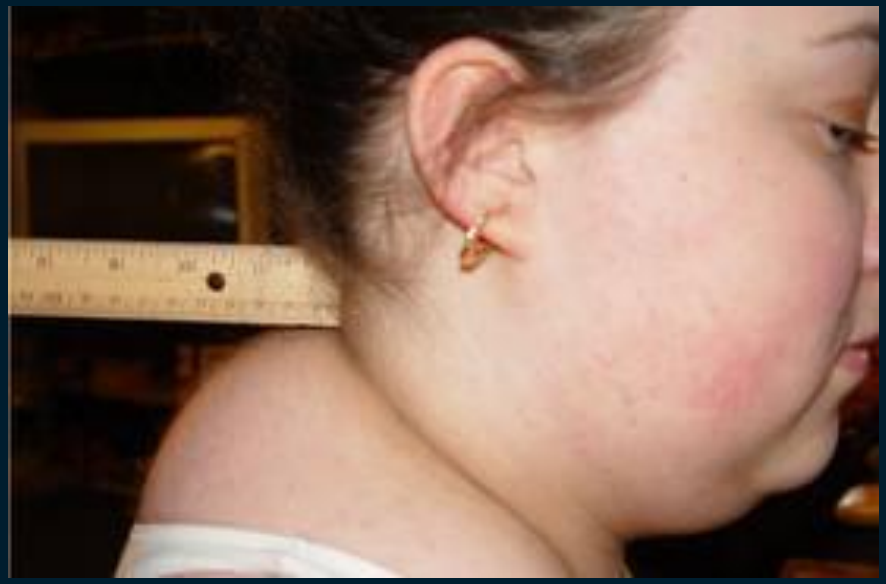
ΠΑΝΣΕΛΗΝΟΕΙΔΕΣ ΠΡΟΣΩΠΕΙΟ

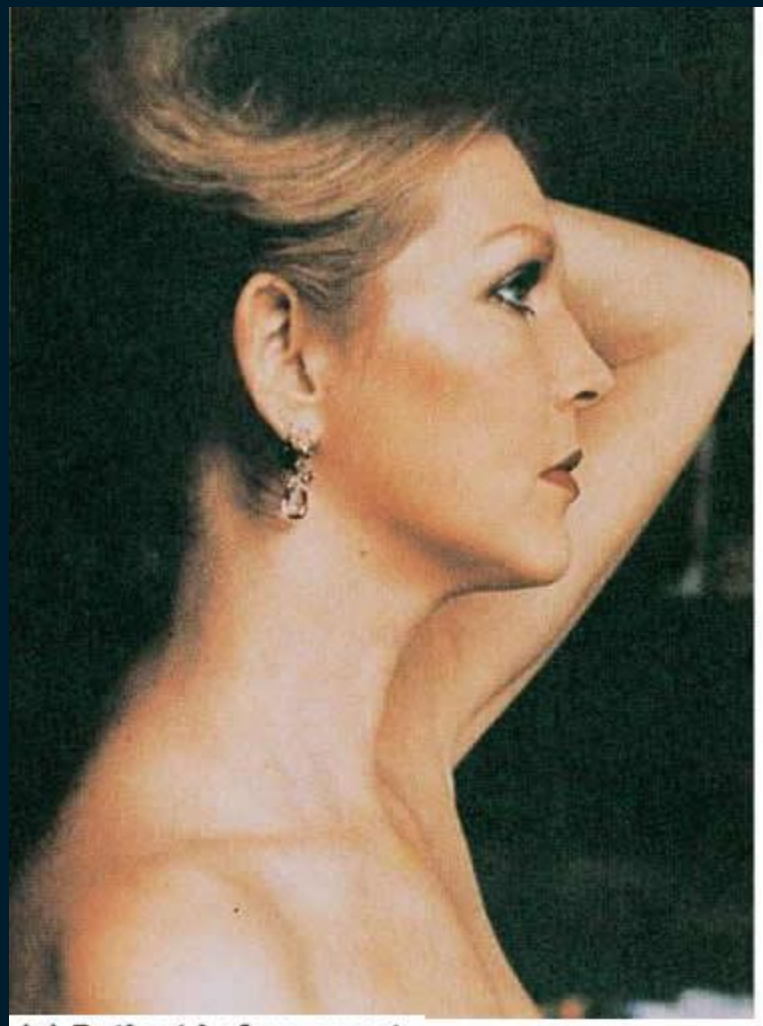




BUFFALO HUMP







(a) Patient before onset.

(b) Same patient with Cushing's syndrome. The white arrow shows the characteristic "buffalo hump" of fat on the upper back.

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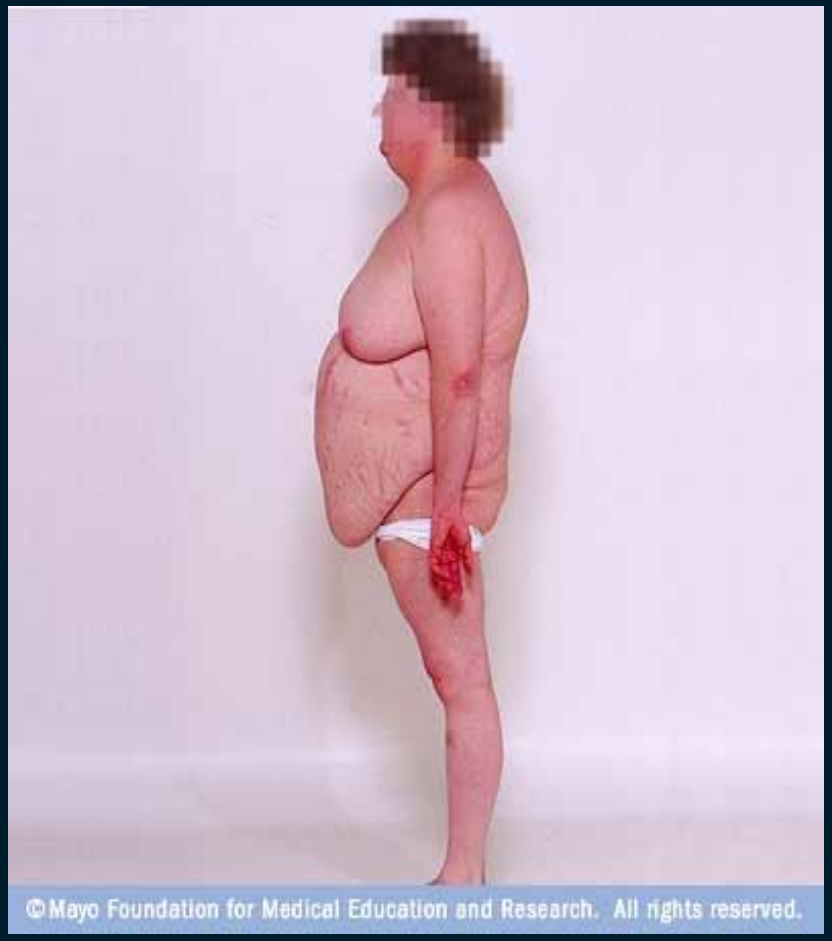

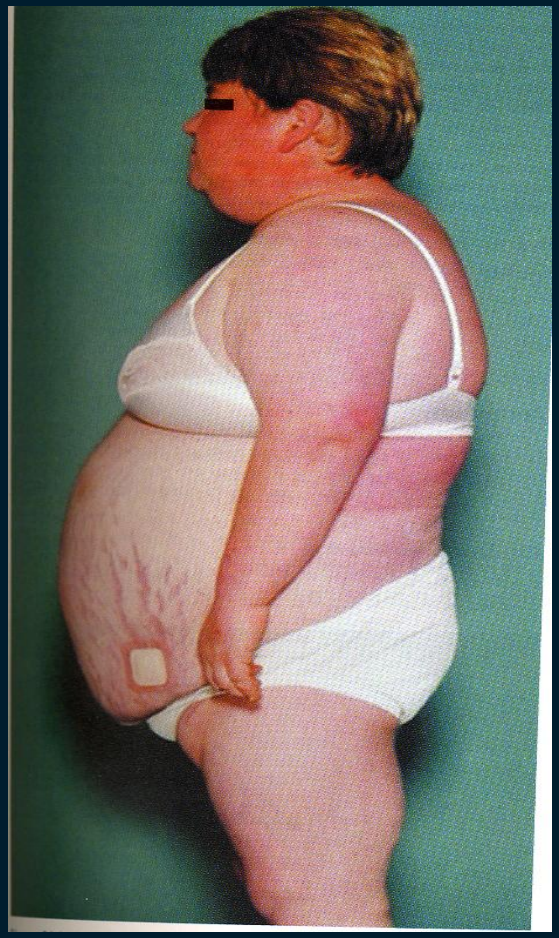

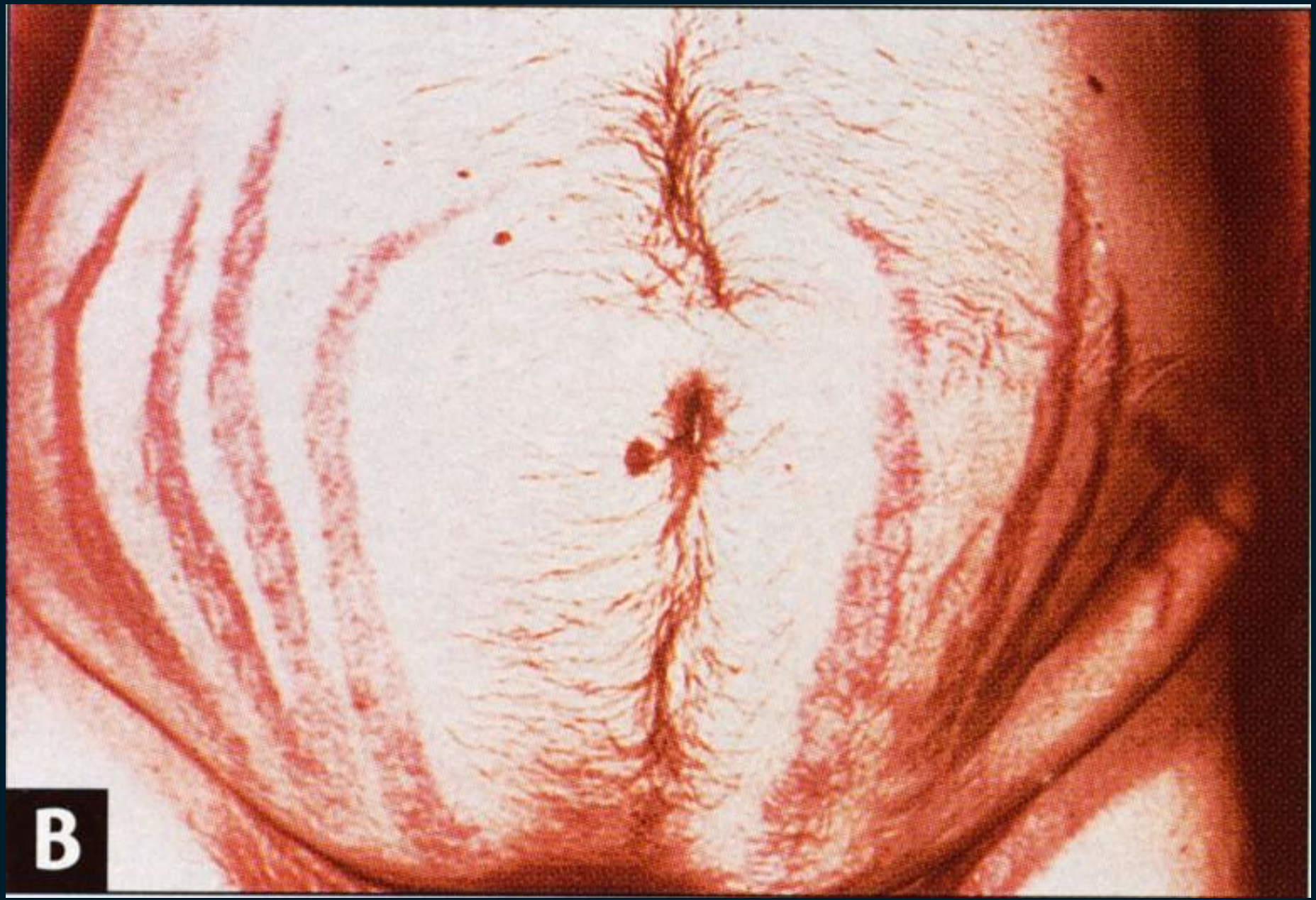
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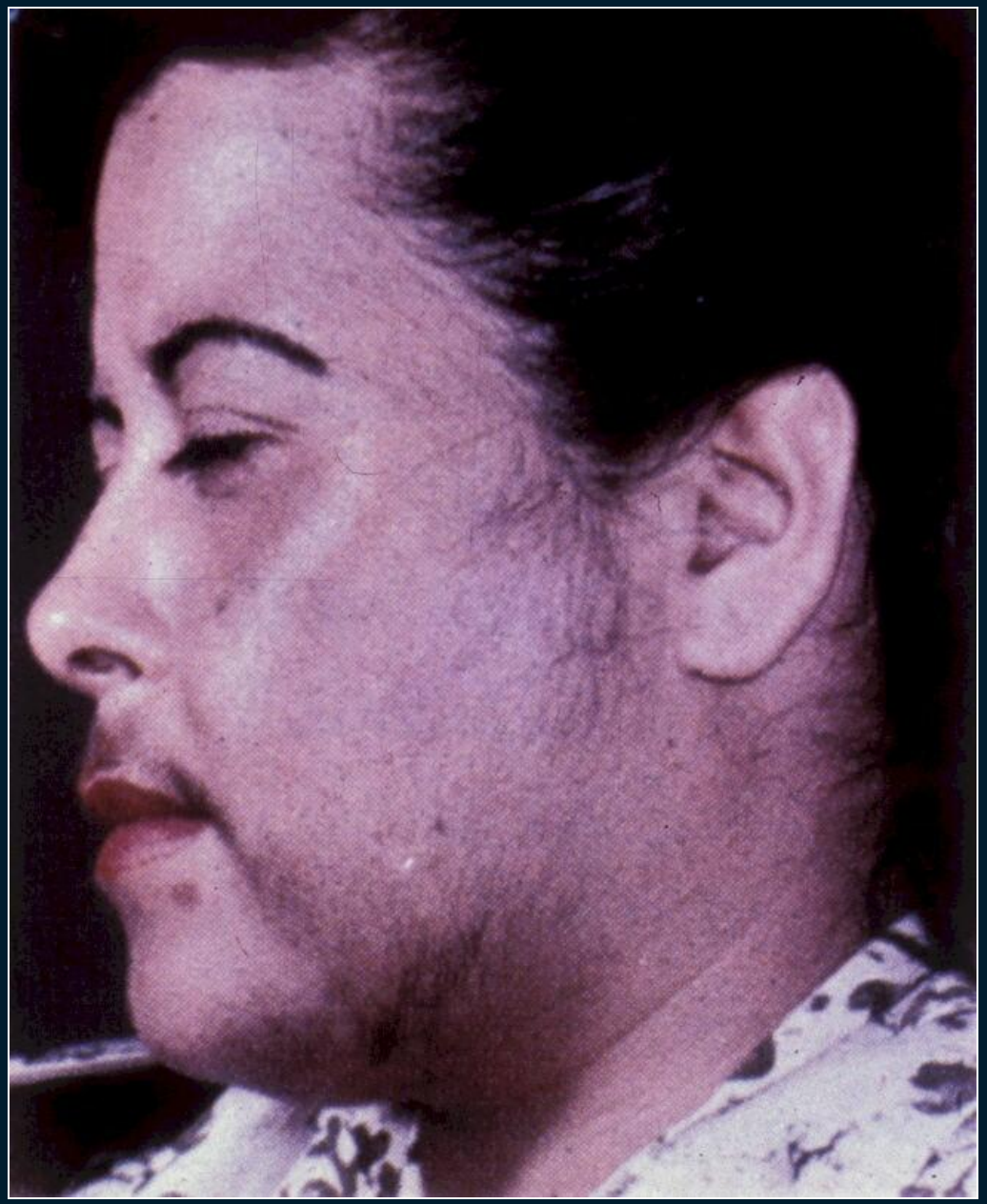


Cushing's Syndrome

- Cushing's disease
  - pituitary tumor
- Adrenal Hyperplasia or Tumor
- Exogenous Glucocorticoids
  - cortisol
  - prednisone
  - dexamethasone

ACTH Independent

- Adrenocortical Adenoma
- Bilateral nodular hyperplasia
- Adrenal carcinoma.

ACTH-Dependent

1. Pituitary microadenoma.
2. Ectopic ACTH secretion:
   - *Small cell carcinoma.*
   - *Fore gut carcinoid.*
   - Ectopic CRH Syndrome:
     - *Medullary thyroid tumor.*
     - *Pancreatic neuro-endocrine tumors*

Ectopic ACTH Secretion

- Rapid evolution of the Cushing;s
- Symptoms of the primary disease:
  - -Small cell carcinoma of the lung
  - -Carcinoid
  - -Medullary Ca of Thyroid
  - -Other primary carcinomas

Cushing's Syndrome

- Screen
  - 24 hr urine production of cortisol
- Diagnosis
  - dexamethasone suppression test

Investigations:

1 : Biochemical diagnosis

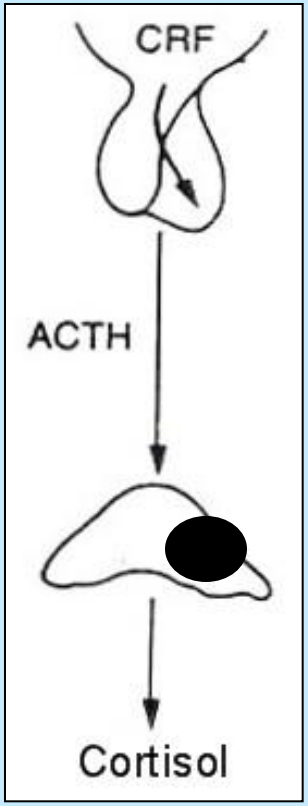
- Persistent increase in cortisol concentration.
- Cortisol suppression by dexamethasone
- Resistant to insulin administration

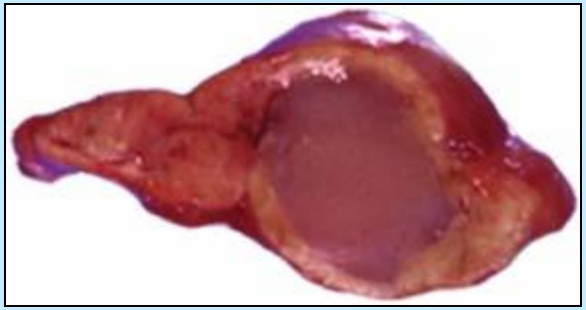
2 : Establishment of the cause

- Low ACTH = Adrenal disease
- High ACTH = Extra- adrenal cause.

Primary Adrenal Hyperfunction

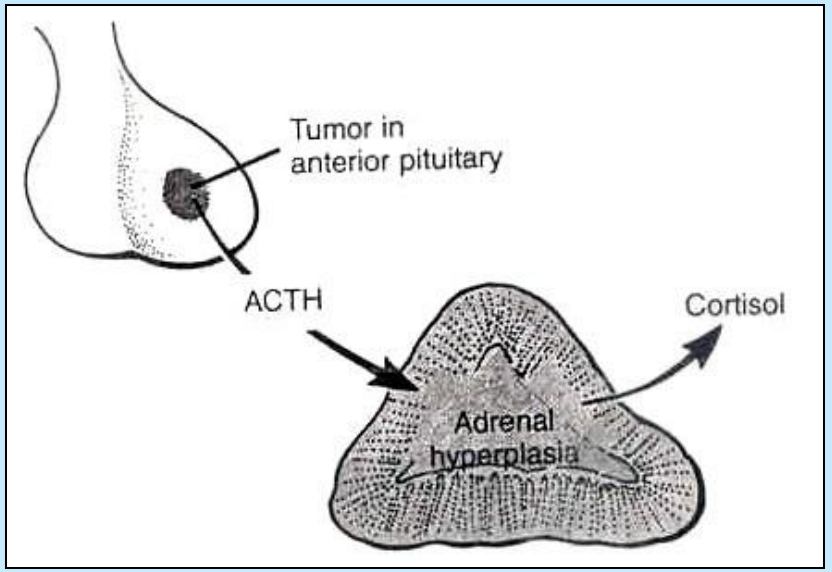
- Laboratory assessment:
  - Baseline: ↑ cortisol, ↑ UFC, ↓ ACTH
  - Lack of diurnal variation (key finding)
  - High Dose Dexamethasone Suppression Test:
    - Cortisol levels remain high (no suppression) suggests Cushings syndrome caused by an autonomous adrenal tumor





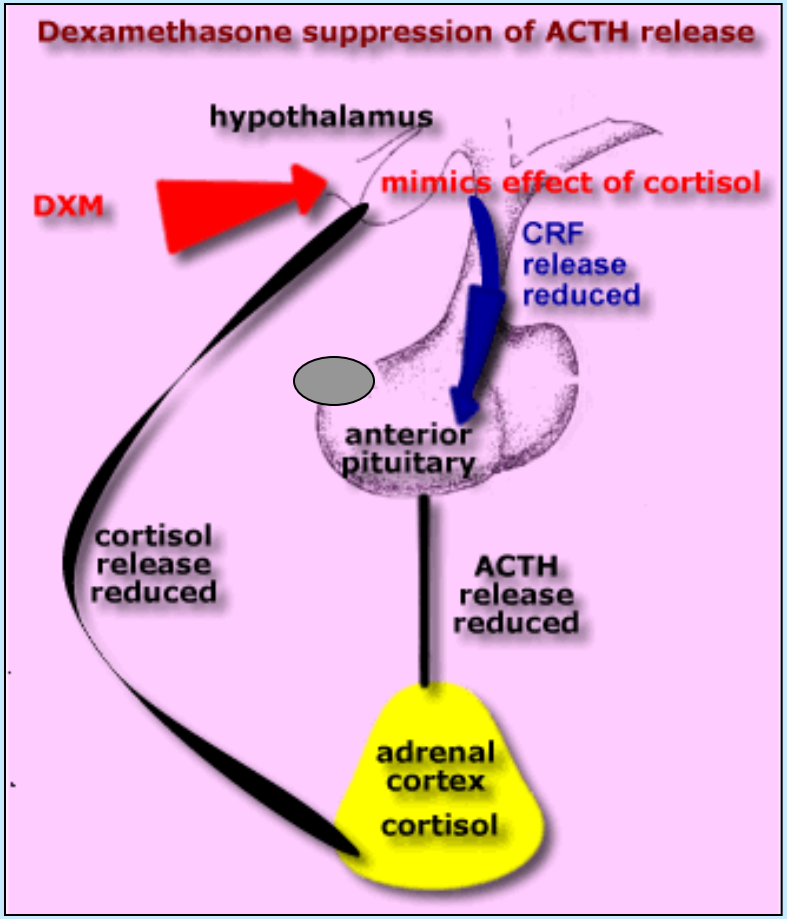
Cushing's Disease

- Caused by ACTH-secreting pituitary adenoma
- Classified as a secondary disorder
- ↑ cortisol, ↑ ACTH
- Symptoms the same as for primary disorder, except hyperpigmentation of skin noted (due to ↑↑ ACTH)



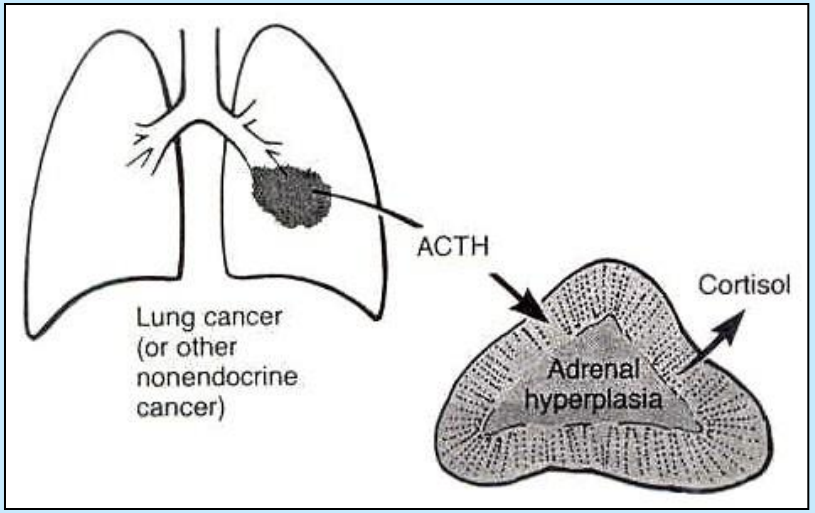
Cushing's Disease

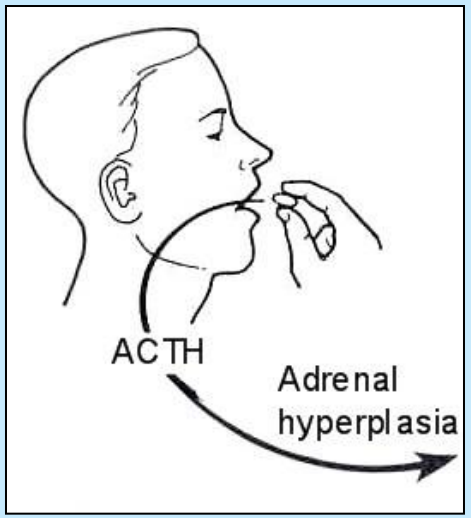
- Laboratory assessment:
  - Baseline: ↑ plasma cortisol, ↑ UFC, ↑ ACTH
  - Lack of diurnal variation (key finding)
  - High Dose Dexamethasone Suppression Test: Suppression of cortisol levels (this is the only condition that shows suppression with high dose dexamethasone)



Secondary Hypercortisolism

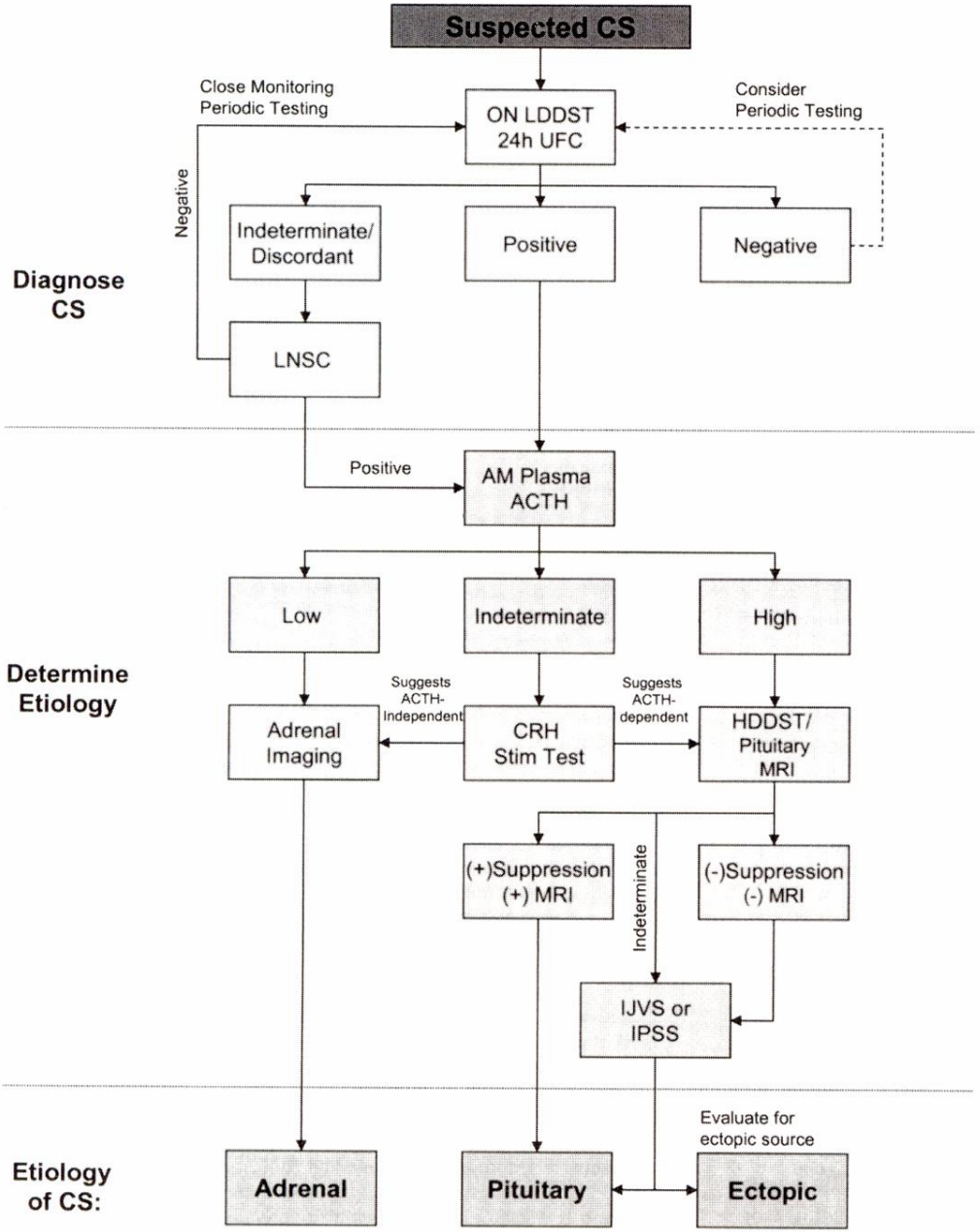
- Caused by:
  - Ectopic ACTH-secreting tumor (oat cell carcinoma lung)
  - Long term ACTH treatment
- ↑ cortisol, ↑ ACTH
- Symptoms the same as for primary disorder, except hyperpigmentation of skin noted





Secondary Hypercortisolism

- Laboratory assessment:
  - Baseline: ↑ plasma cortisol, ↑ UFC, ↑ ACTH
  - Lack of diurnal variation (key finding)
  - High Dose Dexamethasone Suppression Test: Cortisol levels remain elevated (no suppression)

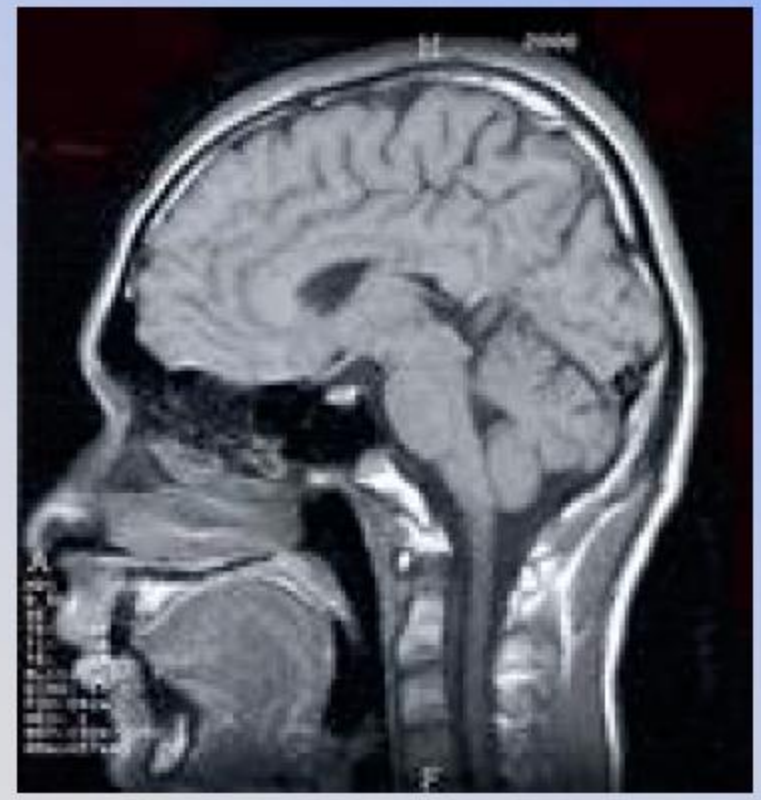


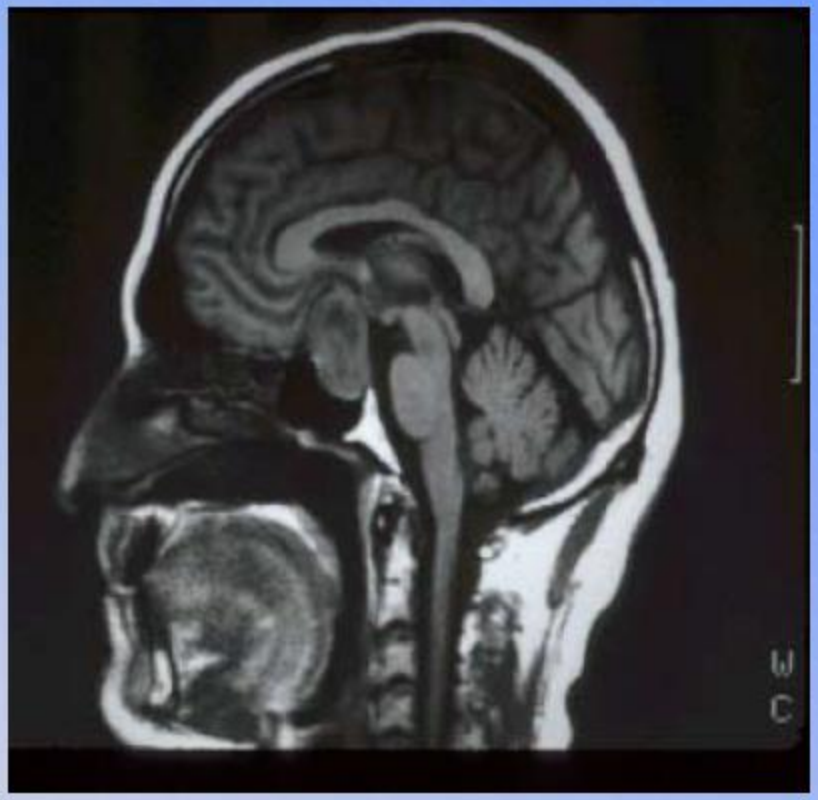
CS: Cushing's Syndrome, ON LDDST: Overnight low-dose dexamethasone suppression test, 24h UFC: 24 hour urine free cortisol, LNSC: Late-night salivary cortisol, HDDST: High-dose dexamethasone suppression test, IJVS: Internal jugular vein sampling, IPPS: Inferior petrosal sinus sampling

Anatomical details

- Pituitary: Skull X ray
  C T
  M R I
- Adrenals: U S
  C T
  M R I
- Scintigraphy - cholesterol scan- N P 59 scan
- Search for ectopic ACTH source
  C T chest
  Angiography

Pituitary Tumor

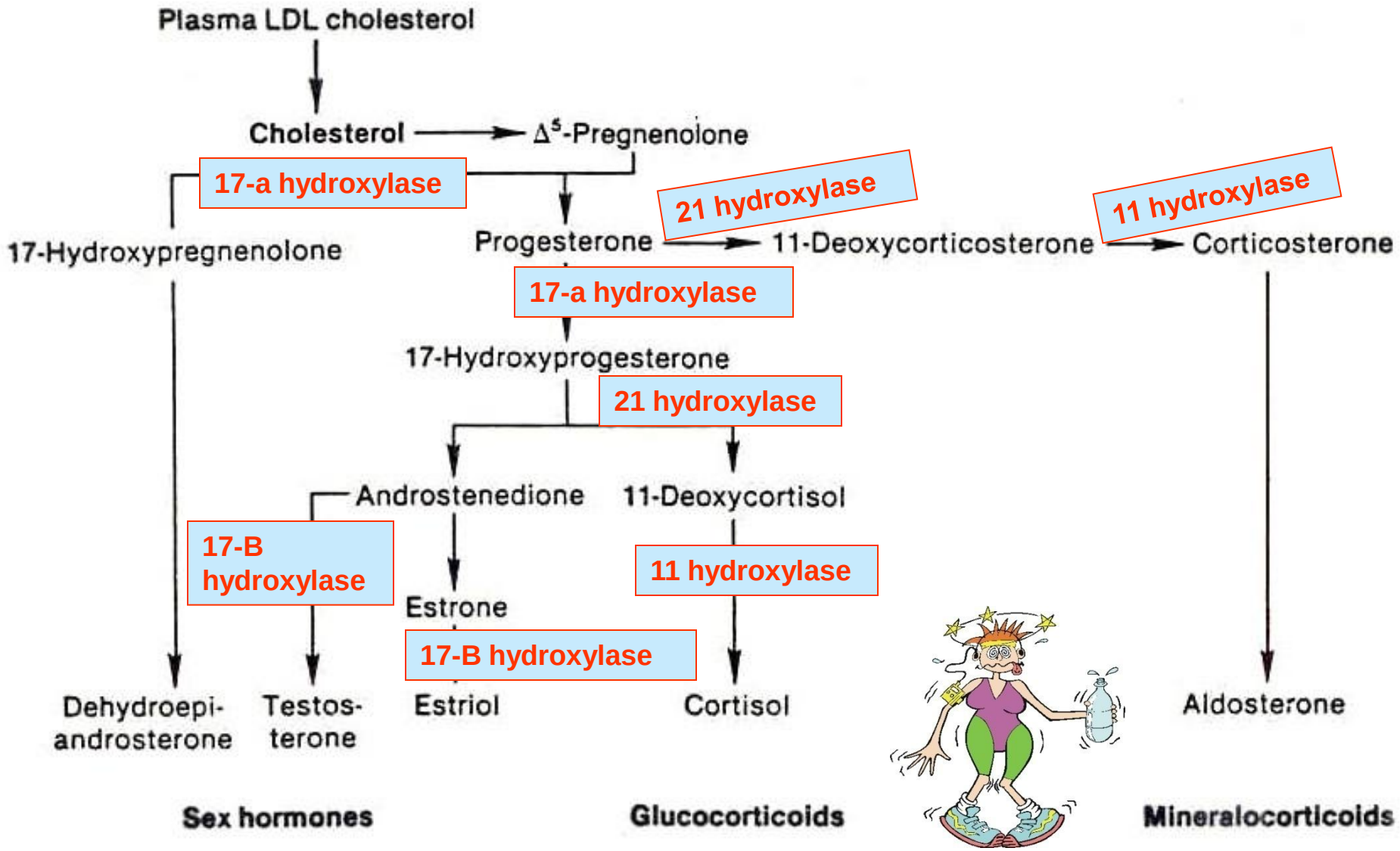




Congenital Adrenal Hyperplasia (CAH)

- Most common adrenal disorder in pediatric population

- Genetic disorder causing a lack of critical enzyme required in the steroid biosynthetic pathway



The lower in the pathway the enzyme deficiency is located,

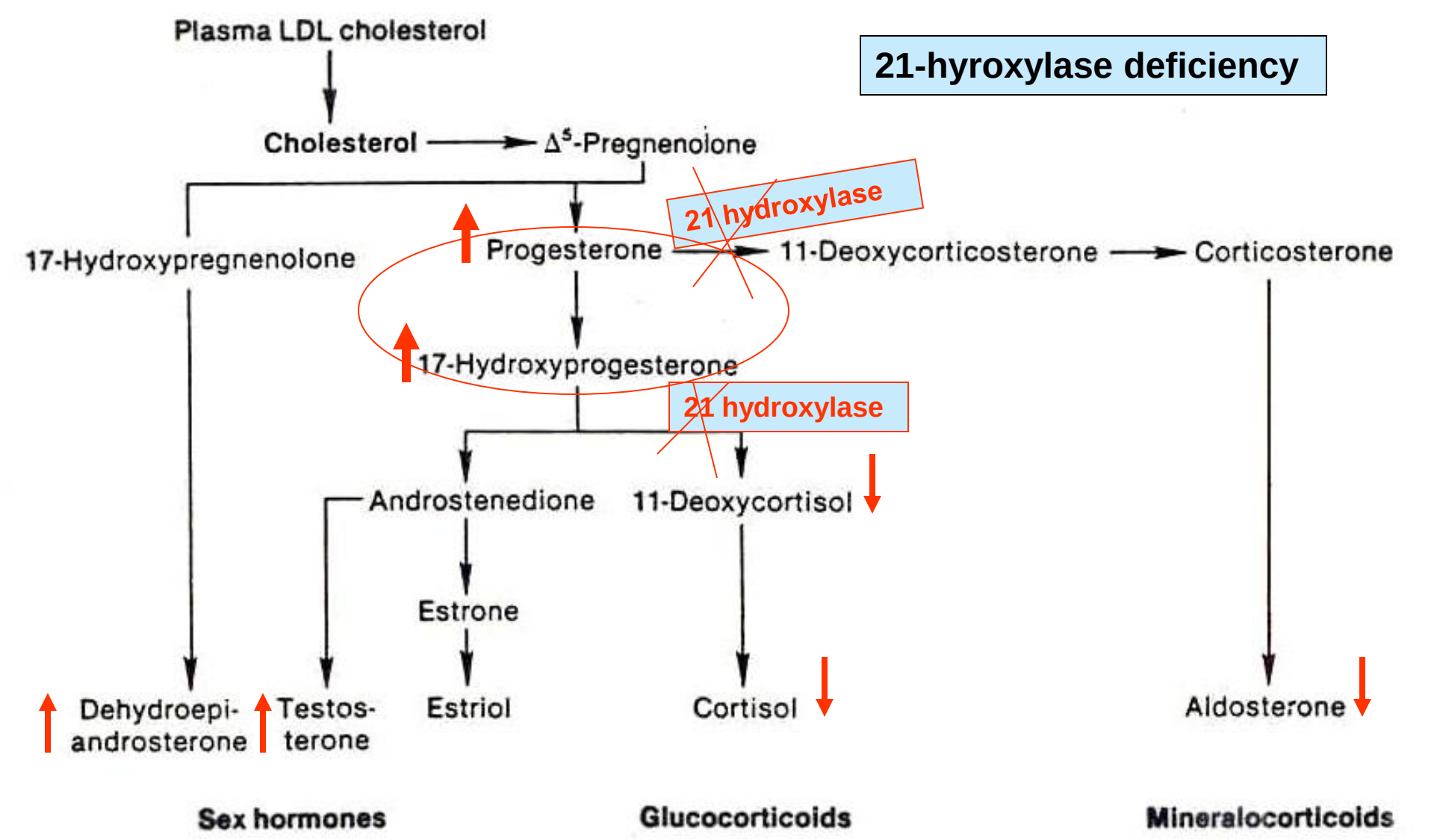
the less severe the symptoms and clinical presentation will be

Congenital Adrenal Hyperplasia (CAH)

- ALWAYS results in decreased cortisol and increased ACTH levels
- Increased ACTH over stimulates adrenal gland causing hyperplasia of adrenal gland
- Because of enzyme deficiency, cortisol remains low, despite over stimulation
- Hormone preceding enzyme deficiency in pathway will be found elevated, and this is what we want to measure in the lab

Congenital Adrenal Hyperplasia (CAH)

- 21-hydroxylase deficiency
  - Most common (95% CAH)
- 11-beta-hydroxylase deficiency
  - Second most common (5% CAH)
- 17-alpha-hydroxylase deficiency
  - ‘Third most common’…extremely rare



Laboratory: Decreased cortisol, aldosterone
Increased 17-OH progesterone, progesterone
Increased TST (DHEA), ACTH

Too Little
Cortisol and Aldosterone

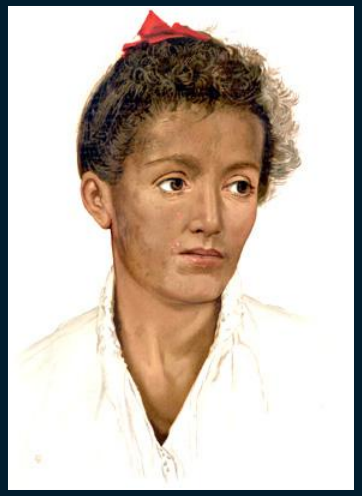
Not Enough Cortisol

- Adrenal Insufficiency
  - low blood pressure
  - nausea
  - low sodium
  - sometimes very tanned

Adrenal Insufficiency

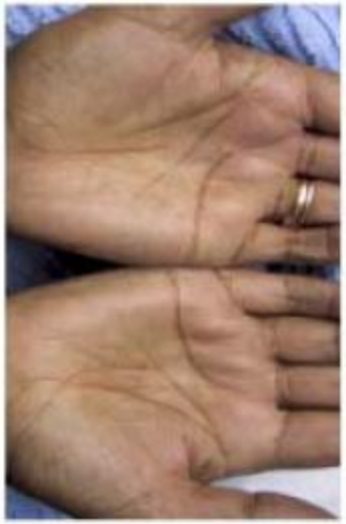
- Addison's Disease
  - auto-immune destruction
- Other
  - hemorrhage into adrenal
  - infection
  - surgical resection
- Adrenal Suppression
  - among those receiving corticosteroids

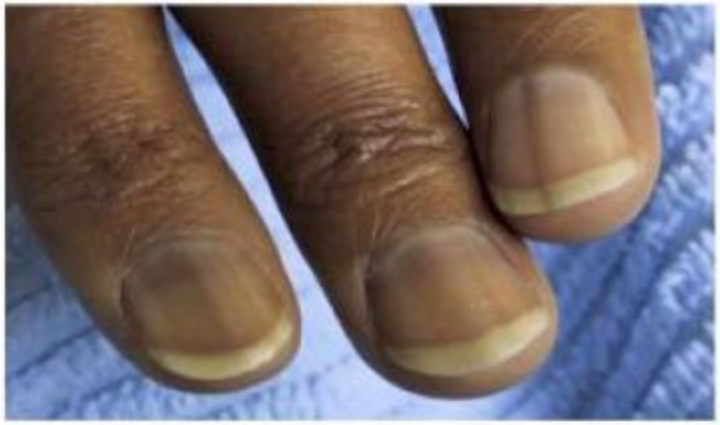
Addison's Disease



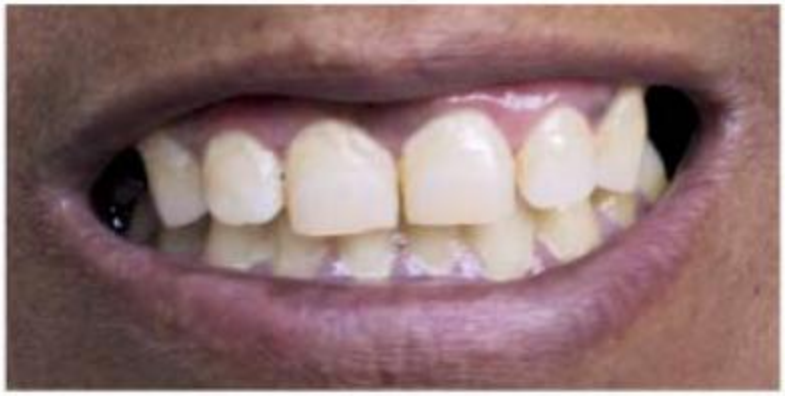
- Symptoms
  - Insiduous (slow and gradual) onset
  - Fatigue, weakness, weight loss, GI disturbances
    Depends on the extent of adrenal failure
  - PP hypoglycemia, stress intolerance, hypotension
  - Hyperpigmentation of skin and mucus membrane due to increased ACTH (mimics MSH)
  - If mineralcorticoid layer destroyed (↓ aldosterone): Hyponatremia, hyperkalemia

Hyperpigmentation





Addison's disease:



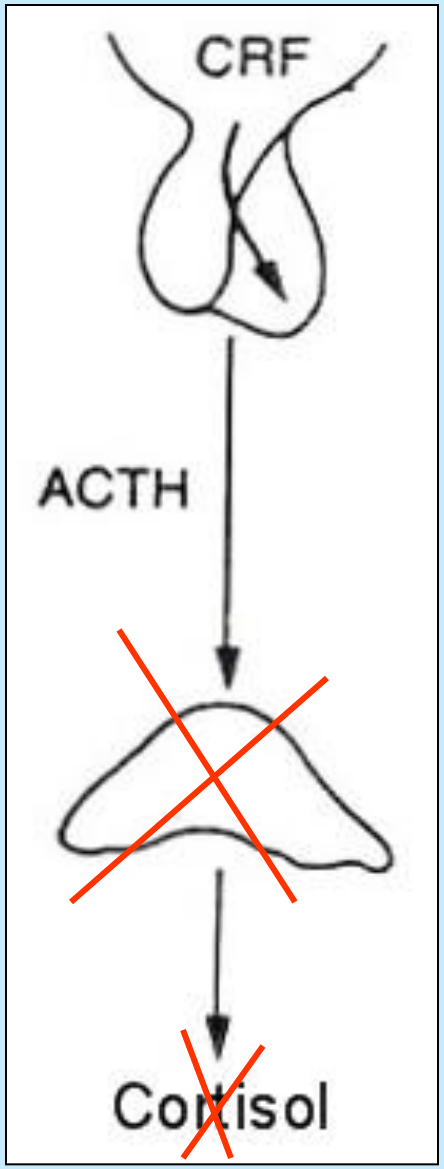
- Note the generalised skin pigmentation (in a Caucasion patient) but especially the deposition in the palmer skin creases, nails and gums.

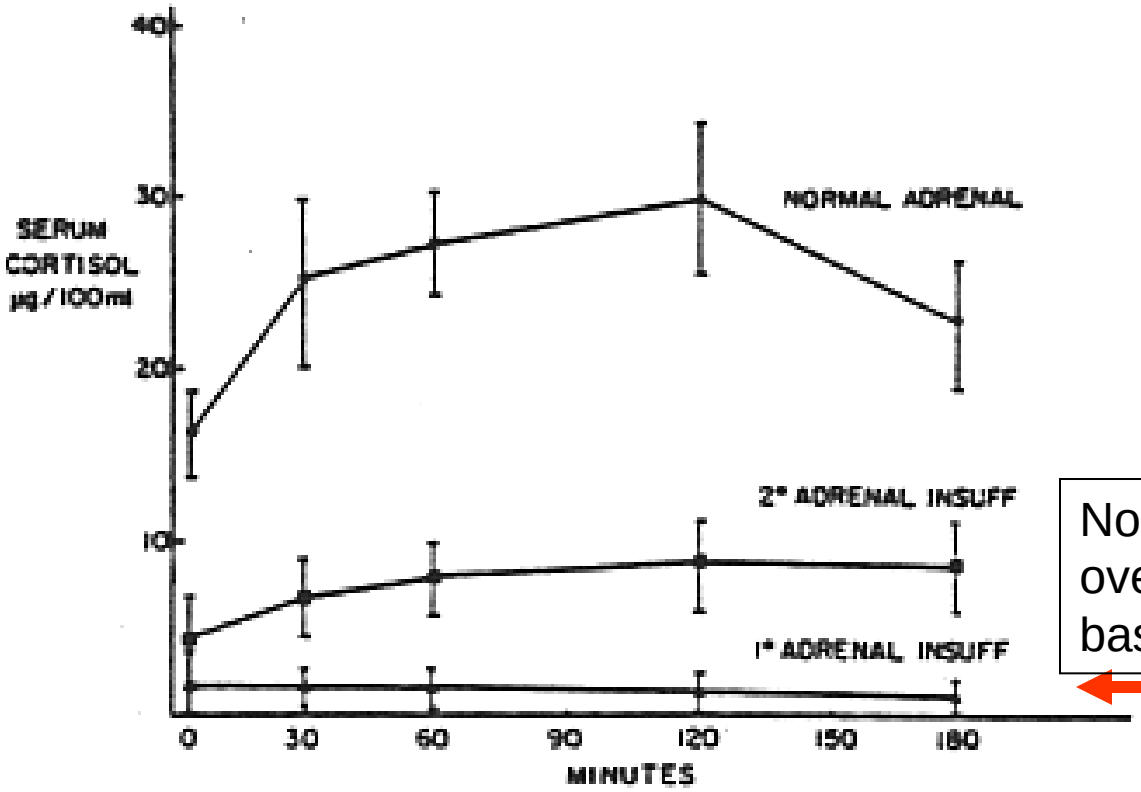
- She was treated many years ago for pulmonary TB. What are the other causes of this condition?

Addison's Disease

- Laboratory assessment:
  - Baseline: ↓ cortisol, ↓ UFC, ↑ ACTH
  - ACTH stimulation test:

    Cortisol levels will not increase over baseline





No change over baseline

Figure 8–1. Serum cortisol response to 0.25 mg of ACTH (cosyntropin as a rapid intravenous bolus) administered to normal subjects and patients with primary adrenal insufficiency (Addison's disease) and secondary adrenal insufficiency (hypopituitarism). There is a clear difference between serum cortisol levels in normals and those with adrenal insufficiency. (Reproduced by permission, Speckart, P. F., Nicoloff, J. T., Bethume, J. E.: Arch. Intern. Med., *128*:761, 1971.)

Addisonian Crisis

- Acute adrenal insufficiency: life threatening event
- Generally, the patient already has an adrenal insufficiency and is on glucocorticoid replacement therapy
- After a prolonged stress event the cortisol reserve is ‘used up’ which means the patient can no longer cope with any additional stressors

Addisonian Crisis

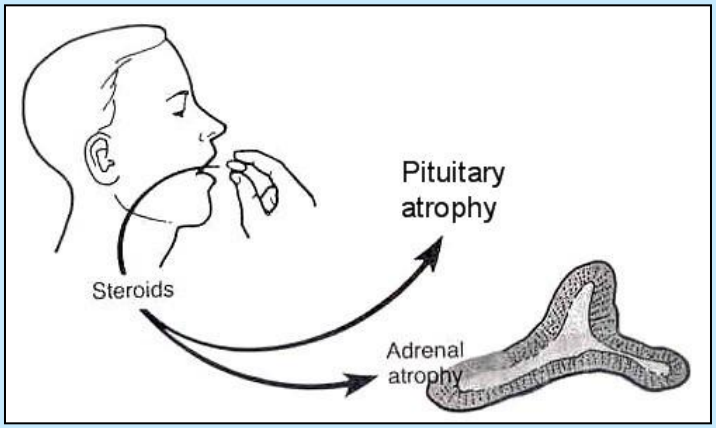
- If stressed, a sudden decrease in cortisol occurs causing the patient to collapse
- Symptoms: rapidly evolves into circulatory shock, vascular collapse, coma and death
- Aggressive treatment (ER)
- Glucocorticoid supplements required during times of stress, illness

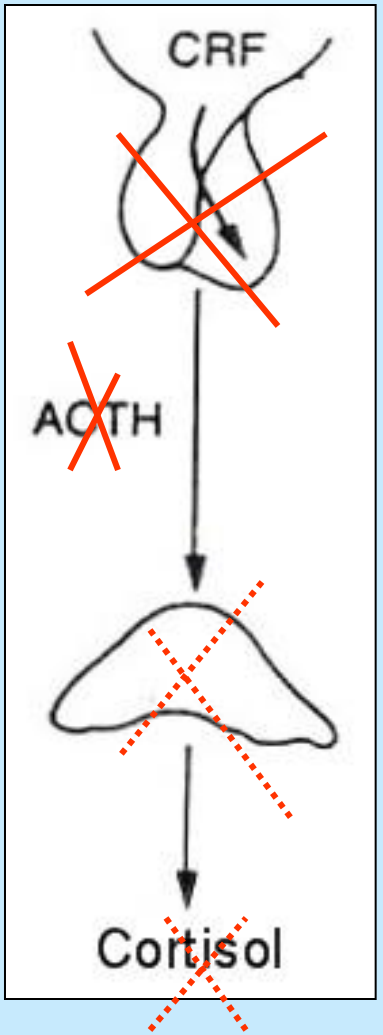
steroid pill

Hypocortisolism, lack ACTH

- Classified as a secondary disorder:
  ↓ cortisol, ↓ ACTH

- Caused by:
  - Pituitary disease (panhypopituitarism)
  - Long term glucocorticoid treatment causing iatrogenic pituitary insufficiency





Hypocortisolism, lack ACTH

- Symptoms:

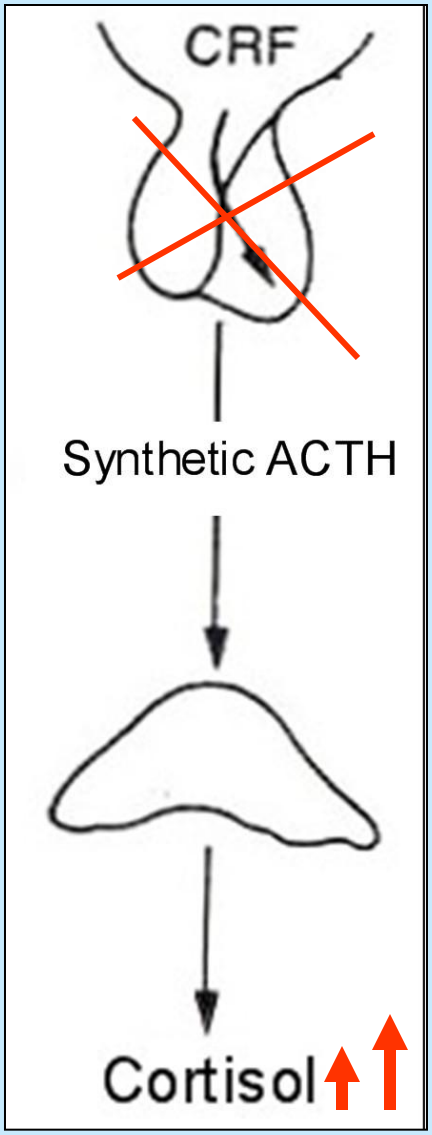
  Same as for primary disease, except no hyperpigmentation (due to lack of ACTH)
  - Fatigue, weakness, weight loss, GI disturbances
  - PP hypoglycemia, stress intolerance, hypotension

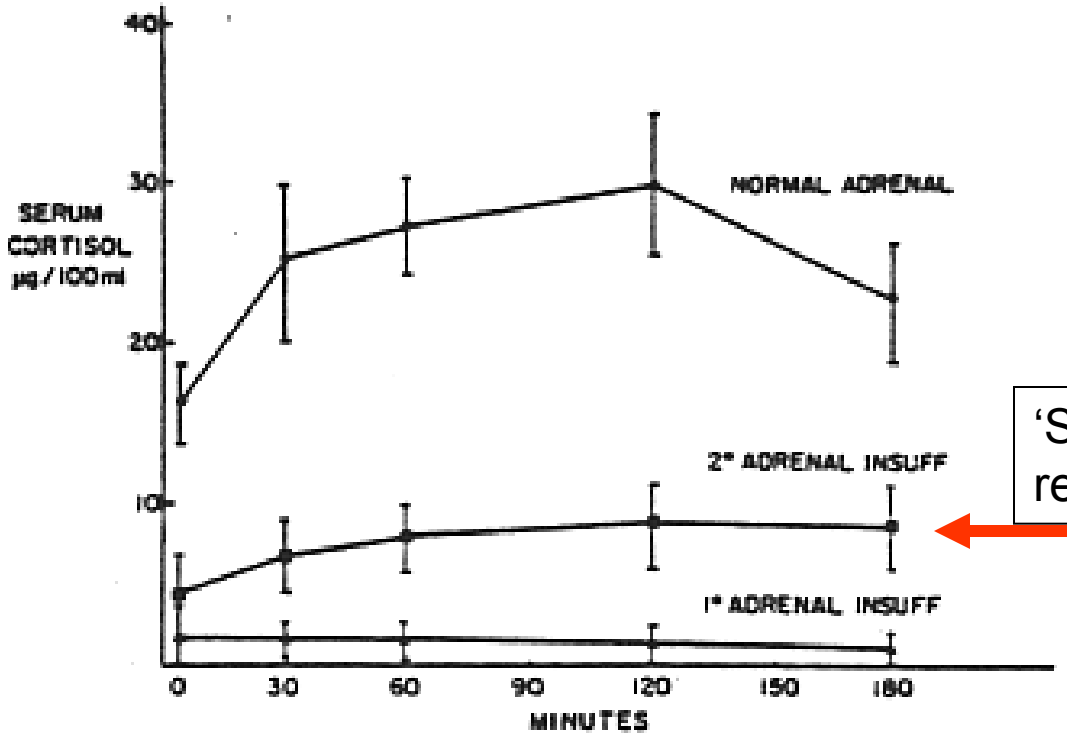
Hypocortisolism, lack ACTH

- Laboratory assessment:
  - Baseline: ↓ cortisol, ↓ UFC, ↓ ACTH
  - ACTH Stimulation Test:

    Progressive staircase rise in cortisol levels over 2-3 days of testing suggests a healthy adrenal gland that was atrophied due to a lack of ACTH stimulation
    - Pituitary dysfunction
    - Hypothalamus dysfunction (rare)
    - Exogenous glucocorticoid treatment (suppresses pituitary ACTH)

steroid pill





'Stair-step response'

Figure 8–1. Serum cortisol response to 0.25 mg of ACTH (cosyntropin as a rapid intravenous bolus) administered to normal subjects and patients with primary adrenal insufficiency (Addison's disease) and secondary adrenal insufficiency (hypopituitarism). There is a clear difference between serum cortisol levels in normals and those with adrenal insufficiency. (Reproduced by permission, Speckart, P. F., Nicoloff, J. T., Bethune, J. E.: Arch. Intern. Med., *128*:761, 1971.)

Hypocortisolism, lack ACTH

- Note:

  Aldosterone levels most often are normal with a secondary disorder because ACTH is not the primary regulator of aldosterone

Too much Adrenaline

Phaeochromocytoma

Phaeochromocytoma

Neuroblastoma

Paraganglioma

Ganglioneuroma

Are derived from the neural crest

Catecholamine Excess

- Pheochromocytoma
  - hypertension
  - palor
  - headaches
  - palpitations
  - anxiety
  - weight loss
- Increased Catecholamines in urine
  - metanephrines
- Treatment is Surgical

Symptoms

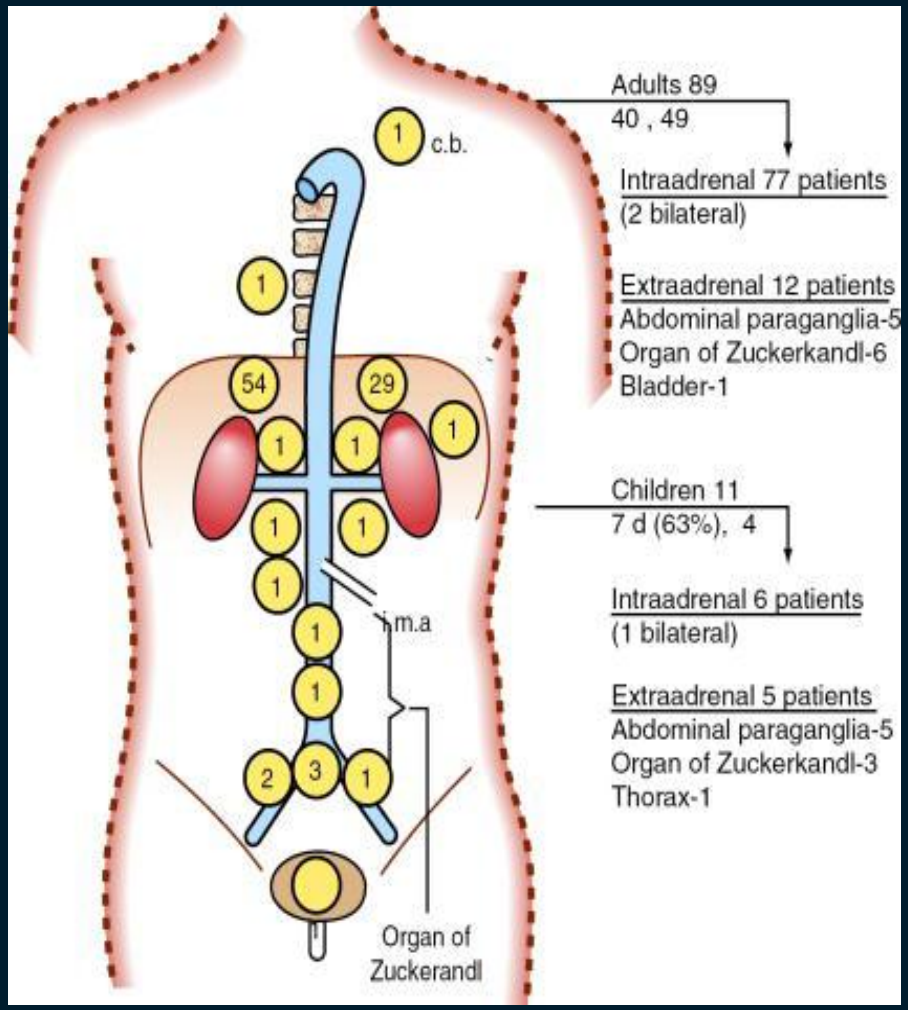
- Attacks often occur spontaneously but may be precipitated by vigorous exercise , twisting and bending, Alcohol, tobacco and drugs : Anesthesia, phenothiazines & tricyclic antidepressants.

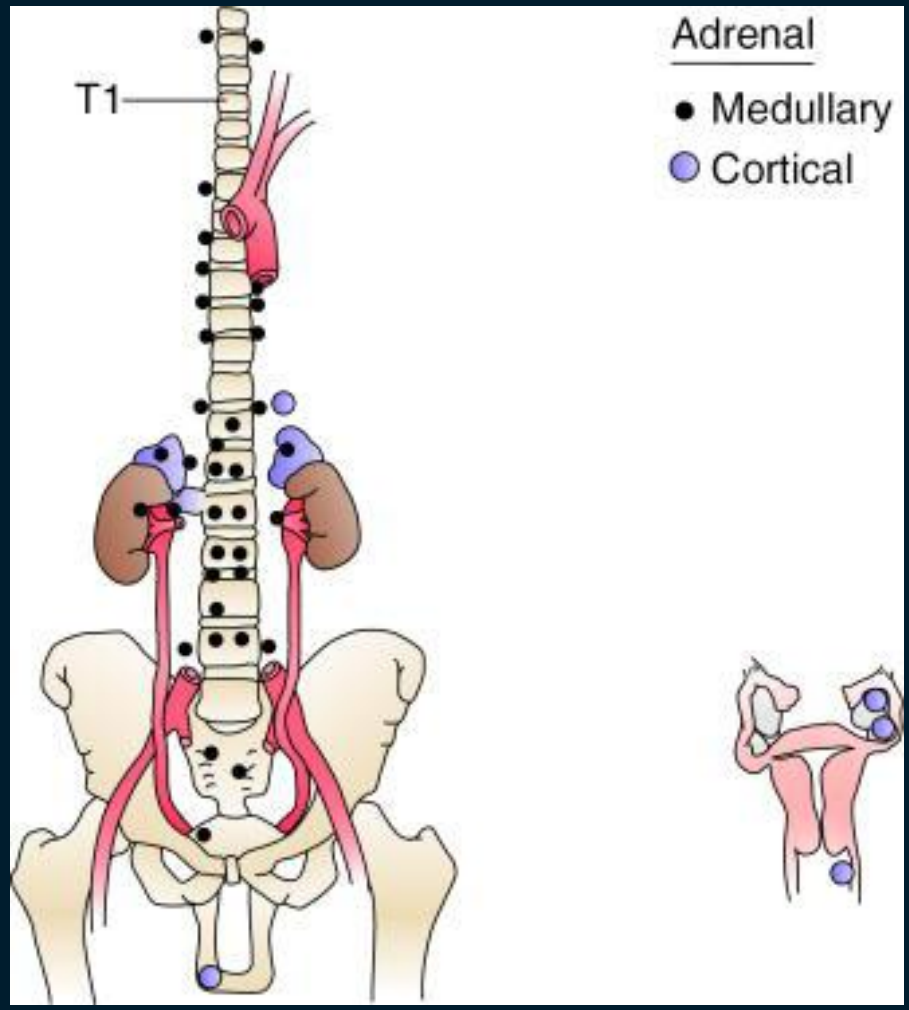
Phaeochromocytoma

- 90% ---solitary – adrenal
- 5 –10% bilateral
- 10%---Exrta-adrenal
- 0.1% of patients investigated for hypertension
- Average size is 5 cm
- Discovered early because of catecholamines effects
- 10% are malignant
- Mostly secrets adrenaline

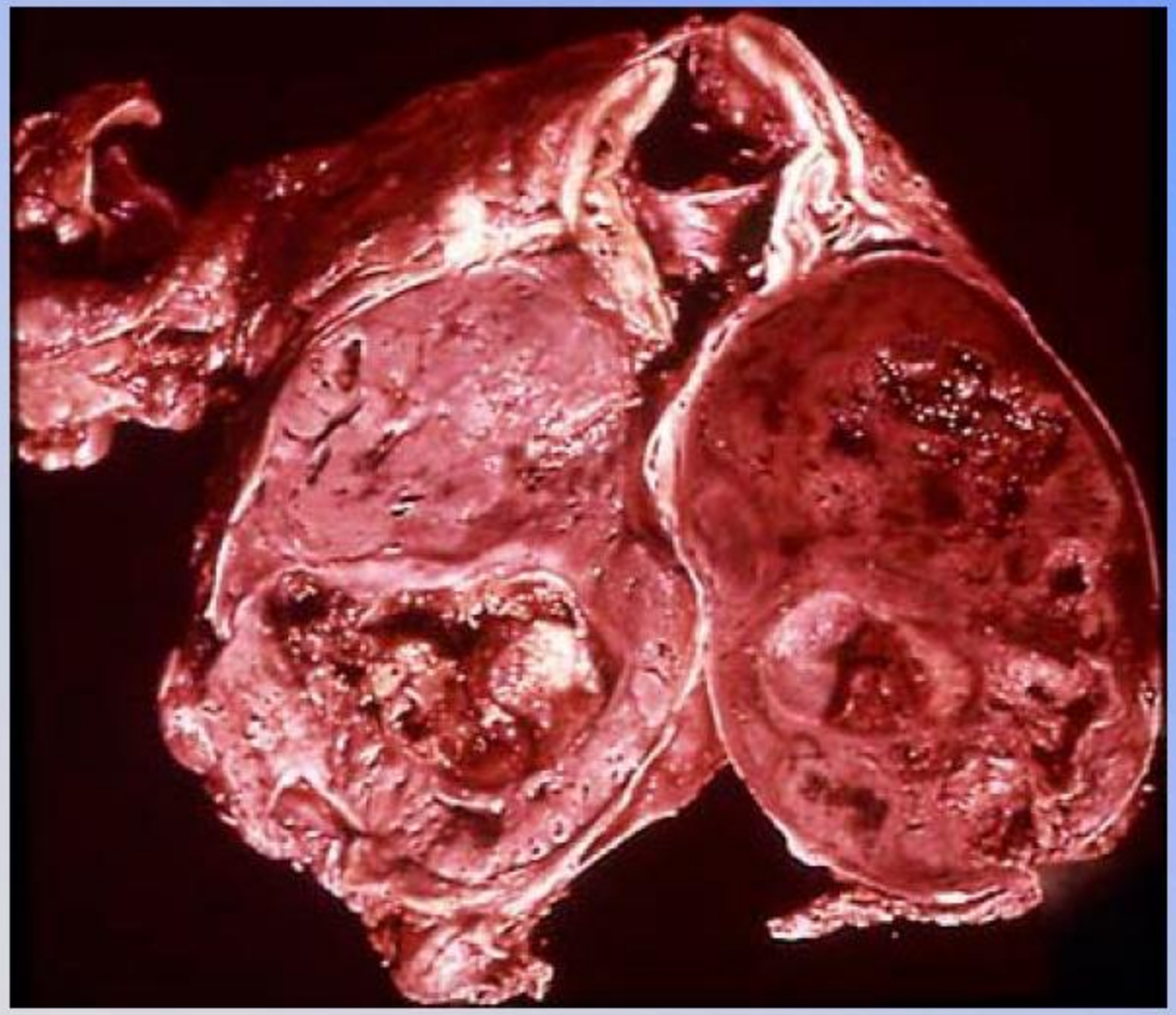
Pheo: ‘Rule of 10’

- 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


Adults 89
40 , 49
Intraadrenal 77 patients
(2 bilateral)
Extraadrenal 12 patients
Abdominal paraganglia-5
Organ of Zuckerkandl-6
Bladder-1
Children 11
7 d (63%), 4
Intraadrenal 6 patients
(1 bilateral)
Extraadrenal 5 patients
Abdominal paraganglia-5
Organ of Zuckerkandl-3
Thorax-1
c.b.
i.m.a
Organ of Zuckerandl


T1
Adrenal
Medullary
Cortical

Pheochromocytoma



Familial Pheo

- MEN 2a
  - 50% Pheo (usually bilateral), MTC, HPT
- MEN 2b
  - 50% Pheo (usually bilatl), MTC, mucosal neuroma, marfanoid habitus
- Von Hippel-Landau
  - 50% Pheo (usually bilat), retinoblastoma, cerebellar hemangioma, nephroma, renal/pancreas cysts
- NF1 (Von Recklinghausen's)
  - 2% Pheo (50% if NF-1 and HTN)
  - Café-au-lait spots, neurofibroma, optic glioma
- Familial paraganglioma
- Familial pheo & islet cell tumor
- Other: Tuberous sclerosis, Sturge-Weber, ataxia-telangectgasia, Carney's Triad (Pheo, Gastric Leiomyoma, Pulm chondroma)

Investigations

- A– 24 hours urinary vanyl mandilic acid (VMA) 60% sensitive.
- Urinary catecholamines . 90% sensitive
- Localization: C T scan

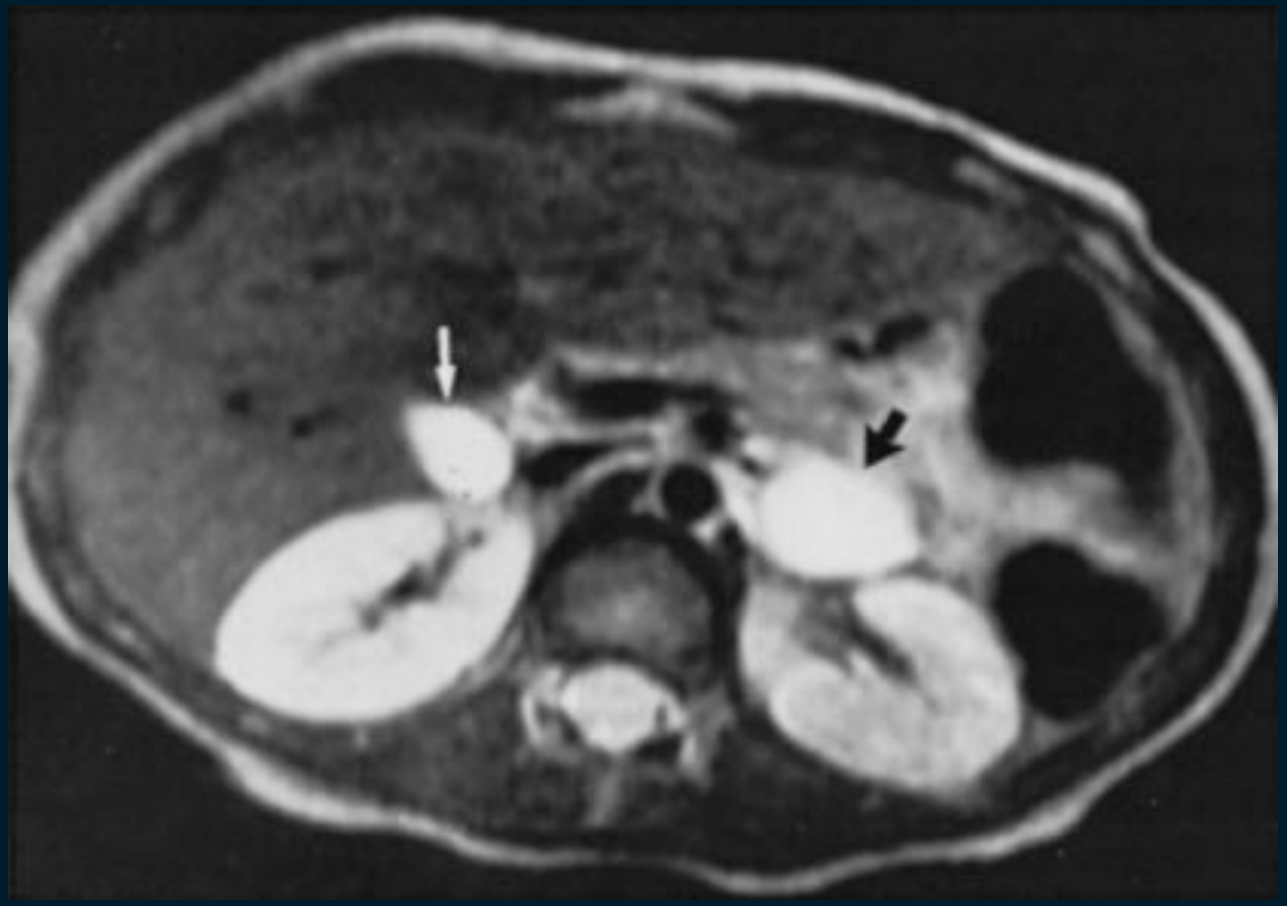
  M R I

  M I B G , isotope scan

Table 37-9 -- Sensitivity and Specificity of Biochemical Tests for Diagnosis of Pheochromocytoma

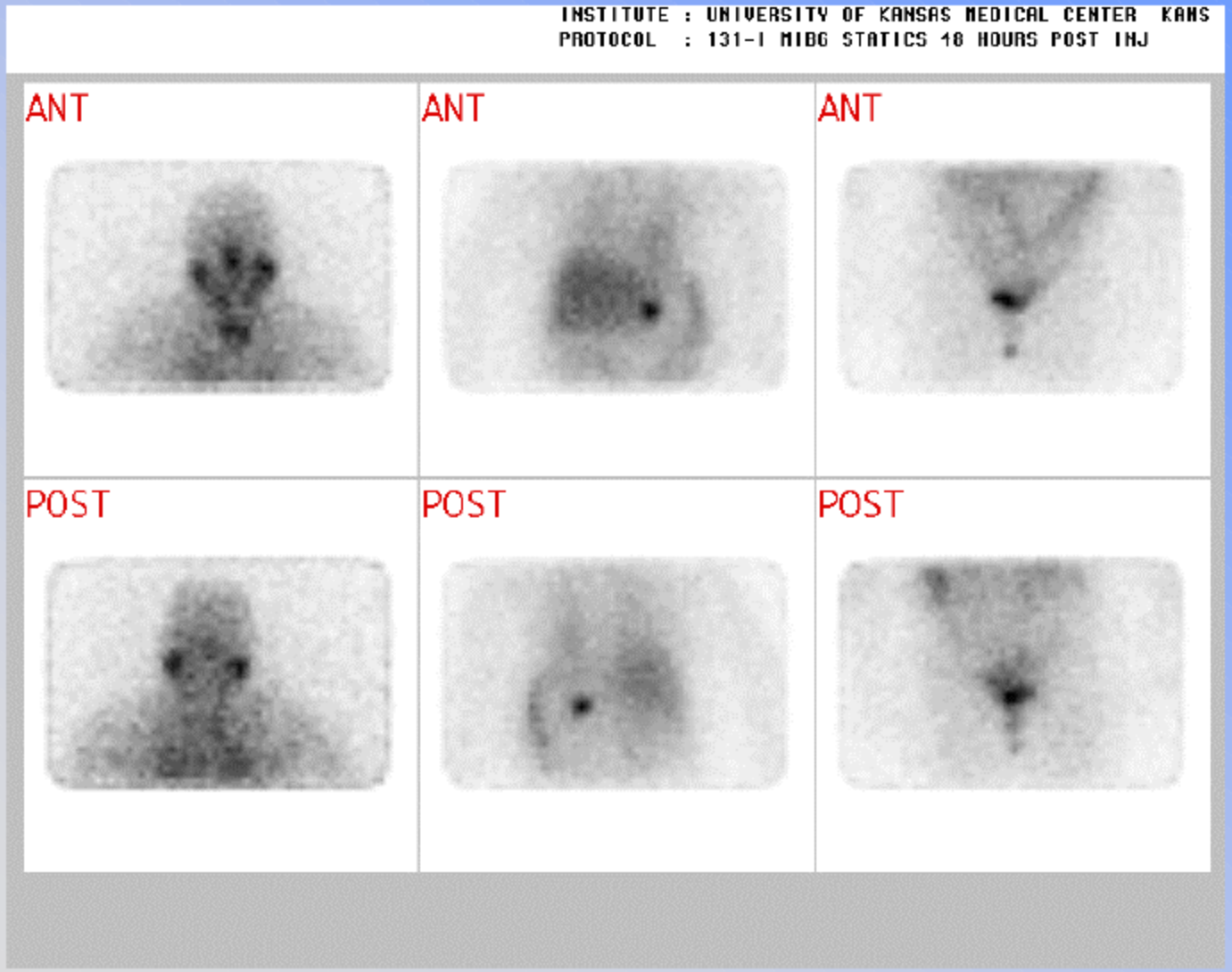
Biochemical Test	Sensitivity (%)	Specificity (%)
Plasma metanephrine level	99	89
Plasma catecholamine level	85	80
Urinary catecholamine level	83	88
Urinary metanephrine level	76	94
Urinary vanillylmandelic acid level	63	94

Ann Intern Med. 134:318, 2001.



T2-weighted MR study of a left-sided **pheochromocytoma** *(black arrow)*. The gallbladder *(white arrow)* has an increased signal intensity because of its high water content. **Pheochromocytomas**, adrenocortical carcinomas, and metastatic lesions to the adrenal gland demonstrate this high signal intensity, possibly because of their high water content.

MIBG scan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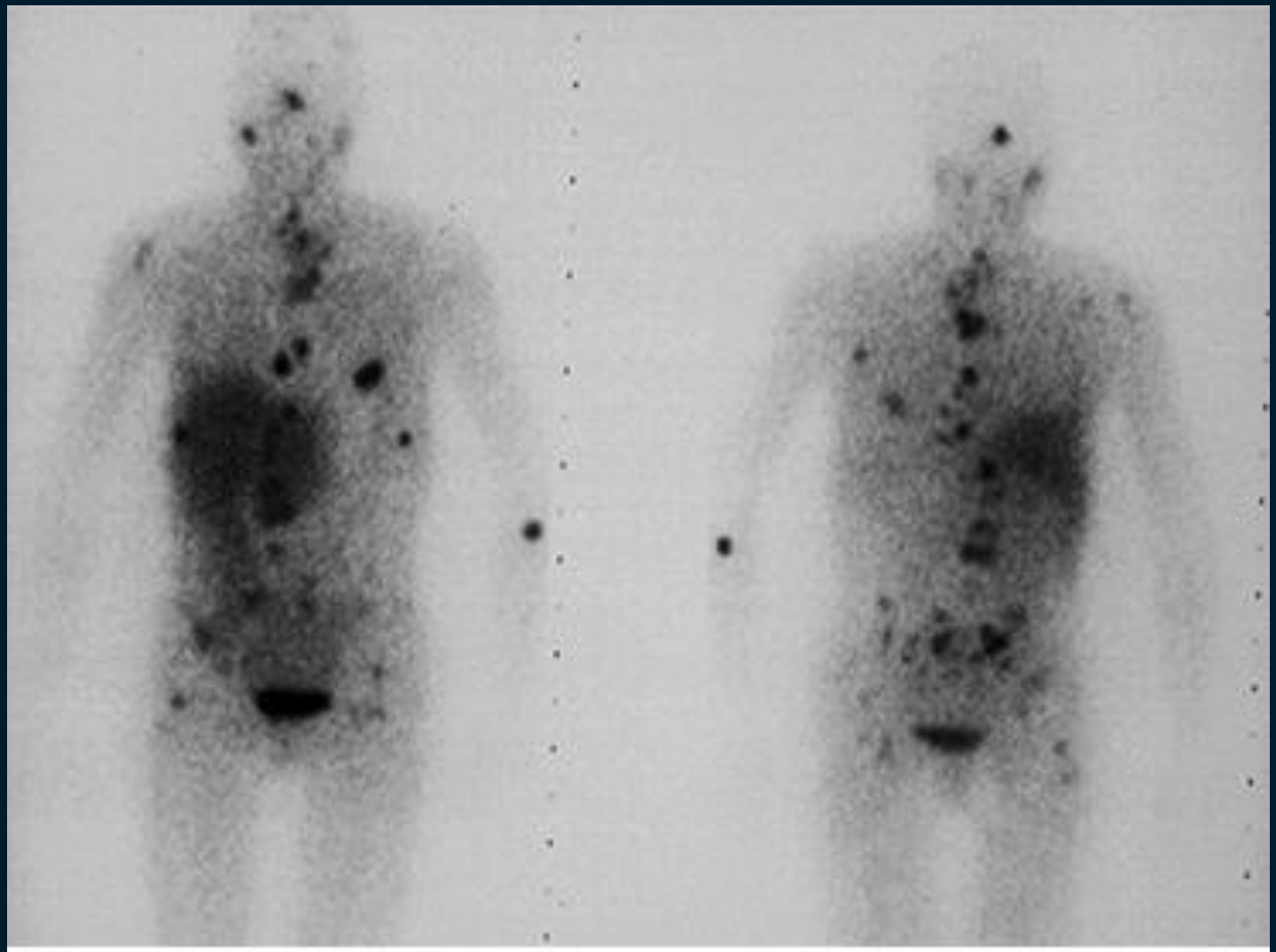

Diffuse metastatic pheochromocytoma 123-I-meta-iodobenzylguanidine scan from a 41-year-old woman shows diffuse metastatic pheochromocytoma. Courtesy of William F Young, Jr, MD.