THE UNIVERSITY OF ARIZONA | COLLEGE OF MEDICINE PHOENIX

Adrenal Disorders

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Objectives

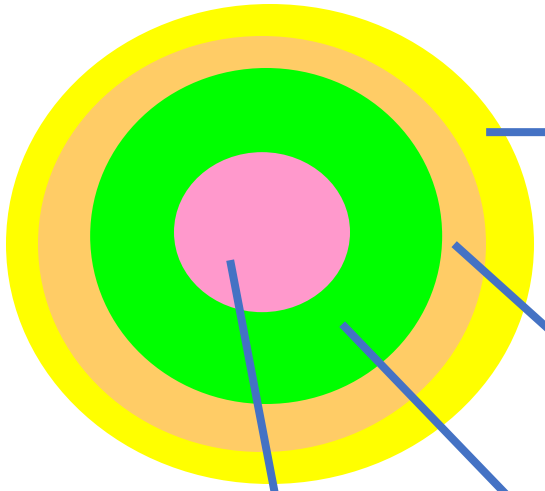
- Review pathogenesis and clinical presentation
  - Adrenal incidentaloma
  - Cortisol excess (Cushing's)
  - Mineralocorticoid excess
- Review principles of diagnosis and therapy for each conditions

A 62-year-old lady comes to see you because she has gained weight and feels depressed. She generally feels weak particularly if she climbs stairs. Her past medical history is also significant for borderline diabetes mellitus. She has been under a lot of stress recently because of the death of her mother and her daughter is undergoing a divorce. On examination: her face is a bit puffy and she has bruises over her arms. There are no abdominal striae. She has a fungal infection in her mouth. 24-hour urine free cortisol is 190 ug/24 hours (normal range 5-55 ug/24hrs).

Which part of the adrenal is most likely affected

a. Zona glomerulosa of the adrenal cortex
b. Zona fasciculata of the adrenal cortex
c. Zona reticularis of the adrenal cortex
d. Adrenal Medulla

Adrenals



Cortex

Zona Glomerulosa

Mineralocorticoids (Aldosterone)

Na+, K+ and water homeostasis

Zona Fasciculata

Glucocorticoids (Cortisol)

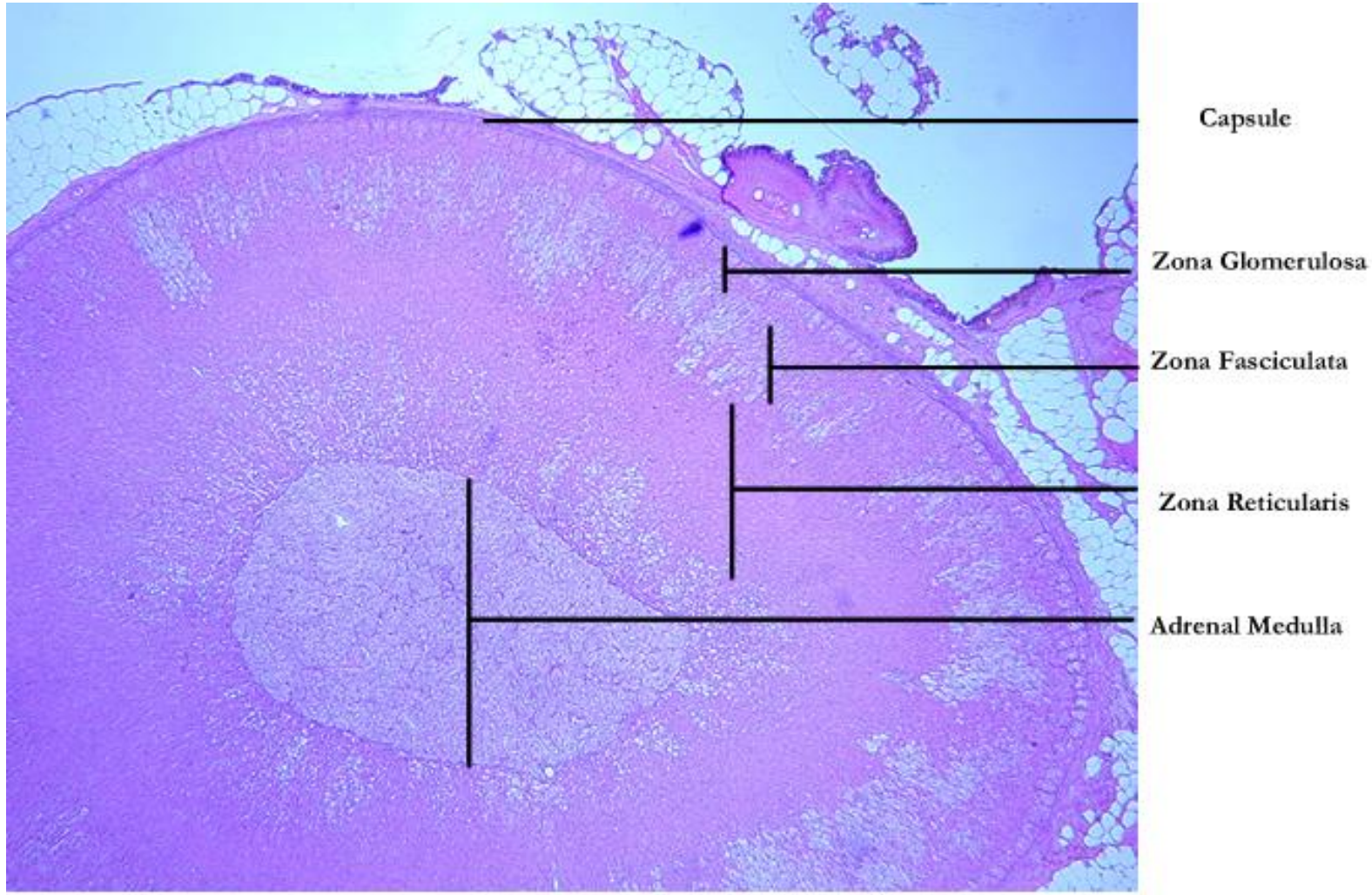
Glucose homeostasis and many others

Zona Reticularis

Sex steroids (androgens)

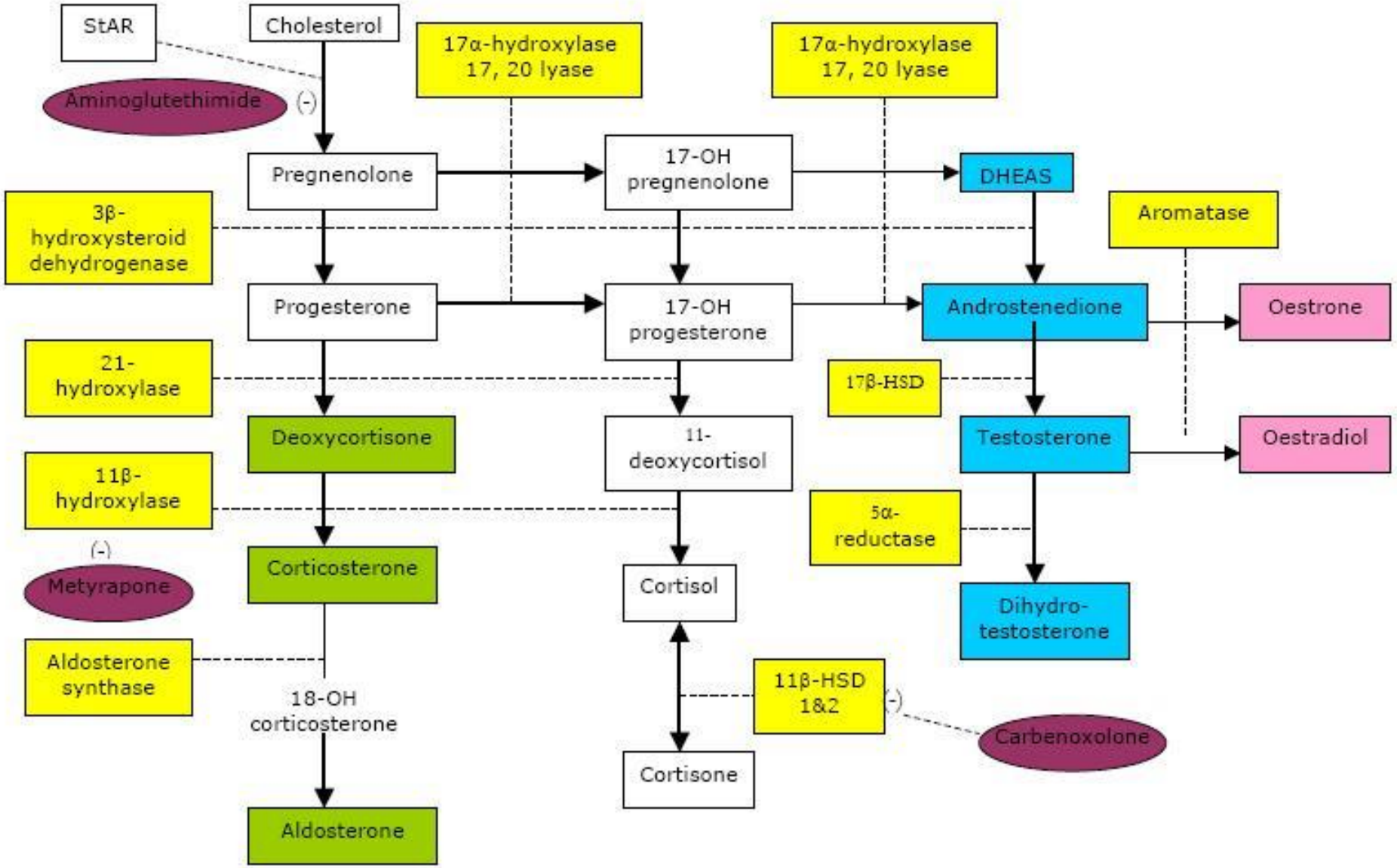
Medulla: "Catecholamines"

Epinephrine, Norepinephrine, dopamine

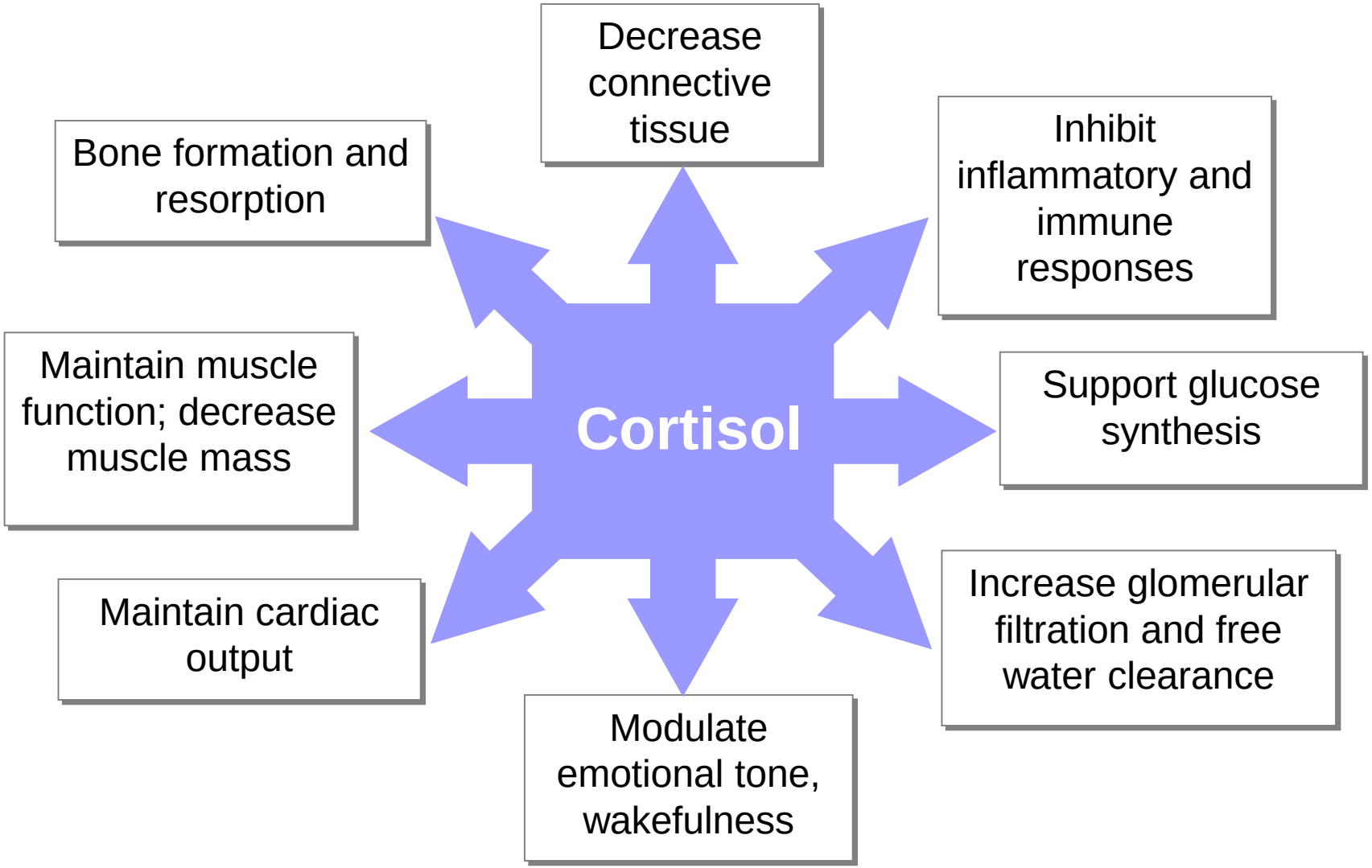


Adrenal Gland (40x)

Biosynthesis steroid Hormones



Cortisol is not just a stress hormone...



What does cortisol do?

Effect on:	How?	Effect of too much cortisol
Blood pressure	• Up-regulates of alpha 1 receptors on arterioles (→ sensitivity to catecholamines) • Binds to aldosterone receptor	Hypertension
Glucose, lipid and protein metabolism	• Increases insulin resistance (→more sugar) • Increases glucose production (→more sugar) • Increases fat and protein catabolism (→decreased lean mass and more sugar)	Diabetes mellitus
Fibroblasts	• Decreases fibroblast activity • Decrease fibril and collagen production	Striae
Bones	• Decreases osteoblast activity → decreases bone formation • Increases bone resorption	Osteoporosis, fractures
Inflammatory and immune responses	• Decreases eosinophils, production of IL-2, leukotrienes, prostaglandines and histamine release • Increases neutrophils	Infection, decreased allergic response
Appetite, sleep	• Modulates sleep, increases appetite	Weight gain

Adrenal cortex diseases

Glucocorticoids	Mineralocorticoids	Androgens
<u>Cushing Syndrome:</u> - **primary:** autonomous adrenal cortisol production - **central:** increased stimulation of adrenal cortisol production (ACTH)	<u>Primary hyperaldosteronism:</u> autonomous adrenal aldosterone production	<u>Hyperandrogenism</u>: In females only: signs of male hormone excess
<u>Adrenal insufficiency:</u> - **primary:** destruction of zona fasciculata or steroidogenesis enzymatic defect - **central:** inadequate stimulation of adrenal cortisol production (ACTH)	<u>Mineralocorticoid deficiency</u> destruction of zona glomerulosa or steroidogenesis enzymatic defect	<u>Androgen deficiency</u> - inadequate stimulation of adrenal cortisol production (ACTH) - destruction of zona reticularis - steroidogenesis enzymatic defect

A 33-year-old man has been referred to you for evaluation of Cushing syndrome. He has had a 20-lb (9.1-kg) weight gain in the past 9 months accompanied by the onset of hypertension and edema. He has noted marked weakness, especially when climbing stairs. His family history is negative for any endocrine disorders. He takes no medications.

On physical examination, he has facial rounding and supraclavicular and dorsocervical fat accumulation. His blood pressure is 168/110 mm Hg, and pulse rate is 94 beats/min. His height is 75 in (190.5 cm), and weight is 220 lb (100 kg) (BMI = 27.5 kg/m2). He has wide, violaceous striae on his abdomen; proximal muscle weakness; and 2+ pretibial edema.

Laboratory test results:

- Sodium = 142 mEq/L (136-142 mEq/L) (SI: 142 mmol/L [136-142 mmol/L])
- Potassium = 3.0 mEq/L (3.5-5.0 mEq/L) (SI: 3.0 mmol/L [3.5-5.0 mmol/L])
- Creatinine = 1.1 mg/dL (0.7-1.3 mg/dL) (SI: 97.2 µmol/L [61.9-114.9 µmol/L])
- Urinary free cortisol = 632 µg/24 h (4-50 µg/24 h) (SI: 1744 nmol/d [11-138 nmol/d])
- Late-night salivary cortisol = 2.1 µg/dL (<0.13 µg/dL) (SI: 58 nmol/L [<3.6 nmol/L])
- DHEA-S = 678 µg/dL (65-334 µg/dL) (SI: 18.4 µmol/L [1.76-9.05 µmol/L])
- Basal plasma ACTH = <5 pg/mL (10-60 pg/mL) (SI: <1.1 pmol/L [2.2-13.2 pmol/L])

Which of the following imaging studies descriptions are most likely in this man?

A. *3 cm adrenal nodule with Hounsfield units = -2*

B. *4 cm adrenal nodule with Hounsfield units = 20 with washout of 58%*

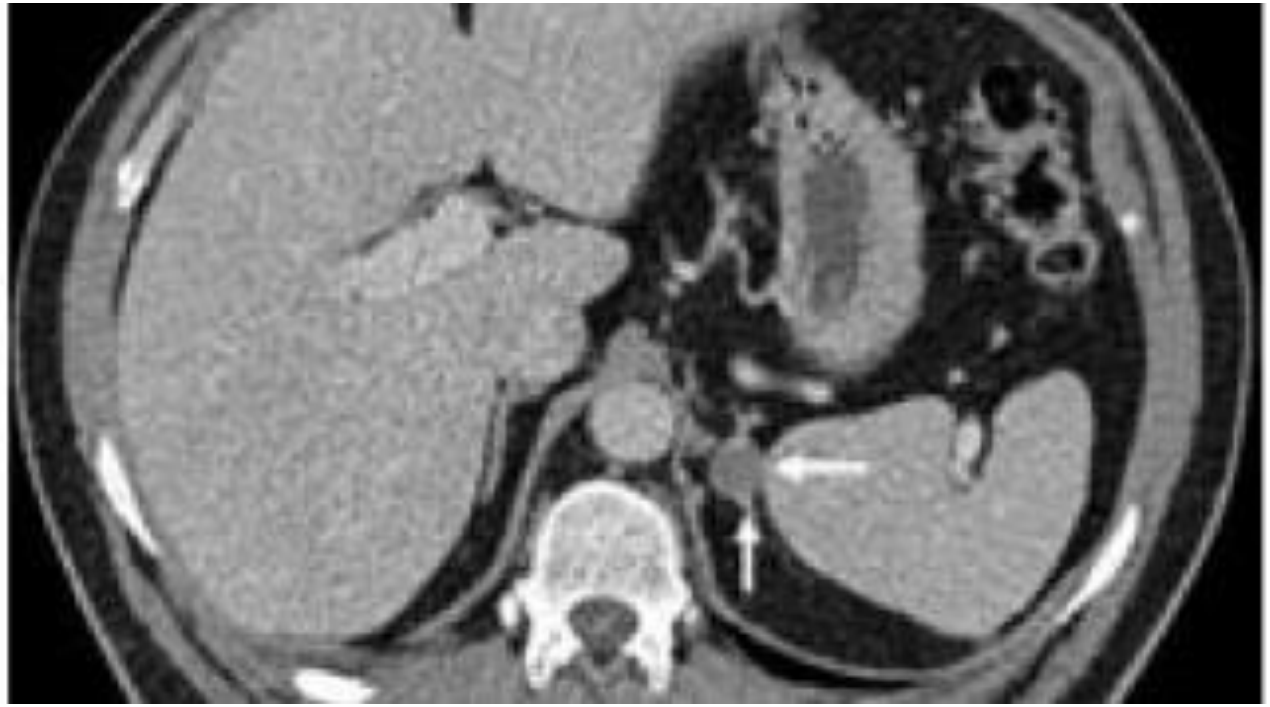
C. *4 cm adrenal nodule with Hounsfield units = 78 with relative enhancement washout of 12%*

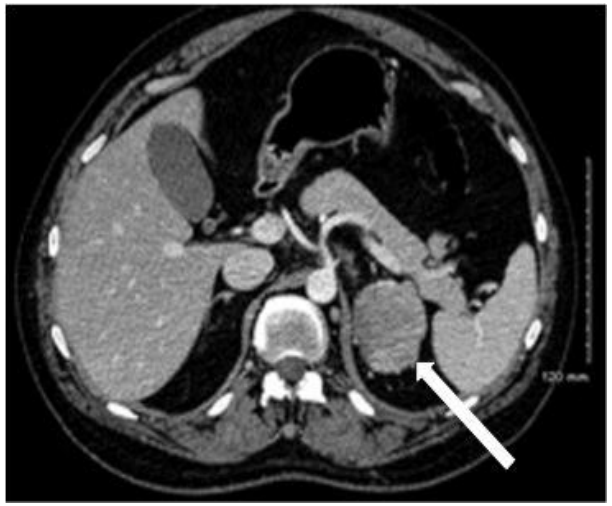
D. *3 cm adrenal nodule with Hounsfield unit = 10*

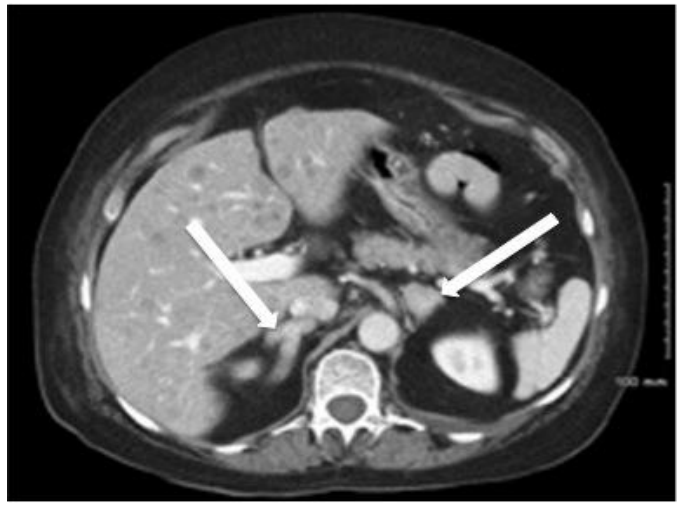
Adrenal incidentaloma

- Detection of an unsuspected adrenal mass on radiologic imaging.
- Patients have no symptoms or clinical evidence of adrenal disease
- Excludes patients undergoing imaging procedures as part of staging and work-up for cancer

Adrenal incidentalomas







Adrenal incidentaloma

- 80% nonfunctioning adenoma
- 5% subclinical Cushing syndrome
- 3% pheochromocytoma
- 1% primary hyperaldosteronism
- <5% adrenocortical carcinoma
- 2.5% metastatic lesion

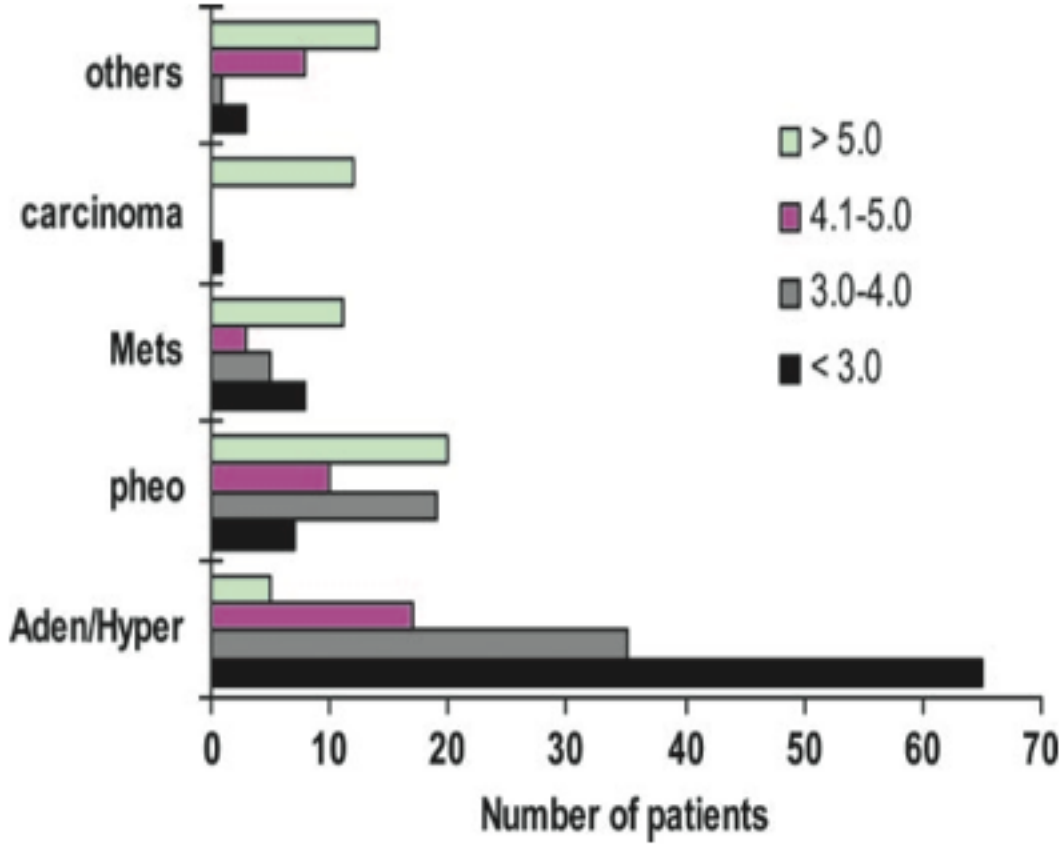
Evaluation

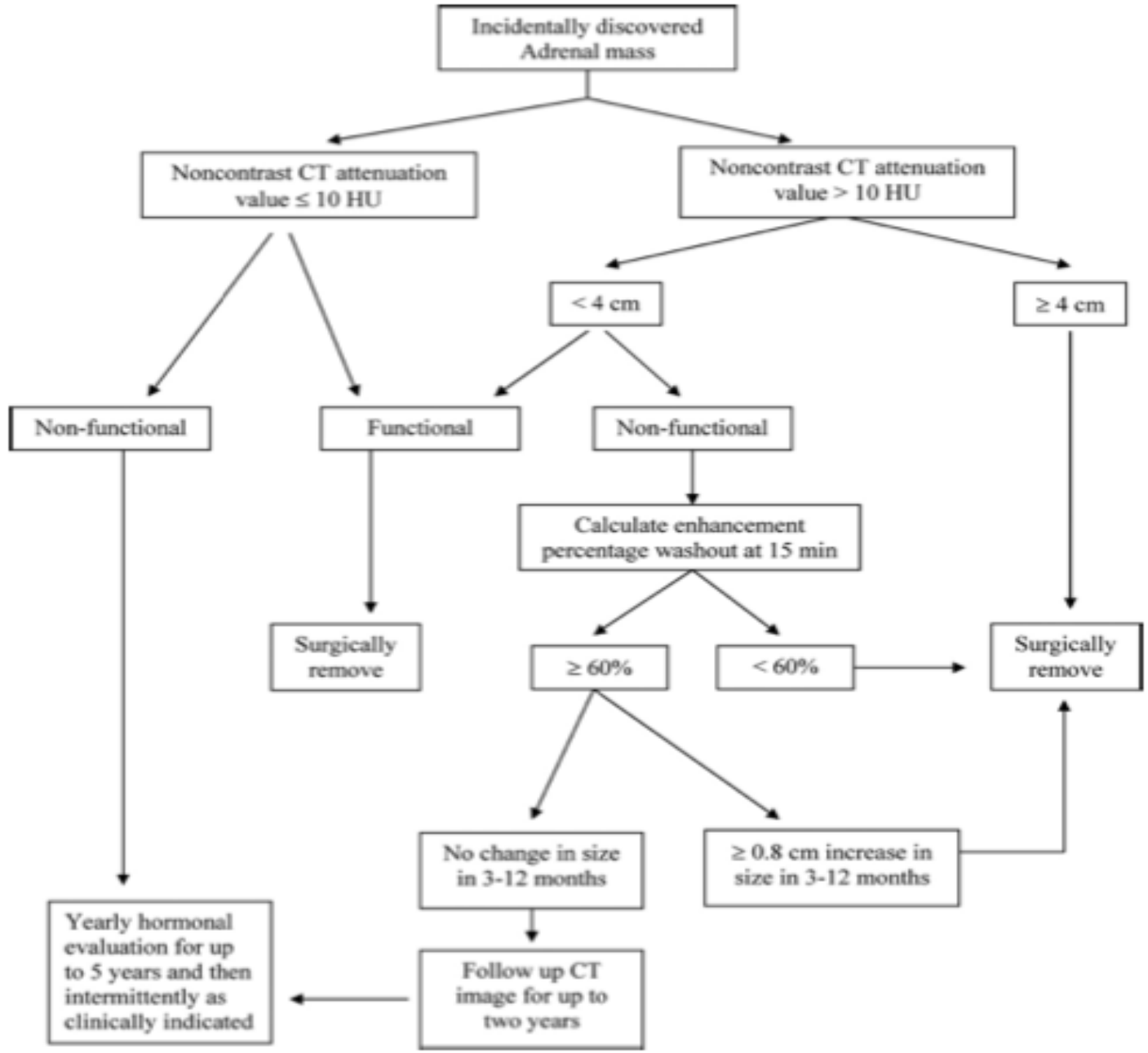
- Is it malignant?
    - features on imaging studies
    - tumor size

Imaging features

- The intracellular lipid content is used to distinguish adenomas from non adenomas
- Adenomas often contain abundant intracytoplasmatic fat and thus have low attenuation **(<10 HU)** on nonenhanced CT scan
- CT scan with enhancement washout is valuable in differentiating lipid poor (noncontrast HU >10) adenomas from non-adenomas
- An absolute enhancement washout percentage of **less than 50%** at 15 minutes after giving contrast strongly suggests a non-adenoma

Tumor size


others
carcinoma
Mets
pheo
Aden/Hyper
> 5.0
4.1-5.0
3.0-4.0
< 3.0
0
10
20
30
40
50
60
70
Number of patients


Incidentally discovered Adrenal mass
Noncontrast CT attenuation value ≤ 10 HU
Noncontrast CT attenuation value > 10 HU
< 4 cm
≥ 4 cm
Non-functional
Functional
Non-functional
Calculate enhancement percentage washout at 15 min
Surgically remove
≥ 60%
< 60%
Surgically remove
No change in size in 3-12 months
≥ 0.8 cm increase in size in 3-12 months
Yearly hormonal evaluation for up to 5 years and then intermittently as clinically indicated
Follow up CT image for up to two years

Evaluation

- Is it functional?
  - 6-20% of patients with adrenal incidentalomas have hormonal abnormalities

- Subclinical Cushing’s syndrome (SCS)

-Cushing’s syndrome

- Pheochromocytoma

- Primary hyperaldosteronism

Subclinical Cushing’s syndrome

- Prevalence of about 5%
- Autonomous cortisol secretion in patients **without typical signs and symptoms** of Cushing’s syndrome
- Increased frequency of hypertension, glucose intolerance, diabetes and possibly osteopenia compared with the general population

Diagnosis

- 1 mg dexamethasone suppression test
- cortisol level of 1.8-5
  - > 5 ug/dL is considered to be clinically significant (specificity is 91%)

Management:
Surgical vs Conservative

- Retrospective study of 41 patients with adrenal incidentaloma and SCS followed for 18-48 months
- Significant improvement in blood pressure and fasting blood glucose who underwent surgery
- Significant worsening of blood pressure and fasting glucose in those who were managed conservatively

Management

- A reasonable strategy is to operate on younger patients (<40 years old) with a recent onset or worsening of diabetes, hypertension or osteoporosis

A 48-year-old woman has sustained 2 left metatarsal fractures in the past 18 months and is found to have low bone density (mean total hip T score of –2.4). She has a history of poorly controlled hypertension, and her cardiologist performs a chest CT to exclude coarctation of the aorta (negative), but a 1.4-cm left adrenal nodule (2 Hounsfield units) is discovered. Her medications are lisinopril, amlodipine, and metoprolol.

On physical examination, her blood pressure is 152/96 mm Hg and pulse rate is 64 beats/min. Her height is 64 in (162.6 cm), and weight is 136 lb (61.8 kg) (BMI = 23.3 kg/m2). Examination findings are normal.

Which of the following would be the most sensitive test for the diagnosis of autonomous cortisol secretion from this nodule?

A.Early-morning serum cortisol measurement

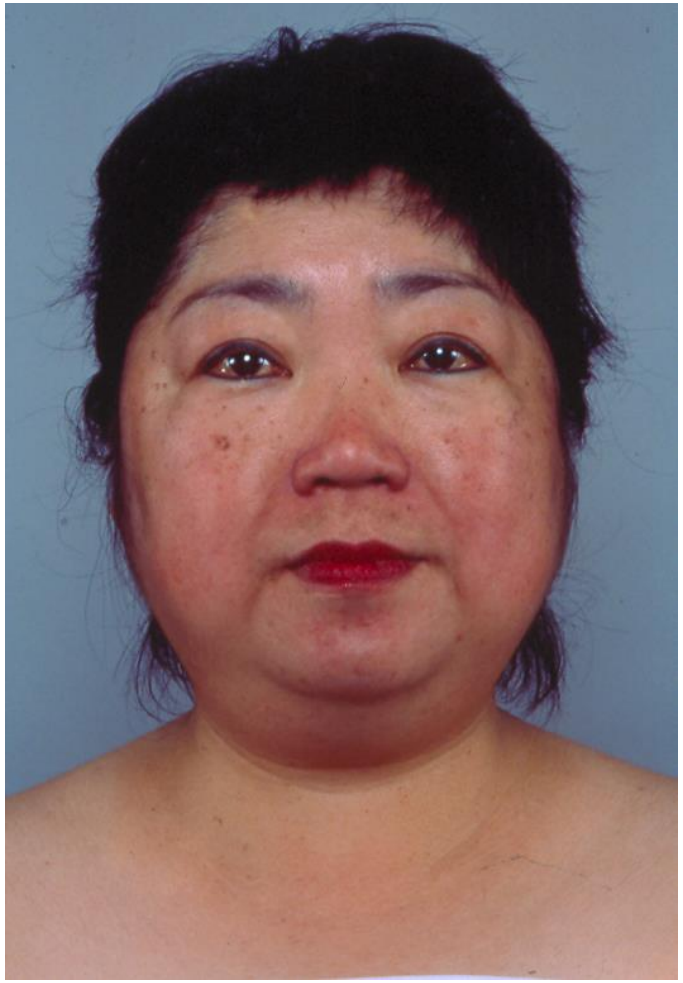
B.24-hour urinary free cortisol measurement

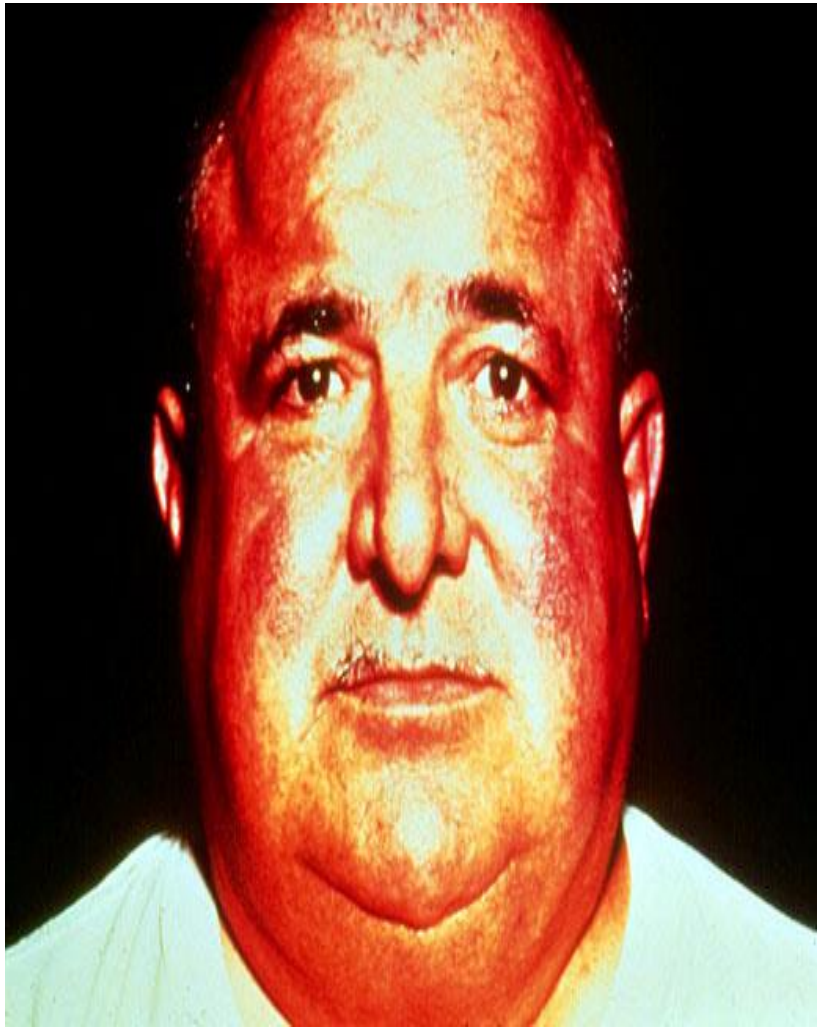
C.Late-night salivary cortisol measurement

D.MRI of adrenal glands

E.Overnight 1-mg dexamethasone suppression test

Cushing's Syndrome – too much cortisol



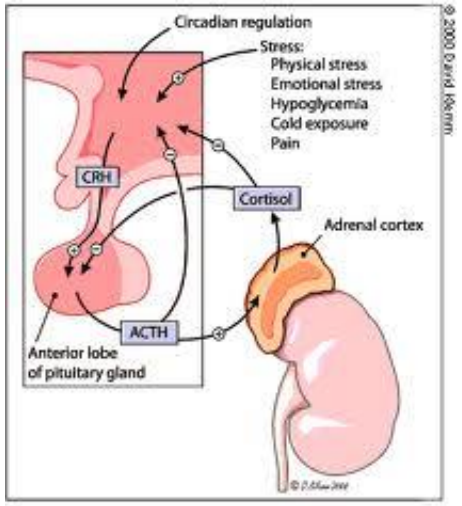


Hypercortisolism

- Which of the following is the most common cause of hypercortisolism?

a. Pituitary (Cushing's disease)
b. Adrenal (Cushing's syndrome)
c. Ectopic ACTH production
d. Prednisone use
e. Ectopic corticotropin releasing hormone (CRH)

Hypercortisolism

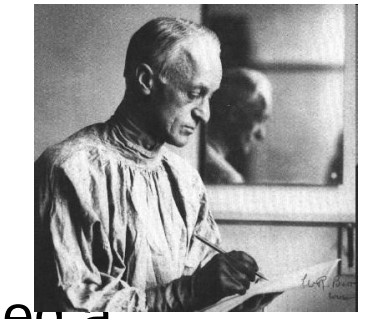


Causes of Hypercortisolism	
Etiology	Frequency
Pituitary adenoma	65%-70%
Ectopic ACTH	10%-15%
Adrenal adenoma	10%
Adrenal cancer	5%-10%

Hypercortisolism

- ACTH dependent Cushing's syndrome:
  - Pituitary adenoma
  - Ectopic ACTH production (often in the lung)
- ACTH independent Cushing's syndrome:
  - Adrenal adenoma
  - Adrenal cancer
  - Adrenal hyperplasia
- Other causes of hypercortisolism:
  - Depression
  - Alcoholism
  - Obesity, and stressful situation

Cushing's Syndrome – too much cortisol



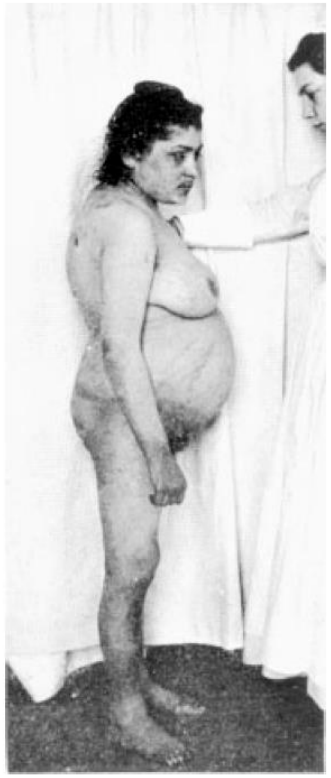
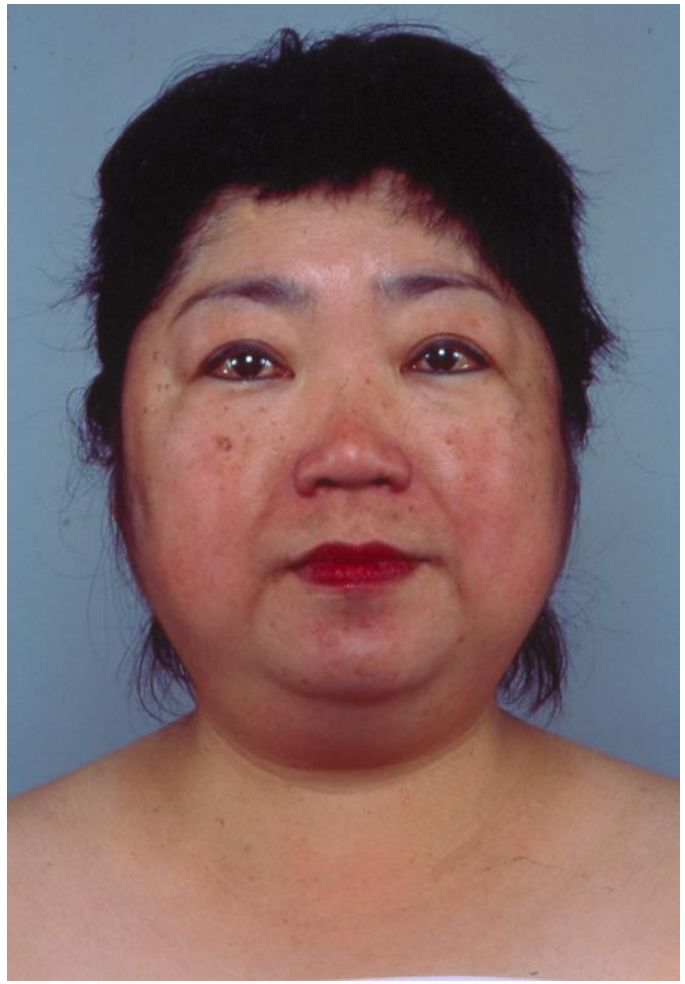


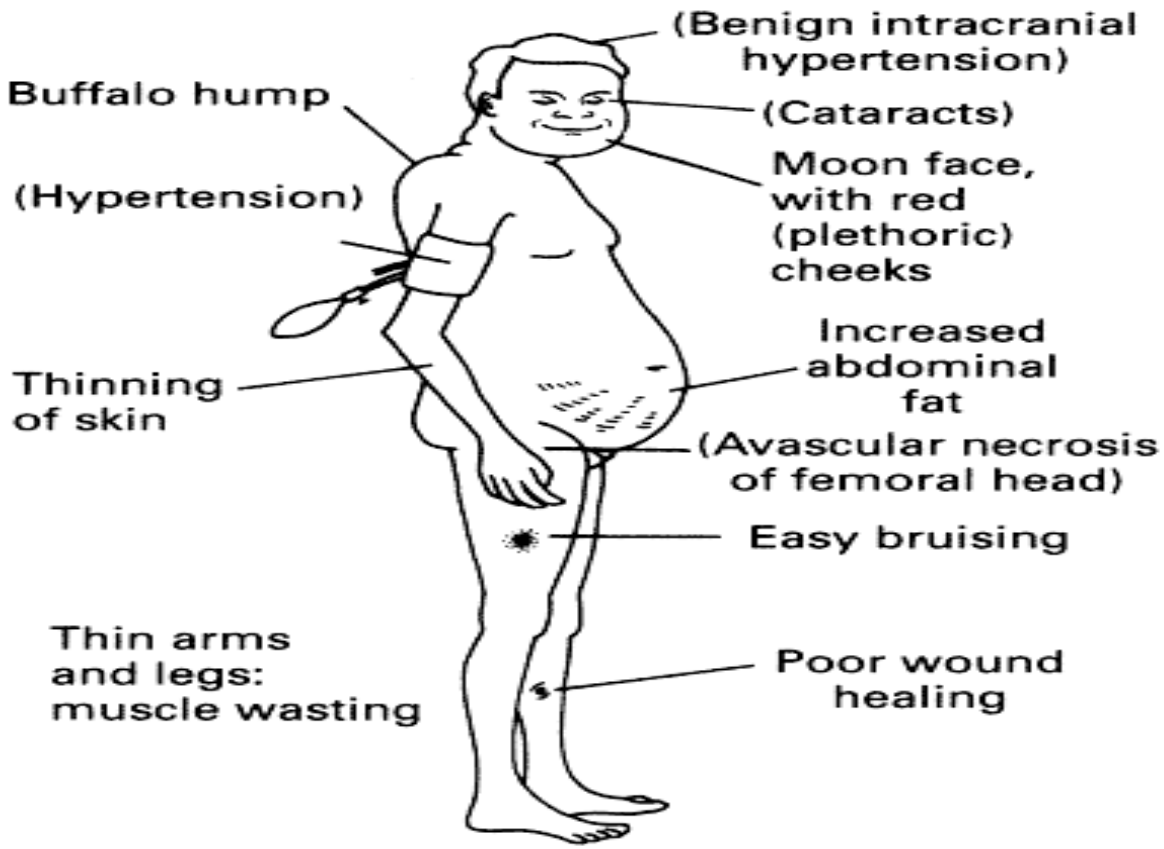
Fig. 3. Minnie G. Harvey Cushing's patient. Reported in The Pituitary Body and its Disorders, 1912.



- Harvey Cushing first described a patient with hypercortisolemia in 1932

- Observed signs/symptoms:
  - Weight gain
  - Muscle weakness
  - Irregular menstrual cycles
  - Headache and vision changes
  - Large round face
  - Striae
  - Insomnia
  - Inability to concentrate
  - Fits of irritability alternating with periods of depression

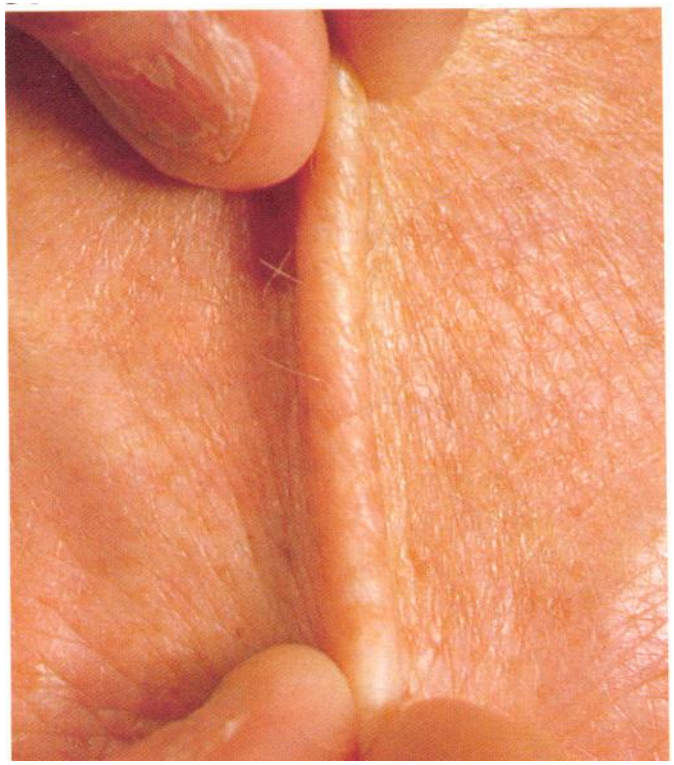
Euphoria
(though sometimes depression or psychotic symptoms, and emotional lability)



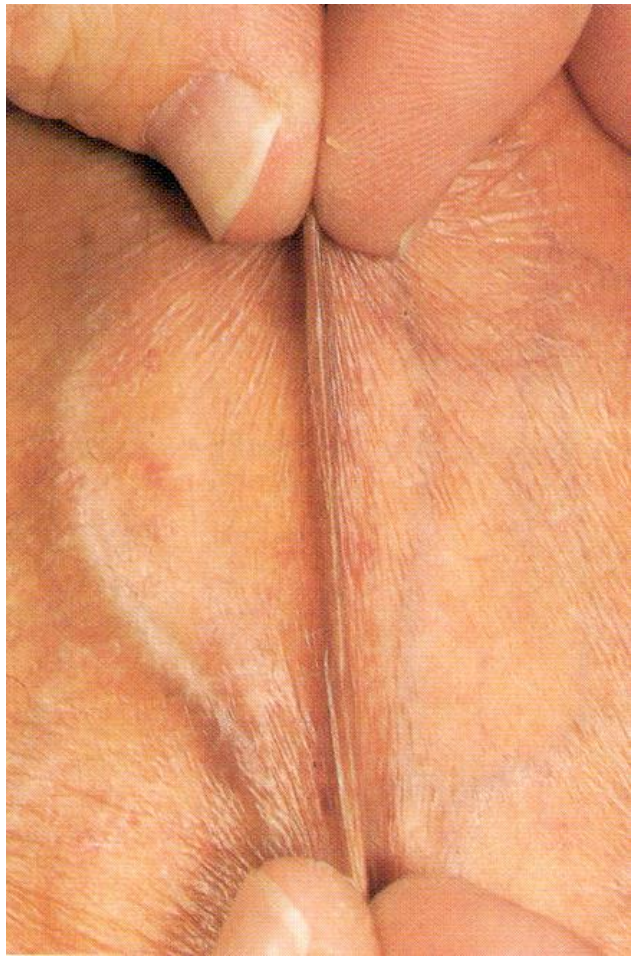
Also:

Osteoporosis
Tendency to hyperglycaemia
Negative nitrogen balance
Increased appetite
Increased susceptibility to infection
Obesity

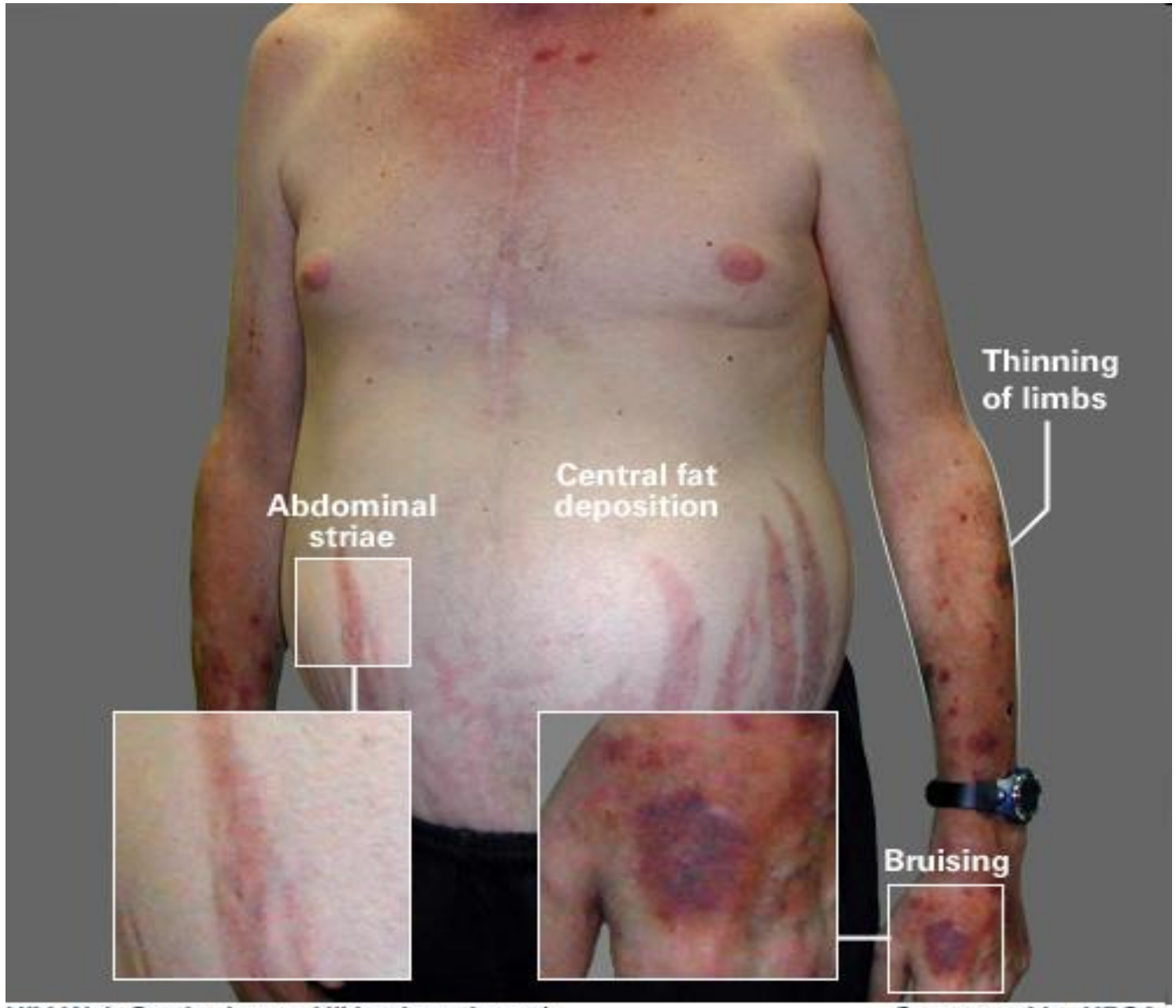
Cushing's Syndrome – thin skin

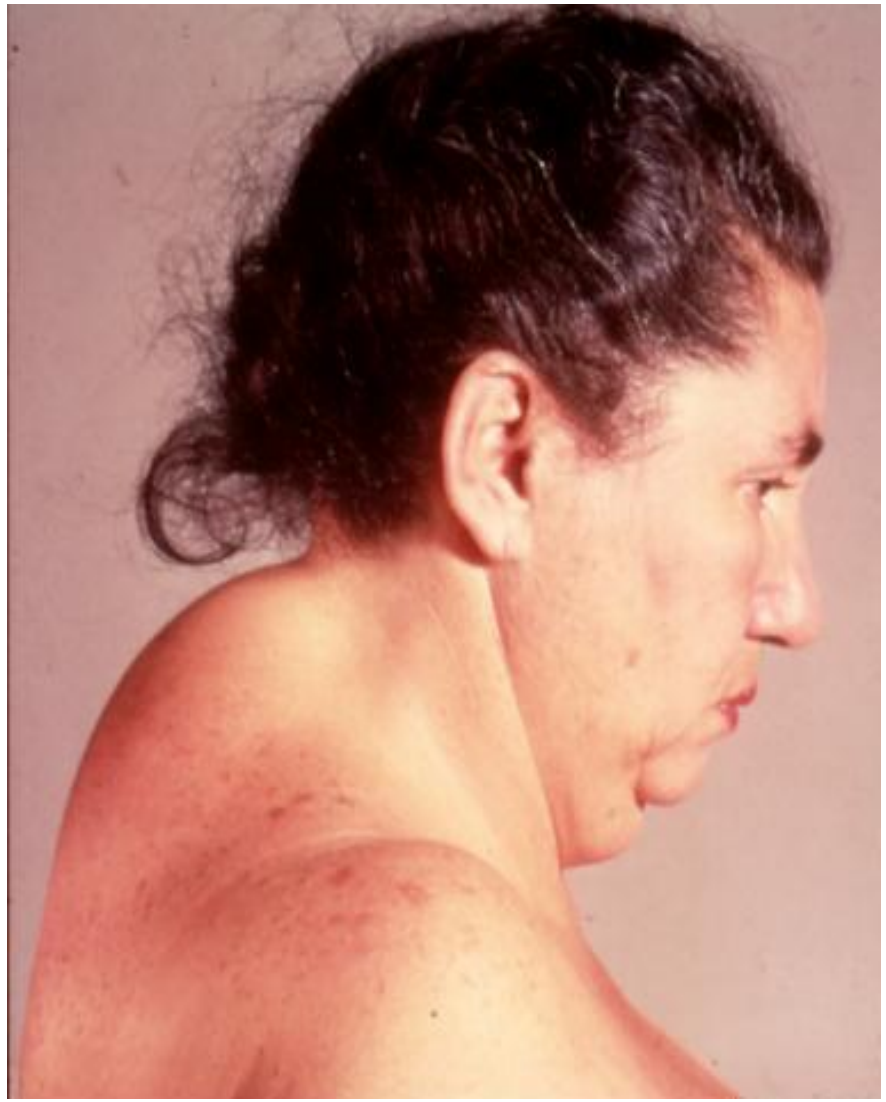


No Cushing's



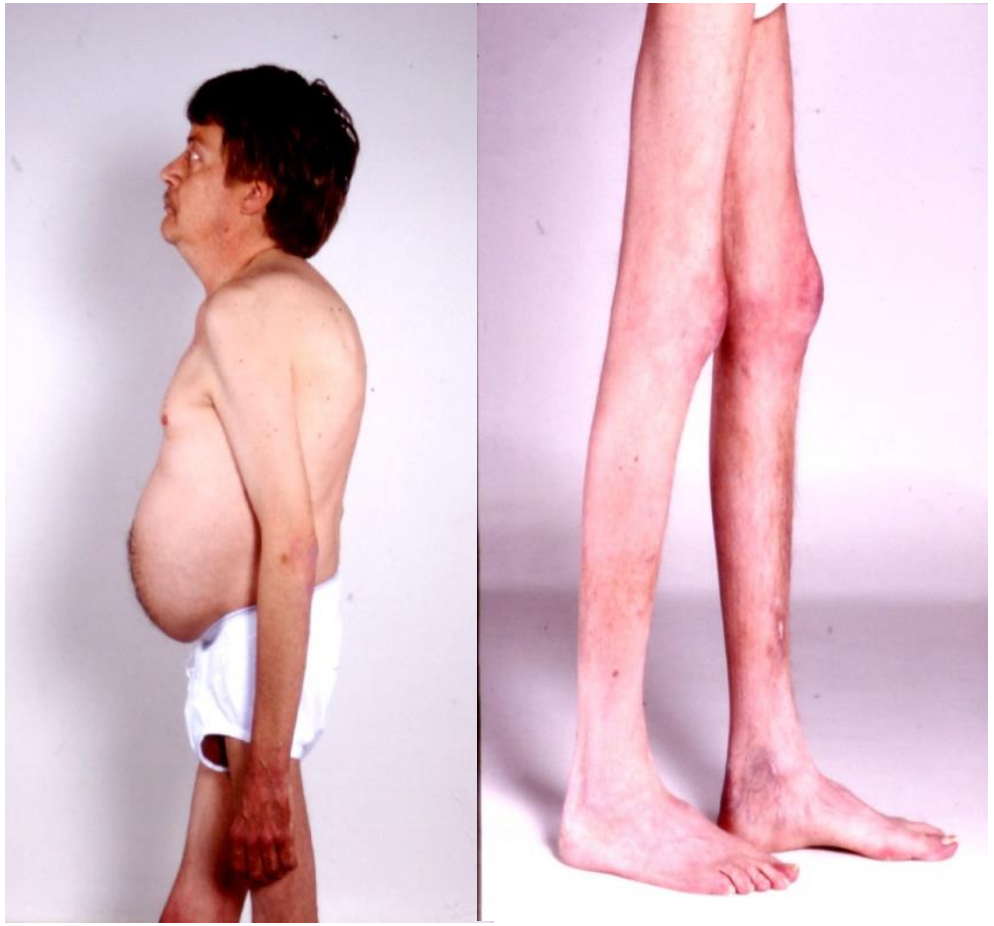
Cushing's


Thinning of limbs
Central fat deposition
Abdominal striae
Bruising
HIV Web Study (www.HIVwebstudy.org)
Supported by HRSA

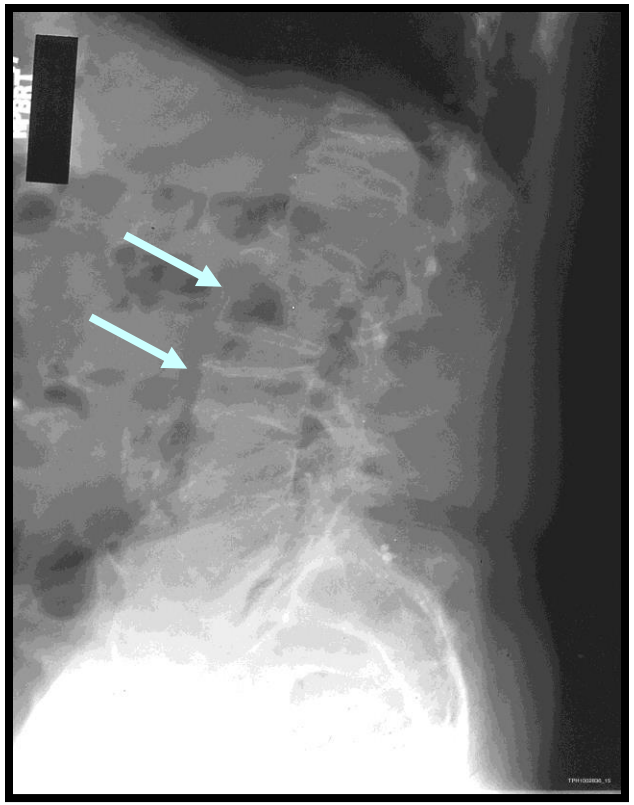


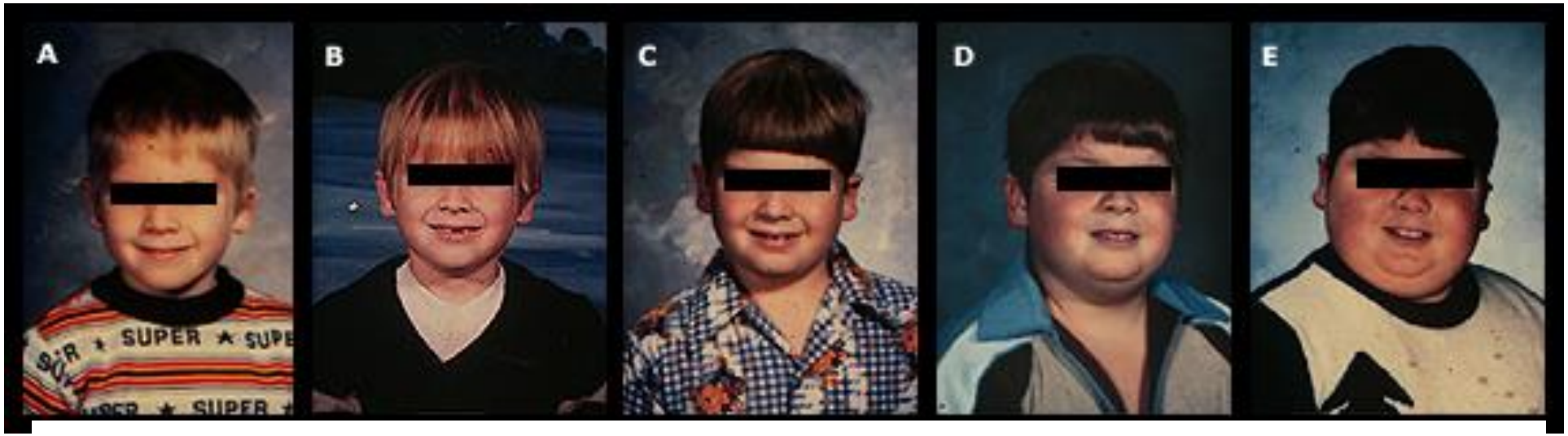
Dorsocervical fat pad

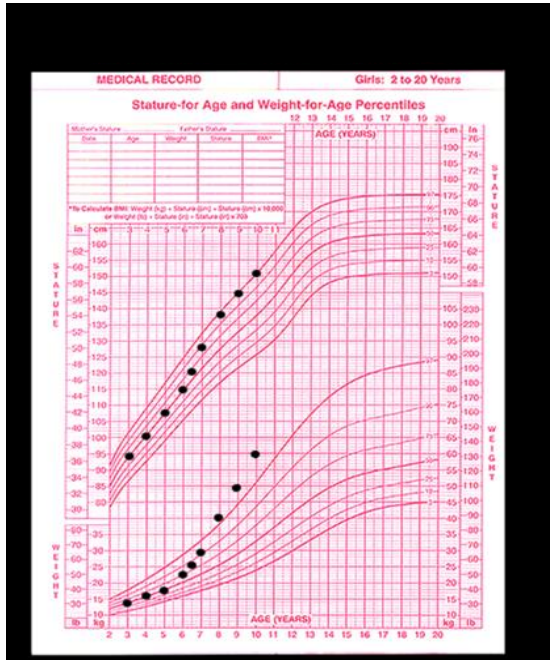
Cushing's syndrome

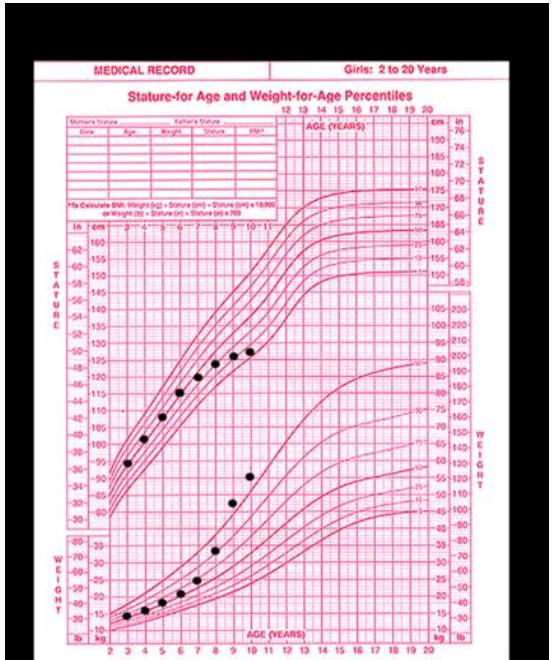


- Central obesity
- Peripheral muscle wasting (proximal myopathy)
- Thoracic compression fractures




A
B
C
D
E

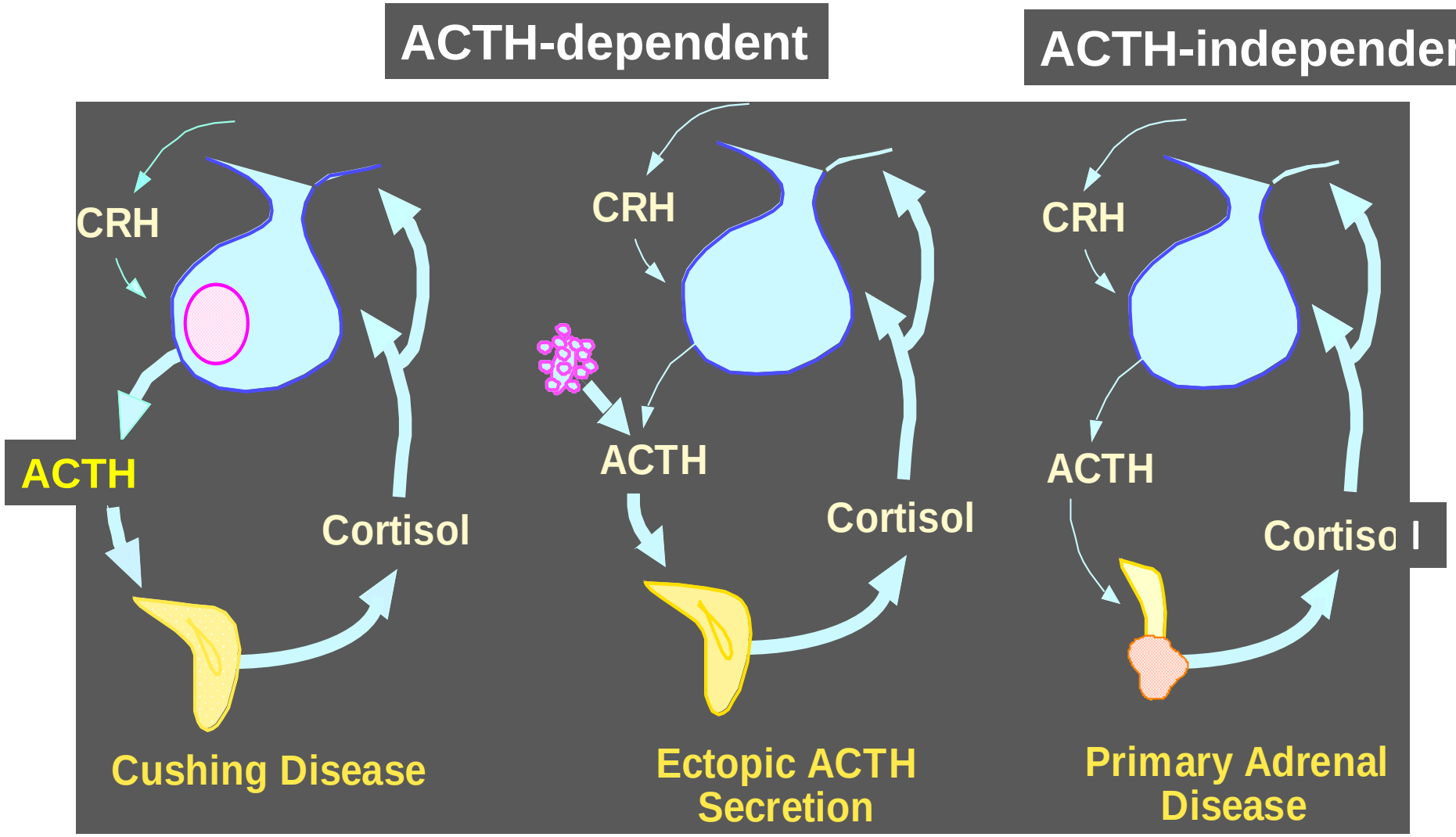

MEDICAL RECORD
Girls: 2 to 20 Years
Stature-for Age and Weight-for-Age Percentiles
AGE (YEARS)
STATURE
WEIGHT


MEDICAL RECORD
Girls: 2 to 20 Years
Stature-for Age and Weight-for-Age Percentiles
AGE (YEARS)
STATURE
WEIGHT

Cushing's Syndrome

- Results from excessive glucocorticoid secretion
- Associated with a distinct clinical phenotype
- 2-3 cases per million per year
- Female : male ratio
  - Cushing's disease 3.5 : 1
  - Ectopic Cushing's 1 : 1

Differential Diagnosis of Cushing's Syndrome



Diagnostic stepwise approach

- Screening and confirmation - Does the patient have Cushing's syndrome? (clinical suspicion plays a big role in interpretation of the result)
- Subtype evaluation – is the Cushing's syndrome ACTH-dependent (pituitary or ectopic source) or ACTH-independent (adrenal adenoma)?
- Localization – where is the source of ACTH secretion in ACTH-dependent disease (pituitary or ectopic)?

Who should be screened?

- Unusual features for age (osteoporosis, HTN)
- Multiple and progressive features (review of old photographs)
- Children with decreasing height percentile and increasing weight
- Adrenal incidentaloma compatible with an adenoma
- Sudden worsening of DM and HTN control
- Recommend against widespread testing in other patient groups

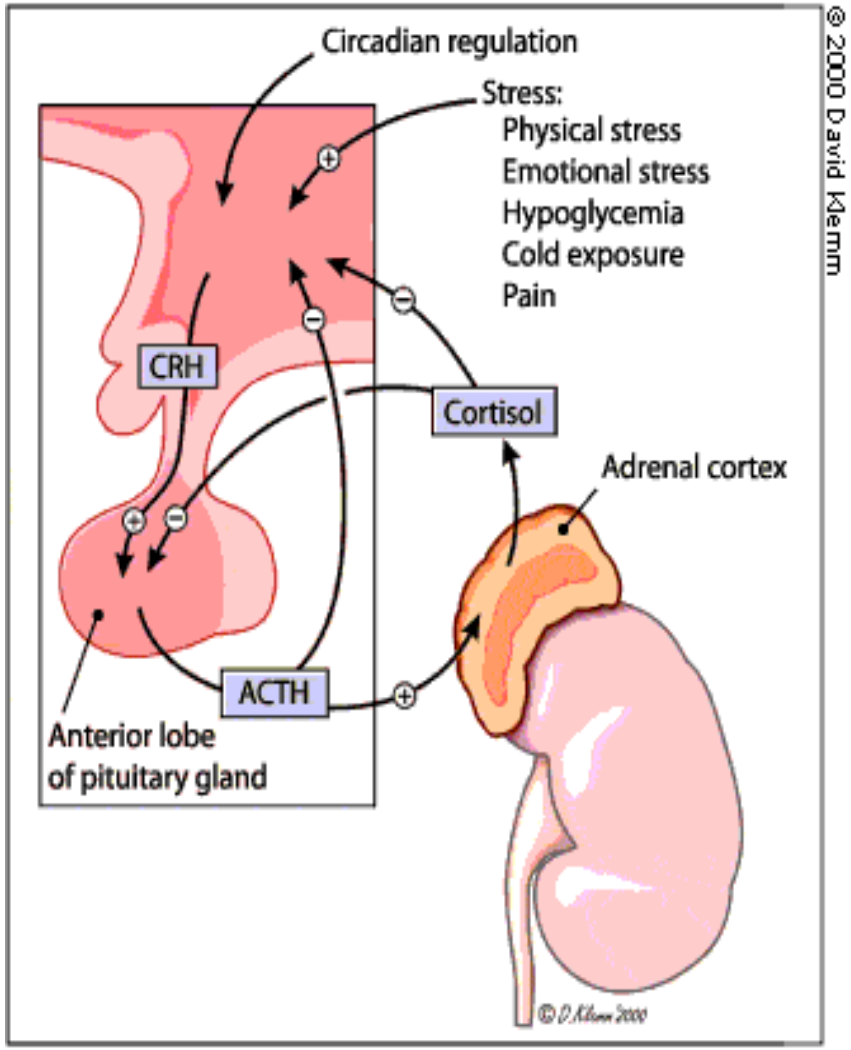
Screening for Cushing's

- Random plasma cortisol level not helpful:
- May be elevated in normal patients
  - pulsatility
  - cortisol-binding globulin (estrogen replacement, oral contraceptives)
  - pseudoCushing's
- May be intermittently normal in patients with Cushing's
  - periodic hormonogenesis

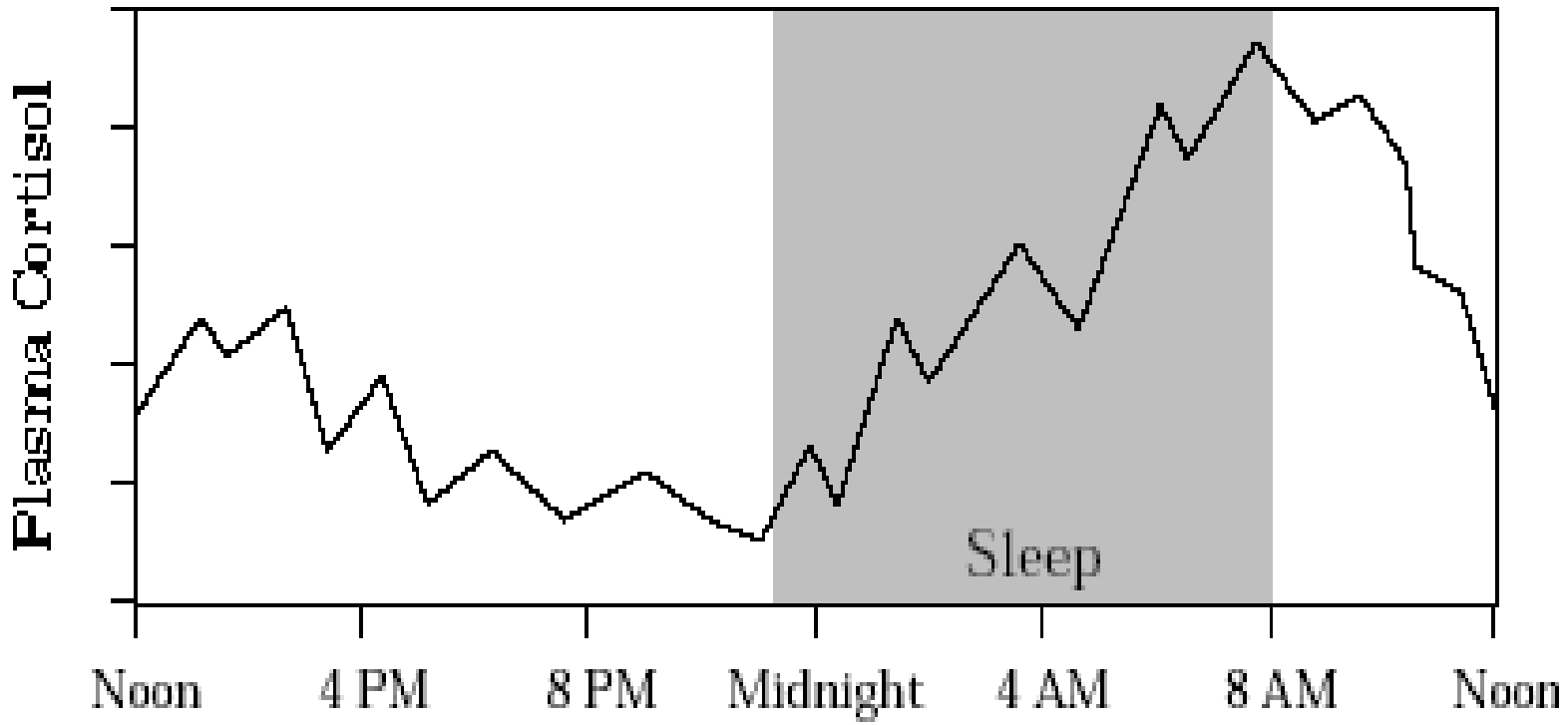
Pseudo Cushing's – activation of CRH

Causes

- Major depression or psychotic disorders
- Stress
  - surgical
  - medical
- Chronic alcoholism



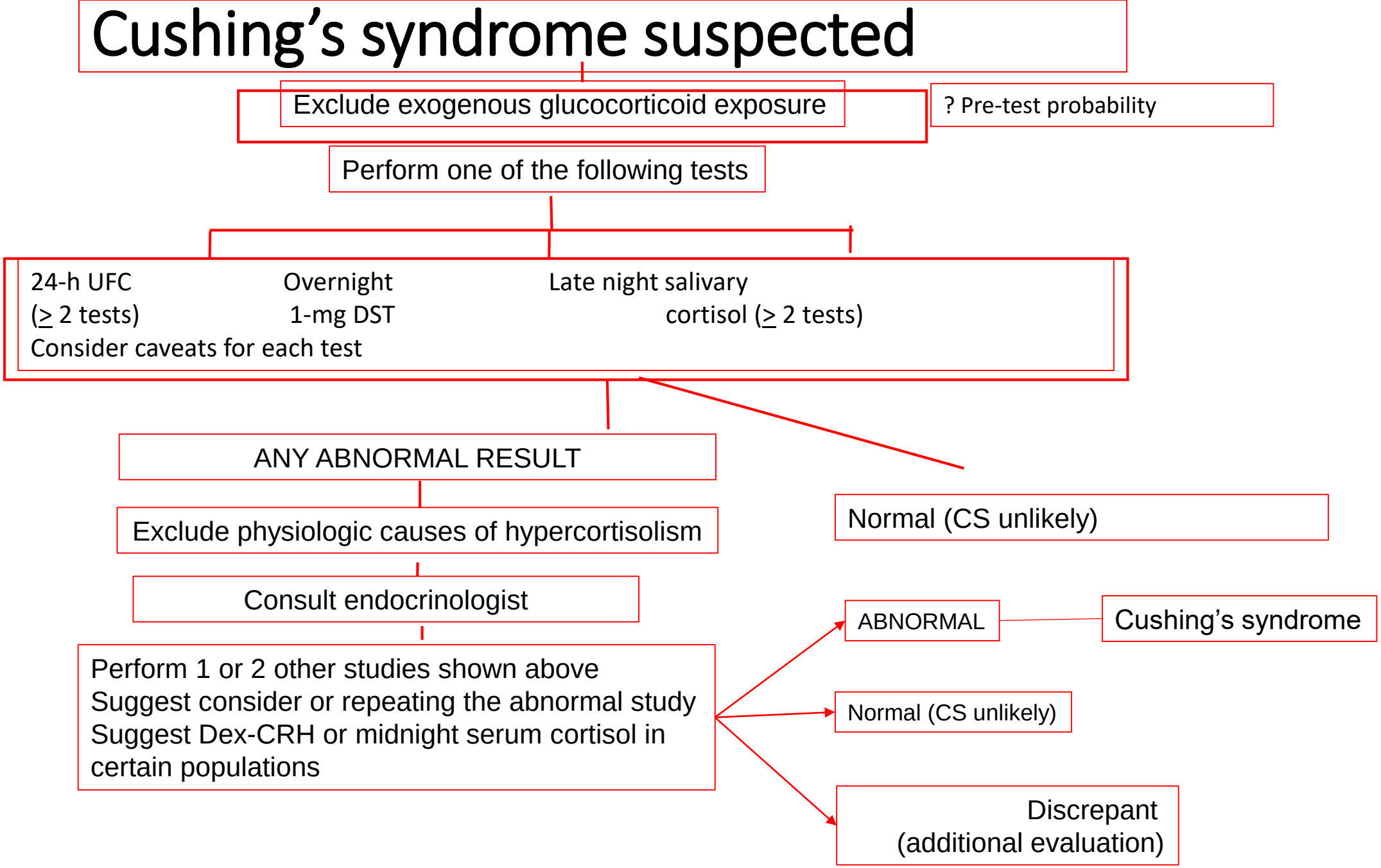
Diurnal Rhythm



Screening for Cushing's

- Options:
- 24 hour urine free cortisol
- Midnight salivary cortisol test
- Dexamethasone suppression tests

- All of these tests must be interpreted in clinical context – clinical features of Cushing's must be present to make a diagnosis


Cushing's syndrome suspected
Exclude exogenous glucocorticoid exposure
? Pre-test probability
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
ANY ABNORMAL RESULT
Exclude physiologic causes of hypercortisolism
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
Normal (CS unlikely)
ABNORMAL
Cushing's syndrome
Normal (CS unlikely)
Discrepant (additional evaluation)

Hypercortisolism

- Which of the following would you do first to confirm the etiology of hypercortisolism in a person with a decreased ACTH level?

a. Inferior petrosal sinus sampling

b. MRI of the pituitary

c. CT of the adrenals

d. High dose dexamethasone suppression test

e. Corticotropin-releasing hormone stimulation and petrosal sinus sampling

Determining the cause of hypercortisolism

- Measurement of Plasma ACTH
  - < 5 pg/mL
    - ACTH-independent
  - > 20 pg/mL
    - ACTH-dependent
    - Higher in Ectopic Cushing's
  - 5 - 20 pg/mL
    - Indeterminate
  - Collect blood into prechilled EDTA tube, place on ice bath. Plasma should be separated rapidly and stored at -40^0 C to avoid degradation & false-negative results

Treatment of Cushing's Syndrome

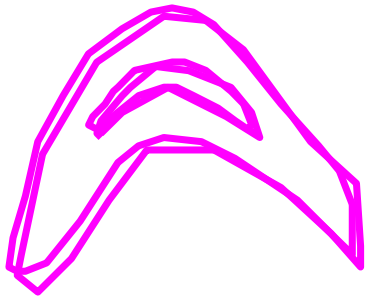
- Cushing's Disease
- Trans-sphenoidal surgery
- Bilateral adrenalectomy
- Medical therapy to block cortisol synthesis or action

- Cushing's Syndrome
- Remove adrenal mass
- Treat source of ectopic ACTH
- Medical therapy to block cortisol synthesis or action

Medical treatment

- Control of hypercortisolemia
  - Before surgery - minimize surgical complications
  - Awaiting results of radiation treatment
  - Surgery unsuccessful or contraindicated
- Control of hypertension and hyperglycemia
- Prophylaxis for opportunistic infection
- Prophylaxis for venous thrombosis

Steroidogenesis Inhibitors



Cortisol

Ketoconazole/etomidate

Metyrapone

Aminoglutethimide

Mitotane

Trilostane

Drugs that decrease ACTH secretion:

Octreotide, Paseriotide, Cabergoline, Bromocriptine

Glucocorticoid antagonist: Mifepristone

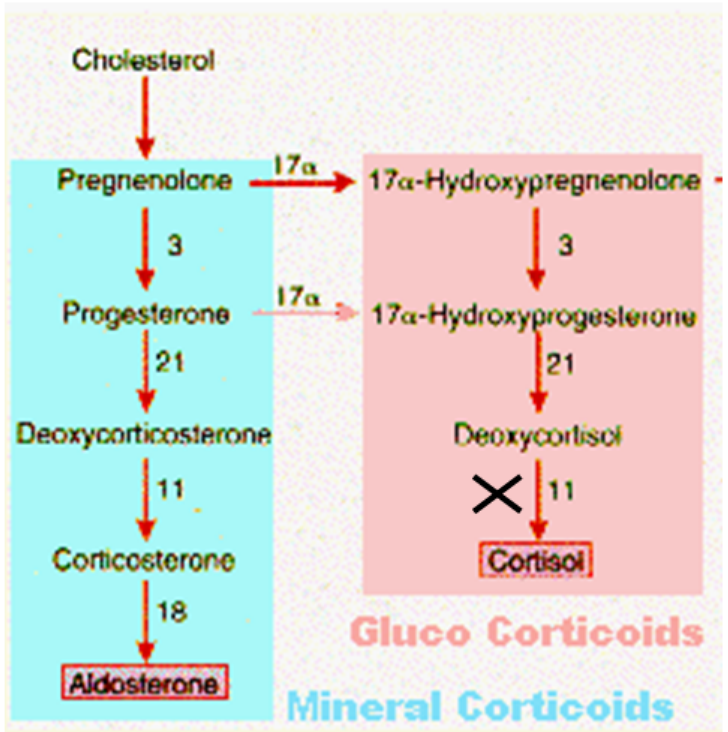
Ketoconazole

Mechanism

- Blocks 11 beta hydroxylase (and other steps in the steroid pathway)

Clinical use

- Medical treatment of Cushing's



Side effects/contraindications

- Symptoms of adrenal insufficiency
- Severe or life threatening/fatal liver disease

Other

- FDA warning issued regarding its use

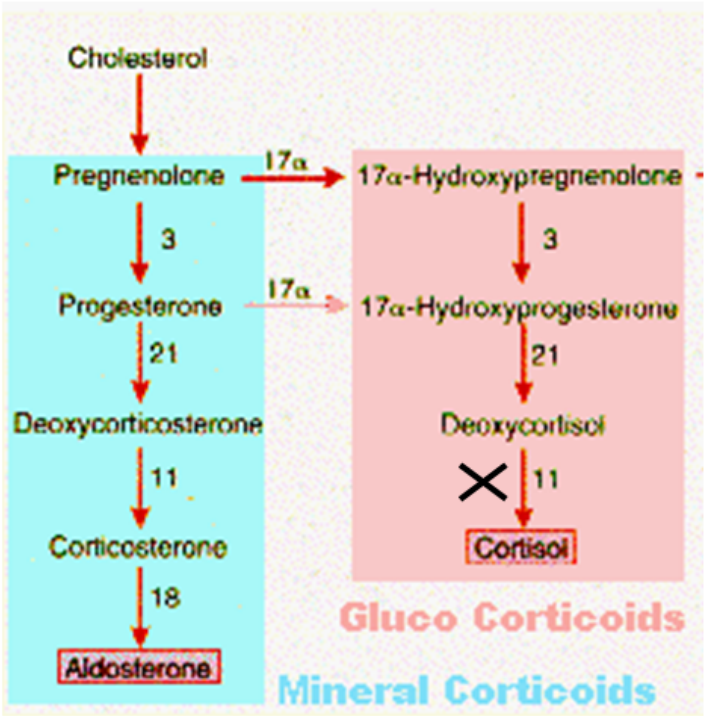
Metyrapone

Mechanism

- Blocks 11 beta hydroxylase

Clinical use

- Medical treatment of Cushings



Side effects/contraindications

- Symptoms of adrenal insufficiency

Other

- Not widely available

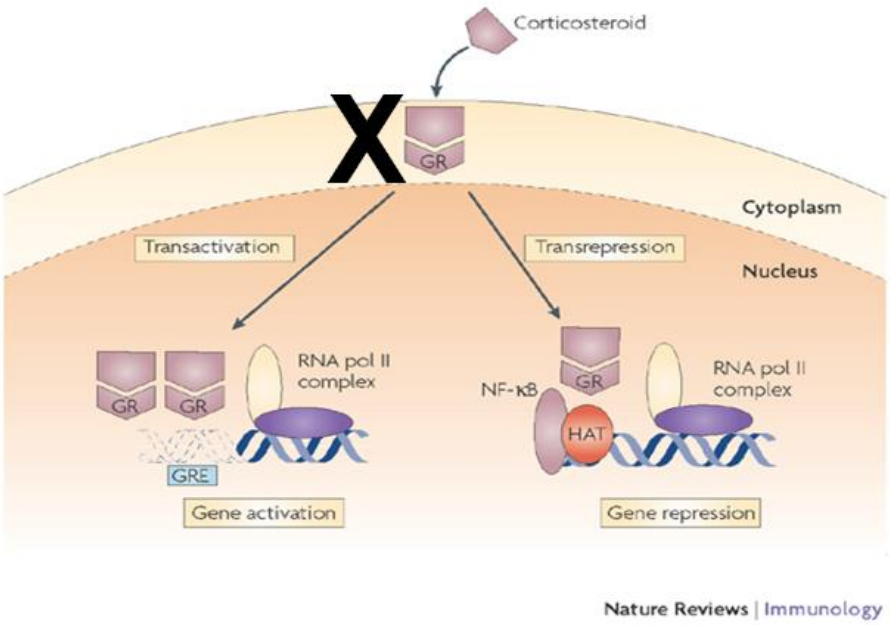
Mifepristone (Korlym)

Mechanism

- Glucocorticoid receptor antagonist

Clinical use

- Medical treatment of Cushing's



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Side effects/contraindications

- Hypokalemia
- GI upset – pain, nausea, vomiting
- Adrenal insufficiency

Other

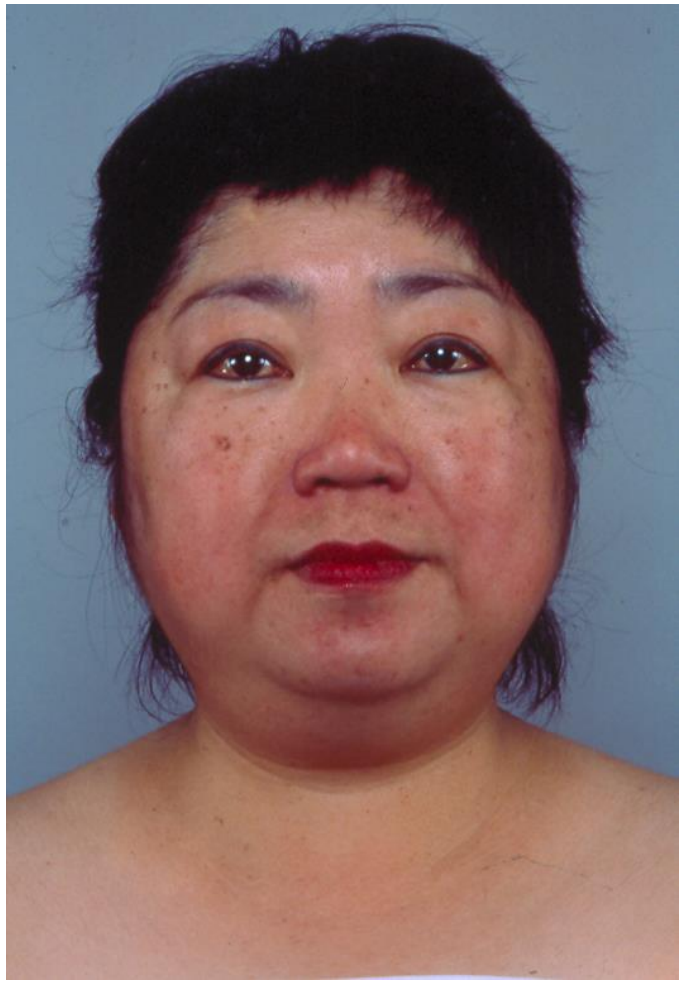
- Also has anti-progesterone activity
- Results in increased cortisol levels

Which drug?

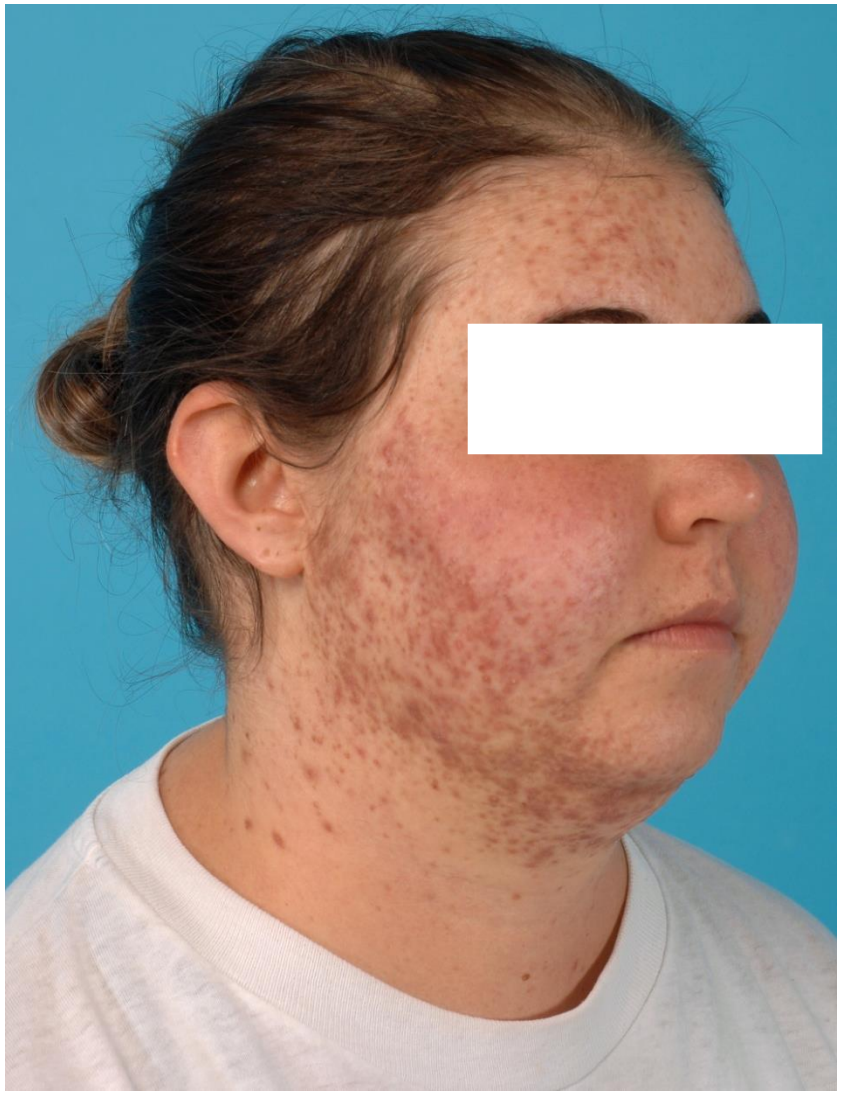
Drug	Pros	Cons
Ketoconazole	Quick action	SE: GI, LFTs (death) Needs stomach acid Drug interactions (CYP3A4 substrate)
Metyrapone	Quick action	SE: GI, hirsutism, acne, HTN, rarely neutropenia, Hard to obtain
Mitotane	Effective	Long wait to efficacy Cannot follow serum cortisol levels SE: GI, neurologic, ↓WBC, teratogenic
Etomidate	Quick action, IV → pts unable to take oral	Needs to be initiated in the ICU Temporary measure
Paseriotide	Effective	Injectible, can worsen/cause diabetes
Mifepristone	FDA approved	Cannot follow serum cortisol levels Anti-progestin (abortifacient, vaginal bleeding), hypokalemia

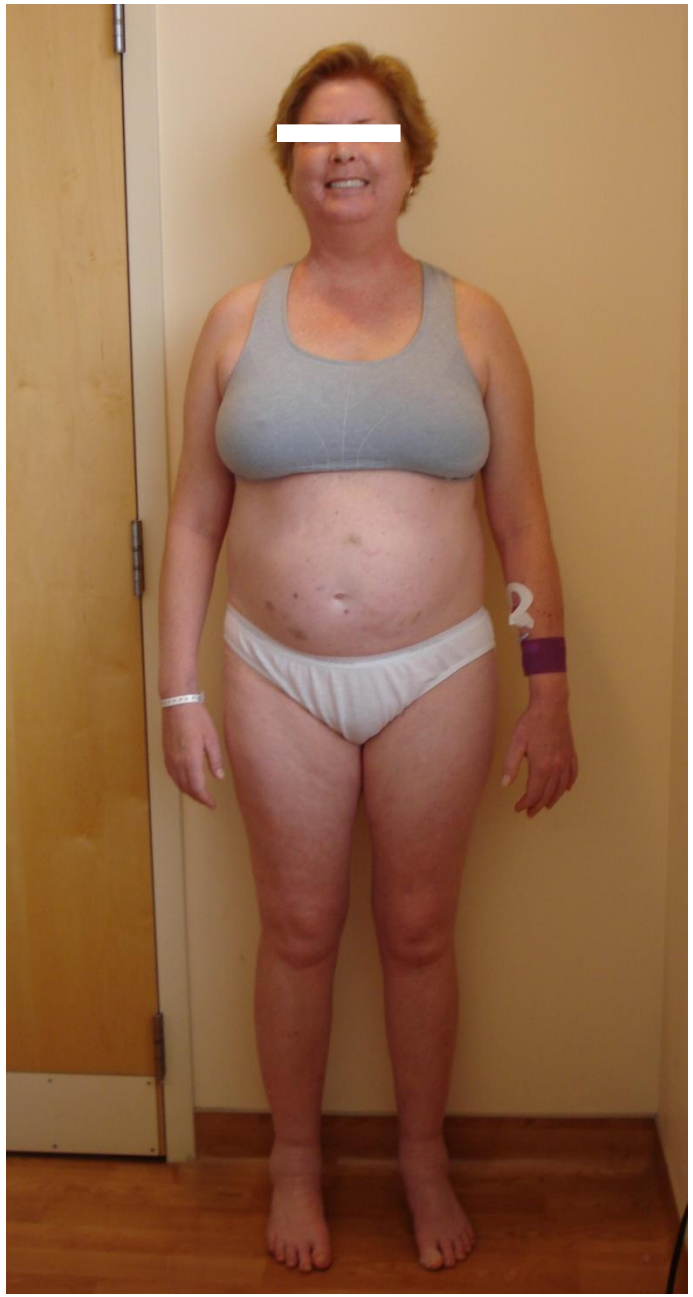
Goal of treatment: UFC in the normal range
Serum cortisol 6-12 mcg/dl (before AM meds)

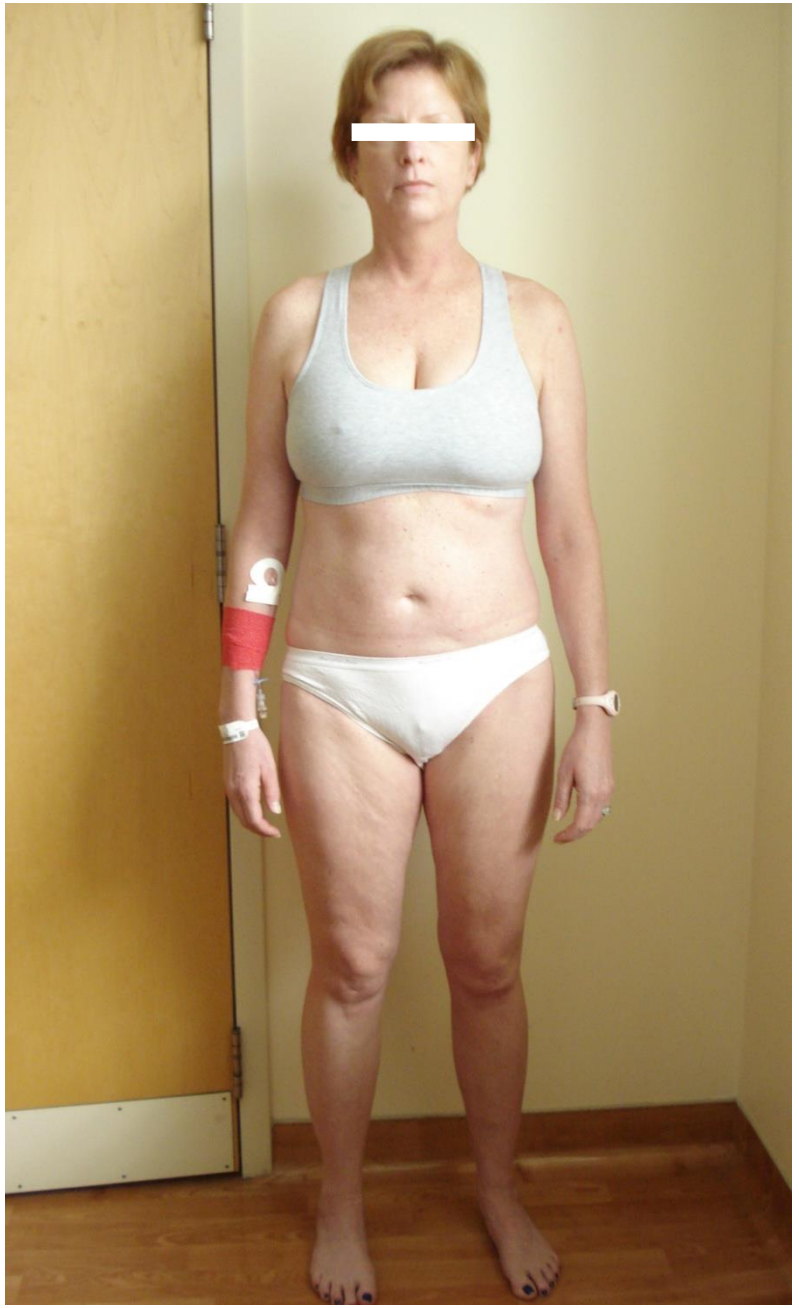
Cushing's syndrome



12 months after cure







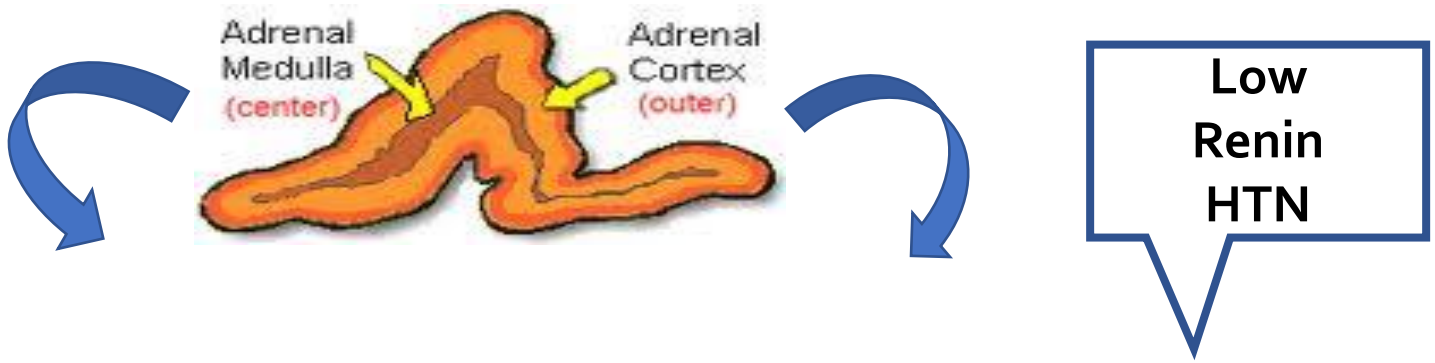
A 33-year-old man has been referred to you for evaluation of Cushing syndrome. He has an 11-year history of HIV infection. He is taking antiretroviral therapy, including didanosine, tenofovir, and ritonavir. His viral load is zero and his CD4 cell count is normal. He has developed asthma in the past 6 months and has been taking fluticasone/salmeterol twice daily and an albuterol metered-dose inhaler as needed. He has gained 30 lb (13.6 kg) in the past 3 months. Hypertension and fasting hyperglycemia have developed.

On physical examination, he has a very cushingoid appearance, with wide, violaceous abdominal striae and proximal muscle weakness.

Which of the following laboratory profiles is most likely to be found in this man?

Answer	Plasma ACTH	DHEA-S	Cortisol
A.	Normal	Normal	Normal
B.	⇑	⇑	⇑
C.	⇓	⇓	⇑
D.	⇓	⇓	⇓
E.	⇑	⇓	⇓

Adrenal Hypertension



Adrenal Medulla

- Pheochromocytoma

Adrenal Cortex

- Cushing's Syndrome
- **Primary Aldosteronism (PA)**
- Congenital Adrenal Hyperplasia (11β or 17α deficiency)
- Familial Glucocorticoid Resistance
- Apparent Mineralocorticoid Excess

A 33-year-old woman returns to your clinic for continued management of her hypertension. She reports compliance with lifestyle modifications and prescribed anti-hypertensive medications including lisinopril, metoprolol, and losartan. She reports feeling fatigued and has noted slight abdominal distention. Her blood pressure at this visit is 155/92 mmHg. Serum laboratory tests show potassium 3.1 mEq/L and sodium 144 mEq/L.

What is the next step?

A. Measure plasma renin and aldo

B. CT abdomen

C. Saline suppression test

D. Start spironolactone

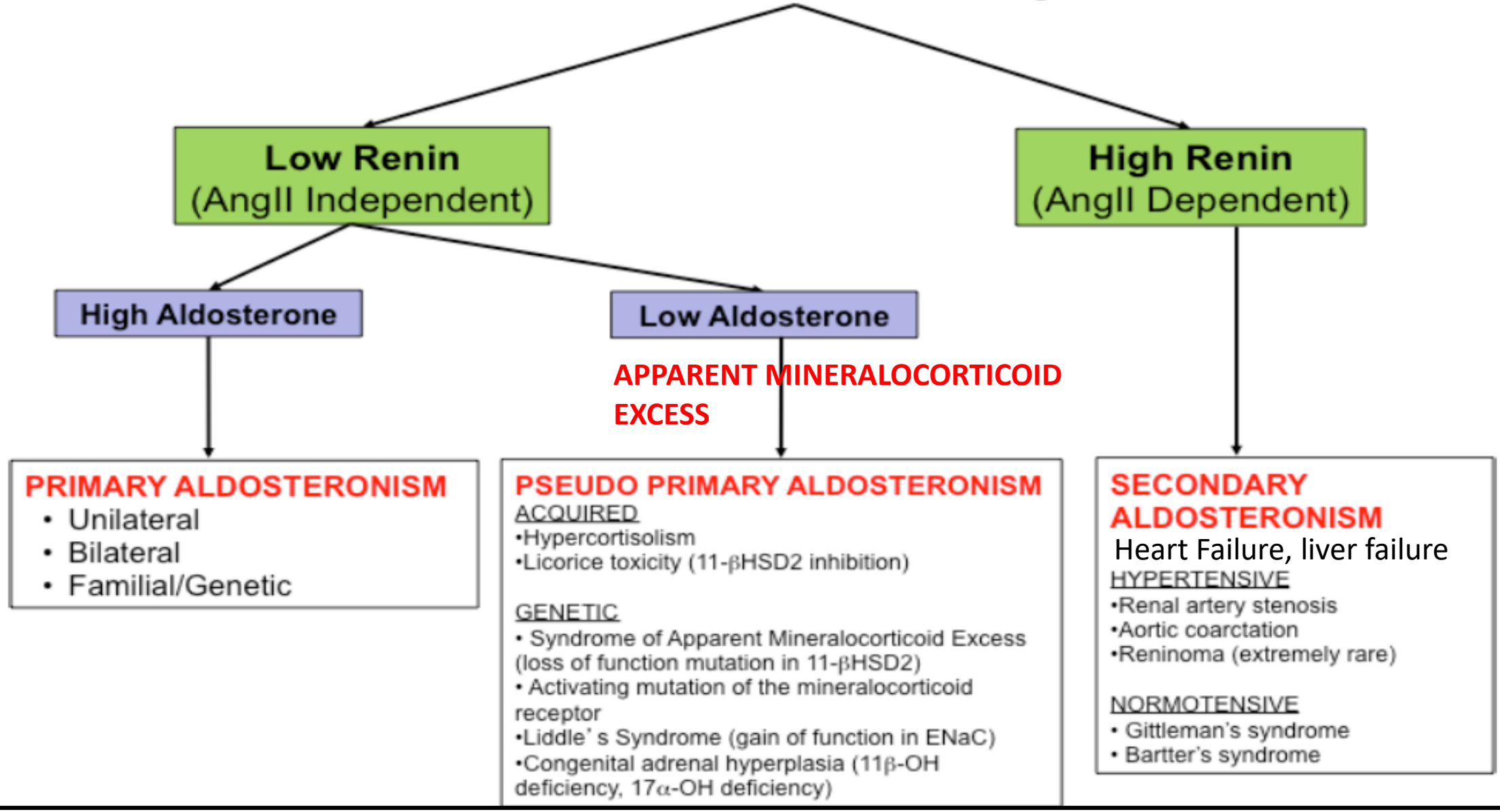
Etiology of Primary Aldosteronism

- **Unilateral Disease**
  - Adenoma (APA) 85% vs. Hyperplasia (IHA) 14% vs Cancer 1%
- **Bilateral Disease**
  - Adenoma (rare) vs. Hyperplasia (IHA)
- **Aldosterone-Producing Adrenocortical Carcinoma**
- **Genetic Diseases**
  - Familial Hyperaldosteronism type I (Glucocorticoid Remediable Aldosteronism)
  - Familial Hyperaldosteronism type II

Prevalence of Primary Aldosteronism

- Used to be LOW: < 1%
- Use of aldosterone to renin ratio (ARR) has allowed detection of many more cases
- Currently, prevalence is at > 10% in both general and specialty settings

Mineralocorticoid Excess Syndrome



Clinical Presentation

- Hypertension is common ranging form mild and intermittent to persistent and severe.

- Hypokalemia
  - frequent cramps, fatigue, muscle weakness, nocturia and polyuria.
  - Metabolic alkalosis may be also present.
  - Renal Cysts

- Adrenal incidentaloma

Differential Diagnosis of Hypertension and Hypokalemia

Suspicion of 2° HTN due to RAAS		
↑Aldo ↑Renin	↑Aldo ↓Renin	↓Aldo ↓Renin
-Renovascular -Hypovolemia -Vascular (other) -LVF	-Adenoma -Hyperplasia -Familial (GRA) -Carcinoma	-Licorice -11-beta HSD mutations -DOC tumor -Cushing Syndrome
-Renin-secreting tumor	-Ectopic Aldosterone secretion	-Liddle's Syndrome -CAH: 11 and 17 hydroxylase -Glucocorticoid resistance

Who should be screened for PA?

Patient Groups	Prevalence of PA
Moderate/severe hypertension JNC 7 Staging: Stage 2 >160/100 **OR** Stage 3 >180/110	Overall: 6.1% Stage 1 (mild): 2% Stage 2 (moderate): 8% Stage 3 (severe): 13%
Resistant/Drug-resistant Hypertension (defined as BP of < 140/90 despite treatment with 3 anti-hypertensive meds	17-23%
Hypertensive patients with spontaneous or diuretic induced hypokalemia	NA
Hypertension with adrenal incidentaloma	Median 2% (range, 1.1%-10%)
Hypertension AND a family history of early onset hypertension or stroke at a young age (<40 yrs)	NA

Screening

- Measurement of morning, ambulatory labs:
  - Aldosterone (>15 ng/ml)
  - Plasma renin activity (PRA) (<0.6 ng/ml/hr)
- Ratio of aldosterone/PRA
  - should be >20
- Interfering Medication*
  - Verapamil, hydralazine, prazosin, terazosin, doxazosin do not interfere with aldo or PRA levels

Caveats to testing with ARR

FALSE POSITIVE ARR

- Beta-Blockers
- Alpha-agonists (clonidine , methyldopa)
- NSAIDs
- Sodium loading
- Old age
- Premenopausal women
- Renal Failure

LOOK AT ALDOSTERONE LEVELS IN THESE CASES

FALSE NEGATIVE ARR

- Hypokalemia
- Sodium restriction
- ACE inhibitor, ARBS
- Diuretics
- K+ sparing diuretics
- Malignant Hypertension

IF ARR IS HIGH IN PATIENTS ON THESE DRUGS, YOU HAVE A POSITIVE SCREENING TEST

Medication effects

Factor	Effect on aldosterone levels	Effect on renin levels	Effect on ARR
Medications			
Beta-adrenergic blockers	↓	↓ ↓	↑ (FP)
Central alpha-2 agonists (e.g., clonidine, alpha-methyldopa	↓	↓ ↓	↑ (FP)
NSAIDs	↓	↓ ↓	↑ (FP)
K+-wasting diuretics	→ ↑	↑ ↑	↓ (FN)
K+-sparing diuretics	↑	↑ ↑	↓ (FN)
ACE inhibitors	↓	↑ ↑	↓ (FN)
ARBs	↓	↑ ↑	↓ (FN)
Ca2+ blockers (DHPs)	→ ↓	↑	↓ (FN)
Renin inhibitors	↓	↓ ↑*	↑ (FP)*
			↓ (FN)*

Testing Conditions

Factor	Effect on aldosterone levels	Effect on renin levels	Effect on ARR
Potassium status			
Hypokalemia	↓	→ ↑	↓ (FN)
Potassium loading	↑	→ ↓	↑ (FP)
Dietary sodium			
Sodium restricted	↑	↑ ↑	↓ (FN)
Sodium loaded	↓	↓ ↓	↑ (FP)
Advancing age	↓	↓ ↓	↑ (FP)
Other conditions			
Renal impairment	→	↓	↑ (FP)
PHA-2	→	↓	↑ (FP)
Pregnancy	↑	↑ ↑	↓ (FN)
Renovascular HT	↑	↑ ↑	↓ (FN)
Malignant HT	↑	↑ ↑	↓ (FN)

Medications that do not interfere with ARR

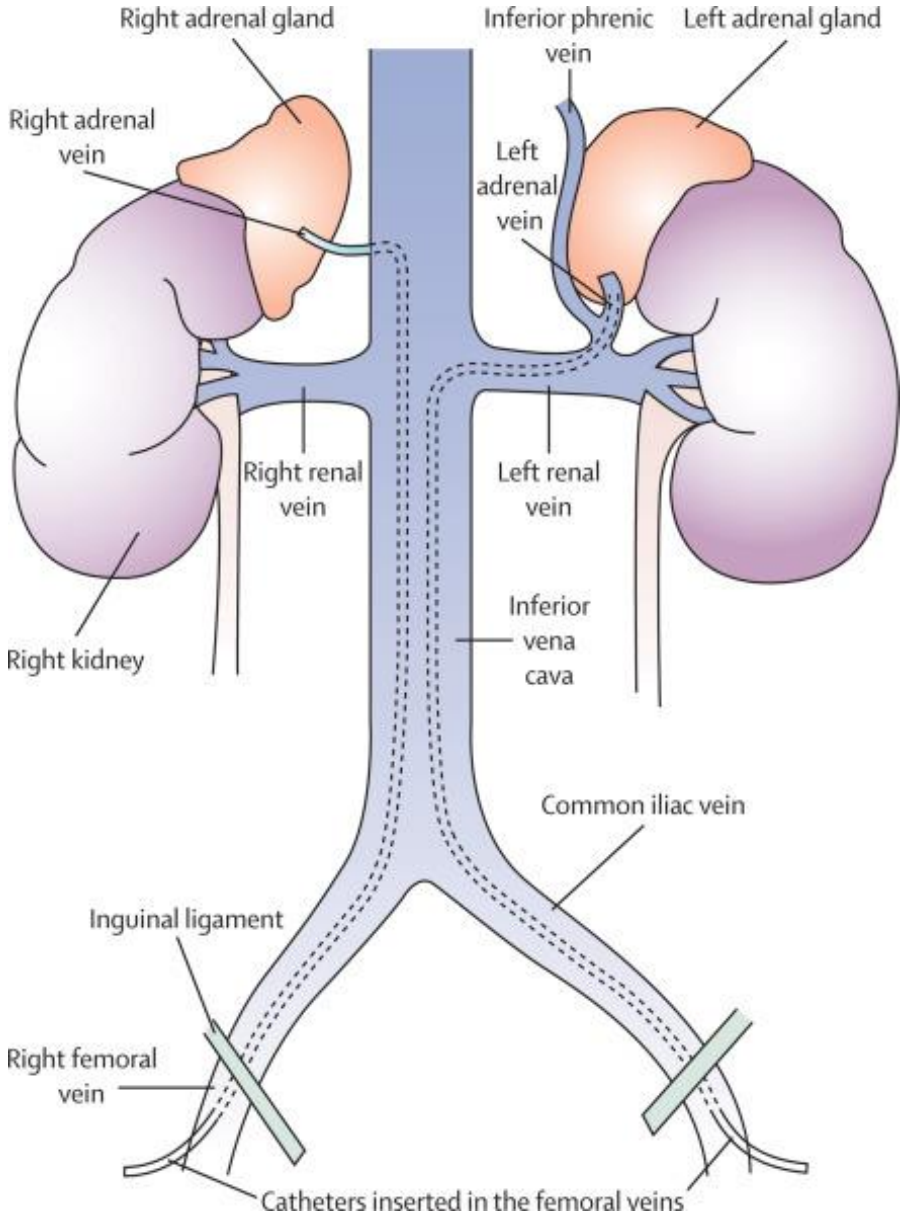
Medication	Dose
Verapamil	120-240 mg BID
Hydralazine	25-75 mg TID
Terazosin	1-10 mg QHS
Prazosin	1-15 mg BID/TID
Doxazosin	1-16 mg QD

Confirmatory testing: Primary Hyperaldosteronism

TEST	METHOD	CUT-OFFS	PRECAUTIONS
ORAL SALT LOADING	Salt load 6g/day for 3 days with adequate K+	Day 4, 24 hr urine aldosterone > 12 mcg, urine Na >200 mmol	Avoid in renal failure, CHF, uncontrolled HTN
SALINE SUPPRESSION TEST	2L normal saline infused over 4 hours (seated/recumbent)	Post-saline Aldosterone >10ng/dl	Avoid in renal failure, CHF, uncontrolled HTN
FLUDROCORTISONE SUPPRESSION TEST	Fludrocortisone 0.1 mg every 6 hrs, K+ tabs every 6 hrs, Na 30 mmol tid qac for 4 days	Day 4 , 10 am aldosterone >6 ng/dl	Cumbersome, not much experience
CAPTOPRIL CHALLENGE TEST	Captopril 25-50 mg once	Aldosterone at 0,1 or 2h Suppression of aldosterone <30%	Substantial False negatives

Unilateral vs. Bilateral

- **AVS**
- Other tests:
  - CT scan
  - ACTH stimulation testing
  - 18-Hydroxycorticosterone levels
  - Posture testing
  - Iodocholesterol scintigraphy



Adrenal Venous Sampling

- Cosyntropin stimulated
  - Minimized stress-induced fluctuations
  - Maximize gradient of cortisol from adrenal vein to IVC
  - Maximize secretion of aldosterone
- Cortisol-corrected aldosterone ratios
  - Proper cannulization (10:1)
  - Lateralization (4:1)
- Downsides:
  - Complications
  - Skilled IR
  - Contrast

Treatment

- Unilateral Adrenalectomy
- Medical Treatment
  - Mineralocorticoid Receptor Antagonists
    - Spironolactone
    - Eplerenone
  - Sodium Channel Antagonists
    - Triamterene
    - Amiloride

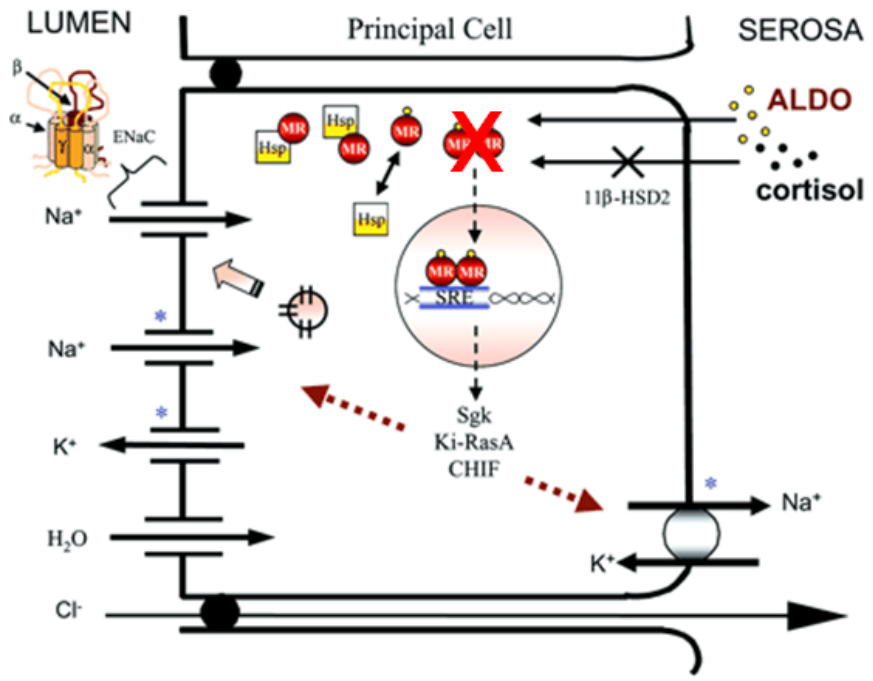
Surgical Cure of Hypertension

- Rule of “Thirds”
  - ~33% cured
  - ~33% reduced BP medications
  - ~33% no change in BP medications
- Who will Benefit?
  - Lack of family hx of HTN
  - Shorter duration of HTN (<6 yrs) +1
  - Female sex +1
  - Two or fewer BP meds +2
  - BMI<25 +1

Spironolactone (Aldactone)

Mechanism

- Aldosterone receptor antagonist
- Inhibits actions of aldosterone



Booth R E et al. Advan in Physiol Edu 2002;26:8-20

Clinical use

- Primary aldosteronism
- Secondary aldosteronism
  - CHF
  - cirrhosis

Side effects/contraindications

- Hyperkalemia
- Gynecomastia
- GI upset

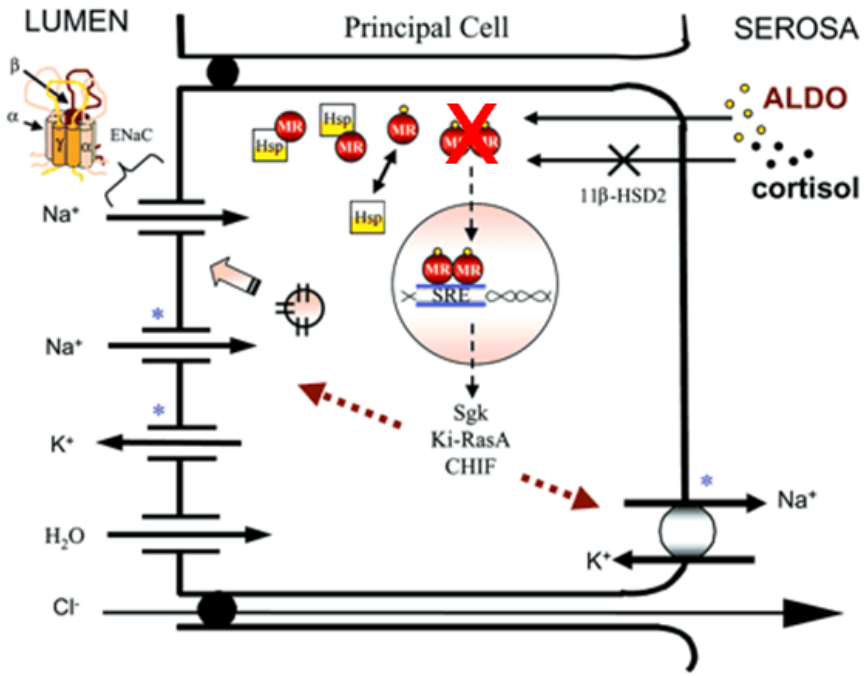
Other

- Blocks action of testosterone at its receptor
- Increases serum estrogen levels

Eplerenone (Inspra)

Mechanism

- Aldosterone receptor antagonist
- Inhibits actions of aldosterone



Booth R E et al. Advan in Physiol Edu 2002;26:8-20

Clinical use

- Primary aldosteronism
- Secondary aldosteronism
  - CHF
  - cirrhosis

Side effects/contraindications

- Hyperkalemia
- GI upset

Other

- Does not have significant testosterone receptor blockade effect

A 60-year-old male has uncontrolled hypertension resistant to multiple antihypertensives. Abdominal CT shows the presence of bilateral adrenal hyperplasia. Which one of the following is consistent with a diagnosis of primary hyperaldosteronism?

A. Decrease ACTH level
B. Increase renin level
C. ARR increase >30
D. Hypokalemic acidosis

Thanks

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THE UNIVERSITY OF ARIZONA | COLLEGE OF MEDICINE PHOENIX

Adrenal Disorders

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ACP education committee

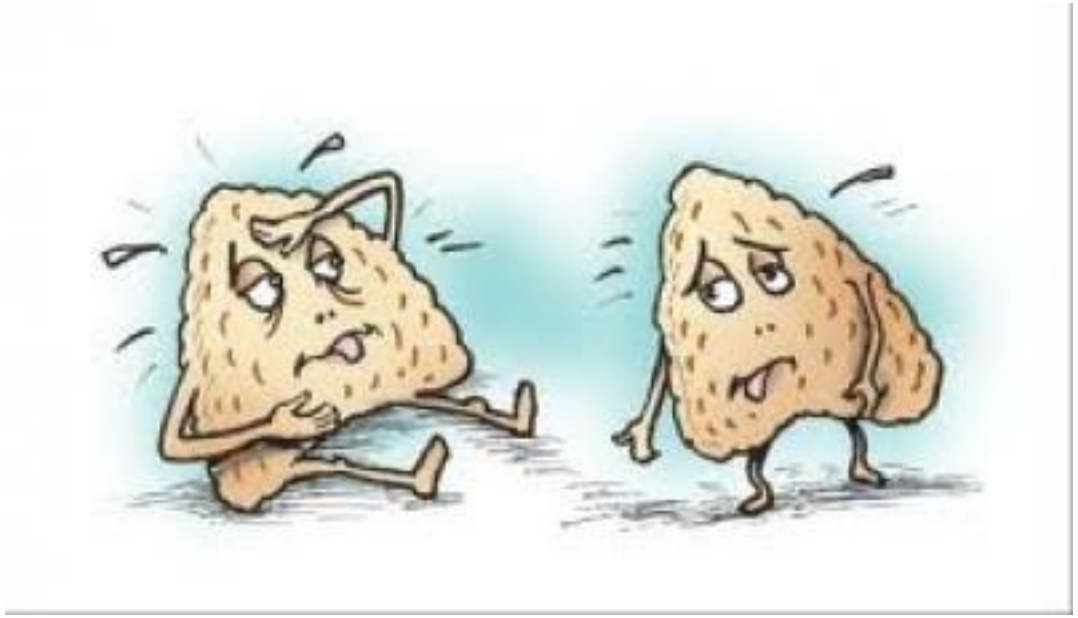
Objectives

- Review pathogenesis and clinical presentation
  - Cortisol deficiency
- Review principles of diagnosis and therapy for each conditions

A 64-year-old has been taking steroids for asthma for 5 years. She undergoes urgent surgery for a perforated ulcer. Two days later, she becomes hypotensive, febrile, and hypoglycemic. What is the most likely diagnosis?

A. Adrenal insufficiency
B. Sepsis
C. Hypovolemia
4.Steroid induced diabetes

Adrenal Insufficiency



Causes of Cortisol Deficiency

Most common is iatrogenic

- All exogenously administered glucocorticoids regardless of dose or route of administration may suppress the HPA axis
- Endogenous cortisol will suppress in 50% of patients who receive intra-articular or oral GC and 5-10% of patient who received inhaled or topical GC

Adrenal insufficiency

Metabolic effects of adrenal disorders		
	Cushing syndrome (hypercortisolism)	Addison disease (hypoadrenalism)
Potassium	Low	High
Blood pressure	High	Low
Glucose	High	Low
Leukocytosis	Neutrophilia	Eosinophilia
Imbalance	Metabolic alkalosis	Metabolic acidosis

Adrenal insufficiency

- Primary adrenal insufficiency (adrenal gland)
  - autoimmune disease, infiltrative disease, malignancy, medications, hemorrhage
- Secondary adrenal insufficiency – (pituitary gland or HT)
  - tumor or hypophysitis
  - exogenous steroids

First Clue: Clinical Manifestation

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

Second Clue: Routine Laboratory Abnormalities

- Hyponatremia: common in primary & secondary AI
  - Why? GC exert negative feedback on vasopressin secretion and deficiency of cortisol may result in nonosmotic stimulation of vasopressin
- Hyperkalemia: due to deficiency of mineralocorticoids but not seen in all primary AI
- Hypercalcemia
- Hypoglycemia – rare more in secondary
- Metabolic Acidosis
- Lymphocytosis, eosinophilia

Imaging abnormalities

- Primary: bilateral adrenal enlargement or masses particular when enlargement is with the normal contour of the adrenal glands
- Atrophic adrenals
  - Secondary: pituitary or sellar mass
- Calcifications – tuberculosis
- Bleeding- hx of anticoagulation use, malignancy, coagulation disorders
- Tumors
- Most times images **cannot rule in or out** the diagnosis and cannot tell if primary or secondary AI.

Causes of AI

- Pituitary or Sellar tumors
- Granulomatous diseases of pituitary or bilateral adrenals
- Autoimmune destruction of Adrenals
- Hypophysitis of Pituitary
- External Bean Radiation to Sella/Pituitary
- Hemorrhage: Bilateral Adrenals, Pituitary Apoplexy, Sheehan's
- Adrenal Infiltration due to Lymphoma
- Infectious Adrenalitis (TB, Fungal, HIV, Syphilis)
- Metastasis: Pituitary or Bilateral Adrenals
- Surgical Resection: Hypophysectomy or bilateral adrenalectomy

A 40-year-old female with a history of HIV and hypertension was brought to the emergency department by her son as she was confused for the past 2 days. She also has been complaining of severe diffuse abdominal pain with nausea and vomiting. Her home medication included megestrol acetate and triumeq (each tablet contains 50 mg dolutegravir, 600 mg abacavir, and 300 mg lamivudine). As per her son, the patient ran out of medication around 2 weeks ago. On physical exam, she was confused. The abdominal exam revealed diffuse tenderness, without rebound tenderness. She had normal deep tendon reflexes. The patient was hypotensive, tachycardiac with hyponatremia, hyperkalemia, and anemia in her laboratory testing. Intravenous fluids were started along with broad-spectrum antibiotics however the patient remained hypotensive requiring vasopressors.

Which of the following is true regarding the patient 's medical condition?

A. The use of triumeq precipitated this medical condition

B. HIV is not considered a risk factor for this condition

C. The use of megestrol acetate precipitate this medical condition

D. There is a decrease in interleukin 1 and 6

Medications

- **Who is at risk? Anyone but particularly in individuals with limited pituitary and/or adrenal reserve**
- Mechanism: Inhibit cortisol biosynthesis- aminoglutethimide (antiepileptic), etomidate (anesthetic-sedative) , ketoconazole (antimycotic) and metyrapone
- Mechanism: Adrenolytic – Mitotane (DDT derivative)
- Mechanism: Drugs that accelerate the metabolism of cortisol and most synthetic glucocorticoids by inducing hepatic CYP3A4 enzyme
  - Phenytoin, barbiturates, and rifampin

Medications

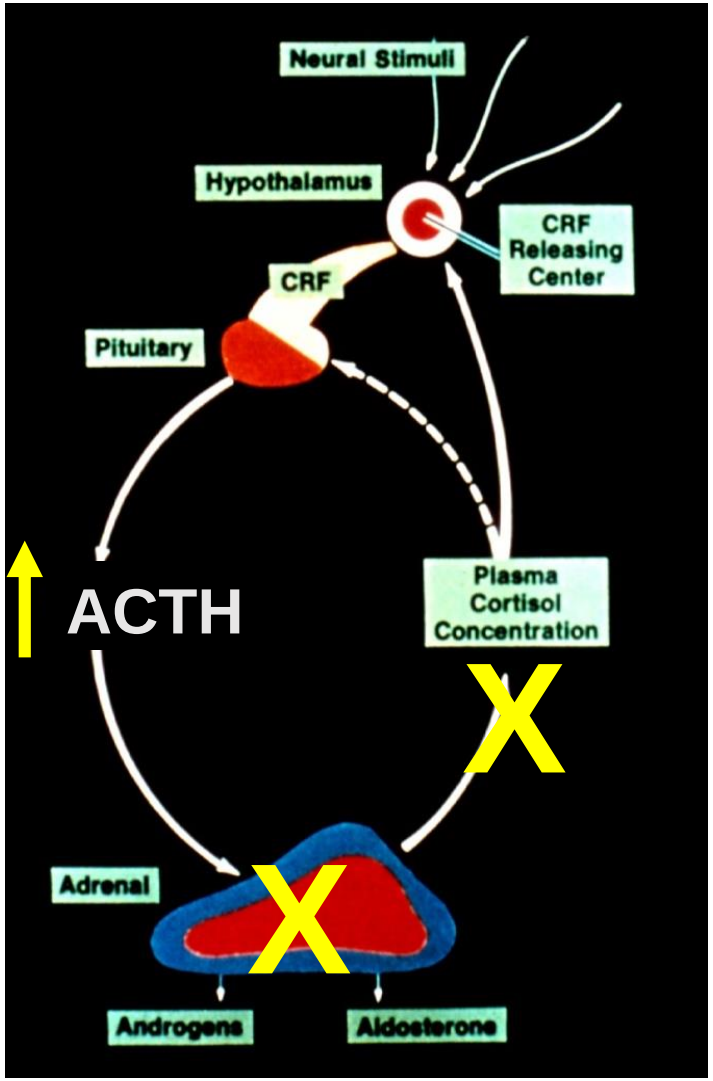
- Opioids- secondary/tertiary ; modify ACTH release
- Psychotropic medication – secondary
- Benzodiazepines (alprazolam), atypical antipsychotics (olanzapine, quetiapine) - secondary
- CTLA-4 monoclonal antibody induced hypophysitis (eg ipilimumab) –secondary
- PD1/PDL1 –adrenalitis (primary)
- GR antagonist (mifepristone) – primary
- Megestrol-secondary

A 27-year-old female patient is 1-month postpartum. She has symptoms of anorexia, weight loss, hyperpigmentation, bowel changes, and lightheadedness on standing. The cosyntropin stimulation test shows random serum cortisol is 11 micrograms/dL. Serum cortisol 1 hour after 0.25 mg cosyntropin is 14 micrograms/dL.

What is the most likely etiology of this patient's illness?

A. Pituitary tumor
B. Autoimmune disease
C. Cushing syndrome
D. Tuberculosis

Primary Adrenal Insufficiency

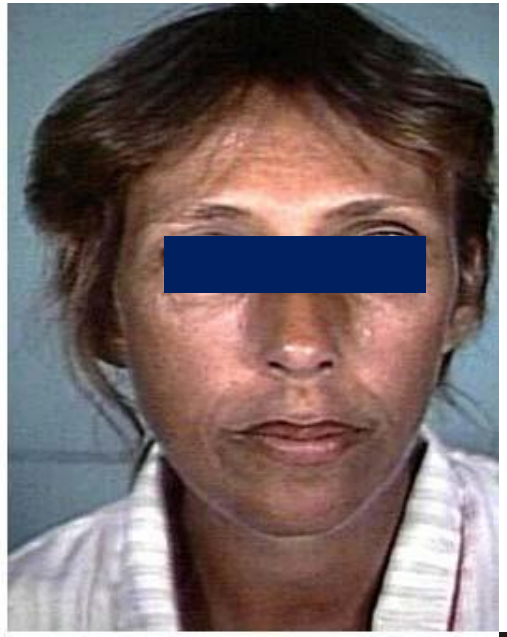


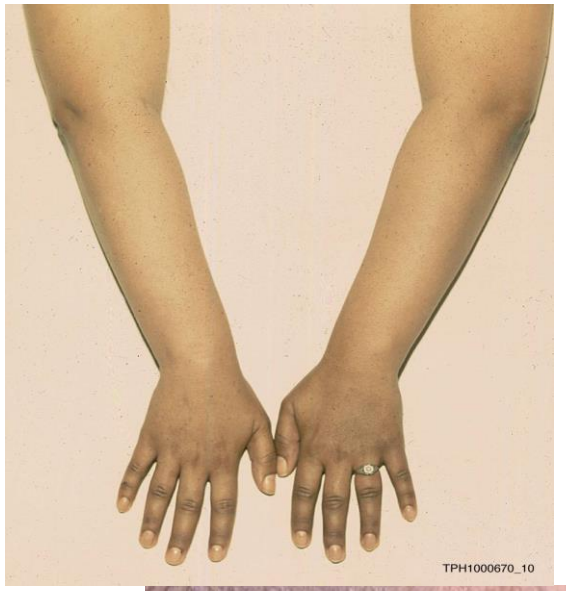
Note: the autoimmune process destroy all layers of the adrenal cortex

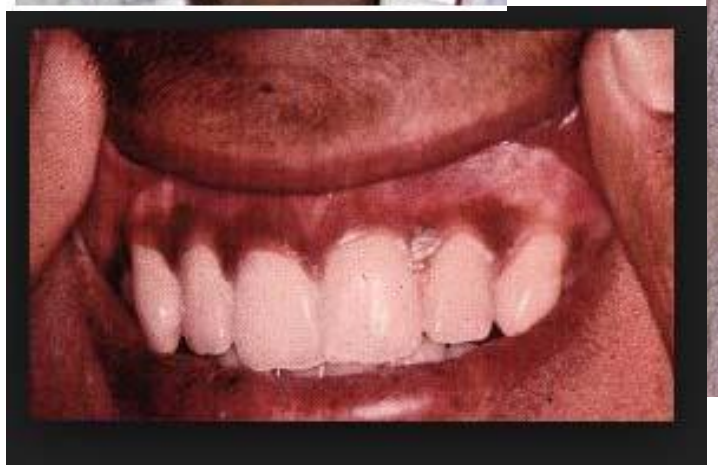
Causes of primary adrenal insufficiency

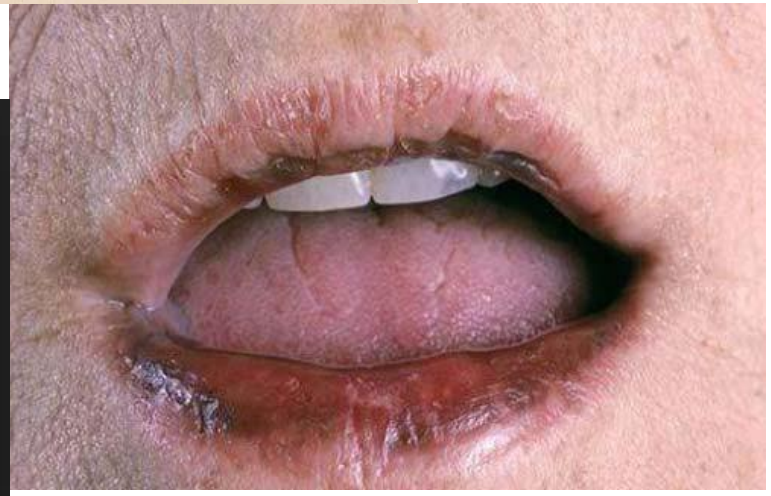
- Autoimmune disease (Addison's disease)
  - 50% of patients have another autoimmune disorder (thyroid disease, vitiligo, type 1 diabetes mellitus, pernicious anemia)
- Infections - HIV, TB, fungal
  - Paracoccidioidomycosis
  - Adrenal glands often calcified
- Infiltrative disease (metastases, lymphoma – bilateral)
- Bilateral hemorrhage
- Bilateral adrenalectomy
- Medications - ketoconazole

Clinical characteristic: PAI









- Fatigue
- Skin darker (stimulation of ACTH production)
- Decreased appetite and nausea
- Dizzy
- Felt like she had the flu

Pigmentation at trauma sites (knuckles, elbows, knees and new scars)

Finding the Etiology AI is important!

- Primary AI is rare! So etiology should be pursued due to additional consequences of the diagnosis
  - Children look for genetic causes
  - 21- hydroxylase Ab
  - Young men Adrenal X- linked leukodystrophy

21 Hydroxylase Antibody

- Cause of autoimmune Addison's disease
- Should be checked in all cases of primary AI
- Sensitivity 90% Sensitivity 100% but immunofluorescence technique is less sensitive
- Young male with primary AI and antibody negative check very long chain fatty acids for Adrenal X- linked leukodystrophy

Polyglandular Autoimmune Syndromes

- Type 1
  - “APECED”
    - Autoimmune PolyEndocrinopathy
    - Chronic Mucocutaneous Candidiasis
    - Ectodermal Dysplasia (dental enamel hypoplasia, pitted nails, alopecia)
  - Autosomal recessive disorder due to mutation in autoimmune regulator (AIRE) gene
  - Onset in infancy
  - Equal gender incidence
  - Classic triad of mucocutaneous candidiasis, AI hypoparathyroidism and Addison’s disease
  - Other manifestations: gonadal failure, hypoplasia of dental enamel, alopecia, vitiligo, intestinal malabsorption, type 1 diabetes, pernicious anemia, hypothyroidism

Polyglandular autoimmune syndromes

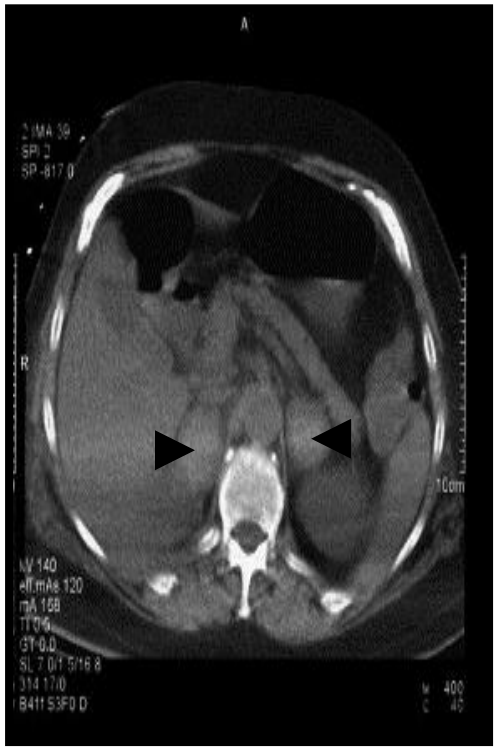
- Type 2
  - HLA-related
  - Multiple types of inheritance described (AD, AR, polygenic)
  - Onset in adulthood
  - Female predominance
  - Autoimmune diseases occurring in multiple endocrine systems
  - Two or more of the following:
    - Primary adrenal insufficiency
    - Graves’ disease
    - AI thyroiditis
    - Type 1 diabetes
    - Primary hypogonadism
    - Myasthenia gravis
    - Celiac disease

Infections of the adrenal gland

- Tuberculosis
  - Major worldwide cause of AI
  - From hematogenous spread
- Fungal (histoplasmosis, cryptococcus)
- CMV
- HIV

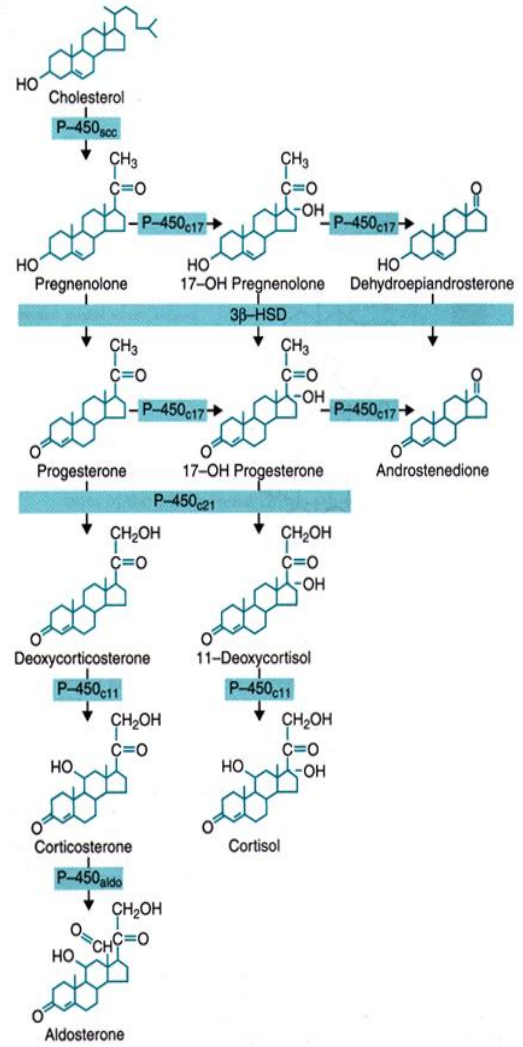
Adrenal hemorrhage

- Adrenal gland is prone to hemorrhage, especially in patients with sepsis, coagulopathy or trauma
- Clues:
  - Hypotension or shock
  - Abdominal or flank pain
  - Fever
  - Drop in hemoglobin
- Waterhouse-Friederichson syndrome
  - Adrenal hemorrhage occurring in patients with sepsis (classically meningococcal sepsis)



Congenital Adrenal Hyperplasia

- Family of autosomal recessive disorders resulting in impaired production of cortisol
- Presentation varies depending on the particular mutation and the particular enzyme involved



Adrenoleukodystrophy

- X-linked recessive disorder
- Mutations in ABCD1 gene
- Defect in oxidation of fatty acids within peroxisomes
  →Elevated serum levels of very-long-chain fatty acids
  →Accumulation in cell membranes
  →Demyelination within the nervous system
- Progressive neurologic dysfunction and adrenal insufficiency

Adrenal hypoplasia congenita

- X-linked
- Mutation in DAX-1 gene
  - Nuclear receptor of unknown function
  - Expressed in adrenal cortex, gonads, and hypothalamus
- Present with congenital adrenal insufficiency and hypogonadotrophic hypogonadism

Metastases to the adrenal gland

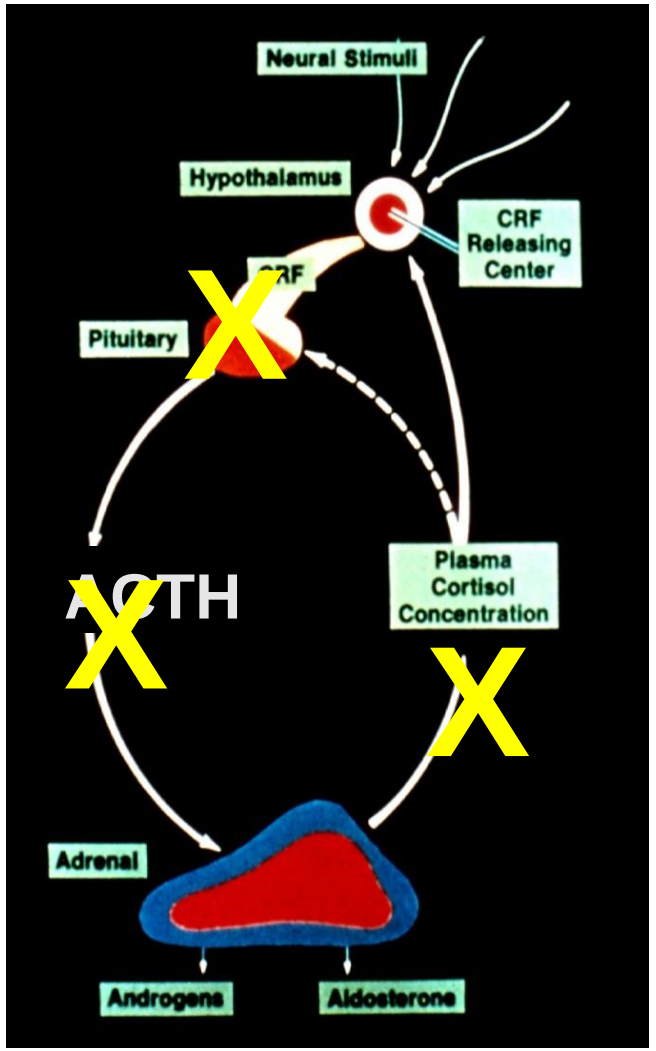
- 40-60% of patients with disseminated breast or lung cancer have adrenal metastases at autopsy
- Frank AI is uncommon

A female presents with anorexia, weight loss, hyperpigmentation, bowel changes, and lightheadedness on standing. The cosyntropin stimulation test shows random serum cortisol of 11 micrograms/dL. Serum cortisol 1 hour after 0.25 mg cosyntropin N is 14 micrograms/dL. Renin level is 10.

Which of the following is an appropriate treatment for this patient?

A. Hydrocortisone 15 and 5 mg mg daily for life
B. Prednisone 5 mg daily for life
C. Hydrocortisone 15 and 5 mg and fludrocortisone 0.1 mg daily for life
D. Dexamethasone 0.5 mg daily for life
E. Dexamethasone 4 mg daily and fludrocortisone 0.1 mg daily for life

Secondary Adrenal Insufficiency



Causes of 2˚ Adrenal Insufficiency

1. Exogenous glucocorticoids
2. Exogenous glucocorticoids
3. Exogenous glucocorticoids
4. Hypothalamic/pituitary disease

H-P disease resulting in 2˚ adrenal insufficiency

- Tumors
- Hemorrhage
- Infarction
- Infiltrative disorders
- Traumatic brain injury

Tumors resulting in 2˚ adrenal insufficiency

- Space-occupying lesions cause hypopituitarism by destroying the pituitary gland or by disrupting the hypothalamic-hypophyseal portal venous system
    - Pituitary adenomas
    - Other CNS tumors (meningioma, epidermoid tumors)
    - Metastases (breast cancer)

Pituitary hemorrhage resulting in 2˚ adrenal insufficiency

- Often due to bleeding into a previously undiagnosed pituitary adenoma
- Severe headache and visual changes may be prominent
- Often called “Pituitary apoplexy”

Pituitary infarction resulting in 2˚ adrenal insufficiency

- Most commonly occurring peripartum (“Sheehan’s syndrome”)
- Hypotension along with vasospasm of the hypophyseal arteries compromise arterial perfusion of the anterior pituitary

Analysis of Laboratory tests in a 50-year-old woman who presents with features of adrenal insufficiency shows normal serum levels of sodium, potassium, and low cortisol levels.

What is the most likely diagnosis?

A. Addison disease
B. Adrenal metastasis from a small cell lung cancer
C. Tuberculosis of the pituitary gland
D. Congenital adrenal Hyperplasia

Infiltrative disease resulting in 2° adrenal insufficiency

- Langerhan's histiocytosis
  - Infiltration of multiple organs by well-differentiated histiocytes
  - Diabetes insipidus, anterior pituitary hormone deficiency
- Sarcoidosis
  - Multisystem granulomatous disorder characterized by the presence of noncaseating granulomas in involved organs
  - Diabetes insipidus, anterior pituitary hormone deficiency

Infiltrative disease resulting in 2˚ adrenal insufficiency

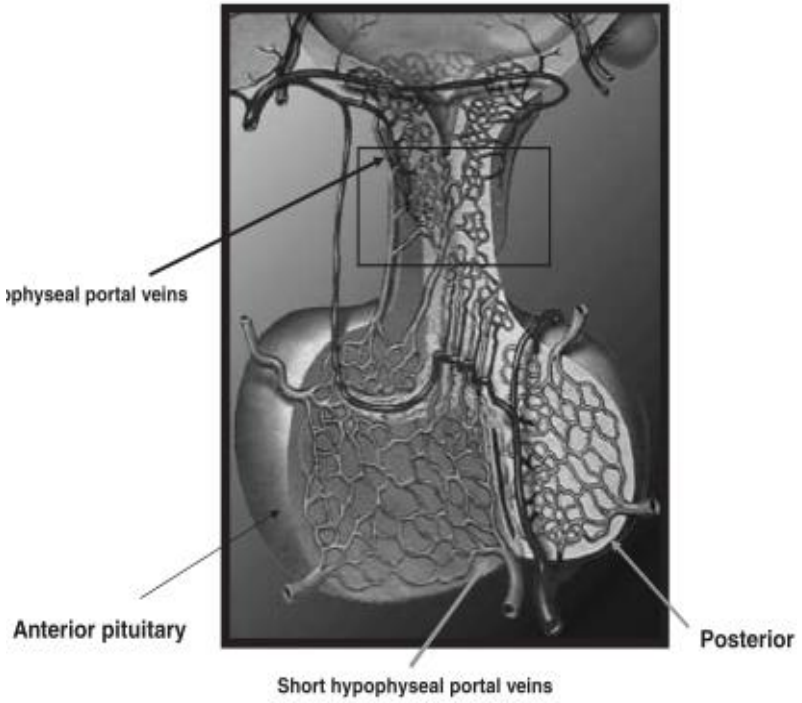
- Hemochromatosis
  - Excessive iron deposition in the tissues
  - Hypogonadotropic hypogonadism
  - Deficiency of TSH, GH and ACTH later in the course of disease

Traumatic brain injury

- Prevalence of hypopituitarism - up to 68.5%
- Mechanisms

  - compression of the pituitary gland and/or hypothalamic nuclei due to edema

  - direct mechanical injury to the hypothalamus, pituitary stalk (hypophysial vessels, portal capillaries) or the gland
- Growth hormone deficiency – most common pituitary deficit



A 25-year-old lady complains of fatigue and body aching. She has lost her appetite and has nausea for the last week. You check a morning total cortisol level and find it is 4ug/dL. She is on no medications.

What is the next best step?

a. Repeat AM cortisol
b. Perform ACTH stim test
c. Start steroid replacement
d. Measure ACTH level

Diagnostic Testing- Basal Serum Cortisol

- Can be used alone to **exclude** all forms of AI in MOST patients
- Cortisol has strong diurnal rhythm
- AM cortisol before 9:00 am is diagnostically useful
- Basal cortisol values < 3 ug/dl highly suggestive but not always diagnostic (clinical correlation needed)
- BUT if cortisol drawn at any time of day is > 10 ug/dl is 99% specific for predicting a cortisol increase greater than 18 ug/dl during an ACTH stim test
- Basal cortisol values 3-10 ug/dl are inconclusive and require additional testing

Diagnostic Testing- ACTH

- AM ACTH value itself not used to excluded adequate cortisol production
- If cortisol is low < 5ug/dl the ACTH is useful to distinguish etiology of AI
  - Primary AI: ACTH > 100 pg/ml
  - Secondary AI: ACTH < 5 pg/ml (or inappropriately low)

Serum Aldosterone & Plasma Renin Activity

- Not deficient in secondary AI
- Only deficient in primary AI
- Aldosterone will be low or undetectable in primary AI but only interpretable with an appropriately elevated renin (>2 ng.ml/h)

250 ug Cosyntropin Stimulation Test

- Indication: Definitively exclude primary adrenal insufficiency or *longstanding* secondary adrenal insufficiency (>2 weeks)
- Protocol: IV or IM bolus with sampling baseline, 30 min and 60 min
- Can be done ANYTIME OF DAY
- NORMAL: A peak cortisol at 30-60min of greater than 18 ug/dl
- Basal cortisol values vary by time of day and clinical status and should never be used as a diagnostic criterion
- Aldosterone normally doubles in response to cosyntropin which can be helpful

Other dynamic testing- recommend endocrine involvement

- Insulin Tolerance Test
  - GOLD STANDARD TEST for all forms of AI
  - Tests the entire HPA axis
  - Measures the counter regulatory hormone response to hypoglycemia
  - Useful in equivocal cases of other dynamic testing & secondary AI
  - Contraindications to test: seizure disorders, significant cardiovascular disease, inability to verbalize symptoms of hypoglycemia

Other diagnosis

- Adrenal Fatigue: Doesn’t exist
- Relative Adrenal Insufficiency: according to endocrinologist doesn’t exist, possibly exists in critical care literature
  - Circulating cortisol is about 10% free hormone and 90% bound
  - The affinity of cortisol for the GC receptor is about .362 ug/dl
  - So a total serum cortisol of 7 ug/dl is about .7 ug/dl free cortisol which is nearly enough to saturate the GC receptor.
  - So during stress even “low” amounts is often enough

A 60-year-old female was found in a semi-comatose condition and brought to the emergency department. On physical exam, her height was 66 inches (167.6 cm), and weight was 123 lb (55.8 kg) (BMI=19.9 kg/m2). Her blood pressure was 80/40 mmHg; her pulse rate was 150 beats/min with temperature 99F. She was disoriented and lethargic with normal deep tendon reflexes. Her home medications include aspirin and ketoconazole prescribed for onychomycosis of her toenails 6 months ago.Laboratory test results demonstrate: hemoglobin 9 g/dl; hematocrit 25%; WBC count 9840 cells/mm3; platelet count 297,000 cells/mm3; creatinine 1.09 mg/dl sodium 128 meq/l; potassium 5.2 mEq/L; chloride 93 mEq/L; and bicarbonate 18 mEq/L. Chest radiography and CT brain didn't reveal any abnormalities. Blood and urine cultures were sent. The patient was started on intravenous fluid resuscitation with broad-spectrum antibiotics.

Which of the following is true regarding this medical condition?

A. Ketoconazole is a precipitating factor
B. The patient can present with hypocalcemia
C. Hyperglycemia is a common manifestation
D. Lymphopenia is a common manifestation

Acute Ill Management with AI

- Aggressive volume replacement with normal saline
- Use of vasocontraction medications
- If not response
  - Hydrocortisone (solu-cortef) as IV bolus or infusion, IM ok as well if no IV access
- Exact dose not critical just get some in ASAP
- 20mg HC will sufficiently raise serum cortisol concentrations

Acute Management of AI

- Presumed maximal output of hydrocortisone during severe stress is 200-300mg/day
- Doses of 50mg q6 will raise serum cortisol to 40-120mg/dl
- MOST IMPORTANT is to continue the dosing until patient is well then can take oral regimen

Acute Management of AI

- Doses of hydrocortisone greater than 40mg/dl per day also have a mineralocorticoid effect so do not need fludrocortisone replacement
- If use dexamethasone, need to give fludrocortisone
- Pts promptly respond to the first dose of hydrocortisone

ACTH Stimulation Test in AI During Critical Illness

- Often does not provide any additional meaningful information when accounting for possible delay in care

Chronic GC replacement

- Hydrocortisone (more physiological steroid)
- 10-12mg/ m2 (BSA)
- Usually Hydrocortisone 15-20mg divided into 2 doses
- Dose to match the normal diurnal rhythm
- Two peaks of cortisol 8am and 4pm
  - 1st dose upon awakening or 30 min prior to arising
  - Next dose 8hrs later and before 5 pm
  - Less preferred is prednisone and dexamethasone since they are long acting and need to be metabolized in the liver to the active hormone
- Side effect: hypercortisolism

Synthetic Steroid Potencies

	Anti-inflam	Glucocort	Mineralo
• Hydrocortisone	1	1	1
• Prednisone	3	4	0.75
• Methylprednisone	6	4	0.5
• Fludrocortisone	0	0	125
• Triamcinolone	5	4	0
• Dexamethasone	26	17→?	0

Note: hydrocortisone (cortisol) has been arbitrarily assigned a potency level of 1 in each of the 3 categories above. For e.g. – prednisone has 4 times glucocorticoid properties compared to cortisol, and 0.75 mineralocorticoid properties compared to cortisol, and 3 times the anti-inflammatory properties of cortisol.

Mineralocorticoid therapy (PAI)

- Mineralocorticoid replacement
  - Fludrocortisone 0.05 to 0.2 mg daily
  - Adjust based on serum potassium
  - absence of edema
  - absence of postural hypotension
  - Not needed in 2˚ adrenal insufficiency
- Liberal salt intake

Treatment

- Treatment of adrenal insufficiency should be initiated as soon as the diagnosis is confirmed, or even sooner if the patient presents in adrenal crisis.
- Patients with primary adrenal insufficiency require life-long glucocorticoid and mineralocorticoid replacement therapy

  - **All patients should wear Medic-alert bracelet!!**

Asked to see pt regarding diagnosis of adrenal fatigue in 19 y/o man complaining of panic attacks accompanied by palpitations and weakness.

Diagnosis of adrenal fatigue made by a salivary cortisol profile.

Pt's mother at the visit

Normal skin pigmentation

124/74 HR 60

BMI 21

PE=normal

Early morning cortisol 1.2 ug/dl

Which of the following testswould you obtain next?

A. Plasma ACTH

B. 250 ug ACTH stimulation test

C. Pitultary MRI

D. DHEA-S

250 ug Stim test was done and peak cortisol was 11.6 ug/dl
Basal ACTH < 5
Total T, Free T4, IGF-1 wnl

Which of the following studies would you get next?

A. Pituitary MRI
B. ITT
C. 1 ug cosyntropin stimulation test
D. Renin level

Pituitary MRI is normal

Which of the following studies would you get next?

A. Measurement of long chain fatty acids

B. 21 Hydroxylase antibodies

C. Synthetic glucocorticoid screen

D. 17 Hydroxyprogestone (Congenital Adrenal hyperplasia)

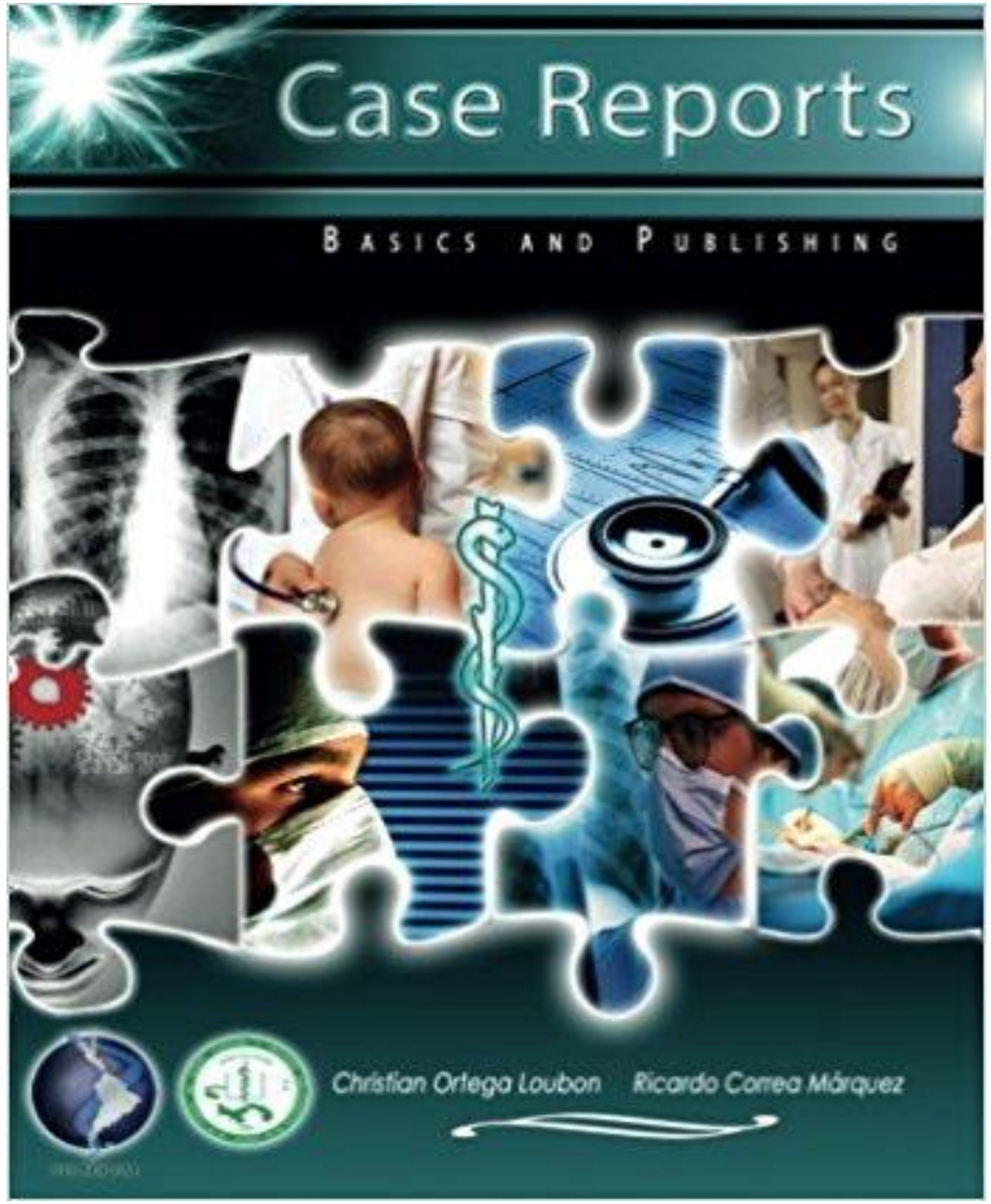
Synthetic GC screen negative

Two weeks later the initial visit, the patient's mother calls you and finds what in his drawer?

Opioid

1. Does he really have adrenal insufficiency?
2. Should you treat?

QUESTIONS!!!!
CASES!!!!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