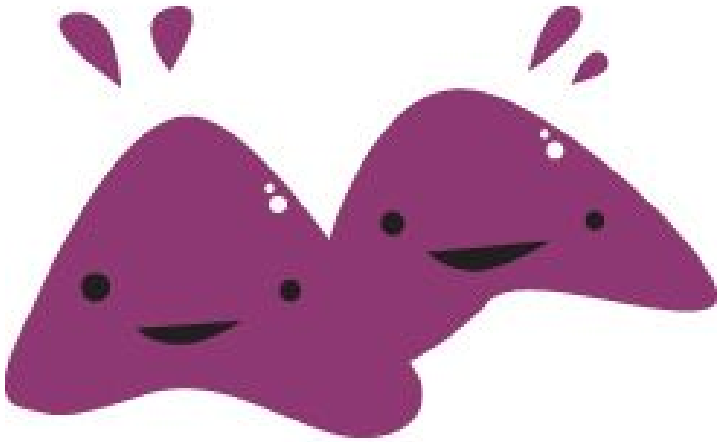

Adrenal Gland

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Color Index:
-Slides -Important -Doctor's Notes -Davidson's Notes -Surgery Recall -Extra

Correction File **Email:** Surgeryteam434@gmail.com

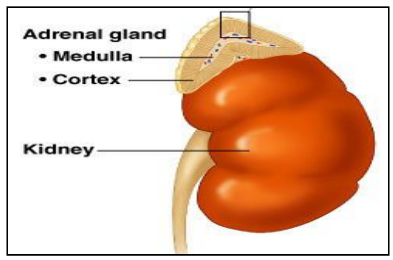
-Patient with 5 years history of steroid she came to the ER with hypotension and tachycardia in examination there was nothing significant apart from that she stopped her steroid …… because the adrenal gland depend on medication so she just stop working and after she stopped her medication she developed these symptoms

- Patient was seen by gynecologist for uterine fibroid she did US , there was a mass on the right adrenal gland what to do ??
this by chance discovered
-Patient, she presented to the ER with hypocalemia and hypertension …….
We will face all of these during this lecture...

Adrenal Glands

Divided into two parts , each with separate functions :

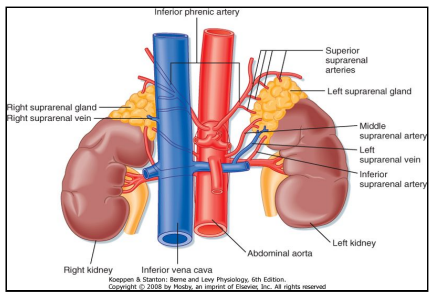
- Adrenal Cortex
- Adrenal Medulla



Blood Supply:
Each gland has 3 arteries and one vein. Arteries comes from:
• Inferior phrenic : superior suprarenal artery
• Abdominal aorta : middle suprarenal artery
• Renal artery : inferior suprarenal artery

left adrenal vein: Left renal vein
right adrenal vein: Inferior vena cava (IVC)

The adrenals are located deeply (retroperitoneal organs), which makes it difficult to remove them. One approach: from the back below 12th rib, enter fascia surrounding adrenal gland > not applicable to all adrenals e.g. big adrenals



Surgical anatomy and development

- Adrenal gland weighs approximately 4g and lies immediately above and medial to the kidneys.
- Each gland has an outer cortex and inner medulla.
- Cortex is derived from mesoderm and medulla is derived from the chromaffin ectodermal cells of the neural crest.
- The medulla is part of the sympathetic nervous system. Its APUD cells secrete the catecholamines, adrenaline (epinephrine), noradrenaline (norepinephrine) and dopamine, and are supplied by preganglionic sympathetic nerves.

The Adrenal Cortex

Three specific zones and each produces a specific class of steroid hormone:

- Zona glomerulosa → mineralocorticoids (**Aldosterone**)
- Zona fasciculata → 1- glucocorticoids (**Cortisol**)

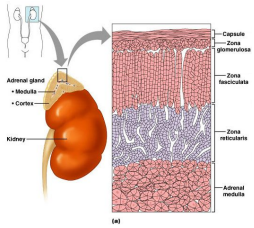
2-Androgenic steroids (androstenedione,

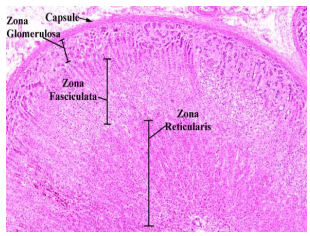
11-hydroxy-androstenedione and testosterone)

- Zona reticularis → androgens
  - Inactive androgen and oestrogen precursor,

    dehydroepiandrosterone sulphate(DHA-S).

- The hormones are circulate either free (5%) or bound to α-globulin.





SUMMARY BOX 20.5

Adrenocortical hormones

- Cortisol secretion is controlled by pituitary adrenocorticotrophic hormone (ACTH). Cortisol protects against stress, maintains blood pressure and aids recovery from injury/shock. Its metabolic activities include protein breakdown, increased gluconeogenesis, reduced glucose utilization and mobilization/redistribution of fat and water
- In excess, cortisol has mineralocorticoid activity, can cause psychosis, and has anti-inflammatory effects (used in transplantation immunosuppression)
- Aldosterone secretion is controlled mainly by angiotensin levels (and thus by renin release from the juxtaglomerular apparatus during decreased renal perfusion)
- Aldosterone conserves sodium (by facilitating its exchange for potassium and hydrogen ions in the kidney) and is a major determinant of extracellular fluid conservation
- Androgenic steroids and dehydroepiandrosterone sulphate (DHA-S) are also secreted by the adrenal cortex. DHA-S is converted to testosterone and oestrogen in fat and liver, and this peripheral aromatization is the main source of oestrogen in postmenopausal women.

why cortex divided into three part ?because each part has it own hormone and every hormone has its own function . so any increase or decrease in this hormone cause specific disease

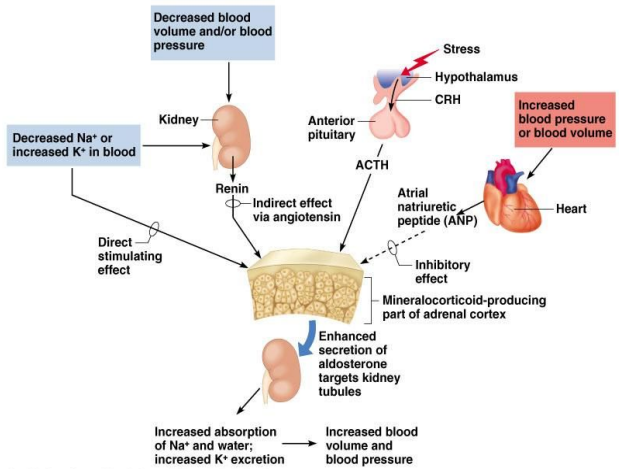
Hormones of the Adrenal Cortex

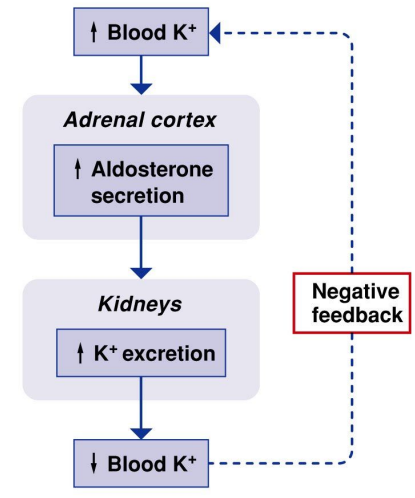
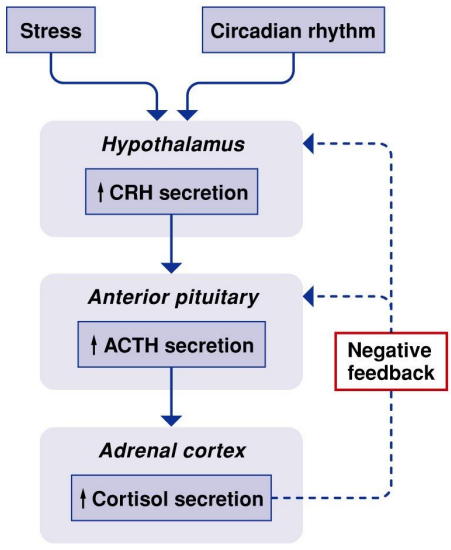
Note

- Direct stimulant of the Adrenal gland is
- Decreased sodium (NA+) level
- increased potassium (K+) level

Enhancing secretion of aldosterone

- Indirect stimulation of the Adrenal gland is :
- decreased blood pressure
- decreased blood volume
- Inhibitory effect :
- increased blood volume
- increased blood pressure



Hormone	Mineralocorticoids (F & E balance) Aldosterone	GLUCOCORTICOIDS CORTISOL
Effect on	Salt : - Na retention - Water retention - K excretion -Hydrogen ion excretion	Responsible for control and & metabolism of: a. CHO (carbohydrates) 1- increase amt.[1] glucose formed 2- increase amt. glucose released b. FATS-control of fat metabolism: stimulates fatty acid mobilization from adipose tissue c. PROTEINS-control of protein metabolism 1- stimulates protein synthesis in liver 2- protein breakdown in tissues d. OTHER functions of cortisol : 1- decrease inflammatory and allergic response 2- decrease immune system therefore prone infection
Regulation	Renin from kidneys controls adrenal cortex production of aldosterone	Regulate metabolism & are critical in stress response
Physiology	 (b) Regulation of aldosterone secretion 	

[1] Amount

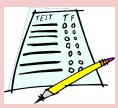
ACTH
(adrenocorticotropic Hormone)

- Produced in anterior pituitary gland
- Circulating levels of cortisol :

1. decreased levels cause stimulation of ACTH
2. increased levels cause decreased release of ACTH

- Affected by :

1. Individual biorhythms
   a. ACTH level are highest 2 hours before and just after awakening
   b. Usually 5AM- 7AM
   c. these gradually decrease rest of day
2. Stress → increase cortisol production and secretion



Test yourself

1. If your Na level is low, will aldosterone secretion increase or decrease ??
2. If your serum K+ level is high, will aldosterone secretion increase or decrease ?
3. RELEASE OF GLUCOCORTICOIDS IS CONTROLLED BY ??
4. Increasing the level of mineralocorticoid activity (aldosterone) , What will happen ?

answers : 1- increased , 2- increased , 3- ACTH, 4 - sodium and water retention , increased blood pressure

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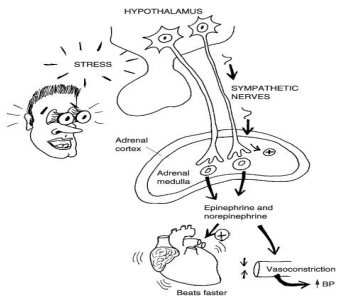
ADRENAL MEDULLA

``Fight or flight ``

★ CATECHOLAMINE RELEASE:

1. Epinephrine
2. Norepinephrine



Diseases of adrenal gland
hyperfunction or hypofunction

CUSHING Syndrome
(TOO MUCH CORTISOL!)

- ❖ Increase Secretion of cortisol from adrenal cortex or high blood circulation of cortisol
- ❖ 4X more frequent in females
- ❖ Usually occurs at 35-50 years of age

ETIOLOGY

- Primary-tumor in the adrenal cortex
- Secondary-tumor on the anterior pituitary gland
- Ectopic ACTH secreting tumor (lunge , pancreas) (it's tumor not found in the pituitary that secretes ACTH, which in turn causes adrenal gland to release cortisol without the normal negative feedback loop)
- Iatrogenic-Steroid administration (the most common cause) (i.e., prescribed prednisone)

SIGNS & SYMPTOMS Cushing's

- **Increase protein catabolism :**
  1. muscle wasting
  2. loss of collagen support (thin, fragile skin, bruises easily)
  3. poor wound healing
- **Increase in CHO metabolism:**
  1. hyperglycemia
  2. Can get diabetes-insulin can't keep up
  3. Polyuria
- **Increase in fat metabolism:**
  1. truncal obesity
  2. buffalo hump
  3. "moon face"
  4. increase weight but decrease strength
- **Increase androgen secretion:**
  1. excessive hair growth
  2. acne
  3. change in voice
  4. receding hairline
- **decrease immune response**
  1. More prone to infection
  2. decrease resistance to stress
  3. Death usually occurs from infection

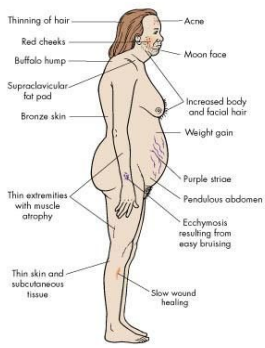


Figure 47-9 Common characteristics of Cushing's syndrome.

1- HYPERALDOSTERONISM
"Conn's Syndrome"

First what does aldosterone do?
Regulates Sodium and Potassium. So balance by causing the kidney to excrete potassium and reabsorb sodium.
What is the normal serum K+ level? 3.5-4.5 (mEq/L)

Case: Patient admitted with **hypokalemia, high sodium** and diagnosed with high blood pressure for the last 2 years Dx is:

"Conn's Syndrome"	
• **Basically it is too much aldosterone secretion** • **Usually caused by adrenal tumor most common in young or middle-aged women.** • **The adenoma is: small, single, canary yellow on bisection & Composed of cells of the glomerulosa type.** • **The high circulating levels of aldosterone suppress renin secretion – a helpful biochemical diagnostic observation.**	
SIGNS & SYMPTOMS	• **Na and water retention (HTN, headaches and visual disturbance (although serious retinopathy is uncommon).** • **K+ (hypokalemia) Worsening hypokalemia, episodes of muscle weakness and nocturnal polyuria.** • **H/A (headache) secondary to HTN - Usually no edema**
DIAGNOSIS ***should be all not just one***	• **Urinary K (Low in blood but high in urine. not specific nor sensitive because some medications can ↑ the potassium)** • **Plasma Na ↑ and K ↓** • **Confirm hypokalaemia:** **By repeated blood sampling and 24-hour urine collections usually → ↑ K excretion.** • **Demonstrate hypersecretion of aldosterone:** • **High plasma aldosterone levels with low plasma renin levels** • **Plasma and/ or urinary aldosterone levels are measured at 4-hourly intervals to allow for diurnal variations** • **Giving the aldosterone antagonist, spironolactone, should ↓ blood pressure and reverse hypokalaemia.** • **CT scan (To rule-out masses)**

- **EKG changes (QRS prolongation because of hypokalemia)**
- **Exclude secondary hyperaldosteronism:**

-Renin levels are ↑ in secondary hyperaldosteronism but undetectable in the primary disease.

-Spironolactone causes further ↑ in renin levels in secondary hyperaldosteronism

- **Localize the adenoma:**

To localize the adenoma we have to use CT or MRI, failure to 'see' an adenoma mean there is no discrete tumour and that the patient has bilateral cortical hyperplasia.

MANAGEMENT
(Doctor said "No need for management will NOT come in EXAM")

- **Surgery(ADRENALECTOMY) but after correcting the hypokalaemia with oral potassium and spironolactone.**

In Adrenal hyperplasia: long-term drug treatment.

PRE-OP

- **Control BP, replace K, control Na and give high dose of steroids**
- **Stabilize hormonally**

Correct fluid and electrolytes Cortisol PM(night) before surgery, AM(morning) of surgery and during OR.

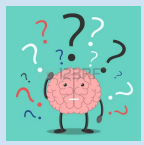
POST-OP

- **ICU-What type of problems to expect? (doctor didn't explain it)**
- **IV cortisol for 24 hours**
- **IM cortisol 2nd day**
- **PO cortisol 3rd day**
- **Poor wound healing**
- **If unilateral- steroids weaned**
- **Other adrenal takes over 6-12 months**
- **Monitor because patient may go into crisis: severe hypotension or severe hypertension**

Secondary hyperaldosteronism:

Hyperaldosteronism is most commonly secondary to excessive renin secretion (and stimulation of the zona glomerulosa by angiotensin) in chronic liver, renal or cardiac disease.

MCQ: which of the following does NOT happens with conn's?
1- Hypokalemia
2- Hyponatremia (Hypernatremia because of HIGH sodium (Na))
3- Water Retention



2- ADDISON'S DISEASE (opposite to Cushing's)

- Hypofunction of adrenal cortex
- Hormones that will be decreased glucocorticoids, mineralocorticoids and androgens

ETIOLOGY	• Idiopathic atrophy • Autoimmune condition Antibodies attack against own adrenal cortex (e.x, SLE) • 90% of tissue destroyed (leading to no secretions) • TB/fungal infections (histoplasmosis) • Iatrogenic causes: adrenalectomy, chemo, anticoagulant treatment
SYMPTOMS & SIGNS	• fatigue, weight loss, anorexia: due to low cortisol. • Changes in skin pigment "small black freckles": due to low cortisol, high ACTH (Adrenocorticotropic hormone) and high MSH (Melanocyte-stimulating hormone) • Muscular weakness: cortisol helps muscles maintain contraction and avoid fatigue but in addison's it's low.
	• Fluid & electrolyte imbalances (opposite of conn's by having hyponatremia and hyperkalemia): due to insufficiency in releasing hormones • BP is low: due to insufficiency in releasing hormones • Hyponatremia: because of low aldosterone • **Hyperkalemia**: because of low aldosterone • Hypoglycemia: because of low cortisol • Androgens are low causing: hair loss and sexual dysfunction • Mental disturbances: anxiety, irritability, etc. • Salt craving: because of low aldosterone
DIAGNOSIS ***not sensitive nor specific***	• Serum cortisol is low **(if low then will be diagnostic for addisons)** • Urinary 17-OHCS[2] and 17 KS[3] is low • K is high • Na is low • Serum glucose is low

[2] 17 hydroxycorticosteroid
[3] 17 Ketosteroid

INTERVENTIONS	• Life long disease so patient must have a sign indicating that he has addison's • Life long hormone replacement • Primary-need oral cortisone 20-25mgs in AM(morning) and 10-12 mg in PM(night) • Change dose PRN[4] for stress • Also need mineralocorticoid-(FLORINEF) • Salt food liberally • Do not fast or omit meals • Eat between meals and snack • Eat diet high in carbs and proteins • Wear medic-alert bracelet • **Kit of 100 mg hydrocortisone IM (IMPORTANT for all patients to have this kit)** • Keep parenteral glucocorticoids at home for injection during illness • Avoid infections/stress
Compilation	• Adrenal crisis • Electrolyte imbalance • Hypoglycemia

In History taking

Any patients coming with adrenal mass you should ask yourself Three questions:

I. Is it functioning (releasing hormones) e.g. causing headache, truncal obesity, HTN(controlled or not? how long?).
II. Previous history of cancer (could be metastasis from breast or skin or Renal Cell Carcinoma (RCC)).
III. Is it benign or malignant

[4] Abbreviation for pro re nata = a latin phrase meaning "as needed".

3- PHEOCHROMOCYTOMA(adrenal medulla mass functioning)

- Rare, benign tumor of the adrenal medulla and sometimes could be malignant
- Oh no...what are we going to see a hypersecretion of?(doctor didn't explain it)
- May be associated with neurofibromatosis, medullary carcinoma of the thyroid (MEN II), Von Hipple–Lindau disease, duodenal ulcer and renal artery stenosis

NEVER take a biopsy if pheochromocytoma was expected.

SIGNS & SYMPTOMS

- Hallmark is hypertension: 200/150 or greater(complaining of headache all the time with uncontrolled even with antihypertensive medications)
- Spells
- Paroxysmal attacks
- bladder distension,emotional distress, exposure to cold.
- NE and Epinephrine released sporadically
- Deep breathing
- Pounding heart
- Headache
- Moist cool hands & feet
- Visual disturbances
- diabetes mellitus

DIAGNOSIS

- By history and examination then tests
- 24 hour urine-VMA[5] (metabolite of Epinephrine)metadrenaline and normetadrenaline levels (serum or urine metanephrines is the most sensitive and specific to know if he has functional pheochromocytoma or not)
- Plasma catecholamines
- CT to locate tumor
- metaiodobenzylguanidine (MIBG) scanning

INTERVENTIONS

PRE-OP

- **Adrenergic blocking agents**

Minipress to lower BP

- **Beta blocking agents**

Inderal to lower HR, BP & force of contraction

- **Diet**

high in vitamin, mineral,calorie, no caffeine

- **Sedatives**
- **Monitor BP.** (+CONTROL IT)
- **Eliminate attacks**
- **If attack- complete bedrest and HOB[6] 45 degrees**

DURING SURGERY

- GIVE REGITINE AND NIPRIDE TO PREVENT HYPERTENSIVE CRISIS(in high BP we give antihypertensive, in hypotension we give fluid)

POST-OP

- BP. may be high initially, BUT CAN BOTTOM OUT
- Volume expanders
- Vasopressors
- Hourly I and O
- Observe for hemorrhage

[5] Vanillylmandelic acid
[6] Head Of Bed

4- Adrenal incidentaloma

- In adrenal Medulla, found by chance, patients asymptomatic, so you must ask the 3 questions, then follow up every 6 months.
- An increase in size is indication of surgery > 5 is the cutoff.
- Mass lesion greater than 1 cm.
- Serendipitously discovered by radiologic examinations. Such as : Computed tomography (CT) or Magnetic resonance imaging (MRI)
- Two questions: 

1- Is it malignancy ? if seen in CT follow up increased by 1 cm or more in a year.

2- Is it functioning ? by asking the 3 questions

Surgical Recall

Cushing's Syndrome

What is the second most common cause? Cushing's disease (most common non iatrogenic cause)

What is Cushing's disease? Cushing's syndrome caused by excess production of ACTH by anterior pituitary

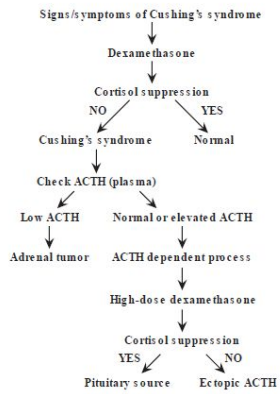
How can cortisol levels be indirectly measured over a short duration? By measuring urine cortisol or the breakdown product of cortisol, 17 hydroxycorticosteroid (17-OHCS), in the urine

What is a direct test of serum cortisol? Serum cortisol level (highest in the morning and lowest at night in healthy patients)

What initial tests should be performed in Cushing's syndrome?
Electrolytes
Serum cortisol
Urine-free cortisol, urine 17-OHCS
Low-dose dexamethasone suppression test
What is the low-dose dexamethasone suppression test? Dexamethasone is a synthetic cortisol that results in negative feedback on ACTH secretion and subsequent cortisol secretion in healthy patients; patients with Cushing's syndrome do not suppress their cortisol secretion

After the dexamethasone test, what is next? Check ACTH levels

What is the workup in a patient suspected of having Cushing's syndrome?



How are the following tumors treated:	
Adrenal adenoma?	Adrenalectomy (almost always unilateral)
Adrenal carcinoma?	Surgical excision (only 33% of cases are operable)
Ectopic ACTH-producing tumor?	Surgical excision, if feasible
Cushing's disease?	transphenoidal adenectomy

Conn's Syndrome

What is the normal physiology for aldosterone secretion?
BP in the renal afferent arteriole is low
Low sodium and hyperkalemia cause renin secretion from juxtaglomerular cells
Renin then converts angiotensinogen to angiotensin I
Angiotensin converting enzyme in the lung then converts angiotensin I to angiotensin II
Angiotensin II then causes the adrenal glomerulosa cells to secrete aldosterone

Classically, what kind of hypertension? Diastolic hypertension

What is the saline infusion test?
Saline infusion will decrease aldosterone levels in normal patients but not in Conn's syndrome

What are the causes of Conn's syndrome?
Adrenal adenoma (66%)
Bilateral idiopathic adrenal hyperplasia (30%)
Adrenal cancer (< 1%)

What is the treatment of the following conditions:	
Adenoma	Unilateral adrenalectomy (laparoscopic)
Unilateral hyperplasia	Unilateral adrenalectomy (laparoscopic)
Bilateral hyperplasia	Spironolactone (usually no surgery)

What are the renin levels in patients with PRIMARY hyperaldosteronism?
Normal or low (key point!), the plasma aldosterone to plasma renin will be > 30

ADDISON'S DISEASE

How do you remember what ADDISON's disease is?
Think: **ADD**ison's disease = **AD**renal **D**own

Pheochromocytoma

Which age group is most likely to be affected?
Any age (children and adults); average age is 40 to 60 years

How can the pheochromocytoma SYMPTOMS triad be remembered?
Think of the first three letters in the word **PHE**ochromocytoma:
Palpitations, **H**eadache and **E**pisodic diaphoresis

What are the other common lab findings?
Hyperglycemia (epinephrine increases glucose, norepinephrine decreases insulin)
Polycythemia (resulting from intravascular volume depletion)

What are the other sites for pheochromocytoma?
Organ of Zuckerkandl, thorax (mediastinum), bladder, scrotum

What is Organ of Zuckerkandl ?
is chromaffin body around abdominal aorta at site of bifurcation and near to inferior mesenteric artery , normally atrophies during childhood, it is considered the most common site of extra adrenal

What is the role of PET scan?
Positron **E**mission **T**omography is helpful in localizing pheochromocytomas that do not accumulate MIBG

What is the localizing option if a tumor is not seen on CT, MRI, or I-MIBG?
IVC venous sampling for catecholamines (gradient will help localize the tumor)

What is the tumor site if epinephrine is elevated?
Must be adrenal or near the adrenal gland (e.g., organ of Zuckerkandl), because non adrenal tumors lack the capability to methylate norepinephrine to epinephrine

Can histology be used to determine malignancy?
No; only distant metastasis or invasion can determine malignancy

What is the classic pheochromocytoma "rule of 10's"?
10% malignant, **10%** bilateral, **10%** in children, **10%** multiple tumors, **10%** extra-adrenal and 10% familial

What is differential diagnosis of pheochromocytoma ?
Renovascular hypertension , hyperthyroidism and carcinoid syndrome

--How can you remember phenoxybenzamine as a medical treatment of pheochromocytoma?
PHEochromocytoma = **PHE**noxybenzamine (alpha- blockers) → increase in intravascular volume

--What is the surgical treatment?
Tumor resection with early ligation of venous drainage (lower possibility of catecholamine release/crisis by tying off drainage) and minimal manipulation

In the patient with pheochromocytoma, what must be ruled out?
MEN type II (almost all cases are bilateral)

Adrenal Incidentaloma

What is the most common cause of incidentaloma?
Nonfunctioning adenoma (>75% of cases)

What is the differential diagnosis ?
Non-functioning adenoma, aldosteronoma and metastatic disease

---

MCQs.

Which of the following could be found in case of addison disease ?

A-Metabolic acidosis B-Hypernatremia C-Severe hypertension D-Hyperkalemia

What is most common site of extra-adrenal pheochromocytoma ?
A- bladder B-Scrotum C-Organ of Zuckerkandl D-Spinal cord

What is the most common cause of Cushing syndrome ?
A-Iatrogenic B-Cushing disease C-Small cell carcinoma D-Adrenal adenoma

Answers : 1- D , 2-C , 3-A