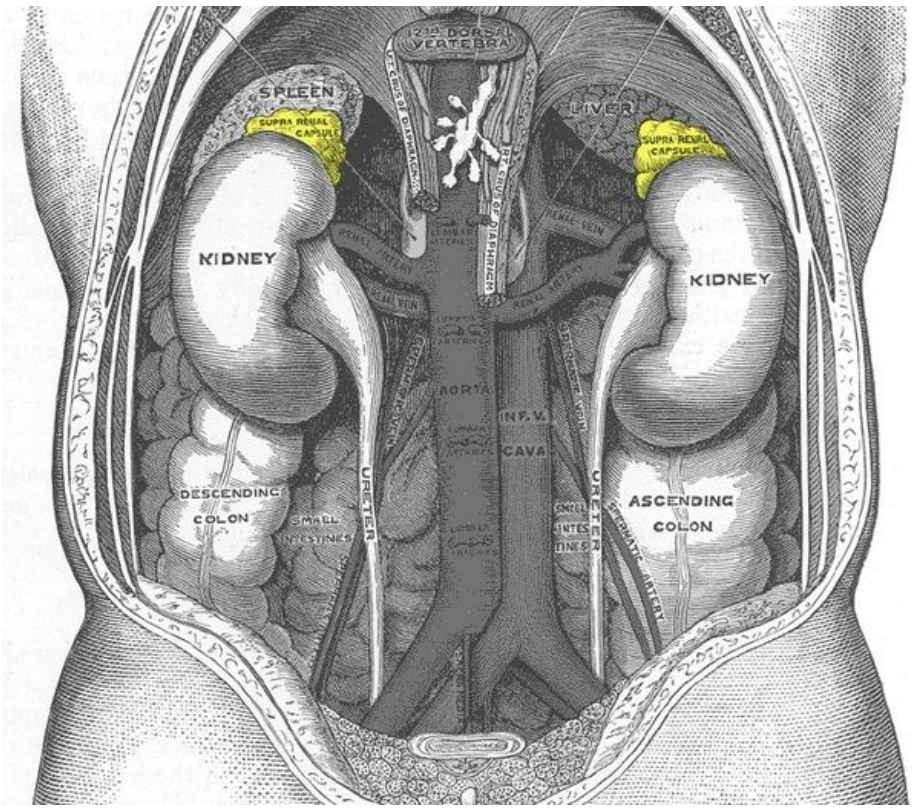
Adrenal gland



Objectives:

- Recognize the variants of hyperadrenalism
- Recognize the variants of hypoadrenalism
- Understand the histopathological features and molecular pathology of both medullary (pheochromocytoma) and adrenocortical neoplasms.

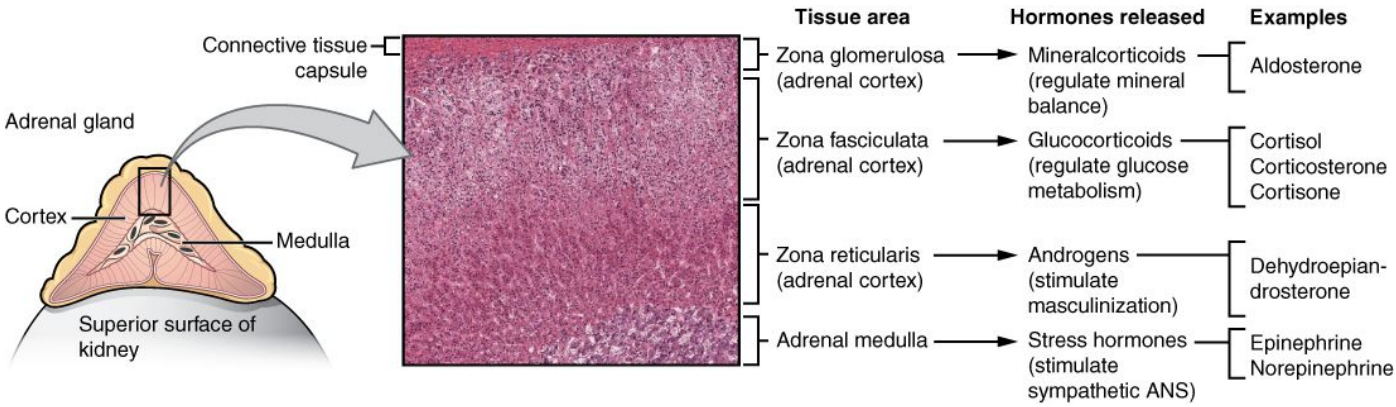
Important note: Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: Pathology Edit

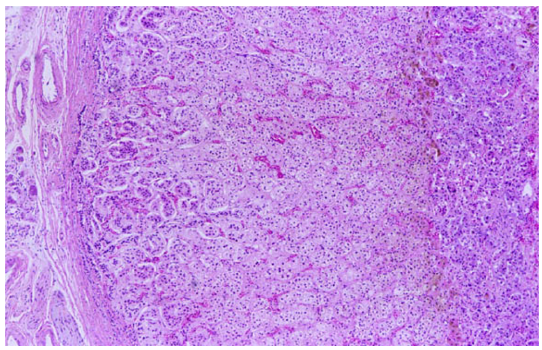
Red: Important
Grey: Extra notes
Green: Dr. Rekaby Notes

Introduction.

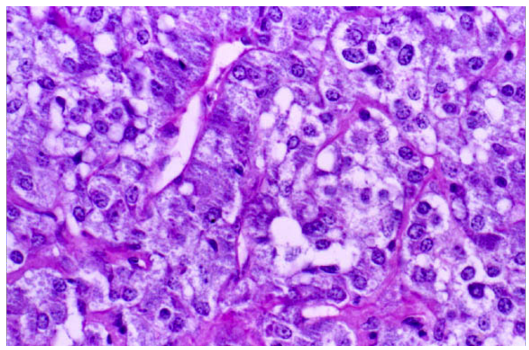
The adrenal glands are paired endocrine organs consisting of two regions, the cortex and medulla, which differ in their development, structure, and function. The cortex consists of three layers of distinct cell types, which secrete different types of steroids.

- Cortex is derived embryologically from **Mesoderm** & medulla is derived from **Neural Ectoderm**.
- Zona fasciculata is the largest layer in cortex → (75%) of total cortex.
- **Chromaffin cells** (pheochromocytes) are neuroendocrine cells found in the medulla. They secrete catecholamines, mainly <u>epinephrine</u>.





Adrenal Cortex



Adrenal Medulla

Adrenocortical Hyperfunction.

There are three distinctive hyperadrenal syndromes:

1. **Cushing syndrome** (↑ cortisol).
2. **Hyperaldosteronism** (↑ aldosterone).
3. **Adrenogenital** or **virilizing syndromes** (↑ androgens).

What is the difference between Cushing syndrome and Cushing's disease??

- **Cushing Syndrome:** is a of Group of symptoms which have certain characteristics and can be caused by different variability of causes e.g.:
- **Cushing Disease** - when you have cushioned features caused by a disease in pituitary causing excess amount of ACTH.

Pathoma video: https://drive.google.com/file/d/0B1EiB7WcXPNYQkE5RXhEYlFUMmM/view

Hypercortisolism (Cushing Syndrome)

Causes of cushing syndrome are divided into two main causes, exogenous & endogenous:

- ***exogenous*:**
  - Most common cause of cushing syndrome is the *administration of exogenous glucocorticoid* ("iatrogenic[1]" Cushing syndrome): "

When do patients need to take exogenous glucocorticoids?

It is used in autoimmune and inflammatory diseases as: Rheumatoid arthritis oncology e.g treatment of Lymphoma & other malignant disease & when it is used with Cytotoxic drugs it enhances their effect.

- ***endogenous*:**

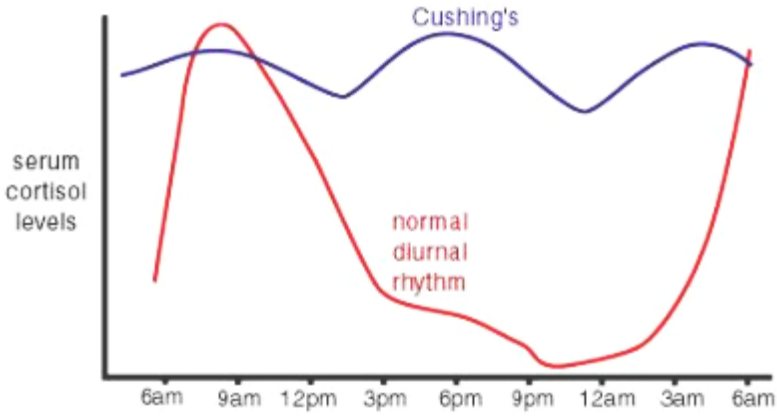
The endogenous causes can, in turn, be divided into those that are ACTH dependent (cortisol needs ACTH to be secreted) and those that are ACTH independent (cortisol is secreted without ACTH stimulation).

Cause	Relative Frequency (%)	Ratio of Females to Males
ACTH-DEPENDENT		
Cushing disease (pituitary adenoma; rarely CRH-dependent pituitary hyperplasia)	70	3.5:1.0
Ectopic corticotropin syndrome (ACTH-secreting pulmonary small-cell carcinoma, bronchial carcinoid) (if removed, person will return back to normal.)	10	1:1
ACTH-INDEPENDENT		
Adrenal adenoma	10	4:1
Adrenal carcinoma	5	1:1
Macronodular hyperplasia (ectopic expression of hormone receptors, including GIPR, LHR, vasopressin and serotonin receptors)	<2	1:1
Primary pigmented nodular adrenal disease (*PRKARIA* and *PDE11* mutations)	<2	1:1
McCune-Albright syndrome (*GNAS* mutations)	<2	1:1

- **Ectopic ACTH syndrome:** there are tumors in the body, especially, carcinoid tumor and oat "small" cell carcinoma of the lungs they secrete proteins that resembles the structure of ACTH, therefore, they stimulate the adrenal glands to secrete Corticosteroids and when this happens the patient may come with Cushing syndrome and he has a carcinoid tumor, sometimes medullary carcinoma can secrete ACTH but RARELY.

[1] of or relating to illness caused by medical examination or treatment.

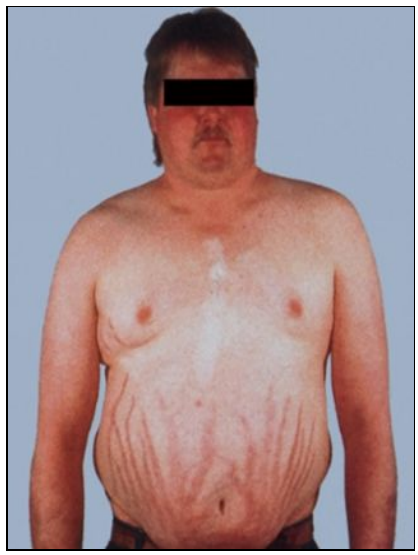
Must know: Secretion of cortisol has a **Diurnal "Circadian" pattern**, so if you want to take a sample from a patient you must follow up the rules, sample should be taken from 8-9 am at its peak "highest" point and then it goes down until 11pm in the evening then we take another sample at night, if it's still high and didn't drop then the patient has a disease of uncontrolled secretion of Cortisol.



Morphology: Could be One of the following abnormalities:

1. **Cortical atrophy:** results from exogenous glucocorticoids.
2. **Diffuse hyperplasia:** individuals with ACTH-dependent Cushing syndrome
3. **Macronodular** (less than 3 cm), or **micronodular** (1-3mm) hyperplasia.
4. **Adenoma** or **carcinoma**. (one of the glands will has the tumor & the other will be atrophied)

Clinical Features of Cushing Syndrome:



1. Obesity or weight gain "Central obesity" 95%
2. Facial plethora[2] 90%
3. Rounded face "Moon-like" 90%
4. Decreased libido "Sex-drive" 90%
5. Thin skin 85%
6. Decrease in linear growth in children 70–80%
7. Menstrual irregularity 80%
8. Hypertension 75%
9. Hirsutism "in females" 75%
10. Depression/emotional liability 70%
11. Easy bruising 65%
12. Glucose intolerance 60%
13. Proximal muscle weakness 60% (for gluconeogenesis) (with thin extremities)
14. Osteopenia or fracture 50%
15. Nephrolithiasis 50
16. immunosuppression → by inhibiting phospholipase A2, histamine IL-2.
17. abdominal straia due to collagen deficiency → rupture of blood vessels

If we are treating a patient with steroids and we want to stop it, you don't stop it suddenly but the dose should be tapered "Gradually" cause there's some kind of dependence, if we don't do it this way the patient might get into **adrenal crisis**, shock, hypotension and severe withdrawal symptoms and flare of original disease.

Diagnosis:

1. **Serum ACTH:**
   - Low → Primary cause (adrenal problem).
   - High → pituitary adenomas and ectopic ACTH. (Secondary cause)
2. **High dose dexamethasone suppression test:**
   - Suppression of ACTH→ pituitary adenomas.
   - Fail of suppression of ACTH→ ectopic ACTH.

[2] احمرار الخدين

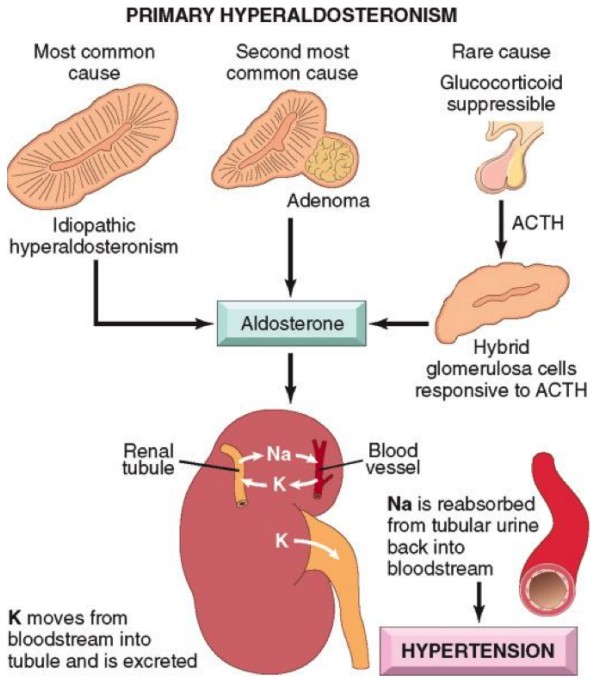
Hyperaldosteronism.

Hyperaldosteronism is a group of conditions characterized by chronic excess in aldosterone secretion. Hyperaldosteronism can be primary or secondary.

	Primary hyperaldosteronism (conn's syndrome)	Secondary hyperaldosteronism
Patho-physiology	Caused by disorder in the adrenal gland itself. There'll be autonomous overproduction of aldosterone, & *suppression of the renin-angiotensin system* and *decrease in plasma renin activity*. (Hyperaldosteronism → sodium reabsorption → water reabsorption → hypertension → inhibition of RAAS system).	Caused by extra-adrenal disorder. **Characterized by:** ● High aldosterone ● High renin
Causes **(from robbins & handouts)**	● Bilateral idiopathic hyperaldosteronism **(most common cause)** → characterized by adrenal gland hyperplasia. ● Aldosterone producing adenoma (most common tumor cause) & Adrenocortical carcinoma. ● Familial hyperaldosteronism (rare).	● Decrease renal perfusion (nephrosclerosis, renal artery stenosis). ● Hypovolemia and edema (CHF, cirrhosis, nephrotic syndrome). ● Pregnancy (estrogen induced increase in renin).

Clinical features:

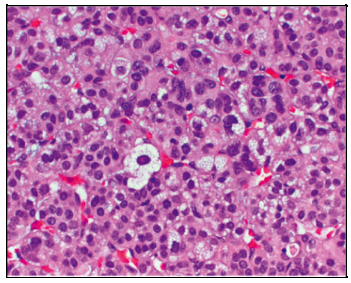
- Hypernatremia (Aldosterone is a hormone that promotes sodium reabsorption)
- **Hypokalemia** results from increased renal potassium and hydrogen excretion → can cause weakness, paraesthesia, visual disturbances and tetany. → metabolic alkalosis.
- The most important feature in hyperaldosteronism is **secondary hypertension** → can lead to left ventricular hypertrophy, stroke and MI.



Aldosterone-producing adenomas, Morphology:

- Solitary.
- Small (<2 cm in diameter).
- Well-circumscribed lesions left > right.
- Thirties and forties.
- **Women** > men.
- Buried within the gland and *do not* produce visible enlargement.
- Bright yellow on cut section.

Investigation: If we want to investigate Hypertension, we must test patient is sitting and standing positions. Because "Renin and aldosterone ratio increases with posture standing because of increased pressure and blood flow to the kidney " if there's no difference between the pressure values the patient is sitting and standing this means there's continuous secretions of aldosterone then we look up for tumor.



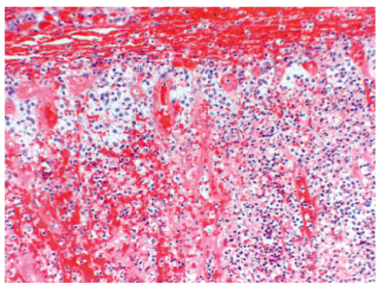
Adrenocortical Insufficiency.

Caused by either **primary adrenal disease** or decreased stimulation of the adrenals due to a deficiency of **ACTH (secondary hypoadrenalism)**.

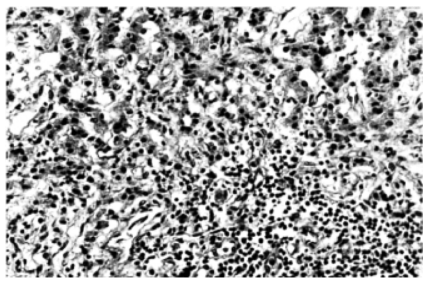
Three patterns of adrenocortical insufficiency:

1. Primary **acute** adrenocortical insufficiency (*adrenal crisis*):
    - Caused by Waterhouse-Friderichsen syndrome, it could be congenital.
2. Primary **chronic** adrenocortical insufficiency (*Addison disease*).
3. **Secondary** adrenocortical insufficiency. (caused by pituitary)

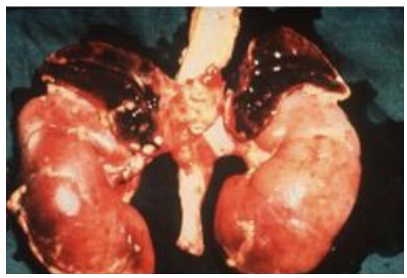
Waterhouse-Friderichsen syndrome: Bilateral Adrenal gland failure due to bleeding into the adrenal glands, induced by septic shock that it in first place caused by Septicemia by severe bacterial infection: Mostly **meningococcus Neisseria meningitidis** (which comes in Al-Hajj), patient has hemorrhagic rash and very high fever.



Necrosis & hemorrhage

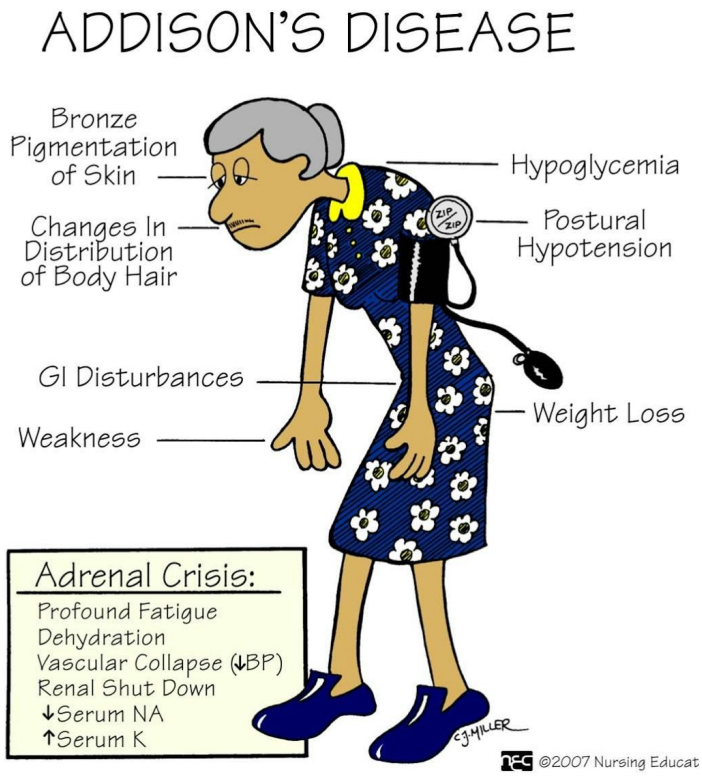


Little residual cortical architecture is discernible (Autoimmune adrenalitis)



Hemorrhagic & shrunken

Acute
Waterhouse-Friderichsen syndrome
Sudden withdrawal of long-term corticosteroid therapy
Stress in patients with underlying chronic adrenal insufficiency
Chronic
Autoimmune adrenalitis (60–70% of cases in developed countries includes APS1 and APS2
Tuberculosis
Acquired immunodeficiency syndrome
Metastatic disease
Systemic amyloidosis
Fungal infections
Hemochromatosis
Sarcoidosis



Addison's disease "Hypoaldosteronism":

Causes: *mnemonic: poor **SAM**, he has Hypoaldosteronism :(*

1- Miliary TB of the adrenal gland	2- Septicemia	3- Autoimmune processes
"still seen in KSA"	"especially Meningococci"	Adrenal gland "especially zona glomerulosa"
	• Happen commonly in kids in low socio-economic countries. • It's called: **"Waterhouse–Friderichsen syndrome (WFS)"**	Is infiltrated by T-lymphocytes causing destruction of zona glomerulosa and patient get symptoms of hypoaldosteronism "Patients may have other autoimmune diseases"

Clinical Presentation:

1. Pigmentation, on the cheeks and forehead, it's usually generalized, and increase around creases and scar tissue "it is thought that the pigmentation is caused by indirect **stimulation of melanocytes** because of the increase of ACTH"[3]
2. Hypotension.
3. Electrolytes imbalance (Hyperkalemia and Hyponatremia).
4. lethargy.
5. Increased fatigability and generalized weakness.

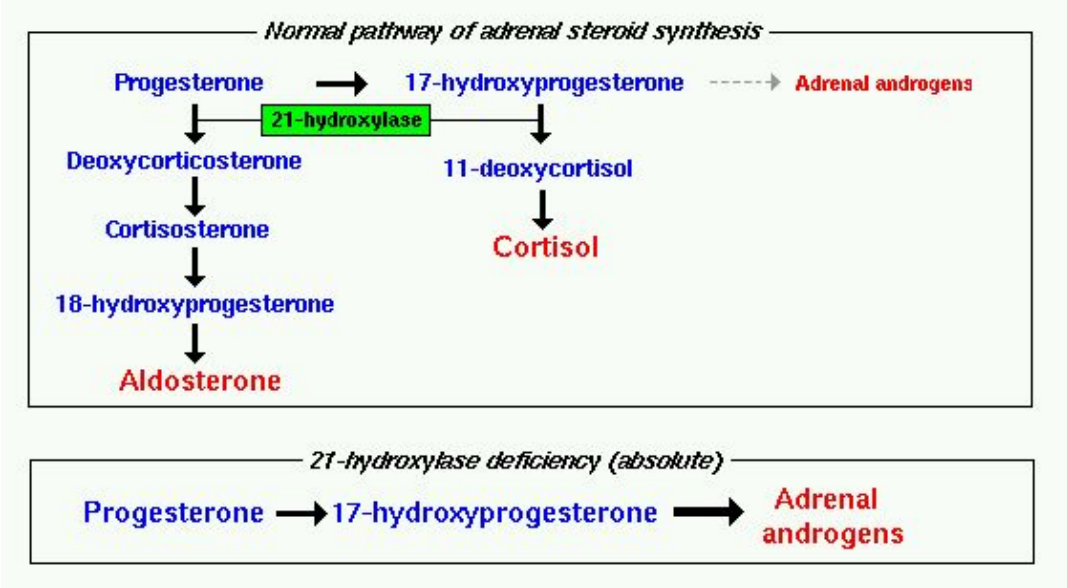
1- Adrenocortical Carcinoma

Difficult to diagnose cause the criteria are not like other malignancies. We rely on **increased weight of adrenal gland**, normally adrenal glands weighs 4g, if someone has cortical nodular hyperplasia it will reach 6 grams, but if there's significant increase in adrenal gland weight "reaching up to 500 g" think about adenocarcinoma "cell atypia and pleomorphism is not really important here for diagnoses of glands" **invasion and increased in size and weight of the adrenal gland are important.**

2- Congenital adrenal hyperplasia (CAH)

- Associated with increased **androgens**, & deficiency of cortisol & aldosterone.
- It can be seen in children, caused by -Deficiency of certain enzymes, especially, **21 or 11 hydroxylase enzyme** (see the picture in next page) "due to abnormal gene" as a result of the deficiency you get accumulation of the substrate of those androgens "estrogen & progesterone" in the patient.
- In kids, manifested as ambiguous genitalia "has both genitals a vagina and a penis".
- If the deficiency is partial "incomplete mutation of the gene" e.g. female has precocious puberty, hirsutism, hoarseness of voice.
- Neonatal screening of those enzymes plays a major rule for improving healthcare.
- Adrenal medullary cells are from neural origin and they resemble the ganglion cells.

[3] **In primary hypoaldosteronism only:** Low Cortisol ⇒ High ACTH synthesis to stimulate adrenals ⇒ melanocyte-stimulating hormone (MSH) and (ACTH) share the same precursor molecule which is pro-opiomelanocortin (POMC) => pigmentations.

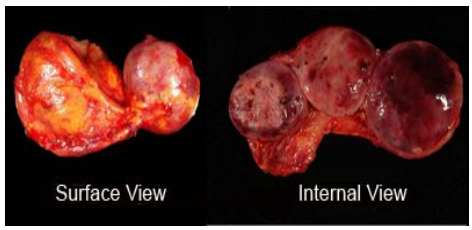


Pheochromocytoma [The 10% tumor].

Tumor of chromaffin cells[4] of the adrenal **medulla**, it can affect the medulla or the paraganglion cells present in the retroperitoneum.

Characteristics:

- Chromaffin cells Secretes catecholamines (Mainly Epinephrine and Norepinephrine) → overproduction produces Hypertension (Which may be intermittent)
- Similar to aldosterone-secreting adenomas, give rise to surgically correctable forms of hypertension.
- 0.1% to 0.3% (fatal)
- Other peptides –Cushing etc…
- Large tumor occupying the adrenal, it could be hemorrhagic pale or pigmented "black".
- Patient present with palpitation, tachycardia, tremor, anxiety, headache, pallor, nausea, sweating, episodic HTN and hypertensive crisis.



Diagnosis: If we suspect pheochromocytoma, we look for the products of the adrenal medulla "Epinephrine & Norepinephrine" and their metabolites (epinephrine → metanephrine, norepinephrine → normetanephrine,and both are broken down to VMA)in the serum (Metanephrine) or urine (24-Hours urine → Metanephrine and Vanillylmandelic acid "VMA"{which will be doubled in presence of this tumor}.
Treatment: Surgical excision.

Rare causes of hypertension:

1. Fibromuscular hyperplasia of the renal artery (Renal artery stenosis) - detected by angiography of renal artery "in young patients"
2. Polycystic kidney disease "adult type" - autosomal recessive, present with abdominal mass
3. Conn's Syndrome "Hyperaldosteronism" - check for electrolytes
4. Pheochromocytoma - check for serum epinephrine & norepinephrine and their metabolite in the urine.

[4] Neural crest-derived cells

"Rule of 10s":

1. 10% of pheochromocytomas arise in association with one of *several familial syndromes* such as **MEN-2A and MEN-2B syndromes** (MEN=Multiple Endocrine Neoplasia), von-Hippel-Lindau, and von-Recklinghausen's neurofibromatosis Type I.
2. 10% of pheochromocytomas are extra-adrenal. **(mostly bladder wall)**
3. 10% of *nonfamilial* adrenal pheochromocytomas are *bilateral*; this percentage may rise to 70% in cases that are associated with familial syndromes.
4. 10% of adrenal pheochromocytomas are biologically *malignant*
5. 10% of adrenal pheochromocytomas in *childhood*
6. 10% located outside of adrenal medulla (e.g. bladder wall or organ of Zuckerkandl[5] at inferior mesenteric artery wall)

Syndrome Components.

- **MEN, type 2A:** Medullary thyroid carcinomas and C-cell hyperplasia, Pheochromocytomas and adrenal medullary hyperplasia, Parathyroid hyperplasia.
- **MEN, type 2B:** Medullary thyroid carcinomas and C-cell hyperplasia, Pheochromocytomas and adrenal medullary hyperplasia, Mucosal neuromas, Marfanoid features.

Marfanoid features (group of symptoms resembling marfan syndrome), include: Long limbs, arms span exceeds the height of the individual, crowded oral maxilla, sometimes with a high arch in the palate, arachnodactyly[6] (Spider fingers), and hypermobility of joints.

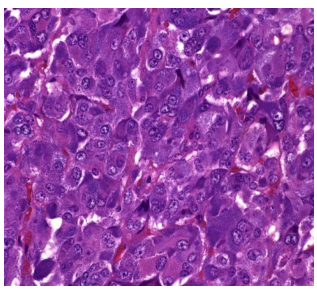
Von Hippel-Lindau.

Inherited disorder characterized by the formation of tumors and fluid-filled sacs (cysts) in many different parts of the body. **The VHL gene is located on the short (p) arm of chromosome 3**.

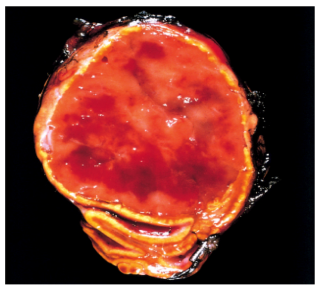
- Renal, hepatic, pancreatic, and epididymal cysts, Renal cell carcinomas, Angiomatosis, Cerebellar, hemangioblastomas, Pheochromocytoma.

Von Recklinghausen's Neurofibromatosis Type I.

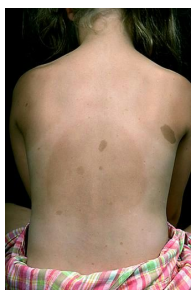
- Café au lait skin spots, Schwannomas, meningiomas, gliomas, Pheochromocytoma.
- Small to large hemorrhagic.
- Well demarcated.
- Polygonal to spindle shaped (chromaffin, chief cells).
- Sustentacular small cells.
- Together, Zellballen nests (polygonal in the center surrounded by sustentacular cells)



Sustentacular small cells



Pheochromocytoma



Café au lait skin spots

[5] The **organ of Zuckerkandl** is a chromaffin body derived from neural crest located at the bifurcation of the aorta or at the origin of the inferior mesenteric artery. It can be the source of pheochromocytoma or paraganglioma.

[6] a condition in which the fingers and toes are abnormally long and slender, in comparison to the palm of the hand and arch of the foot

Summary.

	Disorder	Clinical features	Causes	morphology	Diagnosis
	Adrenal cortex				
HYPERFUNCTION	**Cushing syndrome**	- Moon face. - Buffalo hump. - Hypertension. - Central obesity. - Osteoporosis. - Hirsutism. - Abdominal striae. - Hyperglycaemia - Plethora.	- Exogenous glucocorticoid "iatrogenic". - ACTH-secreting pituitary adenoma. - Ectopic ACTH secretion (e.g. Small cell carcinoma of the lung). - Primary adrenal neoplasm.	1. **Cortical atrophy:** results from exogenous glucocorticoids 2. **Diffuse hyperplasia:** individuals with ACTH-dependent Cushing syndrome.	**Serum ACTH:** - Low → adrenal neoplasms. - High → pituitary adenomas and ectopic ACTH. **High dose dexamethasone suppression test:** - Low → pituitary adenomas. - High → ectopic ACTH.
	Hyper-aldosteronism "Conn syndrome"	- Hypertension. - Hypokalemia. - Hypernatremia. - Metabolic alkalosis. - Muscular weakness.	- Adenoma of the zona glomerulosa. - Bilateral adrenal hyperplasia (rare).	- Solitary, Small. - well circumscribed lesions. - No visible enlargement. - Bright yellow on cut section.	↑ Aldosterone. ↓ Renin. (if the renin levels are raised, then the hyperaldosteronism is secondary)
HYPOFUNCTION	**Acute adreno-cortical insufficiency** "adrenal crisis"	- Hypovolaemic shock. - Hypoglycaemia due to lack of glucocorticoids.	- Rapid steroid treatment withdrawal. - Destruction of the adrenal glands by hemorrhage , which can be complicate bacterial (e.g.meningococcal),Waterhouse-Friderichsen syndrome.	**Waterhouse-Friderichsen syndrome:** Gross: hemorrhage and shrinkage. Microscopically: little residual cortical architecture is discernible.	--
	Chronic adreno-cortical insufficiency "Addison disease"	- Weakness. - Weight loss. - Hypotension - Dehydration. - Hyper-pigmentation. - Hyponatraemia - Hyperkalaemia - Hypoglycaemia.	Autoimmune destruction of the adrenal cortex	--	**Synacthen tests:** - ↑ Cortisol levels → normal. - ↓ Cortisol levels → primary or secondary adrenocortical insufficiency. - Long Synacthen test should then be performed.

	Secondary adreno-cortical insufficiency		- Primary lesions of the pituitary. - Hypothalamic-pituitary-adrenal suppression as a result of long-term steroid therapy	--	Long Synacthen test
	Adrenal medulla				
T U M O R	**Pheochromocytoma**	- Young hypertensive patient. - Palpitations. - Pallor.	Associated with familial syndromes such as: - MEN syndrome. - Von-Hippel-Lindau disease. - Von Recklinghausen's disease.	- Small to large hemorrhagic - Well demarcate - Polygonal to spindle shaped (**chromaffin**, chief cells). - Sustentacular small cells. - Zellballen nests.	Urinary excretion of the catecholamine metabolite vanillylmandelic acid (VMA). Which is at least doubled.

MCQ's.

1) A 19-year-old previously healthy woman has had a mild pharyngitis followed by a high fever over the past 24 hours. When seen in the emergency room, her skin now shows extensive areas of purpura. Vital signs include temperature 39°C, pulse rate 102/minute, respiratory rate 21/minute, and blood pressure 80/55 mm Hg. Laboratory studies show a serum sodium of 115 mmol/L, potassium 5.3 mmol/L, chloride 92 mmol/L, CO2 22 mmol/L, glucose 42 mg/dL, and creatinine 1.1 mg/dL. Which of the following is the most likely diagnosis?

A. Idiopathic adrenalitis
B. Disseminated tuberculosis
C. Reactive systemic amyloidosis
D. Sheehan syndrome
E. Meningococcemia
F. Hemochromatosis

2) A 55-year-old woman has had a 4 kg weight loss over the past 3 months. She exhibits decreased mentation over the past 10 days. On physical examination she is afebrile and hypotensive. Bilateral papilledema is noted. A head CT scan shows marked diffuse cerebral edema with effacement of the lateral ventricles. Laboratory studies show a sodium of 108 mmol/L, potassium 4.0 mmol/L, chloride 83 mmol/L, CO2 14 mmol/L, glucose 82 mg/dL, and creatinine 0.5 mg/dL. Which of the following is most likely to cause these findings?

A. Small cell lung carcinoma
B. Blunt head trauma
C. Hypothalamic glioma
D. Meningitis
E. Pituitary macroadenoma

3) A 48-year-old woman has experienced constant back pain exacerbated by movement over the past month. She reports increasing weakness over the past 3 months. On physical examination her blood pressure is 165/110 mm Hg. She is overweight, with a BMI of 28. A radiograph of the spine reveals a compressed fracture at T10. Laboratory findings include a serum glucose of 155 mg/dL. Which of the following pathologic lesions is most likely to explain her findings?

A) Adrenal cortical carcinoma
B) Anaplastic thyroid carcinoma
C) Empty sella syndrome
D) Pheochromocytoma
E) Multinodular goiter

4) A 33-year-old woman has noted a weight gain of 6 kg over the past year. She has normal menstrual periods. On physical examination her blood pressure is 170/105 mm Hg. Her skin shows marked plethora. Abdominal striae are present. A serum electrolyte panel shows sodium 141 mmol/L, potassium 4.4 mmol/L, chloride 100 mmol/L, CO2 25 mmol/L, glucose 181 mg/dL, and creatinine 1.0 mg/dL. Which of the following radiologic findings would you most expect to be present in this patient?

A 2 cm right adrenal mass with abdominal CT scan
B 4 cm mass at aortic bifurcation with MR imaging
C Multiple pulmonary nodules on chest radiograph
D 10 cm cystic right ovarian lesion by abdominal ultrasound
E 2 cm 'hot' thyroid nodule with Tc99 scintigraphic scan

5) A 50-year-old man has episodic headaches for 3 months. On physical examination his blood pressure is 185/110 mm Hg, with no other remarkable findings. Laboratory studies show sodium 145 mmol/L, potassium 4.3 mmol/L, chloride 103 mmol/L, C02 26 mmol/L, glucose 91 mg/dL, and creatinine 1.3 mg/dL. An abdominal CT scan shows a 7 cm left adrenal mass. During surgery, as the left adrenal gland is removed, there a marked rise in blood pressure. Which of the following laboratory test findings most likely explains his findings?

A Decreased serum cortisol
B Decreased urinary homovanillic acid
C Increased serum ACTH
D Increased urinary free catecholamines
E Elevated serum ANCA

6)A 56-year-old woman has had diffuse, dull, constant abdominal pain for the past 2 months. On physical examination no abnormal findings are noted. An abdominal CT scan shows a 3 cm right adrenal mass. The right adrenal is excised and on microscopic examination the mass is composed of cells resembling adrenal cortex. Which of the following features is the most reliable indicator that this mass is malignant?

A Cellular atypia
B Presence of mitoses
C Invasion
D Size of the mass
E Cellular necrosis

7) A 45-year-old man has a 4 month history of nonfocal, generalized headaches. On physical examination he is found to have a blood pressure of 170/110 mm Hg. Laboratory studies show a serum sodium of 146 mmol/L, potassium 2.3 mmol/L, chloride 103 mmol/L, CO2 27 mmol/L, glucose 82 mg/dL, and creatinine 1.2 mg/dL. His plasma renin activity is 0.1

ng/mL/hr and his serum aldosterone 65 ng/mL. Which of the following is the most likely cause for his findings?

A 21-hydroxylase enzyme deficiency
B Adrenal cortical adenoma
C Pituitary adenoma
D Exogenous corticosteroid administration
E Renal cell carcinoma

8) A 45-year-old woman with severe rheumatoid arthritis has been on chronic corticosteroid therapy for the past 15 years. She is admitted for an orthopedic procedure to correct joint deformity from her disease. She continues to receive her regular dosage of 5 mg of prednisone per day. Three days postoperatively, she develops an aspiration pneumonia with *Klebsiella pneumoniae* cultured from sputum. Five days following the surgery, she becomes obtunded. Laboratory findings at that time include: sodium 105 mmol/L, potassium 5.4 mmol/L, chloride 87 mmol/L, CO2 16 mmol/L, glucose 40 mg/dL, and creatinine 1.1 mg/dL. Which of the following complications is most likely to have occurred in this patient?
A Anterior pituitary necrosis
B Waterhouse-Friderichsen syndrome
C Acute Addisonian crisis
D Conn syndrome
E 21-hydroxylase deficiency

9) A 52-year-old man has weight of 4 kg over the past 6 months, along with bruises on his skin with even minor trauma and back pain. He has smoked 2 packs a cigarettes per day for 35 years. On physical examination he has obesity in a truncal distribution, plethora, and a blood pressure of 160/110 mm Hg. A radiograph of the spine reveals a compressed fracture of T11. Which of the following neoplasms is he most likely to have?
A Pheochromocytoma of bladder
B Follicular carcinoma of thyroid
C Osteosarcoma of femur
D Small cell anaplastic carcinoma of lung
E Neuroendocrine carcinoma of pancreas

10) A clinical study is performed involving subjects who developed Addision disease. They were recorded to have laboratory studies with hyponatremia, hyperkalemia, hypoglycemia, and decreased plasma cortisol. They became hypotensive. In some subjects, this disease had an acute onset over less than 2 days' time. Which of the following conditions is most likely to produce this acute course?
A Waterhouse-Friderichsen syndrome
B Metastatic small cell anaplastic carcinoma
C Disseminated *Mycobacterium tuberculosis infection*
D Reactive systemic amyloidosis
E Blunt force abdominal trauma

11) A 42-year-old man has enlargement of his neck for the past 7 months. He is concerned, because a sister and maternal aunt had thyroid cancer. On physical examination, his thyroid is palpably nodular but nontender. A fine needle aspiration biopsy is performed and cytologic examination shows cells present consistent with a neoplasm. He undergoes total thyroidectomy. Sectioning the resected thyroid reveals four distinct tumor masses from 0.5 to 3 cm in size. These masses are solid and firm, with a tan cut surface. On microscopic examination an immunostain for calcitonin is positive in the nests of dark

blue cells of these masses. He is at greatest risk for developing which of the following neoplasms in the future?
A Astrocytoma
B Pheochromocytoma
C Angiosarcoma
D Gastrinoma
E Renal cell carcinoma

12) A 5-month-old female infant was the product of an uncomplicated pregnancy and was born at term. However, the baby has failure to thrive. On physical examination there is clitoral hypertrophy and poor skin turgor. The baby appears neurologically normal. Laboratory studies show serum sodium 116 mmol/L, potassium 6.2 mmol/L, chloride 83 mmol/L, and CO2 22 mmol/L. There is no history of diarrhea or vomiting. Which of the following inborn errors of metabolism is this infant most likely to have?
A 21-hydroxylase deficiency
B Phenylalanine transferase deficiency
C Galactose-1-uridyl transferase deficiency
D Glucose-6-phosphatase deficiency
E Iodine peroxidase deficiency

ANSWERS: 1-E 2-A 3-A 4-A 5-D 6-C 7-B 8-C 9-D 10-A 11-B 12-A

For any suggestions or questions please don't hesitate to contact us on: Pathology434@gmail.com
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