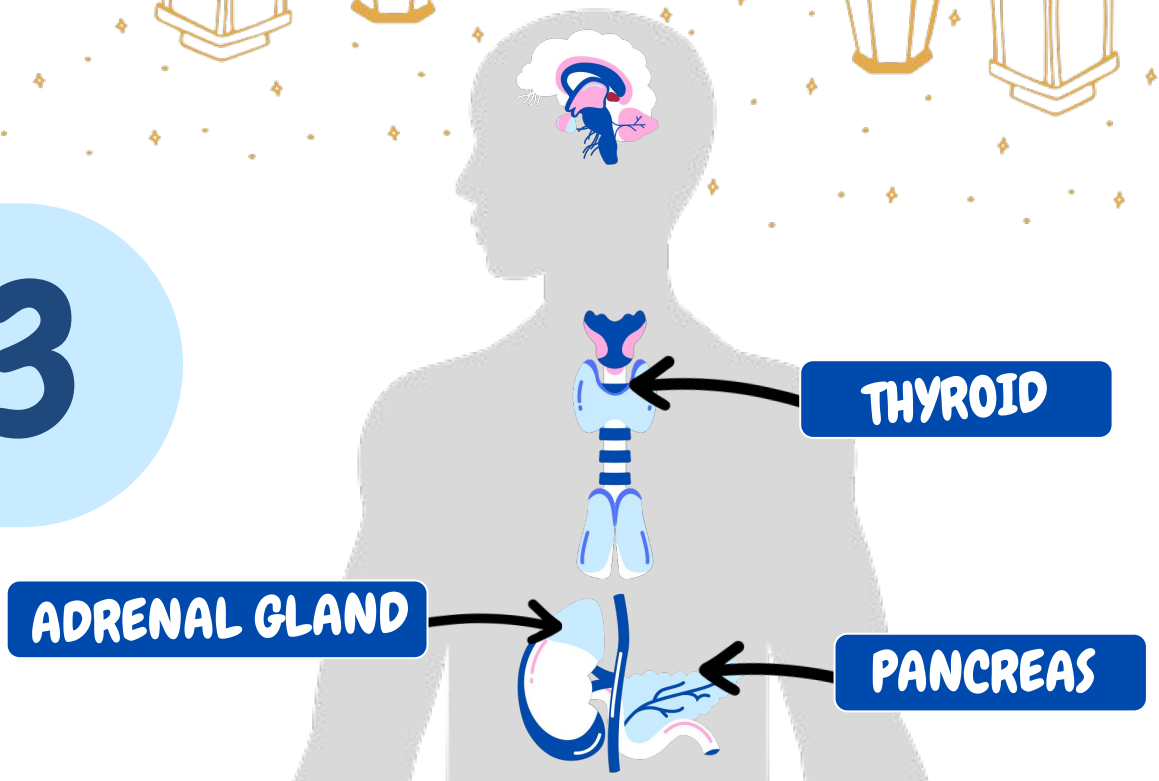
L3



Adrenal gland

Editing File

Color index :
Main text (black)
Female Slides (Pink)
Male Slides (Blue)
Important (Red)
Dr's note (Green)
Extra Info (Grey)

Objectives

- Understand the structure and function of adrenal glands.
- Know the disorders that can cause hypo or hyper function of the adrenal cortex.
- Understand the histopathological features of both medullary (pheochromocytoma) and adrenocortical neoplasms.

THIS LECTURE WAS PRESENTED BY DR.AMANY FATHADDIN & DR.MOHAMMED ALSWAYYED

لا تدع المذاكره تلهيك عن صلاة التراويح و قراءة القران الكريم

IF YOU WANT TO READ THE LECTURE FROM ROBBINS

IF YOU WANT TO READ THE LECTURE FROM FIRST AID

IF YOU WANT TO READ OSMOSIS SUMMARY

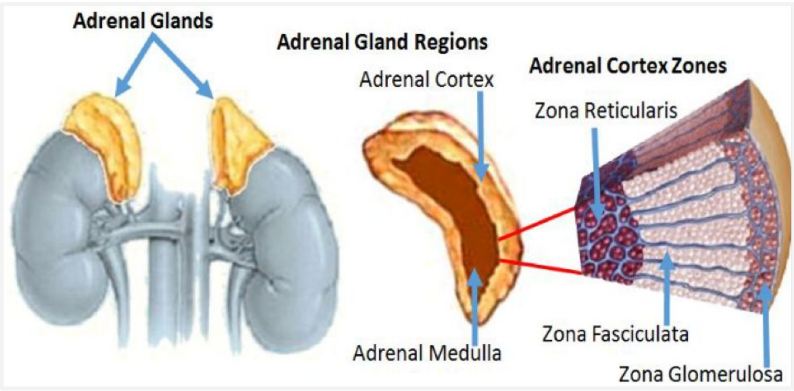
IF YOU WANT TO WATCH OSMOSIS ON CUSHING SYNDROM

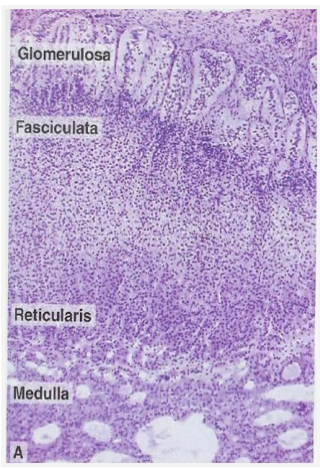
Introduction

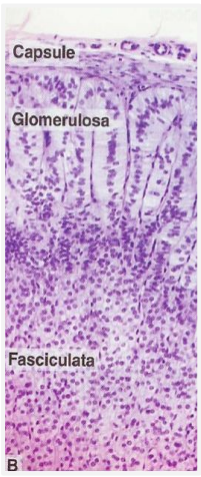
Anatomy of Adrenal gland

The adrenal glands are paired endocrine organs made of cortex and medulla

Cortex	**Zona glomerulosa** Which secretes: Mineralocorticoids (aldosterone)
	zona fasciculata Intervening is the broad zona fasciculata (75%) of the total cortex. Which secretes Glucocorticoids: principally cortisol
	Zona reticularis abuts the medulla. Which secretes:Sex steroids (estrogens and androgens)
Medulla	**adrenal medulla** is composed of chroman cells, which synthesize and secrete catecholamines, mainly epinephrine.





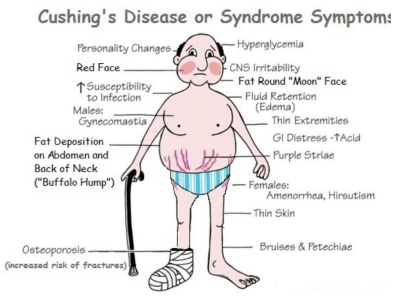


Hyperadrenalism

Overview

There are three distinctive hyperadrenal clinical symptom, each caused by abnormal production of one or more of the hormones produced by the three layers of cortex:

- Cushing syndrome characterized by an excess of cortisol.
- Adrenogenital or virilizing syndrome:caused by an excess of androgen.
- Hyperaldosteronism.



Cushing's syndrome

IMPORTANT

1. Hypercortisolism broadly divided into exogenous and endogenous causes
2. The vast majority of cases of Cushing syndrome are the result of the administration of exogenous glucocorticoids (“**iatrogenic**” Cushing syndrome).
3. The endogenous causes can:
   1-ACTH dependent
   2 ACTH independent

Cushing syndrome

Causes of cushing syndrome

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

Cushing syndrome

1. Cushing's disease

IMPORTANT

Accounts for approximately 70% of cases of spontaneous, endogenous Cushing syndrome.
four times higher among women than among men

In the vast majority of cases, the **pituitary gland** contains an ACTH- producing microadenoma that does not produce mass effects in the brain

The adrenal glands in patients with Cushing disease show variable degrees of bilateral nodular cortical hyperplasia , secondary to the elevated levels of ACTH ("ACTH-dependent") Cushing syndrome

2. Ectopic ACTH

Secretion of ectopic ACTH by non-pituitary tumors accounts for about 10% of cases of Cushing syndrome

In many instances the responsible tumor is a small-cell carcinoma of the lung, although other neoplasms, including carcinoids, medullary carcinomas of the thyroid, and PanNETs, have been associated with the syndrome

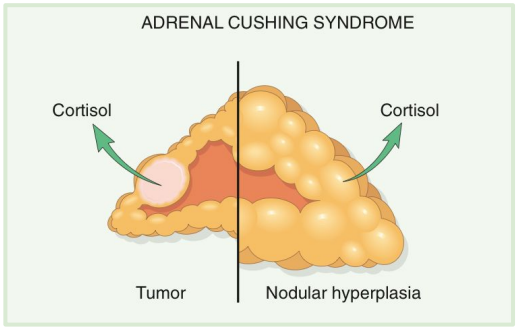
As in the pituitary variant, the adrenal glands undergo bilateral cortical hyperplasia secondary to elevated ACTH

Cushing syndrome

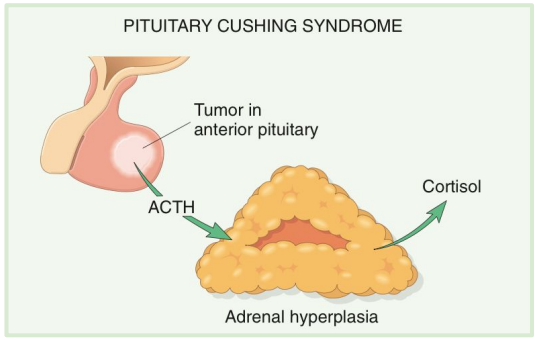
3. Neoplasm and Hyperplasia:

Primary adrenal neoplasms, such as adrenal adenoma and carcinoma, and rarely, primary cortical hyperplasia, are responsible for about 15% to 20% of cases of endogenous Cushing syndrome, also designated ACTH-independent Cushing

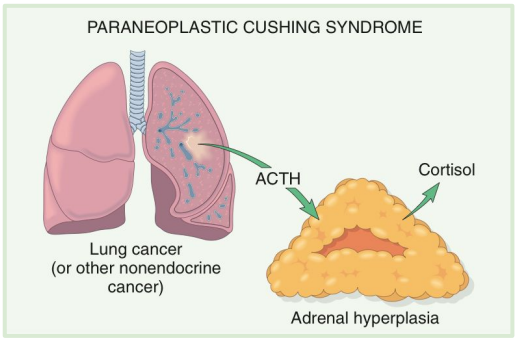
Primary cortical hyperplasia of the adrenal cortices is a rare cause of Cushing syndrome. There are two variants of this entity; the this presents as macro nodules of varying sizes (typically less than 3 cm in diameter) and the second as micronodules (1–3 mm).



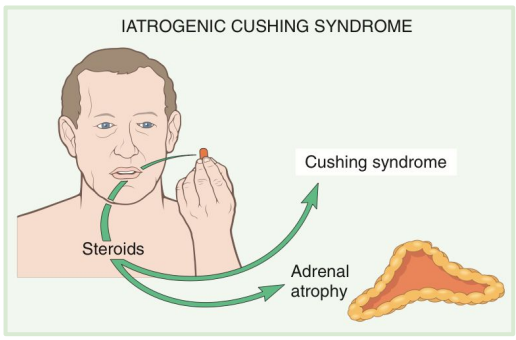
1. Primary neoplasm in the adrenal gland → secretes cortisol → inhibits ACTH secretion → no hyperplasia of the adjacent adrenal gland. 2. Primary nodular hyperplasia of the cortex with the secretion of cortisol



Other common situation: adenoma of pituitary secreting ACTH → continuous stimulation of the adrenal gland → adrenal hyperplasia and increased cortisol



Ectopic secretion (lung cancer that will secrete ACTH)



Administration of cortisone → excessive cortisol level → -ve feedback on the ACTH cells → low ACTH → no stimulation of adrenal gland → adrenal atrophy

Cushing's syndrome

Investigations

1

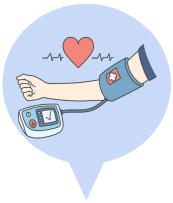
Pituitary and ectopic Cushing syndrome, ACTH levels are elevated and the urine is characterized by high levels of excreted corticosteroids.

2

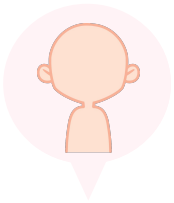
In contrast, ACTH levels are low in Cushing syndrome secondary to adrenal tumors.

Clinical features

IMPORTANT

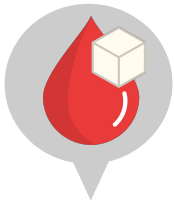


Hypertension and weight gain

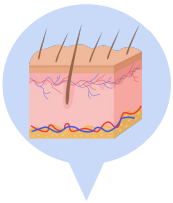


Truncal obesity, "moon face" and accumulation of fat in the posterior neck and back ('buffalo hump")

Proximal limb weakness (atrophy of type 2 fibers)

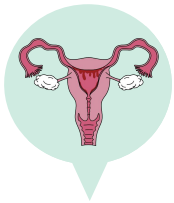


Glucocorticoids induce gluconeogenesis and inhibit uptake of glucose by cells, with resultant hyperglycemia, glycosuria, and polydipsia, mimicking diabetes mellitus

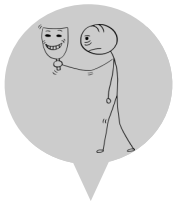


The skin is thin, fragile, and easily bruised; cutaneous striae

Osteoporosis, with consequent increased susceptibility to fractures



Hirsutism and menstrual abnormalities & Increased risk for a variety of infections

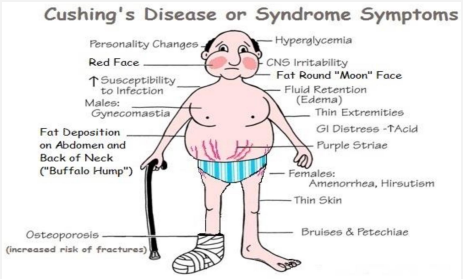


Mental disturbances, including mood swings, depression and frank psychoses

Adrenocortical hyperfunction

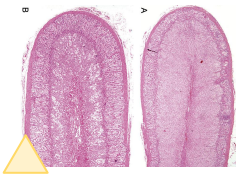
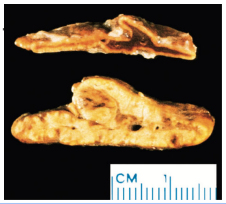
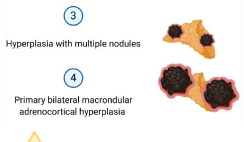
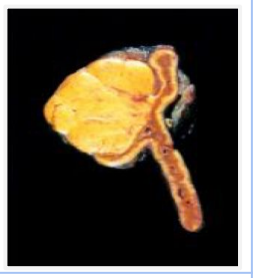
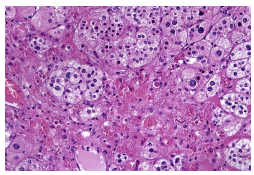
Clinical features

Extra-adrenal Cushing syndrome caused by pituitary or ectopic ACTH secretion usually is associated with increased skin pigmentation secondary to melanocyte-stimulating activity in the ACTH precursor molecule.



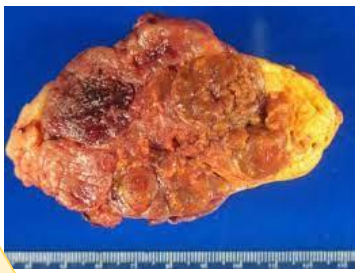
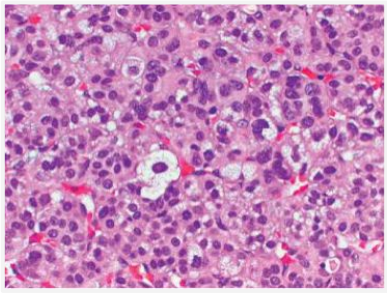
Morphology

Extra pic =

Disorder	Description		Picture
Exogenous cause	**Cortical Atrophy:** results from exogenous glucocorticoids. As the body is dependent on exogenous source, the adrenal glands minimize their function.		
ACTH-dependent	**Diffuse hyperplasia:** individuals with ACTH-dependent Cushing syndrome		
Primary cortical hyperplasia	Cortex replacement by macronodules or 1-3mm darkly pigmented micronodules (pigment is believed to be lipofuscin, which is a wear-and-tear pigment.		
Adenoma	Grossly	• Adrenocortical adenomas are yellow tumors surrounded by thin or well-developed capsules,and most weigh less than 30 g. • The adenoma is distinguished from nodular hyperplasia by its solitary, circumscribed nature	
	Microscopically	• They are composed of cells similar to those encountered in the normal zona fasciculata. • Neoplastic cells are vacuolated because of the presence of intracytoplasmic lipid. • There is mild nuclear pleomorphism. Mitotic activity and necrosis are not seen.	

Adrenocortical hyperfunction

Morphology

Disorder	Description		Picture
Carcinoma	Carcinoma are non encapsulated masses frequently exceeding 200 to 300g in wight having all of the anaplastic characteristics of cancer.		
	Grossly	With functioning tumors, both benign and malignant, the adjacent adrenal cortex and that of the contralateral adrenal gland are atrophic, as a result of suppression of endogenous ACTH by high cortisol levels	
	Microscopically	The pituitary in Cushing syndrome shows changes that vary with different causes. The most common alteration, resulting from high levels of endogenous or exogenous glucocorticoids, is termed **Crooke hyaline change**. In this condition, the normal granula, basophilic cytoplasm of the ACTH-producing cells in the anterior pituitary is replaced by a new homogeneous, lightly basophilic material. This alteration is the result of the accumulation of intermediate keratin filaments in the cytoplasm	 Neoplastic cells are vacuolated because of the presence of intracytoplasmic lipids. There is mild nuclear pleomorphism. Mitotic activity and necrosis aren't seen.
Functional adenomas or carcinomas of the adrenal cortex are not morphologically distinct from non-functioning adrenal neoplasms			

Clinical Note

Exogenous or iatrogenic hypercortisolism is the most common cause. The initial diagnostic approach is to establish hypercortisolism via urinary and salivary cortisol tests along with low-dose dexamethasone suppression test. Once the elevated cortisol levels are confirmed, the etiology is determined based on ACTH levels, confirmatory biochemical tests, and subsequent imaging studies.

Hyperaldosteronism

Osmosis Vid

Hyperaldosteronism
Chronic excess aldosterone secretion

Primary aldosteronism	Secondary hyperaldosteronism
(autonomous overproduction of aldosterone) with resultant suppression of the renin-angiotensin system and decreased plasma renin activity.	in contrast, aldosterone release occurs in response to activation of the renin-angiotensin system: - Decreased renal perfusion - Arterial hypovolemia - Pregnancy

Causes of Primary aldosteronism

Bilateral idiopathic hyperaldosteronism	
characterized by bilateral nodular hyperplasia of the adrenal glands. This is the most common underlying cause of primary hyperaldosteronism, accounting for about 60% of cases. The pathogenesis is unclear. Some have mutations in the KCNJ5 gene. (Most common form of primary hyperaldosteronism)	
Adrenocortical neoplasm	**Rarely, familial hyperaldosteronism**
either an aldosterone-producing adenoma or, rarely, an adrenocortical carcinoma. In approximately 35% of cases, primary hyperaldosteronism is caused by a solitary aldosterone-secreting adenoma, a condition referred to as Conn syndrome	may result from a genetic defect that leads to overactivity of the aldosterone synthase gene, CYP11B2

Hyperaldosteronism

Clinical features

IMPORTANT

01

Hypertension

Primary hyperaldosteronism may be the most common cause of secondary hypertension (i.e., hypertension secondary to an identifiable cause)
(Secondary hypertension can be corrected surgically. In this case, removal of the adenoma will correct the hypertension)

02

Hypernatremia

Aldosterone promotes sodium reabsorption

03

Hypokalemia

results from renal potassium wasting and, when present, can cause a variety of neuromuscular manifestations, including weakness, paresthesias, visual disturbances.

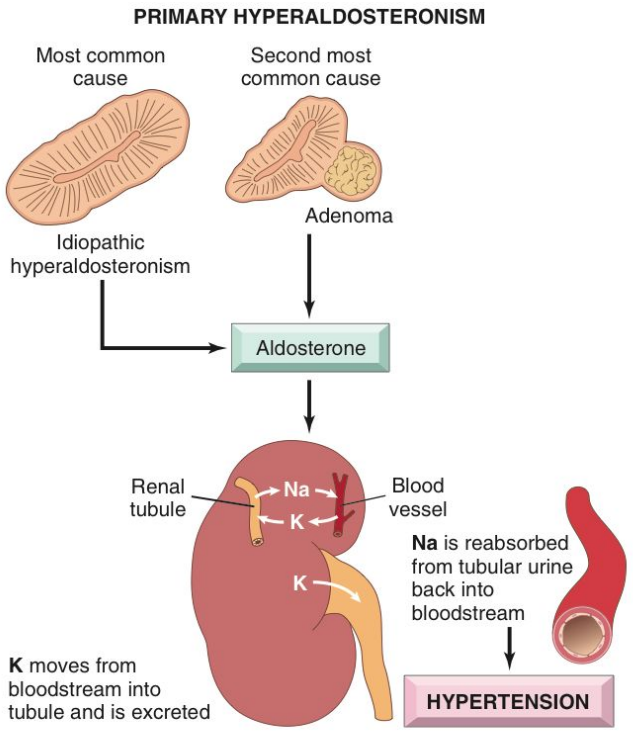
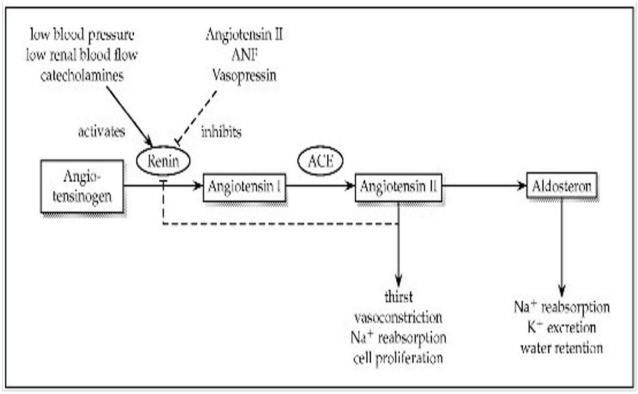


Fig. 20.39 The major causes of primary hyperaldosteronism and its principal effects on the kidney.



Deep Focus Question

What is NOT associated with primary hyperaldosteronism?

A. Hyponatremia
B. Metabolic alkalosis
C. Hypertension
D. Hypokalemia

Answer: A

Hyperaldosteronism

Morphology

Aldosterone-producing adenomas	Bilateral idiopathic hyperplasia
almost always solitary, small (<2 cm in diameter), well-circumscribed lesions. They are bright yellow on cut section and are composed of lipid-laden cortical cells.	is marked by diffuse or focal hyperplasia of cells resembling those of the normal zona glomerulosa.
The cells tend to be uniform in size and shape; occasionally there is some nuclear and cellular pleomorphism.	
A characteristic feature of aldosterone-producing adenomas is the presence of eosinophilic, laminated cytoplasmic inclusions, known as **spironolactone bodies.**	
They do not usually suppress ACTH secretion. Therefore, the adjacent adrenal cortex and that of the contralateral gland are not atrophic.	

Clinical Note

Congenital adrenal hyperplasia (CAH) consists of a group of autosomal recessive disorders that cause a deficiency of an enzyme needed in cortisol, aldosterone, and androgen synthesis. The most common subform of CAH is 21-hydroxylase deficiency, followed by 11β-hydroxylase deficiency. Clinical manifestations depend on the specific enzyme affected. Notably, CAH is the most common cause of ambiguous genitalia in genotypic female individuals. All forms of CAH cause low levels of cortisol, high levels of adrenocorticotropic hormone (ACTH), and adrenal hyperplasia. Laboratory studies help confirm the diagnosis. Lifelong glucocorticoid replacement is needed, and surgical correction of ambiguous genitalia is often performed.

Hypersecretion of sex steroids

The adrenal cortex can secrete excess androgens in either of two settings:

- adrenocortical **neoplasms** (usually virilizing carcinomas)
- **congenital adrenal hyperplasia** (CAH)

1. CAH consists of a group of autosomal recessive disorders characterized by defects in steroid biosynthesis, usually cortisol; the most common subtype is caused by **deficiency** of the **enzyme 21-hydroxylase.**

2. Reduction in cortisol production causes a compensatory increase in ACTH secretion, which in turn stimulates androgen production. So, Cortisol deficiency places persons with CAH at risk for acute adrenal insufficiency

3. Androgens have virilizing effects, including masculinization in females (ambiguous genitalia, oligomenorrhea, hirsutism), precocious puberty in males.

Deep Focus Question

Which of the following statements about congenital adrenal hyperplasia (CAH) is false?

A. CAH results in ambiguous genitalia in male infants.
B. CAH is caused by excessive conversion of cholesterol to sex hormones.
C. CAH may result in ambiguous genitalia in female infants.
D. CAH may result in precocious puberty in both males and females.
E. CAH results from mutations in various genes, regulating hormone formation in the adrenal cortex.

Answer: A

Adrenocortical insufficiency

Osmosis Vid

Adrenocortical insufficiency, or hypofunction, may be caused by either:

1. **Primary** hypoadrenalism (primary adrenal disease):
   - Acute (crisis)
   - chronic (**Addison disease**)
2. **Secondary** hypoadrenalism: Decreased stimulation of the adrenals resulting from a deficiency of ACTH

Table 20.7 Causes of Adrenal Insufficiency

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 (*AIRE* mutations) and APS2 (polygenic)
Infections Tuberculosis Acquired immunodeficiency syndrome Fungal infections
Hemochromatosis
Sarcoidosis
Systemic amyloidosis
Metastatic disease

APS1, APS2, Autoimmune polyendocrine syndrome types 1 and 2; *AIRE,* autoimmune regulator gene.

Deep Focus Question

What is true about CAH?

A. Severity depends on treatment onset.
B. It is an acquired disorder.
C. It is caused by the overproduction of cells in the adrenal gland.
D. It affects aldosterone production but not cortisol.

Answer: C

Deep Focus Question

What is the preferred prenatal treatment for fetuses with two parents who are genetic carriers for CAH?

A. Dexamethasone
B. Estrogen
C. Aldosterone
D. Testosterone
E. Sodium supplementation

Answer: A

Adrenocortical insufficiency
"Waterhouse-Friderichsen syndrome"

Definition

Is a Bilateral adrenal hemorrhage in an infant with overwhelming sepsis, resulting in acute adrenal insufficiency.

Causes

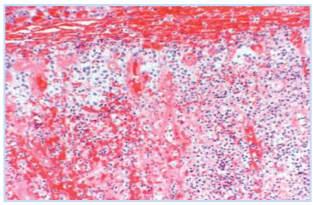
It's is classically associated with **Neisseria meningitidis** septicemia but can also be caused by other organisms, including Pseudomonas spp., pneumococci, and Haemophilus influenzae

Pathogenesis

The pathogenesis remains unclear but probably involves endotoxin-induced vascular injury with associated disseminated intravascular coagulation.

Morphology

At autopsy, the adrenals were grossly hemorrhagic and shrunken; in this photomicrograph, little residual cortical architecture is discernible.



Deep Focus Question

What is most closely associated with Waterhouse-Friderichsen syndrome?

A. Viremia
B. Streptococcus
C. Staphylococcus
D. CMV
E. Meningococcemia

Answer: E

Deep Focus Question

The species of Neisseria genus which is most likely to cause Waterhouse-Friderichsen syndrome is...?

A. Neisseria wadsworthii.
B. ...Neisseria flavescens.
C. ...Neisseria lactamica.
D. ...Neisseria meningitidis.

Answer: D

Chronic Adrenocortical insufficiency
"Addison disease"

Definition

Uncommon disorder resulting from progressive destruction of the adrenal cortex.

Causes

More than 90% of all cases are attributable to one of four disorders:

1. Autoimmune adrenalitis (most common cause) autoimmune destruction of steroid-producing cells, and autoantibodies.
2. Infection: tuberculosis and fungal
3. Acquired immune deficiency syndrome (AIDS)
4. Metastatic neoplasms: Carcinomas of the lung and breast are the source of a majority of metastases in the adrenals.

Morphology

Primary autoimmune adrenalitis	tuberculosis or fungal diseases
Grossly: characterized by irregularly shrunken glands, which may be exceedingly difficult to identify within the suprarenal adipose tissue.	In tuberculosis or fungal diseases, the adrenal architecture may be effaced by a granulomatous inflammatory reaction identical to that encountered in other sites of infection
On histologic examination: the cortex contains only scattered residual cortical cells in a collapsed network of connective tissue. A variable lymphoid infiltrate is present in the cortex and may extend into the subjacent medulla	

Adrenocortical insufficiency

Clinical features

IMPORTANT

Gastrointestinal disturbances are common and include anorexia (loss of appetite), nausea, vomiting, weight loss, and **diarrhea**

In patients with primary adrenal disease, increased levels of ACTH precursor **hormone stimulate melanocytes** with resultant **hyperpigmentation** of the skin and mucosal surfaces

Decreased mineralocorticoid (aldosterone) activity in patients with primary adrenal insufficiency results in potassium retention and sodium loss, with consequent **hyperkalemia, hyponatremia, volume depletion, and hypotension**

Secondary hypoadrenalism is characterized by deficient cortisol and androgen output but normal or **near-normal aldosterone synthesis**

Hypoglycemia occasionally may occur

Stresses such as infections, trauma, or surgical procedures in affected patients may precipitate an **acute adrenal crisis**, manifested by **intractable vomiting, abdominal pain, hypotension, coma, and vascular collapse**. Death follows rapidly unless corticosteroids are replaced immediately

Deep Focus Question

Which condition does NOT improve with induction of mineralocorticoid activity?

A. POTS (paroxysmal orthostatic tachycardia syndrome)
B. Cushing syndrome
C. Addison disease
D. Cerebral salt wasting syndrome
E. Geriatric orthostatic hypotensive syncope

Answer: B

Of note, carcinomas metastatic to the adrenal cortex are significantly more frequent than a primary adrenocortical carcinoma.

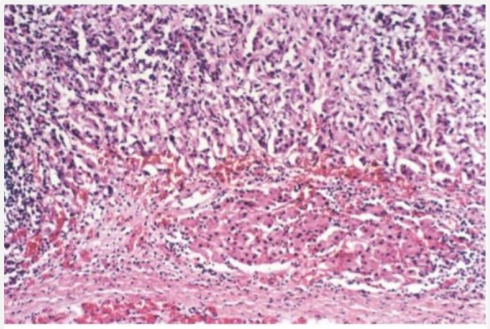


Fig. 20.41 Autoimmune adrenalitis. In addition to loss of all but a subcapsular rim of cortical cells, there is an extensive mononuclear cell infiltrate.

Adrenocortical neoplasms

Definition

While functional adenomas are most commonly associated with hyperaldosteronism and with Cushing syndrome, a virilizing neoplasm is more likely to be a carcinoma , not all adrenocortical neoplasms, however, elaborate steroid hormones

Cortical adenomas:

Most cortical adenomas do not cause hyperfunction and usually are encountered as incidental findings at the time of autopsy or during abdominal imaging for an unrelated cause

Morphology

Grossly	Microscopically
• On cut surface, adenomas usually are yellow to yellow-brown, owing to the presence of lipid within the neoplastic cells • As a general rule they are small	• On microscopic examination adenomas are composed of cells similar to those populating the normal adrenal cortex. • The nuclei tend to be small, although some degree of pleomorphism may be encountered even in benign lesions (**endocrine atypia**) • The cytoplasm of the neoplastic cells ranges from eosinophilic to vacuolated, depending on their lipid content; mitotic activity generally is inconspicuous.

Determination of whether a cortical neoplasm is functional or not is based on clinical evaluation and measurement of the hormone or its metabolites in the laboratory

Adrenocortical carcinomas

Definition

Are rare neoplasms that may occur at any age, including in childhood

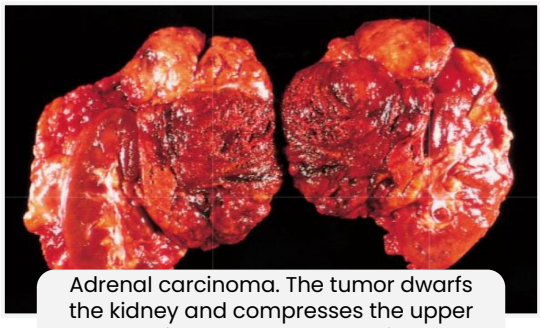
Etiology

Two rare inherited causes of adrenal cortical carcinomas are:

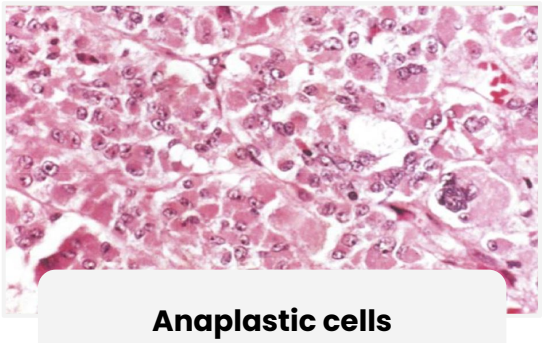
- Li-Fraumeni syndrome
- Beckwith-Wiedemann syndrome

Gross Morphology

- In most cases, adrenocortical carcinomas are large, invasive lesions that efface the native adrenal gland.
- On cut surface, adrenocortical carcinomas typically are variegated, poorly demarcated lesions containing areas of necrosis, hemorrhage, and cystic change



Adrenal carcinoma. The tumor dwarfs the kidney and compresses the upper pole. It is largely hemorrhagic and necrotic.



Anaplastic cells

Pheochromocytoma

IMPORTANT

Pheochromocytoma

Overview

- **Neoplasms composed of chromaffin cells**, which, like their nonneoplastic counterparts, synthesize and release catecholamines
- Similar to aldosterone-secreting adenomas, give rise to surgically correctable forms of **hypertension** (mean if we remove the tumor, the patient will get rid of the hypertension -go away-)

Morphology

Gross

- Range in size from small, circumscribed lesions confined to the adrenal to large, hemorrhagic masses
- On cut surface, smaller pheochromocytomas are yellow-tan, well-defined lesions that compress the adjacent adrenal gland. Larger lesions tend to be hemorrhagic, necrotic, and cystic and typically efface the adrenal gland.

Microscopic

- Polygonal to spindle-shaped chromaffin cells and their supporting cells, compartmentalized into small nests, or **Zellballen**, by a rich vascular network
- The cytoplasm of the neoplastic cells often has a finely granular appearance
- EM reveals variable numbers of membrane-bound, electron-dense granules (neurosecretory granules).

How can you differentiate between benign and malignant Pheochromocytoma?

1. The nuclei of the neoplastic cells are often quite pleomorphic. (so pleomorphism is not enough to diagnose malignancy)
2. Both capsular and vascular invasion may be encountered in benign lesions. (so capsular and vascular invasion aren't enough variants)
3. The mere presence of mitotic figures does not imply malignancy.
4. Therefore, the definitive diagnosis of malignancy in pheochromocytomas is based exclusively on the **presence of metastases.** These may involve regional lymph nodes as well as more distant sites, including liver, lung, and bone.

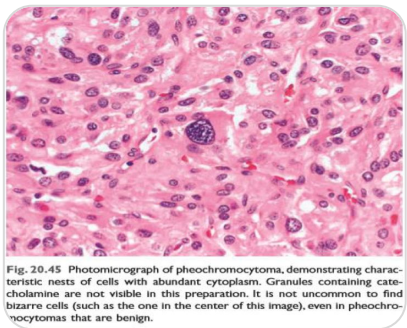
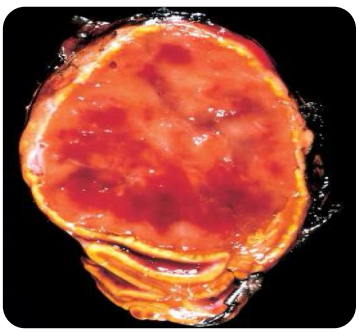


Fig. 20.45 Photomicrograph of pheochromocytoma, demonstrating characteristic nests of cells with abundant cytoplasm. Granules containing catecholamine are not visible in this preparation. It is not uncommon to find bizarre cells (such as the one in the center of this image), even in pheochromocytomas that are benign.



The tumor is enclosed within an attenuated cortex and demonstrates areas of hemorrhage. The comma-shaped residual adrenal gland is seen (lower portion)

Pheochromocytoma

Pheochromocytoma	
Clinical Features	○ The predominant clinical manifestation of pheochromocytoma is **hypertension**. ○ The characteristic presentation with a hypertensive episode is one of abrupt elevation in blood pressure, associated with tachycardia, palpitations, headache, sweating, tremor, and a sense of apprehension. ○ Increased risk of myocardial ischemia, heart failure, renal injury, and stroke (cerebrovascular accident). ○ Sudden cardiac death may occur, probably secondary to catecholamine-induced myocardial irritability and ventricular arrhythmias.
Diagnosis	Is based on demonstration of increased urinary excretion of free catecholamines and their metabolites, such as vanillylmandelic acid and metanephrines

Rule of 10s

- 10% of pheochromocytomas are extra-adrenal (paragangliomas)
- 10% of adrenal pheochromocytomas are bilateral; this proportion may rise to 50% in cases that are associated with familial syndromes.
- 10% of adrenal pheochromocytomas are malignant
- 10% of adrenal pheochromocytomas are not associated with hypertension

One “traditional” 10% rule that has since been modified pertains to familial cases. It is now recognized that as many as 25% of individuals with pheochromocytomas and paragangliomas harbor a germ line mutation in one of at least six known genes, including:

○ RET, which causes type 2 MEN syndromes
○ NF1, which causes type 1 neurofibromatosis
○ VHL, which causes von Hippel-Lindau disease

Keywords

Cushing's syndrome	Cushing's disease	• ACTH- producing microadenoma • adrenal glands show bilateral nodular cortical hyperplasia
	Ectopic ACTH	• small-cell carcinoma of the lung • carcinoids, medullary carcinomas of the thyroid, and PanNET
	• pituitary and ectopic : ACTH levels are elevated • high levels of excreted corticosteroids • secondary to adrenal tumors : ACTH levels are low • moon face , Hypertension , weight gain , Proximal limb weakness , buffalo hump , cutaneous striae	
Adrenocortical hyperfunction	Exogenous	• Cortical Atrophy
	ACTH-dependent	• Diffuse hyperplasia (mentioned above)
	Primary cortical hyperplasia	• Cortex replacement by macronodule or darkly pigmented micronodules • pigment is believed to be lipofuscin, which is a wear-and-tear pigment
	Adenoma	A. Grossly : yellow tumors surrounded by thin or well-developed capsules B. Microscopically : Neoplastic cells are vacuolated because of the presence of intracytoplasmic lipid.
	Carcinoma	A. Grossly : adjacent adrenal cortex and that of the contralateral adrenal gland are atrophic B. Microscopically : Crooke hyaline change , intermediate keratin filaments in the cytoplasm
Hyperaldosteronism	• excess aldosterone secretion • hypertension & hypernatremia & Hypokalemia	
	Primary aldosteronism	• autonomous overproduction of aldosterone • suppression of the renin-angiotensin system and decreased plasma renin activity. • Causes : A. Bilateral idiopathic hyperaldosteronism B. Adrenocortical neoplasm : aldosterone-producing adenoma (Conn syndrome)or adrenocortical carcinoma C. familial hyperaldosteronism : overactivity of the aldosterone synthase gene, CYP11B2
	Secondary hyperaldosteronism	• release occurs in response to activation of the renin-angiotensin system • Decreased renal perfusion , Arterial hypovolemia , Pregnancy
	Aldosterone-producing adenomas	• bright yellow on cut section and are composed of lipid-laden cortical cells. • presence of eosinophilic, laminated cytoplasmic inclusions, known as spironolactone bodies. • adjacent adrenal cortex and contralateral gland are not atrophic.
	Bilateral idiopathic hyperplasia	• bilateral nodular hyperplasia of the adrenal glands • mutations in the KCNJ5 gene

Keywords

Hypersecretion of sex hormones		• adrenocortical neoplasms Or congenital adrenal hyperplasia (CAH) • autosomal recessive disorders • deficiency of the enzyme 21-hydroxylase which stimulates androgen production • masculinization in females (ambiguous genitalia, oligomenorrhea, hirsutism) • precocious (Increase in androgen) puberty in males.
Adrenocortical insufficiency	Waterhouse-Friderichsen syndrome	• Neisseria meningitidis septicemia , sore throat , fever • Maybe Pseudomonas spp., pneumococci, and Haemophilus influenzae. • associated DIC. • hemorrhagic and shrunken adrenal
	Addison disease	• Autoimmune adrenalitis : autoimmune destruction of steroid-producing cells, and autoantibodies. • Infection: tuberculosis and fungal • AIDS • Primary autoimmune adrenalitis: irregularly shrunken glands , cortex contains only scattered residual cortical cells in a collapsed network of connective tissue. • In tuberculosis or fungal diseases, : granulomatous inflammatory
		• diarrhea & hyperpigmentation • hyperkalemia, hyponatremia, volume depletion, and hypotension • intractable vomiting, abdominal pain, hypotension, coma, and vascular collapse.
Adrenocortical neoplasms	adenomas	A. Grossly : yellow to yellow-brown B. Microscopically : endocrine atypia
	Adrenocortical carcinomas	• Two rare inherited causes of are Li-Fraumeni syndrome and Beckwith-Wiedemann syndrome A. Grossly : poorly demarcated lesions containing areas of necrosis, hemorrhage, and cystic change B. Microscopically : Anaplastic cells
Pheochromocytoma		• association with one of several familial syndromes MEN-2A and MEN-2B syndromes (in 10%) • composed of chromaffin cells • RET (causes type 2 MEN) , NF1 (cause type 1 neurofibromatosis) VHL (causes von Hippel-Lindau disease) • Gross : yellow-tan, well-defined lesions • Microscopy: polygonal to spindle-shaped chromaffin cells , small nests, or Zellballen , electron-dense granules • definitive diagnosis of malignancy is based exclusively on the presence of metastases. • hypertension , urinary excretion of free catecholamines , myocardial ischemia

IF YOU WANT A SUMMARY CLICK HERE

MCQs

Question 1

What is the most common cause of spontaneous, endogenous Cushing syndrome?

A. Pituitary adenoma
B. Ectopic ACTH secretion
C. Adrenal adenoma
D. Adrenal carcinoma

Question 2

What is the most common cause of primary hyperaldosteronism?

A. Autonomous overproduction of aldosterone
B. Decreased renal perfusion
C. Activation of the renin-angiotensin system
D. Arterial hypovolemia

Question 3

Which of the following diseases is most commonly associated with KCNJ5 gene mutation?

A. von Hippel-Lindau
B. Bilateral idiopathic hyperaldosteronism,
C. Pheochromocytoma
D. Addison disease

Question 4

Which one of the following is the most common etiology of chronic adrenocortical deficiency?

A. Tuberculous Infection
B. Autoimmune Adrenalitis
C. Waterhouse-friedchicken syndrome
D. Cushing syndrome

1-A \ 2–A \ 3-B \ 4-B

MCQs

Question 5

A 45-year-old male died shortly after having fever and weakness, biopsy of the adrenal gland showed it was hemorrhagic and shrunken, what is the cause?

A. Neisseria Meningitidis

B. Aldosterone-producing adenomas

C. Bilateral idiopathic hyperplasia

D. Adrenocortical adenomas

Question 6

Which of the following manifestations is seen in Conn's syndrome?

A. Hyperkalemia

B. Hyponatremia

C. Hypertension

D. Hypotension

Question 7

What is the definitive diagnosis of malignancy in pheochromocytomas?

A. hemorrhagic masses

B. Zellballen

C. The nuclei of the neoplastic cells are often quite pleomorphic

D. presence of metastases

Question 8

Which of the following is a histopathological feature of pheochromocytoma?

A. Macronodular hyperplasia

B. Pigmented nodular adrenal disease

C. Chromaffin cells

D. Cortical atrophy

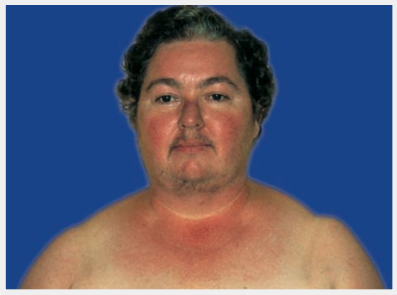
5-A \ 6-C \ 7-D \ 8-C

Cases

1.A 45-year-old man with a recent history of bizarre behavior is seen by a psychiatrist, who recommends evaluation of his endocrine status. On physical examination, the patient appears moderately obese (BMI = 31 kg/m2), with mild hypertension, facial acne, fat accumulation in the supraclavicular fossae, and a protuberant abdomen. Laboratory studies demonstrate a neutrophilic leukocytosis, with a decrease in the percentage of lymphocytes and an absence of eosinophils. The hematocrit and hemoglobin are normal. There is a mild hypokalemia and mild metabolic alkalosis. The fasting serum glucose is within the reference range, but on a 2-hour glucose tolerance test, both the 60- and 120-minute samples had glucose concentrations greater than 200 mg/dL. Laboratory studies show free urinary cortisol of 156 mg per 24 hours (normal = 10 to 100 mg per 24 hours). Which of the following questions would be of most help in establishing a diagnosis?

A.Are you experiencing muscle weakness?	B.Are you experiencing shortness of breath?	C.Are you receiving corticosteroids for some other disease?	D.Have you received recent blood transfusions?

2.A 40-year-old man with a history of diabetes complains of recent changes in his bodily appearance. A photograph of the patient is shown in the image. Laboratory studies reveal elevated serum corticosteroids and low serum corticotropin. Administration of dexamethasone does not lower serum levels of corticosteroids. This patient most likely has a tumor that originates in which of the following anatomic locations?



A.Adrenal cortex, zona fasciculata	B.Adrenal cortex, zona glomerulosa	C.Adrenal medulla	D.Anterior pituitary

3.A 40-year-old man complains of nausea, vomiting, diarrhea, and cramping abdominal pain. His temperature is 38°C (101°F), blood pressure 90/60 mm Hg, and pulse rate 90 per minute. On physical examination, the patient appears dehydrated, with sunken eyeballs, dry tongue, and poor skin turgor. Hyperpigmentation is noted in the palmar creases and the gingival margins. Laboratory results include fasting serum glucose of 62 mg/dL (normal = 70 to 115 mg/dL), BUN of 27 mg/dL (normal = 11 to 23 mg/dL), Na of 122 mEq/L (normal = 136 to 145 mEq/L), and K of 6.5 mEq/L (normal = 3.5 to 5.0 mEq/L). Which of the following is the most likely cause of this patient's symptoms?

A.Autoimmunity	B.Metastatic cancer	C.Sarcoidosis	D.Tuberculosis

1-C \ 2–A \ 3-A

NEED EXPLANATION ? CLICK HERE

Cases

4.A 34-year-old man complains of sudden attacks of dizziness, blurred vision, and excruciating headaches of 4 months in duration. During one of these attacks, his blood pressure was 180/120 mm Hg. The patient's father had been treated for thyroid cancer about 15 years ago. Laboratory studies show normal serum levels of aldosterone, renin, and angiotensin. A 24-hour urinalysis reveals increased metanephrines. Episodic hypertension in this patient is most likely caused by a tumor in which of the following endocrine organs?

A.Adrenal	B.Kidney	C.Parathyroid	D.Pituitary

5.A 46-year-old woman with severe asthma presents with increasing weight and back pain for 9 months. The patient is taking corticosteroids for her asthma. An X-ray of the vertebrae will likely reveal which of the following pathologic findings?

A.Dislocation	B. Osteomalacia	C.Osteomyelitis	D.Osteoporosis

Last Lecture Icons !

BE OUR NEXT LECTURE ICON ! TAKE THIS TOUGH QUIZ !

4-A \ 5–D

NEED EXPLANATION ? CLICK HERE

Cases

EXTRA CASES MAY REQUIRE EXTRA INFO

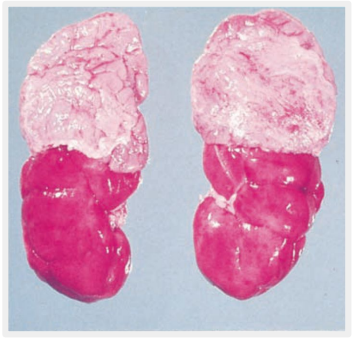
1.Physical examination of a neonate shows peculiar genitalia. Cytogenetic studies reveal a 46, XX karyotype. Laboratory studies will most likely reveal a deficiency of which of the following?

A.Androstenedione	B.Corticotropin	C.21-Hydroxylase	D. Progesterone

2.The infant described in Question 1 is shown to have an autosomal recessive genetic disorder. The infant is expected to manifest which of the following developmental anomalies?

A.Adrenal hyperplasia	B.Bladder diverticulum	C.Cystic renal dysplasia	D.Polycystic ovaries

3. A 7-week-old infant develops severe dehydration and hypotension and expires. The kidneys and adrenal glands at autopsy are shown in the image. Hypovolemic shock in this infant was most likely caused by inadequate synthesis of which of the following hormones?



A.Aldosterone	B.Angiotensin	C.Antidiuretic hormone	D.Atrial natriuretic factor

1-C \ 2–A \ 3-A

Pathology Team

Leader
زياد العتيبي

Leader
لمى العتيبي

- رغد المصلح
- ليان الرويلي
- سلطان البقمي
- محمد العرفج
- عروب المحمود
- ريماز المحمود
- عائشة إبراهيم
- ألين الكلية
- يزيد آل طلحه
- ريما المطيري
- إيلاف معتبي
- شوق الخليفة
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- لؤي الحديثي
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- رند اباالخيل
- ساره العجاجي
- دانه المحيسن
- نوره المحيميد
- معاذ الحضيف
- فيصل الشويعر
- يزيد المطيري
- الجوهرة الوهيبي
- رزان السطيحي