Adrenocorticosteroids

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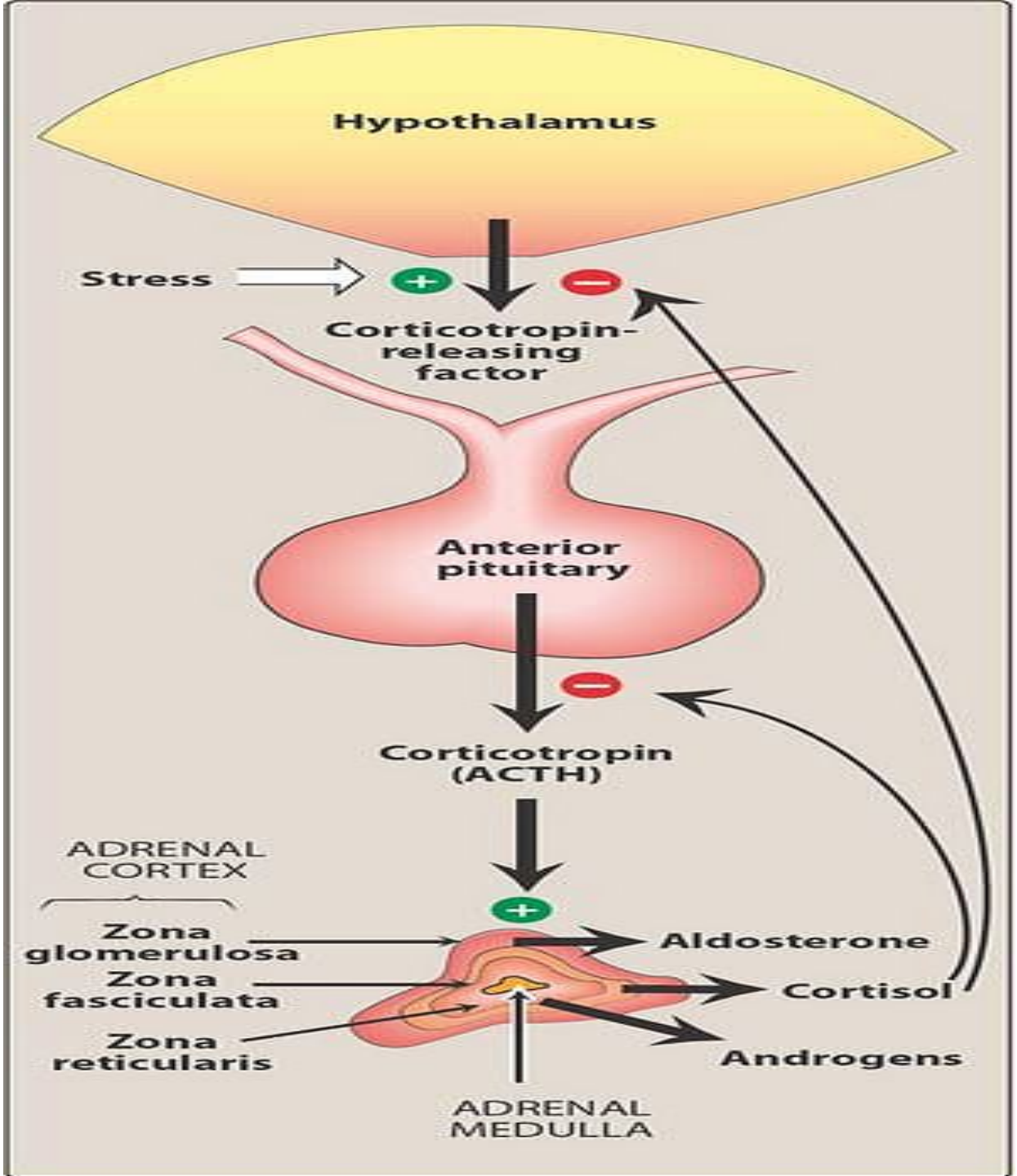
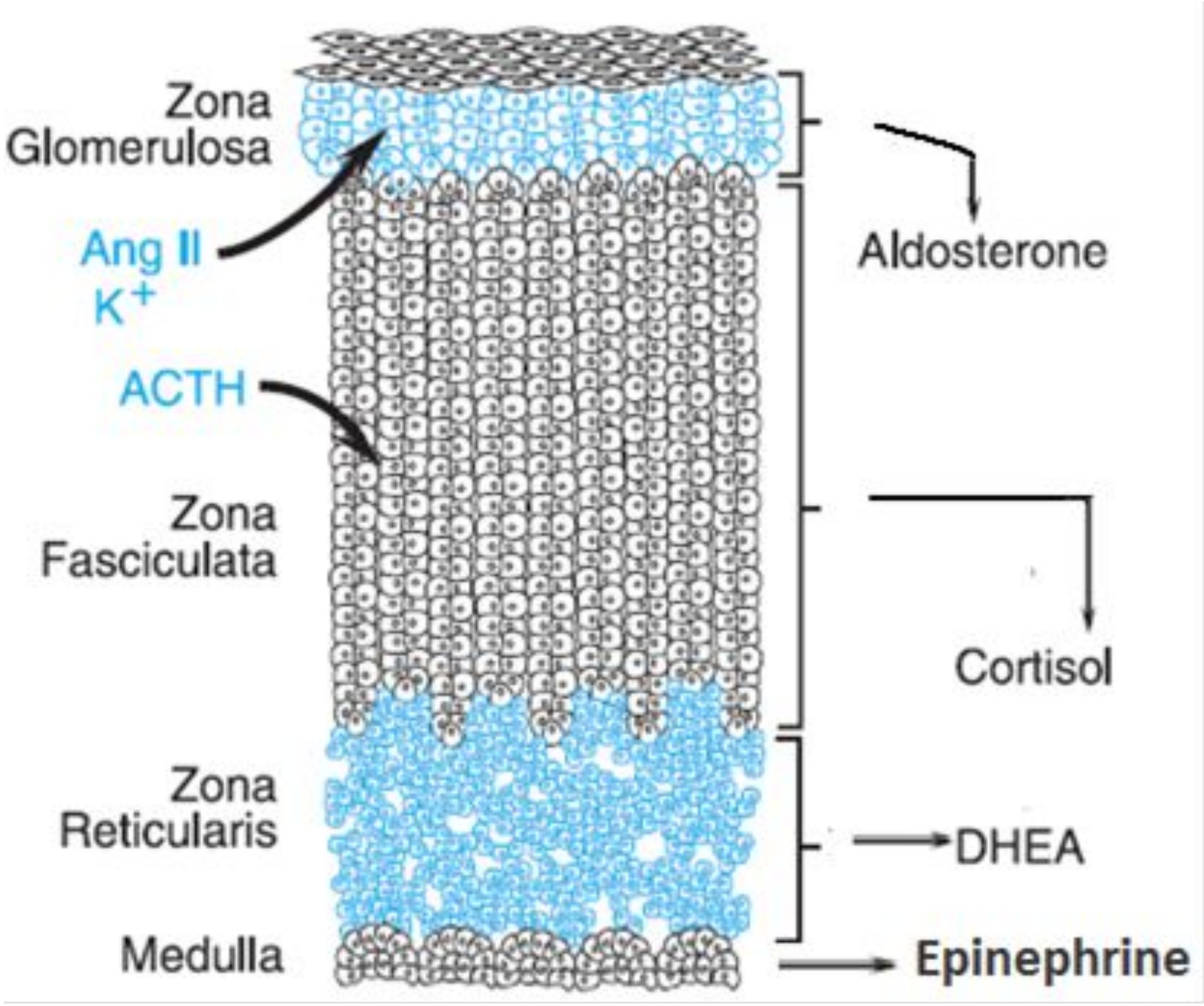
Pharmacology and therapeutics


Hypothalamus
Stress
+
−
Corticotropin-releasing factor
Anterior pituitary
−
Corticotropin (ACTH)
ADRENAL CORTEX
+
Zona glomerulosa
Zona fasciculata
Zona reticularis
Aldosterone
Cortisol
Androgens
ADRENAL MEDULLA

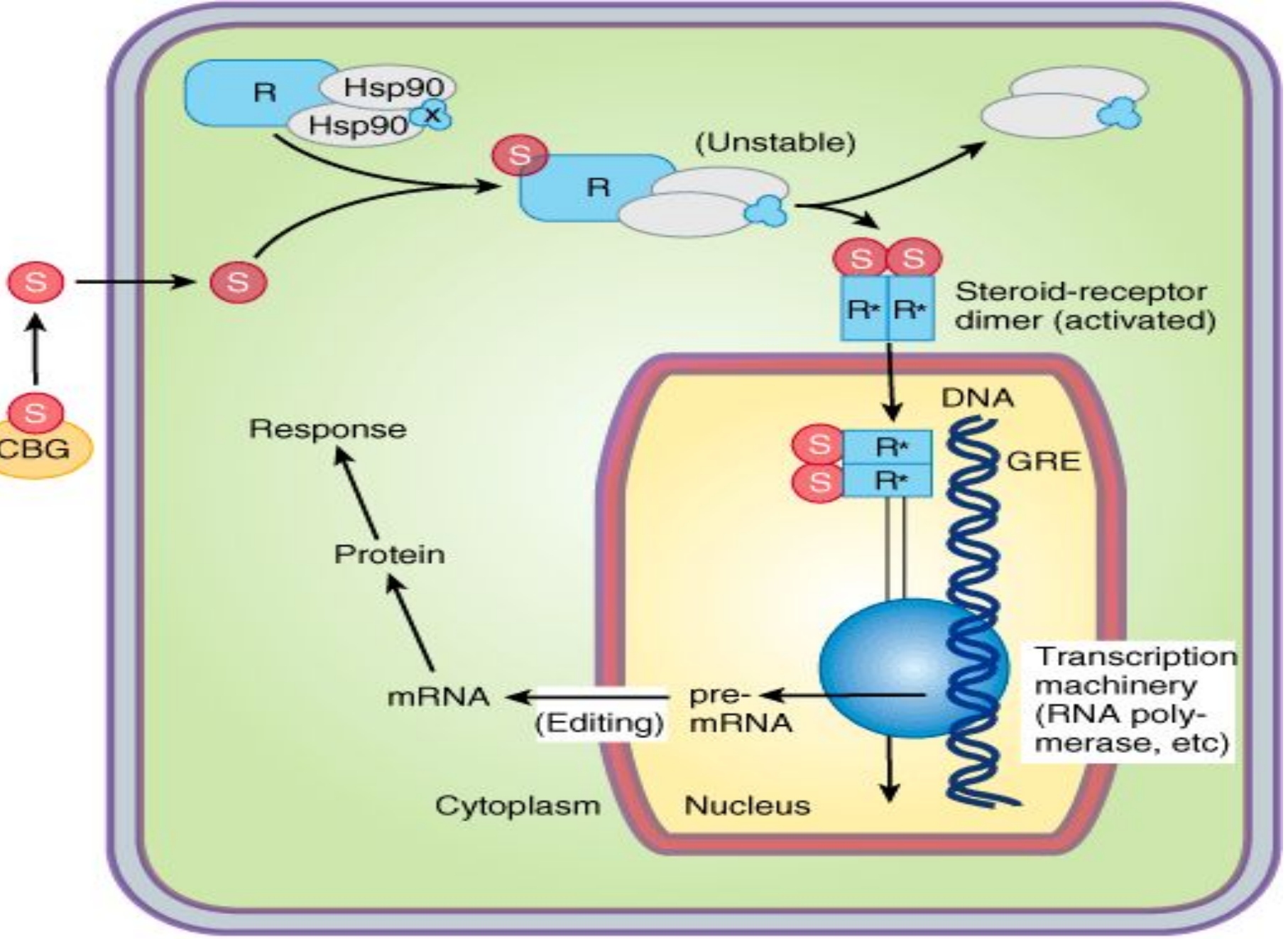

Zona Glomerulosa
Ang II
K+
ACTH
Zona Fasciculata
Zona Reticularis
Medulla
Aldosterone
Cortisol
DHEA
Epinephrine

The adrenal gland consists of the **cortex** and the **medulla**. **The medulla** secretes epinephrine. The adrenal **cortex** is divided into three zones that synthesize various steroids from cholesterol

secrete them The **outer zona glomerulosa** produces mineralocorticoids (for example, aldosterone), which are responsible for regulating salt and water .metabolism

The **middle zona fasciculata** synthesizes . glucocorticoids (for example, cortisol), which are involved with normal metabolism and resistance .to stress

The **inner zona reticularis** secretes adrenal .androgens



ource: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 1th Edition:* http://www.accessmedicine.com

Pharmacological action:

:The effects of cortisol

Metabolic effects:

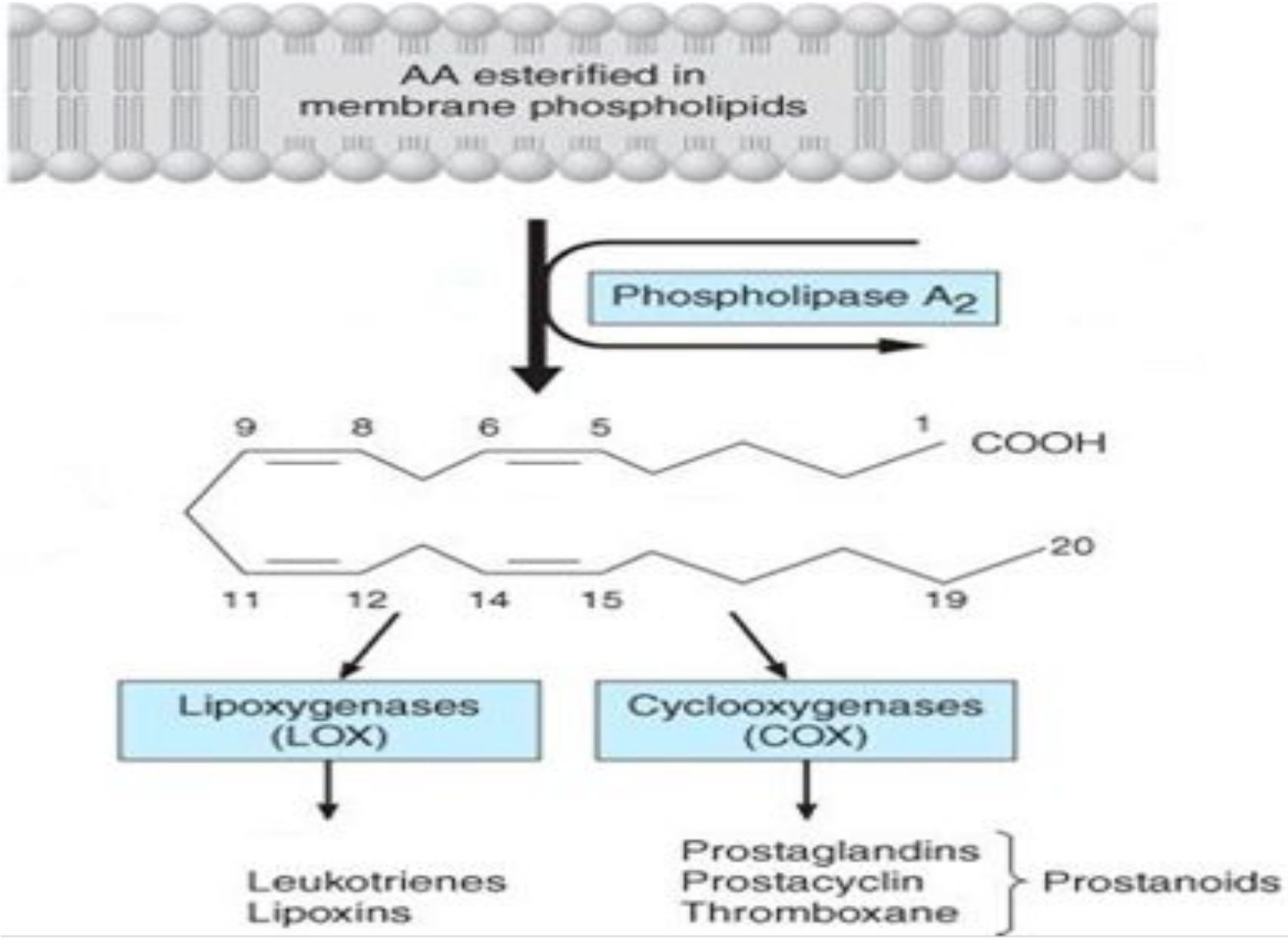
- Glucocorticoids favor gluconeogenesis through increasing amino acid uptake by the liver and kidney and elevating activities of gluconeogenic enzymes.
- They stimulate protein catabolism (except in the liver) and lipolysis (augmenting the action of growth hormone on adipocytes, causing an increase in the activity of hormone-sensitive lipase) in certain parts of the body and lipogenesis in others causing central obesity.

Increase resistance to stress: By raising plasma glucose levels for energy and it can cause a modest rise in blood pressure, apparently by enhancing the vasoconstrictor action of adrenergic stimuli.

Glucocorticoids :3- Alter blood cell levels in:

plasma cause a decrease in eosinophils, basophils, monocytes, and lymphocytes by redistributing them from the circulation to lymphoid tissue. In contrast to this effect, they increase the blood levels of hemoglobin, erythrocytes, .,platelets

4- Anti-inflammatory action: inhibition of phospholipase A2, effects on blood cell and interference with mast cell degranulation results in decreased histamine and capillary permeability **and to suppress immunity.**


AA esterified in membrane phospholipids
Phospholipase A2
9
8
6
5
1
COOH
20
11
12
14
15
19
Lipoxygenases (LOX)
Cyclooxygenases (COX)
Leukotrienes
Lipoxins
Prostaglandins
Prostacyclin
Thromboxane
Prostanoids

:Can have effects on other systems -5

High doses of glucocorticoids stimulate gastric acid and pepsin production and may .exacerbate ulcers

Effects on the central nervous system that .influence mental status have been identified

Chronic glucocorticoid therapy can cause .severe bone loss

production of thyroid-stimulating hormone. and growth hormone production are .increased

	Anti-inflammatory	Salt retention effect	Duration
hydrocotisone	1	1	short
cortisone	0.8	0.8	short
prednisolone	4	0.3	short
Methyl-prednisolone	5	0.1	short
triamcinolone	5	0	intermediate
paramethasone	10	0	intermediate
dexamethasone	**30**	**0**	**long**
betamethasone	**30**	**0**	**long**
aldosterone	**10**	500	
fludrocortisone	**10**	250	

Mineralocorticoids

Mineralocorticoids *help to control the body's water volume and concentration of electrolytes*, especially sodium and potassium by:

1- *Aldosterone* acts on kidney tubules and collecting ducts (also occurs in gastrointestinal mucosa, sweat and salivary glands) causing *a re-absorption of sodium, bicarbonate, and water.*

2- *Decreases reabsorption of potassium*, which, with H^+, is then lost in the urine.

3- *Deoxycorticosterone* (DOC), which also *serves as a precursor of aldosterone* differs from that of aldosterone in that the secretion of DOC is primarily under the control of ACTH.

4- *Fludrocortisone* is a potent steroid with both *glucocorticoid and mineralocorticoid activity*

Pharmacokinetics

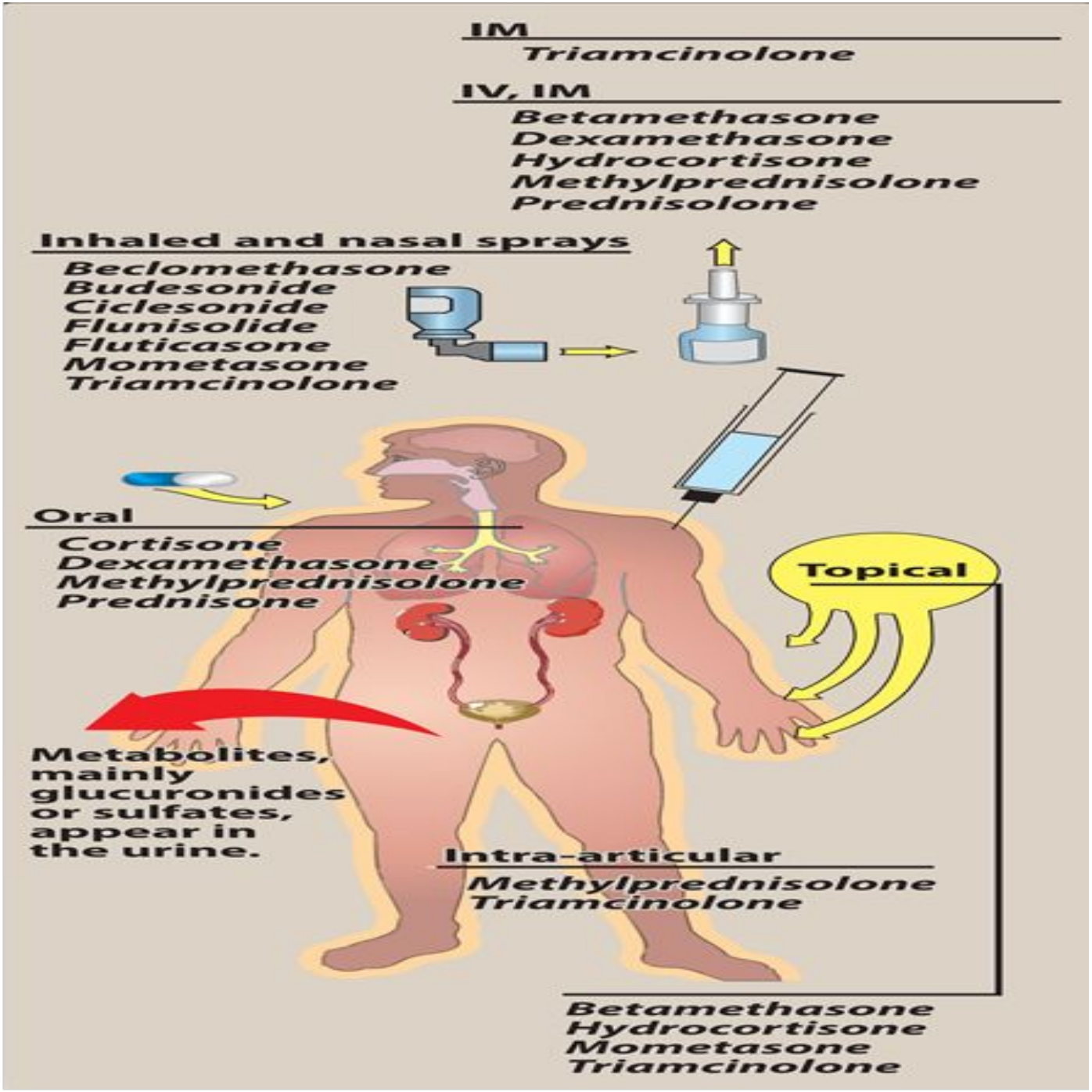
1- Those that are administered orally are readily absorbed from the gastrointestinal tract. Many of them can also be administered intravenously, intramuscularly, intra-articularly, locally and topical applications (creams, intranasal, inhalations, enemas).

2- More than 90 percent of the absorbed glucocorticoids are bound to plasma protein (globulin-CBG).

3- CBG is increased in pregnancy, estrogen administration and in hyperthyroidism. It is decreased by hypothyroidism, genetic defects in synthesis, and protein deficiency states.

4- They are metabolized by the liver.

5- The only glucocorticoid that has no effect on the fetus in pregnancy is prednisone.


IM
Triamcinolone
IV, IM
Betamethasone
Dexamethasone
Hydrocortisone
Methylprednisolone
Prednisolone
Inhaled and nasal sprays
Beclomethasone
Budesonide
Ciclesonide
Flunisolide
Fluticasone
Mometasone
Triamcinolone
Oral
Cortisone
Dexamethasone
Methylprednisolone
Prednisone
Topical
Metabolites, mainly glucuronides or sulfates, appear in the urine.
Intra-articular
Methylprednisolone
Triamcinolone
Betamethasone
Hydrocortisone
Mometasone
Triamcinolone

Therapeutic uses of the adrenal corticosteroids

Replacement therapy for primary adrenocortical -1 insufficiency(addison disease): This disease is caused by adrenal cortex dysfunction

Hydrocortisone is given to correct the deficiency. so that two-thirds is given in the morning and one-third is given in .the afternoon

Replacement therapy for secondary or tertiary -2 adrenocortical insufficiency: These deficiencies are caused by a defect either in CRH production by the hypothalamus (ACTH). corticotropin or by the pituitary

Diagnosis of Cushing's syndrome caused by a glucocorticoids hypersecretion that results either from excessive release of corticotropin by the .anterior pituitary or an adrenal tumor

:Dexamethasone suppression test

Test used to diagnose the cause of an individual's .case of Cushing's syndrome

Dexamethasone this synthetic glucocorticoid suppresses cortisol release in individuals with pituitary-dependent Cushing's syndrome, but it does not suppress glucocorticoid release from .adrenal tumors

Replacement therapy for congenital adrenal -4 hyperplasia is a group of diseases resulting from an enzyme defect in the synthesis of one or more of the adrenal steroid hormones. This condition may lead to virilization in females due to overproduction of adrenal androgens

Treatment of this condition requires administration of sufficient corticosteroids to normalize the patient's hormone levels by suppressing release of CRH and ACTH. This decreases production of ..adrenal androgens

Relief of inflammatory symptoms **-6**

Glucocorticoids dramatically reduce the manifestations of inflammations (for example, rheumatoid and osteoarthritic inflammations, as well as inflammatory conditions of the skin), including the redness, swelling, heat, and tenderness

Treatment of allergies: Glucocorticoids -8 are beneficial in the treatment of the symptoms of bronchial asthma, allergic rhinitis, and allergic reactions due to drugs, .serum and blood transfusion allergy

Acceleration of lung maturation: -9 Respiratory distress syndrome is a problem in premature infant ***(dexamethasone is used).***

effects Adverse

Osteoporosis is the most common adverse -1 effect due to the ability of glucocorticoids to suppress intestinal Ca absorption and inhibit .bone formation

Increased appetite -2

Cushing-like syndrome. redistribution of -3 body fat, puffy face, increased body hair growth, acne, insomnia, and increased .appetite

cataract -3

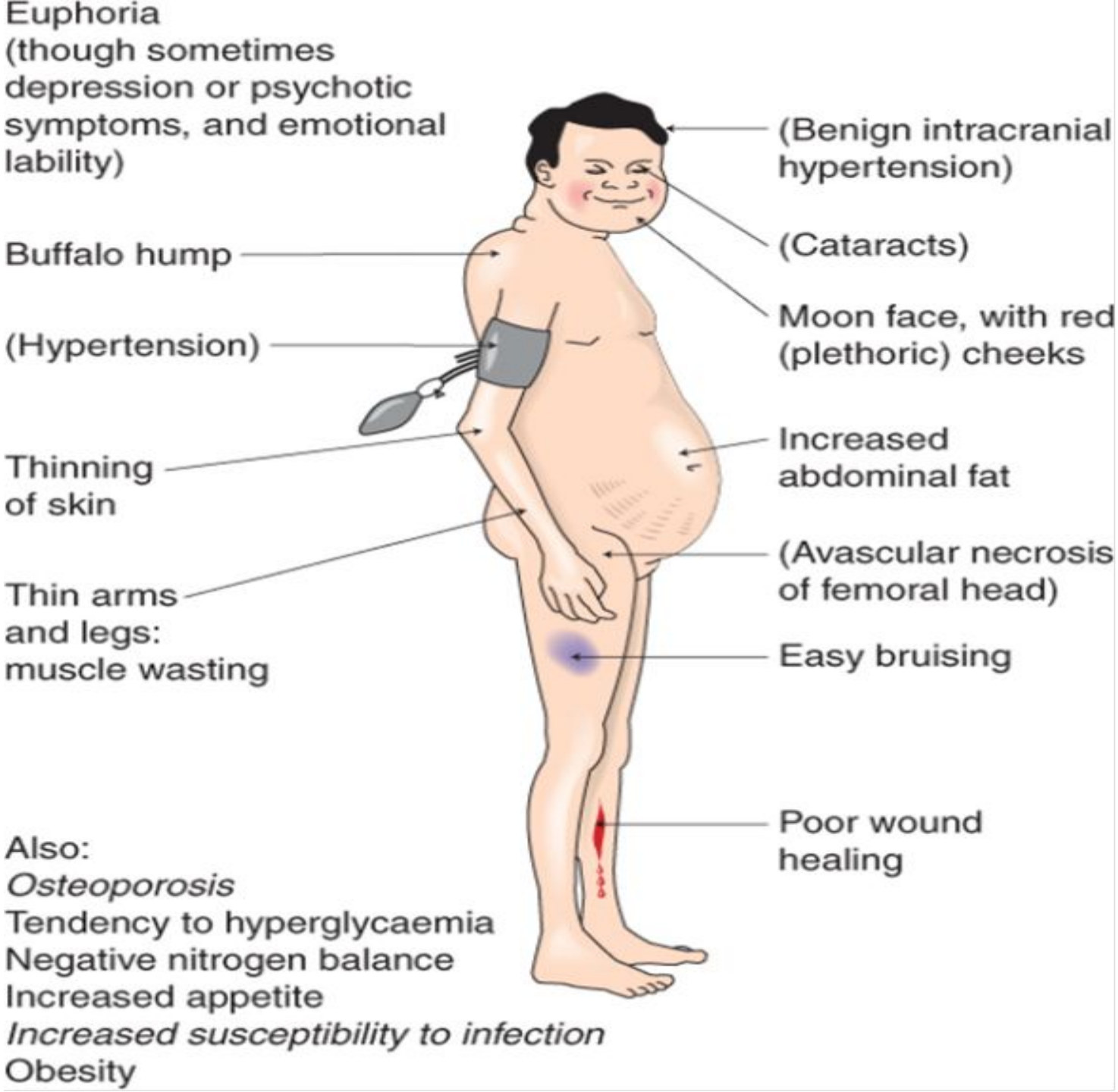
Hyperglycemia may develop and lead to -4 diabetes mellitus. Steroid decrease insulin .receptors sensitivity

.Hypokalemia-5

Withdrawal: abrupt removal of the -6 corticosteroids causes an acute adrenal .insufficiency syndrome that can be lethal

.H.T., peptic ulcer -7

.increase risk of infection -8


Euphoria
(though sometimes depression or psychotic symptoms, and emotional lability)
Buffalo hump
(Hypertension)
Thinning of skin
Thin arms and legs: muscle wasting
(Benign intracranial hypertension)
(Cataracts)
Moon face, with red (plethoric) cheeks
Increased abdominal fat
(Avascular necrosis of femoral head)
Easy bruising
Poor wound healing
Also:
Osteoporosis
Tendency to hyperglycaemia
Negative nitrogen balance
Increased appetite
Increased susceptibility to infection
Obesity

Withdrawal:

Abrupt removal of the corticosteroids causes an acute adrenal insufficiency syndrome that can be lethal. This risk, coupled with the possibility of psychological dependence on the drug and the fact that *withdrawal might cause an exacerbation of the disease*, means the dose must be tapered.

Inhibitors of adrenocorticoid biosynthesis or function

Ketoconazole

Spironolactone

.**:Eplerenone**

.**Aminoglutethimide**

Metyrapone

Mitotane

Mifepristone