

GLUCOCORTICOIZI

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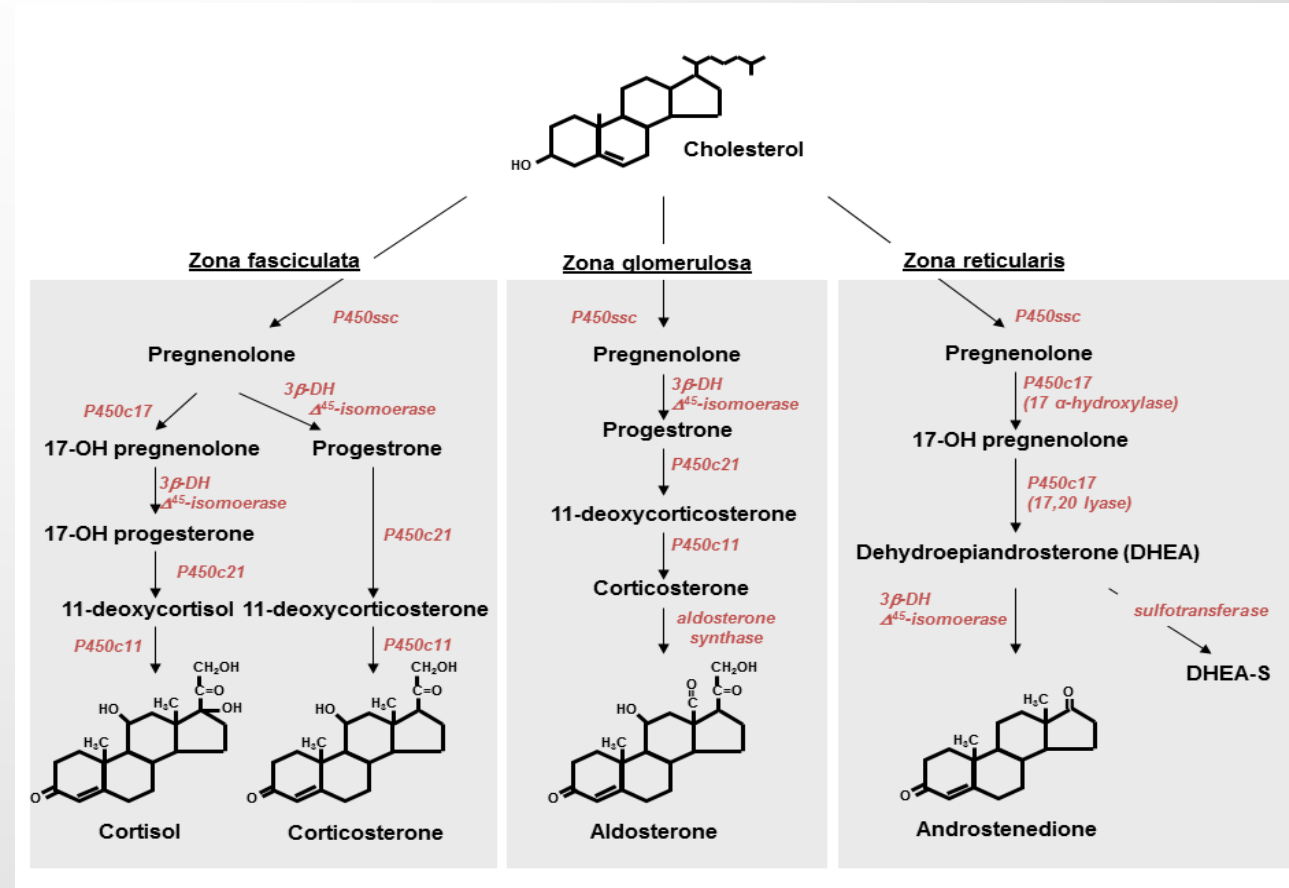
Sinteza: aria fasciculata a adrenosuprarenalei, pornind de la colesterol, sub act. ACTH

Secretie- cortizol=hidro-cortizol-95%

Corticosteron, 5%

- maximum 6-8am si 18 pm

-20mg cortizol/zi



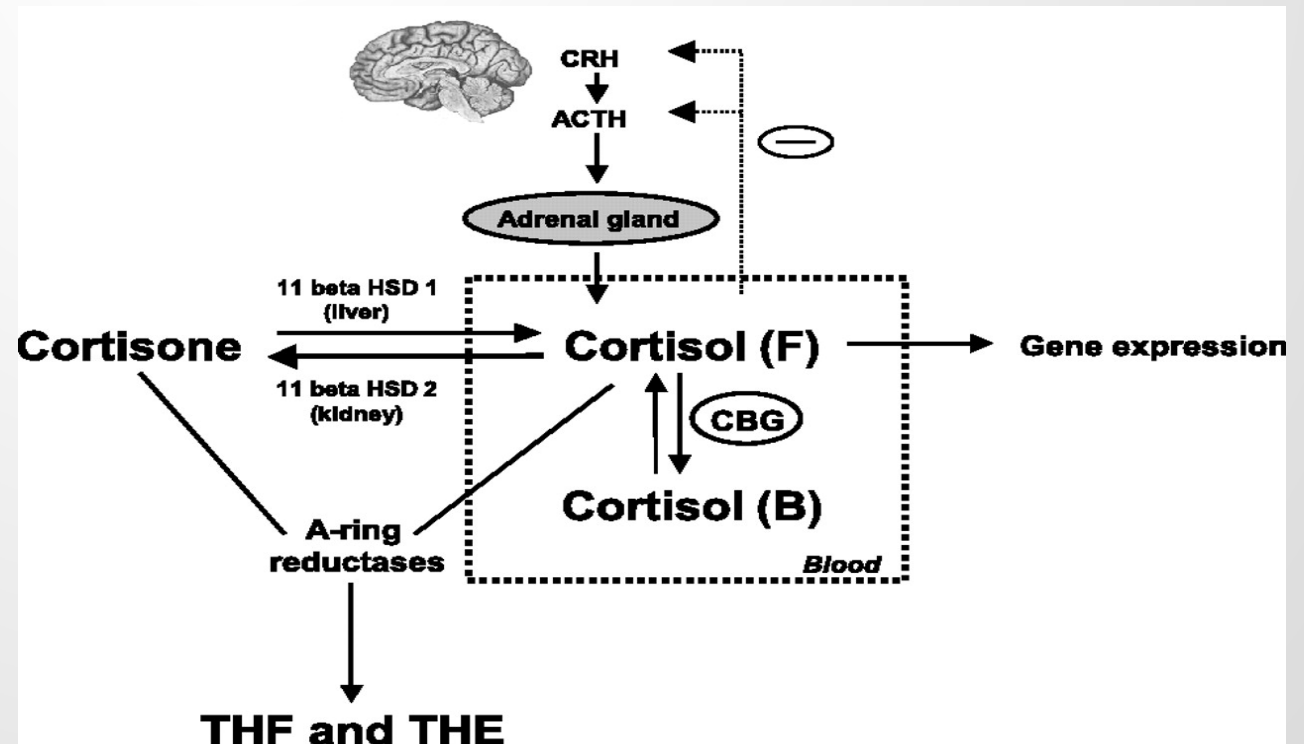
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Transport: 90% legat de CBG

-restul de 10% -efect fiziologic

Metab.: hepatic

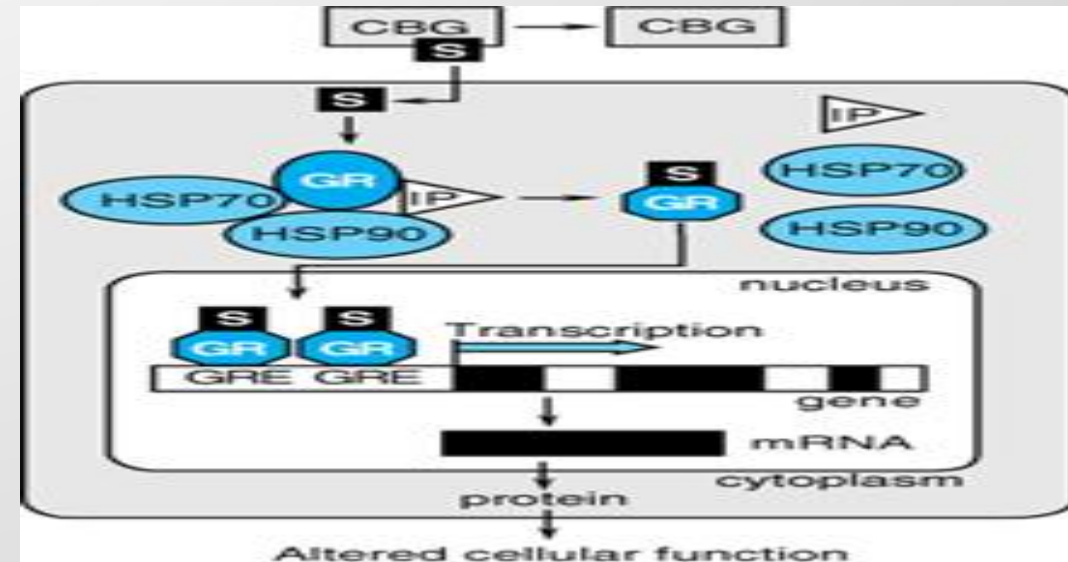
Eliminare: renala



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Mecanism de actiune:

A. Prin intermediul rr pentru Gc, localizati la nivelul tesuturilor tinta



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B. GC se fixeaza pe receptorii membranari cuplati cu prot. G → scad activ. celulara in 1-2 minute

C. Doze foarte mari-altereaza proprietatile fizice si chimice plasmatiche → efect foarte rapid, in cateva secunde

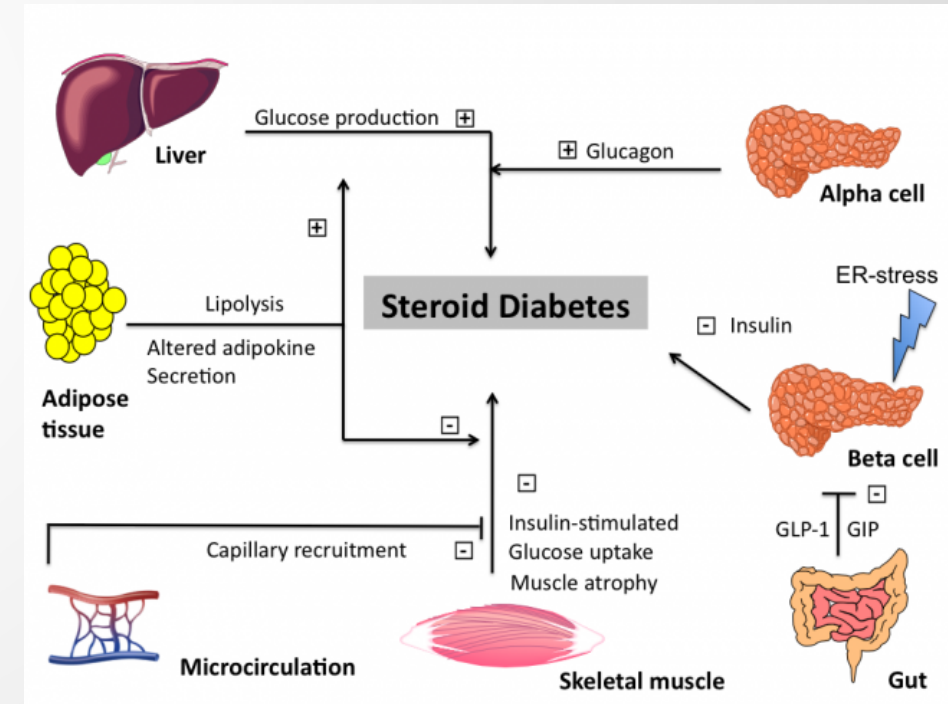
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Efecte:

A. Metabolice: Glucidic:

- ↑ abs. intestinala a glucozei si scad captarea celulara
- stimuleaza neoglucogeneza hepatica
- stimuleaza glicogenoliza hepatica si o inhiba pe cea musculara .

! ↑ glicemia

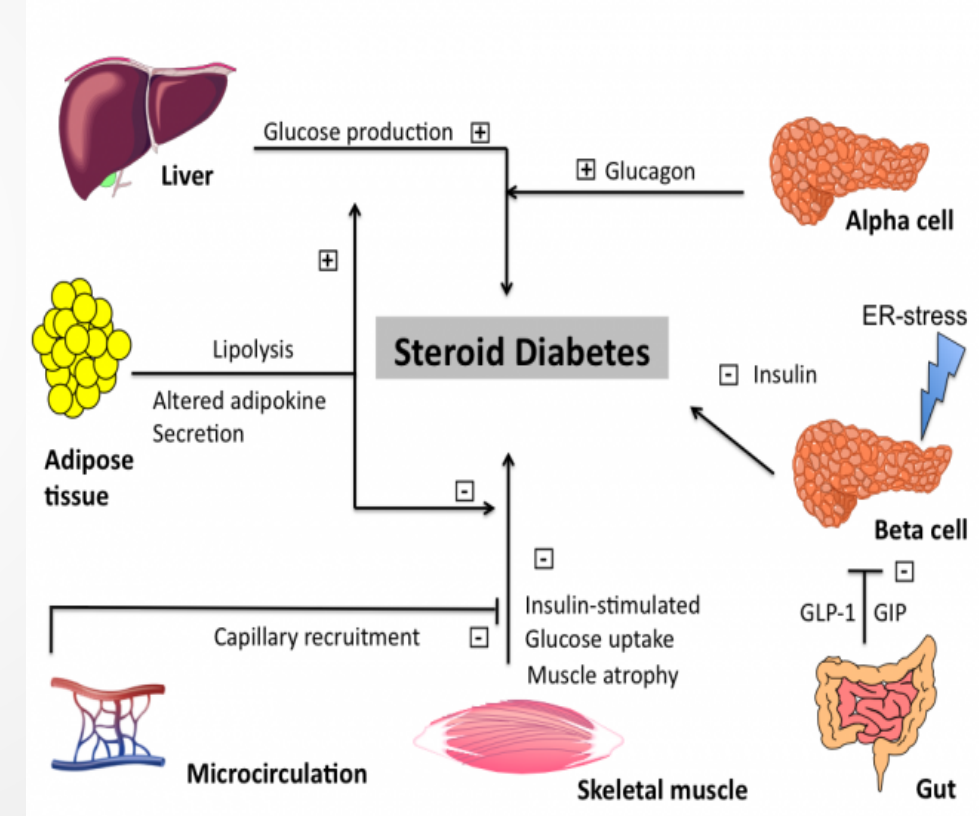


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A. Metabolice:

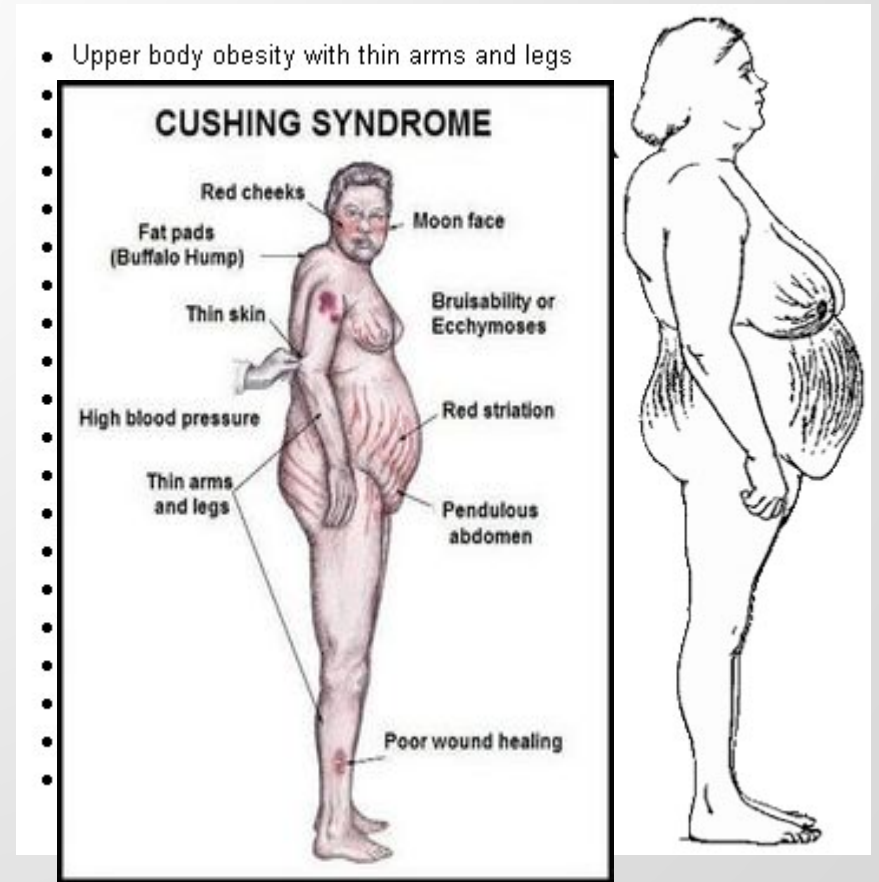
Proteinc: stimuleaza sinteza hepatica si o inhiba pe cea de la nivelul tuturor celorlalte tesuturi →
↑ **efect catabolic**

Lipidic: induce lipoliza → ↓ tesutului adipos



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Lipidic: alterarea raportului lipogeneza/lipoliza-
redistribuirea tesutului adiposo-aspect de “ lamiae
pe scobitori ”



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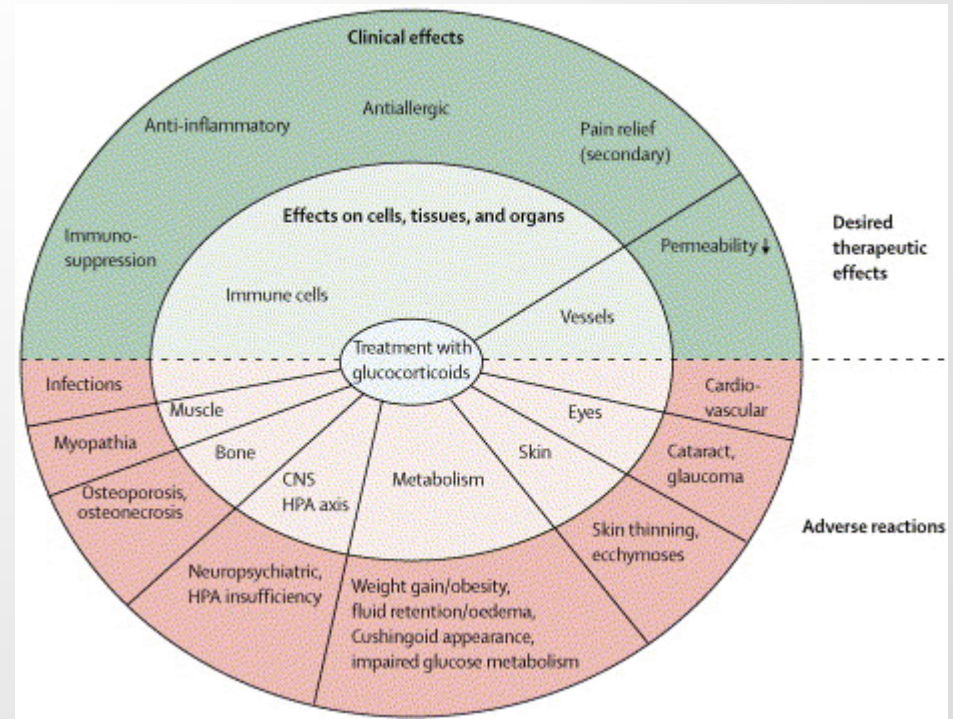
Metabolismul mineral:

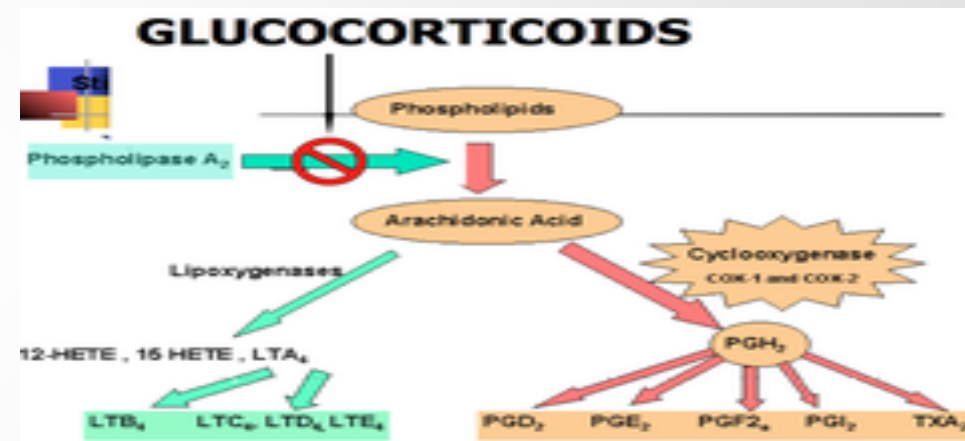
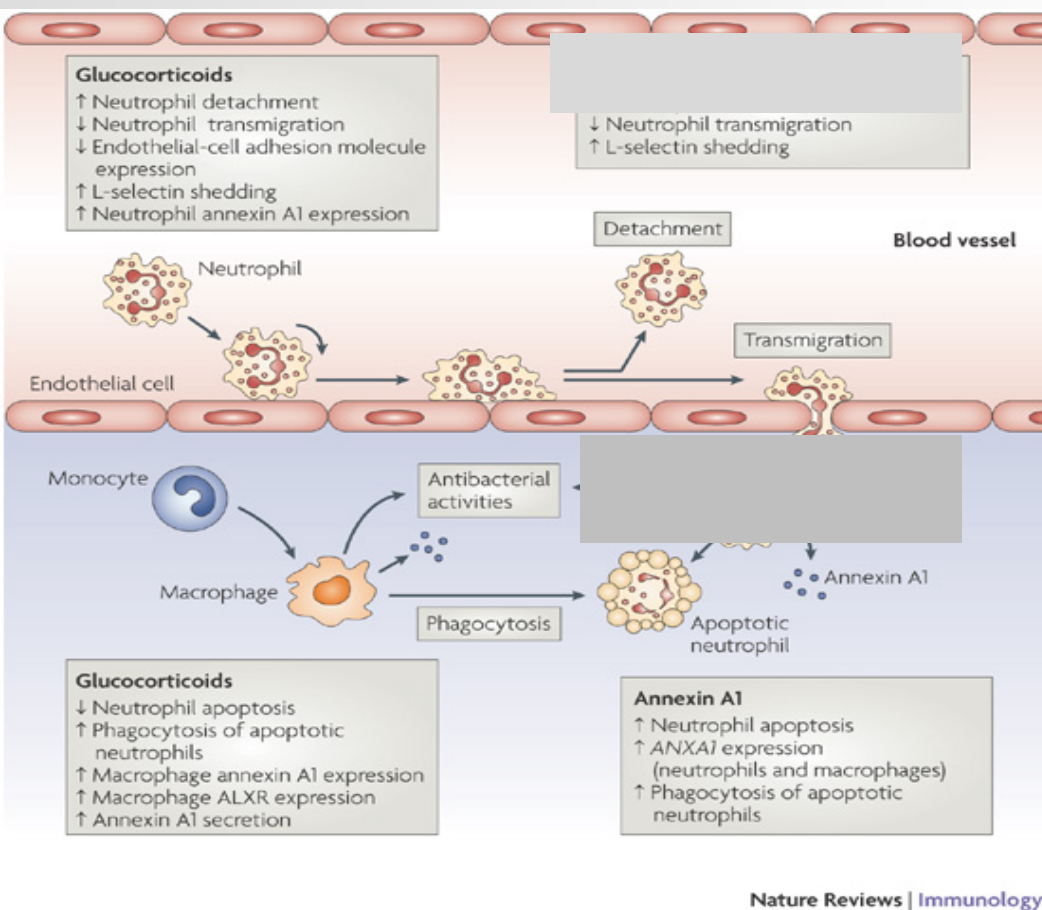
- cresc reabsorbția de sodiu și apă → edeme, ↓ abs. of K and H!
- ↓ abs. intestinală a Ca și cresc eliminarea renală

GC

B. Hematologice:

↑nr de eritrocite, Ne, Le, Tr ,
↓Ly, Mo, Ba, Eo





Efecte:

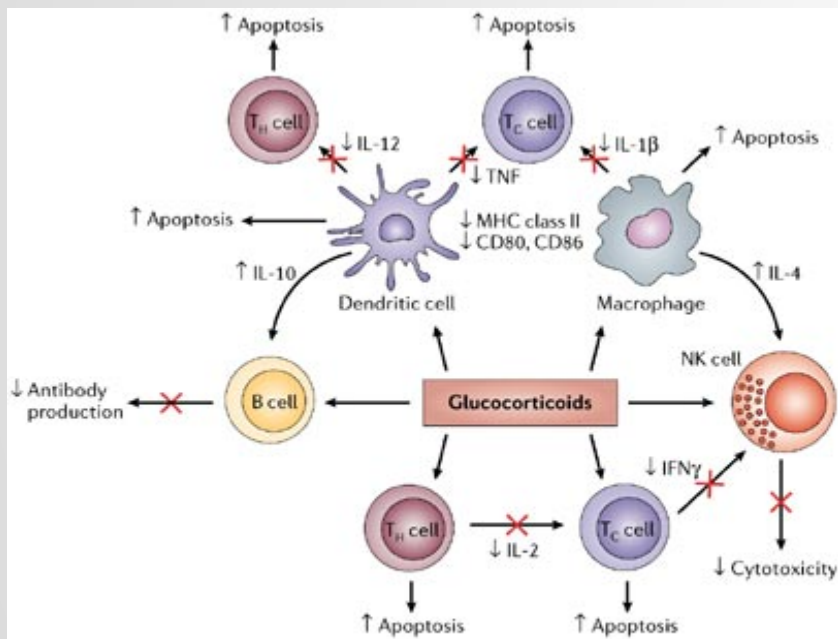
C. Anti-inflamatoare, imunosupresoare, antialergice

Inflamatie:

I. Scad sinteza PG, TX

II. Inhiba expresia moleculelor de adeziune pentru Le si procesul de migrare Le la situsul inflamator

III. Inhiba proliferarea fibroblastica



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Cytokines suppressed by glucocorticoids

IL-1
IL-2
IL-3
IL-4
IL-5
IL-6
IL-13
IL-8
IL-10
GM-CSF
Tumor necrosis factor-alpha
Interferon-gamma

C. Imunosupresie:

- ↓↓Ly
- ↓ productia de cytokine de catre LyT
- ↓ **productia de atc de catre** Ly B-doze mari

C. Antialergice

- inhiba procesul de recunoastere a atg
- blocheaza formarea complexului atg-atc
- blocheaza degranularea mastocitara
- ↓permeabilitatea capilara
- vasoconstrictie

D. Cardiovasculare:

- inotrop pozitiv
- indirect- cresc sensibilitatea miocardului la act. catecolaminelor

E. Muschi scheletici

- fiziologic: cresc tonusul
- tratament indelungat-atrofie, consecutiv catabolismului crescut

F.SNC: efect stimulator

G: Endocrin:

-inhiba secretia de **CRH**

H. Renal: stimuleaza functiile tubulare si glomerulare

GLUCOCORTICIDS

Tissue	Glucocorticoid effects in Immature Cell	High Dose Glucocorticoids in Mature Cell
Bone	 Essential for differentiation in vitro Induces commitment to osteoblast lineage	 Increased Apoptosis Decreased Proliferation Increased Wnt Inhibitor synthesis
Cartilage	 Essential for differentiation in vitro Induces commitment to chondrocyte lineage	 Reduced Collagen and proteoglycan synthesis Reduced Proliferation
Muscle	 Stimulates early differentiation stages	 Increased Proteolysis Increased Atrophy Decrease in Growth Factor expression
Synovium/Skin	 Not essential for differentiation in vitro	 Decreased Inflammatory signalling Reduced Collagen Synthesis Reduced Proliferation
Adipose	 Increased differentiation	 Increased lipoprotein lipase activity Hypertrophy (site dependent)

GLUCOCORTICOIDS

Major Side Effects Associated with Corticosteroid Therapy

Dermatologic and soft tissue

- Skin thinning and purpura
- Cushingoid appearance
- Alopecia
- Acne
- Hirsutism
- Striae
- Hypertrichosis

Eye

- Posterior subcapsular cataract
- Elevated intraocular pressure/glaucoma
- Exophthalmos

Cardiovascular

- Hypertension
- Perturbations of serum lipoproteins
- Premature atherosclerotic disease
- Arrhythmias with pulse infusions

Gastrointestinal

- Gastritis
- Peptic ulcer disease
- Pancreatitis
- Steatohepatitis
- Visceral perforation

Renal

- Hypokalemia
- Fluid volume shifts

Genitourinary and reproductive

- Amenorrhea/Infertility
- Intrauterine growth retardation

Bone

- Osteoporosis
- Avascular necrosis

Muscle

- Myopathy

Neuropsychiatric

- Euphoria
- Dysphoria/depression
- Insomnia/akathisia
- Psychosis
- Pseudo tumor cerebri

Endocrine

- Diabetes mellitus
- Hypothalamic-pituitary-adrenal insufficiency

Infectious disease

- Heightened risk of typical infections
- Opportunistic infections
- Herpes zoster



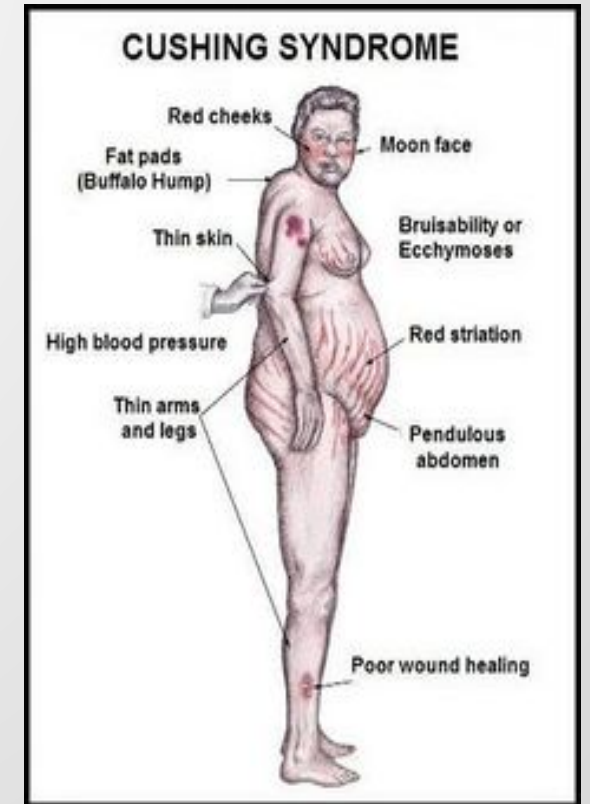
SIDE EFFECTS



EFECTE ADVERSE

A. Metabolice:

- DZ
- atrofie tegumentara
- atrofie musculara
- edeme
- osteomalacie/osteoporoza





EFECTE ADVERSE

B. Cardiovasculare:

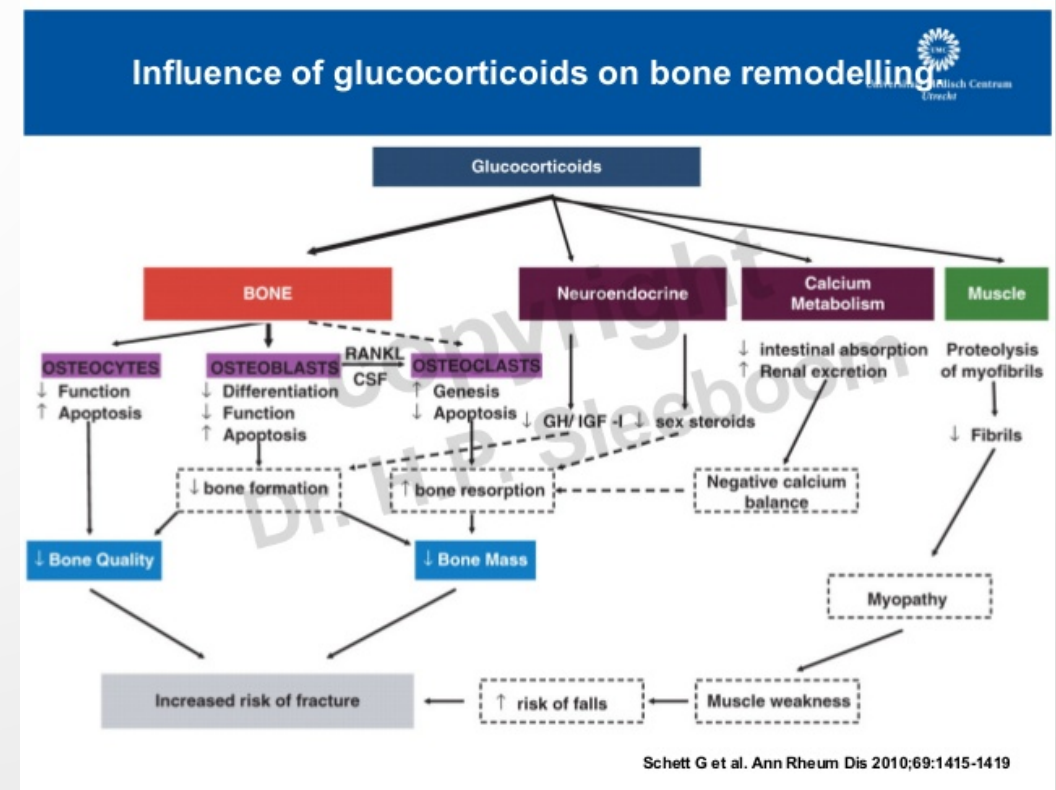
- ↑TA
- accelereza procesul de ateroscleroza

C. Muschi scheletici: atrofie



D. Metabolism osos

- osteoporoza: risc fracturar crescut
- adminstrarea concomitenta de suplimente de Ca, D3 sau tratamentul osteoporozei, cand este diagnosticata





E. Digestive:

- hipersecretie acida, scaderea secretiei de mucus→ administrare concomitenta de IPP
- stetaoza hepatica**



F. Endocrine:

- ICSR
- doze mari ↓ TSH
- tulburari de crestere si dezvoltare
- inhiba functia gonadala
- DZ



G. SNC

Doze mari-euforie, halucinatii

Tratament indelungat—risc de depresie



H. **Sistem imun**: scad rezistenta la infectii

I. **Ocular: cataracta, galucom**

UTILIZARI TERAPEUTICE

A.Efect antiinflamator si imunosupresor:

- afectiuni reumatologice: sistemic, intra-articular
- boli inflamatorii intestinale, boli hepatice autoimune
- astm bronsic, bronista cronica
- boli autoimune hematologice
- anterior transplantului de organ

B. Antialergic: rinite, dermatite, conjunctivite alergice, reactii alergice etc.

C. Medicatie de substitutie in ICSR

D. Soc anafilactic

Tipuri de GC

- Terapie de substitutie: hidrocortizon
- Terapie antiinflamatoare:

Durata scurta: hidrocortizon

Medie: prednisolon; metilprednisolon; triamcinolon

Lunga: dexametazona; betametazona

GLUCOCORTICOIDI

Comparison of representative glucocorticoid preparations

	Equivalent doses* (mg)	Relative antiinflammatory activity	Relative mineralocorticoid activity	Duration of action (hours)
Hydrocortisone (cortisol)	20	1	1	8 to 12
Cortisone acetate	25	0.8	0.8	8 to 12
Prednisone	5	4	0.8	12 to 36
Prednisolone	5	4	0.8	12 to 36
Methylprednisolone	4	5	0.5	12 to 36
Triamcinolone	4	5	0	12 to 36
Fludrocortisone	Not used for an antiinflammatory effect	10	125 [¶]	12 to 36
Dexamethasone	0.75	30	0	36 to 72

* **Equivalent antiinflammatory dose shown is for oral or intravenous (IV) administration.** Relative potency for intraarticular or intramuscular administration may vary considerably.

- **Cortizol and cortizon**

- durata 8-12 ore, efect antiinflamator redus
- in special local, de ex. Intra-ocular : Cortizon acetat, Hidrocortizon (cortizol) acetat-fi 25mg/ml
- hidrocortizon hemisuccinat- singurul hidrosolubil- 2-50mg, pana la 1g/zi

- **Prednison** (cpr 5mg)
- Conc. Plasmatica maxima 2-6h
- Biodisponibilitate 92%
- Legare de prot. plasmatică: 65-91%
- Metabolizat hepatic in prednisolon (activ)
- Tp de $\frac{1}{2}$ 2.6-3h
- Excretie: urinara
- 5-60mg/zi

- **Prednisolon**

- Conc. Plasmatica maxima: 5 min
- Durata 18-36h
- Legare de prot. plasmaticice 65-91%
- Tp de $\frac{1}{2}$ 3.6h
- Excretie urinara
- Doze: in functie de patologie pana la 200mg/zi

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- **Metilprednisolon** (cpr 4;16;32;64mg; flacoane 125;250;500mg-solutie)
- debut 1-2 h (PO); 4-8 zile (IM); 1 sapt. (intra-articular)
- Durata: 30-36 h (PO); 1-4 sapt. (IM)
- Conc. Plasmatica maxima: 31 min (IV)
- Tp de 1/2: 3-3.5 h
- excretie: Urinara majoritar
- efect antiinflamator 4-5> cortizol

- **Dexametazona**-fiole 4;8mg; cpr 4mg.
- Debut: minute-ore, in functie de calea de administrare
- Conc plasmatica maxima:: 8h (IM); 1-2 h (PO)
- Tp de $\frac{1}{2}$: 1.8-3.5 h
- -effect 20-30 X>cortizol
- utilizata in special ca antiinflamator

- **Beclometazona**-in special inhalator
- oral inhalation aerosol:
40mcg/puff
80mcg/puff
- debut: 24 h de la inceputul tratamentului; maximum 3- 4 sapt.
- Durata: 6 h
- Conc. Plasmatica maxima: 10 minute
- Tp de $\frac{1}{2}$ 4h

- **Betametazona**

- Topic
- Injectabil-suspensie 6mg/ml
- Conc plasmatica maxima: IV: 10-36 min
- Tp de $\frac{1}{2}$: 6.5 h
- Tenosinovite, peritendinite
- Afectiuni dermatologice: 1/zi
- RA, osteoartrite: intraarticular

- **Triamcinolon acetonid suspensie injectabila (Kenalog)**
 - 10mg/ml si 40mg/ml
 - IM, intraarticular
-
- **Triamcinolon topic -crema/unguent 0.025%, 0.1%, 0.5%**

- **Clobetazol**

- crema 0.025%, 0.05%;
- spuma 0.05%; gel 0.05%;
- unguent 0.05%;
- lotiune 0.05%;
- solutiie 0.05%.
- Indicatii: psoriazis, dermatoze