Info	
Corticosteroids CC	-its name: cortico = AG cortex, steroids = steroids -it's the mother class -its derivatives are: glucocorticoids GC & mineralocorticoids MC -given in a tapering manner: starter dose is high and goes down as days pass by, when its really low dose; we switch to another drug of the same family(alte-rnation of doses & drugs over time) -its levels in serum are variable during day or night (more at day)
Cortisol	-its from the cortex (hence its name) -it's the reference when measuring (the prototype): its effect regarding Anti-infl & ions retention are equal to 1 cortisol unit, So when saying that a med effect of anti-infl or ions retention is equal to 1, meaning its exactly as effective as cortisol, if we say its 0,5 meaning its half as good, etc…
Addison disease	-is def of CC (adrenocortical insufficiency) -symptoms: (know CC fun & you'll get them easily) hyperkalemia Hyponatremia Hypocalcemia weakness & fatigue weight loss depression anorexia (appetite loss) low BP skin hyperpigmentation
Addison crisis	-is an emergency case of hypersymptoms of Addison disease -presentation: exagg Addison symptoms severe fever sever vomiting, dia & abdominal pain confusion & shock

CC antagonists	
Types	**receptor antagonists** -Aldosterone: <u>spironolactone & eplerenone</u> -GC & progesterone: <u>mifepristone</u> (competitive, treats cushing) **Synthesis antagonists** -aminogluthimide, metyrapone & ketoconazole -ind: adrenal tumor (when surgery is useful due to metastasis)
Ketoconazole	-is: anti-fungal -MOA: inh cytochrome p450 enz (essential for all steroids synth.) -ind: adrenal, prostate & breast tumors & hirsutism
Amino-gluthimide	-MOA: blocks conversion of cholestrole into pregnelone (thus inh synth of all steroid hormones) -ind: adrenocortical hormone-producing tumors -usage: conjugated with other drugs

GC & MC (VIP)		
Hormone	**GC**	**MC**
Synthesized in	Zona fasciculata	Zona glomeruloza
Release form	-cortisol -cortisone -corticosterone	Aldosterone
Regulated by	-ACTH (strongly) -CAT -neuropeptides -cytokines	-ACTH (minutely) -K -neuropeptides -ANP -angiotensin 2 -dopamine
Fun	-metabolisms control (carbs, fat & Pr) -Anti infl effect	-ions retention
Inc in	Cushing	-conn syndrome: Hyperaldosteronism Hypernatremia & hypokalemia Hypervolemia & hypertension
Dec in	Addison	-hyperkalemia -acidosis -hyponatremia -hypotention -wasting -shock

MC (Aldosterone)	
Med	-Aldosterone (present naturally in the body, but given as supp) -fludrocortisone (used as replacement therapy after adrenalectomy)
Ald regulation	-by ACTH & renin-angiotensin system (a system specialized in ions retention maintaining normal blood volume & pressure)
MOA	ID to GC
hl	- Aldosterone: Very short (thus, short activity) - fludrocortisone: prolonged (significant acitivity)

GC drugs (drugs containing GC)		
In from of	Cortisol(hydrocortisone) & cortisone.	
MOA	-simply binding to its normal GC receptor and exerting its effect	
Receptor	**Membranous** -rapid action (non-genetic) -by altering Ca & cAMP -using Pr kinase A&C	**Cytosolic** -slow action (genetic related) -by actv anti-infl (lipocortin) & inh pro-infl (AP1) -by promoting what lessens infl & lessening what promotes infl
Absorption	Have a systemic effect even if given locally (skin, inhalation…)	
Pr binding	-<u>Strongly</u> bound to Corticosteroids Binding Globulin (CBG) & albumin, and can never be used by tissues unless its unbound. -all CC have significant affinity to bind to CBG (GC > MC)	
1st pass effect	-Positive (it activates it - so its normally given inactive!) -cortisone is activated into: hydrocortisone -prednisone is activated into: prednisolone	
Dosage timing	Must follow normal circadian Rhythm (given at early morning) to best mimic normal hormone secretion.	
withdrawal	-if it was given in high doses or for long time, it must be withdrawn taperingly, or it will cause <u>severe adrenocortical insuff</u>	
Effects	**Metabolisms** -Ca: inc excretion & less absorption (anti-Vit D effect) -carbs: inc glucogenesis & dec glucose usage (hyperglycemia) -fat: fat redisposition, causing moon face & buffalo hump By lipolysis & lipogenesis (+over all more lipolysis) -Pr: inc catabolism & dec anabolism muscles atrophy & N imbalance. Lymph & CT atrophy too Uric acid (gout) & bone catabolism (Osteoporosis) Growth disturbance (children) Skin atrophy & capillaries fragility (bruises & stria) **CVS** (causes hypertension, due to Salt in cortisol, causing retint.) -dec vascular permeability(used to treat CNS postsurgery edema) **Anti-infl** (inc neut, dec: lmypho, eosino, basophil, & monocytes) -dec synthesis of infl mediators (no aggregation, migration) -dec Ig affinity to bind to Ag -<u>massive dec in infl cells activity</u> (cell mediated effect “mostly”) -dec complement system (fancy word for immune system) **CNS** (psychosis & euphoria“due to CNS electrolytes disturbance”)	

<table>
<tr><td>intake</td><td colspan="2">-Mostly oral, parenteral is also available(IV, IM & SC)
-very poor skin diffusion</td></tr>
<tr><td rowspan="3">Meds</td><td>Systemics</td><td>(short hl - 12h) “inc Na retention”
-cortisol: Given IV or IM - Emergency use
-cortisone: Given IM - contraind: liver failure

(decent hl - 36h) “high anti-infl & little Na retention”
-prednisolone: given IM & intraticular (in joints)
can be used topically too
-triamcinolone: given IM & intraticular

(long hl - >36h) “high anti-infl & no Na retention”
-dexamethasone: given IM & IV - fluorinated
can be used topically too
-betamethasone: given IM & IV - fluorinated
“Fluorinated: combined with fluorine”</td></tr>
<tr><td>Topicals</td><td>“have good lipid penetration & less ions retention”

(potents)
-betaclomethasone: given as cream
-triamicinolone: given as ointment
“ointment is cream, but a bit thicker”

(moderate)
-fluticasone: given as cream
-mometasone: given as ointment

(safe)
-hydrocortisone acetate: given as ointment

“on sensitive skins -face, babies- never use potents”</td></tr>
<tr><td>Inhalants</td><td>-budesonide & beclomethasone: rapid systemic effect, with almost no toxicity due to super short hl</td></tr>
</table>

Ind	**Supplementary**	<u>(Addison crisis)</u> -parental cortisol & hydrocortisone -correction of electrolytes -treating all worsening factors <u>(Addison disease)</u> -oral: cortisol, fludrocortisone & dexamethasone <u>(cushing)</u> -to diagnose we use: dexamethasone suppres. Test -to treat we use: temporal cortisol (given after the primary treatment of cushing by surgical removal of PG, AG or CC secreting tumor)
	Anti-infl	"we use: prednisolone, dexamethasone & betamethasone" (allergy) serum sickness, angioneurotic edema, asthma, rhinitis, conjunctivitis, eczema& atopic&proliferative skin (Ai) Rheumatoid arthritis, IBS, SLE & nephrotic syndrome (blood pathies) Anemia, thrombocytopenia purpura & agranulocytosis (transplantation) (acute gout that is resistant to gout drugs)
	CNS & tumors	"we use: dexamethasone & betamethasone" -treat CNS tumors (either 1ry or 2ndry) -lessens postsurgery edema -given with cytotoxic chemotherapy as sideeffect preventer -suppresses ACTH release (negative FB) -given in Hodgkin & acute lymphoctic leukemia -addison disease

<table>
<tr><td>Side effects</td><td colspan="5">-iatrogenic cushing (cushing-induced GC)
-hyperglycemia, DM, glycosuria (can be treated by chaning fluorinates)
-muscles atrophy -growth impairment (children)
-antiInfl effect inh tissue healing -hypertension (ions retention)
-fat redistribution -menstrual disturbance
-hairsutism -stria -osteoporosis
-psychosis -acne -peptic ulcers (spec with NSAID)
-femur head avascular necrosis (specifically with GC)
-ocular toxicity: glucogoma cataract (specifically with GC)
-inf wherever its used, cuz it suppresses local immunity there</td></tr>
<tr><td rowspan="2">How to withdraw</td><td rowspan="2">Have it been given for < 1 week?</td><td>Nope</td><td rowspan="2">Was it a Big dose?</td><td>Nope</td><td>Just cut it off</td></tr>
<tr><td>yup</td><td>Yup</td><td>Lessen the dose by <u>2,5 - 5mg</u> every 3 days</td></tr>
<tr><td rowspan="2">How to treat iatrohenic cushing</td><td rowspan="2">Can you stop the med?</td><td>No can do</td><td colspan="3">-treat each symptom separately
Hyperglycemia: antidiabetics
Osteoporosis: bisphosphonates
Peptic ulcers: H2 blockers & PPI</td></tr>
<tr><td>Yup</td><td colspan="3">Then withdraw that shit!</td></tr>
<tr><td>contraind</td><td colspan="5">-DM -heart failure -epilepsy history
-peptic ulcers -osteoporosis
-TB (can only be given if patient had chemotherapy beforehand)</td></tr>
<tr><td>Watchout</td><td colspan="5">-if a patient is on GC and at risk of severe stress (double the dose)
-in children (stop all live vaccines “due to suppressed immunity”)
-in pregnants (avoid fluorinateds & use teratogenicity)
-if newborn with a mother taking high doses of GC, give the newborn low doses of GC & lessens them gradually (to avoid AG cortex insuff)</td></tr>
</table>