Bones	
Components	**Inorganics** -70% -minerals (hydroxyapatite, Ca, PO4) -formed of osteoid mineralization by alkaline phosphatase **Organics** -30% -osteoids (an organic sub produced by osteoblasts)
Cells	**Blasts** -origin: mesenchymal **Clasts** -origin: myloid -made by: monocytes fusion -enz used: collagenase, metalloproteinase & hydrochloric acid
Remodeling regulation	**by systemic hormones:** **PTH** (little blasts & lots clasts /Ca retention /calcitriol production) **Calcitrol** (Ca&PO4 SI abs.“for bone mineralz”/clasts when Ca&PO4 are def) **Calcitonin** (weak in men / clasts) **Estrogen & androgen** (osteoclasts apoptosis / blasts / cytokines & GF release) **GC** (osteoblasts & osteocytes apoptosis / clasts) **Thyroids** (remodeling “both clasts & blasts”) **GH & IGF** (bone growth / endochondral bones formation)

Osteoporosis	
Risk	**Modifiable risks** -smoking -low Ca/Vit D diet -GC -OH -potato-life (sedentive) -estrogen def -poor eye sight -transplantation **Non-modifiable risks** -fractures history -1st degree relative fractures -race (white & Asians) -elders -poor health -demntia -hormone diseases -tumors -metabolic diseases -CT diseases
Treatment	-replace the lost bones (also used as prophylactic "prevention") -enhance blasts & inh clasts (anabolics & anti-resorptives)
Meds	-**thiazide-diuritics & statin** (used as treatment permissive only) -**fluorapatite** (replaces missing Ca, Vit D & Na fluoride) (its normally present in cortical bones) -**teriparatide** (anabolic) -**strontium** (the only med having clasts & blasts effect) -**bisphosphonates / rankle inh / androgen analoges / estrogen analoges / serms / calcitonin** (anti-resorptives)
Ind	Same for all meds, but varies depending on the patient (age…)

Meds	
(1) bisphosphonates (family)	
Structure	Having 2 PO4 (hence its name)
Drugs	**Nitrogenous**(alendronate, iblandronate, risedronate, zoledronate) **Non-N** "not imp" (etidronate, clodronate, tidronate) -3rd generation are the strongest clasts inh: zoledronate
MOA	-replaces bone pyrophosphate, clasts cant break bisphos… -inh clasts forming their little tenticles they use to dissolve bone -inh clasts cholesterol synth, they use cholesterol as a signaling for their metabolisms, so they apoptose -high affinity to bind to Ca (specially hydroxyapatite), so they conc in bones -it remains for months or years in bone (hence given once a week)
Administ.	-orally: on an empty stomach -IV: as a slow fusion (2h) monthly for 1st year taking it, then once every 3 months -to avoid GIT side effects: large water intake -to avoid GERD: give on upright posture (normal standing) -to avoid atrial fibrillation: start IV then switch to oral
Hl	1h
Excretion	Unchanged in urine
Doses	Once a week or twice on consecutive days a month
Ind	-osteoporosis secondry to menopausal or GC -paget disease -hypercalcemia due to tumors
contraind	-taking it within 4h of Ca, Mg or Al containing meds -bone surgery (dental) "cuz it interferes with bone healing" -GERD -renal diseases -peptic ulcers
Side effects	-atrial fibrillation (in women, with alendronate or zolidronate) -jaws osteo-necrosis (with slow IV fusion only) "triggered after dental surgery - due to metalloproteinase activation" -GERD -ulceration -flu symptoms (with IV only)

(2) rankle inhibitors	
Aka	Denosumabs
MOA	-inh RANKL from binding to RANK, which is present on pre-clasts, thus inh clasts formation -binds to mature clasts and apoptose them -does the action of Osteoprotegrin (a sub inh RANKL from binding to RANK)
Administ.	SC (twice a year)
Contraind	-hypocalcemia (Ca & Vit D levels must be corrected before admn) -TB
Side effects	-UTI -URTI -constipation -joints pain -cataract (whitness within eye's pupil, scary…) -eczema & skin rash (eczema: fancy word for skin rash…)
(3) strontium	
Activ frm	DiStrontium
MOA	-blasts: angonize Ca receptors on pre-blasts, forming blasts -clasts: angonize Ca receptors on pre-clasts, inh clasts formation & apoptose mature clasts -inc Osteoprotegrin (lessens clasts)
Adminst	Oral
Binding	-poor to plasma Pr -very strong to bones
Hl	60h
Excretion	In urine
Ind	-severe elders osteoporosis -2ndry to menopause or GC -tumors secreting Ca
Contraind	-severe renal failure -patient hypersens. To it -patients with risk of MI or thrombuses -phenylKetoUria -adminst within 2h of intake of: diary products, antacids, tetracycline & quinolone
Side effect	-MI -GIT disturbance -headache -eczema (goes away within 3 months)

(4,5) androgens & estrogens analogues (sup therapy)	
Estrogen supps	-given to an estrogen def woman with hysterectomy (uterus removed, no estrogen) -given to an estrogen & progestin def W without hysterectomy (uterus is present, but she's def in those, so we give both of them)
Androgen supps	-given to elder men
Hormone replacement Therapy	-at menopausal women, only if menopausal symptoms are present (like hot flashes)
SERM	-selective estrogen receptor modulators -used for elder men or menopausal women
androgens & estrogens fun	-remodeling -clasts apoptosis -release of GF by blasts -inh cytokines that cause resorption

(6) SERMs (raloxifene)	
MOA	-treats only osteoporosis, not all menopausal symptoms -agonist bone effects -antagonist femal sex organ effects
Drugs	**Estradiol** (affects: brain, uterus, Vagina, breasts, bones & CVS) **Raloxifene** (affects: bones & CVS "weakly") "better to use"
Adv raloxifene	-inc bone density (lessens fractures risk by 30%) -no breasts or endotheliums effects -no need to give progestin along it with women with uterus -lessens LDL
Disadv raloxifene	-risk of thrombosis -doesn't treat other post-menopausal symptoms -inc hot flushes -no effect of HDL