Bone Cell Lines

In the bone we have 3 types of cell lines

- The Osteoblasts – The depositing DDs
- The Osteoclasts – The withdrawal Cheques
- The Osteocytes – The Mechano-sensors
- The first two types conduct remodeling
- Trabecular and cortical bone (support)

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Bone Mass Development

- Peak bone mass by age 30-35 years
- 85% bone mass by age 20 years
- This is possible only with adequate calcium intake throughout childhood & exercise
- Bone mass declines from 40 years
- Yearly loss up to 1% in men above 50 yr
- Yearly bone loss up to 5% in women after menopause

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Osteoporosis (OS)

1. A skeletal disorder characterized by compromised bone strength predisposing to increased risk of #
2. A systemic disease – with bone loss; both qualitative and quantitative loss
3. Resultant easy predisposition to fractures with little or minor trauma
4. Up to 20% of bone loss occurs immediately after menopause
5. Resultant Morbidity, Mortality, QUALY
6. Social & Economic burden on the society

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Burden of Osteoporosis

1. Osteoporosis is a major health hazard
2. 124 million Indians currently have or at risk of Osteoporosis (OS)
3. Asian and European women more prone
4. 80% of OS cases are undiagnosed (hidden)
5. 55% of women and 40% men above the age of 50 years have significant bone loss
6. Half of them suffer from # in their lifetime

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OS – Global Burden

1. World wide 323 million fractures in 1990
2. 1.66 million are hip # alone due to OS
3. 1.55 billion # by 2050
4. 6.2 million hip # alone due to OS - 2050
5. Five times this number will have OS
6. 20% of hip # pts die within 1 year
7. 35 to 50% of them lose functionality

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OS – Risk factors

- Life style
  Low calcium and Vitamin D intake
  Low BMI < 19 (Thin frame)
  Limited exercise from childhood
  Smoking, Alcohol, Caffeine
- Genetic
  Female Gender, Asian or European,
  Vitamin D receptor gene, Procollagen, Chr. 11 gene
- ⬆ Age, Post menopausal, Previous #, Family H/o #
- Drugs: Glucocorticoids, Phenytoin, Thyroid hormone

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Risk Factors for OS

- Increasing Age
- Decreasing BMD
- Prior Fragility Fracture
- F H/o OS Fracture
- Menopause < 45 yrs
- Glucocorticoids
- Immobilization
- BMI < 19 (Thin Frame)
- Smoking, Alcohol excess
- Calcium intake < 500 mg
- Anorexia Nervosa
- Propensity to Fall
- DM for > 5 years
- RA, Primary ⬆ PTH
- Malabsorption syndromes
- Chronic Renal Failure
- Transplantation
- Hypogonadism
- Hyperthyroidism
- Eltroxin excess

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Physical Examination

- Wall Occiput Distance – marker of VCF
- Validated with Thoracic, Lumbar X-rays
- Standing straight – heels touching wall
- WOD > 3 cm PPV 69%, NPV 79%
- WOD > 7cm PPV 92%, NPV 76%
- Consider OS in # above 50 years
- Think of OS in ♀ > 50 and ♂ > 65 yrs.
- Ask for old CXRs to Dx vertebral # (VCF)

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Osteoporosis - Types

- Primary Osteoporosis
  - Post Menopausal OS – PMO (Type I)
  - Senile Osteoporosis – SOS (Type II)
- Secondary Osteoporosis
  - Gluco-corticoid induced OS – GIO
  - Other causes of secondary OS
- Osteoporosis with fracture(s)
- OS related # with re-fracture risk
- Osteopenia

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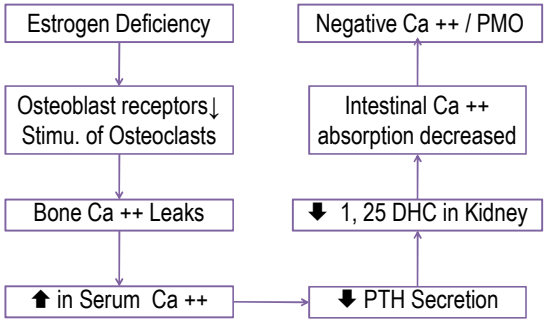
PMO (Type I OS)



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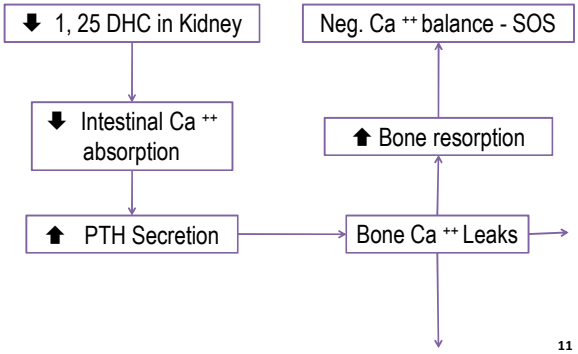
Senile OS (SOS - Type II)



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Gluco-corticoid Induced OS (GIO)

1. Common iatrogenic OS (secondary)
2. 3-6 months continuous use is needed to cause
3. Inhaled steroids in high doses may cause
4. Oral steroid use for chronic asthma, Skin COPD, RA, Inflammatory BD – common causes
5. 50% pts. suffer OS related #
6. Must consider doing BMD
7. Consider drug therapy with Bisphosphonates

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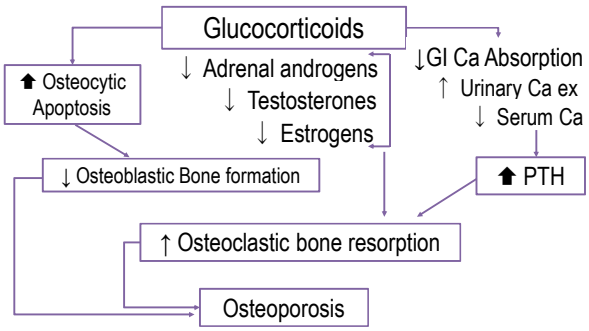
G I O - Pathophysiology



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Tests for Secondary OS

- CBC, ESR
- For PTH – Calcium, Phosphorous
- For Kidney – Creatinine
- Liver – AKP, GOT, GPT, Albumin
- Thyroid – TSH (fasting)
- Testosterone in men
- Estradiol, FSH, Androgens in ♀
- Urinary calcium, free cortisol
- Protein electrophoresis for MM

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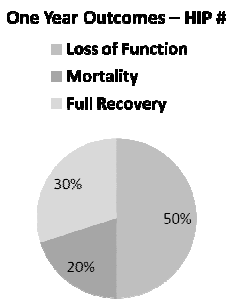
Osteoporotic Fractures

- Hip
- Vertebral Compression (T and L)
- Colles' / Distal Radius
- Proximal Humerus
- Proximal Tibia
- Pelvic bone
- Malleolar ankle #



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Who should have BMD test ? (WHO)

- Anyone sustaining a pathologic fracture
- Anyone with loss of height of >2" or vertebral compression fractures (kyphosis or hump)
- Women > 60; men > 65 age, DM over 5 yrs
- PM women < 60 with risk for osteoporosis
- Patients on Glucocorticoids or Pr. H/0 Rx.
- Patients considering drug therapy for OS
- Follow up of patients on Rx. for osteoporosis

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Advantages of BMD

- BMD values follow normal distribution
- Mean BMD decreases with age in ♀, ♂
- BMD is inversely related to # risk
- WHO adopted BMD to define OS
- Asymptomatic OS can be Dx before #
- BMD is effective in predicting OS #
- Good sensitivity and high specificity

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Short comings of BMD

- BMD values are site specific
- Exposure technique plays a role
- BMD is decreased in osteomalacia
- Cannot differentiate between primary and secondary OS
- Patient management to be based on clinical features - not on BMD alone

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WHO 'T' Score of BMD

T Score =

$$\frac{\text{Patient BMD} - \text{BMD of Young adult}}{\text{Standard deviation of the young adult (same sex)}}$$

Normal BMD = 'T' Score between–1 to + 1 SD

Osteopenia = 'T' Score between –1 and–2.5 SD

Osteoporosis = 'T' Score of –2.5 SD and lower

Osteoporosis (Severe) = 'T' Score of –2.5 SD and lower with associated fractures

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Densitometry - Options

DEXA	Dual Energy X-ray Absorptiometry
SEXA	Single Energy X-ray Absorptiometry
pDEXA	Portable DEXA
QUS	Quantitative Ultrasound
QCT	Quantitative Computed Tomography

Contraindications for DEXA

- Pregnancy – risk versus benefit
- Recent GI contrast studies (< 72 hrs)
- Recent nuclear medicine tests
- Excessive obesity – Weight > 110 kg

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Densitometry - Options

Modality	Reproduci.	Versatility	Cost	Radiation
DEXA	++	++	2000	+
SEXA	+	-	2000	++
pDEXA	+	-	1500	+
QUS	+	-	600	-

pDXA and QUS are for screening, QCT in obese for spine

QCT is sophisticated, accurate but costly (5000)

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Therapeutic Options

- Decrease the risk of fracture
- Maintain bone integrity
- Prevent bone loss and
- Regulate bone turnover
- Relieve symptoms of # and deformity
- Improve mobility and function
- Calcium and Vitamin D
- HRT or ERT – low dose
- Bisphosphonates
- Selective Estrogen Receptor Modulators (SERM)
- Androgens
- Calcitonin
- Future treatment options

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Calcium – How Much ?

Children	800 – 1200 mg
Teens and youngsters	1200 – 1500 mg
Women (25 to 50 yrs)	1000 mg
Men (25 to 60 years)	1000 mg
PM Women on HRT	1000 mg
PM women not on HRT	1500 mg
Men and women > 65 yr	1500 mg
Pregnant and lactating	1200 – 1500 mg

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Bisphosphonates

- Affect the "balance" of bone metabolism;
- They are NOT hormones
- Bind tightly & inhibit Osteoclastic bone resorption
- They increase BMD at spine and hip
- Their efficacy is equal to estrogen
- Randomized trials showed 30-50% reduction in fractures including hip #
- Bone loss will resume after d/c of therapy

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Bisphosphonates

Administering method

- To be taken 30 minutes before Breakfast
- Take with a full tumbler of plain water
- Be in erect position for at least for 1 hr.

Various Biphosphonates

- Alondrenate (Fosamax) 10mg or70mg oral
- Risedronate (Actonel) 5mg or 35mg oral
- Etidronate (cyclical) injectable
- Ibandronate monthly IV injections 0.5 – 2 mg

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SERMs

- Bind to estrogen receptors and exert an estrogen-like effect on bone, not on UT, Breast
- Can increase BMD by 30-50% and decrease spinal # but no effect on hip or other #
- Can be used in prevention & Rx. of PMO
- Contraindicated in pts. with h/o VTE
- May cause - hot flushes, leg cramps, DVT.
- Interact with Warfarin which need to be closely monitored

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SERMs

- Raloxifene (Evista)
- Tamoxifen
- Levormeloxifene
- Idoxifene
- Droloxifene

Mixed estrogen agonist and antagonist activity – They occupy the estrogen receptors and simulate estrogen on bone and increase BMD and reduce OS

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Calcitonin

- 32 AA peptide from the C cells of the Thyroid
- Inhibits osteoclastic activity
- Decreases bone resorption
- Available as nasal spray (Miacalcin)
- Salmon or Human calcitonin spray
- 200 IU daily nasal spray
- 100 IU subcutaneous daily
- Suppositories are weak in action

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New Therapies

- Paratharmone related peptide (PTHrp)
- Teriparatide (Forteo) 20 mcg OD injections
- Tibolone (Gonadomimetic)
- Osteoprotegerin (OCIF) (RANK-L)*
- Vitamin D analogues (Calcipotriol, Tacalcitol)
- Strontium renolate
- Phyto-estrogens

•Receptor Activator of Nuclear Factor kappa B and its Ligand – RANK-L

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Conclusions

- Osteoporosis is a preventable disease
- Good peak bone mass should be attained
- It is not simply aging – like grey hair
- Excellent technology is in place for BMD
- Persons at risk can be identified and Rx.
- Modern Rx. based on RCT is available
- Calcium intake and exercise are essential
- Think of yourself with # hip or # vertebra

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