Osteoarthritis and Osteoporosis

Dr Rakesh Sehrawat
Assistant Professor
Dept. of Orthopaedics
HIMSR and HAHC Hospital
New Delhi

Articular cartilage

- It is **hyaline cartilage**, which is smooth, resilient and enables frictionless movement
- It is **avascular** and has **no nerve supply**
- It **does not have perichondrium**
- It **lacks the ability to properly repair and regenerate itself**.

- **Articular cartilage is divided into 4 zones:**

1. **Superficial zone**: thinnest zone, covers joint surface.
   - Densely packed collagen with little polysaccharide.
   - flattened and ellipsoid shaped chondrocytes arranged parallel to joint surface.
2. **Transition zone**

3. **Middle zone or radial zone or deep zone**: Chondrocytes are spheroidal and most active synthetically.
    - Contains largest diameter collagen fibrils, highest concentration of proteoglycans and lowest concentration of water.
4. **Calcified cartilage zone**: cells are small with very little metabolic activity.

Osteoarthritis or Osteoarthrosis

- **Most common joint disease**
- **Chronic degenerative disorder** of synovial joints primarily involving articular cartilage.
- Non inflammatory condition

- **Progressive softening and disintegration of articular cartilage**: **subchondral bone is denuded (Eburnation)** and becomes hard and glossy,
- New growth of cartilage and bone at joint margins: **osteophytes**
- **Subchondral cysts** and **sclerosis.**
- **Mild synovitis** and **capsular fibrosis**.

Normal ageing vs OA pathology of articular cartilage

Cartilage property	Aging	Osteoarthritis
Total water content	Decreased	Increase in initial stages, decrease in advanced stage
Chondrocyte population and synthetic activity	Decreased	Increased in early stage, decrease in advance stage
Proteolytic enzymes: proteases	Normal	Increased
Proteoglycan content	Decreased	Decreased

Cartilage property	Aging	Osteoarthritis
Collagen	Inc cross-linking	Disrupted collagen organization
Keratan sulphate	Increased	Decreased
Chondritin sulphate 4/6 ratio	Decreased	Increased
Hyaluronate	Increased	Decreased

Causes of OA

A. Primary/ idiopathic OA

- *More common form.*
- Occurs in **old age**
- Weight bearing joints(Hip and Knee) in case of **monoarticular OA**
- Joints of hands are involved in **polyarticular OA**

Risk factors for Primary OA

- Old age
- Overuse
- Obesity
- Family history of OA
- Female sex
- Smoking

B. Secondary OA

- **Underlying primary disease of joint** leads to degeneration of joint.

1. **Trauma:** intra-articular fractures.
2. **Congenital/developmental disorders**: Perthe's, SCFE, varus/valgus deformity, bone dysplasias

3. **Metabolic disease**: Ochronosis (alkaptonuria), hemochromatosis, Wilson's disease, Gaucher's disease
4. **Endocrine disorders**: Acromegaly, hyperparathyroidism, DM, obesity, hypothyroidism
5. **Calcium deposition disease**: **Apatite arthropathy**
6. **Inflammatory**: RA, JRA
7. **Other joint disorders**: AVN, gout, infection, osteopetrosis, paget's disease etc

Joints involved in OA

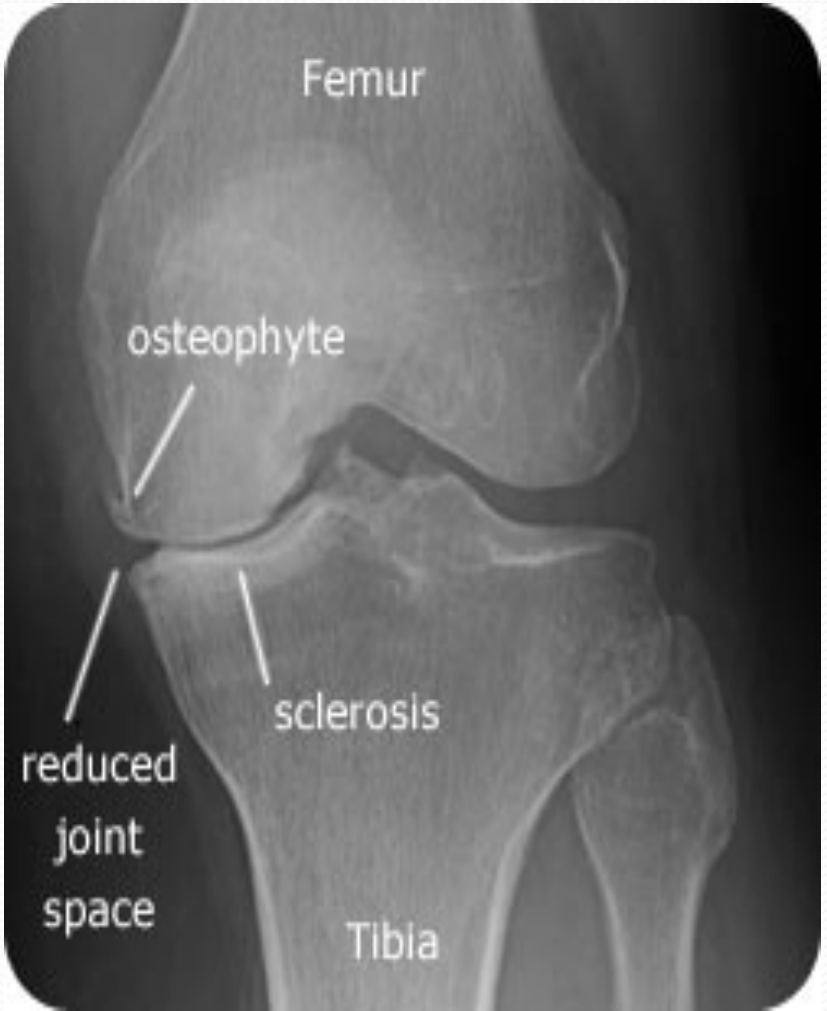
- **Commonly affects Hip, Knee, cervical spine, lumbosacral spine and 1st MTP joint.**
- **Hand: DIP, PIP and 1st CMC jt(base of thumb) are involved** and **MCP jts are spared**.
- **Spared jts: wrist, elbow, MCP, ankle**

OA of hand:

- **Heberden's node**: at **DIP** jt.
- **Bouchard's nodes**: **PIP** jt

Radiological features of OA

- **Narrowing of joint space: earliest**
- Subchondral sclerosis
- Subchondral cyst
- Spurring or lipping of joint from formation of osteophytes
- Loose bodies
- Deformity of joint



- In knee joint medial joint space is affected earliest: **asymmetrical joint space narrowing**, results in varus deformity.

Radiological classification of OA

Ahlbach's classification: applicable to **knee joint**

Type I: joint space narrowing

Type II: total loss of joint space

Type III: < 5mm tibial erosion

Type IV: 5- 10 mm tibial erosion

Type V: > 10 mm tibial erosion or subluxation

Treatment of OA

- **Type I to type III: conservative treatment:**

i. Life style modification

ii. Physiotherapy(exercise)

iii. Pharmacological therapy: NSAID's, intraarticular injection of hyaluronic acid or steroid.

- **Surgery: if conservative treatment fails:**

i. Arthroscopic washout and debridement

ii. High tibial osteotomy

iii. Unicompartmental arthroplasty

iv. Total knee arthroplasty

- **Type IV and V: total knee arthroplasty**

OSTEOPOROSIS

- *Osteoporosis is a systemic skeletal disease*

- *Characterized by*

  1. Low bone density

  2. A micro- architecture deterioration of bone tissue

  3. Enhance bone fragility

  4. Increase the risk of fracture

- **Decreased mass per unit volume of a normally mineralized bone**
- **Commonest metabolic bone disease**
- **Predominant bone resorption with decreased bone formation.**

- **WHO** defines osteoporosis as a **bone density that falls 2.5 standard deviations (SD) below the mean for young healthy adult female —also referred to as a T-score = or < –2.5.**

Definition	Bone Mineral Density Measurement	T-Score
Normal	BMD within 1 SD of the mean bone density for young adult women	T-score ≥ –1
Low bone mass (osteopenia)	BMD 1–2.5 SD below the mean for young-adult women	T-score between –1 and –2.5
Osteoporosis	BMD ≥2.5 SD below the normal mean for young-adult women	T-score ≤ –2.5
Severe or “established” osteoporosis	BMD ≥2.5 SD below the normal mean for young-adult women in a patient who has already experienced ≥1 fractures	T-score ≤ –2.5 (with fragility fracture[s])

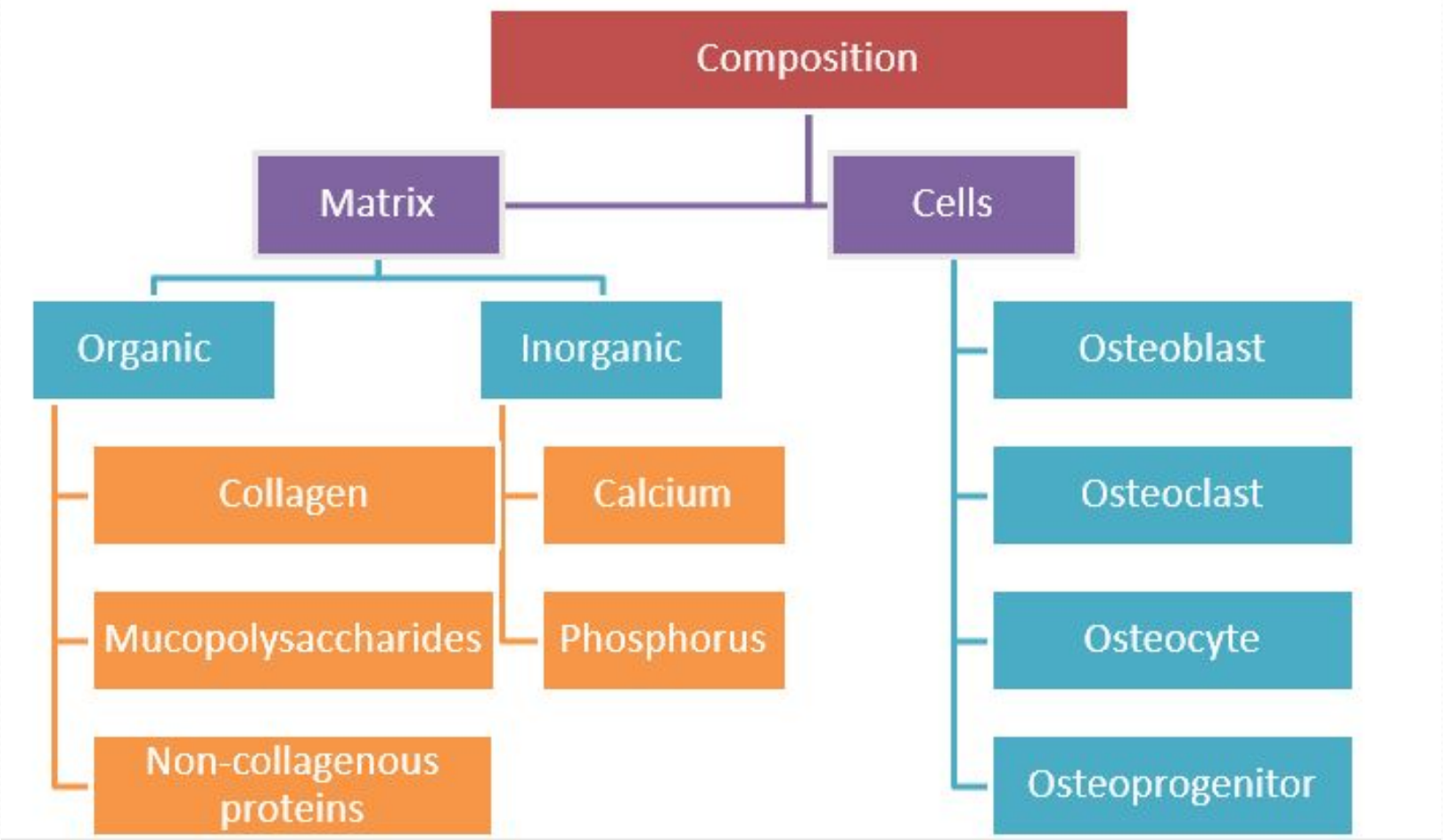
Epidemiology

- 1 in 3 women over 50 years suffer from osteoporosis
- 1 in 5 men over 50 years suffer from osteoporosis
- 15% - 30% men and 30%- 50% women suffer fractures related to osteoporosis in their life time
- Peak incidence
  - Western countries -70 – 80 years
  - India – 50 – 60 years

- **In women it is three times** more common than men because
  1. **Low peak bone mass (PBM)**
  2. **Hormonal changes at menopause**
  3. **Live longer than men**

- Vertebral and wrist fractures are more common in women

Constituents of Bone



Pathophysiology

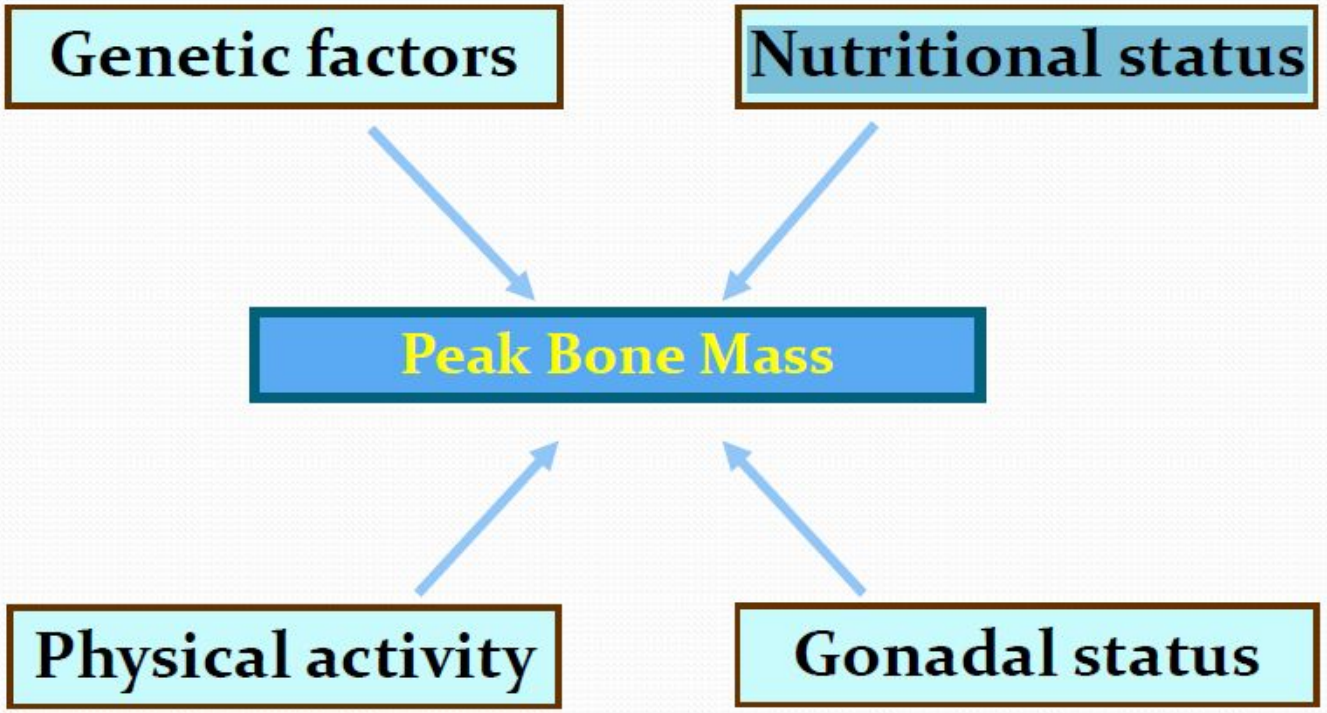
1.PEAK BONE MASS

2.BONE REMODELLING

1. Peak bone mass & Osteoporosis

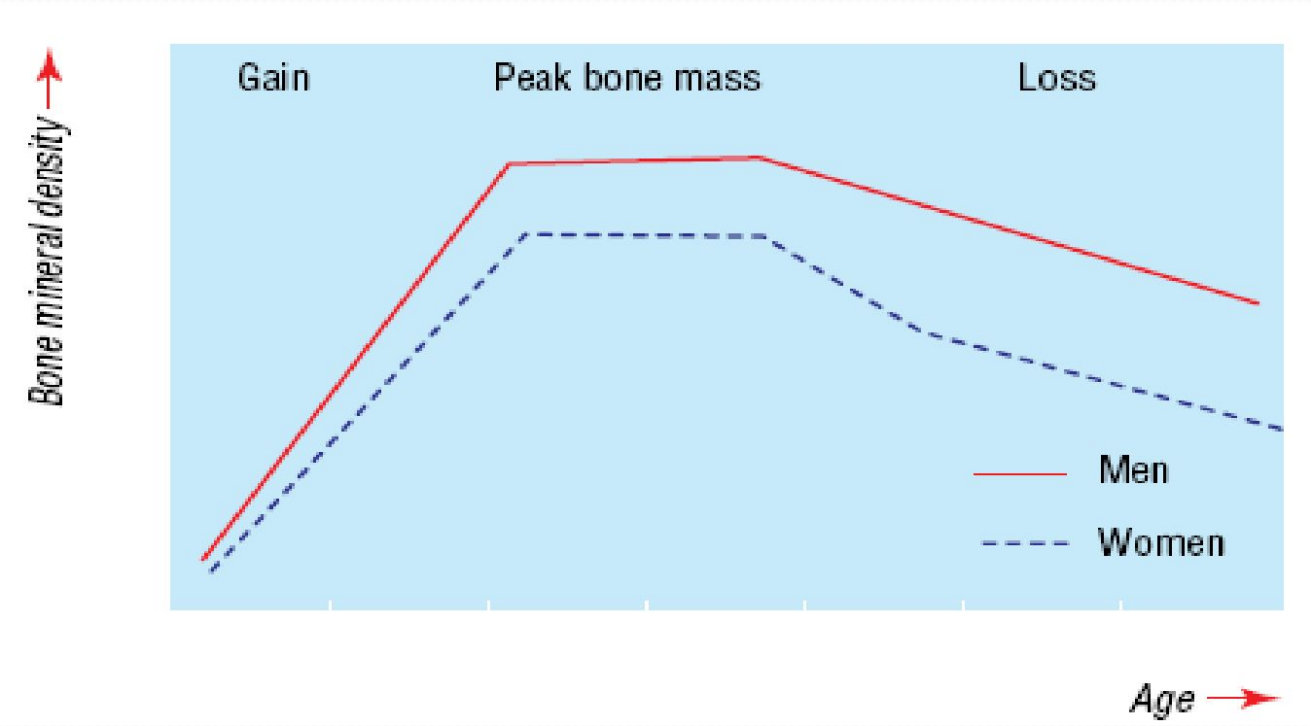
- Peak bone mass is the maximum mass of bone achieved by an individual at skeletal maturity, typically between **ages 25 and 35**
- **After peak bone mass is attained**, both men and women lose bone mass over the remainder of their **lifetimes**
- **Because of the subsequent bone loss, peak bone mass is an important factor in the development of osteoporosis**

Determinants Of Peak Bone Mass



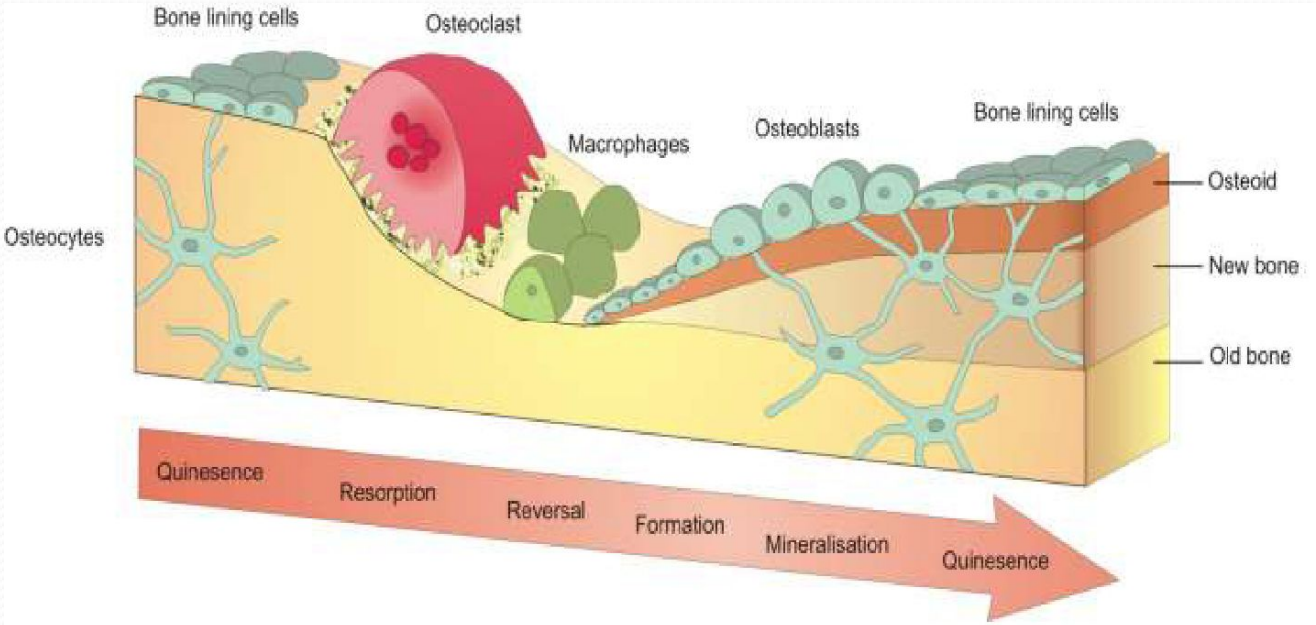
Peak Bone Mass in Women

- Women achieve lesser peak bone mass than men



2. BONE MODELLING AND REMODELLING

- **MODELLING**- during growth, skeleton increases in size by apposition of new bone tissue on outer surface of cortex
- **REMODELLING**- It is a cellular process of bone activity by which both cortical and calculus bone are maintained



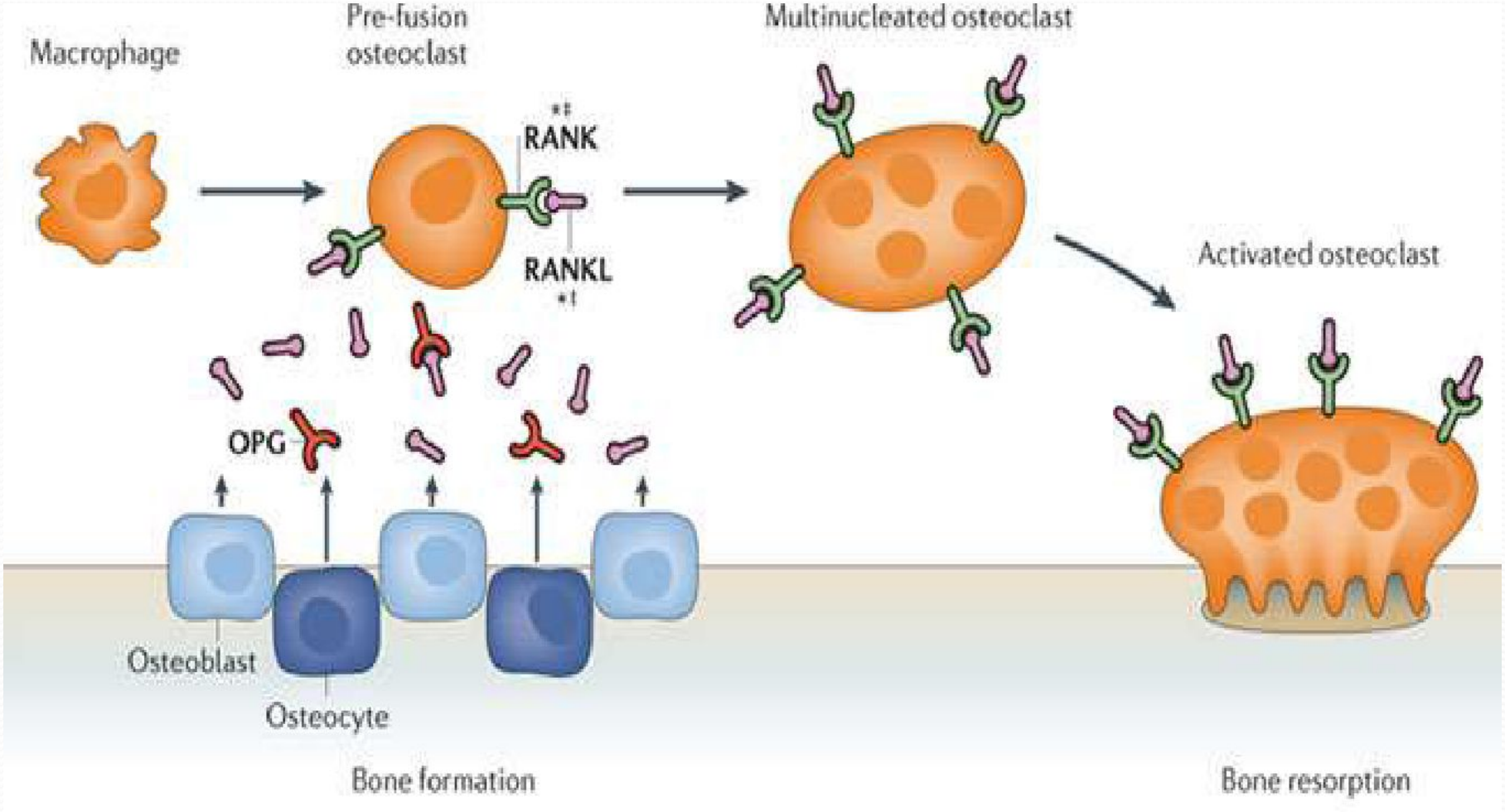
- OSTEOPOROSIS results from bone loss due to age related changes in bone remodelling as well as extrinsic and intrinsic factors that exaggerate this process
- Bone remodelling has two main functions

1. To repair micro damage within skeleton to maintain skeletal strength

2. To supply calcium to maintain serum calcium levels

RANK – RANK L RECEPTOR PATHWAY FOR BONE REMODELLING

- RANK L- the cytokine responsible for communication between osteoblasts and other marrow cells and osteoclasts.(receptor activated nuclear factor kappa ligand)
- Secreted by osteoblast and certain cells of immune system
- RANK- receptor present on osteoclast
- Activation of RANK by RANKL is final common pathway for osteoclast differentiation and functioning
- Osteoprotegerin is humoral decoy for RANK secreted by osteoblasts


Macrophage
Pre-fusion osteoclast
RANK
RANKL
Multinucleated osteoclast
Activated osteoclast
OPG
Osteoblast
Osteocyte
Bone formation
Bone resorption

Hormones & Growth factors regulating bone formation

Factor	Target cells & tissue	Effect
Interleukins (IL-l, IL-3, lL-6, IL-ll)	Bone marrow, osteoclasts	Stimulate osteoclast formation & resorption
Tumor necrosis factor (TNF-a) ; Granulocyte macrophage stimulating factor (GM-CSF)	Osteoclasts	Stimulates bone resorption
Leukemic inhibitory Factor	Osteoblasts, osteoclasts	Stimulates osteoblast and Osteoclast formation in marrow

Factor	Target cells	Effect
Parathyroid Hormone (PTH)	Kidney & Bone	Stimulate production of Vit-D & helps resorption of calcium
Calcitonin	Bone osteoclasts	Inhibits resorptive action of osteoclasts: lowers circulating Calcium.
Calcitriol (1.25-dihydroxy vit-D3)	Bone Osteoblasts Bone Osteoclasts, Kidney, Intestine	-Stimulates collagen, osteopontin, osteocalcin synthesis; -stimulates cell differentiation; -Stimulates Calcium retention -Stimulates calcium absorption
Estrogen	Bone	Stimulates formation of calcitonin receptors, inhibiting resorption,; Stimulate bone formation
Testosterone	Muscle, Bone	Muscle growth, placing stress on bone to stimulate bone formation
Prostaglandins	Osteoclasts	Stimulate resorption and bone formation
Bone Morphogenic protein	Mesenchyme	Stimulate cartilage protein & bone matrix formation; replication

Clinical features

- **SILENT DISEASE:** Asymptomatic unless fracture occurs
- **Mc symptom is back pain** due to **vertebral compression fracture.**
- **Dorsolumbar-spine** is mc involved: **Kyphotic deformity.**
- Loss of Height.
- Other common sites of fracture : **distal radius, neck of femur.**
- **Serum calcium, phosphate and alkaline phosphatase are normal in osteoporosis.**

Risk Factors for Osteoporotic fractures

(Major) with relative risk >2	(Minor) with relative risk 1-2
Age >70	Estrogen deficiency
Menopause <45	Calcium intake <500mg/day
Hypogonadism	Primary hyperparathyroidism
Fragility fracture	Rheumatoid arthritis
Hip fracture h/o in parents	Hypercalciuria
Glucocorticoids	Anticonvulsants
High bone turnover	Diabetes mellitus
Anorexia nervosa	Smoking
<18 BMI	Alcohol
Immobilisation/sedentary life	
Chr. Renal failure	
Transplantation	
Chronic Inflammatory diseases	

Differential Diagnosis

- Hyperparathyroidism
- Paget's disease
- Osteomalacia
- Osteogenesis imperfecta
- Multiple myeloma
- Secondary tumours

Diagnostic Imaging

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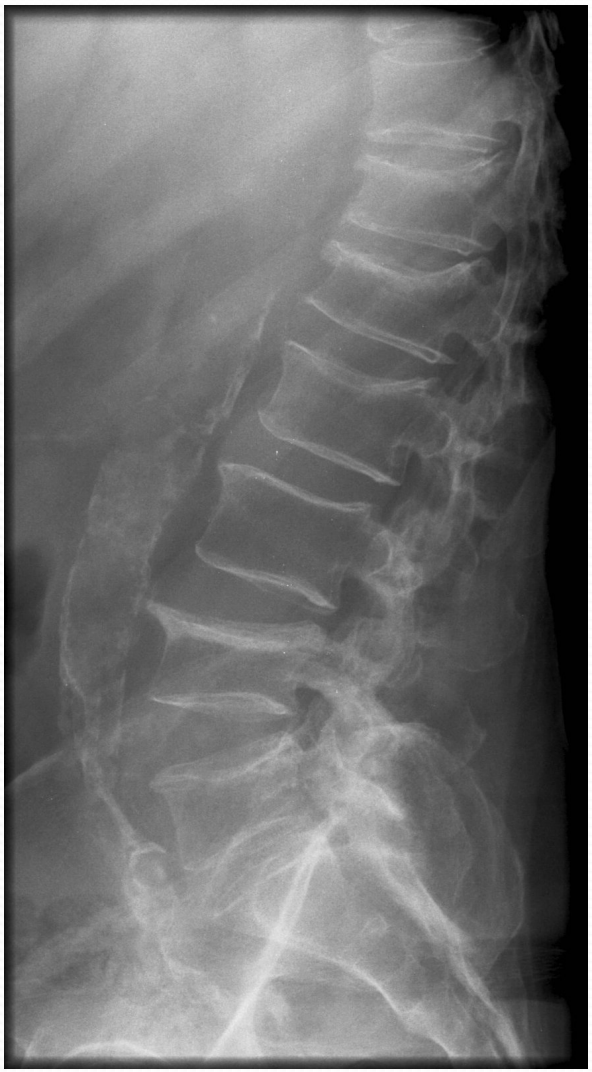
X-Ray

- Atleast 30% of bone mass must be lost before it is visible on xray.
- **Loss of vertical height of vertebrae** due to collapse
- **Cod fish appearance**: disc bulges into the adjacent vertebral bodies, appears biconvex
- **Ground glass appearance** of bones: increased radiolucency



- Post menopausal osteoporosis :Trabecular resorption and cortical resorption
- Senile osteoporosis: Endosteal resorption
- Hyperparathyroidism: Sub periosteal resorption

INDICATIONS FOR VERTEBRAL IMAGING

1. All women age 70 and older and all men age 80 and older if BMD T-Score at the spine, total hip or femoral neck is <-1.0

2. Women age 65 to 69 years and men age 70 to 79 if BMD T-Score at the spine, total hip or femoral neck <-1.5

3. Postmenopausal women and men age 50 and older with specific risk factors like:

A. Low trauma fracture during adulthood {age 50}
B. Historical height loss of 1.5 inches or more {4cm}
C. Prospective height loss of 0.8 inches or more {2cms}
D. Recent or on-going long term glucocorticoid treatment

Conventional radiography

LS SPINE-

- Generalized osteopenia
- Thinning and accentuation of cortex
- Accentuation of primary trabeculae and thinning of secondary trabaculae
- Vertically striated appearance vertebral body

Disadvantages of X-Ray:

- Subjective
- Affected by body habitus , exposure, positioning
- >30% bone loss should be present

- **Singh index:** trabecular pattern of femoral neck is graded into six grades. Used to grade osteoporois on x-ray.
- Metacarpal index and vertebral index
- **Gold standard for diagnosing osteoporosis: DEXA scan**

Bone Mineral Density

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Indications for BMD testing

- In women age 65 and older and men age 70 and older
- In postmenopausal women and men above age 50–69, based on risk factor profile
- In postmenopausal women and men age 50 and older who have had an adult age fracture, to diagnose and determine degree of osteoporosis
- At dual-energy X-ray absorptiometry (DXA) facilities using accepted quality assurance measures

TABLE 19-3 Methods for Bone Mineral Measurement

Ionizing Radiation		Nonionizing Radiation
Gamma Radiation	*X-Ray*	
Single photon absorptiometry (SPA)	Radiogrammetry	
Dual photon absorptiometry (DPA)	Single x-ray absorptiometry (SXA)	Ultrasound
Neutron activationanalysis (NAA)	Dual x-ray absorptiometry (DXA)	Magnetic resonance tomography (MRT)
Compton scatteringtechnique	Quantitative computed tomography (QCT)	

Sites of measurement are the spine, the hip, calcaneum and the wrists

DEXA SCAN

- Commercially introduced in 1987
- Principle – 2 x ray of 70Kv and 140kv are fired on site of measurement with lag time 0f 4ms
- Detector detects accentuation of 2 beams
- Data is fed into computer powered with complex algorithm and calculates BMD

SITES

- Central DEXA- lumbar spine, hip, whole body
- Peripheral DEXA- forearm , calcaneum

CONTRAINDICATIONS-

- Pregnancy
- Recent administration of contrast Agent, nuclear medicine scan
- Radiopaque implant in measurement area
- Marked obesity

- **T-score: compare individual results to those in a young female population**

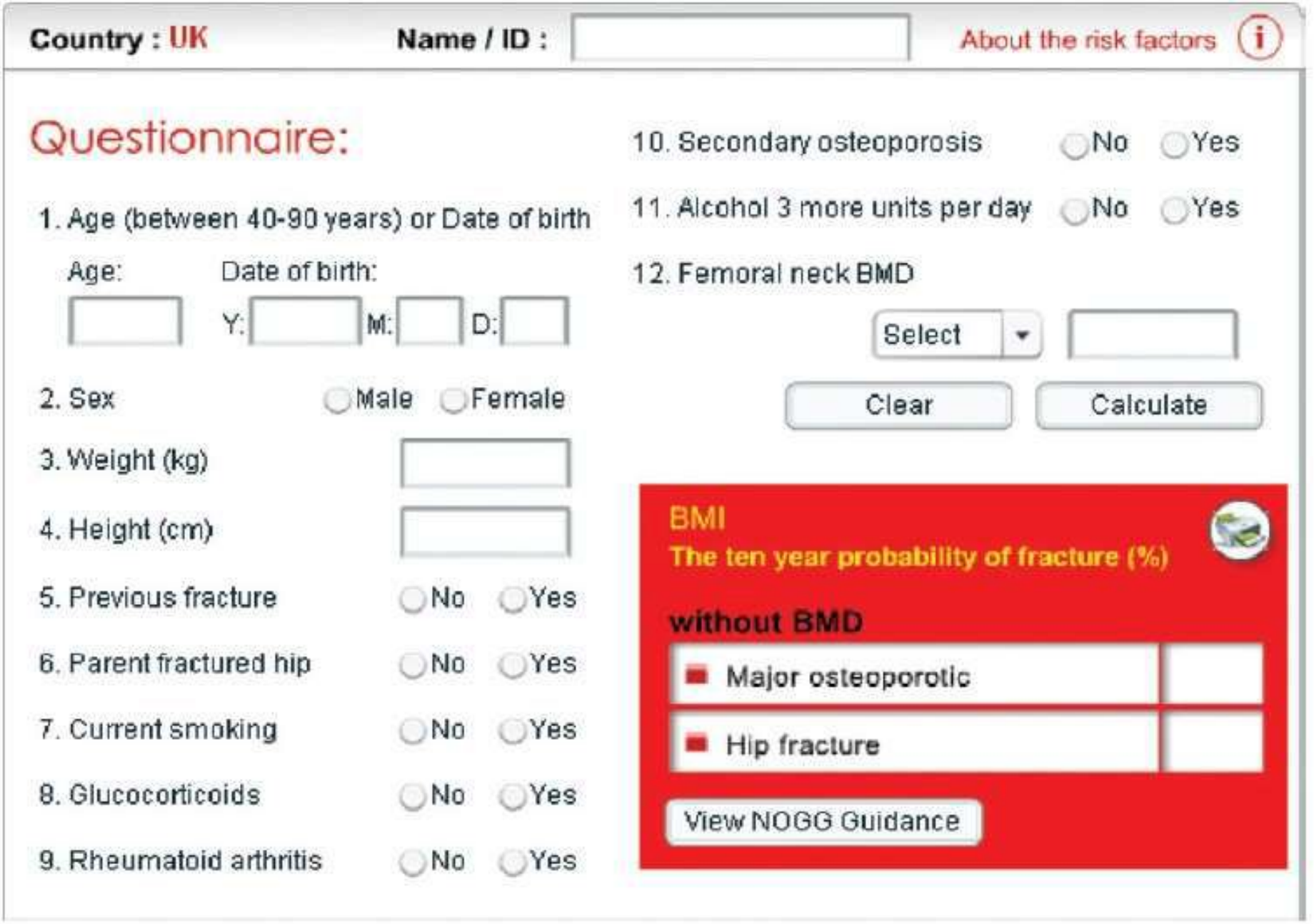
- T-score of 1 equals 1 SD
- **Z-scores**: **compare individual results to those of an age-matched population** that also is matched for race and sex.

- **T-score below –2.5 in the lumbar spine, femoral neck, or total hip has been defined as a diagnosis of osteoporosis.**

WHO FRAX SCORING TOOL

- A web based algorithm designed to calculate the 10 year probability of major osteoporosis related fracture based on clinical risk factors and BMD

- Results evaluated are given in % of risk of patient developing fracture in next 10 years


Country : UK
Name / ID :
About the risk factors
Questionnaire:
1. Age (between 40-90 years) or Date of birth
Age:
Date of birth:
Y:
M:
D:
2. Sex
Male
Female
3. Weight (kg)
4. Height (cm)
5. Previous fracture
No
Yes
6. Parent fractured hip
No
Yes
7. Current smoking
No
Yes
8. Glucocorticoids
No
Yes
9. Rheumatoid arthritis
No
Yes
10. Secondary osteoporosis
No
Yes
11. Alcohol 3 more units per day
No
Yes
12. Femoral neck BMD
Select
Clear
Calculate
BMI
The ten year probability of fracture (%)
without BMD
Major osteoporotic
Hip fracture
View NOGG Guidance

Following assessment of fracture risk using FRAX, the patient can be classified according to the NOGG intervention thresholds: -

- **Low risk** – reassure, give lifestyle advice and reassess in ≤5 years depending on the clinical context

- **Intermediate risk** - measure BMD and recalculate the fracture risk to determine whether the individual's risk lies above or below the intervention threshold

- **High risk** - can be considered for treatment without the need for BMD, although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women

- **Recalculate-** after a minimum of 2 years if the original calculated risk was in the region of the intervention threshold or if the individual's risk factors.

Management

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1.NON PHARMACOLOGICAL – PREVENTION OF OSTEOPOROSIS AND OSTEOPOROTIC FARCTURE.

A.NUTRITION

B.LIFE STYLE MODIFICATIONS

C.PREVENTION OF FALL

D.HIP PROTECTORS

2. BASIC THERAUPETIC MEASURES

A. VIT D AND CALCIUM SUPPLEMENTATION

B. ESTEROGEN AND HRT

3.ANTI RESORBTIVE AGENTS

A.CALCITONIN

B. BISPHOSHPHANTES

C.SERM

D.DONESUMAB

4. DRUGS STIMULATE BONE FORMATION

A.SODIUM FLOURIDE

B.EXOGENOUS PTH

C.VIT D ANALOGUES

5. DRUGS WITH DUAL ACTION

A.STRONTIUM RANELATE

Non Pharmacologic treatment

- Diet Change: for all individuals, a well-balanced die with adequate calcium and vitamin D is essential for healthy bones
- Calcium contributors- Dairy product link milk, yogurt, cheese, ice cream, cottage cheese, and fortified orange juice or soy products
- Most vitamin D comes from sun-induced skin conversion
- Vitamin D contributors- fatty fish, few unfortified foods

Lifestyle Modifications

A. Physical activity-weight bearing and muscle strengthening exercises.
   i. Exercise improves bone strength by 30%to 50%.
   ii. Exercise should be life long.
B. Cessation of smoking, alcohol, high caffeine intake.
C. Adequate sun exposure

Prevention of falls

a) Exercises like balance training, lower limb strengthening exercises
b) Correction of sensory impairment like correction of low vision and hearing impairments
c) Reduce environmental hazards
d) Appropriate reduction of medications
e) Education of individual in behaviour strategies

Hip Protectors

Prevent Direct impact on pelvis

1. Energy absorption type
2. Energy shunting types
3. Crash helmet type
4. Airbag type

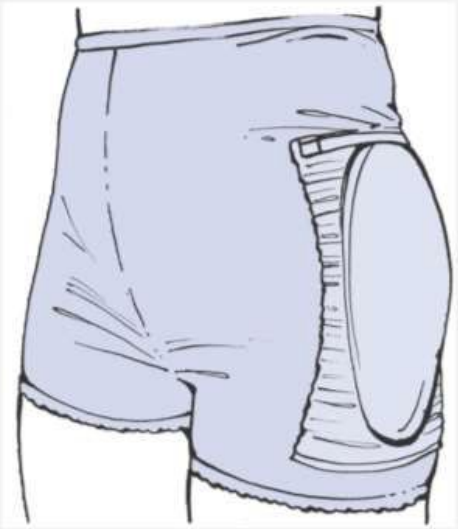


FIGURE 19-6 The hip protector underwear.

Calcium supplements

- More than 90% of a person's bone mass develops before 20 years of age, and half of that bone mass develops from 11-15 years of age. To have strong bones, children and adolescents need to consume enough calcium to build up the bone mass that they will be needed throughout their lives
- Even after age 20, a person can help protect his or her bones. Bone mass can still be built up until the early 30s
- After that, protecting the amount of bone that already exists comes from consuming enough calcium because calcium is essential in maintaining bone mass.
- Adequate calcium intake is also important because the body cannot produce calcium on its own. Every day, the body loses calcium through shedding hair, skin, and nails and through sweat, urine, and faeces. Every day, this lost calcium must be replaced by what a person eats

Calcium Recommended Daily Allowances

Age Range (Years)	Calcium (mg/Day)
9-18	1,300
19-50 51-70 (Men)	1,000
51-70 (Women)	1,200
Over 70	1,200

VIT D

- 800 to 1000 international units (IU) of vitamin D per day for adults age 50 and older

Vit D maintains normal serum calcium levels by activating osteoclasts for bone resorption and increasing intestinal absorption of calcium (increase serum Ca++)

- **Treatment of vitamin D deficiency-**

Adults should be treated with 60,000 IU once a week or the equivalent daily dose (7000 IU vitamin D2 or vitamin D3) for8–12 weeks to achieve a 25(OH)D blood level *of approximately* 30 ng/ml

- This regimen should be followed by maintenance therapy of 1500–2000 IU/day

Pharmacologic therapy

- All patients being considered for treatment of osteoporosis should also be counseled on risk factor reduction including the importance of calcium, vitamin D, and exercise as part of any treatment program for osteoporosis.

- Prior to initiating treatment, patients should be evaluated for secondary causes of osteoporosis and have BMD measurements by central DXA, when available, and vertebral imaging studies when appropriate.

- Biochemical marker levels should be obtained if monitoring of treatment effects is planned

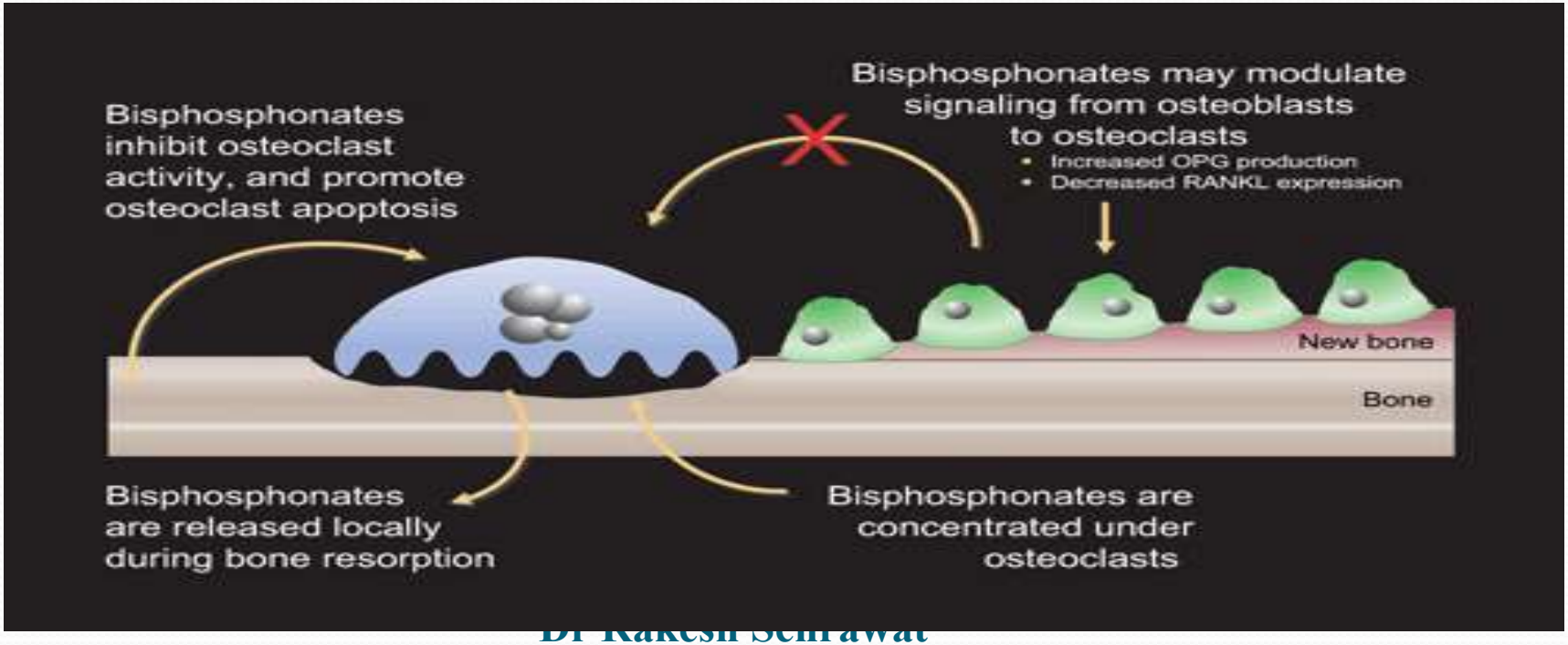
Who should be considered for treatment?

- Postmenopausal women and men age 50 and older presenting with the following should be considered:

1. **A hip or vertebral fracture** (clinically apparent or found on vertebral imaging)
2. T-score ≤−2.5 at the femoral neck, total hip, or lumbar spine
3. Low bone mass (T-score between −1.0 and −2.5 at the femoral neck or lumbar spine)
4. a 10-year probability of a hip fracture ≥3 % or a 10-year probability of a major osteoporosis-related fracture ≥20 %.

Bisphosphonates

- Are analogues of pyrophosphates.
- MOA- attach to bone remodelling sites
- Cause apoptosis of osteoclasts by disrupting cytoskeleton.



- ***Alendronate-***
  - **Prevention** -5 mg daily or 35 mg weekly tablets.
  - **Treatment** -10 mg daily tablet or 70 mg weekly tablet
  - Alendronate is also used in treatment of osteoporosis in men and women taking glucocorticoids

- ***Ibandronate-***
  - Treatment-150 mg monthly tablet, or
  - 3 mg every 3 months by intravenous injection
- ***Risedronate-***
  - Prevention and treatment -5 mg daily tablet; or 35 mg weekly tablet , or, 150 mg monthly tablet

- ***Zoledronic acid***
  - Prevention and treatment -5 mg by intravenous infusion over at least 15 min once yearly for treatment and once every 2 years for prevention

- **Drug administration-**
  - Oral tablets should be taken early morning on empty stomach, 60 mins before breakfast ,and patient should sit upright for 1 hr

- Ibandronate, 3 mg/3 ml prefilled syringe, is given by intravenous injection over 15 to 30 sec. Serum creatinine should be checked before each injection.
- Zoledronic acid, 5 mg in 100 ml is given by intravenous infusion over at least 15 min

- Patients should be well hydrated and may be pre-treated with acetaminophen to reduce the risk of an acute phase reaction (arthralgia, headache, myalgia, fever)

Drug safety

- Side effects for all oral bisphosphonates gastrointestinal problems such as difficulty swallowing and oesophagitis and gastritis
- All bisphosphonates are contraindicated in patients with estimated GFR below 30–35 ml/min
- Osteonecrosis of the jaw (ONJ) can occur with longterm use of bisphosphonates (>5year)
- Although rare, low-trauma atypical femur fractures may be associated with the long-term use of bisphosphonates (e.g., >5 years of use)

Calcitonin

- Treatment of osteoporosis in women who are at least 5 years postmenopausal when alternative treatments are not suitable
- 200 IU delivered as a single daily intranasal spray.
- Intranasal calcitonin can cause rhinitis, epistaxis, and allergic reactions
- Very small increase in the risk of certain cancers

Hormone replacement therapy

- Esterogen with or without progestin is used.
- Also relieves symptoms of postmenopausal symptoms, vulvovaginal atrophy
- Dose-0.625mg daily
- Routes –oral, transdermal

- **Side effects-** increased incidence of coronary heart disease events, strokes, pulmonary embolisms, and invasive breast cancers
- The overall health risks from estrogen exceeds the benefits from use.

Selective Estrogen Receptor Modulator

- Used for both prevention and treatment of osteoporosis
- RALOXIFENE-60mg/day
- Side effects-increased risk of DVT, hot flushes, leg cramps

Tissue selective Esterogen complex- Bazedoxifene.

- Progesterone can be avoided.
- Only for postmenopausal women who have not undergone hysterectomy.

PTH, teriparatide

- Teriparatide is approved for the treatment of osteoporosis in postmenopausal women and men at high risk for fracture.
- It is also approved for treatment in men and women at high risk of fracture with osteoporosis associated with sustained systemic glucocorticoid therapy
- DOSE-20 μg daily subcutaneous injection
- Duration not to exceed 18 to 24 months

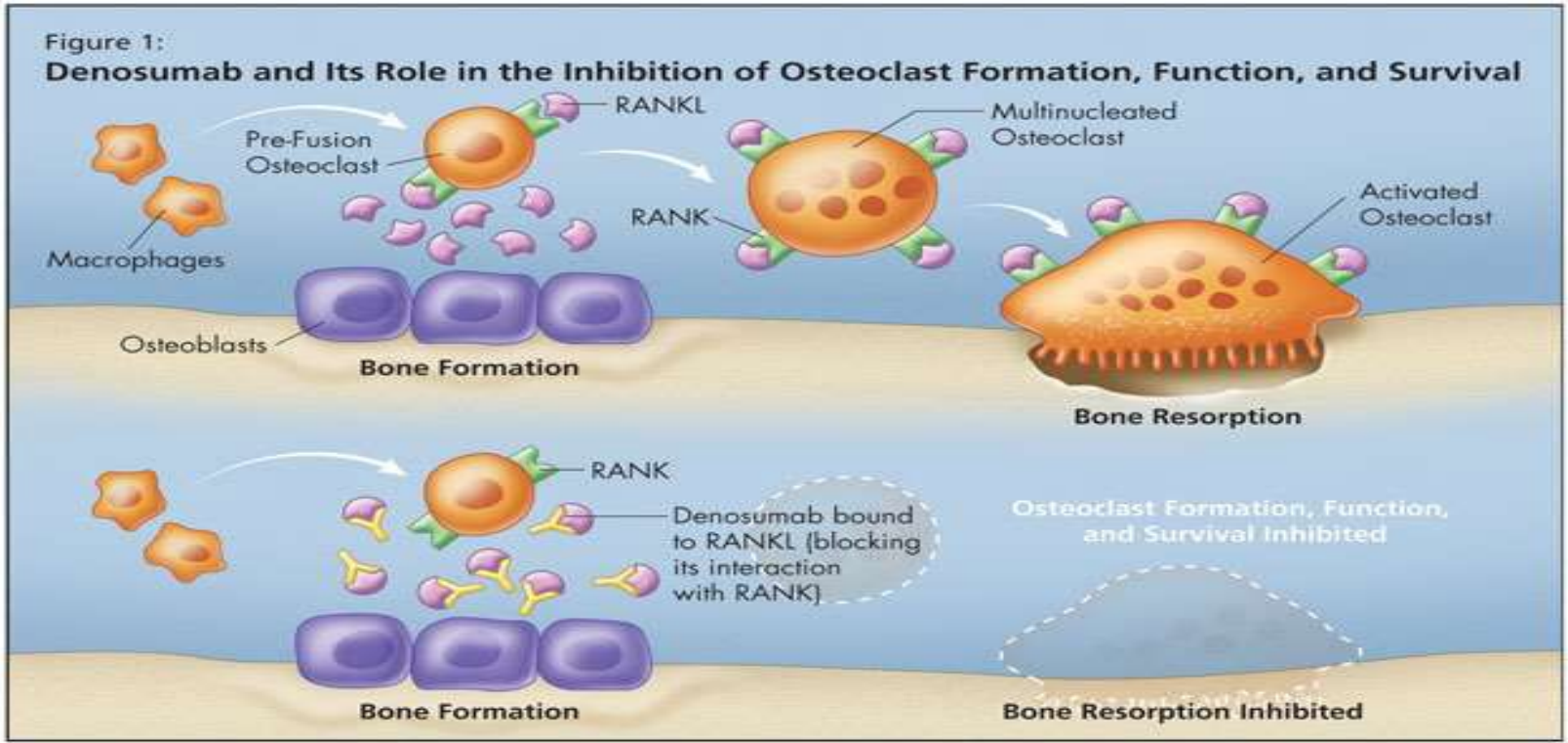
- When treatment is stopped, bone loss can be rapid and alternative agents should be considered to maintain BMD

- **Side effects-** leg cramps, nausea, and dizziness

- **Contraindications**-increased risk of osteosarcoma (e.g., Paget's disease prior radiation therapy of the skeleton), bone metastases, hypercalcemia, or a history of skeletal malignancy

DONESUMAB

- **RANK-L INHIBITOR**
- Dose 60mg/6months S.C
- Used in postmenopausal women
- Side effects-hypocalcemia , cellulitis ,skin rash



Strontium Renelate

- Dual Action:
  - **Inhibit resorption of bone.**
  - **Stimulate bone formation**

Role of Orthopaedicians & surgical management

The goals of surgical treatment of osteoporotic fractures include:

- **Rapid mobilization** and return to normal function and activities.
- **Avoid too much manipulations**
- **Progressive physio therapy**

VERTEBRAL FRACTURES

- **Vertebroplasty** to reduce vertebral fracture–associated pain.
- **Kyphoplasty** to restore height or to treat the deformity associated with osteoporotic vertebral fractures.
- Progressive vertebral collapse or deformity-**pedicle screw fixation.**

THANK YOU

Dr Rakesh Sehrawat