Osteoporosis

- Significant decrease in bone mass per unit volume (or density), that is accompanied by increased fragility. Mineralisation is intact.
  - Loss of trabecular connectivity results in structural loss of strength out of proportion to the loss in mass.
- Osteoporosis is defined in terms of bone mineral density (BMD) < -2.5 standard deviations away from age- and sex-matched medians in the population.
- Regional osteoporosis may be due to disuse, but generalised is more common and subdivided into primary and secondary.

Primary Osteoporosis

Type 1 Post-menopausal = high turnover

- Rapid bone loss in the early post-menopausal period characterised by increased osteoclast activity.
- Women lose bone at an accelerated rate (3% per year) around the menopause and for the first 10 years. 10 times higher than the rate the preceding decade (0.3% per year).

- Risk factors:
  - Caucasian or Asian
  - Family history
  - Anorrrhexia or amenorrhoea
  - Early menopause
  - Early hysterectomy
  - Dietary insufficiencies, malnutrition
  - Smoking
  - Alcohol abuse
  - Chronic lack of exercise

- Classical symptoms/signs
  - Back pain and thoracic kyphosis from thoracic spine wedging
  - Low-energy fractures of the distal radius or other bone.

- NICE guidelines state that in women older than 75 with one fragility fracture, secondary prevention may be started immediately using calcium supplements and bisphosphonates if not contra-indicated. Below the age of 75, DEXA-scans should be performed initially and secondary causes ruled-out.

- Conservative management:
  - Calcium and vitamin D supplements (Chapuy 1994)
  - Maintain activity level
  - Avoid smoking and excessive alcohol
Medical management:

- **HRT**
  - Encouraged in women with risk factors and low BMD on DEXA-scan
  - Contra-indicated if risk factors for breast cancer
  - If no hysterectomy, the risk of uterine carcinoma is offset by use of combined oestrogen and progestogen
- **Bisphosphonates**
  - Risedronate and Alendronate preparations can be given weekly
  - Reduce rate of vertebral and hip fractures (Black 1996)
  - Can have GI side-effects
- **Strontium Ranelate or Raloxifene (SERM)** may be used if cannot comply or intolerant or contra-indicated to bisphosphonates, and have an indicative T-score.
- **Tetrapireotide** may be used if SERMs and bisphosphonates not tolerated or contra-indicated, or if further fragility fractures occur despite treatment, and patient has an indicative T-score for his age.
- **Calcitonin** – available in spray form
- Slow-release fluoride may be combined with calcium supplements

**Type 2 Involutional (Senile) = low turnover**

- Ill-defined syndrome which emerges in very elderly people and is due to a gradual slow-down in osteoblast activity, along with dietary insufficiencies and chronic ill-health
- 15 years after menopause (or men age 70+) there is a steady loss in bone mass of 0.5% per year
  - One in three Caucasian women (33%) by age 70, will have one vertebral insufficiency fracture
- Serum and urinary biochemistry is usually normal unless there is co-existing osteomalacia

**Treatment:**

- Manage any presenting fractures
- Address risk factors:
  - Dietary deficiencies
  - Exposure to sunlight
  - Bisphosphonates may slow further bone loss, but will not restore bone density

**Secondary Osteoporosis**

- **Hypercortisonism:**
  - Suppression of osteoblasts
  - Reduced calcium absorption
  - PTH stimulation
- **Gonadal insufficiency**
  - Present in young girls with ovarian agenesis and primary amenorrhoea (Turner’s syndrome)
  - Can be iatrogenic in female athletes and women with anorexia nervosa
  - Can occur in men with overt hypogonadism, and require testosterone treatment
- Hyperthyroidism will increase overall bone turnover with resorption exceeding formation – fractures usually occur after the menopause due to the cumulative climactic changes and metabolic insult
  - Often a rise in serum ALP, calcium + hypercalciuria
- In myeloma there is bone loss due to overproduction of local osteoclast-activating factors
- Alcohol abuse
  - decrease calcium absorption and increase urinary excretion (diuresis)
  - often accompanied by malnutrition
  - liver failure and toxic effect on osteoblast
  - mild glucocorticoid effect
  - propensity to falls and trauma

**Nutritional**
- malnourished
- malabsorption
- scurvy
- smoking

**Malignancy**
- carcinomata
- myeloma
- leukaemia

**Endocrine**
- thyrotoxicosis
- hyper parathyroid
- Cushing’s
- Hypogonadal

**Other**
- Ank Spond
- Immobility
- RA
- TB
- CRF
- Drugs (alcohol, steroids & heparin)

**2°**

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Osteomalacia

inadequate mineralisation of bones leads to softening (osteomalacia) and deformity (rickets) due to effects of physeal growth and ossification

Causes:

- **Congenital:**
  - Familial X-linked hypophosphataemia (dominant)
    - Mutated hormone blocks renal phosphate tubular reabsorption
    - Requires combined vitamin D and phosphate rx.
  - Fanconi’s syndrome
  - Rare hereditary hypophosphatases
  - Vitamin D-dependent Rickets Type 2
    - Peripheral resistance to vitamin D from a receptor mutation
- **Traumatic** – nil
- **Infective** – hepatitis
- **Neoplastic** – paraneoplastic effect of giant cell tumours or PVNS
- **Circulatory** – nil
- **Autoimmune** – primary biliary cirrhosis
- **Pulmonary** – nil
- **Metabolic:**
  - Gall bladder & liver disease (abnormal absorption of fat soluble Vit D)
  - Crohn’s disease
  - Renal osteodystrophy (lack of 1α hydroxylase)
- **Endocrine** - Pancreatic insufficiency, hypoparathyroidism
- **Degenerative** – elderly with reduced exposure to sunlight
- **Drugs:**
  - Sodium fluoride
  - Bisphosphonate excess
  - Tetracycline excess
  - Phenytoin or rifampicin block metabolism of Vitamin D
- **Iatrogenic**
  - Dietary lack of vitamin D (vegetarians, < 100 iu/day)
  - Complications of thyroid surgery with hypoparathyroidism
  - Bowel resection
- **Psychiatric** – sequelae of paracetamol overdose

Symptoms in children are those of rickets:

- Failure to thrive
- Infants may present with tetani or convulsions
- Deformity of skull (craniotabes)
- Thickening of knee, ankles and wrists from physeal overgrowth
- Enlargement of costochondral junctions – rickety rosary
- Lateral indentation of chest wall – Harrison’s sulcus
- Bowing of tibia from sitting cross-legged
- Bow legs, knock knees or disturbed gait

Symptoms in adults are those of osteomalacia

- Bone pain
- Back ache and proximal muscle weakness before diagnosis is made
- Mild kyphosis from vertebral collapse
- Unexplained pain in hip or long bone, may herald a stress fracture
X-ray signs
- Rickets: thick widened growth plate, with bowing of diaphysis
- Looser zone = thin transverse band of rarefaction in otherwise normal-looking bone
  - Represent stress fractures, caused by pulsating arteries, and which heal with callus lacking calcium
- Codfish vertebra – biconcave
- Spontaneous fractures in pubic rami, femoral neck and below knee
- Trefoil pelvis (champagne glass pelvis) caused by indentation of acetabulum
- Peri-osteal erosions from secondary hyperparathyroidism (medial proximal humerus, femoral neck, lateral distal forearm bones)
- Brown tumours (osteitis fibrosa)
  - Osteoclast resorption with holes filling with fibrous tissue
  - Become confluent

Biochemistry:
- Low calcium and phosphate from vitamin D abnormalities
- High PTH (secondary hyperparathyroidism)
- High ALP (from osteoclast activity)
- Low urinary excretion of calcium
- \([\text{Ca}^{2+}] \times [\text{PO}_4^{-}] < 2.4\)

Bone biopsy will give definitive diagnosis with tetracycline staining showing defective mineralisation.

Management:
- Conservative – dietary advice and modification, sun exposure
- Medical – Adcal D3; may need 400 – 1000 IU per day of Vitamin D
- Surgical – fracture management, osteotomies to treat bowing