OSTEOPOROSIS
An overview of the condition and its treatment
Bone

- 206 bones in the human skeleton
- Provide support, anchorage for muscles and protection for organs e.g. ribs
- Bone is a storage area for calcium and phosphorous salts and has an important role in blood formation
- Before birth the skeleton is made of cartilage most of which is gradually replaced by bone via a process called ossification.
- Bones of the human skeleton can be divided into long bone and flat bones
- Long bones are tubular and weight bearing and are made of a dense outer layer of compact (cortical) bone and central region (medulla) made up of trabecular (spongy) bone
- Trabecular bone makes up most of the short, flat and irregular shaped bones and the epiphyses (ends) of the long bones
- It is much lighter than cortical bone and has a good strength to weight ratio
Bone

- Trabecular bone is more susceptible to the effects of osteoporosis

- Most osteoporotic fractures occur where there are high levels of trabecular bone eg the vertebrae, the neck of femur (hip) and the wrist
Osteoporosis Pathogenesis

- Bone is constantly re-modelled and repaired due to damage caused by daily use.
- Osteoclasts “cut” into old bone (resorption) and osteoblasts fill with organic matrix which becomes mineralised (bone formation or ossification).
- In osteoporosis the net rate of bone resorption exceed rate of bone formation- normally matched.
- Results in a decrease in bone mass and quality.
Bone tissue cells

Basically three:

- **Osteoclasts** - large multi-nuclear cells which release enzymes and acids that digest protein and mineral components of bone (resorption)

- **Osteoblasts** - bone builders, synthesize and secrete collagen and other components to create a matrix which is laid down in the bone. They initiate calcification of the matrix and hence bone formation

- **Osteocytes** - mature bone cells (osteoblasts encased in matrix secretions) responsible for exchange of waste and nutrients.
Bone remodelling process

[Diagram showing bone remodelling process:
- CFU-GM leads to Osteoclasts
- CFU-F leads to Osteoblasts
- Quiescent bone surface covered by lining cells
- Osteoclasts resorbing old bone
- Osteoid becoming mineralized
- Osteoblasts filling the resorption cavity with osteoid]
Definition

• `Osteoporosis is a progressive systemic skeletal disease characterised by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture`.
  World Health Organisation (1994)

• Osteoporosis is a chronic disease that has late clinical consequences and has been referred to as a silent epidemic because there are no associated signs or symptoms before fracture.
Normal v. Osteoporotic bone
Osteoporosis incidence

• There are about **300,000 fragility fractures** every year in the UK

• **1,150 people die every month in the UK as a result of hip fractures**

• In the UK, **one in two women and one in five men** over the age of 50 will break a bone mainly because of poor bone health

National Osteoporosis Society statistics 2012
Risk factors for Osteoporosis

- Age- bone mineral density (BMD) decreases with age

- Hormones- lower levels of oestrogen after menopause accelerate bone loss due to increased activity of osteoclasts.

- Premature menopause or hysterectomy causes earlier acceleration of bone loss. Likewise surgical or chemical castration in men

- Gender- women are at increased risk of osteoporosis as they start out with smaller bones and bone mass compared to men

- Genetic factors- family history of osteoporotic fracture, especially hip fracture, increases risk
Secondary causes of osteoporosis

- Long term corticosteroid use ie 5mg or more prednisolone daily for 3 months or more
- Aromatase inhibitor treatment
- Hyperparathyroidism
- Hyperthyroidism
- Coeliac disease, malabsorption syndromes, inflammatory bowel disease, IBS
- Anorexia
- Renal disease
- Rheumatoid arthritis
- Other drugs- PPI’S, SSRI’s, Anti-epileptics
Modifiable risk factors

- Smoking - BMD lower in smokers
- Alcohol - BMD lower with excess alcohol intake
- Weight - low BMI ie <19 is an indicator of low BMD
- Vitamin D and Calcium - vitamin D required for calcium absorption from intestines, re-absorption from the kidneys and control of parathyroid hormone
- Vitamin D levels and Calcium intake reduced in old age due to reduced exposure to sunlight and changes in the epidermis and poor diet.
- Exercise - weight bearing exercise increases BMD and prolonged bed rest & immobility decreases BMD
Bone Mass

Bone Mass by Age and Sex

Men
Women

Menopause-Associated Bone Loss

Age (years)

Bone Mass

Diagnosis of osteoporosis

- Bone mineral density is main measure for diagnosis
- BMD measured by using Dual Energy X-ray Absorptiometry (DEXA) scan
- Measurements usually made at lumbar spine and hip
- Usually reported as T scores and Z scores
- T score is the number of standard deviations from the peak bone mass of young adults of the same sex
- Z score is the number of standard deviations from the average bone mass of people of same age and sex
- T score between -1 and -2.5 indicates osteopenia
- T score -2.5 or less indicates osteoporosis
Bone Mineral Density Values

World Health Organization (WHO) Osteoporosis Guidelines
DEXA scan results
Criteria for referral for DEXA scan (NHS Glasgow & Clyde)

- Over 50 yrs with a fragility fracture at any site (not attributable to a RTA or a fall from above head height)
- >5mg prednisolone or equivalent per day for more than 3 months
- Over 60 yrs and menopause under 45 yrs
- Over 60 yrs and acquired kyphosis
- Over 60 yrs and significant self-reported height loss
- Over 60 yrs and family history of 1st degree relative with fracture
- Over 60 yrs and family history of 1st degree relative with kyphosis
- Over 60 yrs and family history of 1st degree relative with DEXA confirmed osteoporosis
Treatment of Osteoporosis
Bisphosphonates

- First line treatment for primary and secondary prevention of osteoporotic fractures
- Reduce bone resorption by inhibiting action of osteoclasts
- Available as daily, weekly and monthly oral preparations and 3 monthly and yearly injections
- Daily and weekly- alendronate, risedronate, etidronate
- Monthly- ibandronate
- 3 monthly IV- ibandronate infusion
- Yearly IV- zoledronate infusion
Bisphosphonates cont.

- Oral bisphosphonates have complicated dosage regimes and poor bioavailability
- Strong evidence to support their use
- Alendronate usually first choice due to cost
- GI Side effects are fairly common with oral bisphosphonates
- Recent concerns regarding osteonecrosis of the jaw especially with high dose intravenous versions
Treatment of Osteoporosis - Strontium

- Claims to increase BMD by reducing bone resorption and increasing bone formation by its action on osteoclasts and osteoblasts

- Available as a powder for reconstitution and taken daily usually bedtime

- Avoidance of food required 2 hours before and after administration

- GI side effects of nausea and diarrhoea but usually transient

- Possible slight increase in risk of venous thromboembolism (VTE)

- Possibility of DRESS syndrome occurring (rare)
Treatment of Osteoporosis-others

• Raloxifene - selective oestrogen receptor modulator (SERM) which selectively binds to oestrogen receptors on bone. Reduces incidence of vertebral fractures but no effect on non-vertebral or hip fractures. Carries risk of VTE.
• Teriparatide- a fragment of recombinant human parathyroid hormone. High levels of parathyroid hormone usually cause bone resorption but pulsed doses cause formation. Reduces vertebral and non-vertebral fractures but not hip. Expensive and usually initiated by specialists.
• Calcitonin - hormone produced by thyroid gland. Given as a nasal spray of synthetic calcitonin. Reduces risk of vertebral fracture only.
• Calcium and Vitamin D3 - has an important role on bone formation and remodelling. Calcium is required for bone mineralization and vitamin D keeps parathyroid hormone secretion under control.
Newer Treatments

- **Denosumab** - a human monoclonal antibody to the activator of receptors on osteoclasts resulting in a reduction in their development and activity and resultant increases in BMD
  - Reduces risk of vertebral, non-vertebral and hip fractures
  - Given as a twice yearly s/c injection for 36 months
These medicines increase bone mineral density and reduce fractures.

Why should you consider a patient with osteopenia or osteoporosis for the Chronic Medication Service?
The Problem - Poor Adherence

- Patients stop taking anti-osteoporotic medicines
- Patients take them irregularly
- Patient take them incorrectly
Why patients stop taking

- Studies have shown that after 1 year 1 in 3 patients have stopped taking their Bisphosphonate (other studies as high as 1 in 2)
- Poor understanding of the condition and its treatment
- Long term treatment
- Bisphosphonates (especially) have difficult dosage regimes
- Texture/taste of Calcium & Vitamin D3
- Side-effects
Correct dosage regime

- **Bisphosphonates (alendronate, risedronate....)** must be taken in the morning on an empty stomach and at least 1/2 hour before breakfast
  - Must be taken with a large glass of tap water
  - Must sit upright after taking ie don’t go back to bed!
  - No tea, coffee, juice or other medicines for at least half an hour (do not take calcium and vit D3 for 4 hours)
- **Strontium (Protelos)** no food & calcium 2 hours before and 2 hours after (bedtime is best)
  - Please see individual drug SPC’s
What’s the problem if not taken correctly?

- **Bisphosphonates:**
  - If taken CORRECTLY only 0.64% to 0.39% is absorbed- enough for them to work!
  - If overnight fast/ avoidance of food is not followed absorption is practically ZERO!
  - If taken with tea, coffee, juice.. Absorption reduced by 60%!
  - Oesophageal irritation/ ulceration if insufficient water taken with tablet or lie down after taking

- **Strontium:** 25% absorption if taken correctly, 60%-70% reduction if not
Compliance Aids

• Patients or carers must be able to identify a bisphosphonate in a compliance aid!

• Leave Calcium & Vitamin D3 to later in the day eg lunchtime and teatime
Falls

The most effective way to minimise osteoporotic fragility fractures is to……..

STOP PEOPLE FALLING!!!!

If your Health Board has a Falls Prevention Programme consider referral for your osteoporosis patients who have suffered falls