Osteoporosis
&
metabolic bone disease

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OSTEOPOROSIS

Brittle bone disease
  – Generalised
  – localised / regional
Regional osteoporosis

Immobilisation due to fracture
WHO PROPOSAL

Women with bone density values of more than 2.5 SD below that of normal adult mean value are at risk of fracture = Osteoporosis

Women with bone density values of more than 1 SD below that of normal adult mean value = osteopenia

Fractures – hip = neck of femur
Vertebral
Wrist (Colles’)

Osteoporosis - Generalised

Metabolic bone disease

Low bone mass with microarchitectural deterioration of bone tissue

• Fragility of the skeleton

• Increase in fracture risk

• Normal mineral : collagen - compare to osteomalacia
Bone mineral density give better estimates of osteoporosis than surveys of fractures

Plain x-rays – generally unhelpful as 24-40% bone loss to occur before identify bone loss with accuracy
Life time risk of fracture of women is 40%
mens is 10%

Most individuals over age 70 who have hip fracture do not regain independence – quality of life

Costs reaching £1.7 bn / year

Impact of disease increasing because of aging population
OSTEOPOROSIS
Osteoblasts

Osteocyes
OSTEOPOROSIS

Loss of bone with age

Why?

Ovaries no longer ovulate – oestrogen levels fall

So due to oestrogen or just aging?
Richelson et al. NEJM 1984

<table>
<thead>
<tr>
<th>Age</th>
<th>BMD</th>
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<tbody>
<tr>
<td>Ovariectomised women</td>
<td>54</td>
</tr>
<tr>
<td>Normal menopausal women</td>
<td>52</td>
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<tr>
<td>Postmenopausal women</td>
<td>73</td>
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Mean duration of oestrogen deficiency = 20 years

Bone loss in ovx group equivalent to postmenopausal group

Oestrogen deficiency contributes to bone loss

Not purely accounted for by aging
Bone loss – Ageing or oestrogen?

Premature ovarian failure

Spontaneous – familial, autoimmune
  - athletes, ballerina’s, anorexia

Surgical

Prevention - Hormone replacement therapy
OESTROGEN DEFICIENCY

Increase in bone resorption
  Osteoclast numbers increase - STUDIES
  Biochemical markers become elevated

Increase in bone formation – oestrogen receptors on osteoblasts

Increase in bone turnover / remodelling

Therefore, resorption > formation – Loss of coupling

Net loss in bone mass
How does oestrogen protect against bone loss?

Unclear

Cytokine production altered

RANKL : OPG
Macrophage colony stimulating factor
Transforming growth factor beta
Interleukins IL1, IL6)
Tumour necrosis factor

Ageing – GH – Insulin-like growth factor
Rapid bone loss at menopausal period – 3% / year in the spine for 5 years

0.5% per annum subsequently

Women may lose up to 40% of bone mass

Presentation of disease 20 years after the menopause

Prevention
Prevention - anti-resorptive agents

Oestrogens – more than bone cancer risk – breast and endometrium

to value of lower levels
value of treating at 70 +>

Tamoxifen and other SERMS

Bisphosphonates

Calcitonin

Requirement for ANABOLIC AGENTS
? Parathyroid hormone
If bone loss occurs in all women after the menopause, why does everyone not get osteoporosis?

Peak bone mass – 20 – 30 years of age

More bone available to lose before reaching fracture threshold
  Genetic / familial
  Race
  Sex
RISK FACTORS

Life style / exercise
Smoking
Alcohol
Diet – low calcium

Endocrine diseases –
  hyper and hypo thyroidism
  Addison disease - Adrenal
Risk Factors (continued)

Inflammatory bowel disease
Rheumatoid arthritis

DRUGS
• Steroids
• Anticonvulsants
Osteomalacia and Rickets

Metabolic bone disease

Reduced mineralisation due to low calcium levels

Generally due to disturbance of vitamin D metabolism
7 dehydrocholesterol in skin

Vitamin D (fat soluble vitamin)

25 hydroxylase (Liver)

1α hydroxylase (kidney)
( forms active metabolite)

1,25 (OH)2 D3 mediates effect on

bone – oc form and resorb to release Ca++
renal tubules - increased absorption of Ca++, increase

gut - increased absorption of Ca++ & Vit D

Kidney disease
GI disease

RICKETS and OSTEOMALACIA – BONE BIOPSY
Poor Ca++ absorption leads to HYPOCALCAEMIA → elevated levels of PARATHYROID HORMONE = SECONDARY HYPERPARATHYROIDISM

Primary Hyperparathyroidism

Hyperplasia
Adenomas

Ca++ levels normal or raised
OSTEOMALACIA/RICKETS

• Failure of mineralisation
  – Due to
• Low calcium
  – Due to
• Diet; vit D; fish liver foods
• Milk eggs / Sunlight
• Poor Ca++ absorption in gut
• Renal disease
PAGET’S and OSTEITIS DEFORMANS
Paget Disease of Bone

- Elderly population
- Areas of excessive osteoclastic activity
  - Pain
    - Deformity
      - Osteosarcoma
  - ?virus
  - ?genetic
Osteopetrosis - A phenotype inherited disease

Dense bones
Failure of osteoclastic bone resorption

Osteoclasts are not formed
Or
Osteoclasts are generated but they are inactive

Provides insight into how osteoclasts work
Chronic osteomyelitis

- Chronic disease
- Staph Aureus
- Blood borne
- Children
- New bone /old bone
- Amyloid
- Marjolin’s ulcer