METABOLIC BONE DISEASES

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Normal Bone Metabolism

• Calcium
  – Bone is a reservoir for more than %99 of body calcium
  – Calcium is important
    • nerve and muscle function
    • Clotting
  – Absorbed from duedonum

1,25-(OH)_{2}-vit D_{3}

PTH
Calcium

– The dietary requirement

• 600 mg/day – children
• 1300 mg/day – young adults
• 750 mg/day – adults (25-65 years)
• 1500 mg/day – pregnant
• 2000 mg/day – lactating women
• 1500 mg/day – Postmenopausal / healing fracture
Phosphate

- 85% stored in the bone
- Absorption: Kidney
  - Prox. Tubule
- Molecular pathways & Enzymatic
Parathyroid Hormone

Low concentration of calcium in blood

Release of parathyroid hormone

Effux calcium from bone

Decreased loss of calcium in urine

Enhanced absorption of calcium from intestine

Increased concentration of calcium in blood
Vitamin D

- Activated by UV irradiation
- Utilized from dietary intake
- Hydroxylated to $25(\text{OH})\text{-vit D}_3$ (liver)
- $2^{\text{nd}}$ Hydroxilation $1,25\,(\text{OH})_2\text{-vit D}_3$ (kidney)
VITAMIN D METABOLISM

- **7-DEHYDROCHOLESTEROL**
- **VITAMIN D$_3$ (CHOLECALCIFEROL)**
  - 25-OH-CHOLECALCIFEROL
  - 1,25-(OH)$_2$-CHOLECALCIFEROL
  - 24,25-di-OH-CHOLECALCIFEROL

**Locations:**
- Bone
- Small intestine
Calcitonin

- Peptide
- Thyroid gland
- Inhibits osteoclastic bone resorption
- Osteoclasts have Calcitonin receptors
- Calcitonin decreases serum calcium levels
Increase in Blood Calcium

Increases secretion of calcitonin

Decrease in Blood Calcium

Increases secretion of parathyroid hormone
Metabolic Bone Diseases

• Hypercalcemia
  – Hyperparathyroidism
  – Familial Syndromes
• Hypocalcemia
  – Hypoparathyroidism
  – PHP/Albright’s
  – Renal Osteodystrophy
  – Rickets (Osteomalacia)
    • Vit D- deficient
    • Vit D- dependent
• Osteodense
  – Paget’s Disease
  – Osteopetrosis
• Osteopenia
  – Osteoporosis
  – Scurvy
Primary Hyperparathyroidism

• Over production of PTH
• As a result of parathyroid adenoma
  – Increased plasma Calcium
  – Decreased plasma Phosphate
Primary Hyperparathyroidism

• Clinical Findings
  – Kidney stone
  – Hyperreflexia

• Radiological Findings
  – Osteopenia
  – Osteitis fibrosa cystica
  – Brown’s tumors
    • Increased giant cells, extravasation of RBC’s, hemosiderin staining)
Osteopenia
Brown Tumor
Familial Syndromes

- **Multiple Endocrine Neoplasia (MEN)**
  - Type I and II
  - Pituitary Adenomas
  - Hypercalcemia
Hypercalcemia

• Other Causes
  – Malignancy
  – Lytic bone metastases (multiple myeloma)
  – Hyperthyroidism
  – Vit D intox
  – Prolonged immobilization
  – Addison’s disease
  – Steroid administration
  – Peptic ulcer disease (Milk-Alkali Syndrome)
  – Sarcoidosis
Hypercalcemia

• Treatment
  – Hydration (saline diuresis)
  – Loop diuretics
  – Dialysis (for severe cases)
  – Mobilization (prevents further bone resorption)
  – Specific drug therapy
    • Biphosphonates, mithramycin, calcitonin
Hypoparathyroidism

• Lack of PTH
  – Decrease in plasma Calcium
  – Increase in plasma Phospate

• Clinical Findings
  – Fungal infections of the nails
  – Hair loss
  – Skin pigment loss (vitiligo)

• Iatrogenic hypoparathyroidism most commonly follows thyroidectomy
Pseudohypoparathyroidism (PHP)

- Rare genetic disorder
- Lack of effect of PTH at the target cells
- Receptor abnormality
- Albright hereditary osteodistrophy
  - Short first, fourth, fifth MC and MT
  - Brachydactyly
  - Egzostoses
  - Obesity
  - Diminished Intelligence
Pseudo-Pseudohypoparathyroidism

- Normocalcemic disorder
- Phenotypically similar to PHP
- There is normal response to PTH
Renal Osteodystrophy

• Chronic renal disease
  – High turnover disease
    • Chronically elevated PTH
    • Phosphate retention
    • Hypocalcemia
    • Secondary hiperparathyroidism
  – Low turnover disease
    • Excess deposition of aluminum into bone
    • Normal or reduced serum PTH.
Rickets
(Osteomalacia in Adults)

• Failure of mineralization
• Changes in the physis
  – Increased width and disorientation
• Changes in the bone
  – Cortical thinning, bowing
Causes of Rickets and Osteomalacia

• **Nutritional Deficiency**
  – Vit D deficiency
  – Dietary chelators of calcium
    • Phytates
    • Oxalates (spinach)
  – Phosphorus deficiency
    • Antacid (aluminium containing)

• **Gastrointestinal Absorbtion Defects**
  – Postgastrectomy
  – Biliary disease
  – Inflammatory bowel disease

• **Renal Tubular Defects**
  – Albright’s syndrome
  – Fanconi syndrome
  – Vit D dependent Rickets
  – Renal tubular acidosis
    • Acquired-systemic diseases

• **Other**
  – Heavy metal intox
  – Hypophosphatasia
  – Sodium fluoride
  – High dose diphosphonates
  – Anticonvulsant medication
Rickets

• **Nutritional Rickets**
  – Vitamin D Deficiency Rickets
    • Causes
      – Asian
      – Premature infants
      – Malabsorption
      – Chronic parenteral nutrition
    • Lab: Normal Ca, Low P, Increased PTH, low Vit D
Rickets

- **Clinical Presentation**
  - Rachitic rosary
    - Enlargement of costochondral junction
  - Bowing of the knees
  - ‘Codfish’ vertebrae
  - Retarded bone growth-defect on hypertrophic zone
  - Physial cupping
  - Coxa Vara
  - Muscle hypotonia
  - Dental disease
  - Looser’s zones (pseudofracture on the compression side of bone)
  - Milkman’s fracture (pseudofracture in adults)
  - Waddling gate
Rickets

- Large Forehead
- Rachitic Rosary
- Large Abdomen
- Wide Bones
- Wide Joints
- Retarded growth
- Odd curve to spine or back
- Odd shaped legs
- Wide ankles
Rickets

- Hereditary Vit D dependant
  - Type I
    - Defect 25(OH)Vit D 1α-hydroxylase (renal)
    - Inactive Vit D to active Vit D conversion is defected
    - Autosomal recessive
  
  - Type II
    - The defect is in an intracellular receptor for 1,25(OH)$_2$Vit D
Rickets

• Familial Hypophosphatemic Rickets
  – Vit D- resistant Rickets
  – X-linked dominant
  – Impaired renal tubular reabsorption of phosphate
  – The most commonly encountered form of Rickets

• Treatment
  – Phosphate replacement
  – High-dose Vit D
Hypophosphatasia

- Autosomal recessive disorder
  - Inborn error in the tissue-nonspecific isoenzyme of alkaline phosphatase
- Features are similar to Rickets
- Increased urinary phosphoethanolamine is diagnostic.
Osteoporosis

- Age-related decrease in bone mass
  - associated with loss of estrogen in postmenopausal women
  - Quantitative defect in bone (not qualitative)

- Northern European women
- Smokers
- Heavy drinkers
- Phenitoin
- Low calcium and low-vitamin D diet
Osteoporosis

- Clinical Features
  - Kyphosis
  - Fractures
    - Vertebrae Compression Fractures - wedge shaped defect
    - Hip
    - Distal Radius
Osteoporosis

- **Type I (Postmenopausal)** - Affects trabecular bone
- **Type II (Age-related)** -
  - older than 75
  - Affects both trabecular and cortical bone
  - Related to poor Calcium absorption
  - Hip and pelvis fractures are common
Osteoporosis

• **DIAGNOSIS**
  – Plain radiographs are usually not helpful unless bone loss is > 30%
  – Q-CT (quantitative)
  – DEXA (Dual Energy Xray Absorptiometry)
    • Less radiation
  – Biopsy
    • Is not commonly used
Osteoporosis

• Treatment

- Phosphate
- Diphosphonate

STOPS LOSS

- Calcium
- Vitamin D
- Alendronate
- Calcitonin
- Estrogen
- Mild Exercise
- Raloxifene
- Tamoxifen

BONE GAIN

- Fluoride plus—Calcium
- Vit D
- Estrogen
- Extensive exercise
Proflaxis for Osteoporosis

• Diet with adequate Calcium
• Weight bearing exercise programme
• Hormone replacement therapy at menopause
Idiopathic Transient Osteoporosis of the Hip Joint

- Most common at the third trimester of pregnancy
- Groin pain, limited ROM, localised osteopenia
- Self limited
- Tends to resolve spontaneously after 6-8 months
- Treatment: Limited weight bearing, analgesics
Osteomalacia

• Adult form of Rickets
• Defect in mineralization
  – Vitamin D-deficient diets
  – GI disorders
  – Renal Osteodysrophy
  – Aluminium containing Phosphate binding antacids
  – Chronic alcoholism
<table>
<thead>
<tr>
<th></th>
<th>Osteoporosis</th>
<th>Osteomalacia</th>
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</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Elderly</td>
<td>Any age</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Pain at the fracture site</td>
<td>Generalized pain</td>
</tr>
<tr>
<td><strong>Serum Ca$$^{++}$$</strong></td>
<td>Normal</td>
<td>Low/ Normal</td>
</tr>
<tr>
<td><strong>Serum P$_i$</strong></td>
<td>Normal</td>
<td>Low/ Normal</td>
</tr>
<tr>
<td><strong>Alkaline Phosphatase</strong></td>
<td>Normal</td>
<td>Elevated</td>
</tr>
<tr>
<td><strong>Mineralization</strong></td>
<td>Normal</td>
<td>Decreased</td>
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Increased Osteodensity

- Osteopetrosis (Marble Bone Disease)
- Osteopoikilosis (Spotted Bone Disease)
Osteopetrosis

- Increased sclerosis and obliteration of the medullary canal
- Decreased osteoclastic (chondroclast) function
- Failure of bone resorption
- Tx: Bone marrow transplantation
  - Calcitriol (high dose)
Osteopoikilosis

- Spotted Bone Disease
- Islands of deep cortical bone appear within the medullary cavity and the cancellous bone of the long bones
- Asymptomatic
Paget Disease

- Remodelling disease
- Bone resorption
- Disordered bone formation
  - Patients older than 50
  - Common sites: femur, pelvis, tibia, skull
  - Usually asymptomatic
- Three phase
  - Lytic phase
  - Mixt phase
  - Sclerotic phase
Paget Disease

• Lab:
  – Increased ALP
  – Increased urinary markers of bone turnover
  – Normal Calcium

• Clinical features
  – Bowing of femur or tibia
  – Arthritis of the hip
  – Lumbar stenosis
Paget Disease

• Treatment:
  – Biphosphonates
  – Calcitonin
Thank you...

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