• Nothing to disclose
Pretest Question

• 90% of bone mass is accumulated by
  1. 5 years age
  2. 10 years age
  3. Pubertal age
  4. 12 years age
  5. 18 years age
Overview

• Determinants of bone health
  • Calcium
  • Vitamin D

• Assessment of bone health in children
  • Bone density testing
  • Treatment

• Rickets
Bone Health

- Bone strength is largely determined by bone mass achieved in childhood and adolescence
  - 40% of bone mass is attained in adolescence
  - 90% by 18 yrs age
  - Peak bone mass by late twenties

- Bone mass attained is the most important determinant of life-long skeletal health and risk of osteoporosis
Factors Affecting Bone Mass

Nonmodifiable
- Genetics
- Gender
- Ethnicity

Modifiable
- Nutrition
  - Calcium
  - Vitamin D
  - Sodium
  - Protein
  - Soda
- Exercise and lifestyle
- Body weight and composition
- Hormonal status
Peak Bone Mass

Fig. 1. Diagrammatic representation of the bone mass life-line in individuals who achieve their full genetic potential for skeletal mass and in those who do not. (The magnitude of the difference between the curves is not intended to be to scale.) Along the bottom of the graph are arrayed several of the factors known to be of particular importance. (© Robert P. Heaney 1999, used with permission.)
Factors Affecting Bone Mass

• Inadequate nutrition, inadequate physical activity and chronic inflammation can lead to compromised peak bone mass
  • Increased risk for osteoporosis and fracture

• Nutrition and physical activity function synergistically to improve bone acquisition and maintenance.
Bone Health

• Bone development relies on the processes of modeling and remodeling
  • Osteoblast driven bone formation
  • Osteoclast driven bone resorption

• Imbalance between resorption and formation may result in abnormal bone mineral accretion.
Bone health

• Increased prevalence and detection of decreased mineralization in children has helped us understand that adult bone disease originates in earlier years
Bone health

• Fetal bone health
  • Maternal vitamin D influences neonatal calcium levels, bone mineral density and bone size and therefore influence long-term fracture risk.
  • BMD z-scores tend to track in childhood

• Childhood
  • Vitamin D, calcium
  • Weight bearing exercise
Calcium
## Recommended Daily Allowance For Calcium

<table>
<thead>
<tr>
<th>Age</th>
<th>Calcium</th>
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<tbody>
<tr>
<td></td>
<td>RDA (mg/d) (Intake That Meets Needs of ≥97.5% of Population)</td>
</tr>
<tr>
<td>Infants</td>
<td></td>
</tr>
<tr>
<td>0–6 mo</td>
<td>200$^b$</td>
</tr>
<tr>
<td>6–12 mo</td>
<td>260$^b$</td>
</tr>
<tr>
<td>1–3 y</td>
<td>700</td>
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<tr>
<td>4–8 y</td>
<td>1000</td>
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<tr>
<td>9–13 y</td>
<td>1300</td>
</tr>
<tr>
<td>14–18 y</td>
<td>1300</td>
</tr>
</tbody>
</table>
Dietary Calcium Sources

• 1 cup milk is 300 mg
• 1 cup yoghurt 300 mg
• 1.5 oz cheese 300 mg
• Other sources green leafy vegetables, legumes, nuts, fortified cereals
Calcium Supplements?

- Calcium supplementation showed no beneficial effects on BMD - meta-analysis of RCT’s.
  - Concluded unlikely to result in reduction of fracture risk

- Emphasis on establishing healthy dietary behaviors that include balanced diets to meet RDA for calcium
  - Dietary sources have better bioavailability
  - Establishes life long healthy behaviors.
Vitamin D

• Synthesized in skin from 7-dehydrocholesterol on exposure to sunlight-----25 hydroxylation in liver

• 25 hydroxy vitamin D is a good indicator of Vitamin D stores
  • Half life of 2-3 weeks

• Second hydroxylation in Kidney -----1,25 hydroxy Vitamin D, the active form of vitamin D
  • Half life of few hrs
  • Increases calcium absorption from intestine and renal reabsorption of calcium
Vitamin D

• Vitamin D is essential for bone mineralization
  • Intestinal calcium absorption
  • Bone mineral accretion

• Deficiency leads to suboptimal bone mineralization and rickets
  • Insufficient bone mineral accrual may ultimately lead to osteoporosis, increased fracture risk

• Adequate Vitamin D status is crucial to maximize peak bone mass

• Other benefits
  • Cardiometabolic
  • Immunity
  • Cancer
Vitamin D Sources

• Sunlight (blocked by sunscreen)
• Fatty fish, mushroom
• Fortified foods
  • Milk (100IU per cup)
  • Cereal
  • Yoghurt
  • Cheese
• Multivitamins, Vitamin D supplements
• Human milk is a poor source of Vitamin D
Vitamin D Supplementation in Infants

- Breast fed and partially breast fed infants should be supplemented with 400IU/ day
  - Start within a few days after birth and continue until they meet RDA from diet from fortified formula or cows milk
- >1 yr to adolescence- 600IU daily
### Recommended Daily Allowance for Vitamin D

<table>
<thead>
<tr>
<th>Age Group</th>
<th>RDA (IU/d) (Intake That Meets Needs of ≥97.5% of Population)</th>
<th>UL (IU/d)(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
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<td></td>
</tr>
<tr>
<td>0–6 mo</td>
<td>400(^b)</td>
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<tr>
<td>6–12 mo</td>
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<tr>
<td>9–13 y</td>
<td>600</td>
<td>4000</td>
</tr>
<tr>
<td>14–18 y</td>
<td>600</td>
<td>4000</td>
</tr>
</tbody>
</table>
Prevalence of Vitamin D deficiency (VDD)

• VDD is the most common nutritional deficiency worldwide

• Variable prevalence 17 to 47% of adolescents are deficient
  • African, Hispanic/Asian descent
  • Obese higher risk due to sequestration in fat tissue
  • Medications – glucocorticoids, anticonvulsants
  • Health concern even in sunny areas
Vitamin D Deficiency

- 25 hydroxyvitamin D is best indicator of Vitamin D status

- Wide range of terminology
  - Deficiency
  - Sufficiency
  - Insufficiency
  - Optimal
  - Suboptimal
Vitamin D Deficiency Cut offs

• Deficiency
  • <30 ng/ml (Endocrine society and 7 other societies)
  • <20 ng/ml (AAP, Institute of medicine)

• Most commonly accepted threshold for adequacy is above 30 ng/ml
Assessment of Vitamin D Status

• Reflects endogenous synthesis and dietary intake

• Routine screening not recommended
  • Vitamin D supplementation is cheap and safe

• Endocrine society recommends screening at risk children
  • Obesity, black and Hispanic children
  • Malabsorption syndromes
  • Glucocorticoid, anti-convulsant, antifungal, antiretroviral medications
Treatment of Vitamin D Deficiency

• Oral route preferred
• D2 plant sources; D3 animal sources
• D3 may be better than D2
  • No difference seen in children

• 2000IU/ day for 3 months
• 50,000 weekly doses for 6-8 weeks for adherence
• Maintenance dose after treatment dose 400-1000IU/ day
Other Dietary Factors

• Poor calcium absorption with diets with
  • High sodium
  • Low protein
  • Carbonated beverages
Exercise

• Mechanical loading increases bone formation

• Weight bearing exercise increase bone mineral accrual
  • Site specific increases based on loading
  • Immobilization causes rapid decline in bone mass

• Healthy body weight associated with optimal BMD
Conditions Associated With Reduced Bone Mass

Genetic conditions
- Osteogenesis imperfecta
- Idiopathic juvenile osteoporosis
- Turner syndrome

Chronic illness
- Cystic fibrosis
- Connective tissue disorders (lupus, juvenile idiopathic arthritis, juvenile dermatomyositis)
- Inflammatory bowel disease, celiac disease
- Chronic renal failure
- Childhood cancer
- Cerebral palsy
- Chronic immobilization

Eating disorders, including anorexia nervosa, bulimia nervosa, eating disorders not otherwise specified, and the female athlete triad

Endocrine conditions
- Cushing syndrome
- Hypogonadism
- Hyperthyroidism
- Hyperparathyroidism
- Growth hormone deficiency
- Diabetes mellitus

Medications
- Glucocorticoids
- Anticonvulsants
- Chemotherapy
- Leuprolide acetate
- Proton pump inhibitors
- Selective serotonin reuptake inhibitors
- DMPA
Assessment of Bone Health
Bone mineral density (BMD) assessment in children- Challenges

• Assessment of BMD in growing child presents a challenge for accuracy and consistency
• BMD varies with age and gender, and must be analyzed by comparing results to age and gender based normative data
• BMD also varies with race, height, lean mass and pubertal stage
• Comparison of longitudinal data in the same patient is complicated because of the process of growth.
Dual Energy X-ray Absorptiometry (DXA)

- Comprehensive bone health assessment in pediatric and adolescent patients
- Bone mineral density in childhood study (BMDCS) demonstrated that DXA measures of areal BMD Z-scores track through childhood.
  - Assist in diagnosis of patients with significant fracture history
  - Routine assessment in those at high risk for fractures
  - To monitor response to treatments
DXA

• DXA remains the preferred method of assessment of bone mass
  • Availability
  • Speed-5 min
  • Precision
  • Safety
  • Low cost
  • Low radiation exposure- 1/10th of CXR
  • Robust normative data
Densitometry methods

• pQCT measures
  • volumetric bone mineral density
  • Identifies trabecular and cortical bone separately
  • Largely a research tool due to lack of standardized scanning protocols and reference data

• Quantitative Ultrasound
  • Portable
  • Limited by lack of precision
Which skeletal sites should be studied by DXA?

• Preferred sites: Lumbar spine and total body less head (TBLH)
  • Cranium excluded as head contributes considerable mass to the whole body and changes little with time, which can mask subtler changes to Whole body bone mass

• Distal radius is an alternative skeletal site (obese subjects)
Which skeletal sites should be studied by DXA?

- Lateral distal femur is valuable for patients with immobilization disorders (CP, muscular dystrophy) or those with contractures that preclude proper positioning for spine or whole body.
  - robust reference data available
  - correlate well with increased lower extremity fragility fracture risk in non-ambulatory children
Indications for Densitometry

• Primary bone disorders
  • Idiopathic juvenile osteoporosis
  • Osteogenesis imperfecta

• Secondary bone disorders
  • Inflammation
    • Inflammatory bowel disease
    • Juvenile idiopathic arthritis
    • Cystic fibrosis
  • Immobilization
    • Cerebral palsy
    • Myopathies
  • Endocrine disturbance
    • Turner syndrome
    • Anorexia nervosa
  • Cancer and therapies with adverse effects on bone
    • Acute lymphoblastic leukemia
    • After chemotherapy for childhood cancer
  • Hematologic disorders
    • Thalassemia
Timing of scans

• In patients with primary bone disease or at risk of secondary bone disease, a DXA scan should be performed when the patient may benefit from interventions and DXA results will influence that management

• Minimum interval between scans should be between approximately a year
International Society For Clinical Densitometry (ISCD)-Reporting and Interpretation

• Bone mass is reported as bone mineral content (BMC) and density (aBMD)

• Z-scores (standard deviation by age) should be used before age 20 years (not T-score)

• Choose reference data collected using similar DXA manufacturer and software as patient

• aBMD is an areal not volumetric measure, resulting in lower values in smaller individuals
  
  • Children with delayed growth- height adjustment recommended

• Gold standard pediatric reference data from bone mineral density in childhood study
Factors to consider before ordering a DXA

• Disease severity

• Feasibility
  • Can the patient lie still
  • Contractures or hardware in region of interest
  • Are there vertebral fractures
  • Experience of the center with pediatric patients
  • Will findings influence clinical management

Risks from interpretation not radiation exposure
  • Therapeutic decisions should NOT be based on DXA findings alone
Bone densitometry and fracture prediction

• Low BMC and low aBMD are linked to fracture risk

• Low spine aBMD Z-score linked to spine fractures

• Bone mass at lateral distal femur a better predictor than spine aBMD in immobilized children
DXA reporting

• ISCD recommends
  • Height adjusted Z-score (rather than actual age) in children with short stature or growth delay
  • Serial DXA’s should compare same sites as baseline testing

• Osteoporosis diagnosis requires
  • Low aBMD Z-score <-2 and clinically significant fracture history

• Clinically significant fracture history
  • Long bone fracture of lower extremities
  • Vertebral compression fracture
  • Two or more long bone fractures of upper extremities

• For those with low BMD and no fractures- use low bone density
  • Terms like osteopenia should be avoided
Comprehensive skeletal assessment

- Genetic, inflammatory, nutritional, biomechanical and endocrine risk factors should be considered
- Basic laboratory assessment for skeletal fragility
  - CBC, ESR
  - Ca, phos, PTH, 25 vitamin d, magnesium, Alkaline phosphatase, BUN, creatinine
  - Thyroid function tests
  - Celiac screen
  - LH, FSH
  - IGF-1
  - Urine calcium/ creatinine
  - Genetic screen for OI
Summary

• DXA is the preferred method for assessment of bone mass
• Appropriate interpretation includes adjustments for delayed growth and puberty and use of age, sex and ethnic specific normative data
• Diagnosis of osteoporosis is based on both low bone mass for age and a significant fracture history
Management of Low Bone Density
Interventions

• Monitor Vitamin D levels

• Optimize calcium and Vitamin D to meet recommended amounts for age

• Treatment of underlying cause
  • Sex steroids for hypogonadism
  • Weight gain in anorexia nervosa

• Increases in skeletal loading through physical therapy, standing on vibrating platforms, weight bearing exercise

• Bisphosphonate therapy
Bisphosphonate therapy

- Oral- Alendronate
- IV- Pamidronate, Zoledronic acid
- IV preferred
  - Zoledronic acid infusion widely preferred shorter infusion time and given every 6 months
- Reserved for those with osteoporosis.
Rickets due to Vitamin D deficiency
An 8-month-old infant presents with the primary complaint of irritability. He has been exclusively breastfed since birth. His mother was not interested in providing any supplemental foods because her milk supply has been adequate. Physical examination reveals a fussy infant who has frontal bossing and whose weight and height are both at the 25th percentile. The infant becomes irritable with movement of the left arm. Arm radiography reveals a humeral fracture and bowing of both radii. Chest radiography demonstrates enlargement of the costochondral junctions.

Of the following, the MOST likely diagnosis is

• A. Congenital syphilis
• B. Osteogenesis imperfecta
• C. Vitamin D deficient rickets
• D. Child physical abuse
• E. Vitamin E deficiency
A 7-month-old child presents for a follow-up office visit after undergoing a Kasai procedure for biliary atresia at 6 weeks of age. The mother states that the boy is irritable when his right arm is moved. On physical examination, the infant is jaundiced. You detect tenderness in the anterior radial head. Radiography of the affected region demonstrates metaphyseal fraying (Item Q33) and a fracture.

Of the following, the MOST appropriate laboratory studies to obtain next are

• A. calcium, phosphorus and DEXA scan
• B. calcium, phosphorus and 1,25 Vitamin D
• C. Calcium, phosphorus, 25 Vitamin D
• D. calcium, phosphorus and magnesium
• E. calcium, phosphorus and PTH
Vitamin D deficiency

• Decreased intake/absorption or production
  • Lack of exposure to sun
  • Dietary deficiency
  • Malabsorption

• Increased catabolism-anticonvulsants

• Defective Vitamin D hydroxylation
Clinical features

• Growth retardation
• Metaphyseal widening
• Frontal bossing
• Rachitic rosary
• Bowing of legs
• Subluxation of epiphyseal plates and fractures
• Tetany and seizures
Rickets
Radiographic changes

Cupping, fraying, metaphyseal widening
Diagnosis

- (Low serum calcium)
- (Low serum phosphorus)
- High alkaline phosphatase
- High PTH
- Low serum 25 OH vitamin D

- Rx
  - Vitamin D and calcium replacement
Thank you for your attention
Case scenario’s
Case 1

• 15 year old female athlete with primary amenorrhea, height at 3\textsuperscript{rd} centile, BMI of 15, had 1 stress fracture. Mother has osteoporosis’ by DXA, but no history of fractures.

Would you order a DXA and why or why not?
Which skeletal sites would be preferred?
What are the potential pitfalls in interpretation of results?
What other tests might you order?
Case 1

• Likely exercise induced primary amenorrhea
• No fragility fractures
• If DXA done- need to adjust for height and delayed maturity
• How will DXA change management
• Rule out ovarian insufficiency-FSH, prolactin, celiac screen, TFT’s, CBC, ESR
Case 2

• 11 year old wheel chair bound boy with cerebral palsy and seizures. No history of fractures.

Would you order a DXA and why or why not?
Which skeletal sites would be preferred?
What are the potential pitfalls in interpretation of results?
What other tests might you order?
Case 2

- This child is at increased risk of fragility fractures due to immobilization and antiepileptic's
- No fractures
- If DXA done- lateral distal femur
Case 3

- Healthy 7 year old boy with 5 fractures, starting at age 3 years- right tibia, right femur, right forearmX2, left radius.

Would you order a DXA and why or why not?
Which skeletal sites would be preferred?
What are the potential pitfalls in interpretation of results?
What other tests might you order?
Case 3

• Fracture history in otherwise healthy 7 year old is concerning.
• Important to review nature of trauma
• DXA indicated- WB, spine
• Additional testing including OI testing
Case 4

- 9 year old with JRA on high dose glucocorticoids for 2 years. Complaining of back pain. Ht at 50\textsuperscript{th} centile, wt at 80\textsuperscript{th} centile.

Would you order a DXA and why or why not?
Which skeletal sites would be preferred?
What are the potential pitfalls in interpretation of results?
What other tests might you order?
Case 4

- Back pain in this setting is worrisome for vertebral fractures
- DXA can be useful as baseline before treatment.