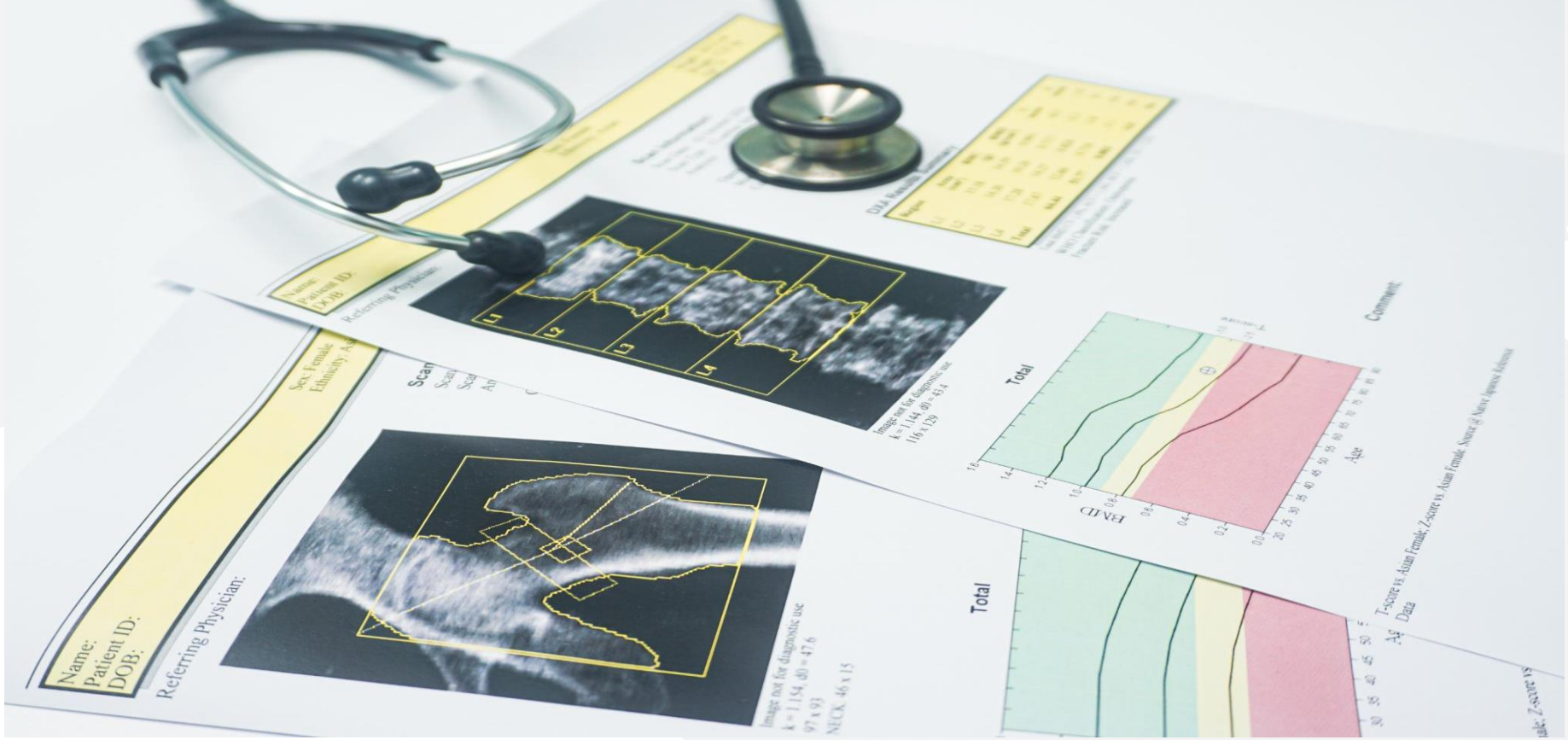

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Management of Low Bone Mineral Density (BMD) in Children with Spina Bifida

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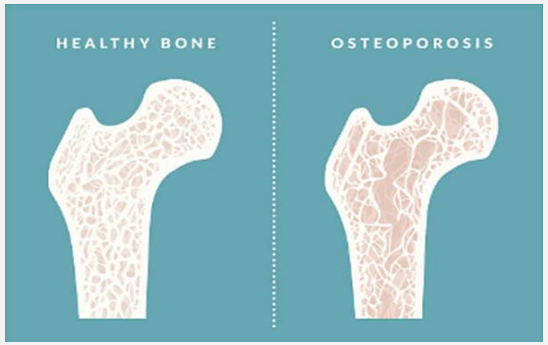

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Learning Objectives

- Define the Extent of the Problem
- Identify Risk Factors Leading to Decreased BMD in SB
- Discuss Work-up Algorithm for Children with SB and Low BMD
- Discuss Treatment of low BMD/Osteoporosis
- Summary of recommendation

Spina Bifida (SB) : Classification

Spina Bifida Occulta (Closed Spinal Dysraphism)

- Failure of fusion of posterior vertebral arches
- **Skin intact**; no exposed neural tissue
- Often **asymptomatic**
- May have cutaneous markers:
  - Tuft of hair
  - Dermal sinus
  - Lipoma
  - Hemangioma

Open Spina Bifida (Aperta)

- Neural tissue exposed or covered by thin membrane
  Often associated with **neurologic deficits**
- **A. Meningocele**
- Herniation of **meninges only**
- Spinal cord stays in normal position
- Neurologic deficits **mild or absent**
- Least severe open form
- **B. Myelomeningocele (MMC)**
- Herniation of **meninges + spinal cord**
- **Most common and most severe** form
- Significant neurologic impairment:
  - Motor & sensory loss below lesion
  - Neurogenic bladder/bowel
- Common associations:
  - **Hydrocephalus**
  - **Chiari II malformation**
- Highest risk for low BMD and fractures

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Guidelines for the Care of People with Spina Bifida

Osteoporosis and Bone Health

Workgroup members: **Alex Van Speybroeck, MD; Joe O'Neal, MD; Brad Dicianno, MD; Leslie Morse, DO; Devonne Elkins, MD, FACP, FAAP**

Osteoporosis and Bone Health 2023

Fracture Risk and Clinical Impact

- Fracture risk is highest in 2-10 years old with SB.
- Lower extremity fractures are most common
- Fractures can worsen mobility, independence, and chronic pain
- Delayed diagnosis is common due to altered sensation
- Bowel sensitive and decrease calcium intake
- Further consideration should be given to those individuals with or at risk for the development of chronic kidney disease (CKD)
  - The impact that CKD has on mineral and bone metabolism.
  - Individuals with CKD are at risk of developing CKD-mineral and bone disorder (CKD-MBD) which results in decreased calcitriol, increasing serum phosphorus levels with resultant pulling of calcium from bones.
  - Further, this is associated with increasing PTH from the kidneys resulting in further leaching of calcium from the bones. It is important to monitor calcium, phosphorus, PTH and vitamin D in these individuals especially for individuals with SB who are already at risk of decreased bone mineralization, osteoporosis, and fractures.
  - Dietary and pharmacological treatments may be necessitated to address CKD-MBD. These may include decreasing dietary phosphorus, calcitriol, calcium supplementation, phosphate binders, dialysis, or renal transplantation.

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Risks for Decreased BMD in SB Children

- **Patients with SB have significantly reduced bone mineral density (BMD) and are at high risk for osteoporosis and pathologic fractures.** Studies consistently demonstrate BMD Z-scores 1-2 standard deviations below normal, with approximately 65% of children with spina bifida having low bone density for age.

  Szalay EA, Cheema A. Clinical Orthopedics and Related Research. 2011.

- The relationship between spina bifida and osteoporosis is multifactorial.
  - **Non-ambulatory status is the most significant risk factor**, with wheelchair-dependent patients showing BMD approximately 1 standard deviation lower than ambulatory patients and a 10-fold increased risk of fracture
  - **Higher neurological lesion levels** (thoracic and high lumbar) correlate with worse bone health due to greater immobility.
  - **Additional** contributing factors include vitamin D deficiency, hypophosphatemia, and increased urinary calcium excretion in non-ambulatory patients.
  - **Medications**

  Kafadar I, Kilic BA, Yilmaz FK, Kilic M. Journal of the International Society for Pediatric Neurosurgery. 2016.

Overview of Risk Factors & Mechanisms

Mechanical Factors

Reduced physical activity in SB limits mechanical stress needed for bone formation and maintenance.

Nutritional Deficiencies

Inadequate calcium and vitamin D intake and insufficient sunlight impair bone mineralization in SB individuals.

Pharmacological Impacts

Long-term antiepileptic drug use disrupts vitamin D metabolism, reducing calcium absorption and promoting bone loss.

Developmental Challenges

Low body mass, delayed growth, and hormonal imbalances further weaken skeletal development in SB.

Fracture patterns and timing in SB

- Fracture prevalence is highest in childhood (10.9/1000 patient-years) and decreases in adolescence and adulthood.

Osteoporosis International 2017

- The distal femur and femoral shaft are the most common fracture sites in children, though these fractures become rare in adulthood.

Developmental Medicine and Child Neurology. 2010.

- Spontaneous or low-impact fractures are common, particularly in non-ambulatory patients with higher lesion levels.
- Patients who experience one fracture have a 3.1-fold increased risk of subsequent fractures.

Osteoporosis International 2017

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Wolff's Law: states that **bone adapts to the mechanical loads placed upon it**—its internal structure and external shape change in response to stress.

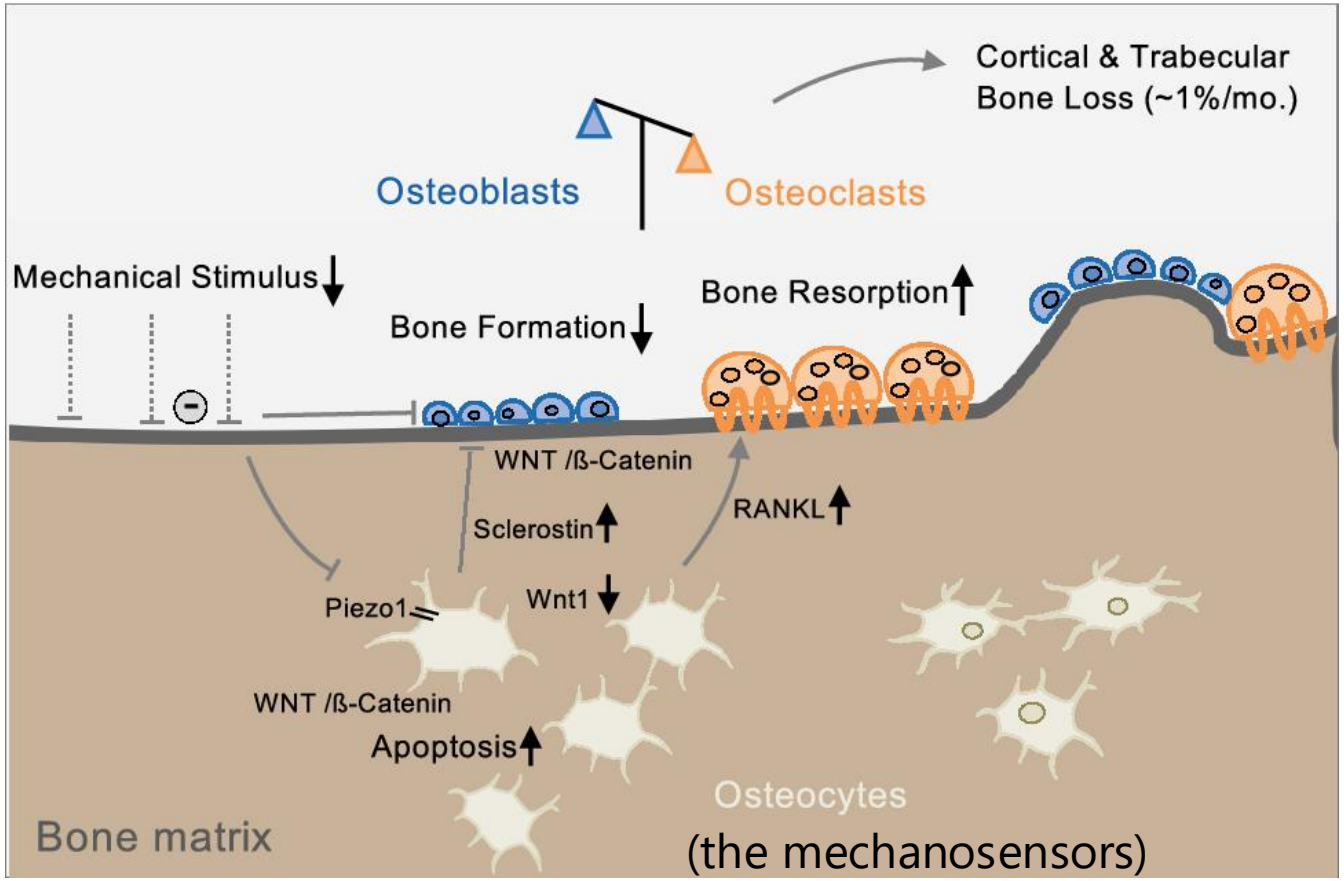
- Highly loaded regions → **thicker lamellae, trabecular alignment**
- Low loaded regions → **trabecular thinning, cortical porosity**

This explains:

•Why athletes have higher bone mass

•Why immobilization causes rapid bone loss

Mechanotransduction: Turning Load Into Signals



Cellular Outcomes
With Mechanical Loading:
- ↓ Sclerostin (removes inhibition on Wnt signaling)
- ↑ Osteoblast activity
- ↑ Bone formation
- ↓ Osteoclast formation
- ↑ Periosteal bone apposition

With Mechanical Unloading (e.g., bedrest, spaceflight):
- ↑ Sclerostin
- ↑ RANKL
- ↑ Osteoclast-mediated bone resorption
- ↓ Osteoblast activity
- Net bone loss

Bone is a highly dynamic tissue that constantly remodels in response to mechanical forces. This ability—**mechanosensation**—allows bone to strengthen when loaded and weaken when unloaded. It's the biological basis for exercise-induced bone formation, disuse osteoporosis, and Wolff's Law.

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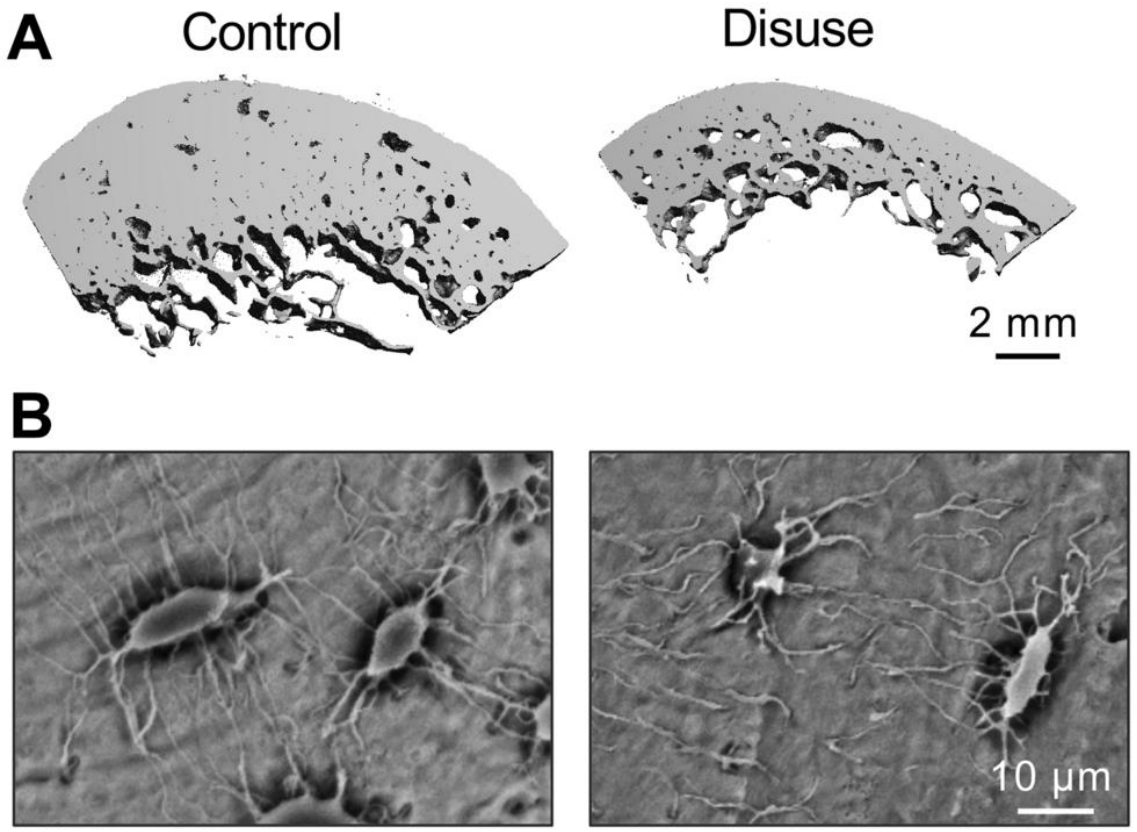

Micromorphological changes in cortical bone after immobilization. **a** µ-CT images demonstrating profound cortical changes, including a decrease in cortical thickness and an increase in cortical porosity, in individuals after long-term bed rest. **b** SEM images of acid-etched plastic-embedded cortical bone sections revealing decreased canalicular connectivity of osteocytes after immobilization, underlining the role of osteocytes in mechano-transduction. Images were obtained from representative samples obtained in the context of a previous study

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Nutritional Deficiencies

Feeding Challenges in SB

Children with SB face feeding difficulties, hindering intake of calcium and vitamin D essential for bones.

Calcium and Vitamin D Role

Calcium is vital for bone mineralization; vitamin D enhances calcium absorption in the gut.

Impact of Deficiencies on Bone Health

Nutritional deficits weaken bones, lower bone mineral density, and increase fracture risk over time.

Nutritional Intervention Strategies

Dietary assessments and supplementation optimize intake, supporting bone health and development in SB individuals.

Antiepileptic Medications

Vitamin D Metabolism Disruption

AEDs accelerate vitamin D catabolism, reducing active vitamin D and impairing calcium absorption in the gut.

Bone Demineralization Process

Reduced calcium triggers parathyroid hormone release, increasing bone resorption and causing bone density loss over time.

Impact on Vulnerable Populations

Children and adolescents with SB are more susceptible to bone loss due to long-term AED therapy.

Need for Monitoring and Intervention

Regular monitoring of vitamin D, calcium, and bone density is essential for managing osteoporosis risk in AED patients.

Developmental Factors

Impact on Skeletal Growth

Delayed growth in children with SB is linked to nutritional deficits, hormonal imbalances, and reduced physical activity.

Bone Mineral Density Issues

Low body weight and short stature correlate with decreased bone mineral density, increasing osteoporosis risk.

Effect of Sedentary Behavior

Sedentary lifestyle reduces mechanical and metabolic stimuli needed for healthy bone development in SB patients.

Mitigation Strategies

Early nutritional support, growth monitoring, and tailored physical activity programs help improve bone health outcomes.

Work up of Children with SB

- Lab Assessment
  - 25 (OH) Vit D
    - Dark skinned, Obesity, IBD, malabsorption syndrome, eating disorders, antiseizure meds, proteinuria
  - Bone biochemistry
    - BUN , Cr, electrolytes, Ca, Pi, Alk Phosphatase
    - PTH
    - Urine Ca/Cr
  - Bone turnover markers
    - CTX: Serum marker of bone resorption
    - PINP: Serum marker of bone formation
  - Genetic Testing
- X-Ray
  - Spot skeletal views for focal abnormalities
  - Skeletal survey for systemic bone disease
  - DXA vs QCT

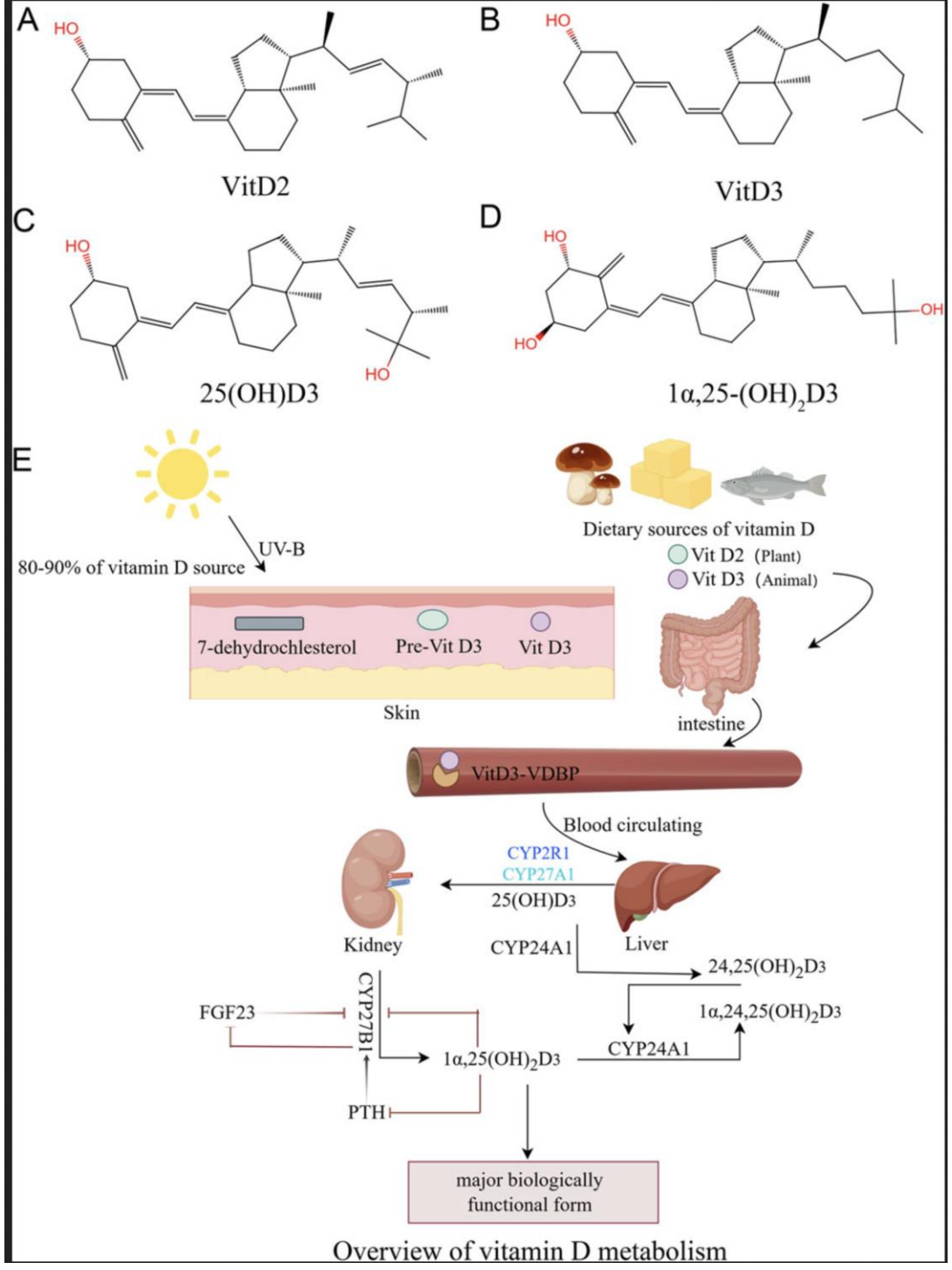
Guidance on Dual-Energy X-ray Absorptiometry Interpretation in Children and Adolescents Younger Than 20 Years*

- Only z scores, which compare BMD with age- and sex-matched peers, should be used.
- T scores, which compare BMD with the PBM of healthy young adults aged 20-40 years, should not be used and should not appear in reports or on dual-energy x-ray absorptiometry printouts.
- The diagnosis of osteoporosis should not be made solely based on densitometric criteria.
    - Pediatric osteoporosis requires either ≥1 low-trauma vertebral fracture (with or without low BMD), or
    - Low BMD for age (Z-score ≤-2) plus a significant fracture history (≥2 long bone fractures before age 10 or ≥3 before age 19). (*Pedaitrics* 2016)
- Terms such as low bone density for chronologic age or below the expected range for age may be used if the z score is lower than −2.0 SDS;
- TBLH scans are the preferred skeletal sites for measurements. The value of BMD to predict fractures in children and adolescents is not clearly determined.
- Adjustments made to BMD or BMC for Height age, pubertal stage, skeletal maturity, or body composition should be clearly stated in the report; there is no agreement on standards for such adjustments.
- Serial BMD studies should be done preferably using the same machine

QCT vs DXA

- **QCT demonstrates higher sensitivity for detecting osteoporosis** compared to DXA in the same population. A 2025 meta-analysis found QCT identifies significantly more osteoporosis cases than DXA, with one study showing QCT detected osteoporosis in 87.7% of patients with pathologic fractures versus only 28.9% by DXA. QCT's superior fracture prediction (AUC 0.802 vs 0.76 for DXA) reflects its ability to measure trabecular bone, which undergoes age-related loss faster than cortical bone. Availability, cost, radiation, makes its clinical use limited.
- **DXA has important limitations** that can lead to underdiagnosis. Osteophytes, ligament calcification, spinal degeneration, and abdominal aortic calcification artificially elevate lumbar DXA measurements. Central obesity (BMI >35) increases the distance from X-ray source to detector, further overestimating BMD. More widely used.

The Lancet, 83: 1, 2025



Overview of vitamin D metabolism

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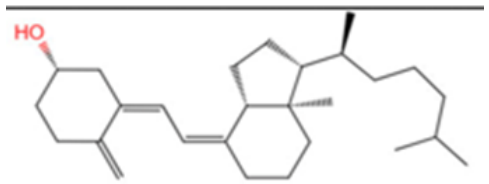
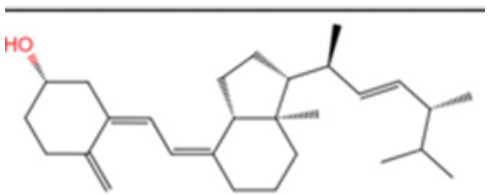
	Cholecalciferol (D_3)	Ergocalciferol (D_2)
Source	Animals (Lanolin)	Plant
Potency	~3× higher potency	Baseline potency
Serum 25-OH-D increase	~45 ng/mL over 12 weeks	~24 ng/mL over 12 weeks
Dose equivalence	50,000 IU D_3 = 93,500 IU D_2	Requires ~2× dose for same effect
Serum stability	Better-maintained levels	Faster decline after dosing
Clinical preference	Preferred choice for supplementation	Less preferred, esp. on equal IU basis



VitD3



VitD2

Conclusion:
Cholecalciferol (Vitamin D_3) is the preferred form due to its superior potency, bioavailability, and sustained ability to raise serum Vitamin D levels compared to ergocalciferol (Vitamin D_2).

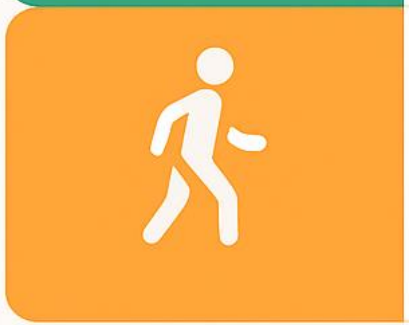
Pediatric Bone Health Summary

Vitamin D (AAP vs NIH)

- Infants: AAP 400 IU/day | NIH 400 IU/day (10 µg)
- Children & Adolescents: AAP 600 IU/day | NIH 600 IU/day (15 µg)

Calcium (NIH)

- 1–3 yrs: 700 mg
- 4–8 yrs: 1.000 mg
- 9–18 yrs: 1.300 mg



Lifestyle Tips

- Weight-bearing activities (walking, dancing, jogging)
- Resistance exercises for muscle strength
- Balanced nutrition with calcium-rich foods

Source: AAP & NIH Office of Dietary Supplements

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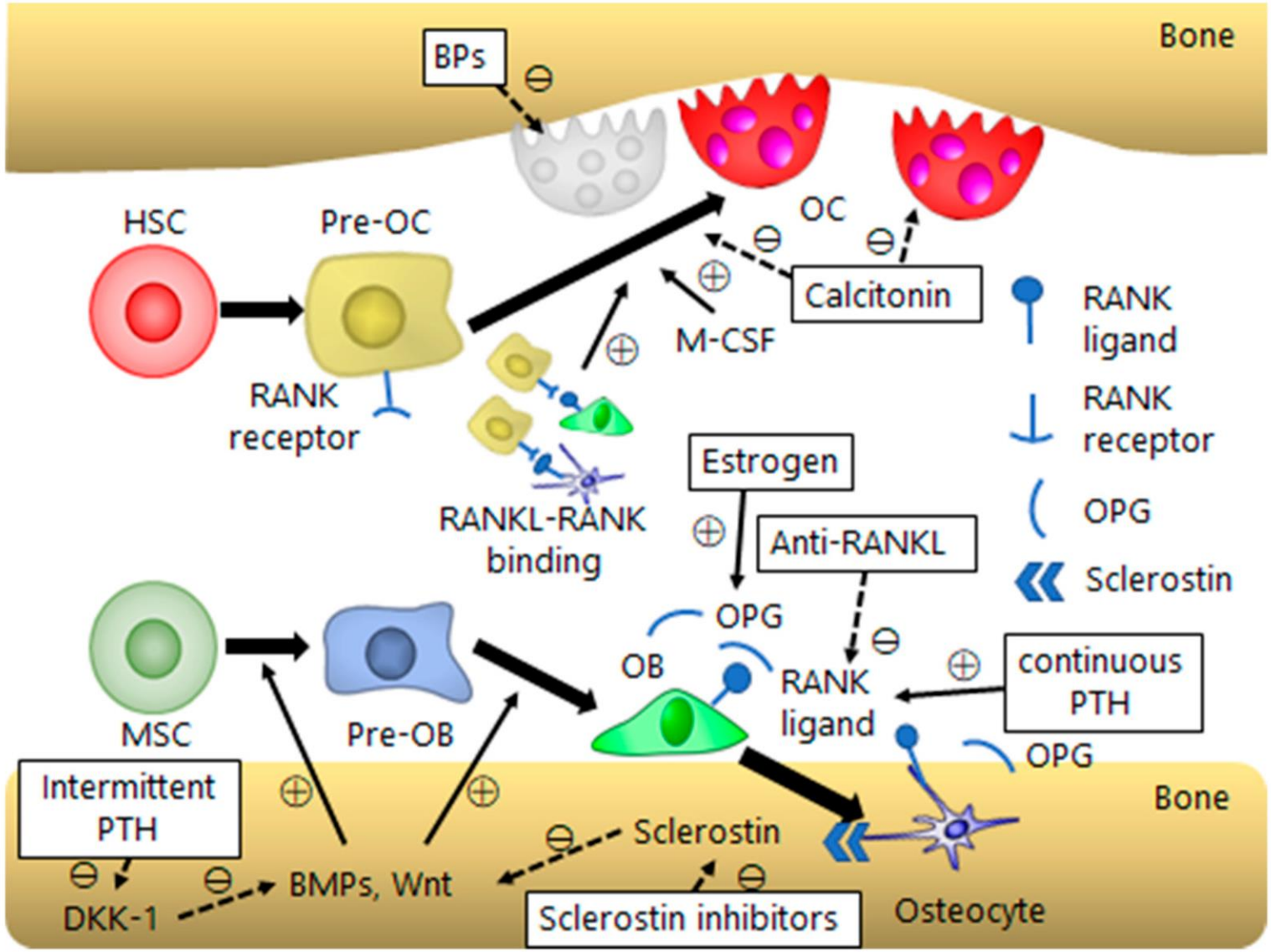

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Bisphosphonate Use in Children with SB/CP

Indications

- Low BMD (Z-score ≤ −2) **plus**:
  - History of fragility fractures **or**
  - Vertebral compression fractures (with or without low BMD)
- Recurrent long-bone fractures despite optimization of nutrition and mobility

Limitations & Risks

- Acute-phase reaction (fever, myalgia) after first infusion
- Transient hypocalcemia (ensure vitamin D and calcium repletion)
- Unknown long-term effects on growing bone (use specialist oversight)
- Adjunct to mechanical loading or nutrition optimization

Benefits

- ↑ Lumbar spine and total body BMD
- ↓ Fracture incidence in moderate–severe CP/SB
- ↓ Bone pain, ↑ quality of life
- Improved vertebral morphology in compression fractures

Clinical Practice Points

- Reserved for **specialist-guided therapy** (endocrinology/bone health)
- Given **after correction** of vitamin D, calcium, and secondary causes
- Treatment duration is finite (often 1–3 years), with reassessment

- **Rhodes JT, et al.** Assessment and management of low bone mineral density in children with cerebral palsy. *JPOSNA.* 2024; 7.

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Treatment Algorithm Summary (Based on Evidence Updates, 2011 → 2016 → 2025)

Step 1: Screen

•Identify risk factors (mobility, nutrition, medications, fractures).

•Obtain DXA scan and labs (vitamin D levels, calcium, phosphate).

•Spine x-ray?

Step 2: Correct Modifiable Factors

•Optimize nutrition (increase dietary calcium, add vitamin D).

•Address underweight or growth faltering.

•Modify medications when possible.

Step 3: Implement Therapies

•Encourage safe weight-bearing opportunities (standers, supported ambulation) though evidence remains limited.

- Initiate bisphosphonate/Sclerostin ab therapies when:
- Low BMD is confirmed **and/or**
- Fragility fractures are present.

  Supported by *probable evidence*.

Step 4: Follow-Up

•Repeat DXA and labs annually or biennially depending on risk severity.

•Monitor fracture occurrence, pubertal development, and nutritional progress.

•Adjust treatment (e.g., pause bisphosphonates after improvement).

Summary

Reduced Mechanical Loading

Limited mobility in SB reduces weight-bearing activity, essential for bone growth and strength.

Nutritional Deficiencies

Inadequate calcium and vitamin D intake impair bone mineralization and contribute to osteoporosis risk.

Medication Effects

Long-term antiepileptic medication disrupts vitamin D metabolism, accelerating bone loss in individuals with SB.

Developmental Challenges

Low BMI and delayed growth hinder optimal bone mass development during critical skeletal growth periods.

- Let’s do questions!
- Or we can all just pretend everything

  made perfect sense and stop here.