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Metabolic Bone Diseases

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Faculty Disclosures

Eileen Lydon, ANP-BC:

• Speakers Bureau: Abbvie, Regeneron

Metabolic Bone Diseases

Disorders of bone strength usually caused by abnormalities of minerals (calcium or phosphorus), vitamin D, Bone mass or bone structure

Most Common Metabolic Bone Diseases

- Osteoporosis
- Osteomalacia (Adults)
- Osteopetrosis
- Parathyroid Disorders
- Paget's Diseases
- Renal Osteodystrophy
- Osteogenesis imperfecta
- Rickets (Children)

Mature Bone Structure and Metabolism

- Bone is a dynamic tissue-remodeled constantly
- Structure is suitable for mobility and protection
- Reservoir for <u>calcium</u>, <u>phosphorus</u>, magnesium, sodium and other ions
- Remodeled by osteoblasts, osteoclasts, and osteocytes



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"Soft bones", which is caused by impaired mineralization of the bone matrix (osteoid), due to inadequate amounts of phosphorus and calcium

- Most common cause is vitamin d deficiency which results in decreased calcium absorption
 - Dietary
 - Lack of sun exposure
 - Bowel and kidney disorders celiac
 - Bariatric Surgery

McDermott, M. Rheumatology Secrets. 2020.

Normal Bone



Bone=Green; Osteoid=Orange

Osteomalacia



Increased Osteoid

Hormonal Control Loop for Vitamin D Metabolism



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Osteomalacia

- Symptoms and findings
 - Bone pain
 - Muscle weakness
 - Increased fractures
 - Low vitamin D 25 OH, serum and urinary calcium, phosphorus
 - Elevated parathyroid hormone and alkaline phosphatase
- Treatment:
 - Vitamin D and Calcium

Primary Hyperparathyroidism

- Disorder of calcium metabolism, characterized by hypercalcemia, and elevated or inappropriately normal parathyroid hormone (PTH)
- Almost always due to overgrowth of parathyroid tissue, as a single gland (80%), or multiple gland (15-20%)
- Another variant serum calcium normal and PTH elevated, in absence of any other cause

Secondary Causes of Hyperparathyroidism

- Vitamin D deficiency
- Malabsorption syndromes
- Renal insufficiency
- Primary hypercalciuria
- Other metabolic bone diseases
- Lithium and thiazide diuretics
- Bisphosphonate or denosumab therapies

Billezikian, J, P et al. Lancet. 2018.

Primary Hyperparathyroidism

- Excessive resorption of calcium from bone
 - Osteitis fibrosis cystica
 - Salt and pepper degranulation of the skull
 - Tapering of the distal clavicle
 - Subperiosteal resorption of the distal phalanges
 - Bone cysts and brown tumors
- Can be associated with fractures, skeletal deformities, bone pain, chondrocalcinosis, and kidney stones

Periosteal Bone Resorption



Salt and Pepper Skull



Treatment

- Most often mild hypercalcemia, however life threatening hypercalcemia can occur
- Parathyroid surgery usually results in cure of the disease
 - Risk of kidney stones, bone mineral density, and risk of fractures are improved after surgery
- Asymptomatic primary hyperparathyroidism often managed conservatively

Paget's Disease of Bone

A chronic condition characterized by focal areas of abnormal osteoclasts that cause excessive bone resorption, followed by abnormal bone formation resulting in disorganized, weak bone

Paget's Disease: An Osteoclast-Mediated Disorder

Histology of Pagetic Bone



Courtesy of Pierre Delmas, MD.



Courtesy of the Paget Foundation.

Paget's

- Localized areas of excessive bone resorption and formation
 - May have only one affected bone or have lesions in multiple bones
 - New lesions rarely develop in previously unaffected bone after diagnosis

Pagetic Bone Is Weaker Than Normal Bone

Normal

Pagetic





Siris ES, Roodman GD. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 5th ed. Washington, DC: ASBMR; 2003: 495-506.

Paget's

- Second most common metabolic bone disease
- Affects about 2% of the US population > 55 years
- 15-30% have positive family histories
- Most common in people of Northern European descent

Siris ES, Roodman GD. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 5th ed. Washington, DC: ASBMR; 2003: 495-506; Altman RD, et al. *J Bone Miner Res.* 2000; 15:461-465.

Common Sites of Involvement

- Can occur in any bone, but most commonly
 - Skull
 - Vertebrae
 - Pelvis
 - Femur
 - Tibia

Siris ES, Roodman GD. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 5th ed. Washington, DC: ASBMR; 2003: 495-506.

Paget's Clinical Presentation

- Usually mild or asymptomatic
- Diagnosis based on incidental findings
 - Elevated serum alkaline phosphatase
 - Radiological findings
- May present with symptoms that are nonspecific

Siris ES, Roodman GD. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 5th ed. Washington, DC: ASBMR; 2003: 495-506; Altman RD. In: Coe FL, Favus MJ, eds. *Disorder of Bone and Mineral Metabolism.* 2nd ed. Philadelphia, Pa: Lippincott Williams & Wilkens; 2002:985-1020.

Paget's Disease-Bowing of Tibia



Complications of Paget's Disease: Complete (Chalk-Stick) Fracture in a Femur



Courtesy of Pierre Delmas, MD.

Diagnosing Paget's Disease

- Laboratory tests
 - Alkaline phosphatase, a marker of bone formation
 - Any level above normal, especially in the absence of elevated liver enzymes
 - Bone-specific alkaline phosphatase may be more reliable
 - Elevated markers of bone resorption
- Radiographs
- Bone scan to assess extent of disease

Lyles KW, et al. J Bone Miner Res. 2001; 16: 1379-1387; Selby PL, et al. Bone. 2002; 31: 366-373.

Management of Paget's Disease

- Bisphosphonates (IV zoledronic acid 5 mg)
- Subcutaneous calcitonin (rarely used)
- NSAIDSs, analgesics opioids
 - Pain relief
- Surgery

- Fractures, bone deformities, osteoarthritis

Lyles KW, et al. J Bone Miner Res. 2001; 16: 1379-1387; Selby PL, et al. Bone. 2002; 31: 366-373.

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