PHYLOGENTIC DISORDERS OF SKELETAL SYSTEM

SUBMITTED BY
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INTRODUCTION:

- **Phylogenetics** is the study of evolutionary relationships among biological entities - often species, individuals or genes (which may be referred to as taxa). The major elements of **phylogenetics** are summarised on the great events.
- Some of the evolutionary diseases of skeletal system in human beings are as follows....

PAGET'S DISEASE:

- is a condition involving cellular remodeling and deformity of one or more bones. The affected bones show signs of dysregulated bone remodeling at the microscopic level, specifically excessive bone breakdown and subsequent disorganized new bone formation. These structural changes cause the bone to weaken, which may result in deformity, pain, fracture or arthritis of associated joints.
- The symptoms of this disesase are :
- Mild or early cases of Pagets are asymptomatic, and so most people are diagnosed with Paget's disease incidentally during medical evaluation for another problem. Approximately 35% of patients with Paget's have symptoms related to the disease when they are first diagnosed. Overall, the most common symptom is bone pain. When symptoms do occur, they may be confused with those of arthritis or other disorders, and so diagnosis may be delayed.
- Paget's may first be noticed as an increasing deformity of a person's bones.
- Paget's disease affecting the skull may cause frontal bossing, increased hat size, and headaches. Often patients may develop loss of hearing in one or both ears due to auditory foramen narrowing and resultant compression of the nerves in the inner ear. Rarely, skull involvement may lead to compression of the nerves that supply the eye, leading to vision loss.

HYPERPHOSPHATASIA

- Hereditary hyperphosphatasia is a rare genetic bone disorder (osteopathy) that usually becomes apparent during infancy or early childhood. Affected individuals develop progressive skeletal malformations especially in the long bones of the arms and legs. Skeletal malformations in the legs may cause problems walking and may eventually result in short stature. Additional symptoms include pain, fractures of affected bones, and muscle weakness. Because the biochemical and radiographic findings of hereditary hyperphosphatasia are similar to those of Paget's disease (a focal skeletal disorder of adults characterized by abnormal bone turnover), the disorder is sometimes referred to as juvenile Paget's disease. However, despite these similarities, the two disorders are distinct. Hereditary hyperphosphatasia is inherited in an autosomal recessive pattern.
- Its symptoms include

- The severity of symptoms associated with hereditary hyperphosphatasia varies from patient to patient. Symptoms usually become apparent during infancy or early childhood usually between 2 and 3 years of age. Most individuals develop widening and bowing of the long bones of the legs eventually resulting in problems walking and short stature. Thickening of the upper domelike portion of the skull (calvaria) is another common finding.
- Additional symptoms include pain, fractures of affected bones, abnormal front-to-back and side-to-side curvature of the spine (kyphoscoliosis) and muscle weakness. Deafness is common – it arises because of an impaired ability of the auditory nerves to transmit input to the brain (sensorineural hearing loss).

KENNY COFFEY SYNDROME

- Kenny-Caffey syndrome is a rare hereditary skeletal disorder characterized by thickening of the long bones, thin marrow cavities in the bones (medullary stenosis), and abnormalities affecting the head and eyes. Most cases are obvious at birth (congenital). The primary outcome of Kenny-Caffey syndrome is short stature. Mental abilities are rarely affected. Individuals with Kenny-Caffey syndrome may also have recurrent episodes of low levels of calcium in the blood stream (hypocalcemia) that is caused by insufficient production of parathyroid hormones (hpoparathyroidism). In most cases, Kenny-Caffey syndrome is inherited in an autosomal dominant pattern. Other cases are inherited in an autosomal recessive pattern, linked to the TBCE gene. (For more information on this disorder, choose “Kenny Caffey” as your search term in the Rare Disease Database.)
- Benign hyperphosphatasia is a biochemical finding unaccompanied by skeletal changes.

OSTEOPOROSIS

- A condition in which bones become weak and brittle.
- The body constantly absorbs and replaces bone tissue. With osteoporosis, new bone creation doesn't keep up with old bone removal. A lifelong lack of calcium plays a role in the development of **osteoporosis**. Low calcium intake contributes to diminished bone density, early bone loss and an increased risk of fractures. Eating disorders. Severely restricting food intake and being underweight weakens bone in .both men and women.
- The symptoms of this disease are as follows

- There typically are no symptoms in the early stages of bone loss. But once your bones have been weakened by osteoporosis, you might have signs and symptoms that include:
- Back pain, caused by a fractured or collapsed vertebra
- Loss of height over time
- A stooped posture
- A bone that breaks much more easily than expected
- A number of factors can increase the likelihood that you'll develop osteoporosis — including your age, race, lifestyle choices, and medical conditions and treatments.

OSTEOMALACIA

- **Osteomalacia** refers to a marked softening of your bones, most often caused by severe vitamin D deficiency. The softened bones of children and young adults with **osteomalacia** can lead to bowing during growth, especially in weight-bearing bones of the legs. **Osteomalacia** in older adults can lead to fractures.

  These problems can be caused by:

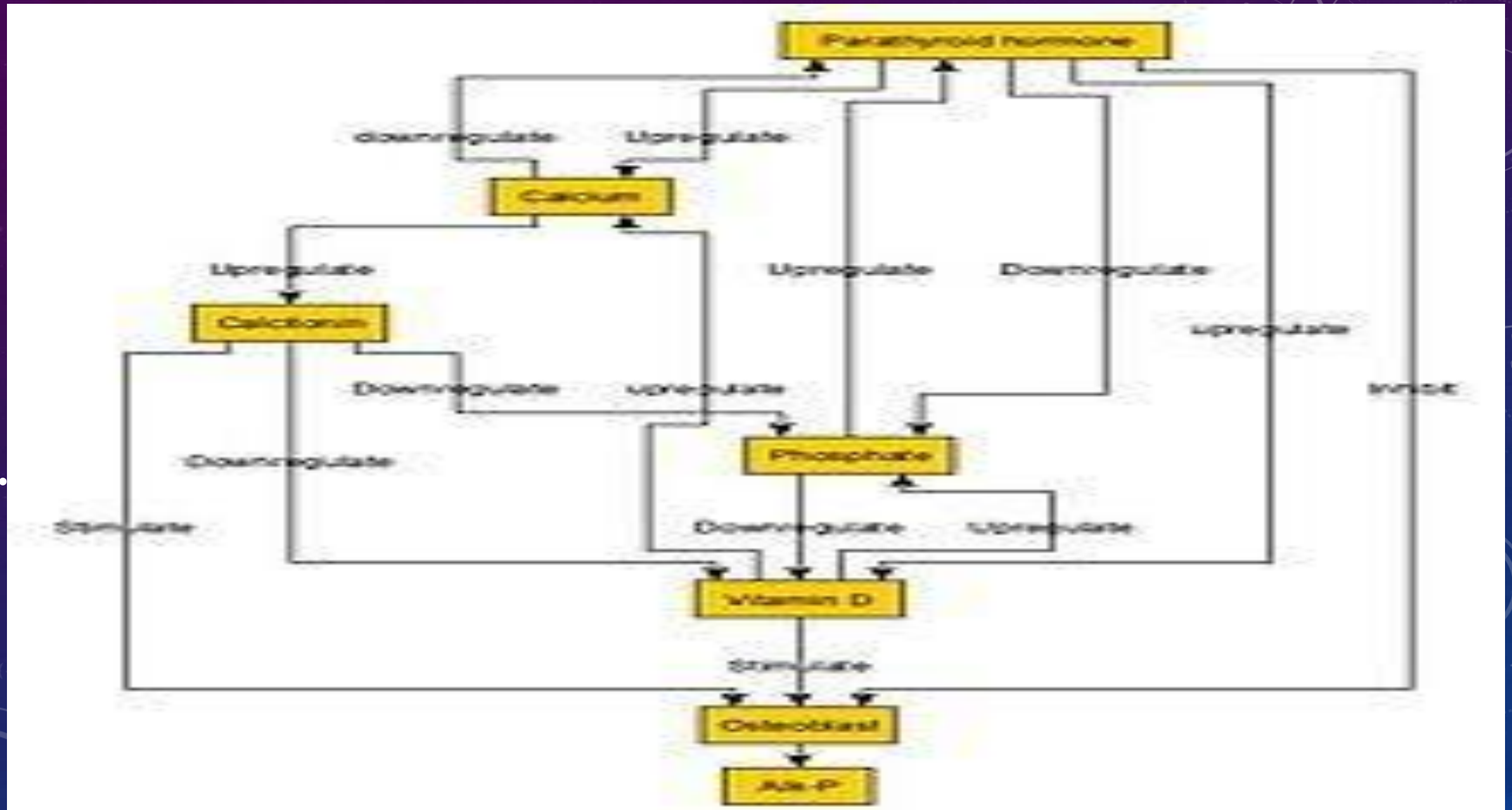
- **Vitamin D deficiency.** Sunlight produces vitamin D in your skin. Dietary vitamin D is usually from foods to which the vitamin has been added, such as cow's milk.
- People who live in areas where sunlight is limited, get little exposure to sunlight or eat a diet low in vitamin D can develop osteomalacia. Vitamin D deficiency is the most common cause of osteomalacia worldwide.

ITS SYMPTOMS ARE :

- Symptoms
- When osteomalacia is in its early stages, you might not have symptoms, although signs of osteomalacia might show on an X-ray or other diagnostic tests. As osteomalacia progresses, you might develop bone pain and muscle weakness.
- The dull, aching pain associated with osteomalacia most commonly affects the lower back, pelvis, hips, legs and ribs. The pain might be worse at night or when you put pressure on the bones. The pain is rarely relieved completely by rest.
- Decreased muscle tone and leg weakness can cause a waddling gait and make walking slower and more difficult.

OSTEOPETROSIS

- **Osteopetrosis**, literally "stone bone", also known as **marble bone disease** or Albers-Schönberg disease, is an extremely rare inherited disorder whereby the bones harden, becoming denser, in contrast to more prevalent conditions like osteoporosis, in which the bones become less dense and more brittle, or osteomalacia, in which the bones soften. Osteopetrosis can cause bones to dissolve and break. It is one of the hereditary causes of osteosclerosis. It is considered to be the prototype of osteosclerosing dysplasias. The cause of the disease is understood to be malfunctioning osteoclasts and their inability to resorb bone. Although human osteopetrosis is a heterogeneous disorder encompassing different molecular lesions and a range of clinical features, all forms share a single pathogenic nexus in the osteoclast. The exact molecular defects or location of the mutations taking place are unknown.


Parathyroid hormone
downregulate
Upregulate
Calcium
Upregulate
Upregulate
Downregulate
Calcitonin
upregulate
Downregulate
upregulate
Phosphate
Downregulate
Upregulate
Vitamin D
Osteoblast
Alk-P

- However, serious forms can result in ...
- Stunted growth, deformity, and increased likelihood of fractures
- Patients suffer anemia, recurrent infections, and hepatosplenomegaly due to bone expansion leading to bone marrow narrowing and extramedullary hematopoiesis
- It can also result in blindness, facial paralysis, and deafness, due to the increased pressure put on the nerves by the extra bone
- Abnormal cortical bone morphology
- Abnormal form of the vertebral bodies
- Abnormality of temperature regulation
- Abnormality of the ribs

OSTEOPENIA

- A condition that occurs when the body doesn't make new bone as quickly as it reabsorbs old bone.
- Causes include a low-calcium diet, smoking, age-related hormone changes, and certain diseases and medications. Women are most at risk.
- You can take action to prevent osteopenia. The right exercise and food choices may help keep your bones strong. If you have osteopenia, ask your doctor about how you can improve and prevent worsening so you can avoid osteoporosis.

- Aging is the most common risk factor for osteopenia. After your bone mass peaks, your body breaks down old bone faster than it builds new bone. That means you lose some bone density.
- Women lose bone more quickly after menopause, due to lower estrogen levels. If you lose too much, your bone mass may drop low enough to be considered osteopenia.
- **Osteopenia symptoms**
- Osteopenia doesn’t usually cause symptoms. Losing bone density doesn’t cause pain.

THANK YOU

- *Submitted to: PhD Anna Zhukova mam*