

# Clinical Case on calcified tissue disorders

# Case presentation 1

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- A 39-year-old female was referred to the Hospital Dentistry Clinic evaluation of severe halitosis, gingival bleeding, and tooth mobility. The patient initially presented to the Emergency Department with a chief complaint of swelling and bruising of the right lower extremity. The patient's medical history revealed significant findings.
- The patient had been previously admitted for swelling and bruising of the right lower extremity, which was present for more than 6 weeks. The patient had a history of mental retardation and was under the primary care of her mother.
- Records revealed no past surgical history, no known drug or food allergies, and the patient was not currently taking medication. The patient had no history of tobacco or alcohol use.
- The patient's diet remained essentially unchanged for years, consisting solely of processed macaroni and cheese, peanut butter, and sweetened carbonated beverages.
- The patient's serum vitamin C level was less than 0.12 mg/dL.

# Case presentation 1

- The patient's clinical signs and symptoms included cutaneous abnormalities with purpura in all extremities along with petechiae. She also exhibited delayed wound healing in an ulcer on the right arm.
- Oral findings were consistent with generalized severe chronic periodontitis. The patient's panoramic radiograph revealed severe bone loss and a hopeless prognosis for retaining any teeth. The patient presented with significant gingival hyperplastic lesions. Areas of gingival tissues exhibited necrosis. Spontaneous gingival hemorrhage was evident.



# Case presentation 1

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- What are the clinical signs and symptoms of Vit C deficiency?
- What is the normal daily intake of Vit C needed?
- What food sources are rich in Vit C
- What is the molecular process affected in Scurvy?
- What is the importance of the collagen modifications affected in Scurvy?
- What other conditions also present symptoms similar to scurvy?

# Diseases associated with abnormalities in collagen synthesis

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- Scurvy-deficiency of ascorbic acid (Vit C).
  - Impaired function of prolyl and lysyl hydroxylases.
  - Decreased formation of hydrogen bonds and cross-linking
  - Decreased tensile strength
  - Symptoms-bleeding gums, loose teeth, subcutaneous hemorrhage, poor wound healing

## Case presentation 2

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- A 24-year-old woman presented with low back pain after water-tubing. Her medical history included a distal radius fracture at age 9 and several digital fractures in childhood. She denied smoking or consuming alcohol, she had adequate calcium intake, and her menstrual history was non-contributory. Her father, who had been diagnosed with osteoporosis, had had more than a dozen fractures, including a hip fracture at age 54. Her sister, age 35, also had osteoporosis.
- On examination, the patient was 167 cm tall and weighed 52 kg. She had blue-gray sclera and normal dentition. A mid-peak ejection murmur was heard over the left sternal border. Musculoskeletal examination demonstrated scoliosis and paralumbar tenderness. Other systems were intact. Lumbar radiographs confirmed an L1 compression fracture, and computed tomography demonstrated fracture stability without cord impingement. Osteoporosis was suspected, and dual-energy x-ray absorptiometry assessment of bone mineral density confirmed severe disease in the lumbar spine and femoral neck. Secondary causes of osteoporosis were ruled out. Owing to her physician high index of suspicion, a diagnosis of OI was pursued.

# Case presentation 2

- Osteogenesis imperfecta



## Case presentation 2

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- How many types of OI are identified and what causes each type?
- Describe how the molecular alterations affect the structure and function of bone.
- What are the clinical signs and symptoms of OI
- What is dentinogenesis imperfecta and what causes it?
- What are the clinical signs and symptoms of DI?

# Case presentation 2

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- Dentinogenesis imperfecta



# Diseases associated with abnormalities in collagen synthesis

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- Osteogenesis imperfecta-brittle bone syndrome
  - mutations in the collagen genes prevent stable triple helix formation and leads to unfolding of protein at body temp.
  - Eight types, type II usually lethal, type III also high rate of mortality
  - Bone fragility with frequent fractures, blue sclera, opalescent dentin, hearing loss, hump-backs

# Diseases associated with abnormalities in collagen synthesis

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- What other diseases are associated with abnormalities in collagen synthesis?
- Describe the molecular changes involved.

# Diseases associated with abnormalities in collagen synthesis

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- Ehlers-Danlos syndrome
  - Inherited disorder of connective tissue due to defects in the collagen molecule
  - 11 types described, type I (severe) and type II (mild) are the most common
  - Type IV is the most serious due to rupture of large vessels secondary to abnormalities in the collagen type III molecule
  - The defects in collagen could be secondary to defective removal of propeptides by aminoprocollagen peptidase (type VII), deficiency of lysyl hydroxylase (type VI), or mutations in type I collagen genes (VII)
  - Common clinical findings include hypermobility of joints, hyperextensibility of skin, abnormal tissue fragility
  - Periodontal disease and hyperextensibility of the tongue can be present

# Diseases associated with abnormalities in collagen synthesis

Gene or Enzyme	Disease <sup>2</sup>
<i>COL1A1, COL1A2</i>	Osteogenesis imperfecta, type I <sup>3</sup> (MIM 1566200) Osteoporosis <sup>4</sup> (MIM 166710) Ehlers-Danlos syndrome type VII auto- somal dominant (130060)
<i>COL2A1</i>	Severe chondrodysplasias Osteoarthritis <sup>4</sup> (MIM 120140)
<i>COL3A1</i>	Ehlers-Danlos syndrome type IV (MIM 130050)
<i>COL4A3–COL4A6</i>	Alport syndrome (including both auto- somal and X-linked forms) (MIM 104200)
<i>COL7A1</i>	Epidermolysis bullosa, dystrophic (MIM 131750)
<i>COL10A1</i>	Schmid metaphysial chondrodysplasia (MIM 156500)
Lysyl hydroxylase	Ehlers-Danlos syndrome type VI (MIM 225400)
Procollagen N- proteinase	Ehlers-Danlos syndrome type VII autosomal recessive (MIM 225410)
Lysyl hydroxylase	Menkes disease <sup>5</sup> (MIM 309400)

# Case presentation 3

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- A 31-year-old female patient presented with considerable dental sensitivity and wear of her teeth. Her primary concerns included extreme sensitivity; dissatisfaction with size, shape, and shade of teeth; and poor masticatory efficiency. She was very conscious about the appearance of her teeth and reported that her primary dentition was affected in same manner.
- A detailed medical history, dental history, and social history was obtained but was noncontributory. The patient was questioned further about the presence of similar abnormalities in her family. She stated her grandfather had a similar defect in his teeth.

# Case presentation 3

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- An extraoral examination revealed no abnormalities. Intraoral examination revealed a full complement of the permanent dentition. The incisal aspects of maxillary and mandibular anteriors were completely worn away exposing the pulp chambers. The occlusal aspects of all the posterior teeth were also severely worn, however, the cervical and proximal enamel was found to be normal. The crowns were short and thin with the tooth surfaces being rough and dull. Deep carious lesions were seen in the right and left mandibular molars. The attrition of the molars resulted in a decrease of the vertical dimension of occlusion. The gingival status was found to be good and well maintained. The oral hygiene of the patient was satisfactory.
- A panoramic radiographic examination of the teeth revealed generalized defective enamel on all the teeth. The enamel of the teeth appeared to have the same radiodensity as dentin and the morphology of the roots were normal. The pulp chambers were normal with no evidence of calcification. The cementum, lamina dura, and bony trabeculations were within normal limits.

# Case presentation 3

- Amelogenesis imperfecta



# Case presentation 3

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- What is amelogenesis imperfecta?
- What causes AI?
- How is AI classified by types or groups?
- What is the role of the gene products mutated in AI?
- What are the clinical characteristics of AI?
- How is AI different from DI?

# Diseases that affect matrix calcification

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- Amelogenesis imperfecta
  - Disorder of tooth development where tooth enamel formation is defective leaving it weak and prone to damage
  - Genetic mutations have been identified as causing this condition. Genes affected encode for proteins involved in the formation of the enamel: AMELX, ENAM, MMP20
  - There are 4 general types divided in 14 subtypes
    - ❖ Type I: hypoplastic
    - ❖ Type II: hypomaturation
    - ❖ Type III: hypocalcified
    - ❖ Type IV: hypomaturation, hypocalcified, taurodontism

# Diseases that affect matrix calcification

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- Amelogenesis imperfecta
  - The function of the genes known to be muted
    - ✦ AMELX-amelogenin, X-linked: protein encoded by this gene helps control the size and shape of the hydroxyapatite crystal
    - ✦ ENAM-enamelin: the protein encoded by this gene appears to function as a nucleation center for the deposition of hydroxyapatite
    - ✦ MMP20-enamelysin: encodes an enzyme that helps degrade and remove amelogenins and ameloblastin reducing the organic content during enamel maturation
  - Clinical presentation of AI
    - ✦ Small teeth, discoloration of teeth, pitted or grooved teeth, rapid wear and breakage, increased risk of caries
  - Difference between DI and AI
    - ✦ DI presents changes in the size of the pulp chamber, DI has no increased risk of caries