the Child Dental Patient with

Lysosomal storage disorder
(Mucopolysaccharidosis)

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MPS type VI Definition

- **Mucopolysaccharidosis VI** (MPS VI), also known as **Maroteaux-Lamy syndrome**, is a progressive autosomal recessive lysosomal storage disorder with multisystem involvement which was first described by Dr.Pierre Maroteaux and Dr.Maurice Lamy in 1963.
- The underlying cause of the disease is **deficient activity of the enzyme *N*-acetylgalactosamine 4-sulfatase** (arylsulfatase B (ASB)), which is involved in the degradation of the glycosaminoglycans (GAGs) dermatan sulfate and chondroitin 4-sulfate.
- This enzyme deficiency leads to the **accumulation of partially degraded GAGs in tissues and organs**, which in turn causes an array of clinical manifestations that progressively worsen with age.
- **Dermatan sulfate is an important component of bones, cartilage and connective tissues**, but also has a role as cofactor or receptor for growth factors, cytokines, adhesion molecules and chemokines and serves as a regulator of enzyme activity and signaling molecules in response to cellular damage

MPS type VI Diagnosis

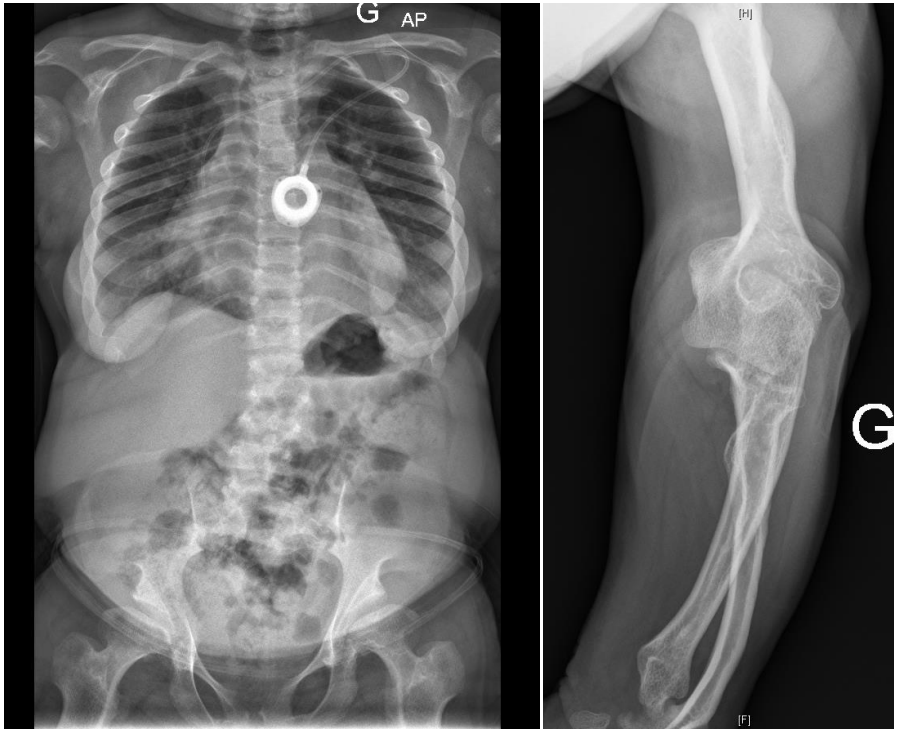
- Diagnosis of MPS VI relies on presence of **clinical features**, **increased GAG levels in urine** or low ASB activity in dried blood spots, and **measurement of enzyme activity** levels in leukocytes or fibroblasts.
- The clinical manifestations of MPS VI are believed to be directly or indirectly caused by accumulation of dermatan sulfate in tissues and organs.

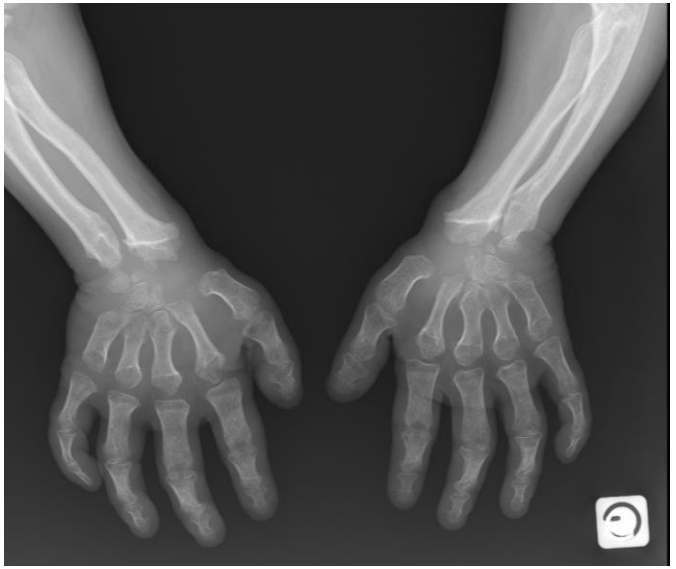
MPS type VI Prevalence

- MPS VI is **very rare**, with incidence estimates ranging from 0.36 to 1.30 per 100,000 live births, depending on the country or ethnic population examined.
- The highest incidence has been reported for the Turkish population in Germany, which may be due to a high degree of consanguinity in this population; the lowest incidence has been reported for Sweden
- Due to the lack of newborn screening programs for MPS VI and the difficulties in diagnosing the disease, the reported incidence rates are probably underestimated

Clinical features of MPS VI

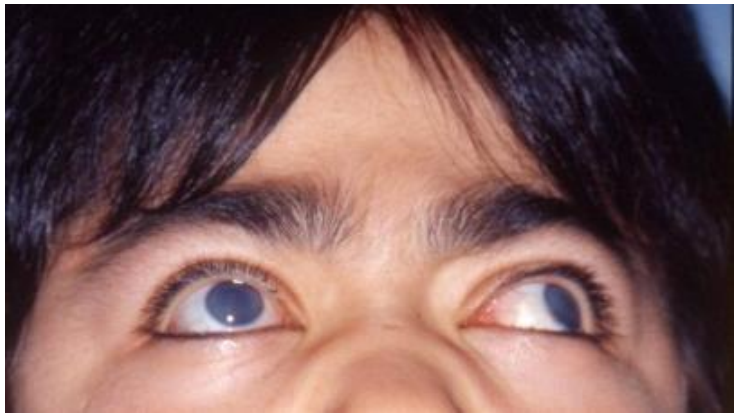
- **Disease manifestations, age of symptom onset and rate of disease progression vary widely among MPS VI patients**
- The **skeleton** is generally one of the most severely affected organs in these patients; These patients also frequently show scoliosis or kyphosis, hip dysplasia, genu valgum and claw hand deformities, as well as joint stiffness, joint pain and flexion contractures
- Musculoskeletal disease can result in **short stature** (adult height below 120 cm in rapidly progressing patients), low body weight, nerve entrapment syndromes such as spinal cord compression, nerve root compression and carpal tunnel syndrome, and **poor mobility**





Clinical features of MPS VI

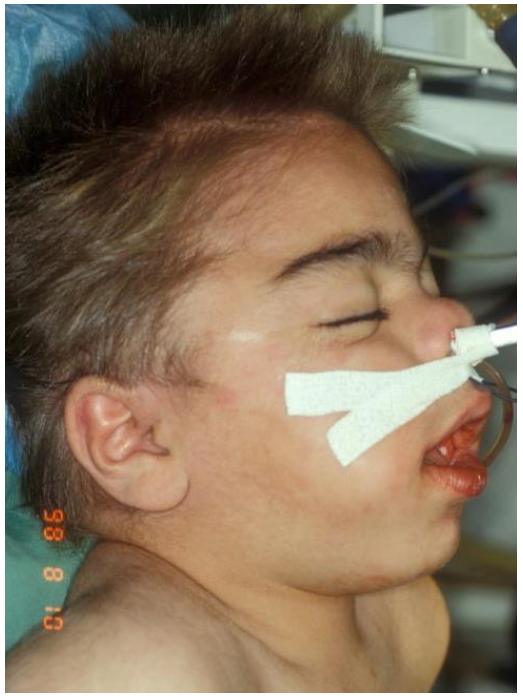
- Cardiac valve abnormalities (mitral and aortic valves) = the most common finding
- Compromised pulmonary function
- Patients may develop frequent sinusitis or otitis media, recurrent bronchitis or pneumonia, sleep disordered breathing, and even respiratory failure
- Hepatosplenomegaly
- Umbilical and inguinal hernias
- Impaired vision (due to corneal clouding, high hyperopia, optic nerve injury, or retinopathy) ⇨ reduced visual acuity or even blindness
- Impaired hearing
- Delayed pubertal development



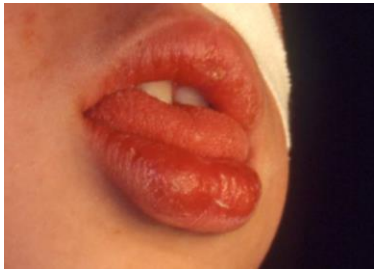
Quality of life in MPS VI

- Because of the high morbidity, frequent surgeries, and constant monitoring required to manage the common infections and other clinical manifestations, most MPS VI patients have a poor quality of life
- Activities of daily living can also be considerably limited due to impairments in vision, hearing, mobility, and functional capacity

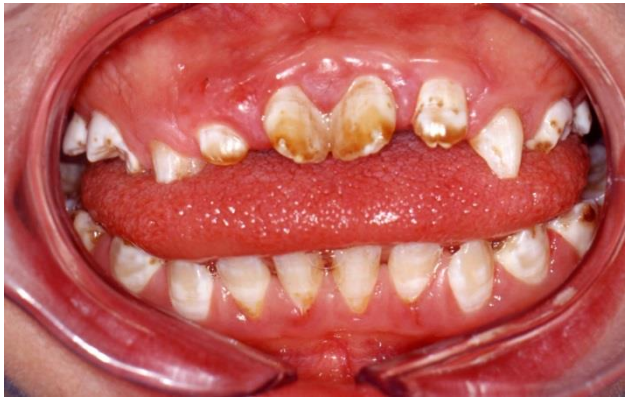
Craniofacial and dental features



- Coarse facial features with:
  - hirsutism
  - frontal bossing
  - depressed nasal bridge



- Oral and dental abnormalities:
  - enlarged tongue
  - gingival hypertrophy
  - unerupted and impacted permanent teeth
  - hyperplastic tooth follicles
  - malposition of unerupted teeth
  - taurodontism
  - long tooth roots
  - maloclusion - anterior open bite
  - hypoplastic mandibular condyles



Management of MPS VI

- Recent therapies directly target the underlying cause of the disease, i.e. the deficiency of the ASB enzyme
- The therapies currently available consist in replacing or repairing the deficient enzyme:
  - weekly intravenous infusions with recombinant human ASB or galsulfase
  - hematopoietic stem cell transplantation which restores the endogenous production of deficient enzyme through the transplantation of multipotent hematopoietic stem cells from a healthy donor

- Medical and surgical treatment of disease manifestations:
  - Patients with MPS VI need continuous management of disease manifestations, including use of adaptive or supportive devices, physiotherapy, occupational therapy, symptom-based medications, and surgical interventions
  - A multi-disciplinary management approach is required to detect and monitor disease manifestations

Anesthetic risk

Interventions requiring general anesthesia can be very dangerous in patients with MPS VI who are at high risk of perioperative morbidity and mortality

- Respiratory function in patients with MPS VI can be impaired due to airway abnormalities, which may be caused directly by GAG deposition in the mouth, nose, throat, and upper and lower airways, or indirectly by cranial and spinal abnormalities (e.g.,flattened nasal bridge, short neck, high epiglottis, mandibular abnormalities, abnormal cervical vertebrae)
- Many patients also show reduced ventilatory capacity due to altered chest wall shape and structure, diaphragmatic weakness, or compromised diaphragm excursion
- Intubation difficulties or failure (sometimes requiring emergency tracheostomy) are also an issue

Thus, airway obstruction (after induction or extubation) and restrictive pulmonary disease, often in combination with cardiovascular manifestations, pose a serious anesthetic risk to MPS VI patients. Because of this high anesthetic risk, the advantages of surgery should always be balanced against the associated risks for each individual patient and the procedures should be performed by experienced personnel