Early traces of a lysosomal storage disease

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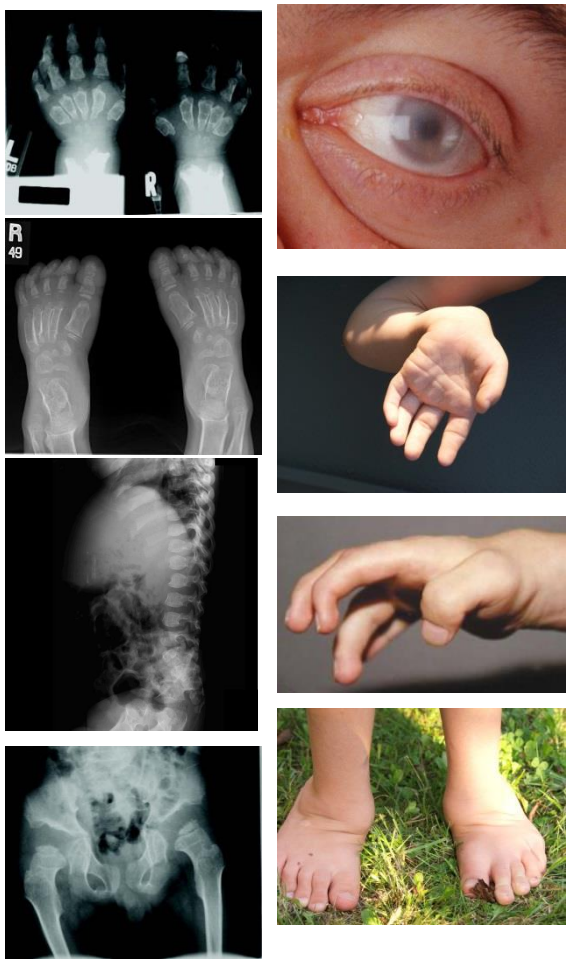
Overview

- What is “dysostosis multiplex”?
- First descriptions of these specific bone changes in Mucopolysaccharidosis (MPS)
- Other lysosomal diseases with dysostosis multiplex
- Earlier findings interpreted as dysostosis multiplex
- Austrian Medieval skeleton

From last year: Characteristics of MPS



Dysostosis multiplex

- MPS is a group of rare genetic diseases in the extracellular matrix of the conncetive tissue
- Connective tissue is represented all over the body – therefore MPS are multisystemic disorders
- Clinical spectrum: from very severe forms with early death to very mild - better: attenuated - forms with survival until late adulthood (in all types of MPS)
- MPS cause increasing organ dysfunctions with advancing age

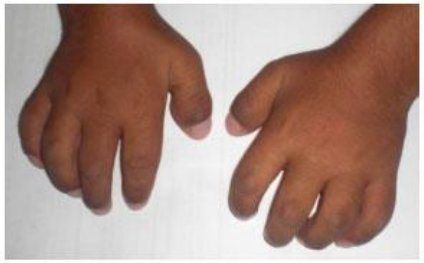
- **X-rays of the bones are part of the diagnostic pathway**

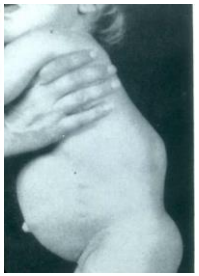
What is “dysostosis multiplex”?

Skeletal changes in all bones and joints

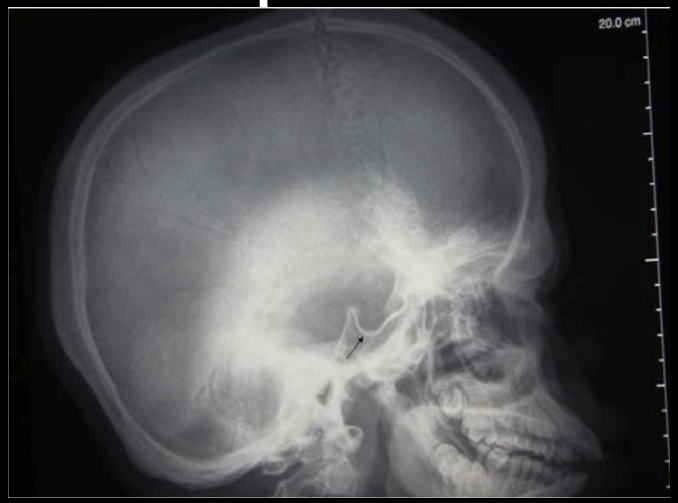
- Macrocephaly, sclerosis of the skull (thick), j-shaped sella turcica
- Saddle nose, small or large mandibula
- Malformation of the vertebral bones (ovoid, platyspondyly), broad ribs, severe changes in cervical spine and thoracolumbal spine (thoracolumbal „gibbus“)
- Changes in the acetabular roof, flattening of the femoral heads
- Cone shaped metacarpals

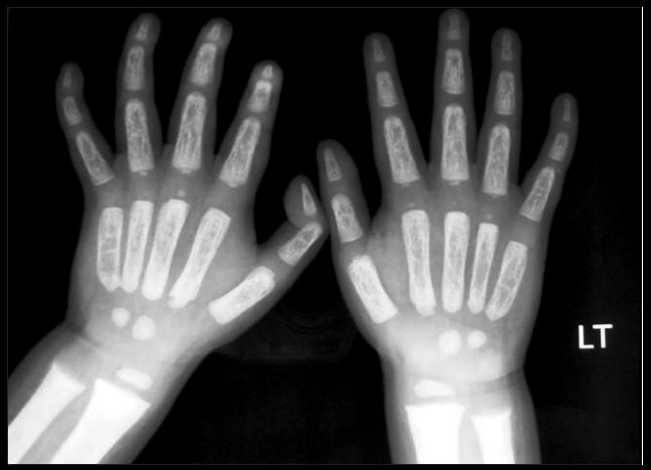
Bone changes and related clinical signs

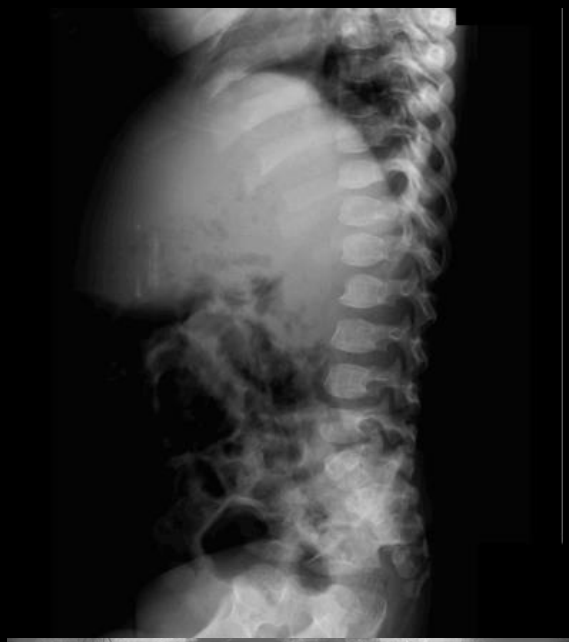


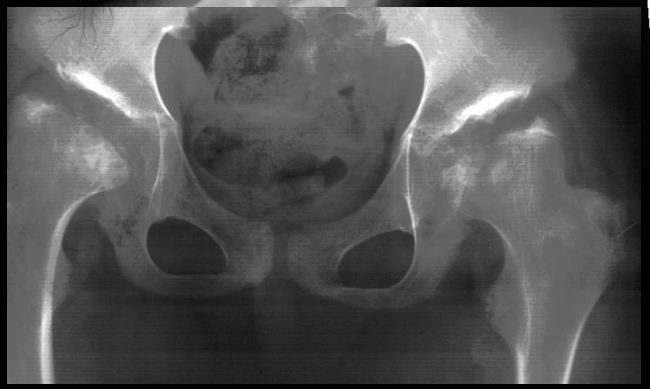


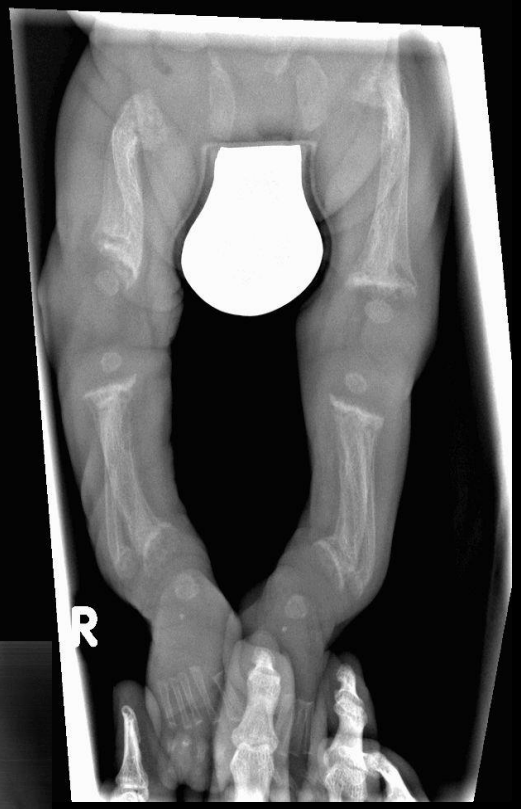
Typical radiological findings in dysostosis multiplex





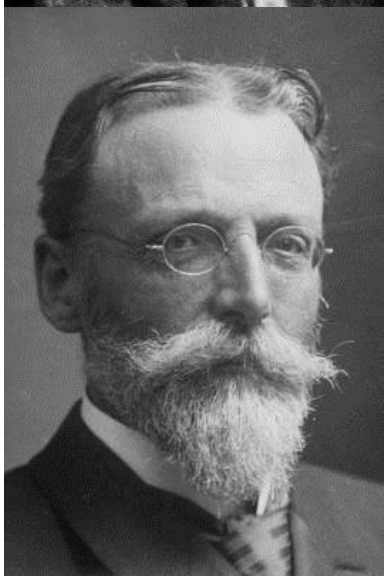






First descriptions of these specific bone changes in Mucopolysaccharidosis (MPS)

First publication about „dysostosis multiplex“



Prof.Meinrad von Pfaundler (Austria), Gertrud Hurler (Germany):

1919: First presentation: „Demonstrationen über einen Typus kindlicher Dysostose“

Published 1919: MMWS: „Über einen Typus multipler Abartungen, vorwiegend am Skelettsystem“

In 1973: MPS I - Morbus Hurler (Pfaundler-Hurler) – enzyme deficiency: Iduronidase

Other lysosomal diseases with dysostosis multiplex

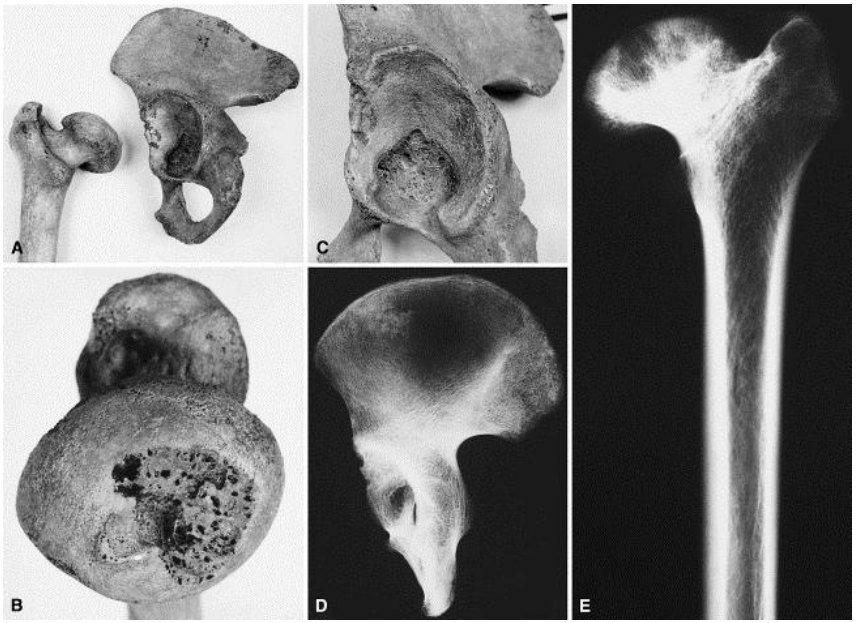
Differential diagnoses

- Mucopolysaccharidoses
- Mucolipidoses
- Glycoproteinoses: alpha-mannosidosis, fucosidosis, GM1-gangliosidosis, aspartylglucosaminuria, sialidosis…

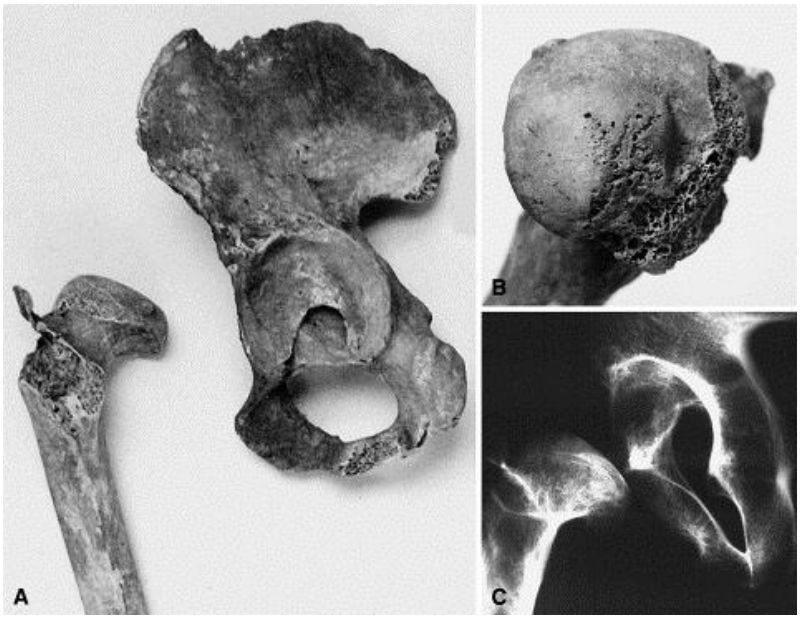
- **= from the group of lysosomal storage diseases**

Earlier findings - interpreted as dysostosis multiplex

Earlier findings interpreted as Legg-Calvé-Perthes Disease, probably MPS or gangliosidosis *(Smrcka V et al. Clin Orthop Pelat Res 2009; 467:293-297)*



Man, older than 50 years, end of the 5th to 6th century, South Moravia, Langobard cemetery, Czech Republic



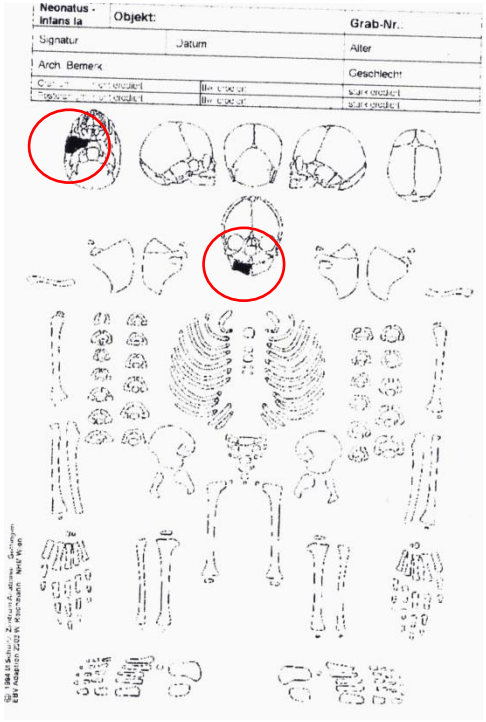
Adult man, 9th to 10th century, Branýsek/Bohemia, Czech Republik

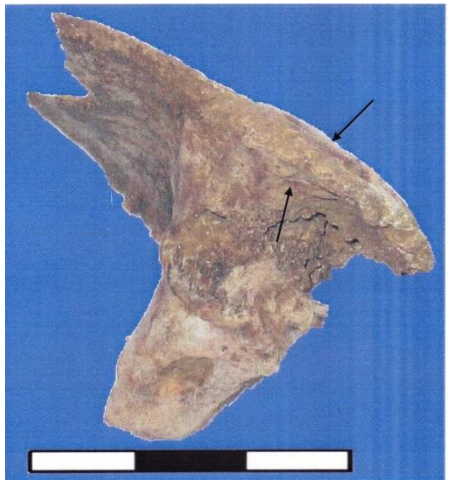
(M. Ghamra Kozma, 2008)

Early findings interpreted as MPS

Egypt, early dynasty (3000 b.c.):
Humeri with possible Mucopolysaccharidosis;
about 14 years old person.

British Natural Museum London, nach:
DJ Ortner, WGL Putschar, 1985





Saladorf, Austria, 4th century:
Population from Pannonia and Noricum,temporal bone and part of maxilla

P Pail in: *Diploma Thesis, University of Vienna, 2009*

Austrian Medieval Skeleton

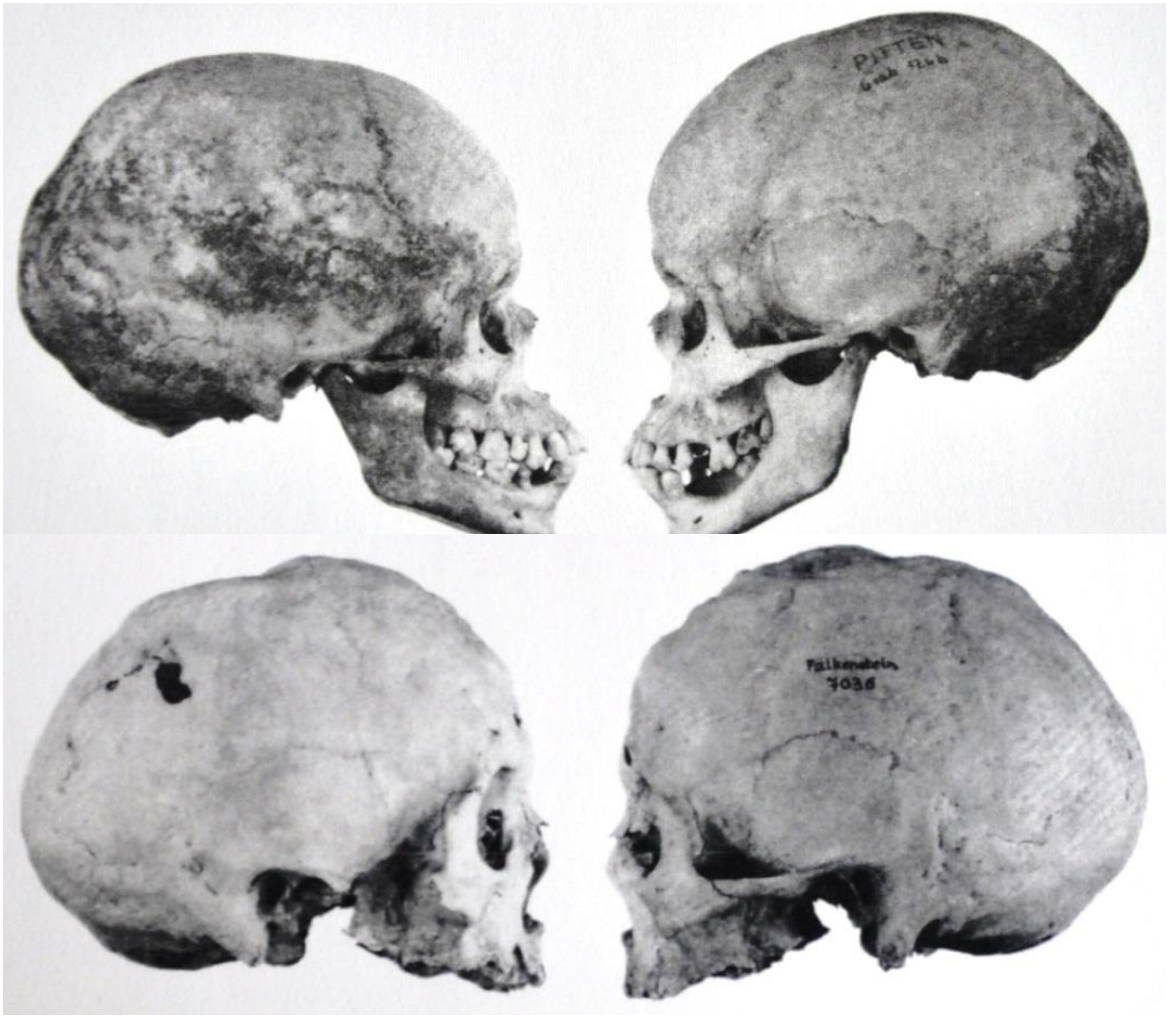
Skeleton from Pitten, Lower Austria, 9th century

- Found between 1970 – 1973
- Young male adult, 20 – 30 years old
- Burial position at the edge of the cemetery – mental retardation?
- Skull form resembled picture of *R Virchow (1862)*
- Authors interpreted and published as Pfaundler-Hurler-syndrome
- Authors:
  - *Szilvássy J, Kritscher H, Ann Naturhist Mus Wien 1981; 85/A: 73-84*
  - *Schultz M, Kritscher H, Szilvássy J. Ann Maturhist Mus Wien 1984; 86/a:89-93*

- **Reevaluation of the skeletal findings – dysostosis multiplex?**

  Kircher SG: JSM Biochemistry & Molecular Biology 2017;4(2)

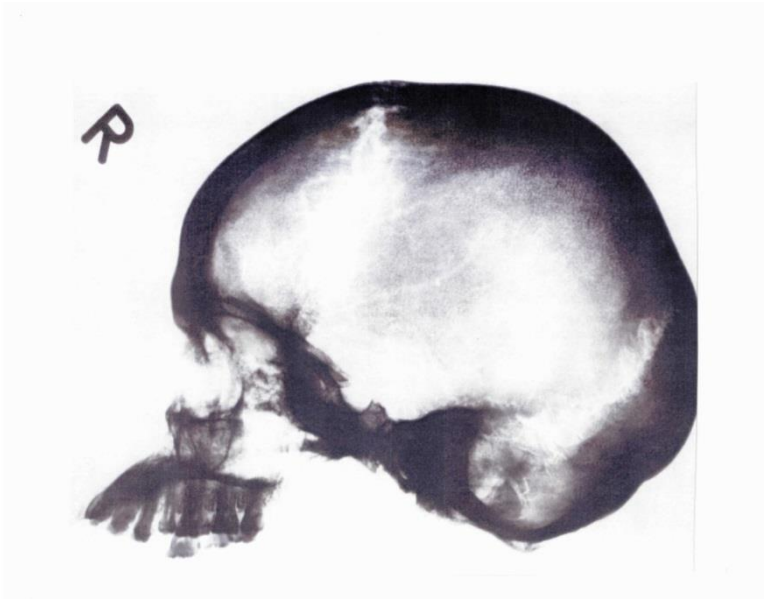
What are the signs of dysostosis multiplex? Skull - form



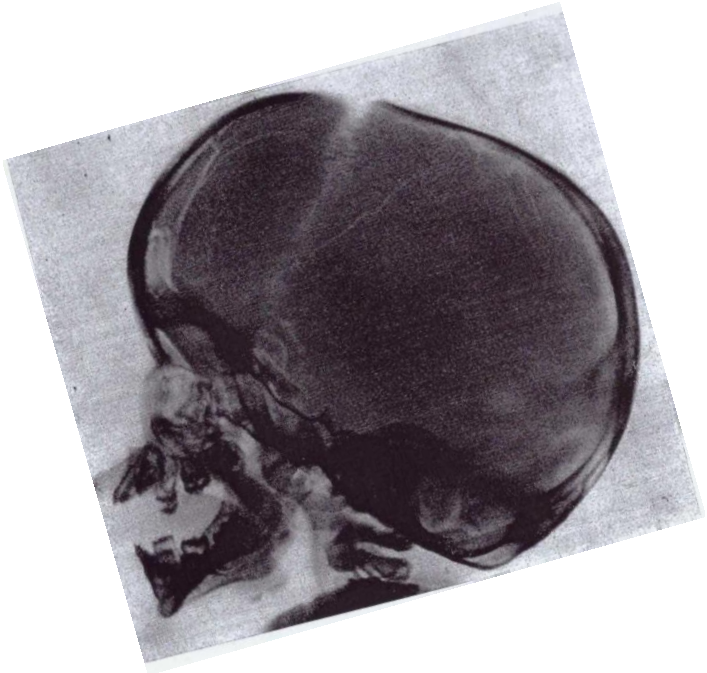
Medieval skeleton

Comparison: Medieval skull man, 40 years old, suffered from syhillis.
Bauer G, Szilvássy J, Kritscher H. Ann Naturhist Mus Wien 1983; 85/A: 59-72

What are the signs of dysostosis multiplex? Skull – x-rays

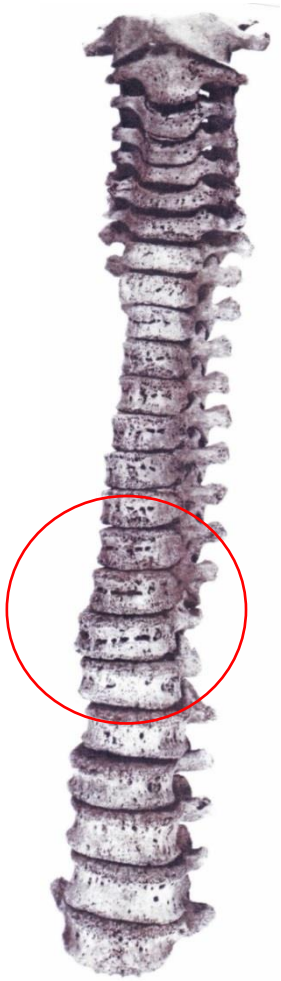


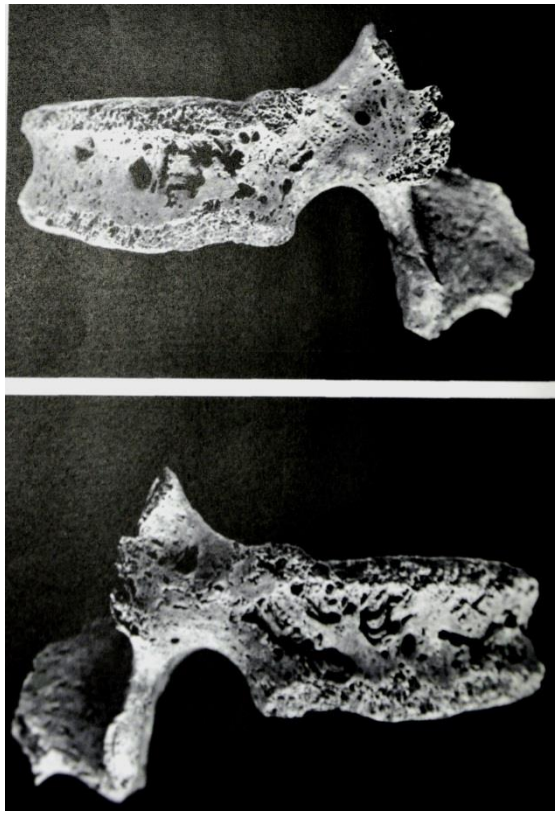
Medieval
Skeleton – X-ray



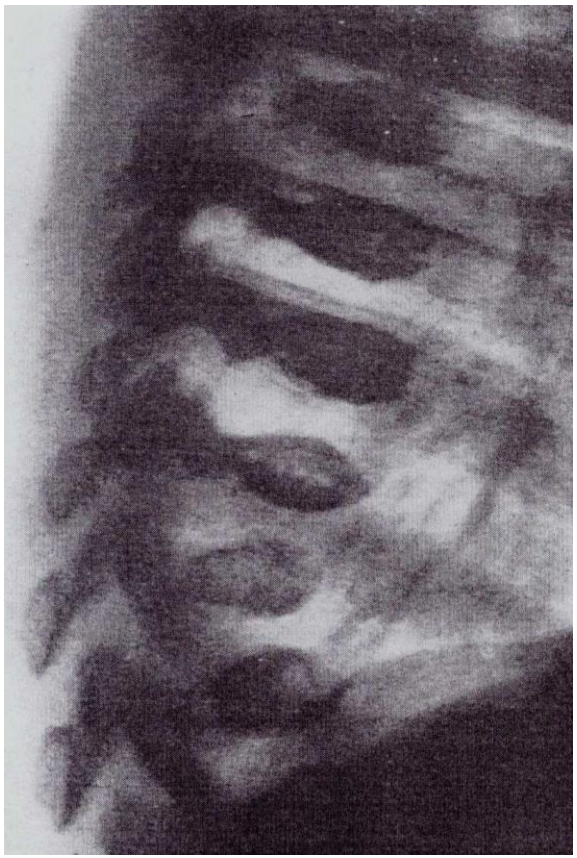
Comparison: Ullrich O. Chapter X: Die Pfaundler-Hurlersche Krankheit.
In: Ergebnisse der Inneren Medizin, 1943, Editors: M.v.Pfaundler, A. Schittenhelm

What are the signs of dysostosis multiplex? Spine, vertebral bodies



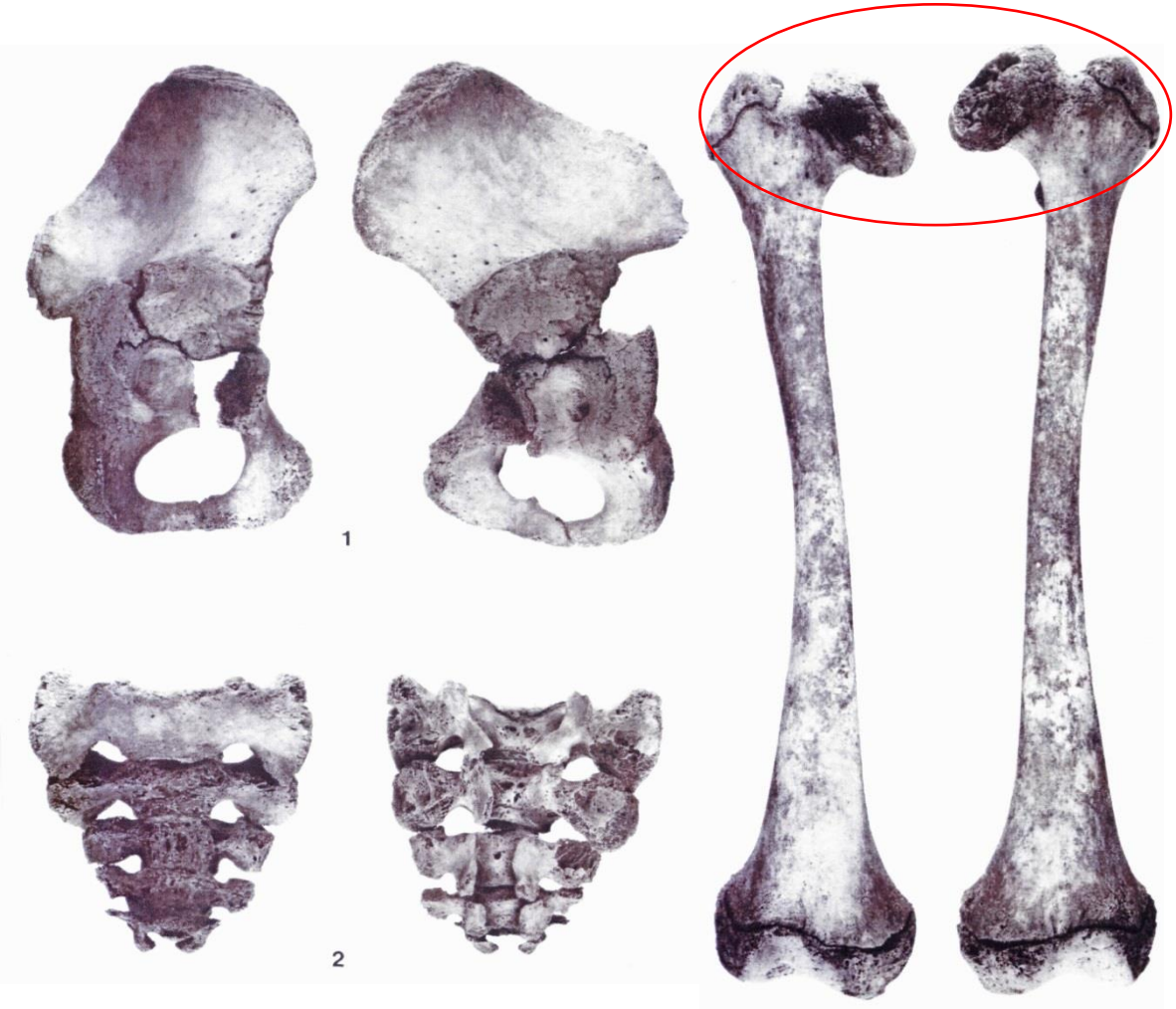


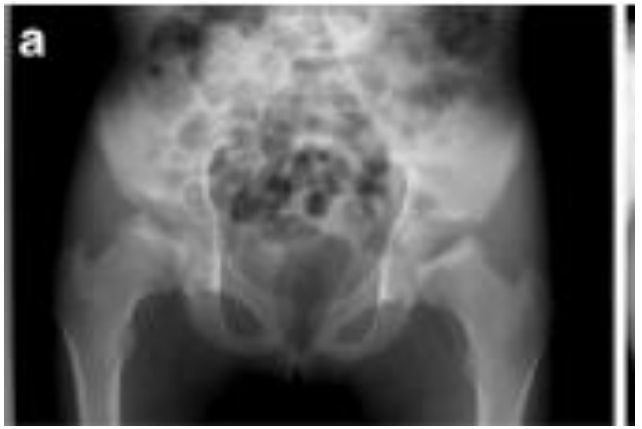
Thoracal vertebra 11



Feldman N et al. Osteochondrodystrophia deformans (Morquio Brailsford Disease). *Arch Dis Childh 1950; 279-288.*

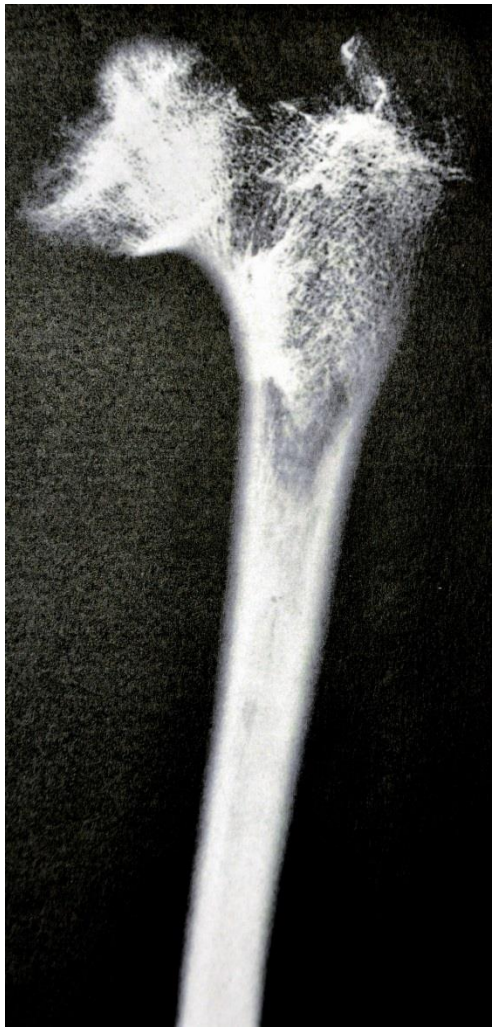
What are the signs of dysostosis multiplex? Pelvis and femoral heads





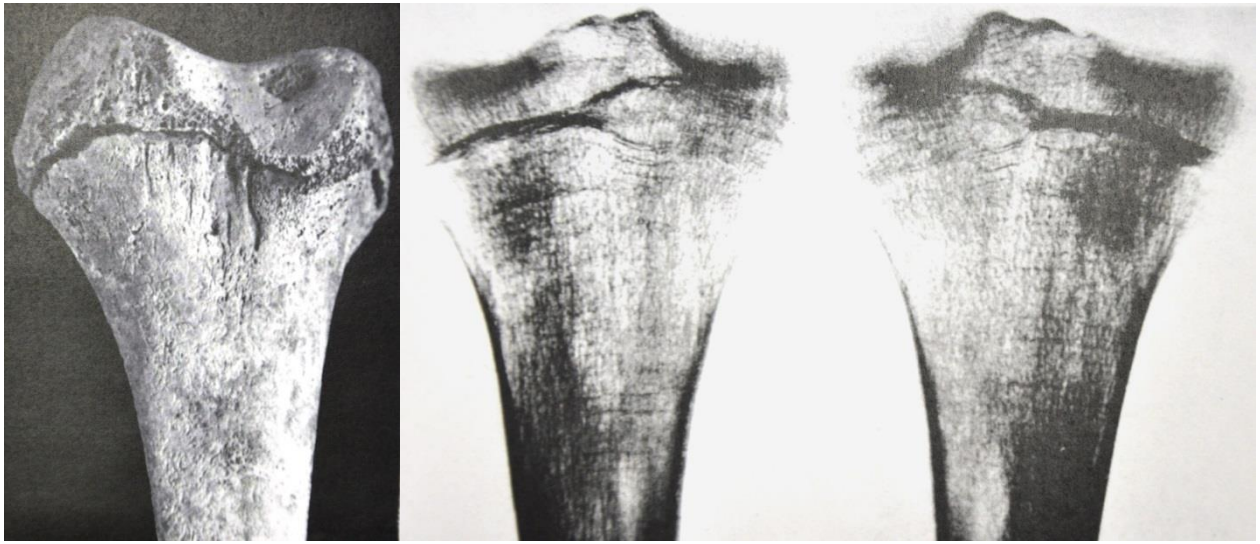
Girl, 8 years old, diagnosed: MPS VI (Maroteaux-Lamy).
Lachman RS et al. Skeletal Radiol 2014; 43:359-369

What are the signs of dysostosis multiplex? Lower extremities

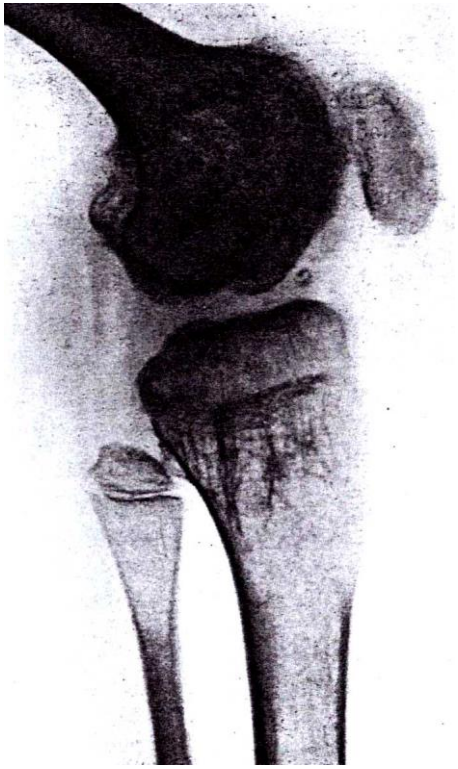


Early traces of a lysosomal storage disease, S.G.Kircher, 2017

What are the signs of dysostosis multiplex? Knee-joints (tibiae)



Medieval Skeleton: Harris lines in X-ray. Observed in diseases with inborn disturbances of osteochondrotic maturation *Harris HA. Brit J Radiol 1931; 4:561-588*



Sur une form de dystropie osseuse familiale. *Morquio L. Arch Méd Enf Paris 1929; 32:129-135*

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