# Unfolding Clinical Events Following a Diagnosis of MPS

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# Important concepts to consider

- Progressive disorders
  - Multisystem involvement
  - Rate of progression is highly variable
- Disease complications do not necessarily correlate with each other
- Disease specific approaches
- Symptom specific approaches
- Anticipatory guidance

# Heterogeneity of the LSDs

Each LSD represents a spectrum of disease from early severe to attenuated

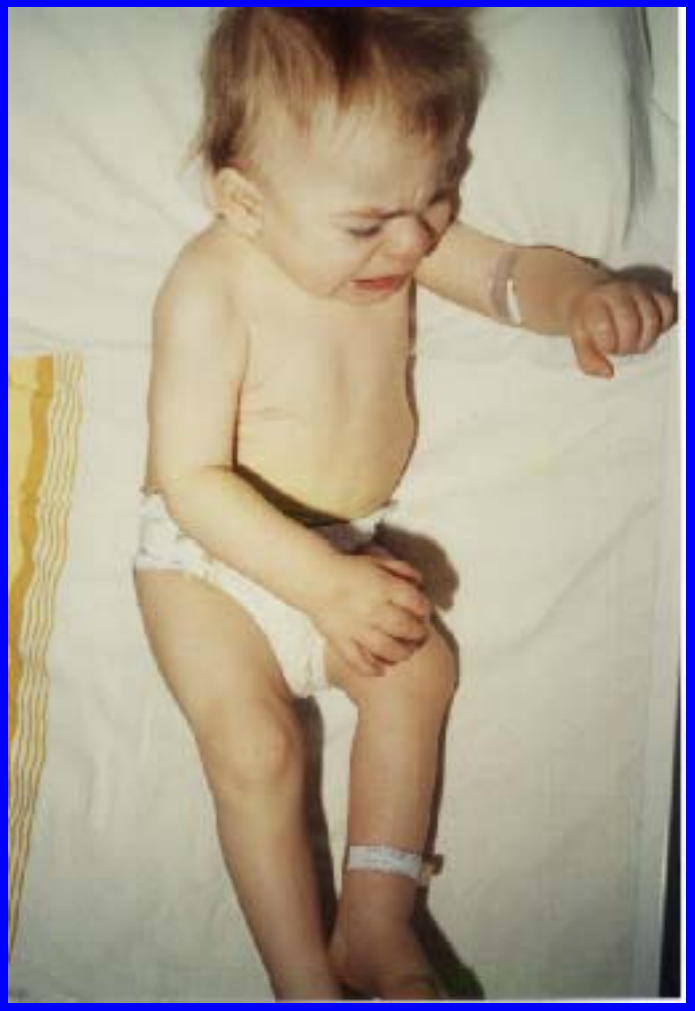
| Hurler syndrome | Hurler/Scheie | Scheie syndrome |
|---|---|---|
| • early diagnosis<br>• developmental delay<br>• hepatosplenomegaly<br>• skeletal involvement<br>• corneal clouding<br>• joint involvement<br>• deafness<br>• cardiac involvement<br>• death in first decade | • little or no intellectual defect<br>• respiratory disease<br>• obstructive airway disease<br>• cardiovascular disease<br>• joint stiffness/contractures<br>• skeletal abnormalities<br>• decreased visual acuity<br>• death in teens and 20's | • later diagnosis<br>• normal intelligence<br>• hepatosplenomegaly<br>• joint involvement<br>• nerve entrapment<br>• deafness<br>• cardiac involvement<br>• normal life span |

# MPS I Clinical heterogeneity

## A spectrum of disease

Hurler syndrome  Hurler/Scheie  Scheie syndrome

# Severe MPS I



18 months

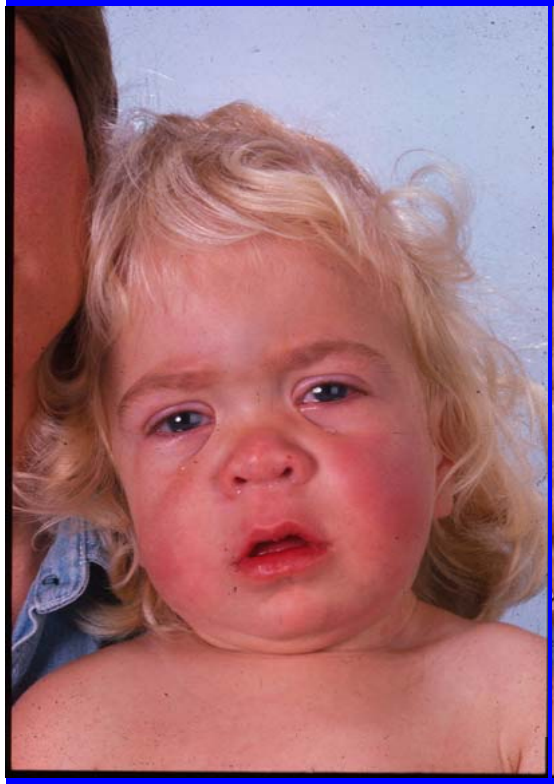
# MPS I

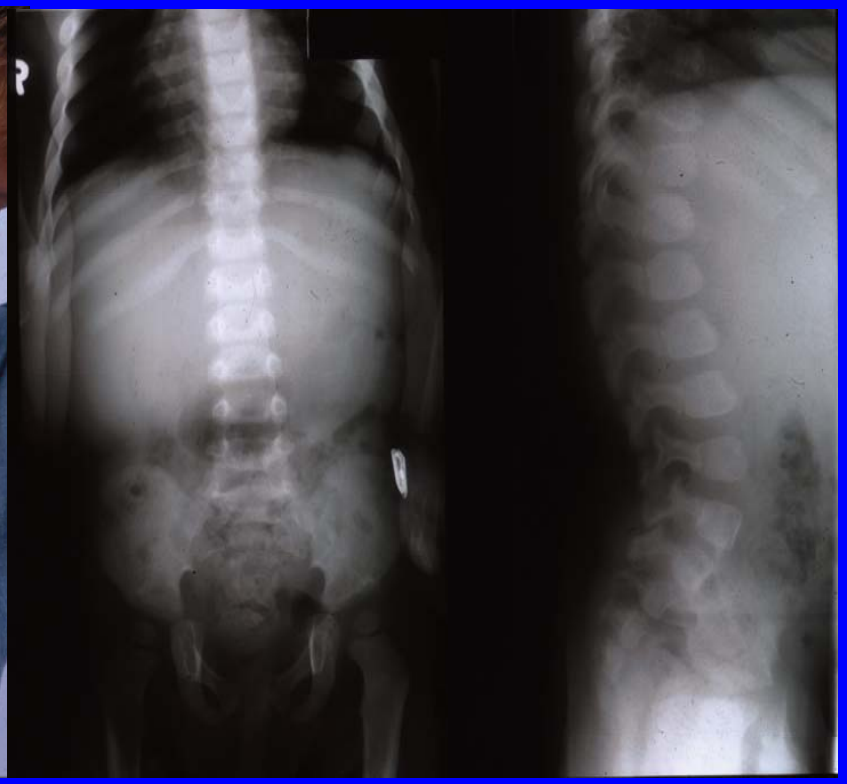
# MPS I


14 yrs

5 yrs

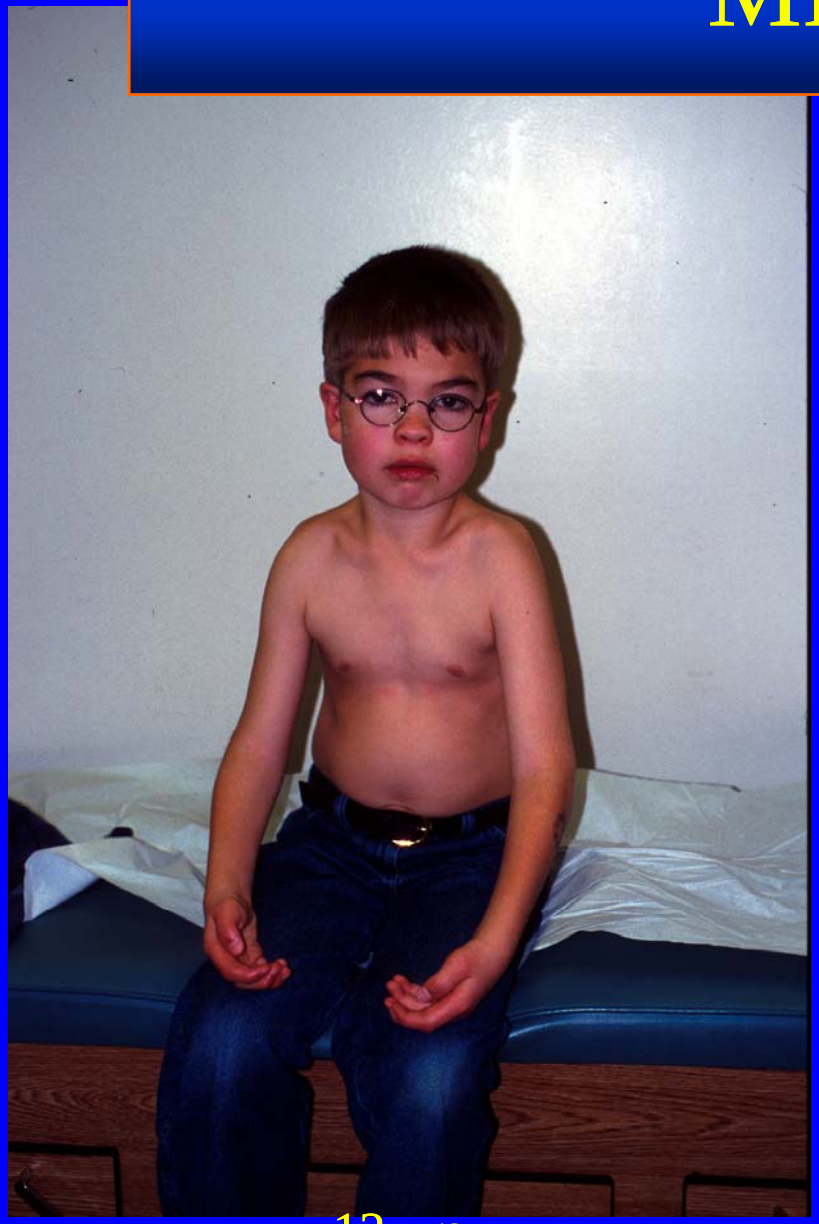
# MPS I





18 months

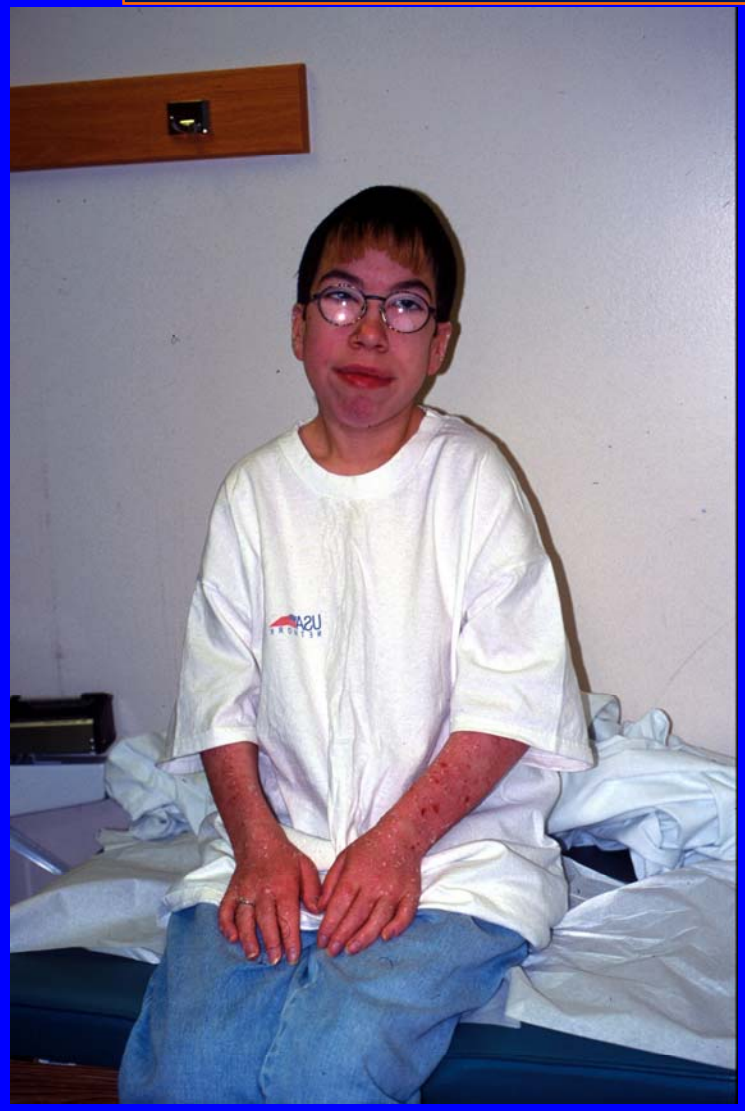
# MPS I



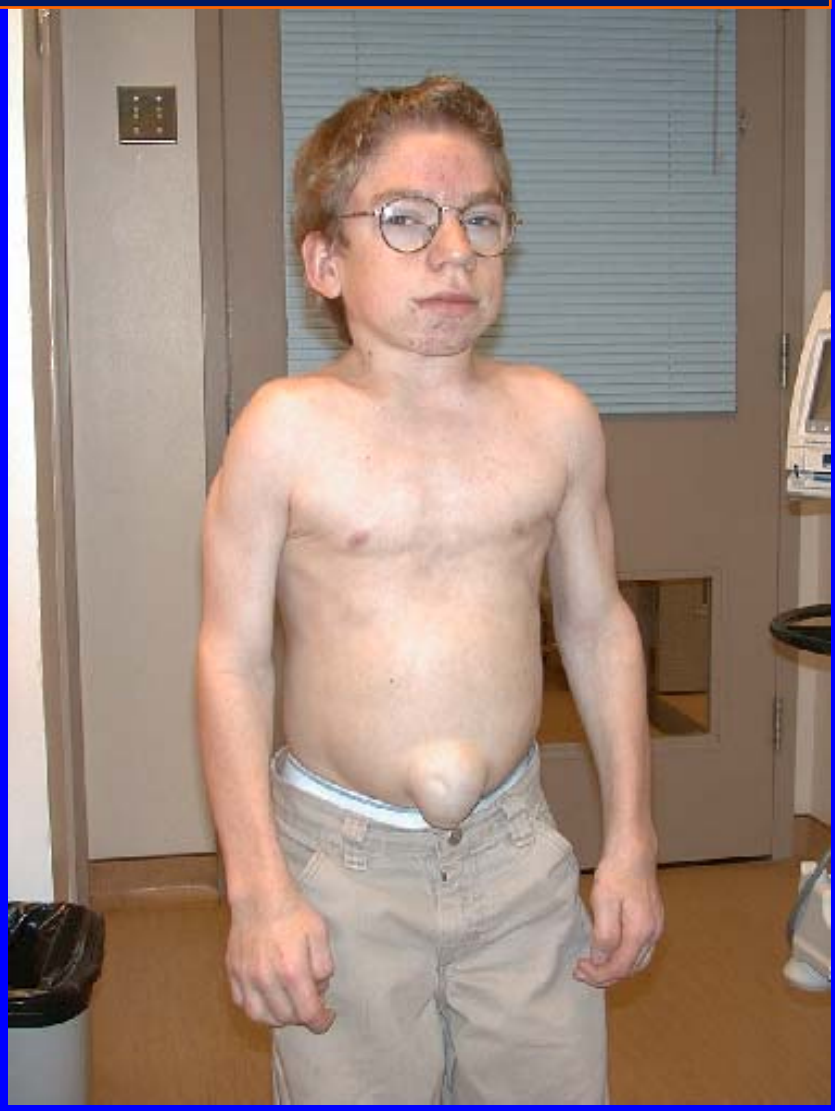
12 yrs

12 yrs

# MPS I

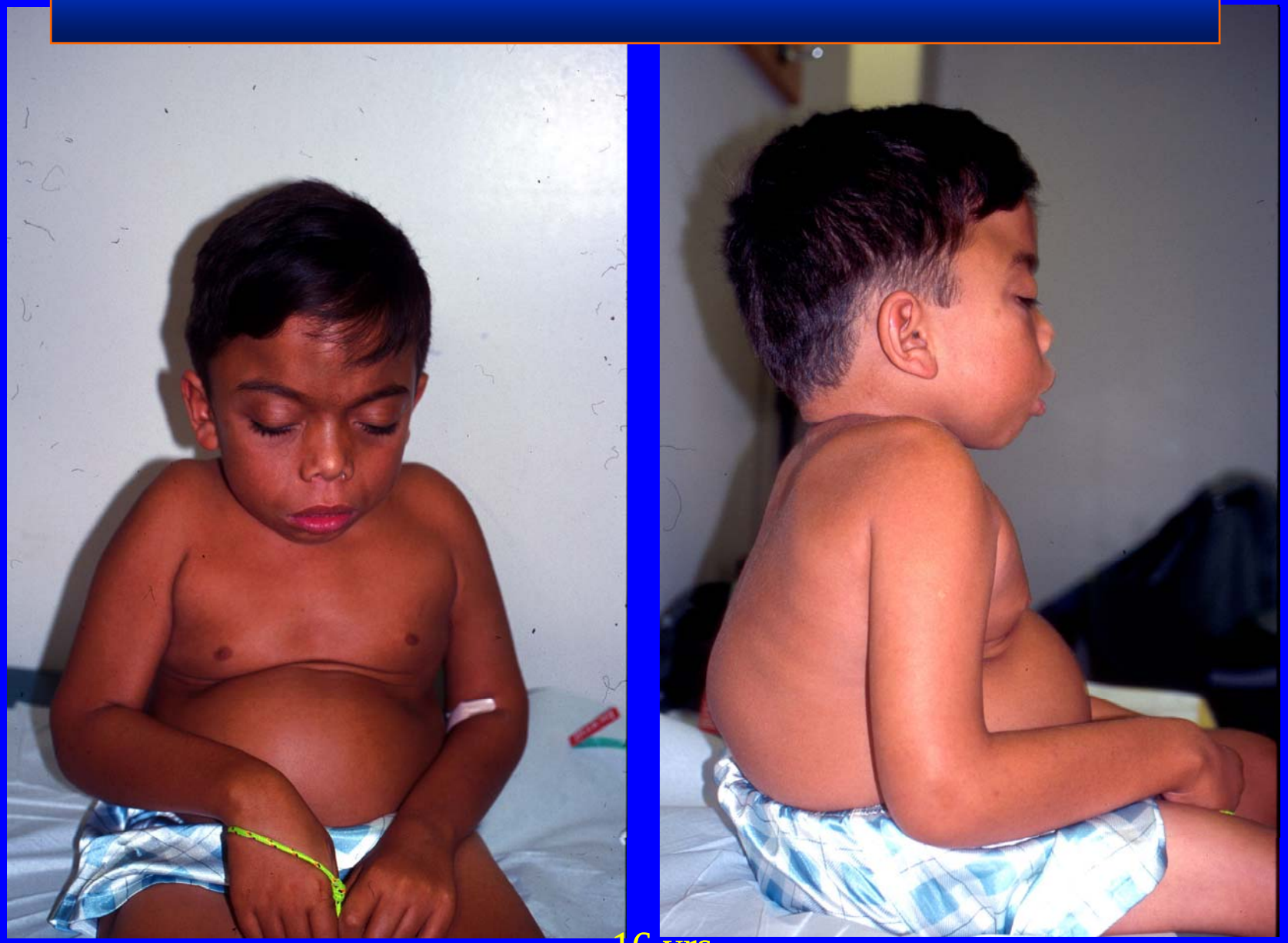


21 yrs



17 yrs

# MPS I



16 yrs

# Important concepts to consider

- Multi-organ involvement
  - Each MPS will have a series of organ systems that are more prominently involved
  - No real correlation between each organ system
- Most disease complications do not have acute onset but rather slow insidious onset

# Important concepts to consider

- MPSs in which ERT is currently used
  - ERT does not cure the conditions but changes the natural history of disease
- Anticipatory guidance and early intervention is the corner stone of management of the MPSs

# Primary Neurological Involvement

- Consideration in
  - MPS III (all types), MPS VII
  - Subgroup of individuals with MPS I, II
- Manifestations
  - Usually normal early motor milestones
  - Speech and language delay is the most common early manifestation
    - Timing
      - MPS I and III early: 14-16 months
      - MPS II: not obvious till age 2 -3 years

# Primary neurological involvement

- Speech and language delay, behavioral concerns
- Development continues but at a slower rate until the age of 5-6 when development plateaus
- Developmental regression: age 6-10
  - Loss of skills previously attained
  - Development of wasting of the lower limb muscles and spasticity
  - Seizures (60% MPS II, 80-90% of MPS III)
- Sleep disturbance
  - Common in MPS III

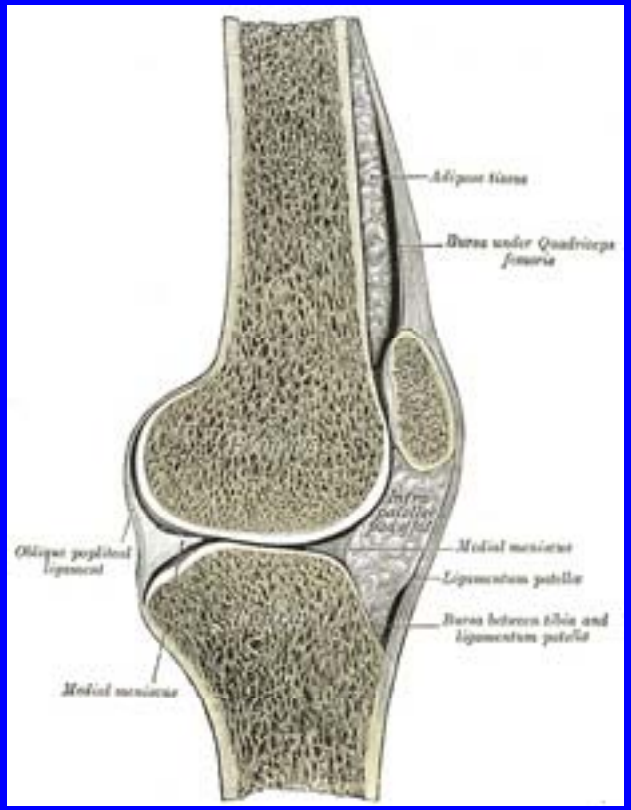
# Additional Neurological Involvement

- Hearing loss
  - Conductive and neurosensory
- Visual issues
  - Corneal clouding: MPS I, VI, VII
  - Retinal dysfunction: MPS I, II, VII
    - Night blindness
- Abnormal spinal fluid resorption

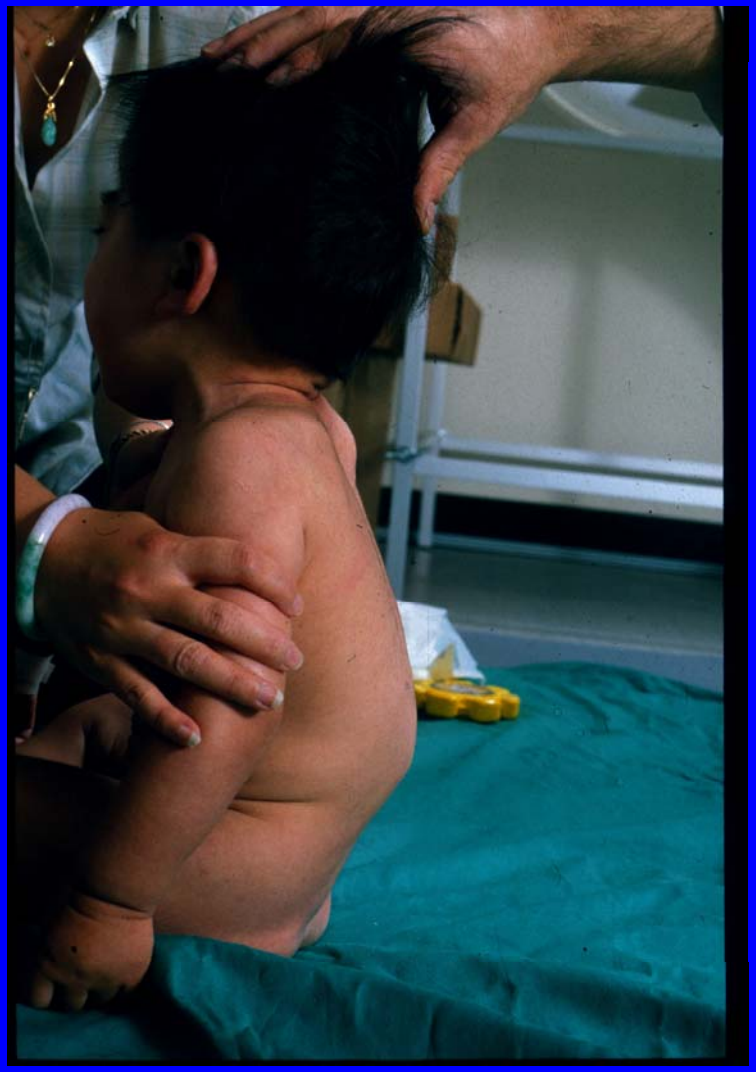
# Skeletal Involvement

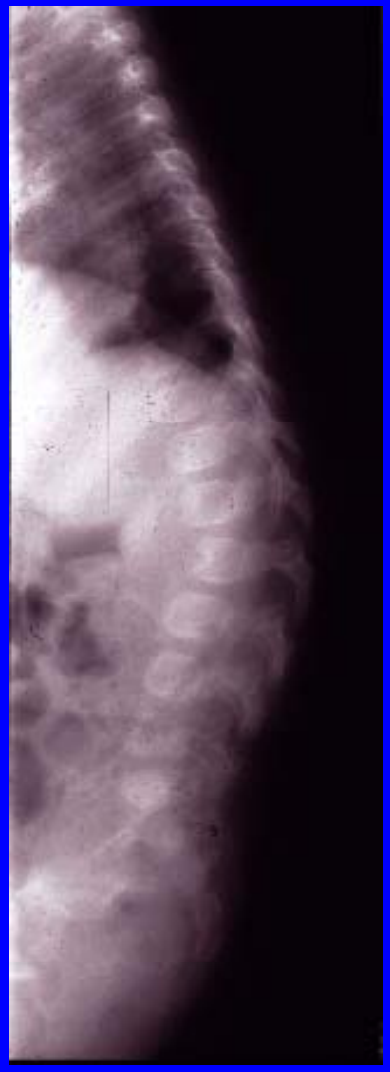
- MPS I, II, VI
  - Restriction of motion about large joints
    - Shoulders, hips initially
    - Smaller joints
  - Reduced growth velocity with growth plateau by the age of 7-9 in more severely affected individuals.

# Joint and Skeletal Disease

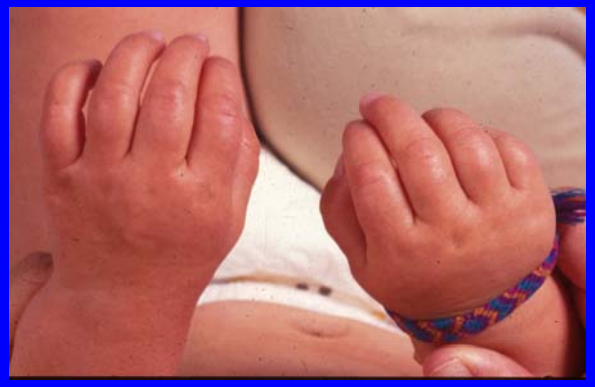


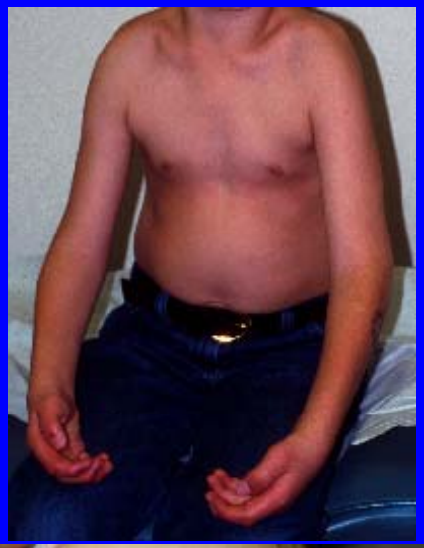
# Joint and Skeletal Disease

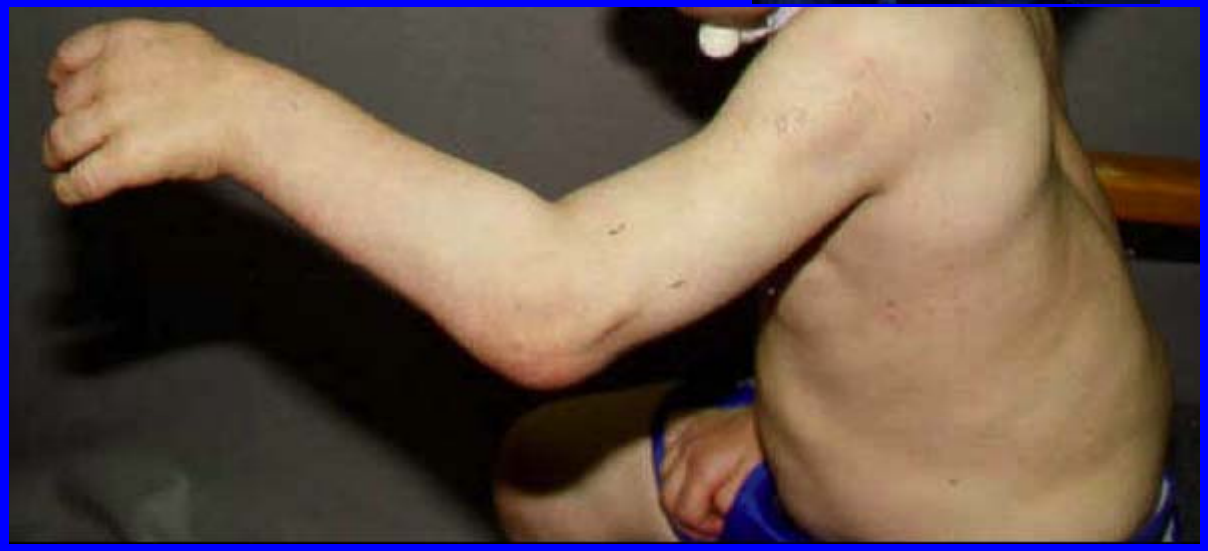




# Joint Restriction and Stiffness







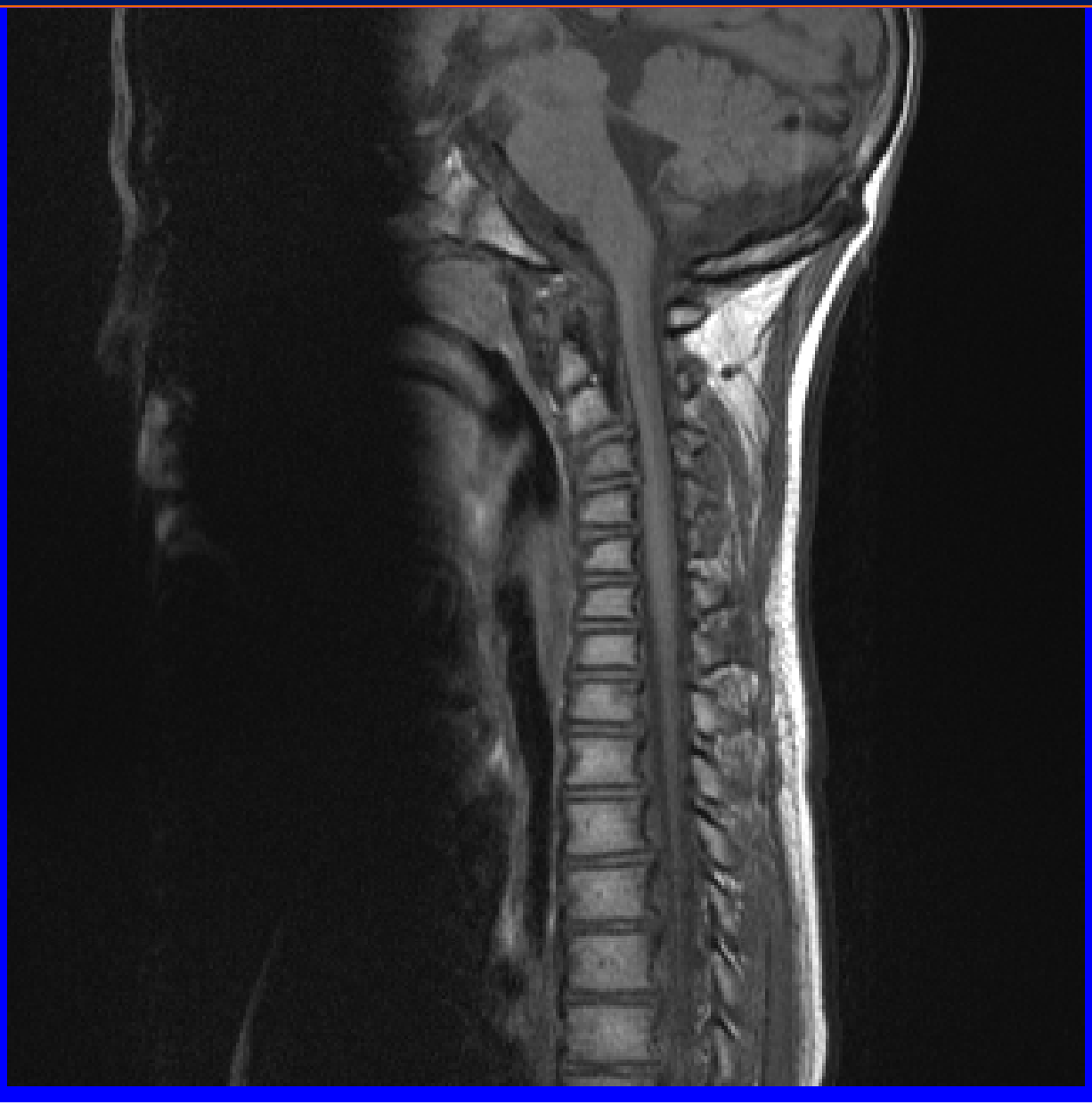
# !!Skeletal Involvement

- MPS IV
  - Joint hyper-mobility
  - Linear growth failure as early as 4 years of age
    - Involves all bones
  - Progressive scoliosis and kyphosis

# Spinal Cord

- All of the MPSs have possible spinal cord concerns:
  - MPS III much less likely.
- The cord involvement is complex and involves the vertebrae, discs and the lining (meninges of the cord)
- Both instability and compression of the cord are possible at any level.
  - Symptoms
    - Altered sensation in the extremities
    - Increased reflexes during physical exam
    - Bowel and/or bladder control abnormalities
  - Evaluation:
    - Detailed X rays of the neck and spine
    - MRI of the spine
    - Nerve conduction studies

# Spinal Cord



# Cardiac Involvement

- MPS I, II, III, VI, VII
  - All involve the cardiac valves
  - Progressive thickening
    - can be documented within the first 2 years
  - Eventually valves will leak
    - Replacement could be required
  - Small proportion of patients develop cardiomyopathy

# Personal/Family

- Recognize the importance of this.
- Actively do things to encourage the health of your family.