Mucopolysaccharidosis

Fatma Al-Jasmi, MBBS, FRCPC, FCCMG

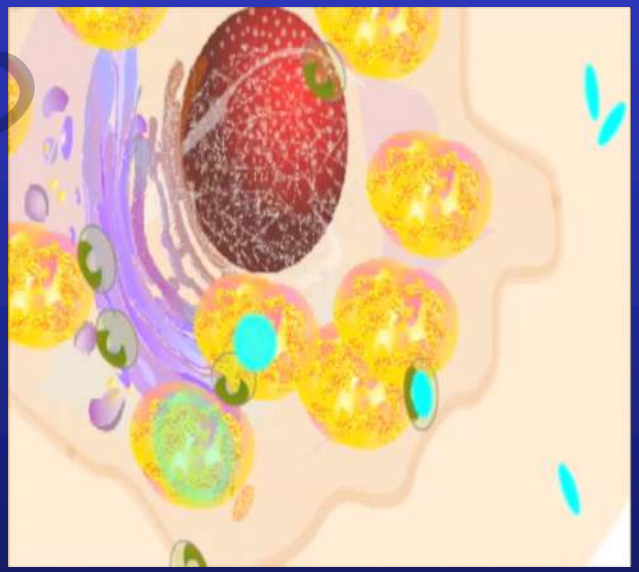
Metabolic Consultant and Assistant Professor of Pediatric
Department of Pediatric, Faculty of Medicine and Health Science,
UAE University, Al Ain, UAE.

Outline

- Characteristics of MPS
- Diagnosis
- Management

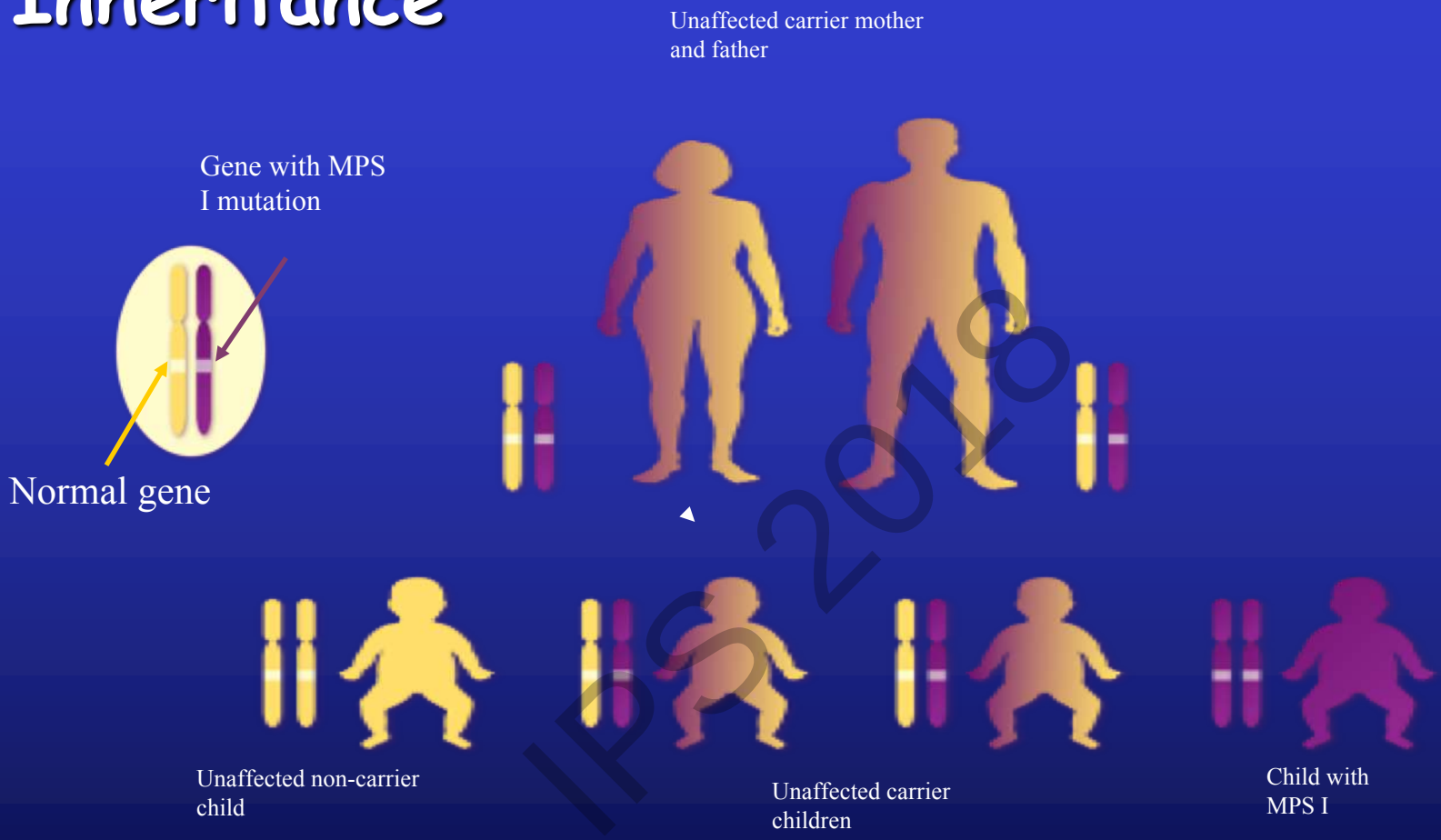
MPS

- The mucopolysaccharidoses (MPS) are heterogenous group of lysosomal storage disorders
- MPS I result from deficiency of **α-L- iduronidase**
- **α-L-iduronidase** degrades GAGs in the lysosomes.



Deficiency of this enzyme lead to accumulation of partially degraded GAGs in the lysosomes, resulting in cellular dysfunction and clinical abnormalities

Inheritance



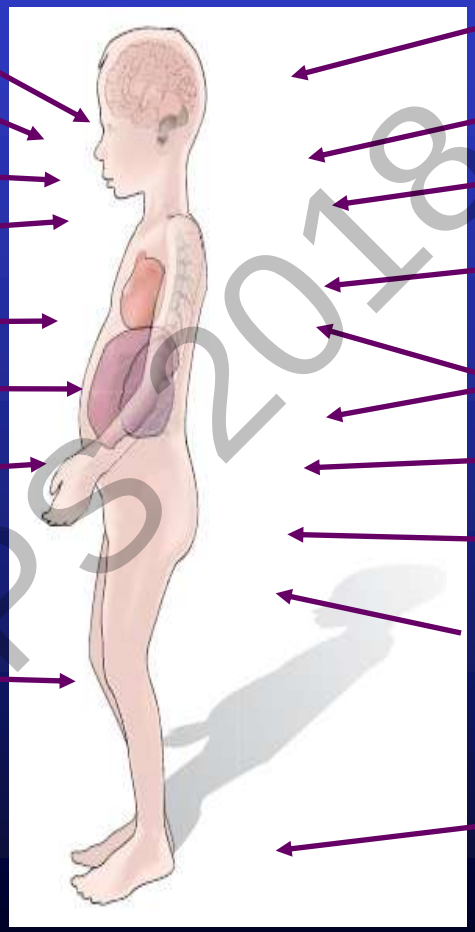
Autosomal recessive inheritance

- Both parents must be carriers of MPS
- 25% chance with each birth that the child will have MPS

CHARACTERISTICS OF DISEASE

Progressive disease

Multi-Systemic disease



Corneal clouding

Coarsening of facial features

Chronic rhinitis, otitis

Enlarged tongue

Cardiovascular disease

Hepatosplenomegaly

Umbilical, inguinal hernia

Knock-knees

Cognitive impairment

Microsomia, hydrocephalus

Obstructive airway disease

Kyphosis, gibbus deformity

Restrictive of joint mobility

Carpal tunnel syndrome

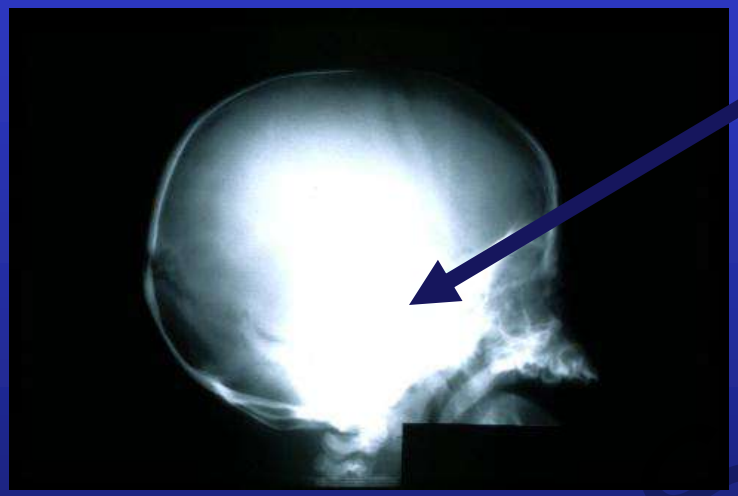
Chronic diarrhea

Abnormal gait due
to hip deformity

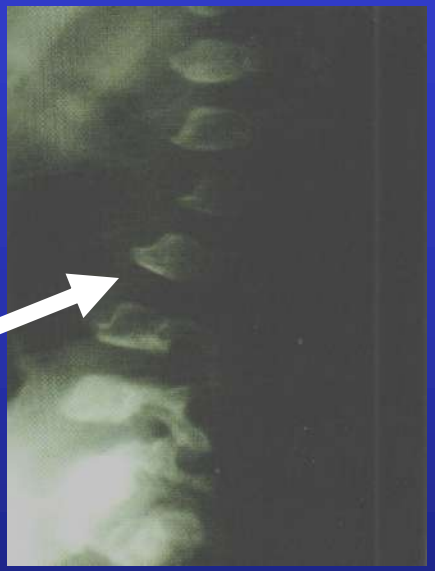
Toe-walking

DIAGNOSIS

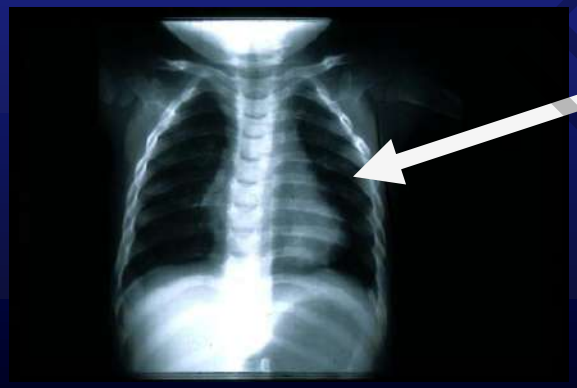
Dysostosis multiplex...



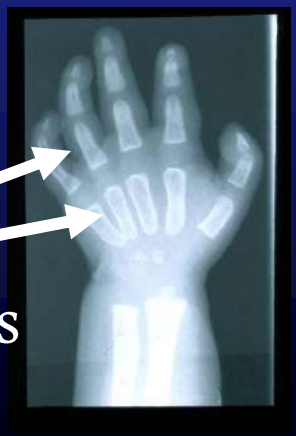
J-shaped sella



Wedging of vertebrae

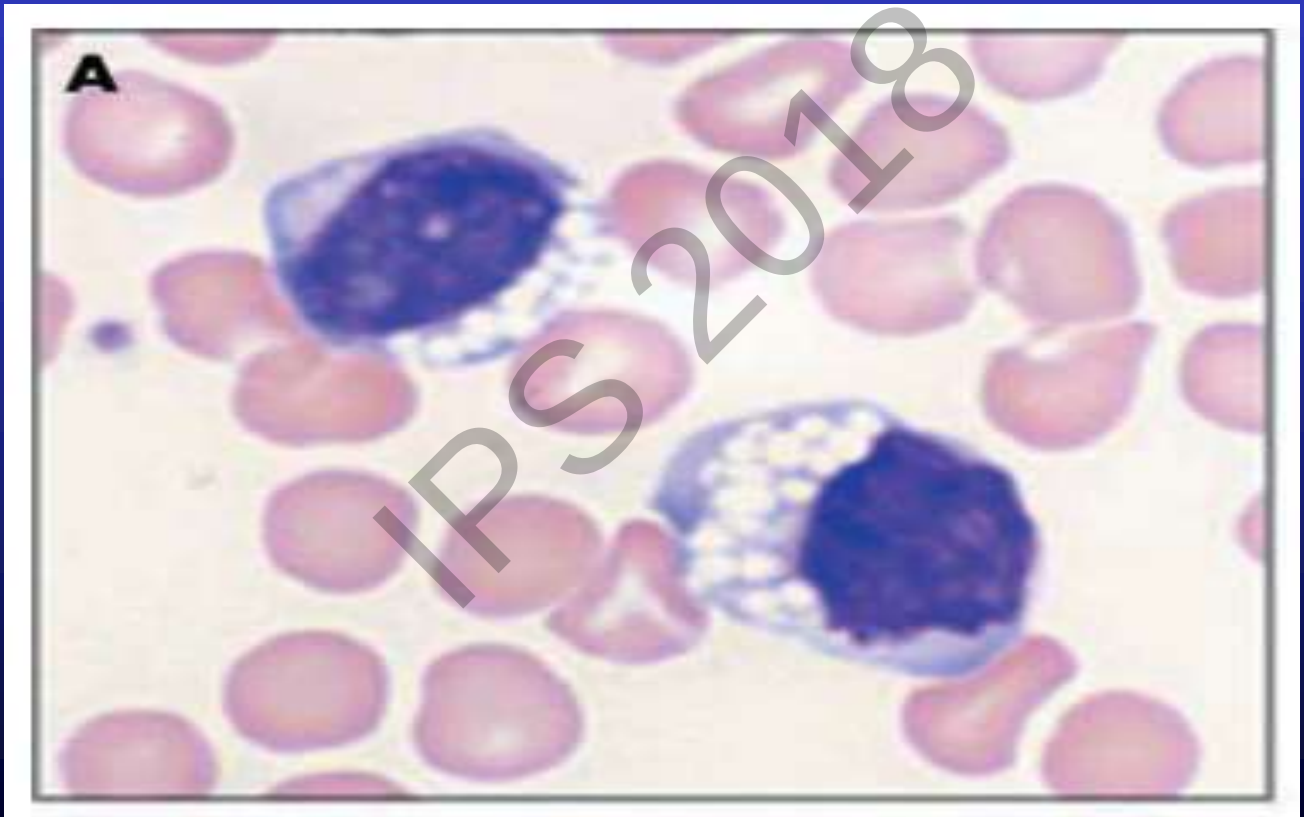


Thickened ribs



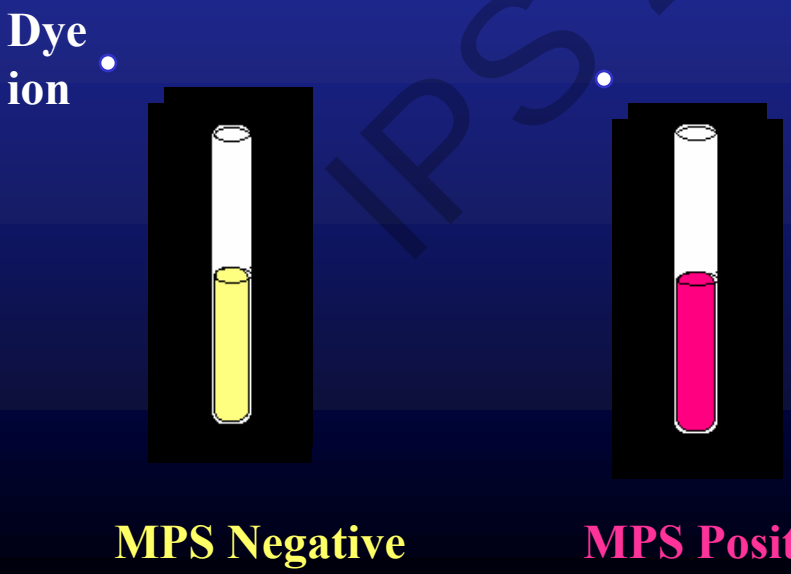
Bullet-shaped phalanges & metacarpals

Vaculated Lymphocyte



Urine MPS Screening Test

- Screening test for excess acidic mucopolysaccharide in urine.
- In the presence of excess MPS, the positive charge of the dye ion pairs with the negative charge of the MPS changing the color of solution from blue/purple to pink



False positive result are common especially in young infants

Thin-layer chromatography

Keratan sulphate

Heparan Sulfate

Dermatan sulphate

Standard

Negative control

Patient

1- Clinical Presentation:
History and Physical examination

2- Screening test:
Skeletal survey
Blood film
Urine MPS

3-Enzymology:
α-L-Iduronidase

4- Molecular genetic testing:
IDUA

MANAGEMENT


THE PATIENTS KNOW MORE ABOUT THEIR DISEASES THAN ME. I MUST GET FASTER MODEM, HIGHER SPEED INTERNET ACCESS THAN THEM

Management:

1- Supportive treatment

2- Enzyme replacement therapy

3- Bone Marrow Transplant

In General

- Hurler patient should be managed at tertiary center by multidisciplinary team with MPS I experience

Supportive Management

Symptoms	Management
Hydrocephalus	Ventriculoperitoneal shunt
Learning disabilities	Standard interventions
Spinal cord compression, cervical instability	**Surgical intervention**
Corneal clouding	Corneal transplant
Deafness	Ear tubes, hearing aids
Otitis media	Ear tubes
Sleep apnea/ Airway obstruction	Tonsillectomy, adenoidectomy Continuous positive pressure ventilation (CPAP or BiPAP) with oxygen enrichment Tracheotomy
Cardiac valve disease	**Valvular replacement**
Umbilical and inguinal hernias	Hernia repair surgery
Bone and joint manifestations	Physical therapy, corset, orthopedic surgery
Carpal tunnel syndrome	**Neurosurgical decompression**

Muenzer et al. *Pediatrics* 2009;123:19-29

Hematopoietic Stem Cell Transplantation (HSCT)

- HSCT is employed as a vehicle for delivering missing enzyme to other tissues in the body.

- HSCT donor cells can be:
  - HLA-matched bone marrow (better results)
  - Umbilical cord blood cells

Disadvantages of HSCT:

- Finding HLA- compatible donor in case of BMT
- Graft versus host disease.
- Cost.
- Morbidity and mortality (> 15–20% mortality) because of the toxicity of the conditioning regimen, bone marrow ablation.

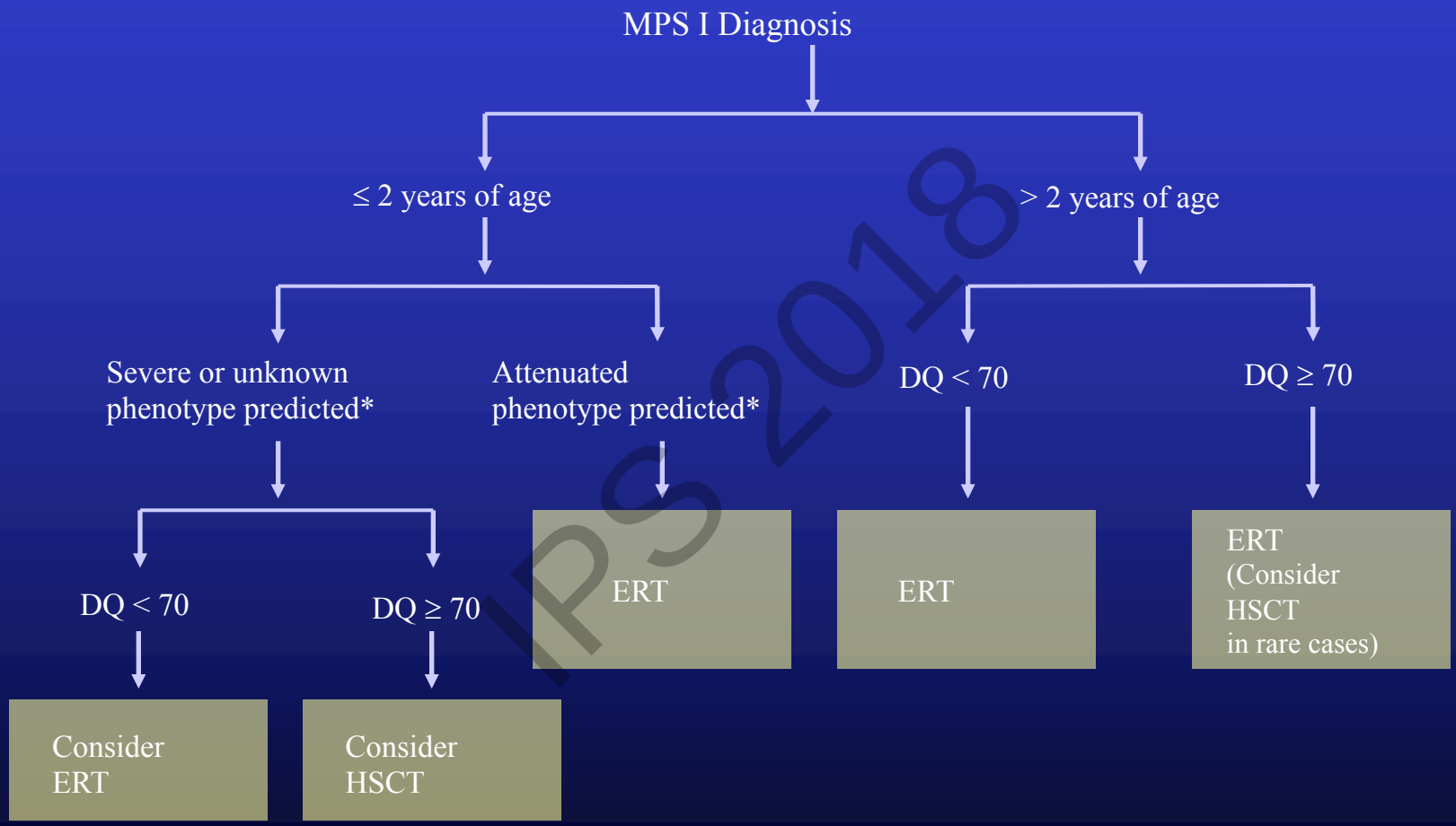
Criteria for HSCT:

- Age less than 18-24 months

  OR

- Development score ≥70

Treatment algorithm for MPS I



DQ = Developmental quotient
ERT = Enzyme replacement therapy
HSCT = Hematopoietic stem cell transplant

From Muenzer et al. *Pediatrics* 2009;123:19-29

Management

Supportive Management

(e.g., hernia repair, tonsillectomy, orthopedic surgery, CPAP)

Enzyme replacement therapy

(Aldurazyme)

Hematopoietic stem cell transplantation

In conclusion…

- Early diagnosis is the key for better prognosis

- Pediatrician are the frontier…

THANK YOU