

# Cas clinique

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**SMHP, Ecole du Val de Grâce, le 29 mars 2013**

# Case

- **At 9 years of age :**
  - **Growth retardation**
  - **Went to France with his parents**
  - **Originating from northern Africa**
  - **Mild spleen enlargement**
  - **The customs officer says : « he cannot enter in France before antituberculous therapy »**
  - **Lost to follow-up for 30 years ...**

# Case

- **At 39 years of age :**
  - **Normal height**
  - **Shortness of breath, tobacco**
  - **Moderate liver and spleen enlargement**
  
  - **Chest X ray**



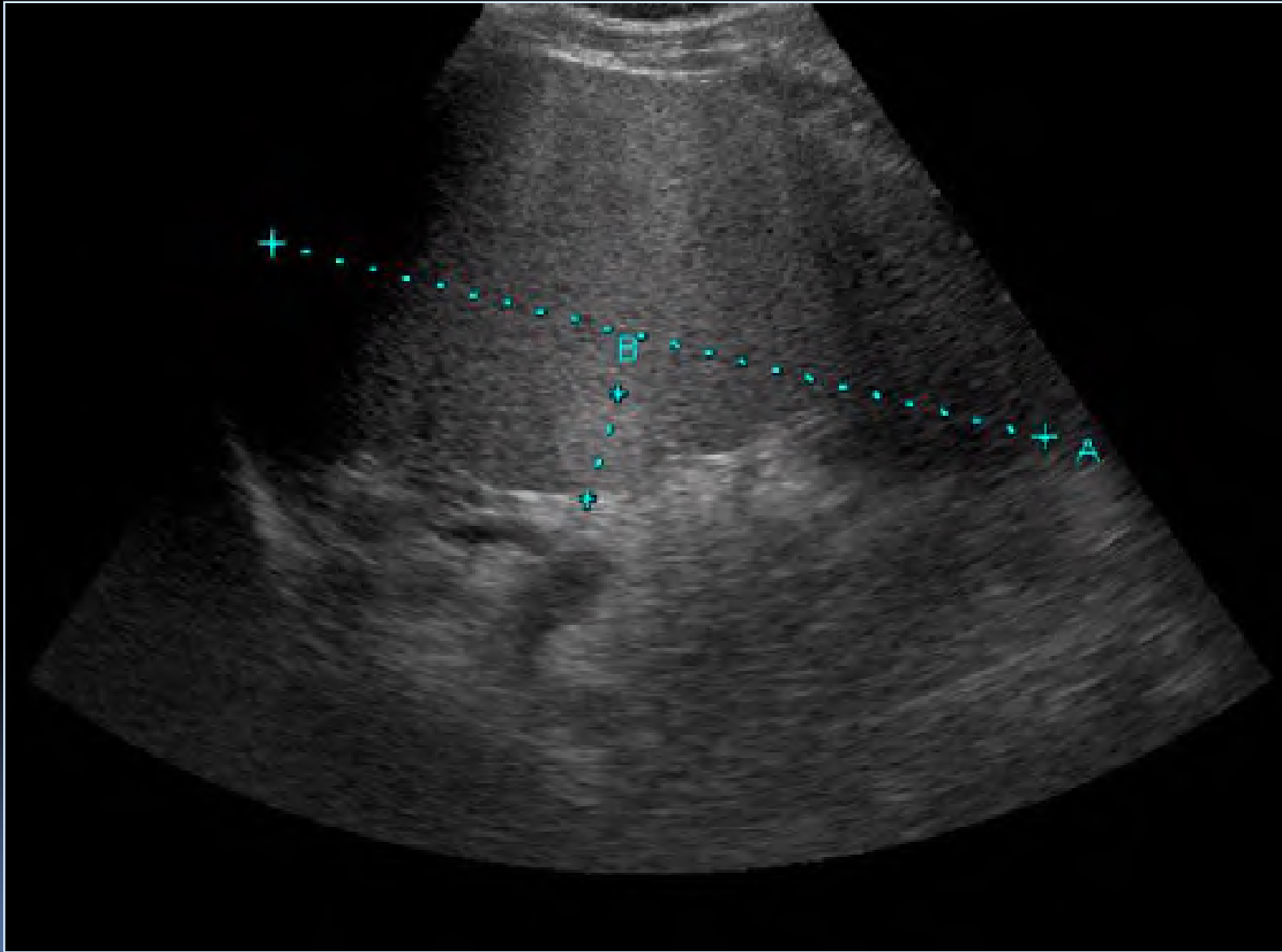
# Case

- **Interstitial lung disease**
- **Restrictive lung disease physiology**
- **Mild pulmonary gas exchange**
  
- **Thorax CT scan : Interstitial lung disease**

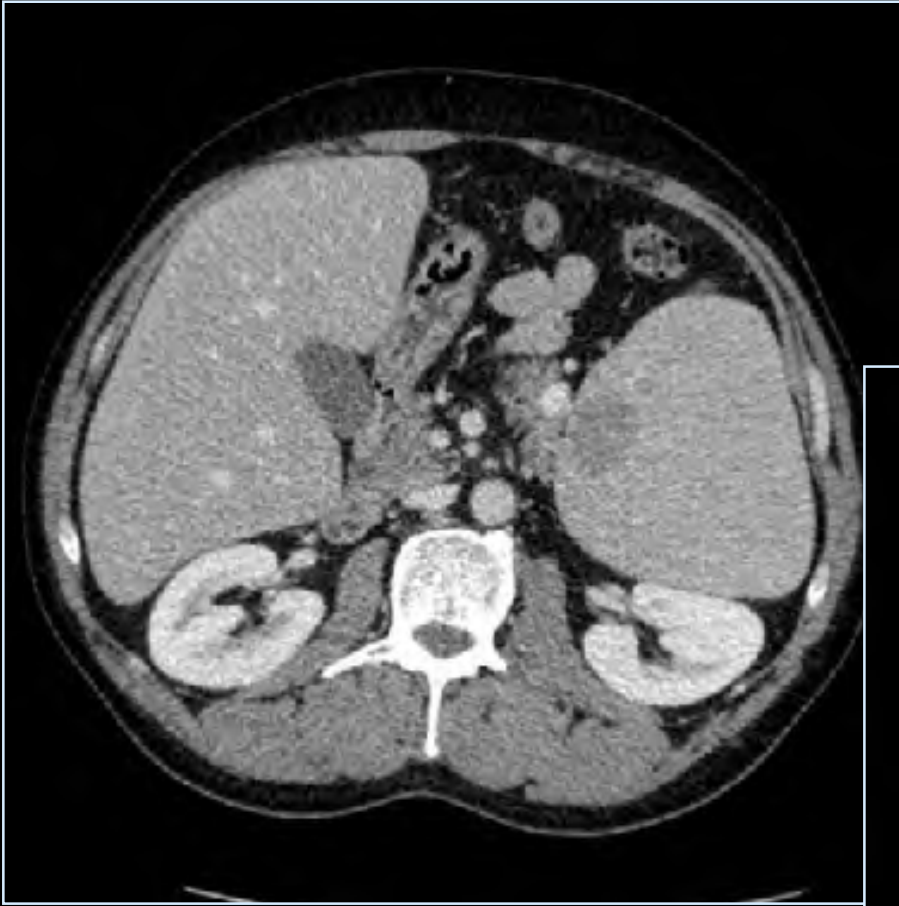


# Case

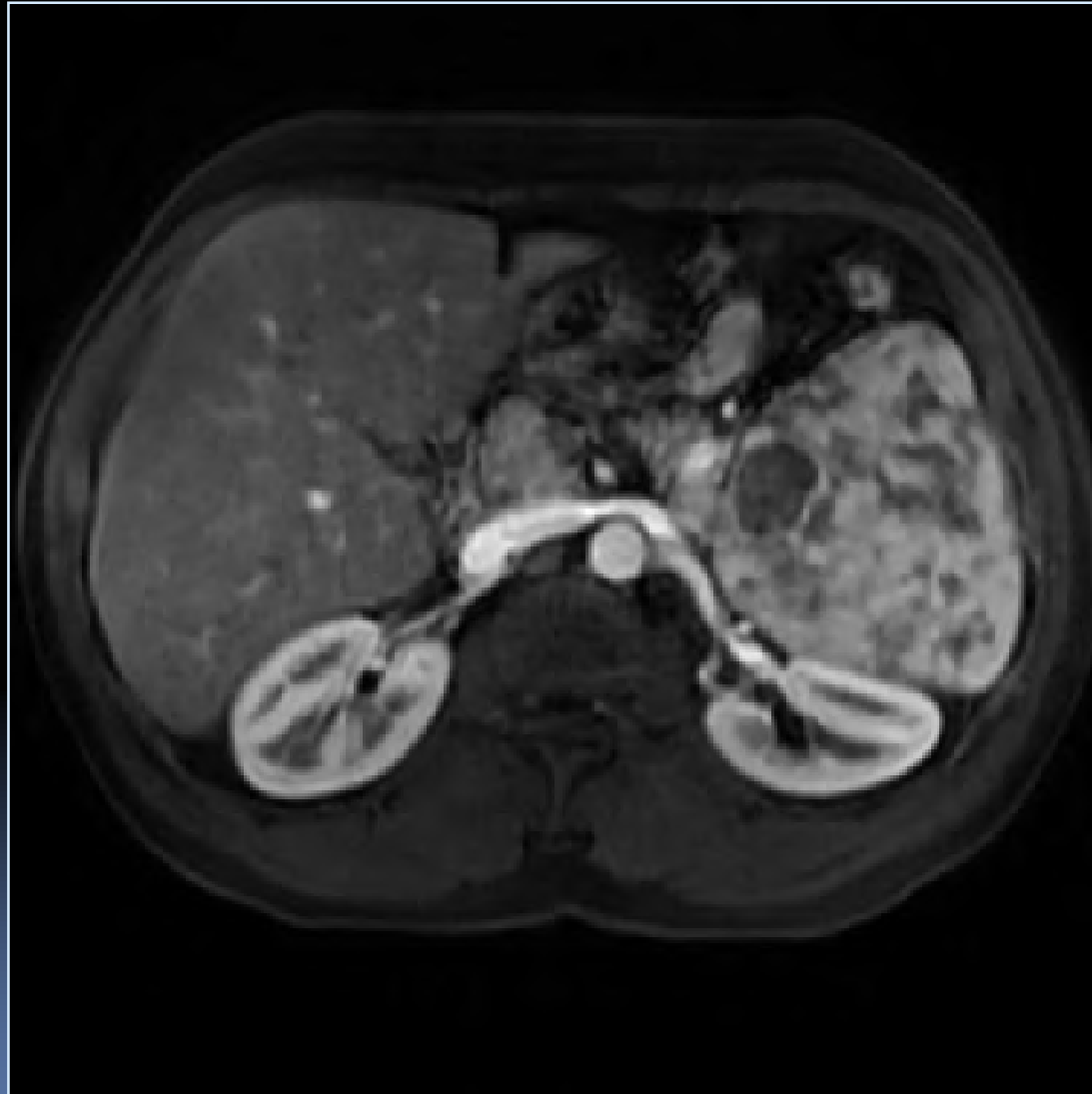
- **Interstitial lung disease**
- **Restrictive lung disease physiology**
- **Mild pulmonary gas exchange**
  
- **Thorax CT scan : Interstitial lung disease**
  
- **Abdominal sonography and CT scan**







# MRI



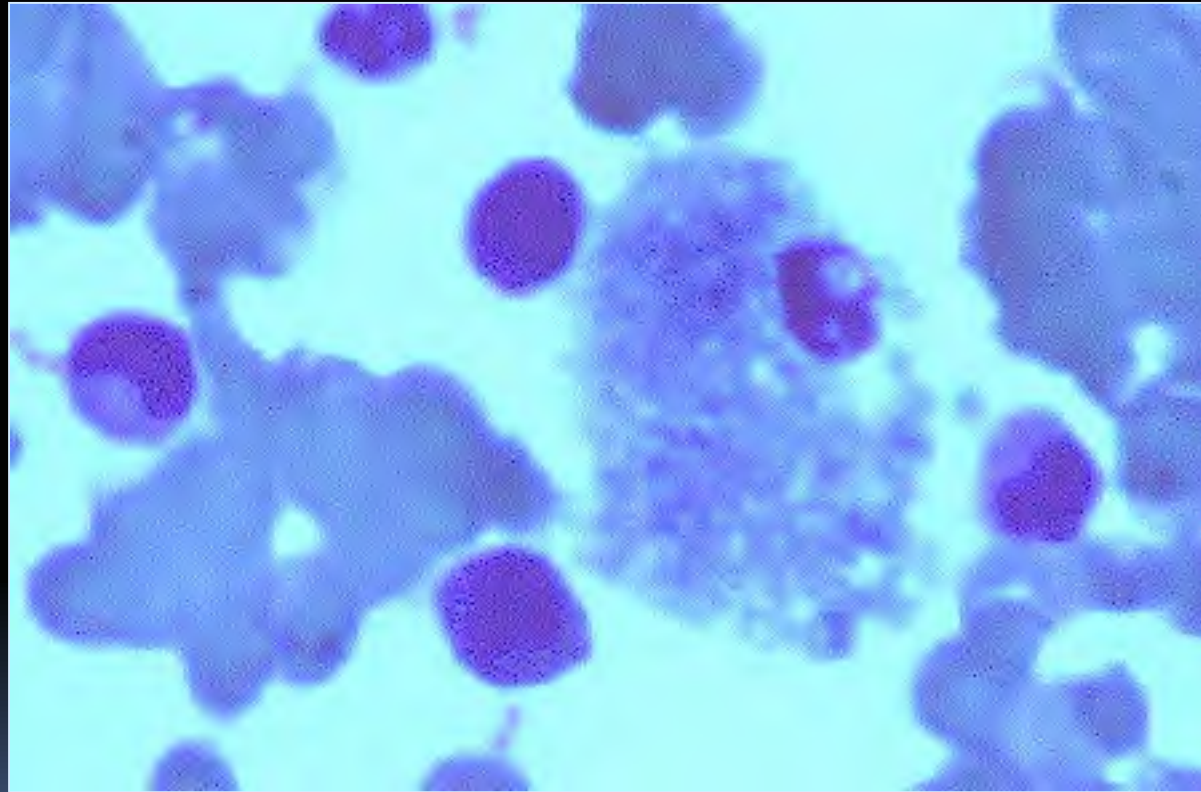
# MRI



# Case

- **No cardiomyopathy**
- **Ophthalmologic exam : cherry red spot**
- **No skeletal deformity, no arthritis**
- **Neurological exam : normal**
- **Hb 110g/l, Leuko 5 000, platelets 100 000**
- **Low HDLc, High LDLc and TG**
- **Chitotriosidase : 5 N**
- **Iron, copper : normal**

# Niemann-Pick cells (bone marrow)



# Niemann Pick type B

- **SMPD1 = sphingomyelin phosphodiesterase 1 = acid sphingomyelinase (ASM)**
  - Cultured skin fibroblasts or leucocytes
- **AR, 11p15.1-p15.4**
- **0.4 to 0.6/100 000 newborns**
- **Missense mutations : 59% of all alleles**
- **R 608 del**
  - 42% of patients
  - 25% of all alleles

# Splenectomy ?



**Monoclonal IgM kappa**

# The answer is NO

- **Lymphoma ?**
- **No fever, no lymph node**
- **Splenectomized patients have been noted to undergo rapid deterioration of their pulmonary status**



# Maladie de Niemann Pick B (10 cas)

- ▶ 9 hommes, 1 femme
- ▶ Age au diagnostic :
  - ▶ Pédiatrique dans 7 cas (6 mois – 7 ans)
  - ▶ Age adulte dans 3 cas (39, 46, 54 ans)
  - ▶ Consanguinité dans 2 cas
- ▶ 1 décès à 31 ans (cirrhose grave, forme A-B)
- ▶ Symptômes pulmonaires et HSM constants
  - ▶ Troubles digestifs précoces
  - ▶ Hypertrophie des surrénales (2 cas)
  - ▶ Pneumothorax (2 cas)

# Niemann Pick type B

- **Initial presentation**
  - Spleen 78%
  - Liver 73%
- **Symptoms**
  - Bleeding 49%
  - Pulmonary infections 42%
  - Shortness of breath 42%
  - Joint/limb pain : 39%

*McGovern MM, et al. Paediatrics 2008.*

# Niemann Pick type B

- **Skeletal manifestations**

- **Pediatric patients (n=20)**

- 5/20 : skeletal fractures
- Average bone age delay : 1.6 years
- BMC and BMD decreased vs controls

- **Adult patients (n=26)**

- Osteopenia or osteoporosis (> 50%)
- Splenomegaly – Z scores (inv. Correlated)

*Wasserstein M, et al. J Inherit Metab Dis 2012.*

# Treatment ?

- **Stop tobacco**
- **Risk of coronary artery disease**
  - **Atherogenic lipid profile**
- **No specific treatment is available**
- **Quality of life seems to be normal in some cases**

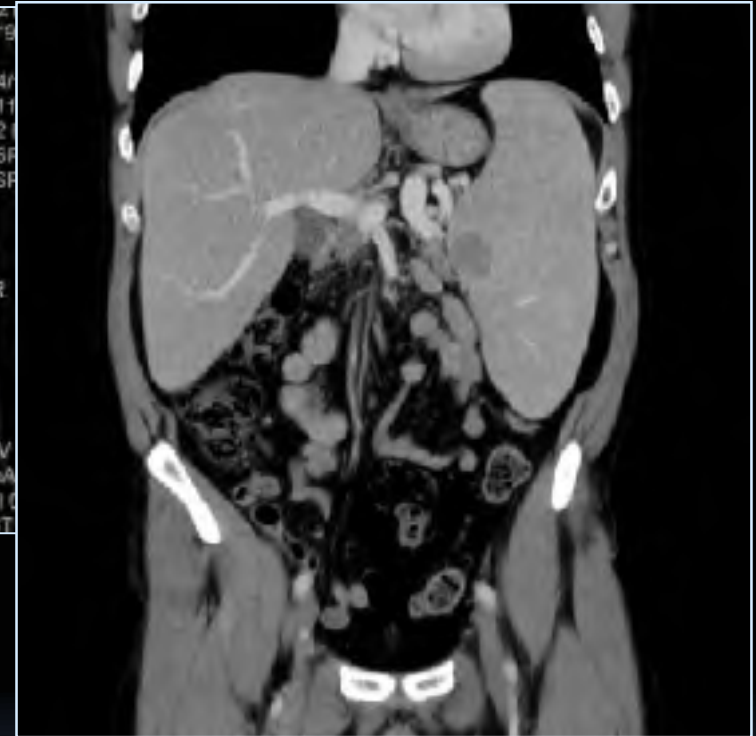
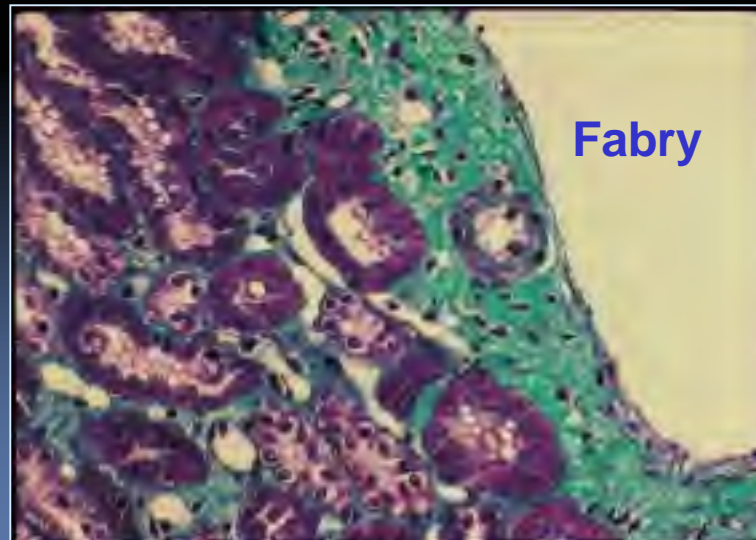
# Tableaux cliniques

- ▶ **Macrophage**

**Gaucher  
type 1**



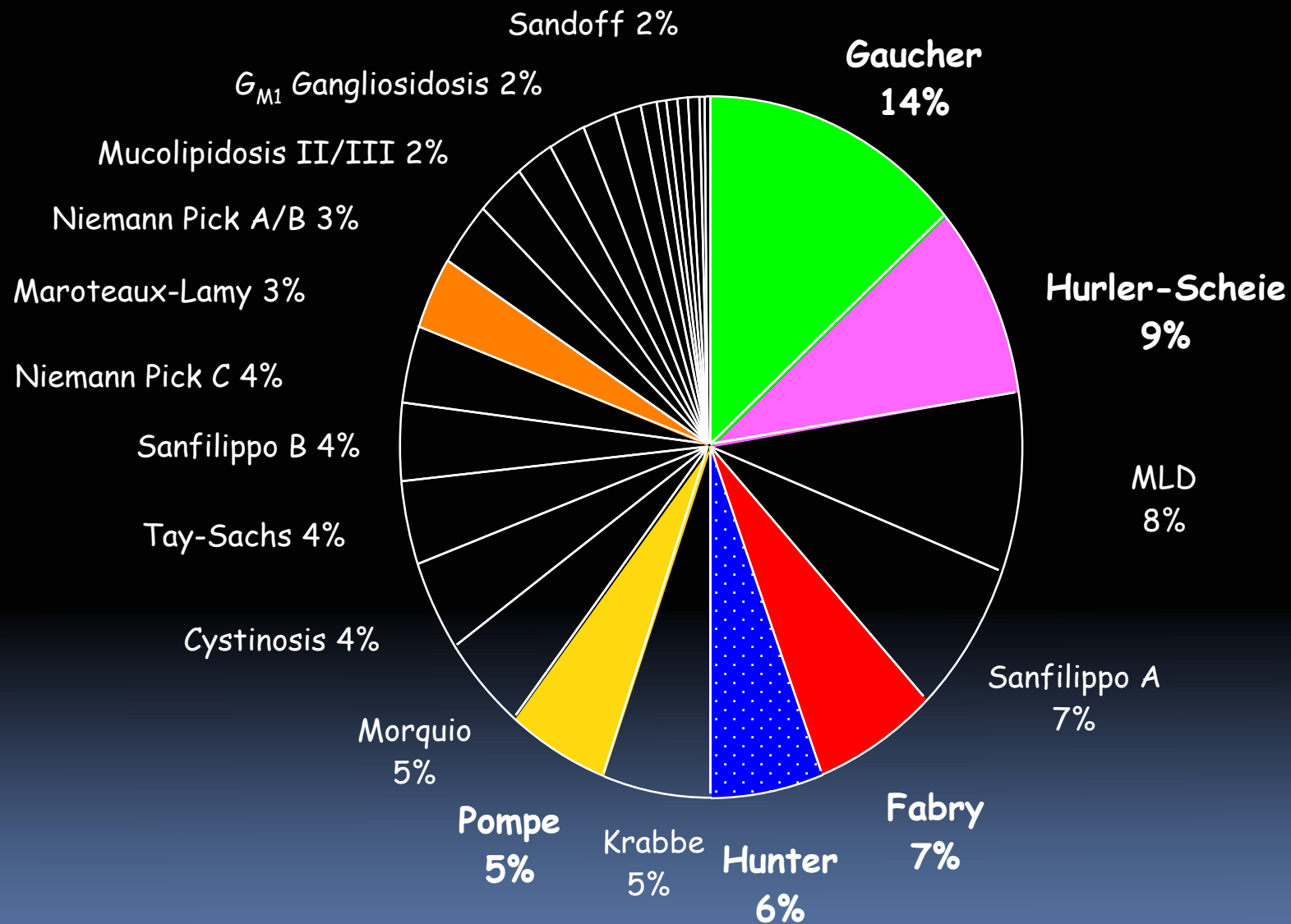
- ▶ **Cellule endothéliale**



**Niemann-Pick  
type B**



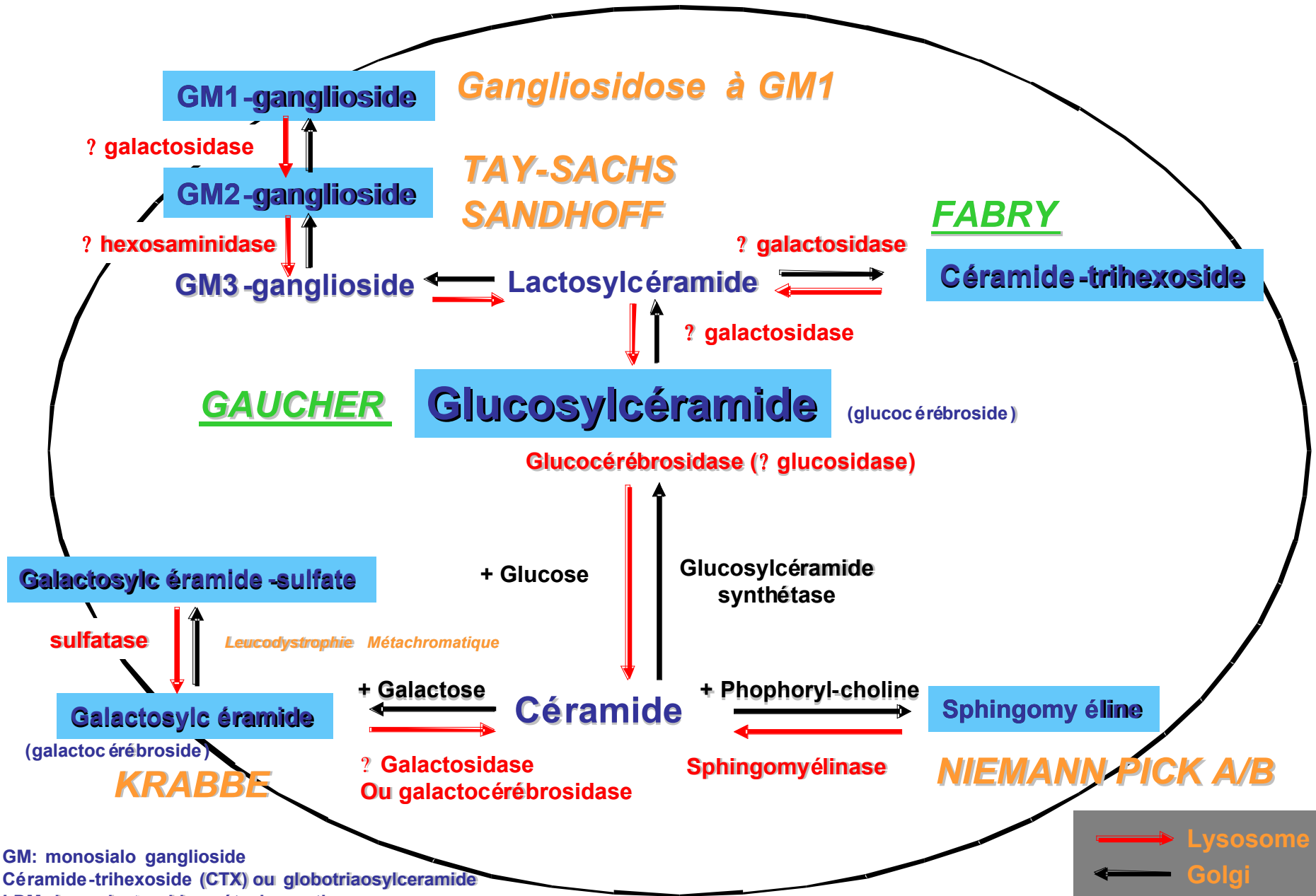
# Lysosomal storage disorders



With Courtesy GM Pastores, New York.

(Australia 1980-1996; Meikle et al., 1999)

# Métabolisme des glycolipides



GM: monosialo ganglioside  
 Céramide-trihexoside (CTX) ou globotriaosylceramide  
 LDM: leucodystrophie métachromatique