# CME Series on Lysosomal Disorders


# Clinical considerations of the impact of pregnancy in Lysosomal diseases

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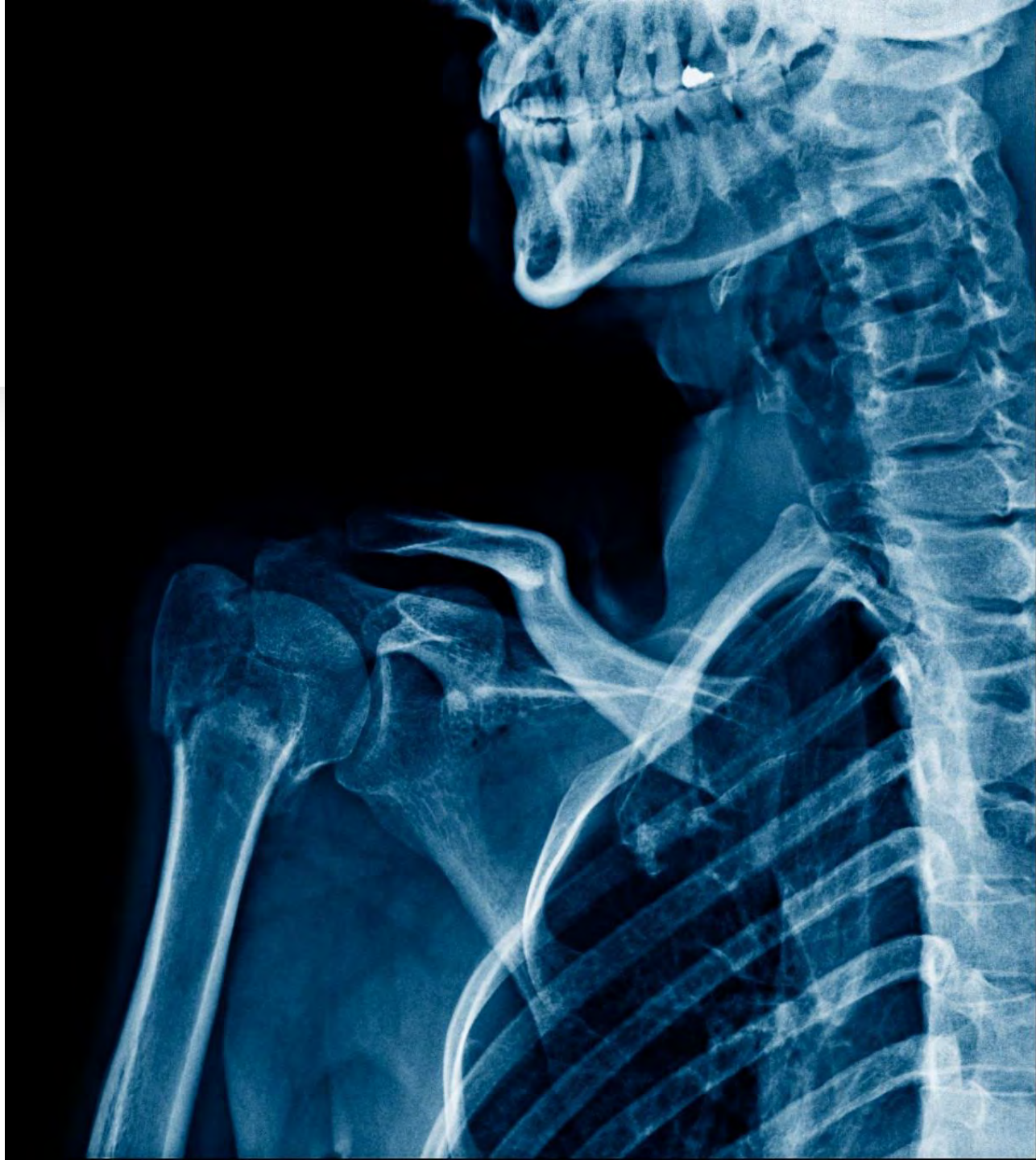
# Lysosomal Diseases & Pregnancy

- LDs involve multi-organ systems including hematologic, skeletal, visceral, and neuromuscular pathways.
- Pregnancy imposes additional metabolic, cardiovascular, and respiratory stress that may unmask or worsen symptoms.
- Enzyme Replacement Therapy (ERT) has improved outcomes but requires individualized planning.
- Early interdisciplinary involvement is crucial: genetics, MFM, anesthesia, metabolism, cardiology.



# Gaucher Disease & Pregnancy

- GD can affect reproductive events due to **thrombocytopenia, anemia, organomegaly, and bone disease**.
- **Menorrhagia** significantly more common in untreated GD (50%) vs treated (28.9%).
- **ERT improves pregnancy outcomes:**
  - *Spontaneous abortion*: 13.8% untreated vs **1.7% with ERT**.
  - *Delivery complications*: 39% untreated vs **6.5% with ERT**.
  - *Postpartum complications*: 21% untreated vs **7% with ERT**.
- No evidence of fetal harm from imiglucerase; breastfeeding while on ERT appears safe.
- GD diagnosis can occur p**during or after a pregnancy**, highlighting the need for heightened clinical suspicion.

**Zimran et al., 2009** The female Gaucher patient

# Pompe Disease and Pregnancy

- **Delayed diagnosis :** most pregnancies occurred **before diagnosis of LOPD**.
- **Pregnancy as a metabolic stressor:**
  - Symptoms may **worsen during pregnancy** (muscle weakness, back pain).
  - ~84% reported **back pain** during pregnancy (page 5, symptom chart).
- **Respiratory considerations:** rare in this cohort, but critical when present—risk of hypoventilation and decreased fetal oxygenation.
- **Pregnancy outcomes:**
  - 86% live births; spontaneous miscarriage rate 12%; **stillbirth slightly increased (3.8% vs 0.2–0.7%)** (Figure 1A, page 5).
  - Delivery mode similar to national averages; **anesthesia complications higher (5% vs 0.1%)** (Figure 1D).
- **ERT exposure:**
  - Several pregnancies exposed to ERT showed **no fetal adverse events**.
  - Symptoms often worsen during pregnancy and improve postpartum in patients on ERT.

# Pregnancy outcomes in females with LOPD compared with the National Data

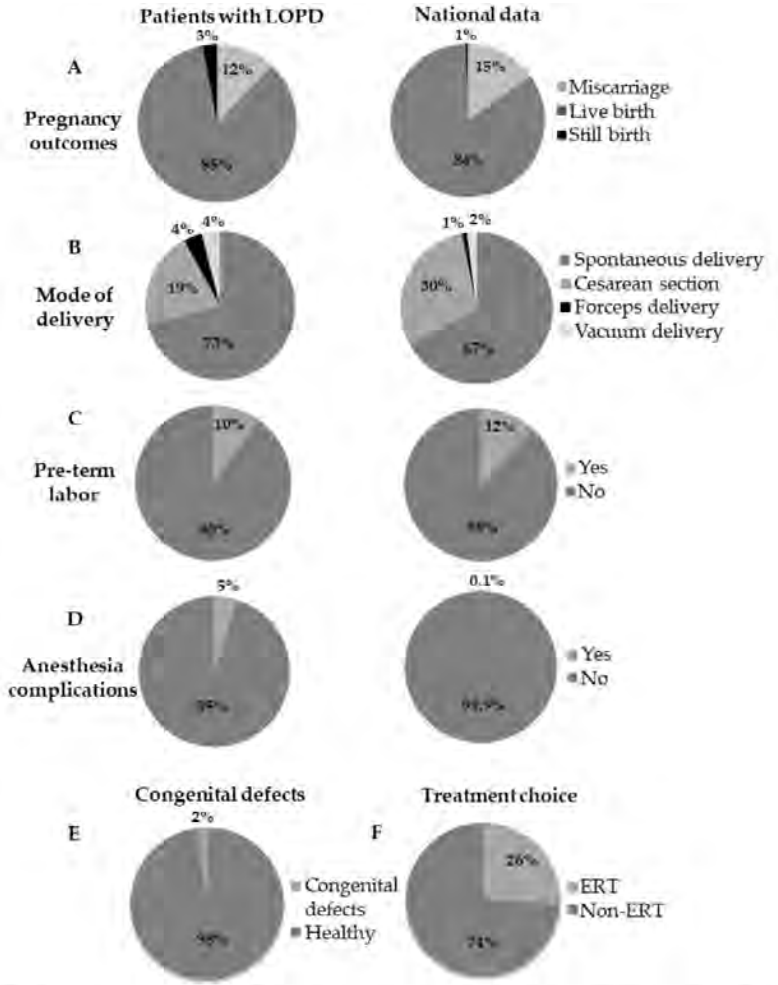
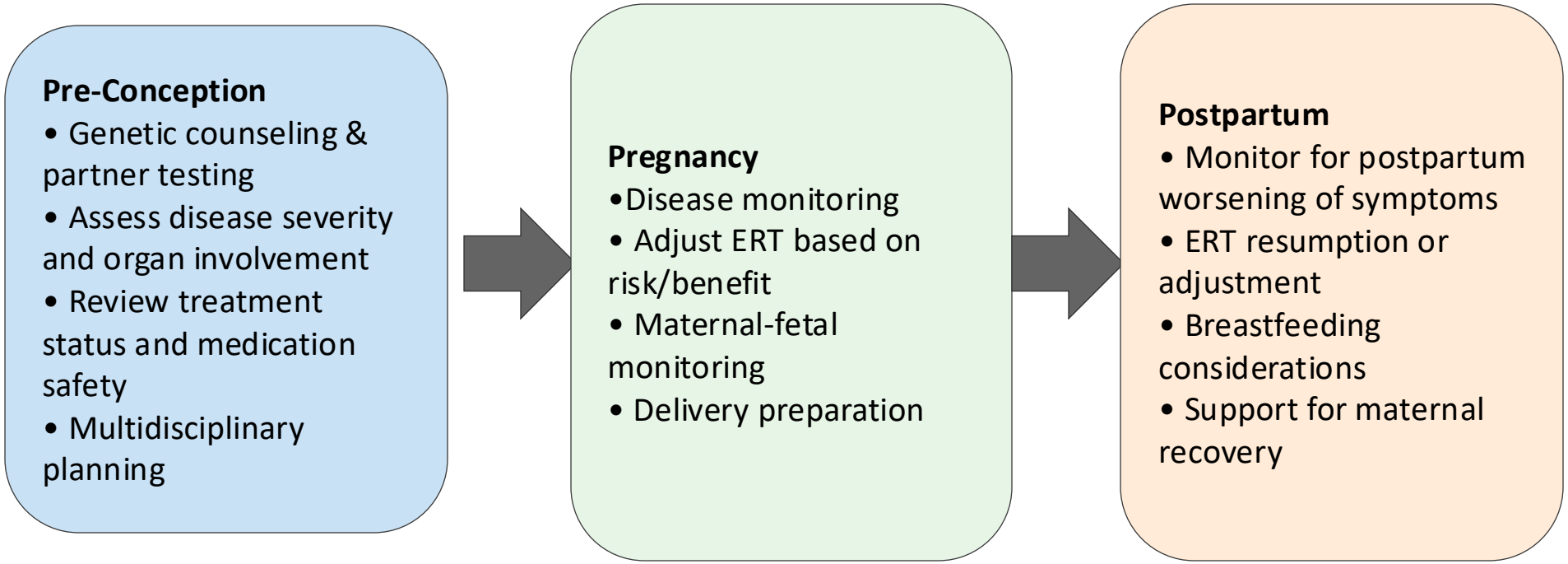



**Figure 1.** Pregnancy outcomes in LOPD: The frequency of pregnancy related events in 25 female patients with LOPD in comparison to the national data. This includes: (**A**) pregnancy outcomes; (**B**) mode of delivery; (**C**) pre-term labor; (**D**) anesthesia complications during delivery; along with (**E**) examining frequency of congenital defects in the study cohort; and (**F**) examining treatment decisions in pregnant patient with LOPD.

# Pre-Conception → Pregnancy → Postpartum



# Maternal & Fetal Considerations in Lysosomal Disorders

## MATERNAL RISKS

- Exacerbation of weakness and fatigue
- Respiratory compromise (e.g., Pompe)
- Thrombocytopenia / bleeding risk (Gaucher)
- Worsening hepatosplenomegaly
- Higher anesthesia vulnerability

## FETAL RISKS

- Growth restriction due to maternal hypoxia
- Risk of prematurity
- Rare but reported stillbirth risk in some LSDs
- Influence of maternal inflammation / immune activation

Exposure to LD specific therapy

# Pregnancy and Lysosomal Disorders:  Outline

- Introduction to LDs and the reproductive system
- The multidisciplinary team:  Role of the gynecologist/obstetrician/genetic counselor
- Best practices and resources to plan, prepare and manage pregnancy in persons with LDs.
- Overview of  therapy during pregnancy

# Pregnancy and Other Reproductive Issues in Lysosomal Disorders

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# Disclosures

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# Learning Objectives

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- Describe the role of the gynecologist, obstetrician, and genetic counselor in the team approach to care of people with LSDs
- Describe best practices for discussing pregnancy options for people with LSDs
- Describe best practices to manage pregnancy in people with LSDs
- Describe research trends involving pregnancy in persons with LSDs

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# Lysosomal Storage Disorders

# Introduction: LSDs

- Single gene disorders, most autosomal recessive
  - 3 are X-linked: Fabry, Hunter, and Danon Disease
- 70% related to loss of/defective enzyme, remainder are due to defects in enzyme activator or associated proteins
- 70 LSDs have been described thus far
- Variable ages at presentation
- Disease usually related to accumulation of substrate in organs, leading to specific presentation
- Individually rare, cumulatively common

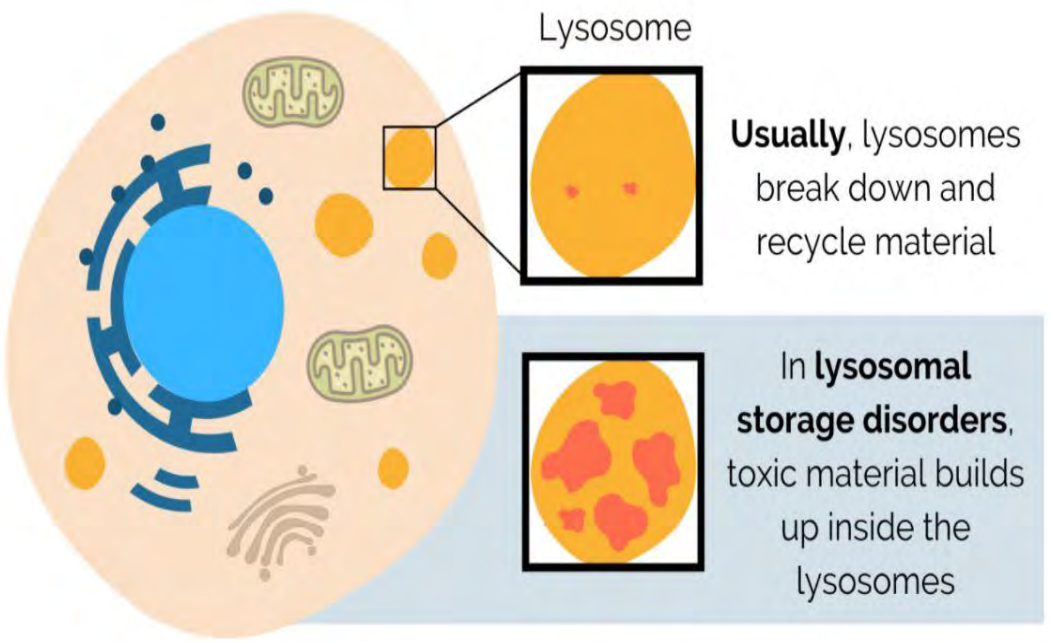



*Image Courtesy: Sanfilippo Children's Foundation*

Rajkumar V, Dumpa V. Lysosomal Storage Disease. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563270/

# Types of LSDs

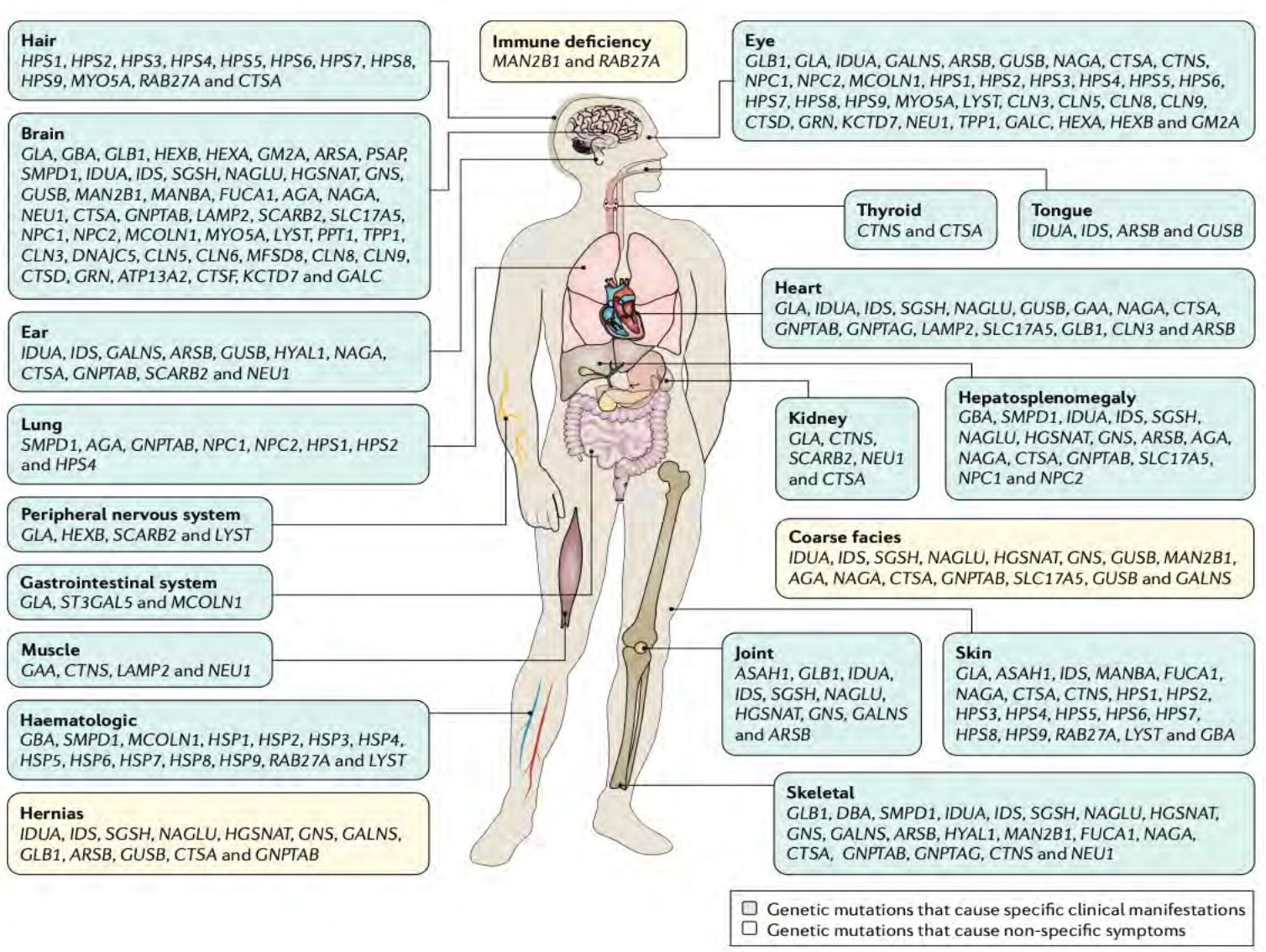
| Sphingolipidosis | MPS | Lipofuscinosis | Sialic Acid | Mucolipidosis | Miscellaneous |
|---|---|---|---|---|---|
| GM2 Gangliosidosis<br>Niemann Pick A,B,C<br>Gaucher (1, 2, 3)<br>Fabry<br>Metachromatic Leukodystrophy<br>Krabbe<br>GM1 Gangliosidosis<br>Multiple Sulfatase Deficiency<br>Oligosaccharidosis | Hurler (Scheie)<br>Hunter<br>SanFilippo<br>Morquio<br>Maroteaux-Lamy<br>Sly | CLN1 to CLN14 | Galactosialidosis<br>Infantile<br>Salla Disease<br>Sialuria | Sialidosis I/II<br>I-Cell<br>Pseudo-Hurler<br>Mucolipidosis IV | Lysosomal acid lipase deficiency<br>Pompe<br>Danon<br>Cystinosis |

*Not mentioned: Disorders of Lysosome Related Organelles (LROs) e.g. Chediak-Higashi or Hermansky Pudlak Syndrome

Rajkumar V, Dumpa V. Lysosomal Storage Disease. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563270/

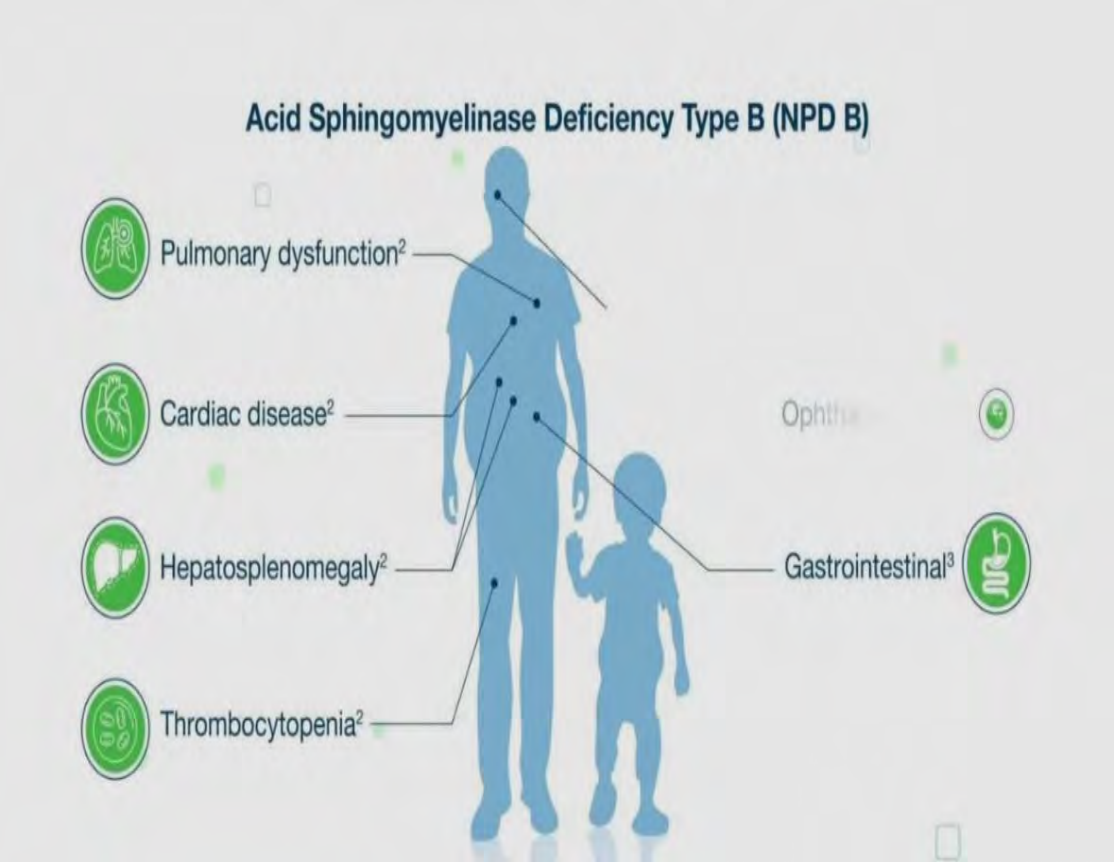
# LSDs: End Organ Impact

- Myriad of end organ impacts
- Location of substrate accumulation determines phenotype
- Multi-system disease



# LSDs: Niemann Pick Disease (Type B)

- Acid sphingomyelinase deficiency
- Variants in *SMPD1*
- Attenuated disease due to residual enzyme function
- Presentation: late childhood – early adulthood; “chronic visceral form”
- Recombinant Enzyme Therapy available (Olipudase alfa)
  - Improvements in pulmonary function
  - Improvements in hepatic and splenic size

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# Gaucher Disease (Type 1)

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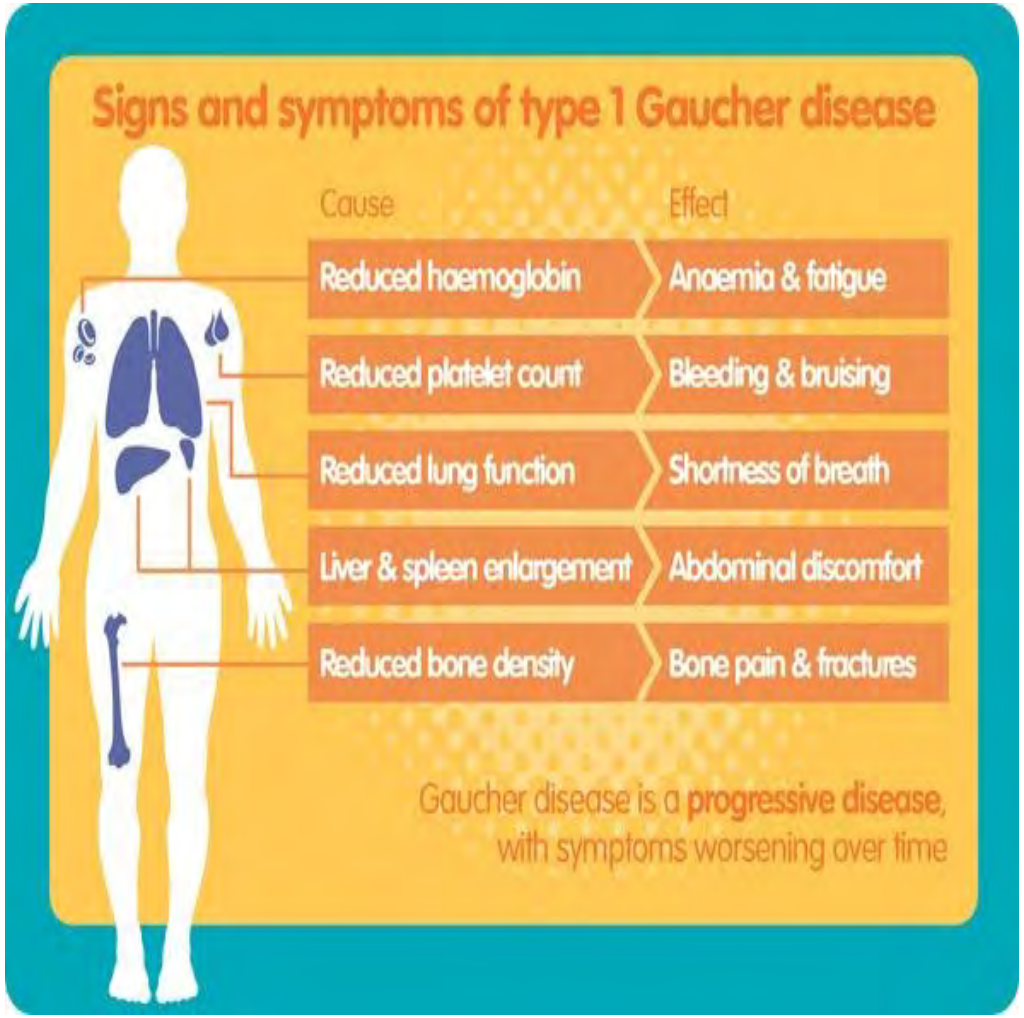
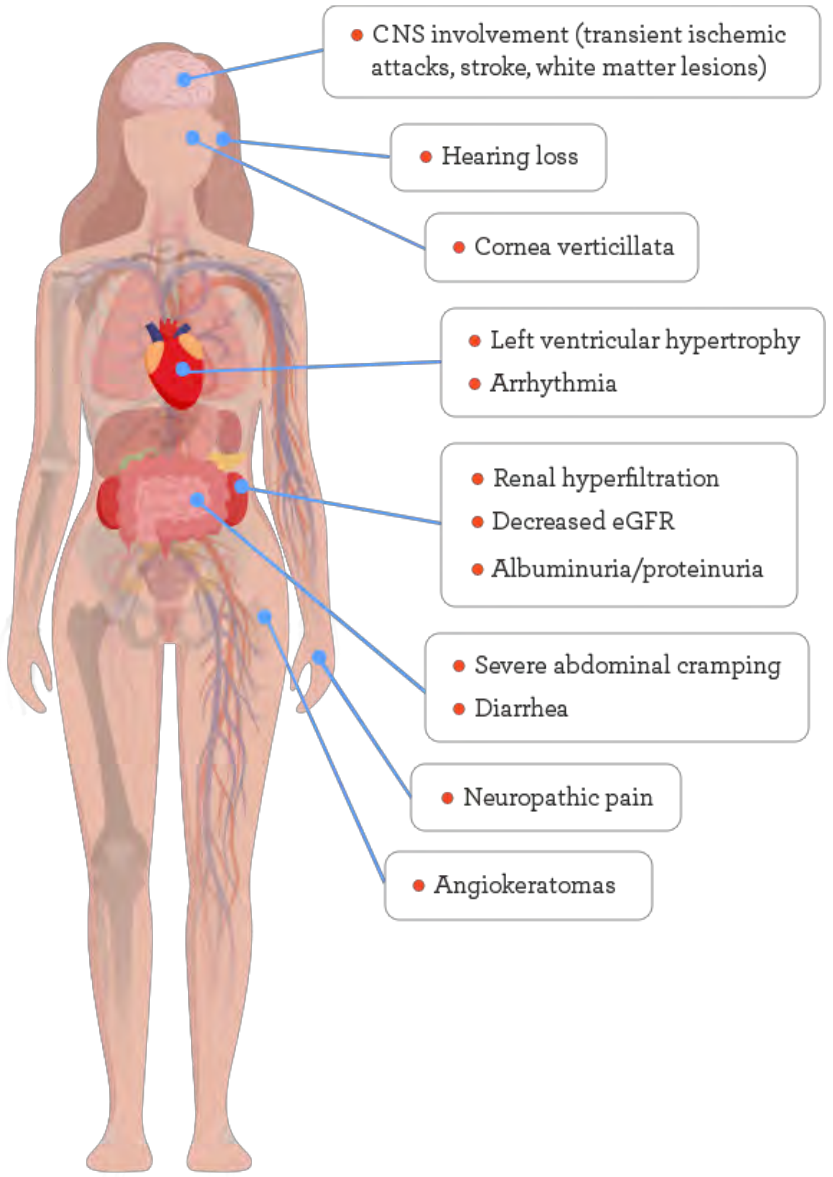
- Autosomal recessive
- Variants in *GBA1,* glucocerebrosidase
- Type 1 is most common (90%)
- Multi-organ involvement
  - Skeletal: bone necrosis, osteoperosis, focal lytic or sclerotic lesions
  - Secondary neurologic disease (spine due to boney injure)
  - Splenic manifestations
  - Hepatomegaly
  - Hematologic abnormalities: anemia, thrombocytopenia, coagulation deficiencies
  - Pulmonary involvement
- Tx: Enzyme Replacement Therapy or Substrate Reductive Therapy




Hughes DA, Pastores GM. Gaucher Disease. 2000 Jul 27 [Updated 2023 Dec 7]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1269/

# Fabry Disease

- Most common of the LSDs
- Loss of alpha-galactosidase A
- Pathogenic variant in *GLA*
- X linked – females with variable presentation and severity
- Tx: Enzyme Replacement Therapy with or without chaperone therapy

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# MPS Disorders

- Longer life expectancies with enzyme replacement therapy and hematopoietic stem cell transplantation
- Variable phenotype/age of presentation depending on disorder/substrate
- Multi-organ involvement:
  - Skeletal/joint issues
  - Spinal anomalies
  - Cardiopulmonary compromise
  - High risk airway
  - Hepatosplenomegaly
  - Impaired vision and hearing


Stewart FJ, Bentley A, Burton BK, Guffon N, Hale SL, Harmatz PR, Kircher SG, Kochhar PK, Mitchell JJ, Plöckinger U, Graham S, Sande S, Sisic Z, Johnston TA. Pregnancy in patients with mucopolysaccharidosis: a case series. Mol Genet Metab Rep. 2016 Aug 29;8:111-5. doi: 10.1016/j.ymgmr.2016.08.002. PMID: 27622143; PMCID: PMC5007877.

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# Puberty

- Delays in menarche described in several LSDs, best studied in most common disorders (Gaucher, Fabry)
  - Up to 60% of patients with Gaucher[1]
  - Linear growth limited in many conditions

- Menorrhagia
  - Significant issue in conditions with thrombocytopenia and coagulation disorders (Gaucher disease, MPS disorders)
  - Can exacerbate existing anemia
  - Often require active management to reduce bleeding severity

Meijon-Ortigueira MDM, Solares I, Muñoz-Delgado C, Stanescu S, Morado M, Pascual-Izquierdo C, Villalon Blanco L, Belanger Quintana A, Menéndez-Conde CP, Morales-Conejo M, Villarrubia-Espinosa J. Women with Gaucher Disease. Biomedicines. 2024 Mar 5;12(3):579. doi: 10.3390/biomedicines12030579. PMID: 38540192; PMCID: PMC10968251.

# Menorrhagia Management

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- Multi-disciplinary team:
  - Metabolic specialist: ERT and/or substrate therapy
    - Natural history studies showing improvement in linear growth, less disease progression
  - Pediatric Adolescent and Gynecology Specialist
    - Often have more experience working with recently pubertal patients
    - Pediatric equipment available
    - Placement of IUD or Nexplanon with local anesthetic and/or sedation as necessary
  - Endocrinology
    - Growth hormone therapy
    - Can consider additional
- What methods are most recommended
  - Most experience with OCPs
  - Depo-provera is associated with transient bone density loss in general population, with limited long term data in patient with LSDs (theoretical risk of worsening existing bone disease)
  - LARC methods available, but not well described in this population
- Desperate need for more data!

Gold J.I., Gold N.B., DeLeon D.D., Ganetzky R. Contraceptive use in women with inherited metabolic disorders: A retrospective study and literature review. Orphanet J. Rare Dis. 2022;17:41. doi: 10.1186/s13023-022-02188-x.
Zimran A, Morris E, Mengel E, Kaplan P, Belmatoug N, Hughes DA, Malinova V, Heitner R, Sobreira E, Mrsić M, Granovsky-Grisaru S, Amato D, vom Dahl S. The female Gaucher patient: the impact of enzyme replacement therapy around key reproductive events (menstruation, pregnancy and menopause). Blood Cells Mol Dis. 2009 Nov-Dec;43(3):264-88. doi: 10.1016/j.bcmd.2009.04.003. Epub 2009 Jun 6. PMID: 19502088.

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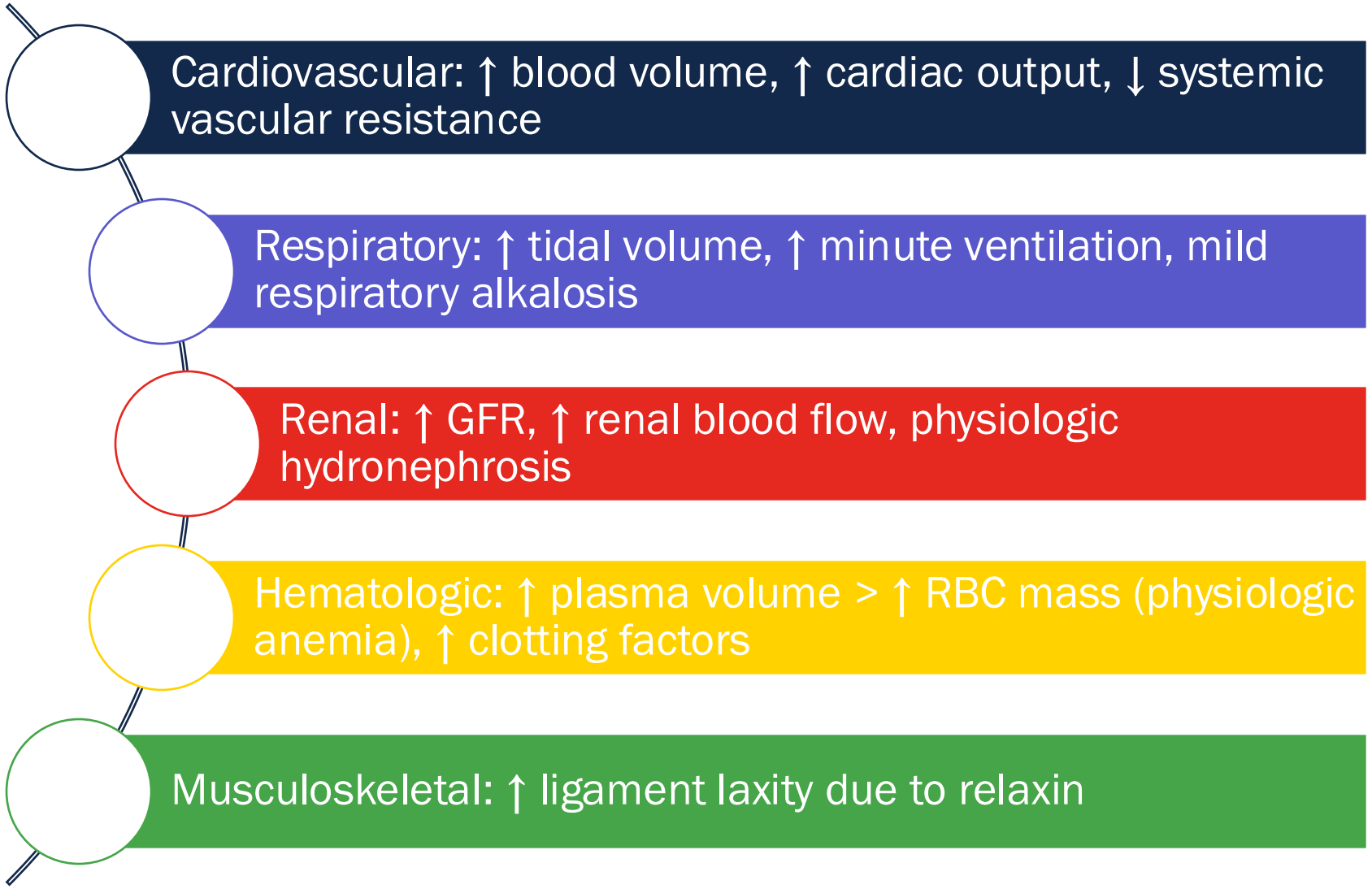
# Pregnancy

# Physiologic Changes of Pregnancy



# Establishing A Care Team

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- Clinical/Metabolic Geneticist
- Maternal Fetal Medicine
- Genetic Counseling
- Anesthesiology
- Subspecialists:
  - Physical Medicine/Therapy
  - Cardiology
  - Pulmonology
  - Hematology
- Family Supports
- Social Work

# Preconception Care

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# Review of Risks/Outlining a Care Plan

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| | |
|---|---|
| Cardiac Risk | • Echocardiogram/Cardiology Evaluation |
| Pulmonary Risk | • Baseline PFTs, up to date with periodic pulmonary assessment per primary care |
| Skeletal Risks | • Anesthesia risk – discuss neuraxial anesthesia feasibility |
| Hepatic/Splenic disease | • Assess baseline liver function (hepatic failure is a contraindication to pregnancy)<br>• Up to date with vaccinations if asplenia |
| Anemia | • baseline CBC and coagulation function testing PRIOR to pregnancy |

# Understanding Pregnancy Risks

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- Increased risk of:
  - Worsening of maternal disease
  - Preterm Birth
  - Cesarean delivery
  - Hemorrhage
  - Theoretical increased risks of:
    - Hypertensive disorders of pregnancy
    - Gestational diabetes
    - Fetal growth restriction
- However, such extrapolations are from other populations with rare disease! There is very limited data in pregnancy, and most data is drawn from case reports/case series.

Zimran A, Morris E, Mengel E, Kaplan P, Belmatoug N, Hughes DA, Malinova V, Heitner R, Sobreira E, Mrsić M, Granovsky-Grisaru S, Amato D, vom Dahl S. The female Gaucher patient: the impact of enzyme replacement therapy around key reproductive events (menstruation, pregnancy and menopause). Blood Cells Mol Dis. 2009 Nov-Dec;43(3):264-88. doi: 10.1016/j.bcmd.2009.04.003. Epub 2009 Jun 6. PMID: 19502088.
Lau H, Belmatoug N, Deegan P, Goker-Alpan O, Schwartz IVD, Shankar SP, Panahloo Z, Zimran A. Reported outcomes of 453 pregnancies in patients with Gaucher disease: An analysis from the Gaucher outcome survey. Blood Cells Mol Dis. 2018 Feb;68:226-231. doi: 10.1016/j.bcmd.2016.10.003. Epub 2016 Oct 20. PMID: 27839985.

# Impact of ERT

- When ERT is available…
  - Limited data in pregnancy leads to guarded recommendations around use
  - Results in shared decision making, best done in the preconception period
- Gaucher Disease
  - Significant evidence suggests improvement in maternal/fetal outcomes including reduced risk of hemorrhage associated with use of ERT
  - No increased risk of birth defects or pregnancy loss
- Fabry Disease
  - Although not ‘recommended’ – have suggested decreased progression of symptoms in female patients with severe phenotype (case reports)

Elstein D, Hughes D, Goker-Alpan O, Stivel M, Baris HN, Cohen IJ, Granovsky-Grisaru S, Samueloff A, Mehta A, Zimran A. Outcome of pregnancies in women receiving velaglucerase alfa for Gaucher disease. J Obstet Gynaecol Res. 2014 Apr;40(4):968-75. doi: 10.1111/jog.12254. Epub 2014 Feb 26. Erratum in: J Obstet Gynaecol Res. 2014 Sep;40(9):2088. PMID: 24612151.

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Cohen Y, Frydman D, Rotem R, Kofman R, Zimran A, Revel-Vilk S, Grisaru-Granovsky S. Risk of postpartum hemorrhage in multiparous women with Gaucher disease: A call for reconsidering enzyme replacement therapy in all pregnant patients. J Inherit Metab Dis. 2021 Sep;44(5):1165-1173. doi: 10.1002/jimd.12382. Epub 2021 May 5. PMID: 33829536.

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# When Pregnancy is Not Recommended

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- Strict Contraindications (~50% mortality)
  - Pulmonary Arterial Hypertension (of any severity)
  - mWHO Class IV Heart Disease
    - severe LV dysfunction EF < 30%
    - severe mitral or aortic stenosis
- Relative Contraindications
  - Sleep apnea with right sided heart strain
  - HFpEF
  - ILD with baseline oxygen therapy, recent exacerbation, or declining lung function parameters
  - Severe anesthetic risk

# Prenatal Screening, Genetic Counseling, Diagnosis

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- Best time for genetic counseling is pre-conception
  - Partner carrier screening
  - Carrier risk assessment for other conditions
- Plan for prenatal screening and/or diagnosis
  - Review of prenatal screening options
  - Review of risks versus benefits of prenatal diagnosis
  - Discussion regarding newborn screening (state-dependent)

*Image Courtesy: https://www.cdc.gov/genomics-and-health/counseling-testing/genetic-counseling.html*

# Reproductive Options

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- Also best discussed in the preconception period!
- IVF and embryo selection for at risk couples
- Gestational carrier
- Adoption
- Criteria for when termination of pregnancy may be considered.

# Considerations for Antenatal Care

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- Care with a Maternal Fetal Medicine Specialist
- Should be seen by metabolic specialist every trimester
- Routine screening (pulmonary function, cardiac function) should be continued during pregnancy
- Subspecialty care continues during pregnancy (with frequency determined by need)
- Repeat genetic counseling during pregnancy
- Level II Ultrasound
- Antenatal testing based on disease severity
- Screening for complications as appropriate: preterm birth, fetal growth restriction, hypertensive disease, gestational diabetes

# Considerations for Delivery Care

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- Patients should be delivered at a high risk pregnancy care center with maternal fetal medicine specialists available and high-risk anesthesia teams
- Critical Decisions:
  - Labor or cesarean delivery (shared decision making, MSK status, ability to have neuraxial anesthesia, airway issues)
  - Is there a need for telemetry? (most labor and delivery units do not have continuous tele!)
  - Fluid management
  - Bleeding risk and preparation
    - IV access, blood crossed and available, other products (platelets, coagulation factors) proximity to operating room, other obstetric hemorrhage management agents (prostaglandins, Pitocin, tranexamic acid, tamponade balloon)

# Postpartum Care

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- Continue ERT in postpartum period
- Breastfeeding
  - Limited data regarding breastfeeding and ERT in multitude of LSDs
  - Gaucher disease – levels of recombinant enzymes secreted in breast milk are very low, thus ERT should be continued
- Calcium Supplementation
  - In conditions with lytic bone disease, Calcium and Vitamin D should be supplemented due to heavy bony remodeling that happens in the postpartum period

Paskulin L, Dornelles AD, Quevedo A, Nalin T, Tirelli KM, Vairo F, Schwartz IVD. Breastfeeding in patients with Gaucher disease: Is taliglucerase alfa safe? Mol Genet Metab Rep. 2019 Jan 16;18:30-31. doi: 10.1016/j.ymgmr.2018.11.004. PMID: 30705823; PMCID: PMC6349462.

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# Areas for Research

# Critical Gaps in Data

- Pregnancy management guidelines:
  - Risk of fetal growth restriction
  - Risk of stillbirth
  - What is optimal mode of delivery?
- Enzyme Replacement Therapy:
  - How does remaining on ERT change natural history of disease:
    - Puberty, menarche
    - Fertility and trying to conceive
    - Maternal and fetal pregnancy outcomes
- Contraception: limited data

Stewart FJ, Bentley A, Burton BK, Guffon N, Hale SL, Harmatz PR, Kircher SG, Kochhar PK, Mitchell JJ, Plöckinger U, Graham S, Sande S, Sisic Z, Johnston TA. Pregnancy in patients with mucopolysaccharidosis: a case series. Mol Genet Metab Rep. 2016 Aug 29;8:111-5. doi: 10.1016/j.ymgmr.2016.08.002. PMID: 27622143; PMCID: PMC5007877.
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Lukina E., Balwani M., Belmatoug N., Watman N., Hughes D., Gaemers S.J.M., Foster M.C., Lewis G., Peterschmitt M.J. Pregnancy outcome in women with Gaucher disease type 1 who had unplanned pregnancies during eliglustat clinical trials. JIMD Rep. 2021;57:76–84. doi: 10.1002/jmd2.12172.

# Therapy and Pregnancy: Gaucher Type 1

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- Not FDA approved for use in pregnancy
- Significant data that ERT:
  - Is safe for use in pregnancy
  - Does not increase the risk of fetal malformations or miscarriage
  - Improves pregnancy outcomes in terms of decreased bleeding risk and decreased maternal disease progression during pregnancy
- SRT is FDA approved for use in Gaucher type 1
  - However limited human pregnancy data and animal studies show increased risk of teratogenicity
  - Lukina et. al – 18 patients pregnant on Eliglustat phase 2 and 3 clinical trials
    - 14 healthy infants
    - 3 elective terminations
    - One ectopic
    - One spontaneous abortion
    - One stillbirth
  - Unclear if there is increased risk based on these data

**APPROVED GAUCHER DISEASE TREATMENTS**

| Therapeutic strategy | Brand names | Administration method | Mechanism |
|---|---|---|---|
| Enzyme replacement therapy | • Cerezyme<br>• VPRIV<br>• Elelyso | Intravenous  | Provides a lab-made version of the missing GCase enzyme |
| Substrate reduction therapy | • Cerdelga<br>• Zavesca | Oral  | Lowers the production of the fatty molecules that accumulate and cause Gaucher disease symptoms |


Lukina E, Balwani M, Belmatoug N, Watman N, Hughes D, Gaemers SJM, Foster MC, Lewis G, Peterschmitt MJ. Pregnancy outcome in women with Gaucher disease type 1 who had unplanned pregnancies during eliglustat clinical trials. JIMD Rep. 2020 Oct 18;57(1):76-84. doi: 10.1002/jmd2.12172. PMID: 33473343; PMCID: PMC7802626.

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Zimran A, Morris E, Mengel E, Kaplan P, Belmatoug N, Hughes DA, Malinova V, Heitner R, Sobreira E, Mrsić M, Granovsky-Grisaru S, Amato D, vom Dahl S. The female Gaucher patient: the impact of enzyme replacement therapy around key reproductive events (menstruation, pregnancy and menopause). Blood Cells Mol Dis. 2009 Nov-Dec;43(3):264-88. doi: 10.1016/j.bcmd.2009.04.003. Epub 2009 Jun 6. PMID: 19502088.

# ERT and other disorders

- Fabry Disease
  - Diagnostic and management barriers “X-linked disease”
    - Few women represented in clinical studies of natural history
    - Diagnostic barriers due to variable presentation
  - Limited data about use of ERT in pregnancy
  - Not currently recommended  due to limited data, but case series suggest it is safe and does not pose increased maternal/fetal risk
- Pompe
  - Case studies suggest safety, but no clear guidance
  - Typical recommendation is to remain on ERT if on prior to pregnancy, or consider starting if there is disease progression

Hopkin RJ, Laney D, Kazemi S, Walter A. Fabry disease in females: organ involvement and clinical outcomes compared with the general population (103/150 characters). Orphanet J Rare Dis. 2025 Aug 13;20(1):433. doi: 10.1186/s13023-025-03922-x. PMID: 40804726; PMCID: PMC12351852.

Fernández P, Fernández SO, Gonzalez JGM, Fernández T, Fernández CC, Fernández SP. Enzyme Replacement Therapy in Pregnant Women with Fabry Disease: A Case Series. JIMD Rep. 2019;45:77-81. doi: 10.1007/8904_2018_141. Epub 2018 Nov 8. PMID: 30406505; PMCID: PMC6336548.

de Vries JM, Brugma JD, Ozkan L, Steegers EA, Reuser AJ, van Doorn PA, van der Ploeg AT. First experience with enzyme replacement therapy during pregnancy and lactation in Pompe disease. Mol Genet Metab. 2011 Dec;104(4):552-5. doi: 10.1016/j.ymgme.2011.09.012. Epub 2011 Sep 16. PMID: 21967859.

# Diagnosing Affected Pregnancies

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- Gaps in access to carrier screening
  - Less than half of pregnant women receive complete carrier risk assessment
  - ACOG guidelines (2016) recommend Tier 1 screening: SMA, hemoglobinopathies, and CF; consider Fragile X based on family history.
  - ACMG (2022) recommends Tier 3 screening (frequency of 1/200)
- Additional factors:
  - Insurance coverage of carrier screening
  - Partner screening (coverage, availability, location)
- Gaps in access to genetic testing
  - MFM referral
  - Access to CVS/amniocentesis providers

Hull LE, Flannery K, Kaimal A, Sepucha K, Rehm HL, Haas JS. Multilevel barriers and facilitators to widespread use of preconception carrier screening in the United States. Genet Med. 2023 Dec;25(12):100946. doi: 10.1016/j.gim.2023.100946. Epub 2023 Jul 30. PMID: 37534745; PMCID: PMC10825062.
Best S, Long J, Theodorou T, Hatem S, Lake R, Archibald A, Freeman L, Braithwaite J. Health practitioners' perceptions of the barriers and enablers to the implementation of reproductive genetic carrier screening: A systematic review. Prenat Diagn. 2021 May;41(6):708-719. doi: 10.1002/pd.5914. Epub 2021 Mar 5. PMID: 33533079; PMCID: PMC8252081.

# Access to Fetal Therapy:

## Diseases Included in the PEARL Clinical Trial

We are testing the safety and feasibility of prenatal enzyme replacement therapy for these lysosomal storage diseases:

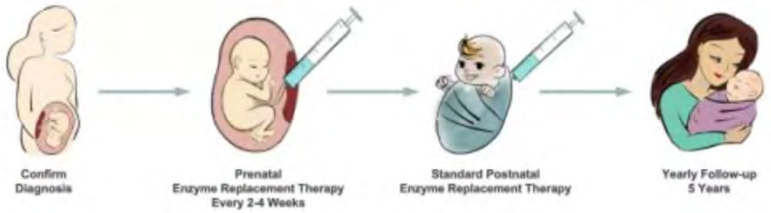
- Mucopolysaccharidosis (MPS) 1, or Hurler syndrome
- Mucopolysaccharidosis (MPS) 2, or Hunter syndrome
- Mucopolysaccharidosis (MPS) 4a, or Morquio syndrome
- Mucopolysaccharidosis (MPS) 6, or Maroteaux-Lamy syndrome
- Mucopolysaccharidosis (MPS) 7, or Sly syndrome
- Infantile-onset Pompe disease (IOPD)
- Neuronopathic Gaucher disease (types 2 and 3)
- Lysosomal Acid Lipase (LAL) deficiency, or Wolman disease

University of California San Francisco

Pearl Trial

Prenatal Enzyme Replacement for Lysosomal Storage Diseases

Study Timeline




## Study Team

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**Dane Munar**
Clinical Research Coordinator

NCT04532047

# Prospect of Fetal Therapy

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ORIGINAL ARTICLE | BRIEF REPORT

## In Utero Enzyme-Replacement Therapy for Infantile-Onset Pompe's Disease

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## Intrauterine enzyme replacement therapies for lysosomal storage disorders: Current developments and promising future prospects

Akos Herzeg[1,2], Beltran Borges[1,2], Billie R. Lianoglou[1,2], Juan Gonzalez-Velez[1,3], Emma Canepa[1,2], Dane Munar[1], Sarah P. Young[4], Deeksha Bali[4], Michel H. Gelb[5], Pranesh Chakraborty[6], Priya S. Kishnani[4], Paul Harmatz[7], Jennifer L. Cohen[4], Tippi C. MacKenzie[1,2,7]

# Newborn Screening

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- Recommended Uniform Screening Program (RUSP) 1/2023:
  - Pompe
  - Krabbe
  - MPS Type I
  - MPS Type II
- Challenges:
  - Late-affecting conditions with variable presentation timing/phenotype
  - Interpretation of results
  - Adequate follow up protocols
  - Timely referral/evaluation with a LSD provider team

https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp

Terrell A, Sapp K, Graham B, McPheron M, Wetherill L. Exploratory Study on the Challenges of Newborn Screening for Lysosomal Storage Disorders Emphasizes the Need for Multitier Testing and Collaborative Approaches to Management. JIMD Rep. 2025 Jun 16;66(4):e70027. doi: 10.1002/jmd2.70027. PMID: 40524786; PMCID: PMC12169912.

# Conclusions

- Management of menarche and pregnancy for patients with LSDs can be complex and requires a specialized care team
- ERT has significant benefit for female patients with LSDs during critical reproductive stages
- Pregnancy information/care plan is best determined in the pre-conception period with a multi-disciplinary team
- Significant gaps in current literature and many unanswered questions

# Questions

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- Thank you
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