Gaucher's Disease

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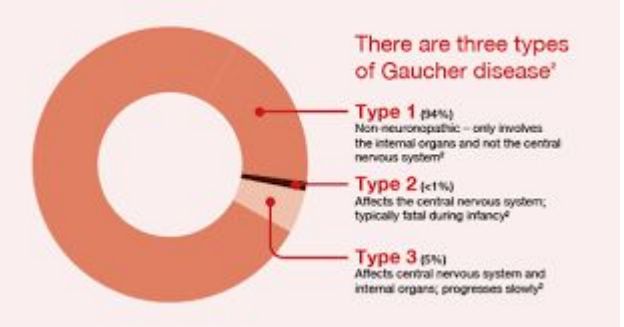
What is Gaucher's Disease?

- It's an inherited metabolic disorder.
- There's an insufficient production of glucocerebrosidase.
- Lipids accumulate in the body and brain
- Symptoms appear in childhood and adulthoo
- There are three types.



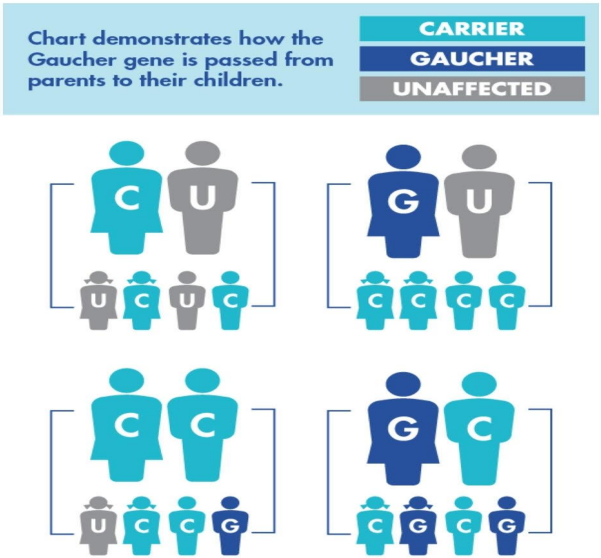
Gaucher's Disease

- It can affects male and female in equal numbers. But it is more common in Ashkenazi Jewish ancestry, where the incidence may be as high as 1 in 450 births.
- It causes fatty substances called lipids to build up in certain organs such as the spleen and liver.
- Organs can become very large and not work well. It can also affect the lungs, brain, eyes, and bones.
- It can be hard to diagnose because there are many different symptoms.

Cause

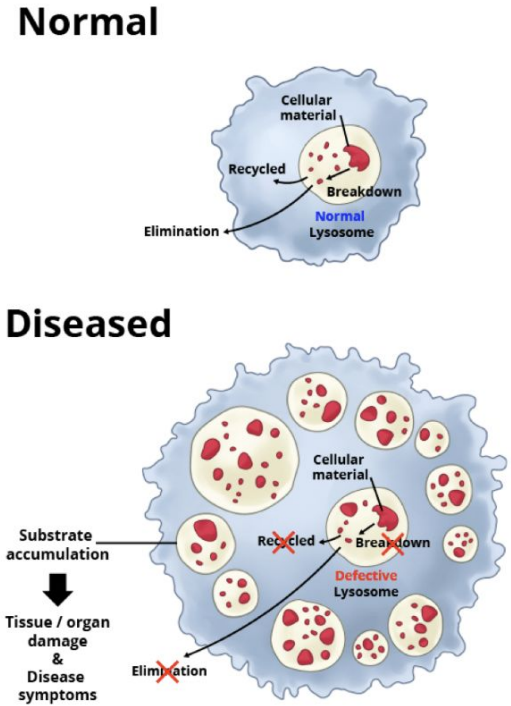
- Gaucher disease is caused by mutations in the *GBA* gene.
- It is an autosomal recessive disorder
- When one Gaucher gene in the pair is abnormal, the child is an asymptomatic carrier who can pass that abnormal gene to his or her children.
- When both genes in the pair are defective, a person will have Gaucher disease.

The chart below shows how parents pass the Gaucher gene to their children.



Cause

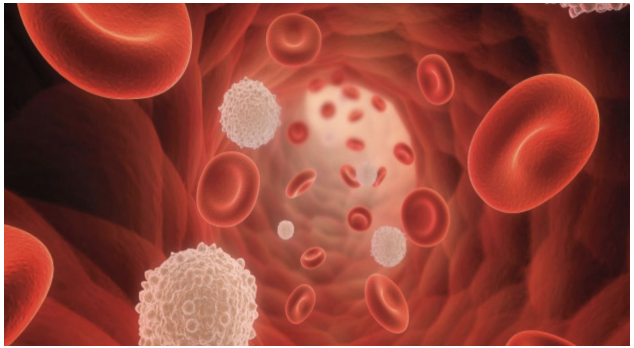
- GBA gene provides instructions for making beta-glucocerebrosidase (GCase)
- This enzyme is active in lysosomes
- All types of Gaucher disease are also called lysosomal storage disorders.
    - Lysosomes in the macrophages become progressively enlarged and filled with undigested glucocerebroside.
- Looks like “crumpled tissue paper” under a microscope



Signs and Symptoms

Type 1 (non neuropathic)

- Usually bruise easily due to low blood platelets
- Feel fatigued due to anemia
- May have an enlarged liver and spleen



Signs and Symptoms

Type 2 (acute infantile neuropathic Gaucher disease)

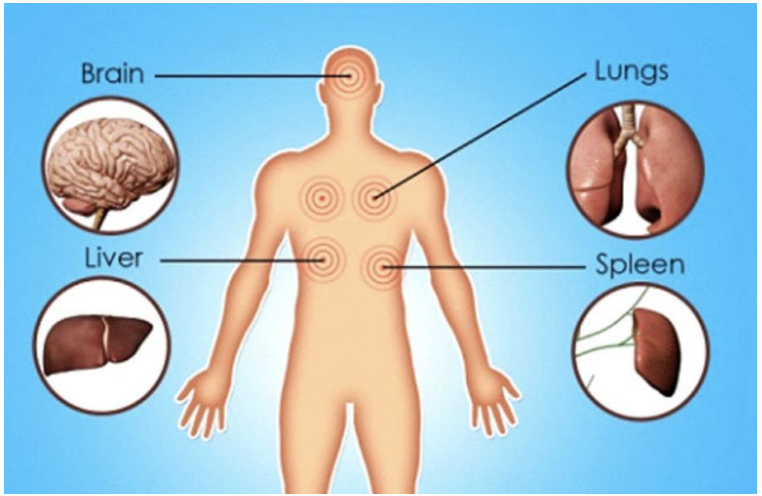
Symptoms include:

- Extensive brain damage
- Seizures
- Spasticity
- Poor ability to suck and swallow
- Enlarged liver and spleen

Signs and Symptoms

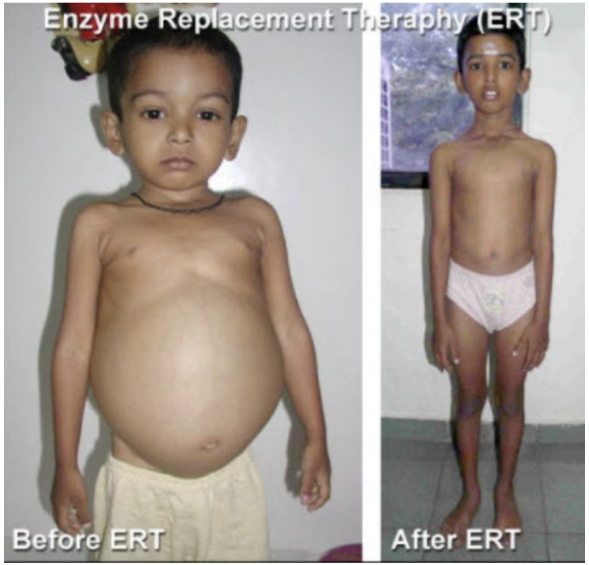
Type 3 (chronic neuropathic Gaucher disease) includes:

- Signs of brain involvement
- Seizures
- Skeletal irregularities
- Eye movement disorders
- Cognitive deficit
- Poor coordination
- Enlarged liver and spleen
- Breathing problems
- Blood disorders



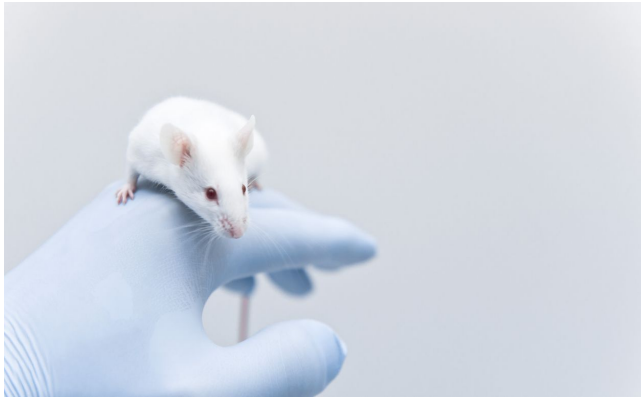
Treatment

- Two categories:
    - Enzyme replacement therapy
    - Substrate reduction therapy
- Gene therapy clinical trials



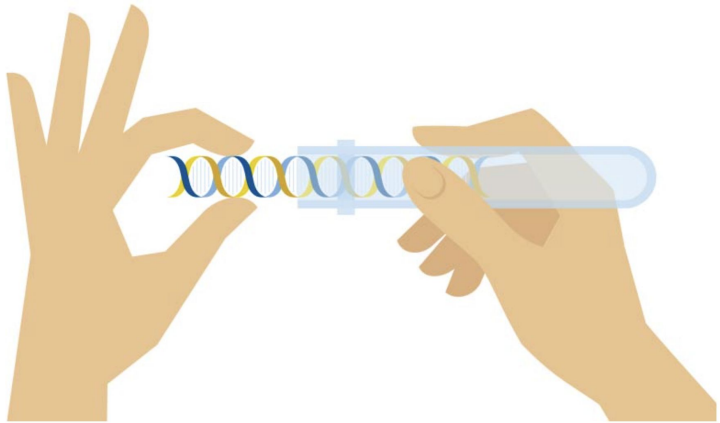
Gene Therapy

- Gene therapy is a potential strategy for the treatment of GD.
- Progress seen on mice
- Clinical trials in humans
- In vivo or Ex vivo approach



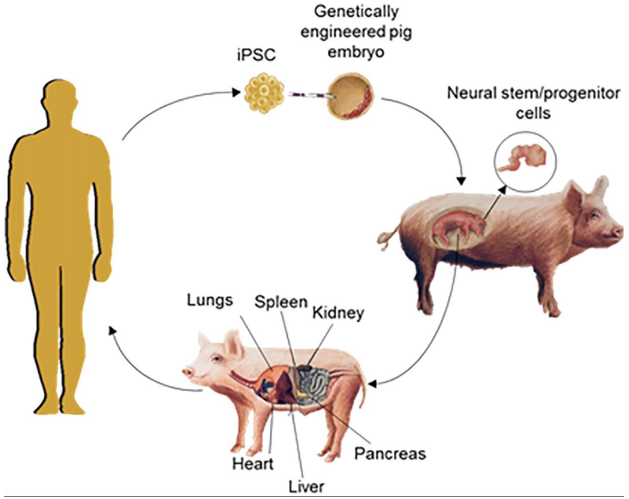
Prevention

- No prevention
- Find out if you are a carrier
- Early treatment may prevent damage to bones and organs (Type 1)



Ethical Implications

- Misuse of stem cells
- Concern for human cloning or also human-animal chimeras.



References

Gaucher disease: Causes, symptoms & treatment. Cleveland Clinic. (n.d.). Retrieved from https://my.clevelandclinic.org/health/diseases/16234-gaucher-disease#:~:text=There%20is%20no%20way%20to,family%2C%20talk%20to%20your%20provider.

Massaro, G., Geard, A. F., Liu, W., Coombe-Tennant, O., Waddington, S. N., Baruteau, J., Gissen, P., & Rahim, A. A. (2021). Gene Therapy for Lysosomal Storage Disorders: Ongoing Studies and Clinical Development. *Biomolecules*, *11*(4), 611. https://doi.org/10.3390/biom11040611

Mehta A, Kuter DJ, Salek SS, Belmatoug N, Bembi B, Bright J, Vom Dahl S, Deodato F, Di Rocco M, Göker-Alpan O, Hughes DA, Lukina EA, Machaczka M, Mengel E, Nagral A, Nakamura K, Narita A, Oliveri B, Pastores G, Pérez-López J, Ramaswami U, Schwartz IV, Szer J, Weinreb NJ, Zimran A. Presenting signs and patient co-variables in Gaucher disease: outcome of the Gaucher Earlier Diagnosis Consensus (GED-C) Delphi initiative. Intern Med J. 2019 May;49(5):578-591. doi: 10.1111/imj.14156. Erratum in: Intern Med J. 2019 Aug;49(8):1059. PMID: 30414226; PMCID: PMC6852187.

Sam, R., Ryan, E., Daykin, E., & Sidransky, E. (2021). Current and emerging pharmacotherapy for Gaucher disease in pediatric populations. *Expert opinion on pharmacotherapy*, *22*(11), 1489–1503. https://doi.org/10.1080/14656566.2021.1902989

Stone WL, Basit H, Master SR. Gaucher Disease. [Updated 2022 Jun 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK448080/

U.S. Department of Health and Human Services. (n.d.). *Gaucher disease*. National Institute of Neurological Disorders and Stroke. Retrieved April 14, 2023, from https://www.ninds.nih.gov/health-information/disorders/gaucher-disease

Volarevic, V., Markovic, B. S., Gazdic, M., Volarevic, A., Jovicic, N., Arsenijevic, N., Armstrong, L., Djonov, V., Lako, M., & Stojkovic, M. (2018). Ethical and Safety Issues of Stem Cell-Based Therapy. *International journal of medical sciences*, *15*(1), 36–45. https://doi.org/10.7150/ijms.21666