



## Hope for Effective Treatment for Rare (Orphan) Diseases

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There is no universally accepted definition for rare diseases. The definitions used in the medical literature and by national health plans are similarly divided, with definitions ranging from 1/1,000 to 1/200,000 [1]. The World Health Organization (WHO) defines rare diseases as those that affect fewer than 1 In 2000 individuals or fewer in the general population. There are currently over 7000 known rare diseases impacting more than 300 million people globally, with 70% of these conditions starting in childhood. Many cause chronic debilitation, are life-threatening or lead to significant long-term health impairments [2].

Many people use the terms “orphan disease” and “rare disease” interchangeably. But Orphan diseases often refer to diseases (including rare ones) that researchers aren’t investigating much, or at all due to cost. Even if the treatment is available, it is unaffordable e.g. Gaucher disease, Hunter’s disease, Spinal muscular atrophy (SMA).

Three main groups of causes of rare diseases include

- **Genetics:** Either a genetic mutation from a parent germline or a random occurrence without any family history
- **Germs (microbes):** These cause infections which may be very rare in some countries e.g. Tuberculosis in United States of America and Leptospirosis in Malaysia
- **Toxins:** Asbestosis can lead to mesothelioma, a rare lung condition

Some examples of rare diseases are Duchenne Muscular Dystrophy, Tay Sach disease, Gaucher disease, Maple syrup disease, Erlen Danlos syndrome, Huntington chorea, etc. This paper will focus on orphan diseases of genetic and chromosomal basis.

Newborn screenings provide diagnosis of some diseases that have no detectable signs in newborns. such as cystic fibrosis, sickle cell anemia etc. Potential for neonatal screening will continue to expand with the availability of successful treatment for rare diseases. We remember the story of Phenylketonuria, a rare disease with an incidence in Caucasian population approximately 1 in 10,000 to 1 in 15,000. With the understanding of the basic mechanism of the disease we now can treat this condition with good long term health and developmental outcome if dietary treatment is started early and closely monitored.

Available treatment for rare or orphan diseases of genetic or chromosomal origin includes:

- Medications
- Nutritional supplements or dietary changes
- Occupational, speech, Physiotherapy, special educational training and physical devices
- Surgical correction of cardiac, gastrointestinal, neurological abnormalities etc.
- Medical devices

Many rare diseases of genetic or chromosomal origin do not yet have effective treatment. Very often such cases have multisystem involvement requiring multidisciplinary management. Not only are these diseases given very little attention in research because of the cost involved and treatment if at all available is often unaffordable even for the rich. Hence most of these cases are left to follow the course of the disease and receive only the available conventional medical and rehabilitation services.

There has been clinical research done on enzyme replacement therapy (ERT) to treat conditions such as lysosomal storage disorders eg Gaucher Disease, Fabry disease, Pompe Disease and mucopolysaccharidosis eg Hunter syndrome. These products are very expensive due to high development and manufacturing costs for a very small number of patients. Treatment has to be lifelong. Safety and efficacy are still challenges faced [3] (Ries, M 2017).

Gene therapy is another possible treatment approach for orphan diseases but is still very much in clinical trial phases [4] (Ginn SL., et al. 2024)

More recently, extracellular vesicles (EVs) have been proposed as a bio-platform for ERT delivery for Gaucher disease. These EVs, encompassing exosomes, microvesicles, and apoptotic bodies, are sub-cellular entities (40-5000 nm diameter) secreted by cells in a constitutive or inducible manner [4-6] (Hugel B et al 2005, Ratajczak J., et al. 2006, Camussi., et al. 2010). Importantly, more than conferring enzyme protection, EVs may enable enzymes to reach the Central Nervous System (CNS) as EVs are able to cross the Blood brain barrier (BBB). This is a new venue in the field of ERT [7] (Silva., et al.).

Human stem cell therapy is still experimental. Genetic modification of stem cells can potentially make stem cell-based products more effective. Patient-specific induced pluripotent stem cells (iPS) can be genetically manipulated and transplanted back into the patient. Stem cells secrete paracrine factors that could become new therapeutic tools in the treatment of orphan diseases. Gene therapy and stem cell therapy with DNA repair are promising approaches to the treatment of rare, intractable diseases. These are still very much in the research phase [9] (M Ian Philips 2012).

One therapeutic modality that is ignored but has been getting attention with increasing publications is stem cell xenotransplantation (SCXT), a personalised and integrative form of therapy. In reality physicians have been treating medical disorders untreatable in conventional medicine with this protocol of cell therapy including rare genetic and chromosomal abnormalities for more than 50 years. This includes orphan genetic diseases such as Duchenne muscular dystrophy, Tay Sach disease, Friedrich's ataxia, Fabry's disease, osteogenesis imperfecta and lysosomal storage diseases such as metachromatic leukodystrophy etc. Orphan diseases of chromosomal origin that have been treated include Turner syndrome, Prader Willi's syndrome, Klinefelter syndrome, Noonan syndrome (Schmid F 1983).

Thousands of children with Down syndrome, a more common chromosomal disorder, have been treated with fetal precursor stem cell xenotransplantation in Europe for many decades, with thousands of published case studies. Clearly if the protocol is strictly followed, the aim of mitigating/eliminating the ever-increasing delay in development with increasing age in children with Down syndrome can be achieved [10-14] (Neihans P 1960, Schmid F 1983, Kuhnau WW 1983, Molnar EM 2006, Abdul Halim A J 2017). Many researchers now believe that stem cell xenotransplantation is safe. If the cells are processed correctly, adhering to the 2003 Food and Drug Administration guideline and the ensuing World Health Organization consensus papers, the concerns of xenogeneic disease transmission can be effectively managed through donor selection or recipient management measures [15] (Cooper, D. K. C., et al. 2017). There are about 6000 known genetic diseases and only a few of them have any known treatment. Some have been treated with stem cell xenotransplantation with success. There are many that have been treated, but no medical reports have been written, or no one has attempted to do it. So for a newly diagnosed infant with a genetic disease with no known treatment, there is no harm in using this protocol to treat. Either an improvement will be seen or there is no change in the condition of the child. The revitalising effects of SCXT should improve the health status of the majority of patients [16] (Molnar EM 2006, Abdul Halim A J 2022). On compassionate ground this classical form of stem cell transplantation which is safe should be made available to families and patients with rare orphan diseases of genetic and chromosomal origin.

In conclusion, only a very small fraction of orphan diseases currently have effective treatments. Possible therapeutic solutions currently and in the future for patients with orphan diseases include gene therapy, enzyme replacement therapy and stem cell transplantation. As our understanding of orphan diseases grows and technological capabilities advance, there is hope for much more effective preventive strategies, diagnostic capability and effective treatment protocols in the future thereby improving the quality of life for millions of families, affected children and individuals affected by these rare conditions.

Bibliography

1. "Rare diseases: what are we talking about?". Rare diseases centre – Venetian Region – Italy (2022).
2. WHO Eighteenth meeting, 10 February 2025 EB156/SR/18.
3. Ries M. "Enzyme replacement therapy and beyond-in memoiriam Roscoe O. Brady, M.D. (1923–2016)". *Journal of Inherited Metabolic Disease* 40.3 (2017): 343-356.
4. Hugel B., et al. "Membrane microparticles: two sides of the coin". *Physiology (Bethesda)* 20 (2005): 22-27.
5. Ratajczak J., et al. "Membrane-derived microvesicles: important and underappreciated mediators of cell-to-cell communication". *Leukemia* 20 (2006): 1487-1495.
6. Camussi G., et al. "Exosomes/microvesicles as a mechanism of cell-to-cell communication". *Kidney International* 78 (2010).
7. Silva., et al. *Rare Disease Orphan Drugs* 1 (2022): 13.
8. Ginn SL., et al. "Gene therapy clinical trials worldwide to 2023—an update". *The Journal of Gene Medicine* 26.8 (2024).
9. M Ian Phillips. "Gene, stem cell, and future therapies for orphan diseases Review". *Clinical Pharmacology Therapy* 92.2 (2012): 182-192.
10. Niehans P. "Introduction to Cell Therapy". Pageant Books, Inc. New York, (1960).
11. Schmid F. "Cell therapy, a New Dimension of Medicine". Ott Publishing, Thun, Switzerland, (1983).
12. Wolfram W Kuhnau and Michael L Culbert. "Live Cell Therapy". My Life with a Medical Breakthrough. Arts Graficas de B.C. in Mexico, (1983).
13. Abdul Halim AJ. "Hope for Untreatable Medical Disorders with Live Cell Therapy". London: Troubador Publishing Ltd, (2017).
14. Abdul Halim Abdul Jalil and Mohamed Lokman Md Isa. "Live cell therapy: Past, present and future". *Journal of Reproductive Biotechnology and Fertility* 11 (2022).
15. Cooper DK C., et al. "Regulation of Clinical Xenotransplantation-Time for a Reappraisal". *Transplantation* 101.8 (2017): 1766-1769.
16. Molnar EM. "Textbook of Stem Cell Transplantation". *Medical and Engineering Publishers* (2006).